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College of Science

Department of Chemistry

Synthesis and Characterization a Series of New Isatin Derivtives With Some Complexes

A Thesis Submitted to the
Council of the College of Science, University of
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202١ A.D

144٢ A.H

بِسْمِ اللَّـهِ الرَّحْمَنِ الرَّحِيمِ

ۚ وَأَنْزَلَ اللَّهُ عَلَيْكَ الْكِتَابَ وَالْحِكْمَةَ وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ ۚ وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا

صدق آلله العظيم

سورة النساء/آية{١١٣}

Dedication

To the last of the prophets and messengers, our noble messenger and our example, Muhammad(peace be upon him).

To the source of my strength, my pride, and my family will give them all thanks and gratitude, especially my beloved mother, my husband, brother and sister, and finally all thanks to my beloved children (Adam and Anas) for the burden they have carried with me in order to achieve my dream.

OMNIA...

Acknowledgeme

First of all, I thank Allah for inspiring me with strength, patience and willingness

to perform this work, I would like to express my sincere gratitude to my supervisor,

Dr. Wasan Baqir Ali and Dr.Areej Ali Jaraullah

for their support and encouragement, their guidance and special advice to enrich throughout this work.

Special thanks are extended to the Dean, Chairman, and the staff of the Chemistry

Finally, Many thanks to my husband and my family And my kids And my girlfriend(Khitam).

The soul of my girlfriend who left us (Nawras)

I must express my very profound gratitude to of my colleagues in the study for providing me with unfailing support and continuous encouragement throughout my years of investigation and through the process of

researching and writing this thesis. thanks for everyone help me to complete this thesis.

Abstract

In this thesis, new compounds, have been successfully synthesized from isatin **,** and their purity confirmed by thin layer chromatography**.** The chemical structures of the synthesized compounds (O_1- O_{15}) were determined by some spectroscopy techniques such as [FTIR and 1H-NMR]**.** Compound O_{15} was used as a ligand in the synthesis of new complexes through its reaction with transition elements salts such as ($CoCl_2$**.**$6H_2O$**,** $NiCl_2$**.**$6H_2O$**,** $CuCl_2$**.**$2H_2O$**,** and $ZnCl_2$**).** The new complexes have been distinguished using UV-Vis**,** FTIR **,** atomic absorption spectroscopy**,** elemental analysis**,** magnetic susceptibility**,** and conductivity measurements**.** Some physical properties of synthesized compounds and complexes were determined such as melting points**,** and colors**.** The current study included these steps **:**

1- Synthesis of new compound (6H-indolo[2,3-b]quinoxaline-2-carboxylic acid)[O_1], by the reaction of isatin with 3,4-diaminobenzoic acid **.**

2- Synthesis of (2- Methyl -6H-Indolo[2,3-b] Quinoxaline [O_2]), by the reaction of isatin with 4- methyl o-phenylenediamine, and then reaction of [O_2] **,** with phenyl isothiocyanate to synthesis (2-Methyl-indolo[2,3-b] Quinoxaline-6-carbothioic acid phenyl amide[O_3]) **.** Also, it interacts [O_2] with benzyl chloride to synthesis (6-benzyl-2-Methyl-6H-Indolo[2,3-b] Quinoxaline [O_4]) **.**

3- Synthesis of compounds N- alkyl isatin [O_5 -O_8] from the reaction of isatin with different haloalkanes **.**

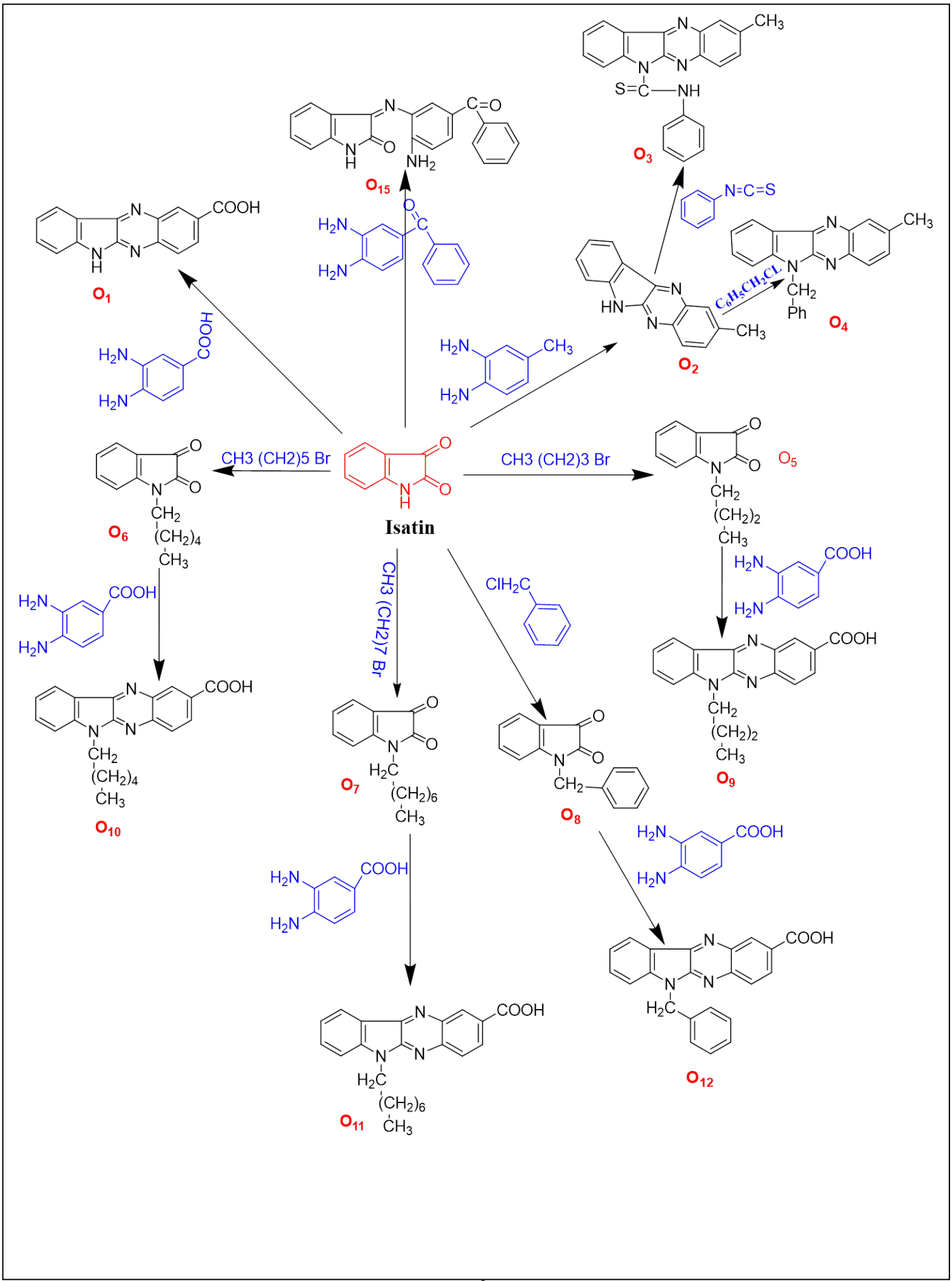
4- Synthesis of compounds [O_9 - O_{12}] by the reaction of 3,4-diaminobenzoic acid with N- alkyl isatin to get new and effective replacement reactions compounds**.**

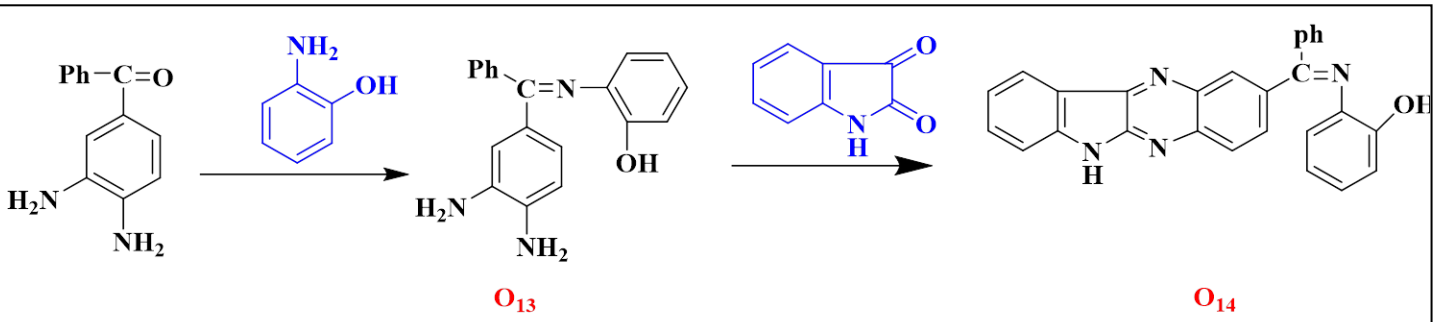
5- New two schiff's base were synthesized by two steps from the reaction of 3,4- di aminobenzophenone with o-amino phenol to produce the compound [O_{13}]**,** and then the schiff's base [O_{13}] reaction with isatin to produce compound [O_{14}]**.**

i

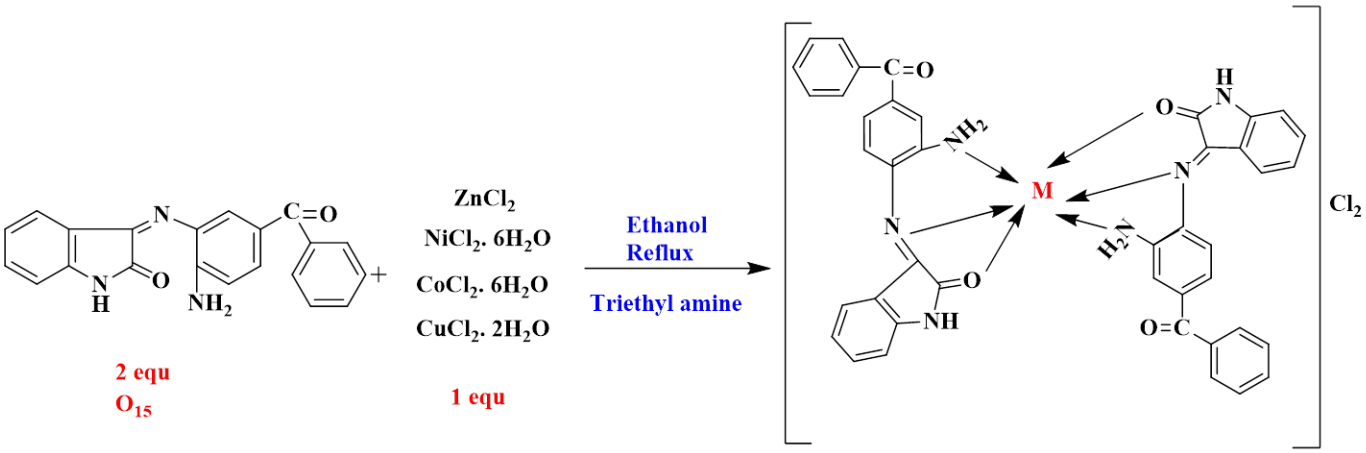
6- reaction of isatin with 3,4-di aminobenzphenone to produce a new compound 3-(2-amino-5-b-benzoyl-phenylimino)-1,3di hydro-indol-2-one [O_{15}]**,** and its complexes [$Co(O_{15})_2$]Cl_2, [$Ni(O_{15})_2$]Cl_2, [$Cu(O_{15})_2$]Cl_2, and [$Zn(O_{15})_2$]Cl_2 **.**

7- Finally the biological activity of some synthesized compounds was evaluated against two types of bacteria (E.colias) and (S. Aureus)**.** Where most of these compounds exhibited good to acceptable antibacterial activity against two strains of bacteria used **.**


Isatin
CH3 (CH2)5 Br
CH3 (CH2)3 Br
CH3 (CH2)7 Br
ClH2C
C6H5CH2Cl
N=C=S
O1
O2
O3
O4
O5
O6
O7
O8
O9
O10
O11
O12
O15



O_{13} O_{14}



2 equ
O_{15}

1 equ

M = Ni^{II} .Co^{II} , Zn^{II} ,Cu^{II}

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List of abbreviations

Abbreviation	Meaning
^{1}H-NMR	*Proton Nuclear Magnetic Resonance*
F.T-IR	*Fourier-transform infrared*
UV-Vis	*Ultraviolet-Visible*
DMSO	*Dimethyl sulfoxide*
M.P.	*Melting point*
M.Wt	*Molecular weight*
TLC	*Thin layer chromatography*
S.aureus	*Staphylococcus aureus*
&	*And*
Ar	*Aromatic ring*
C.H.N	*Elemental-Analysis (carbon, hydrogen and nitrogen)*
E.coli	*Escherichia coli*
Cm	*Centimeter*
g	*Gram*
μm	*Micrometer*
%	*Percent (per cent)*
δ	*Chemical shifts*
H	*Hour(s)*
Min	*Minute*
MHz	*Megahertz*
ppm	*Parts per million*
s	*Singlet*
Cal	*Calculated*
λ	*Wave length*
Cond.	*Conductivity*
DMF	*Dimethyl formamide*
C.T.	*Charge Transfer*
Oh	*Octahedral*
^{0}C	*Degree Celsius*
$\bar{\upsilon}$	*Wave number*
μ_{eff}	*Magnetic torque*
Mmol	*Millimol*
B.M	*Bohr Magneton*
Mm	*Millimeter*
L : M	*Ratio Ligand:Metal*
rt	*Room temperature*
P.t.	*Proton trancefare*
Cat.	*Catalyst*

Chapter one

Preface &previous studies

1.1. Preface

The heterocyclic compounds are highly significant for a broad range of synthetic, industrial and pharmaceutical uses. The compounds of heterocyclic have broad - spectrum of biological activities such as antibacterial, antifungal, antiviral, antiprotozoal and anthelmintic activity. Mostly Include at least one carbon. Whereas atoms, which don't have (C) and (H), are referred to as heteroatoms, this is often comparable to all carbon skeleton [1]**.** The heterocyclic chemistry emphasizes mainly on unsaturated derivatives with unstrained 5 or 6-membered rings such as furan(C_4H_4O), thiophene pyrrole(C_4H_5N), and pyridine(C_5H_5N.). Heterocycles as pyridine, thiophene pyrrole and furan(C_4H_4O). being fused to benzene rings (C_6H_6) Which led to the development of both of (C_9H_7N,) and benzothiophene,(C_8H_7N,) and benzo-furan (C_8H_6O), respectively. The merger of two benzene rings. A third large class of compounds have advanced, including acridine, dibenzothiophene carbazole, and dibenzo-furan unsaturated rings can be classified based on the in corporation of the hetero atoms in to the conjugated (pi) system. It is categorized in to three rings, four, five, and six members**.** The most common hetero cyclics are those with 5 or 6 rings contains homogeneous atoms [2]**.** They are classified into three, four, five, and six-membered rings. The most common hetero cycles are those having five or six-membered rings and containing hetero atoms of nitrogen (N), oxygen (O), or sulfur (S) [3]**.** Indole is an organic compound with the formula C_8H_7N, a heterogeneous ring aromatic compound ,consisting of a hexagonal ring of gasoline integrated with a pentagram containing a nitrogen atom (pyrrol ring). The indole ring enters into the structure of many natural products**.** Properties of the indole are found in the form of a colorless and bright solid powder**.** These compounds are very plenty in nature, are an important source of pharmacologically active vehicles. Indole alkaloids have anticancer activity via different anti-proliferative mechanisms, and some of them, such as vinblastine and vincristine, have already utilized in clinics or under clinical estimations for the therapy for cancer [4]**.**

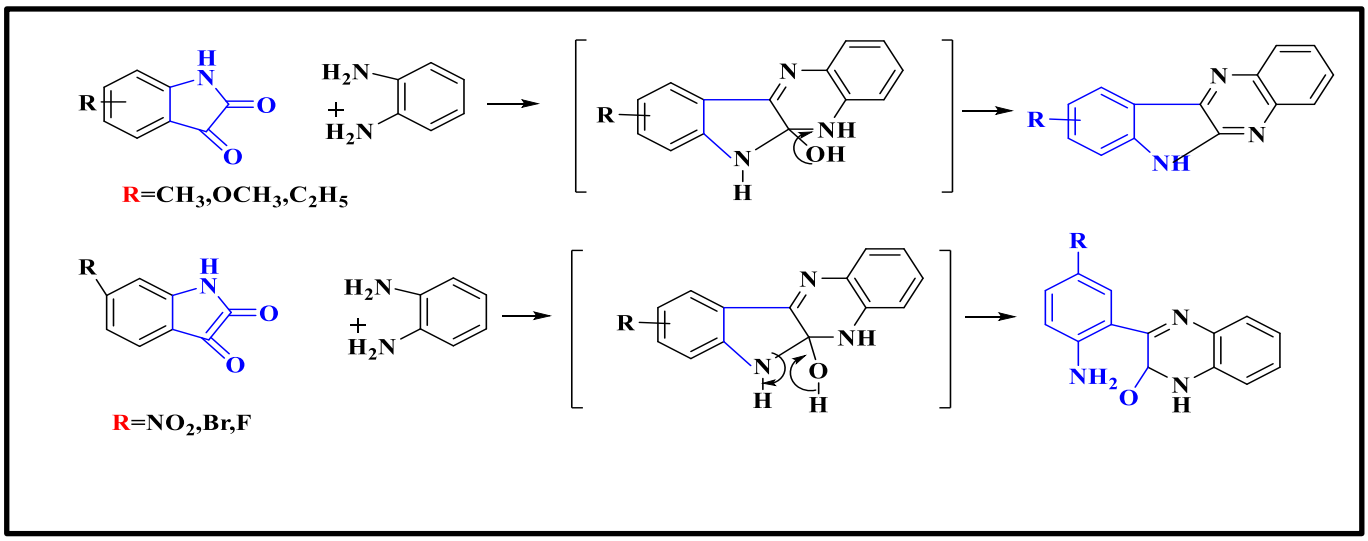
Quinoline is a heterogeneous ring-based nitrogen compound whose molecular formula C_9H_7N is the result of the of fased of the perydine part with the benzene ring**.** It is widely used mainly as an intermediate in the manufacture of other products**.** Potential exposure to quinolone may occur from the inhalation of cigarette smoke. It breaks down quickly in the atmosphere and water**.** Acute (short-term) inhalation exposure to quinoline vapors irritates the eyes, nose, and throat and may cause headaches, dizziness, and nausea in humans [5]**.**

Schiff bases are generally known as imines or azomethines and act as ligands in various metal complexes. They are formed as condensation products from primary amines and aldehydes or ketones. However, aldehydes react faster than ketones in condensation reactions due to steric and electronic effects [6]**.** These days, there search coordination chemistry with Schiff's base expanded greatly. The importance of Schiff base complexes for material science, catalysis, bioinorganic chemistry, separation and encapsulation processes, and forming of compounds with unusual properties and structures have been well recognized and reviewed [7]**.** They display wide ringe of activities biological such as anti-fungal, anti-bacterial ,anti-malarial, anti-proliferative ,anti- inflammatory, antiviral, ant -pyreticproperties and are widely used it is widely used for industrial purposes [8]**.**

1. 2 . Literature review

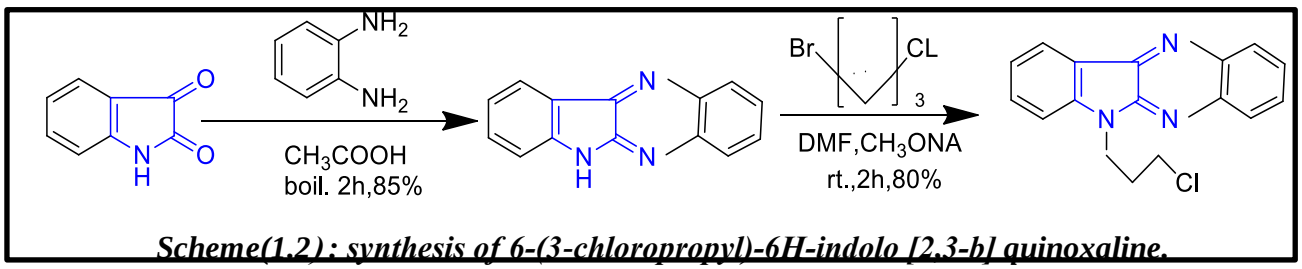
Dowlatabadi R. et al.(2011) Studied the reaction of several substituted isatin with ortho-phenylenediamine in acetic acid. While electron-donor substituents on isatin shift the reaction toward classical 6H-indolo[2,3-b] quinoxaline ring closure,

electron-withdrawing groups enhance the formation of 3-(2′-amino-5′-substituted)-quinoxaline-2(1H)-ones as shown in scheme (1.1) [9].



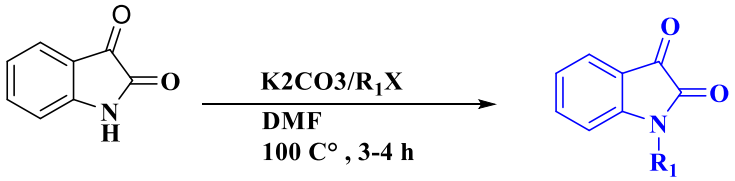
Scheme(1. 1): reaction of substituted isatin with ortho-phenylene diamine .

Shibinskaya M. O. et al. (2012) synthesized 6-(3-chloropropyl)-6H-indolo-[2,3-b] quinoxaline with 80% yield via indole quinoxaline alkylation by 1-bromo-3-chloropropane. Alkylation of 6H-Indolo-[2,3-b] quinoxaline was carried out in dimethylfor mamide at room temperature in the presence of equimolar quantity of sodium methylate as shown in scheme(1.2)[10].

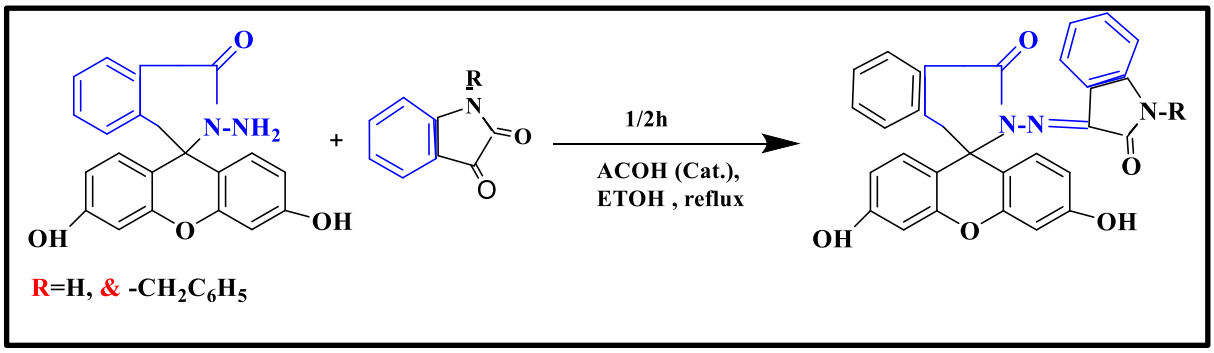


Scheme(1.2) : synthesis of 6-(3-chloropropyl)-6H-indolo [2,3-b] quinoxaline.

Kadi A. A. et al. (2015) synthesized N-alkyl/benzyl isatin derivatives from isatin and alkyl/benzyl halides in presence of K_2CO_3 in DMF and excellent to quantitative yields (~95%) were obtained. Isatins and benzyl-isatins were condensed with fluorescein hydrazide to form fluorescein hydrazone as shown in scheme(1. 3). N-Alkyl/benzyl substituted isatin derivatives are intermediates and synthetic precursors for the preparation of biologically active heterocycles. [11].

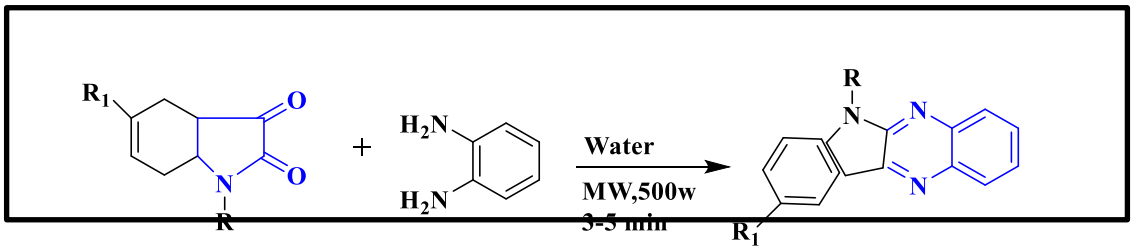


R_1=CH_3, C_2H_2 ,C_4H_9 ,C_6H_{13}, $CH_2CH(CH_3)_2$, $CH(CH_3)C_2H_5$, $CH_2C_6H_5$, & CH_2-(3-OCH_3)C_4H_6



Scheme(1. 3): Synthesis of N-substituted isatin derivatives.

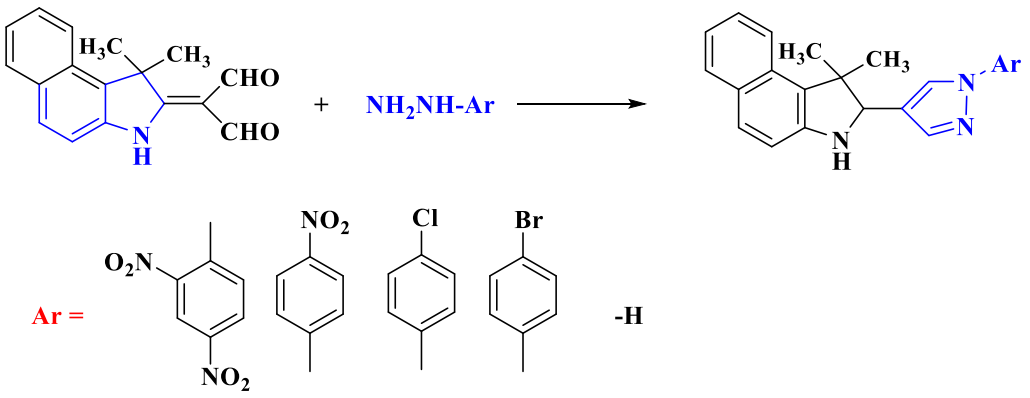
Bajpai S. et al. (2017) prepared of quinoxaline derivatives from reaction of isatin derivatives with o-phenylenediamine in water under microwave irradiation as shown in scheme (1. 4). The microwave method environmentally friendly, inexpensive, and highly effective to give the products in good to excellent yields. [12].



R= $COCH_3$, CH_2Ph and $CH_2CH_2CH_3$
R_1= Cl and H

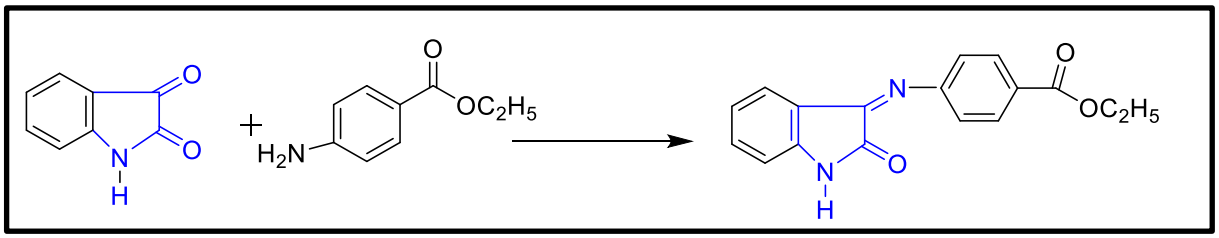
Scheme(1 .4): The reaction of isatin derivatives with o-phenylenediamine.

Ali W.B. (2018) synthesized new series of pyrazole derivatives by refluxing hydrazine derivatives with 2-(1,1-Dimethyl1,3- dihydro-benzo[e]indol-2-ylidene) malon aldehyde as shown in scheme (1. 5).The compounds were identified by FT-IR and ^{1}H-NMR spectral data. [13].



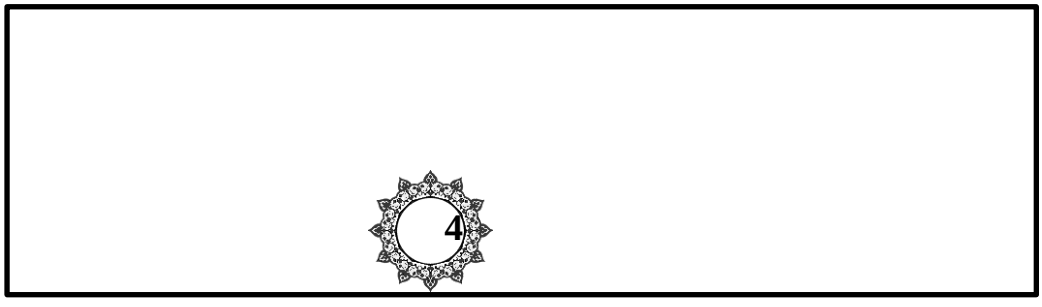
Scheme(1. 5): synthesis of pyrazole derivatives.

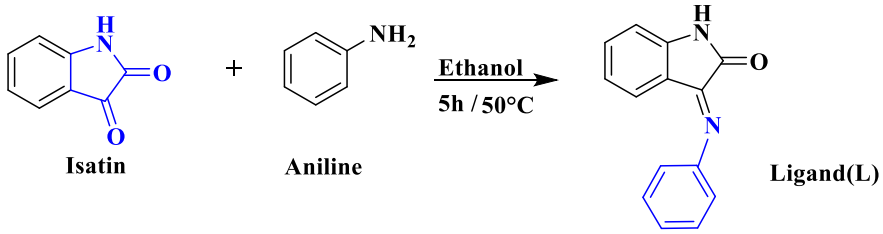
Al-Azawi K.F. (2018) Synthesized successfully new compound, ethyl 4-amino N-(3-isatinyl) benzoate in high yield from reaction of ethyl 4-aminobenzoate with isatin in (1:1) molar ratio as illustrated in the scheme (1.6), and its inhibition impact on corrosion of MS (mild steel) in hydrochloric acid as corrosive solution was examined via weight loss and scanning electron microscope techniques.[14].

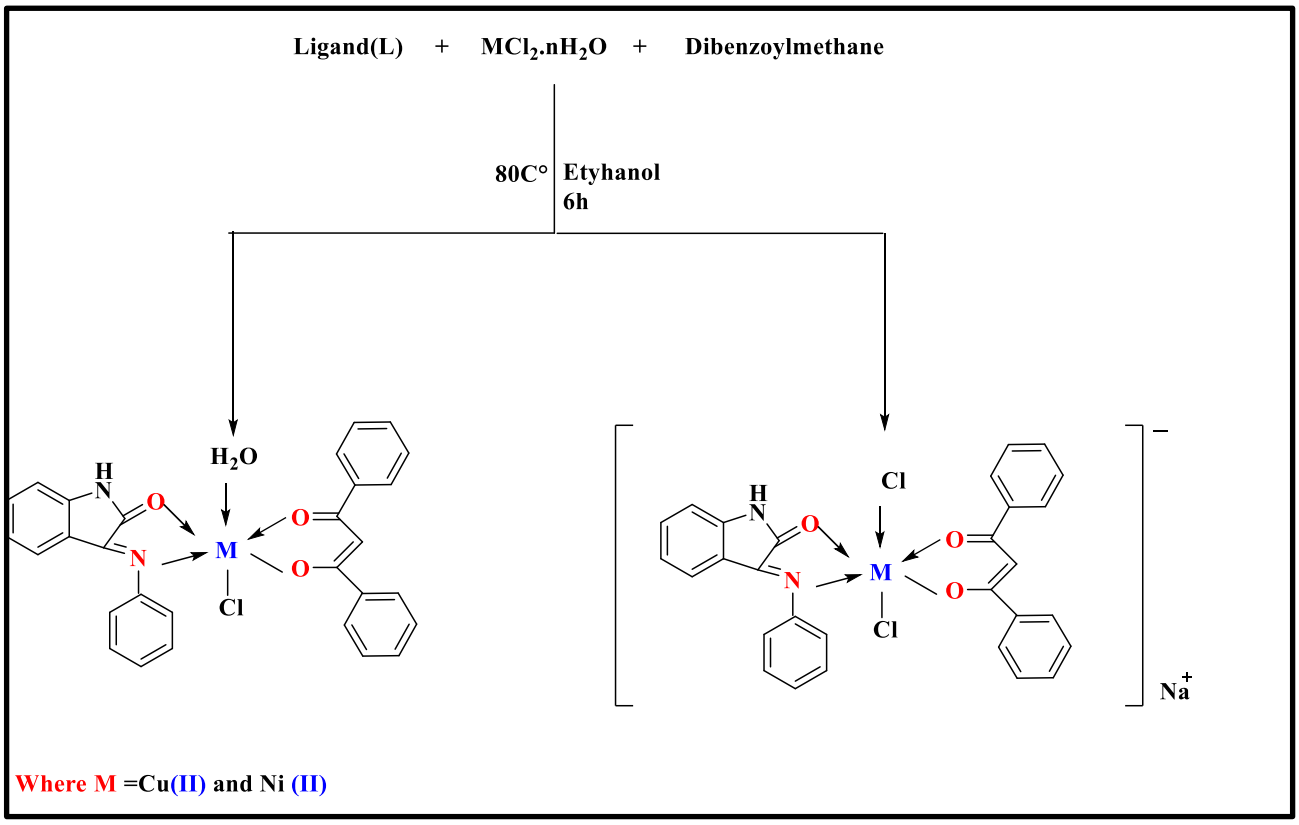


Scheme(1. 6): synthesis of inhibitor (ethyl 4-amino N-(3-isatinyl) benzoate).

Dar O.A. et. al.(2019) synthesized 3-(phenylimino)indolin-2-oneligand(L) from the reaction isatin with aniline in the ratio of 1:1 and then synthesis of mixed ligand complexes from reaction of dibenzoylmethane, schiff baseas ligands with $[M(Cl)_2.nH_2O]$ where M= Ni(II) and Cu(II) ions and n=6 and 2 as shown in scheme (1.7)[15] .



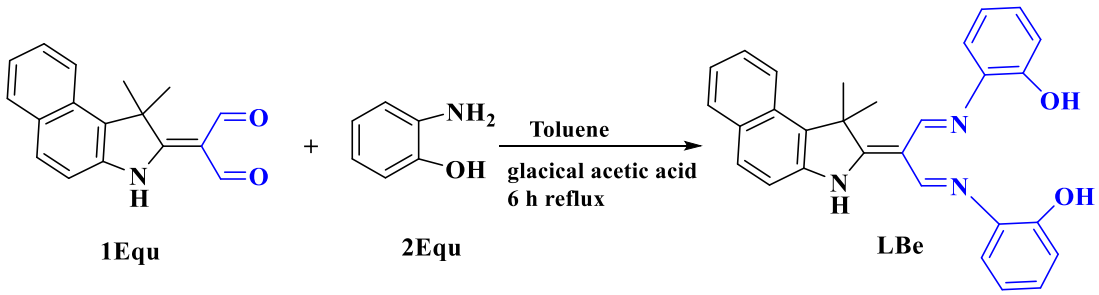




Scheme(1. 7): Synthesis of isatin based ligand (L) and mixed ligand complexes.

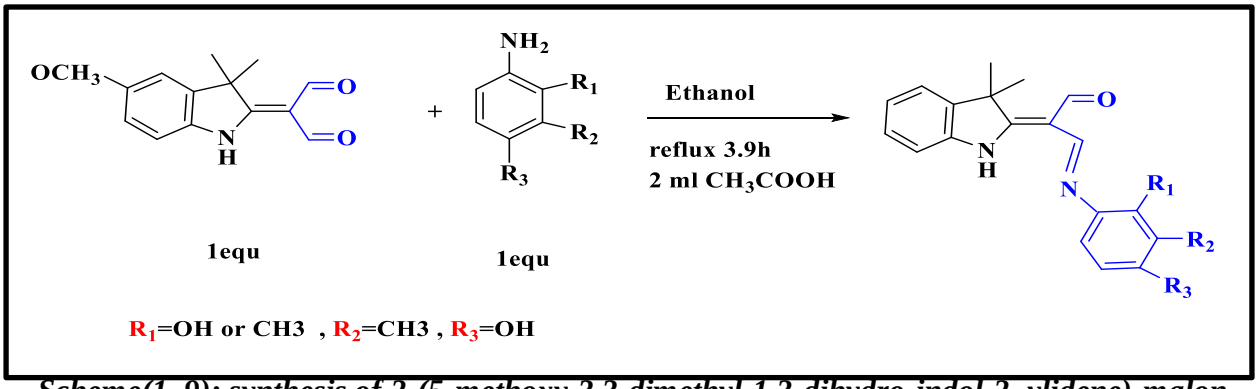
Hameed R. F. et al. (2019) synthesized new ligand 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e] indol-2-ylidene) propane-1,3-diylidene) bis (azanylylidene) diphenol LBe by the condensation reaction of 2-hydoxy aniline with 2-(1,1-dimethyl-1,3- dihydro-2H-benzo[e]indol-2-ylidene) malon aldehyde in ratio 2:1 as illustrated in the scheme (1. 8). This compound used as ligand to synthesis a series of metal complexes by its reaction with different metal chlorides in a molar ratio 1:1 and 1:2 of M:L in ethanol. Cytotoxicity effect of ligand and its complexes have

been evaluated against Hella cell line (cervical cancer) in two exposure times 24 and 48 hours.[16].



Scheme(1. 8): Synthesis of h2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e]indol-2-ylidene)propane-1,3-diylidene)j bis (azanylylidene) diphenol .

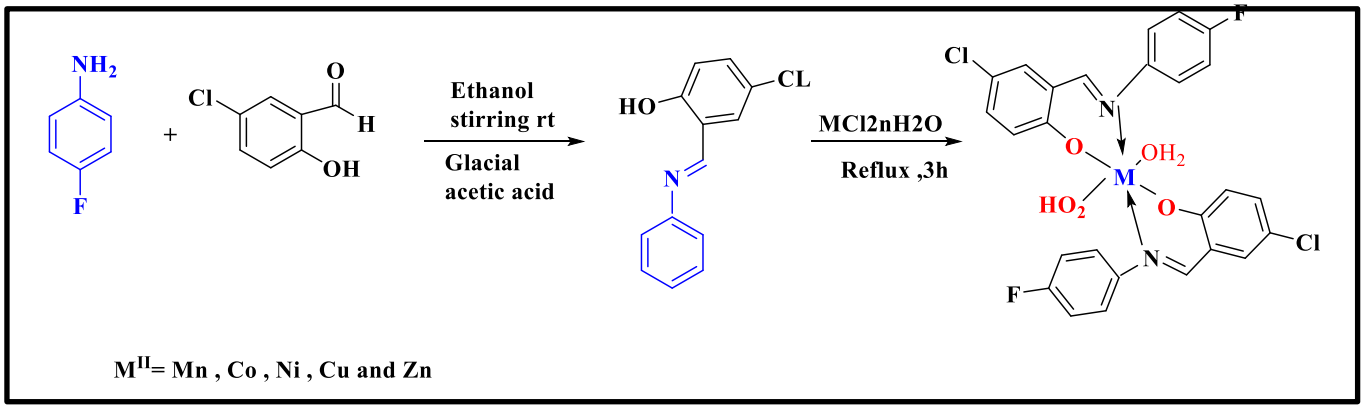
Rusul Adnan Nafia R. A. and Faraj F. L.(2019) synthesized three new Schiff bases by the reaction of 2-(5-methoxy-3,3-dimethyl-1,3-dihydro-indol-2-ylidene)-malon aldehyde with substituted aniline as shown in scheme (1. 9).The chemical structures were characterized by FT-IR, ^{1}H ,and APT^{13}C NMR .The biological activity of the new synthesized compounds screened on Lymphatic Cell in metaphase in Human Blood ,which was revealed different results[17].



Scheme(1. 9): synthesis of 2-(5-methoxy-3,3-dimethyl-1,3-dihydro-indol-2- ylidene)-malon aldehyde.

Ommenya K. F. et al. (2020) synthesized 4-chloro-2-{(E)-[(4-fluorophenyl)

imino]methyl}phenol, from reaction of 5-chlorosalicylaldehyde and 4-fluoroaniline at room temperature. A new series of Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) complexes was synthesized in a methanolic medium as shown in scheme (1.10). Elemental analysis, FT-IR, UV-Vis, and NMR spectral data, molar conductance measurements, and melting point were used to characterize the ligand and the metal complexes. The ligand and its metal (II) complexes were tested in vitro to evaluate their bactericidal activity against Gram **(-)** bacteria (Escherichia coli and Pseudomonas aeruginosa) and Gram **(+)** bacteria (Bacillus subtilis and Staphylococcus typhi) using the disc diffusion method. Antibacterial evaluation results revealed that the metal (II) complexes exhibited higher antibacterial activity than the free ligand as shown in scheme (1. ١٠). [18].



scheme(1. 10):synthesis of ligand and its complexes.

1.3. The aim of the study

The major objectives of the present study are **:**

1. Synthesis of indole derivatives are gained more attention due to their wide spectrum applications in biological and pharmacological fields. Accordingly, the main focus of the current project was to synthesize a new chain of indole derivatives as pure compounds **.**
2. Characterization of the synthesized organic compounds by (FT-IR and ^{1}H-NMR) spectroscopy **.**
3. Synthesis of new Schiff base and used it as a ligand to prepared complexes with Co(II), Ni(II), Cu(II), and Zn(II) ions **.**

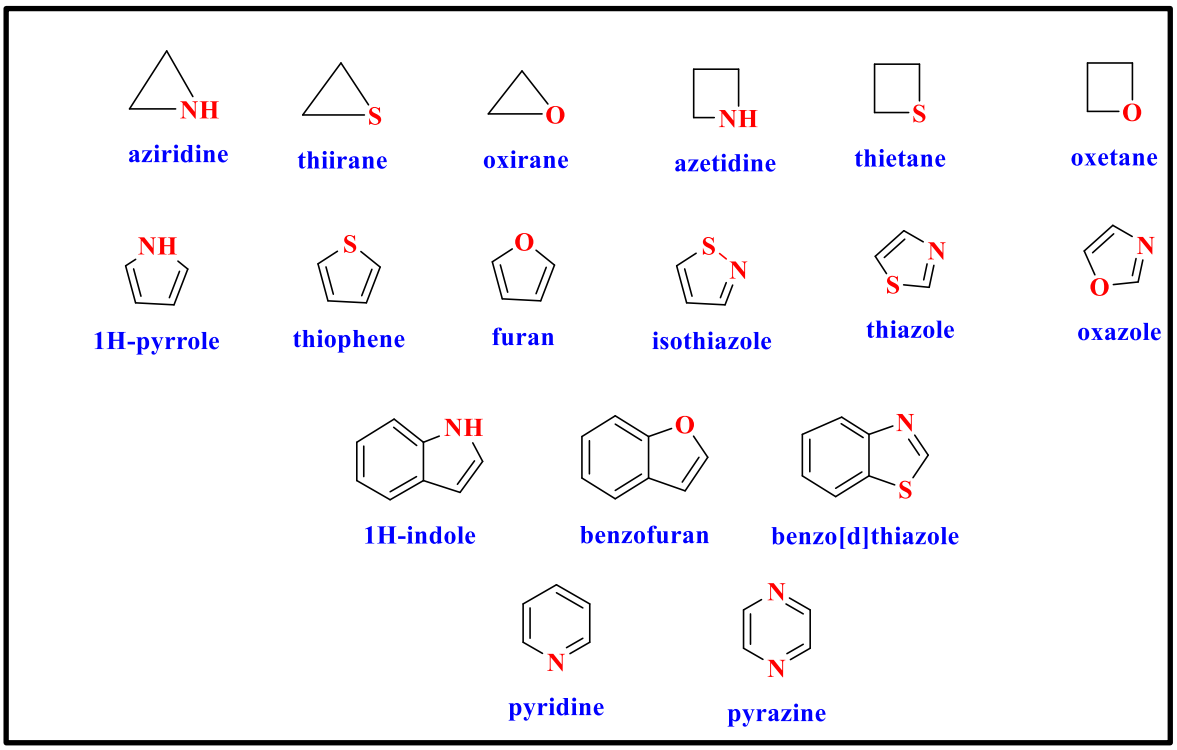
4. Characterization of the ligand and the complexes through the use of FT-IR , uv-vis spectroscopy, elemental analysis (C.H.N.S). metal analysis, magnetic susceptibility, and conductivity measurements .
5. Measurment the biological activity of the synthesis compounds and know their effectiveness against bacteria of both positive and negative types.

Chapter Two

Introduction

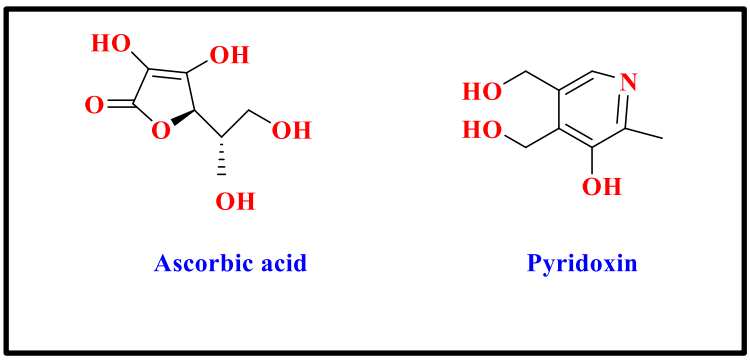
2. 1 Heterocyclic compounds

Heterocyclic compounds are cyclic organic compounds that contain at least one heterocyclic atom, and the most common heterocyclic atoms are nitrogen, oxygen, and sulfur, [19].The cyclic compounds can be five or six members it may contain a one heterocyclic atom as pyrrole ,furan and thiophene, or two heterocyclic atoms as in pyrazine which is composed of two nitroges atom, or the oxazole ring, which contains nitrogen and oxygen [20]. These heterocyclic rings can be combined with a benzene ring to form compound like indole compounds and benzothiozole [21and 22], as shown in figure (2. 1).



Figure(٢. ١): Simple aromatic rings and nonaromatic rings.

In nature, made up heterocyclic compounds are consist of materials important to life. For example DNA is made of long chains of heterocyclic groups (nucleotides) [23], and the rest of the sugars and polysaccharides too, for example, their derivatives, including Ascorbic acid , are found in the form of five rings (furans) or six broken rings (piran) with one atom of oxygen. Nitrogen, such as vitamin B6 (pyridoxine), which is a derivative of pyridine, is essential in the metabolism of amino acids [24], as shown in Figure (2.2).



Figure(2. 2):Vitamin C and Pyridoxine.

The importance of heterocyclic compounds. They are primarily used as medicines [٢٥], antioxidants [٢٦], as inhibitors [٢٧]of corrosion[٢٨], as copolymers, Dyeing materials[٢٩]. They are used in the synthesis of other organic materials as automobiles compunds, compunds certain natural products, antibiotics such as penicillin, cephalosporin; alkaloids such as vinblastine, morphine, heterocyclic moiety [٣٠]. Most of the heterocyclic compounds have biological activity, so they are used as antibiotics[٣١], anti-cancer[٣٢], anti-fungal, anti-bacterial, anti-inflammatory[٣٣], anti-microbial, in addition to having these compounds biological and pharmacological effectiveness [٣٤].

2. 2 Indole

A title of indole is the portmanteau of the terms indigo and oleum, as indole was first extracted by treating with oleum indigo dye [3٥]. It has a two-ring structure consisting of the amalgamation of (a benzene ring and a pyrrol nucleus at position 2, 3 of the pyrrol ring),as shown in Figure (٢. 3).

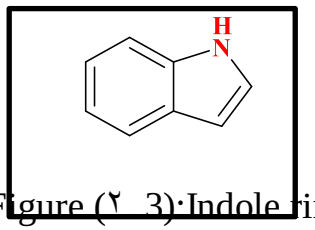


Figure (٢. 3):Indole ring

In fact, relatively high concentration of indole has been found in coal tar and animal feces and sewage, constituting the major contributor to odor pollution. Indole has long been regarded as a typical N-heterocyclic aromatic pollutant due to its toxicity and potential mutagenicity [3٦]. That indole can cause toxicity animal hemolysi, hemoglobin urine pyrosis, temporary skin irritation, tumor formation and

plant low pigmentation for microorganisms, indole can induce bacterial membrane and oxidant toxicity, prevent cell division by modulating membrane potential, inhibit adenosine triphosphate production and protein folding, and cause reparable DNA[3٧]. The biological importance of indole and its derivatives many naturally occurring biological activities and have found application in the pharmaceutical and other industries [3٨]. Many different types of alkaloids, which are compounds seen to be “like alkali” (having an amine group), the first extraction of these compounds was done using acid. The alkaloids have been isolated from various sources like fungi, mosses, frogs, and even mammals[3٩]. Natural products containing the indole nucleus heteroauxin (indole 3- acetic acid). This acid is important in plant physiology because of the part it plays as a promoter of the growth of seed scattered tryptophan derivatives are abundantly found in variety of naturally found compound that exhibit various physiological properties [٤٠] as shown in Figure (2. 4).

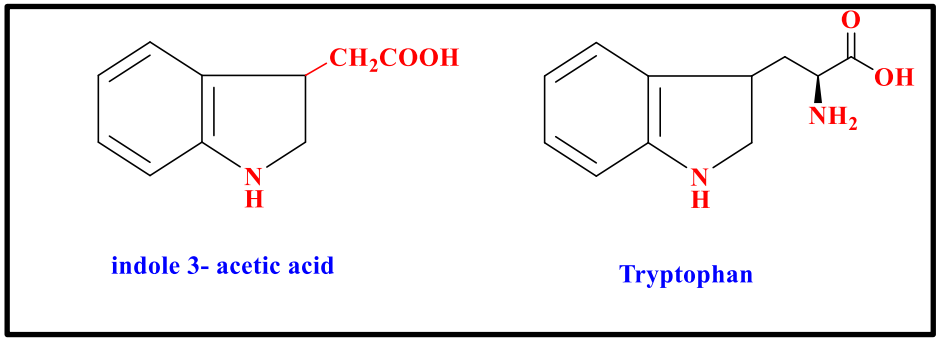


Figure (٢. 4) :Indole 3- acetic acid and Tryptophan.

٢.٢.١ *Pharmacological activities of indole derivatives*

indole analogues accountable for anti-cancer, anti-convulsant, anti-microbial, anti-tubercular, anti-malarial, antiviral, anti-diabetic . as shown in Figure (2. ٥). [٤١and ٤٢].

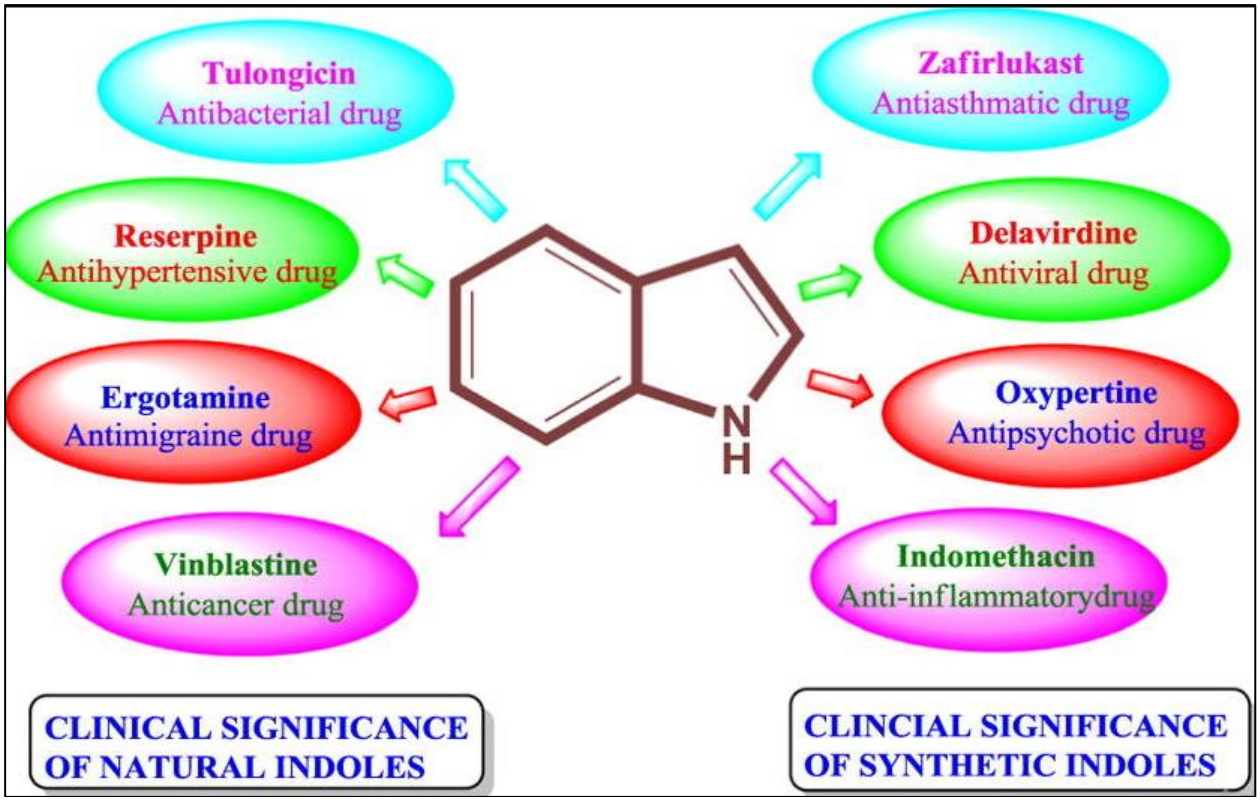


Figure (٢. ٥): Pharmacological activities of indole derivatives

2.2 .2 Reactivity of indole as aromatic ring.

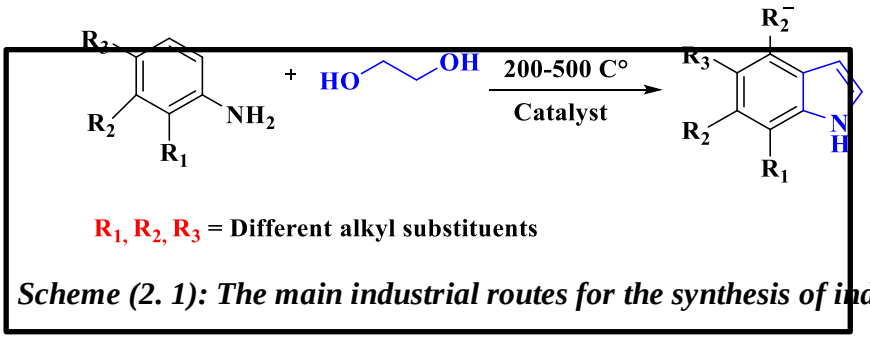
Indole is aromatic heterocyclic, but exhibit very distinctive reactivity. Here are some general rules [٤٣ and ٤٤] **:**

- The nitrogen is not basic. (pKa= 3.6) .
- Indole can readily undergo aromatic electrophillic substitution. The C_3 position is the most nucleophillic , followed by the N and C_2 positions.
- The C_2 and C_3 bond can often react like alkenes.
- Indole can be deprotonated at nitrogen. The resulting salts can be good nucleophiles.

- Highly ionic salts (e.g. Li^+, K^+) favours N substitution.
- Softer counter ions favours C_3 substitution.
- When N is substituted, C_2 can be deprotonated .

٢.٢. ٣ *General methods for indole synthesis*

A variety of industrial and laboratory methods. The main industrial routes start from aniline via vapor-phase reaction with ethyleneglycol in the presence of catalysts . Reaction of aniline and ethyleneglycol to give indole. In general, reactions are conducted between 200 and 500 °C. Yields can be as high as 60%. other precursors to indole include form toluidine, 2-ethylaniline, and 2-(2-nitrophenyl) ethanol, all of which undergo cyclizations, as shown in scheme (2.1) [4٥].

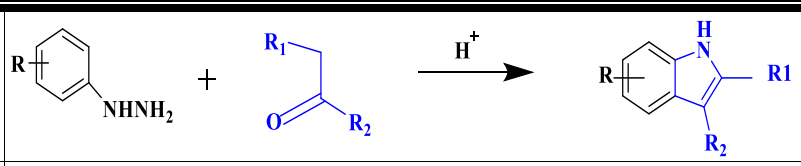
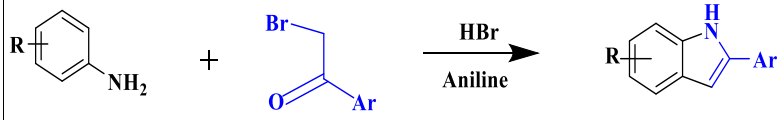
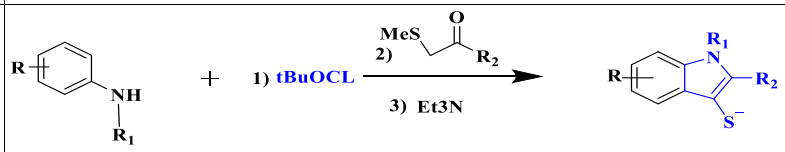
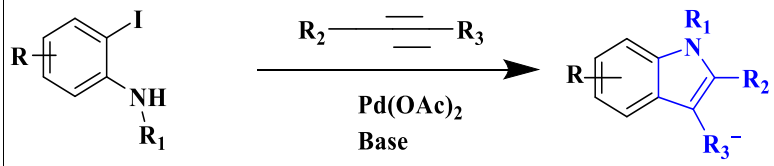
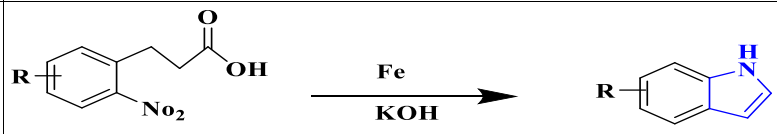
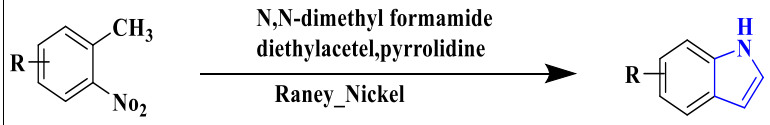
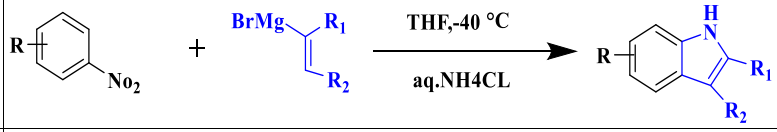
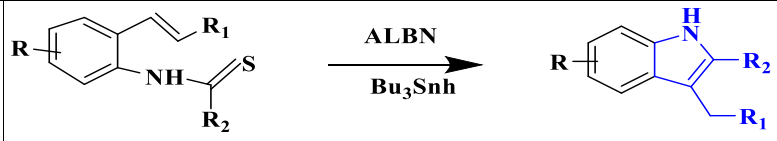
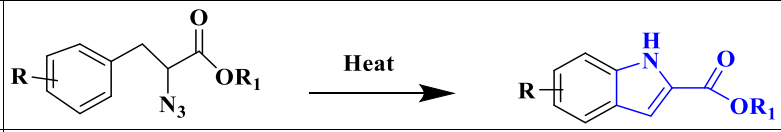
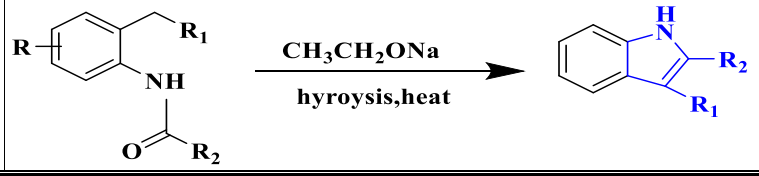


Scheme (2. 1): The main industrial routes for the synthesis of indole.

indole is prepared in the laboratory in a number of important ways, as illustrated in Table (2- 1).

Table (2- 1): Some importance methods for indole derivatives synthesis

Comp. No.	Methods	Reactions	Ref.

1	*Fisher indole synthesis*		[٤٦]
2	*Bi schier_ mohlah indole synthesis*		[٤٧]
3	*Gassman indol synthesis*		[٤٨]
4	*Larock indole synthesis*		[٤٩]
5	*Baeyer_emerling indole synthesis*		[٥٠]
6	*Lemigruber _ batcho indole synthesis*		[٥١]
7	*Bartoli indole synthesis*		[٥٢]
8	*Fukuyama indole synthesis*		[٥٣]
9	*Hametsberger indole synthesis*		[٥٤]
10	*Madelung indole synthesis*		[55]

٢. 3Quinoline

Charles Gerhardt 1842 discovery of quinoline as a result of the dramatic decomposition of quinline and of cinchonine antedates. Quinolines are the class of

organic compound of the hetero aromatic series characterized through a double-ring structure comprised of benzene and a pyridine ring fused at two adjacent carbon atoms [Figure (2.6) shown below]. The benzene ring includes six carbon atoms, whereas the pyridine ring includes five carbon atoms and a nitrogen atom (compare by the structure of naphthalene below). The simplest member of the quinoline family is quinolone it self, a compound having molecular structure C_9H_7N [٥٦ and ٥٧] .

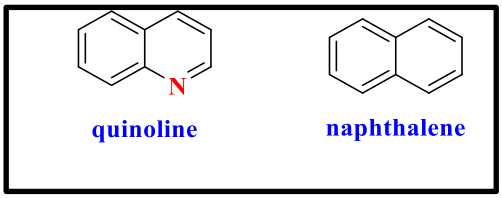


Figure (2. ٦): Structures of quinoline and naphthalene.

Quinoline is an important building material for the production of new medicines and is produced by numerous natural compounds, such as alkaloids from the cinchona plant, which exhibit various biological activities. Quinoline would be used in the production of anti-radiation products, but it is important to establish radiation interaction properties [٥٨]. In biomedical research, the synthesis in quinoline derivatives has become widespread due to the effectiveness of synthetic methods and the relative low-cost processing of these compounds, that could also be processed on a wide scale. It is an important heterocyclic derivative that serves as a building block for many pharmacological synthetic compounds. Quinoline and its derivatives are commonly used in antimalarial drugs, fungicides, antibiotics, dyes, and flavoring agents [٥٩]. And its derivatives also have important roles in other biological compounds that are involved in cardiovascular, anticancer, and anti-inflammatory activities [٦٠].

2. 3. 1 General physical and chemical properties of quinoline

Quinoline is really a hygroscopic solvent with a heavy taste that is colourless strong odor .On exposure to light, it becomes yellow and becomes brown afterward.

Quinoline is really only partially soluble in cold water, but it dissolves readily in most organic solvents and boiling water. This can be predicted that the benzene ring in quinoline would experience electrophilic substitution by electrophiles however be resistant to oxidation and reduction even as the pyridine ring would act as a base, experience nucleophilic substitution and reduction however be resistant to oxidation and electrophilic substitution as electrophilic substitution of the benzene ring is easier[٦١] .Quinoline is a weak base (pKa 4.9).It is a slightly weaker base compare to pyridine (pKa 5.2). It generally undergoes electrophilic substitution at positions 5

Comp . No.	Methods	Reactions	Ref.

and 8 of the benzene ring. Nucleophilic substitution takes place mostly at positions 2 and 4 of the pyridine ring. Reduction of the pyridine ring is fairly easy however reduction of the benzene ring is comparatively difficult[٦٢]. The oxidation of both rings is difficult. It generally undergoes substitution In two places ,electrophilic .The electrophilic exchange reaction prefers benzin (i.e. occurs on the benzene ring), while the necleophile reaction occurs on the peridine ring [٦٣].

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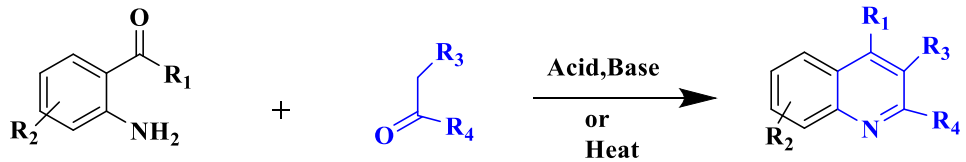
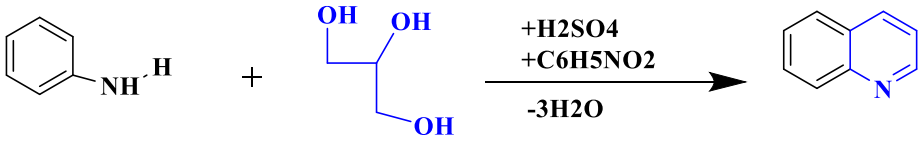
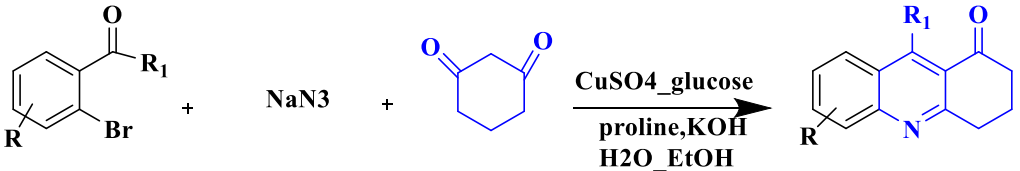
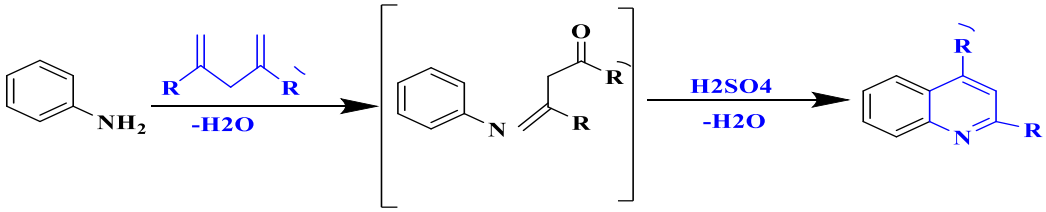
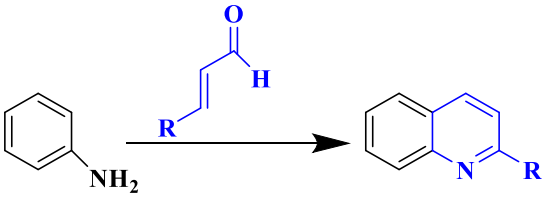
2. 3. 2 Synthesis of quinoline and its derivatives

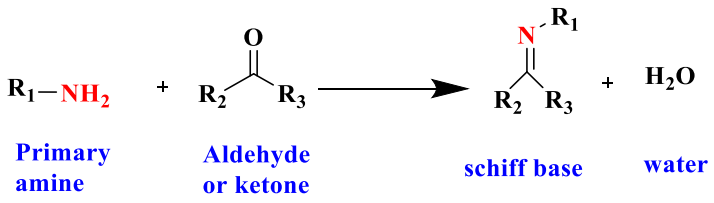
Quinolines are mostly synthesized using a variety of reactions from a basic aniline. It is not brought in combination of benzene with pyridine, but rather a cyclization process of aniline with a ketone compound containing the methyl [6٤]. Table (2-2) explain Some importance methods for quinoline synthesis.

Table (2- 2): Some importance methods for quinoline synthesis.

1	***Gould–Jacob quinoline synthesis***		[6٥]
2	***Skraup quinoline synthesis***		[6٦]
3	***Modified Friedländer quinoline synthesis***		[6٧]
4	***Combes / Conrad – Limpach quinoline synthesis***		[6٨]
5	***Doebner–von Miller quinoline synthesis***		[6٩]

٢.٤ *Schiff bases*

Schiff bases are aldehyde- or ketone-like compounds in which the carbonyl group is replaced by an imine or azomethine group. They are widely used for industrial purposes and also exhibit a broad range of biological activities. [٧٠]. These compounds were reported by a german chemist Hugo Schiff in 1864 and therefore referred to his name [٧١] .The majority of the Schiff bases are represented by the general formula $R_1R_2C=NR_3$ [٧٢].While some of these have the general formula $R_1CH=NR_2$, in which carbon is attached with a hydrogen atom instead of an alkyl or aryl group [7٣]. Usually, stable Schiff bases are those which are formed from the condensation reaction of aromatic amines and aromatic aldehydes [7٤]. as shown in scheme (2.4).



Scheme (2.2): Preparation of Schiff base.

2. 4. 1 Schiff base important metal complexes

Biological activities depend upon the type of substituent attached to the aromatic ring .The attention of Schiff bases, as well as their metallic complexes, is increasing due to their remarkable catalytic and biological applications [7٥]. Schiff bases also function as versatile ligands and can coordinate with a number of metal atoms or ions in various oxidation states and geometries. Schiff bases can form complexes with d-block elements and lanthanides [7٦]. Schiff bases are capable of coordinating with metal ions via the imine nitrogen and other groups linked to the Schiff base [7٧].Schiff bases are called privileged ligands since they can be prepared simply by condensation between aldehydes and primary amines [7٨]. Most of the Schiff bases have nitrogen or oxygen donor atoms, but sometimes sulfur or selenium can replace oxygen atom [7٩]. Schiff bases may serve as monodentate, bidentate, tridentate or tetradentate ligands depending upon the number of donor atoms present in the molecule. They can make chelates (typically five or six-membered) on reaction with metal ion [٨٠]. Some of the Schiff bases in combinations with metal ions are used as insecticides, fungicides, and herbicides [٨١]. Antioxidants are naturally occurring chemical substances that protect the living body from damage caused by harmful molecules called free radicals. These are produced by body cells in response to free radicles [٨٣ and ٨4]. The free radicals play a significant role in the etiology of numerous diseases, including cancer, diabetes, liver injury, autoimmune disorders, cardiac diseases, atherosclerosis, and aging [85]. Therefore antioxidants that have the potential to scavenge the free radicals play a significant role in the curing and preventions of these diseases [86]. Antioxidants are widely used as catalysts in antibiotics such as anti-inflammatory, antifungal, antibacterial, antivirus and in industries as anticorrosion [87]. Nowadays, synthetic antioxidants have major use as

compared to natural antioxidants because they are cheaper and effective [88 and ^9].

Chapter Three
Experimental Work

3. 1Chemicals

All starting materials and solvents used in this study were purchased from different companies, as listed in Table (3.1). These materials used as it is without any purification or modification .

Table 3. 1: Chemicals and solvents used in the chemistry part

No.	Chemicals	Chemical formula	Supplied from	Purity%
1	**Benzyl chloride**	$C_6H_5CH_2Cl$	**Aldrich**	98
2	**1-Bromo butane**	C_4H_9Br	**Aldrich**	98
3	**1-Bromo hexane**	$C_6H_{13}Br$	**Aldrich**	98
4	**1- Bromo octane**	$C_8H_{17}Br$	**Aldrich**	98
5	**Cobalt(II) chloride hexahydrate**	$CoCl_2.6H_2O$	**Aldrich**	96
6	**Cupric(II) chloride dihydrate**	$CuCl_2.2H_2O$	**ACS**	99
7	**3,4-Diaminobenzoic acid**	$C_7H_8N_2O_2$	**Aldrich**	97
8	**3,4-Diaminobenzophenon**	$C_{13}H_{12}N_2O$	**Aldrich**	97
9	**Dimethyl formamide (DMF)**	C_3H_7NO	**Merck**	99.5
10	**Dimethyl sulfoxide (DMSO)**	$C_2H_6OS.$	**BDH**	98
11	**Ethanol**	C_2H_6O	**Scharlu**	99.9
12	**Ethylacetate**	$C_4H_8O_2$	**Aldrich**	99
13	**Glacial acetic acid**	$C_2H_4O_2$	**BDH**	99.9
14	**Hexane**	C_6H_{14}	**BDH**	99
15	**Isatin**	$C_8H_5NO_2$	**Aldrich**	99
16	**4-Methyl-*o* -phenylenediamine**	$C_6H_{10}N_2$	**Fluka**	98
17	**Nickel(II)chloride hexahydrate**	$NiCl_2 .6H_2O$	**CDH**	99
18	***o*-Amino phenol**	C_6H_7NO	**Aldrich**	98
19	**Potassium carbonate**	K_2CO_3	**BDH**	96
20	**Sodium bicarbonate**	$NaHCO_3$	**BDH**	96
21	**Triethylamine**	$N(CH_2CH_3)_3$	**Fluka**	99
22	**Zinc (II) chloride anhydrous**	$ZnCl_2$	**SCRC**	99.9

3. 2. Instruments

- **Melting Points:** The melting points of the compounds and the metal-complexes were determined by open capillary tube in the Stuartsmplo electronic apparatus, at the Department of Chemistry, College of Science, University of Diyala.

- **FT-IR Spectra:** Infrared spectra of the synthesized compounds were recorded in (KBr) disc by using PERKIN ELMER SPEACTRUM-65 / Germany at Department of Chemistry, College of Science, University of Diyala.

- **Nuclear Magnetic Resonance Spectrometer (NMR):** ^{1}H NMR the spectra were recorded on a Bruke 400 MHz spectrometer in Jordan, University of Science and Technology, College of Science, Irbid City.

- **Antibacterial Activity:** The antibacterial activity of most compounds was evaluated at the. University of Baghdad . Center for Biological Research.

- **Electronic Spectra (uv-vis):** The electronic spectra of the ligand and its complexes were obtained by using UV-Visible (V-650) JAPAN pectrophotometer type Cary 100 at range (800-200) nm, with quartz cell of (1.0 cm) length and the concentration of (1×10^{-3} M), at Department of Chemistry, College of Science, University of Diyala .

- **Elemental-Analysis:** The elemental analysis (C.H.N.S) of ligand and its complexes was carried out by Eager 300 for EA1112 instrument in central Device labortoray College of science, University of Tehran, Iran.

- **Atomic Absorption:** The metals percentage of the complexes was measured using atomic absorption technique by Shimadzu Atomic Absorption 680 Flam Spectrophotometer for the determination of (Co^{2+}, Ni^{2+},Cu^{2+}, and Zn^{2+}) metal ions.

- **Magnetic Susceptibility:** The magnetic susceptibility of the complexes was measured by using (Balance Johnson Mattey). The μ_{eff} was determined in the solid

state by Faraday's method at Department of Chemistry , College of Science , Mustansiriyah University. Using onlya spin magnetic momenta a ccording to the following equation .

$$\mu_{eff} = 2.82 \sqrt{X_A . T} \text{ B.M}$$

$$X_A = X_M - (-D)$$

$$X_M = Xg * M.Wt$$

Where:

T= Room temperature in degree K

X_A= Atomic susceptibility

X_M = Molar susceptibility

X_g = Gramic susceptibility

D = Diamagnetic correction factor

• **Conductivity measurements:** Electrical measurements conductivity (Λ_m) of the complexes were registered at (25ºC) for (0.001 Molar) solution of the samples in [DMSO] by using (conductivity meter, inolab / Germany) at Department of Chemistry ,College of Science , University of Diyala and the determination of cell constant was made using the following relationship:

Where, (Λ_m) =molar conductance (Ω^{-1} cm^2 mol^{-1}), (C)= concentration ($mole.L^{-1}$) and (K)= specific conductance (Ω cm^{-1}).

• **Ultraviolet Cabinet:** Thin Layer Chromatography (TLC) for organic compounds was performed by using CM-10A /SPECTROLINE /USA and mixture of solvents (Ethyl acetate and n-hexane) at Department of Chemistry, College of Science, University of Diyala.

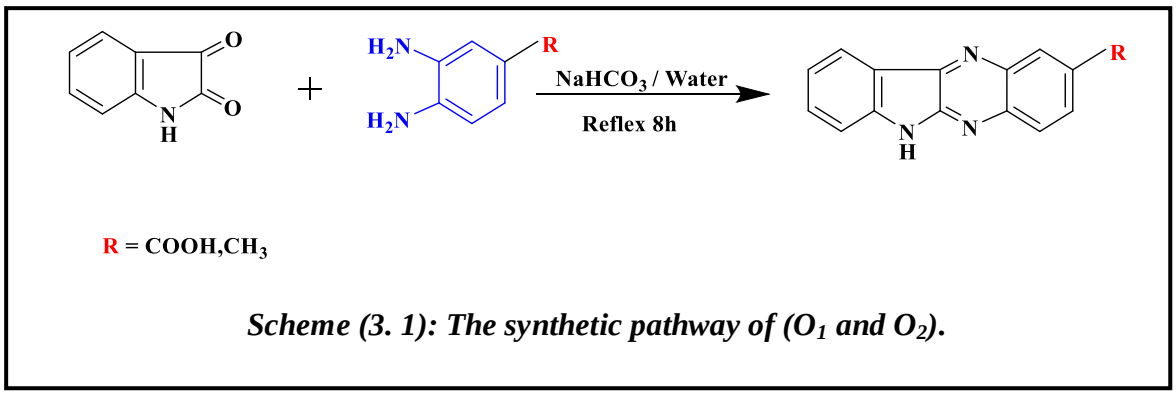
• **Rotary vacuum evaporator :**The solvents were evaporated by using Heldove apparatus, Heivap, Germany at Department of Chemistry , College of Science University of Diyala.

3. 3 Synthetic methods of the compounds.

3. 3. 1 General method for the synthesis of the compounds [O_1 and O_2]

Isatin (1.71g , 11.6 mmol)) has been resolved in the aqueous solution of

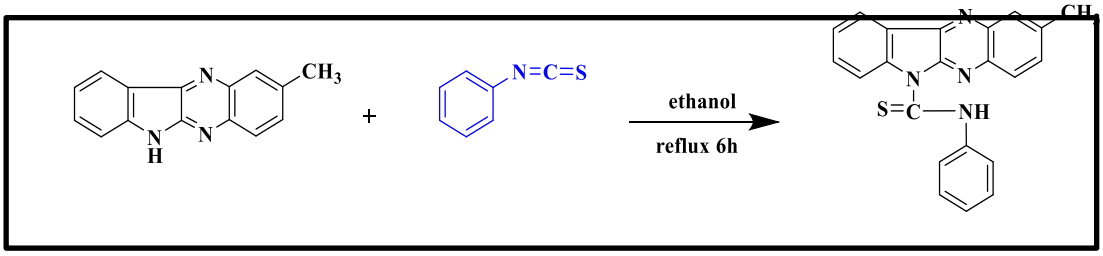
sodium bicarbonate (2.38 g, 28.3 mmol in 80 mL water). 3,4-diamino benzoic acid or 4- methyl-o-phenylenediamine (13.2mmol) was added and refluxed the mixture 8 h. The completion of the reaction was checked by using TLC mobile phase (ethylacetate :hexane 1:3). After cooling acetic acid was used to acidify the mixture and allowed to remain overnight. The mixture was filtered and the precipitate formed washed by H_2O distilled ,and recrystallized using absolute ethanol [90]. Scheme (3. 1) demonstrate the synthetic pathway of **(O_1 and O_2) .**



Scheme (3. 1): The synthetic pathway of (O_1 and O_2).

3. 3. 2 Synthesis of (2-methyl-indolo[2,3-b]quinoxaline-6)-carbothioic acid phenylamide [O_3].

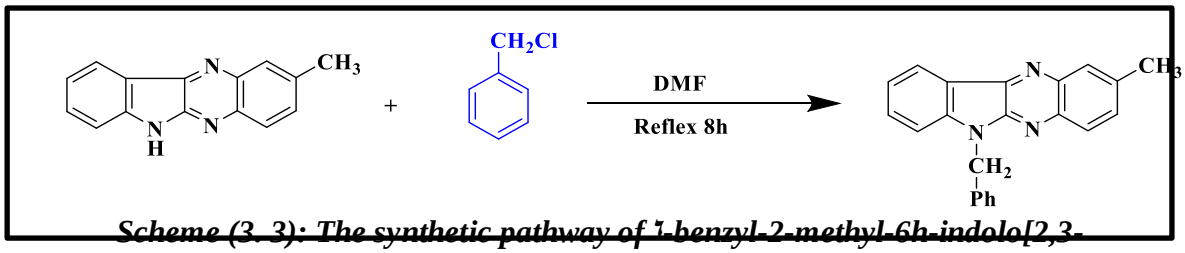
A mixture of (0.2g ,0.85mmol)of (2-methyl-6H-indolo[2,3-b] quinoxaline) [O_2] and (0.11g , 0.85 mmol) of phenyl isothiocyanate in absolute ethanol 20 mL was refluxed at 78ºC for 6 h in a water bath. The solvent evaporated under the reduced pressure, the precipitate is filtered, and washed with hexane and dried in an oven to give pure light brown precipitate. Scheme (3. 2) demonstrate the synthetic pathway of **(O_3).**



Scheme (3. 2): The synthetic pathway of (2-methyl-in dolo [2,3-b]quinoxaline-6-carbothioic acid pheny lamide)(O_3).

3. 3. 3 Synthesis of ٦-Benzyl-2-methyl-6h-indolo[2,3-b]quinoxaline [O_4].

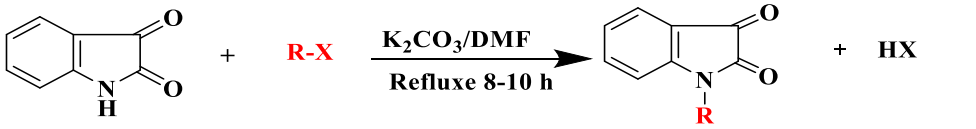
(0.2g, ٠.٨١mmol) 2-methyl-6H-indolo[2,3-b] quinoxaline[O_2] dissolved in 1٥ ml DMF. Then added potassium carbonate (٠.٢٧g, ٢mmol) and (٠.11g,٠.88mmol) of benzyl chloride that dissolved in ١٥mL DMF. The mixture was refluxing for 8h in oil bath. The solvent was reduced and the brown precipitate is filtered and washed with hexane, and dried in an oven to give precipitate pure brown-black. Scheme (3. 3) demonstrate the synthetic pathway of **(O_4).**

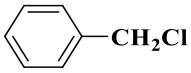


***Scheme (3. 3): The synthetic pathway of ٦-benzyl-2-methyl-6h-indolo[2,3-b]quinoxaline*.(O_4).**

٣ .٣. ٤ General method for the synthesis of the compounds [O_5 –O_8].

Isatin (1.03g, 7 mmol) was dissolved in the aqueous solution of refluxed Potassium carbonate (1.٣٨g, 10 mmol) in DMF 15mL, the corresponding alkyl halide (7.7mmol) in DMF 15mL it is added to this solution and the mixture is reflexed in an oil- bath at suitable temperature for 8-10 h it was monitored by TLC .When the reaction was completed, the reaction mixture was poured in to ice-water . the mixture was filtered and the precipitate formed by H_2O distilled, ,and recrystallized using absolute ethanol. [91]. Scheme (3. 4) demonstrate the synthetic pathway of **(O_5–O_8).**

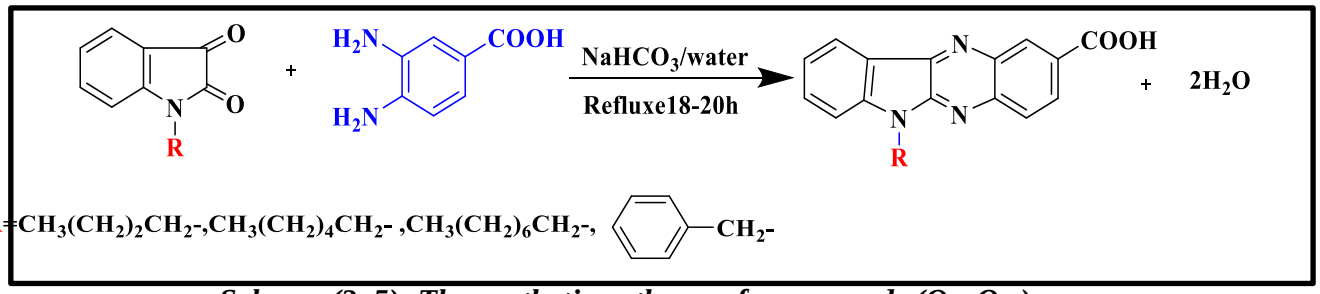


R-X= $CH_3(CH_2)_2CH_2$ Br ,$CH_3(CH_2)_4CH_2Br$, $CH_3(CH_2)_6CH_2Br$, 

Scheme (3. 4): The synthetic pathway of compounds (O_5–O_8).

3. 3. 5 General method for the synthesis of compounds[O_9 – O_{12}].

A mixture of O_5 - O_8 (N- alkyl isatin) (١١mmol) It was dissolved in solution of aqueous sodium bicarbonate ($NaHCO_3$). (2.38 g, 28.3 mmol in 80 mL water) with (13mmol) of 3,4-diaminobenzoic acid was added and the mixture was refluxed for 18-20h. The completion from the reaction it was checked by using TLC mobile phase (ethyl acetate: hexane 1:3).After cooling solution was acidified with acetic acid and left to stay over night . The solution was filtered and the precipitate formed washed by H_2O, ,and recrystallized using absolute ethanol. Scheme (3. 5) demonstrate the synthetic pathway of (**O_9 and O_{12}**).

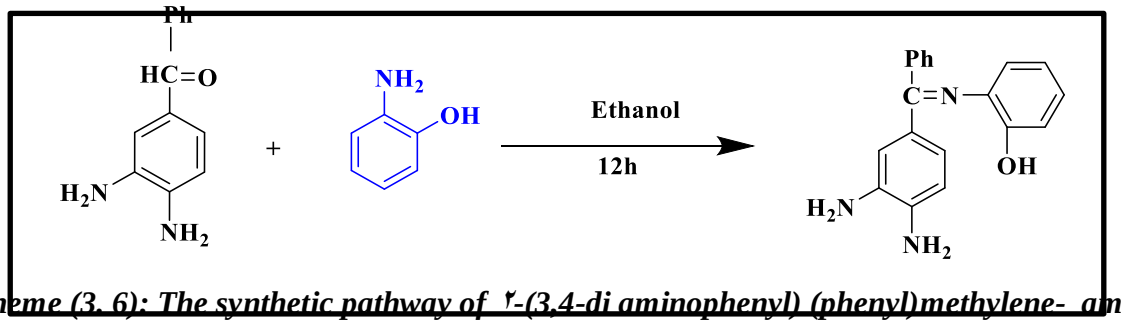


Scheme (3. 5): The synthetic pathway of compounds (O_9–O_{12}).

3. 3. 6 Synthesis of 2-(3,4-di aminophenyl)(phenyl) methylene-aminophenol[O_{13}].

A solution of 3,4-diaminobenzophenone (0.48 g,2.3 mmol)in absolute ethanol (15 ml) was added to (0.25g ,2.3 mmol) o-Amino phenol that dissolved in 10 mL ethanol with 5-6 drops of glacial acetic acid CH_3COOH .The mixture was reflaxed at 78ºC for 12 h in a water bath. The solvent evaporated underneath the low pressure, and the

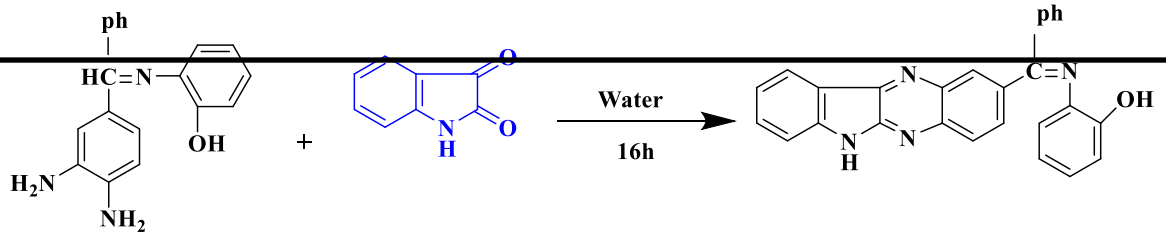
brown precipitate is filtered off, also recrystallized it using C_2H_5OH to give pure brown yellow precipitate. Scheme (3. 6) demonstrate the synthetic pathway of (**O_{13}**).



Scheme (3. 6): The synthetic pathway of ٢-(3,4-di aminophenyl) (phenyl)methylene- amino phenol (O_{13}).

3. 3. 6. 1 Synthesis of Z-2(1-6H-Iindol[2,3-b]quinoxaline-2yl)ethylidene amino phenol [O_{14}].

Isatin (0.34 g, 2.32mmol) was dissolveed in the aqueous solution of sodium bicarbonate (0.47 g, 5.66mmol in 80 mL water). ٢-(3,4-di aminophenyl)(phenyl) methylene-amino phenol (0.80 g, 2.64mmol) (O_{13}) was added and refluxed the mixture 16 h . The completion of the reaction was checked by using TLC mobile phase (ethyl acetate :hexane 1:3).The solution was cooled to room temperature ,acidify by using acetic acid, allowed to remain overnight, and filtered in second day, washed with distilled H_2O and desiccated also recrystallized using C_2H_5OH give pure brown precipitate . Scheme (3. 7) demonstrate the synthetic pathway of (**O_{14}**).

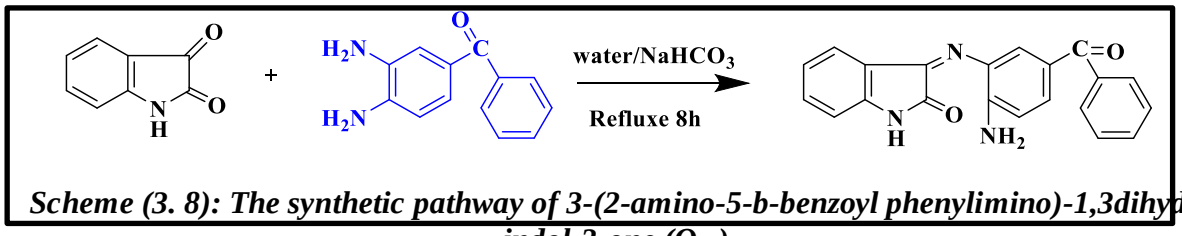


Scheme (3. 7): The synthetic pathway of Z-2(1-6H-Iindol[2,3-b]quinoxaline-2yl) ethylidene amino phenol (O_{14}).

3. 3. 7 Synthesis of 3-(2-amino-5-b-benzoylphenylimino)-1,3-dihydro-indol-2-one [O_{15}].

Isatin (1.71g , 11.6 mmol)) was dissolved in the aqueous solution of sodium bicarbonate (2.38 g, 28.3mmol in 80 mL water). 3,4-diaminobenzophenone (2.46g

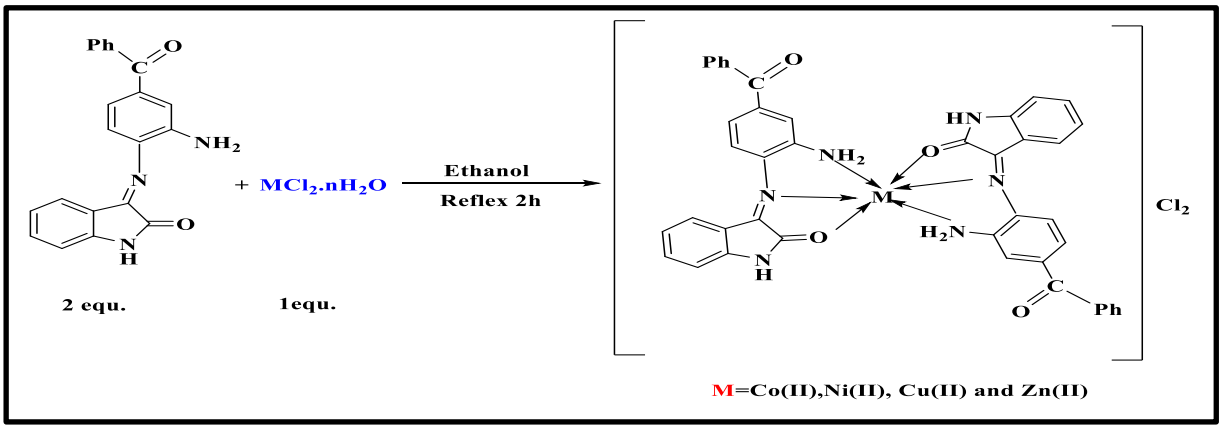
,11.6 mmol) was added and refluxed the mixture 8 h. The completion of the reaction was checked by using TLC mobile phase (ethyl acetate :hexane 1:3). After cooling acetic acid was used to acidify the is solution and allowed to remain overnight. the solution was filtered and the precipitate formed washed by H_2O distilled, and recrystallized using absolute ethanol to give pure bright yellow precipitate. Scheme (3. 8) demonstrate the synthetic pathway of (**O_{15}**).



Scheme (3. 8): The synthetic pathway of 3-(2-amino-5-b-benzoyl phenylimino)-1,3dihydro-indol-2-one (O_{15}).

3. 3. 7. 1 Synthesis of complexes[$M(C_{21}H_{15}N_3O_2)_2]Cl_2$.

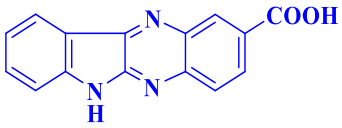
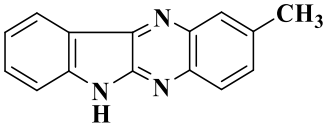
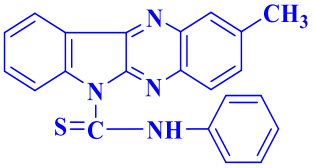
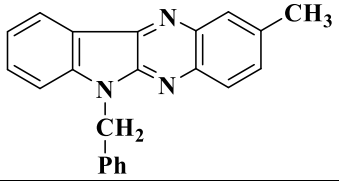
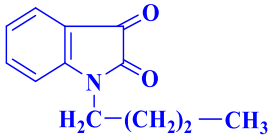
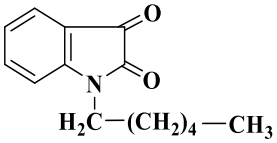
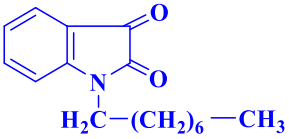
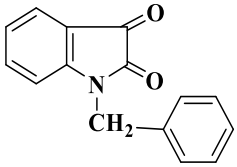
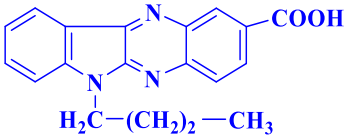
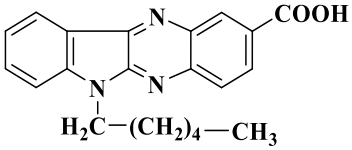
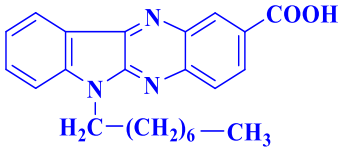
(0.29 mmol) of metal chloride such as ($CoCl_2.6H_2O$, $NiCl_2.6H_2O$, $CuCl_2.2H_2O$ and $ZnCl_2$) was dissolved in (25 ml) of ethanol, then the solution was added into a solution of ligand (O_{15}) (0.2 g, 0.58 mmol). The mixture was placed in 100 ml round bottom flask, and a few drops of triethyl amine were added and the mix was refluxed on a water bath at 78°C. The refluxing was continued for 2h, then cooled. The solid precipitate is filtered, washed with H_2O, and dried in an oven at 50°C. Scheme (3. 9) demonstrate the synthetic pathway of (**O_{15}**).

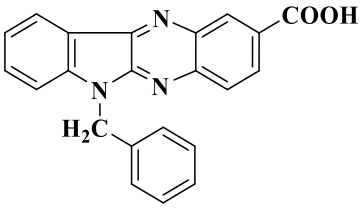
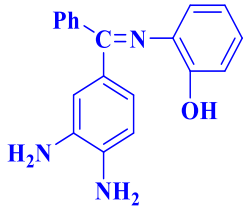
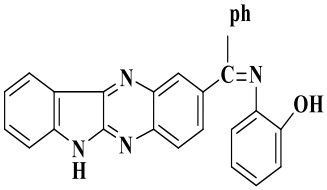
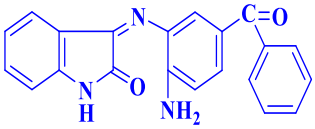
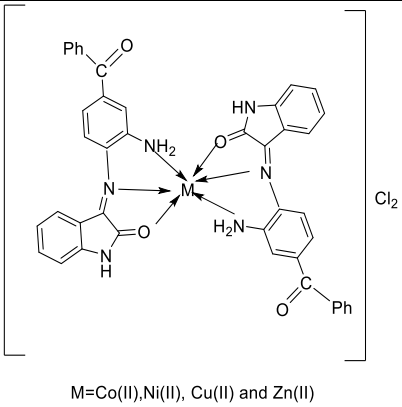


Scheme (3. 9): The synthetic pathway of complexes with O_{15} ligand

Comp. No.	Comp. Structure	Molecular Formula	Comp. name

Table 3.2 : The structures and nomenclatures of the synthesized compounds

O_1		$C_{١٥}H_{٩}N_3O_{٢}$	6H-indolo[2,3-b]quinoxaline-2-carboxylic acid
O_2		$C_{15}H_{11}N_3$	2-methyl-6H-indolo[2,3-b]quinoxaline
O_3		$C_{22}H_{16}N_4S$	2-methyl-indolo[2,3-b]quinoxaline-6-carbothioic acid phenylamide
O_4		$C_{22}H_{17}N_3$	٦-benzyl-2-methyl-6h-indolo[2,3-b]quinoxaline
O_5		$C_{12}H_{13}NO_2$	1-Butyl-1H-indole-2,3-dione
O_6		$C_{14}H_{17}NO_2$	1-Hexyl-1H-indole-2,3-dione
O_7		$C_{16}H_{21}NO_2$	1-Octyl-1H-indole-2,3-dione
O_8		$C_{15}H_{11}NO_2$	1-Benzyl-1H-indole-2,3-dione
O_9		$C_{19}H_{17}N_3O_2$	6-Butyl-6H-indolo[2,3-b]quionxaline-2-carboxylic acid
O_{10}		$C_{21}H_{21}N_3O_2$	6-Hexyl-6H-indolo[2,3-b]quionxaline-2-Carboxylic acid
O_{11}		$C_{23}H_{25}N_3O_2$	6-Octyl-6H-indolo[2,3-b]quionxaline-2-carboxylic acid

O_{12}		**$C_{22}H_{15}N_3O_2$**	**6-Benzyl-6H-indolo[2,3-b]quionxaline-2-carboxylic acid**
O_{13}		**$C_{19}H_{17}N_3O$**	**2-(((3,4-diaminophenyl)(phenyl)methylene)amino)phenol**
O_{14}		**$C_{22}H_{16}N_4O$**	**(Z)-2-((1-(6H-indolo[2,3-b]quinoxalin-2-yl)ethylidene)amino)phenol**
O_{15}		**$C_{21}H_{15}N_3O_2$**	**3-(2-amino-5-b-benzoyl phenylimino)-1,3dihydro-indol-2-one**
$[M(O_{15})_2]Cl_2$	 M=Co(II),Ni(II), Cu(II) and Zn(II)	**$[M(C_{21}H_{15}N_3O_2)_2]Cl_2$**	**[Bis(3-(2-amino-5-b-benzoyl phenylimino)-1,3dihydro-indol-2-one)Metal(II)]Chloride**

3. 4 Biological activity

Some of the vehicles produced have been inspected their antibacterial activities toward two strains of bacteria (***E.colias***) a gram-negative and (***S. Aureus***) as a gram-positive bacteria by using mueller hinton agar diffusion method(66) in nutrient agar medium. This is sterile agar media were poured into petri dishes and allowed to solidify. Microbial suspensions were spread on the medium surface by the sterile triangular ring. stainless steel sterile cylinder of 8mm was used to make cavities, and the solution of the test compounds in DMSO (200 mg/ml) were added into each

cavity with help allowed a micropipette to spread for 1 hour, Then the plates were incubated for 24 h. at 37°C . The areas of inhibition that appeared around the cups were measured in mm. STREPTOMTCIN used as standard antibiotics. The isolates used in this study were multidrug resistant to antibiotics.

Chapter Four

Results and discussion

4. 1 Introduction

The indole and the other heterocyclic compounds derived from are an important

organic compounds in the organic synthesis and many derivatives that showed their biological effect against many diseases. Therefore, we have been synthesized a series of new compounds of Schiff bases and indole [2,3-b] quinoxaline from 3,4-diaminotoluene, 3,4-diaminobenzoic acid, and 3,4- diaminobenzophenone with isatin compounds that are widely used in pharmaceutical chemistry and the development of drugs. The physical properties of compounds (O_1-O_{15}) were registered ***in Table (4. 4).***

4. 2 Synthesis and identification of 6H-indolo [2,3-b] quinoxaline-2-carboxylic acid [O_1] and 2-methyl-6H-indolo[2,3-b] quinoxaline [O_2].

Compound (O_1) was synthesized through the reaction of isatin with 3,4-di amino benzoic acid with a structure appears in ***Figure (4. 1).***

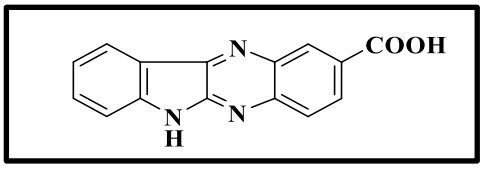


Figure (4. 1): The chemical structure of compound O_1

Where as compound (O_2) was synthesized through the reaction of isatin with 4-methyl-o-phenylenediamine as appears in ***Figure (4. 2).***

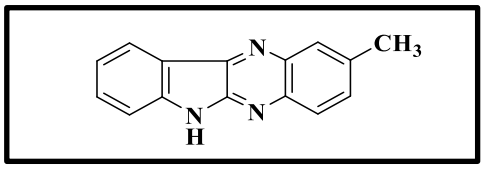
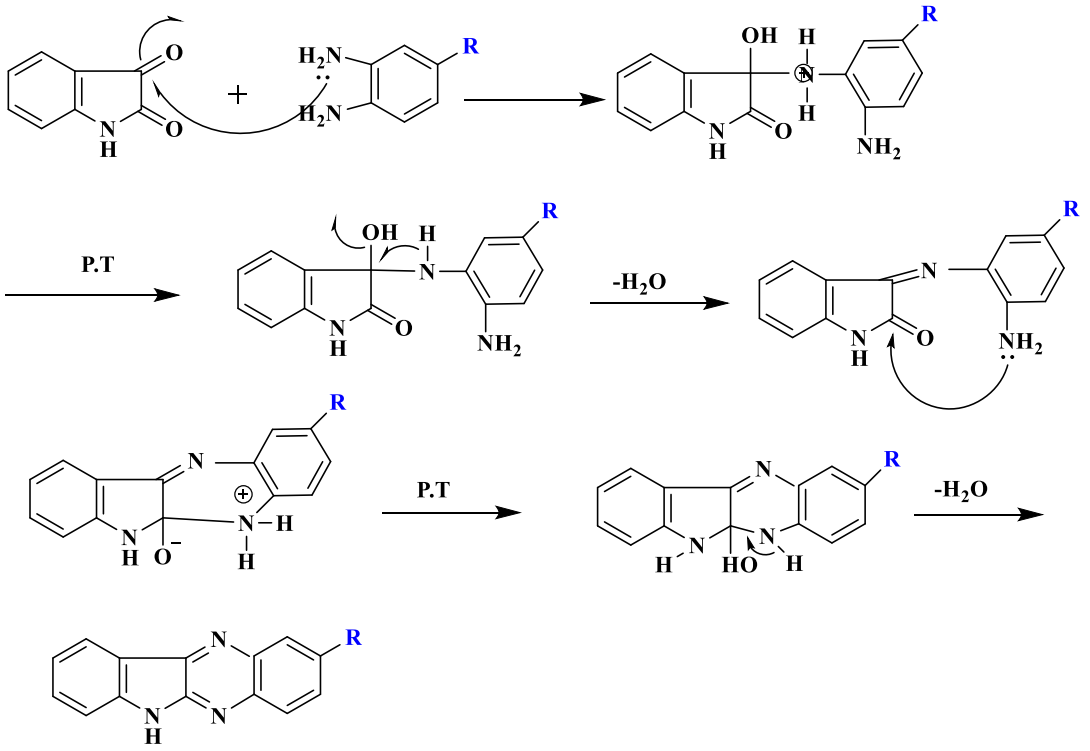


Figure (4. 2): The chemical structure of compound O_2

The suggested mechanism of the closure ring reaction is explains in the scheme(4. 1).



R =CH3 ,COOH

Scheme (4. 1): The mechanism for the synthesis of (O_1-O_2) compounds.

The structure of the compound O_1 was proved by FT-IR spectrum as illustrated in ***Figure (4.3)*** and ***Table (4.1)***.The FT-IR spectrum shows absorption band range between (٣365-2500 cm^{-1}) was attributed to O-H group (broad). Bond absorption at 1667 cm^{-1} was due to stretching vibration of C=O. New clear absorption band at 1564 cm^{-1} was due to C=N stretching vibration . [92].

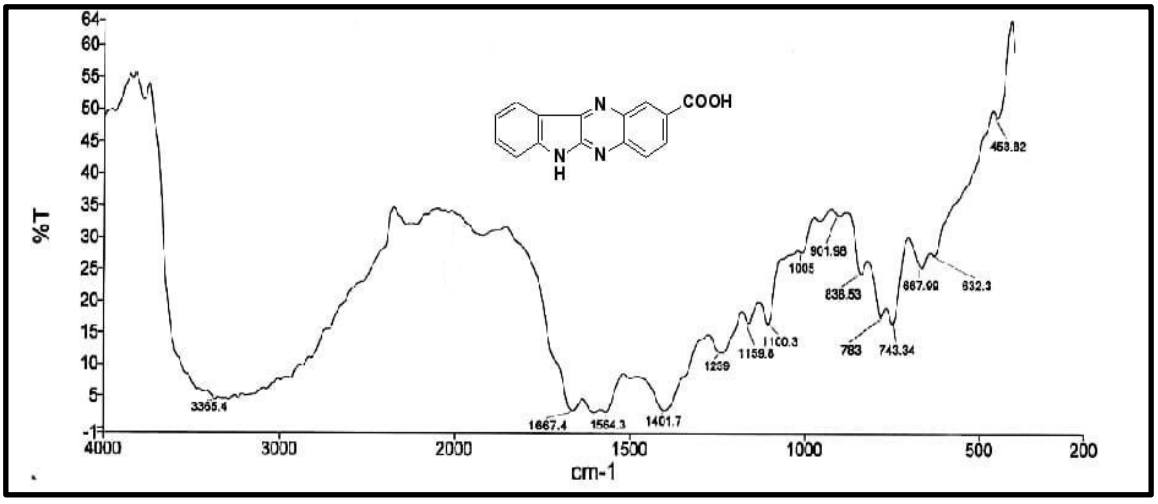


Figure (4. 3): FT-IR spectrum in of (O_1) compound

The structure of the synthesized compound O_2 was confirmed by FT-IR and

^{1}H-NMR spectroscopy. The FT-IR spectrum of compound O_2 as illustrated in ***Figure (4. 4)*** and ***Table (4. 1)*** shows absorption bands at 3321cm^{-1} was attributed to bonding of NH group. Absorption band at 3029 cm^{-1} was due to C-H aromatic, as well as absorption band at 2919 cm^{-1} was due to C-H aliphatic. Bond absorption at 1615 cm^{-1} was due to C=N stretching vibration

The ^{1}H-NMR spectra of the compound (O_2), ***Figure (4.5)***shows the following chemical shifts (DMSO-d_6, ppm): 10.04(s,1H, N-H) , 6.5-8.04 (m, 7H, Ar-H), 1.21 (s, 3H, CH_3) .

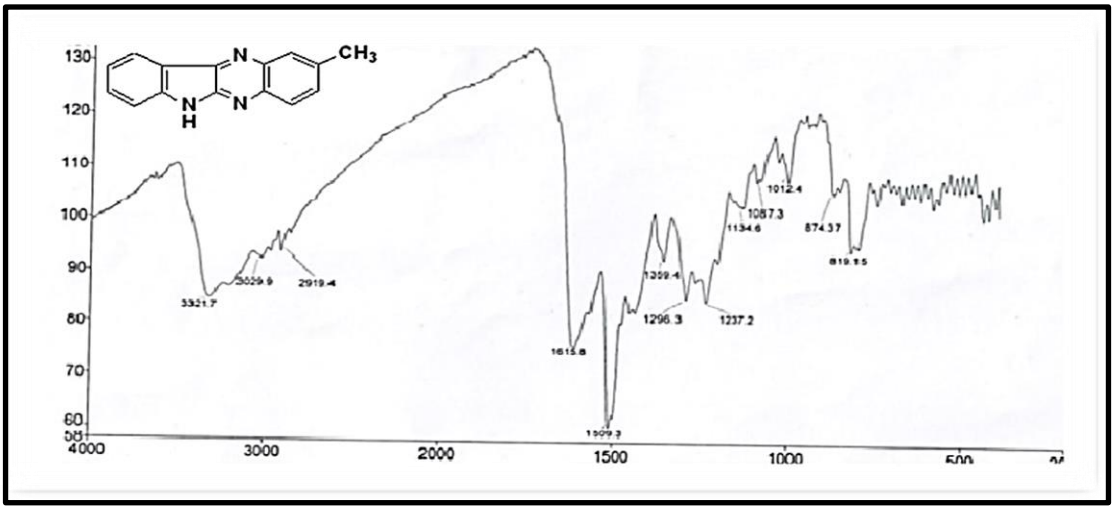


Figure (4.4): FT-IR spectrum in of (O_2) compound.

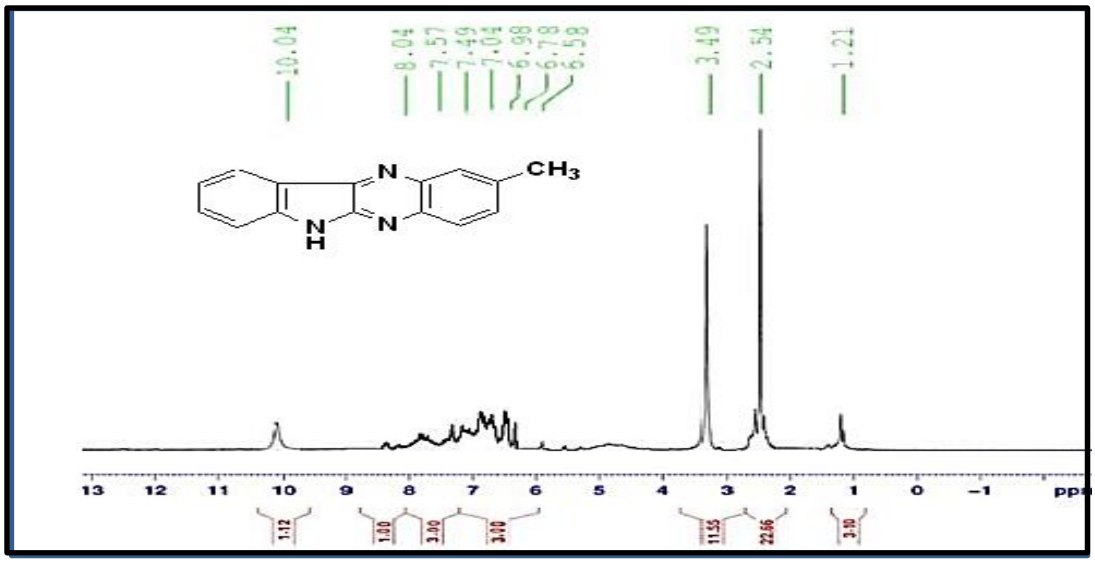


Figure (4. 5): ^{1}H NMR spectrum of compound 2-Methyl-6H-Indolo[2,3-b]quinoxaline(O_2).

4. 3 Synthesis and identification of 2-methyl-indolo[2,3-b] quinoxaline-6-

carbothioic acid phenylamide [O_3]

Compound (O_3) was synthesized through the reaction of 2-methyl-6H-indolo [2,3-b] quinoxaline (O_2) with phenyl isothiocyanate with a structure appears in ***Figure (4.6).***

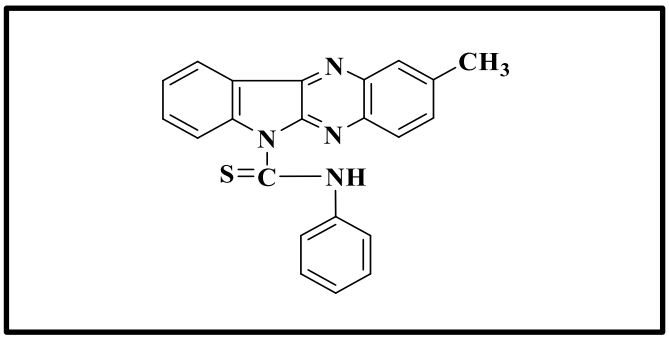
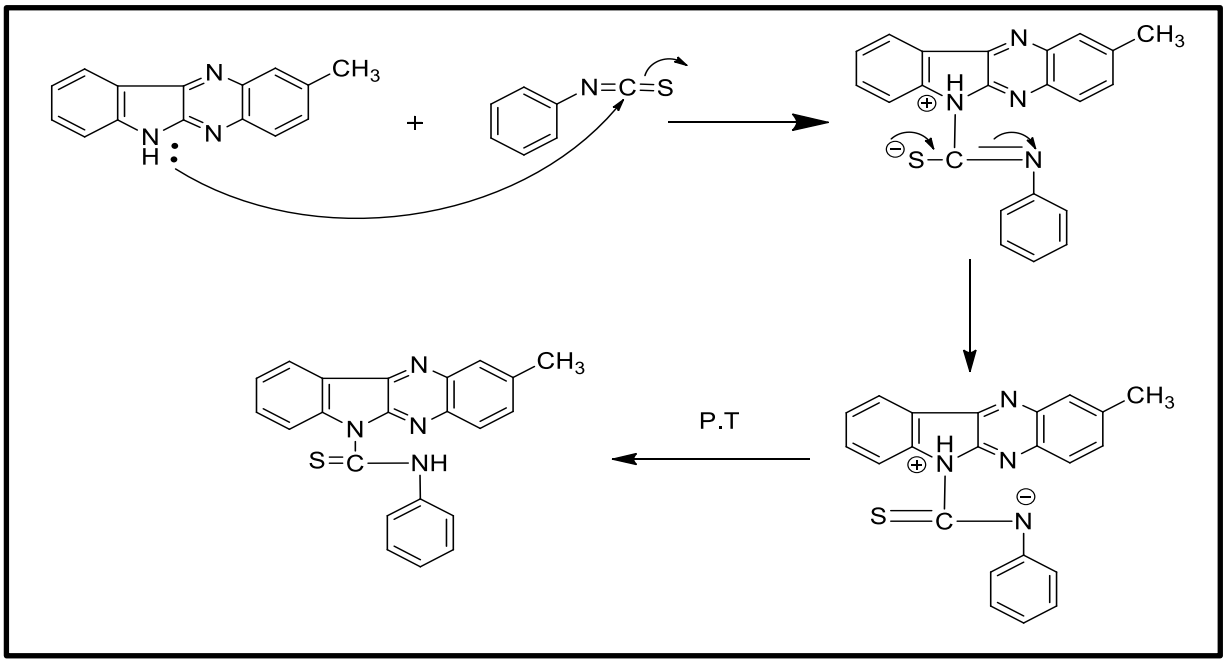


Figure (4. 6): The chemical structure of compound (O_3).

The suggested mechanism for the synthesis of compound O_3 is shown in scheme (4. 2).



Scheme (4. 2): The mechanism of the synthesis of (O_3).

The FT-IR spectrum of compound O_3 ***Figure (4. 7)*** and ***Table (4. 1)*** were

indicated the absorption bands at 3211 cm^{-1} was attributed to stretching vibration of N-H. Absorption band at 3027 cm^{-1} was due to C-H aromatic and absorption band at 2981 cm^{-1} was due to C-H aliphatic .Whereas absorption band at 1655 cm^{-1} was due to C=N stretching vibration. The bands at 1527 cm^{-1} and 1442cm^{-1} are due to the C=C aromatic.

The ^{1}H-NMR spectrum of compound (O_3) ***Figure (4. 8)*** shows the chemical shifts (DMSO-d_6, ppm): 6.60-7.37(m,12H, Ar-H) , 5.37(s, 1H, N-H) , and 1.28 (s,3H, CH_3) .

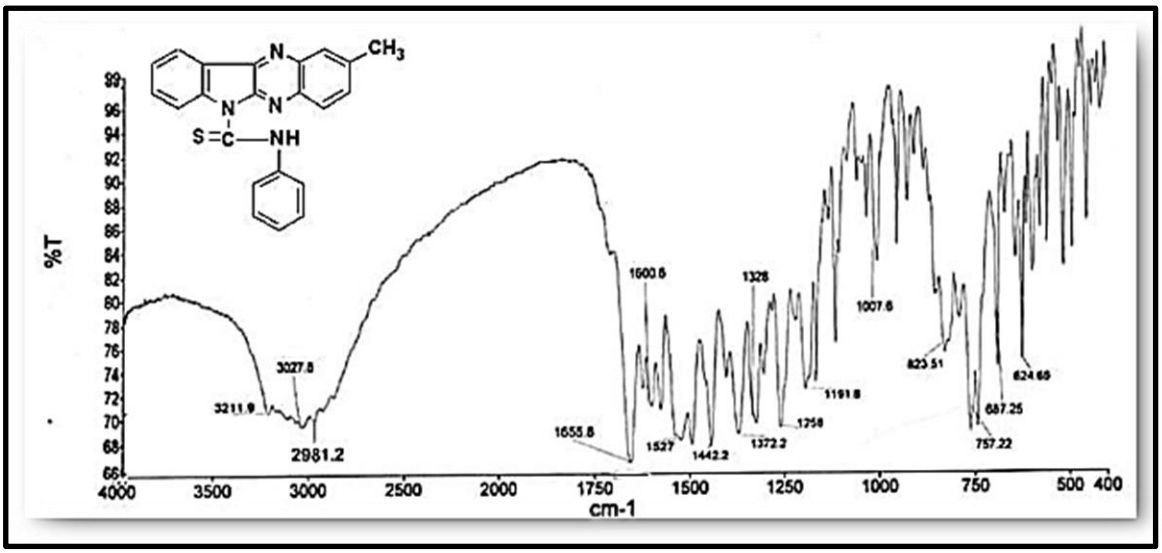


Figure (4. 7): FT-IR spectrum in of (O_3) compound.

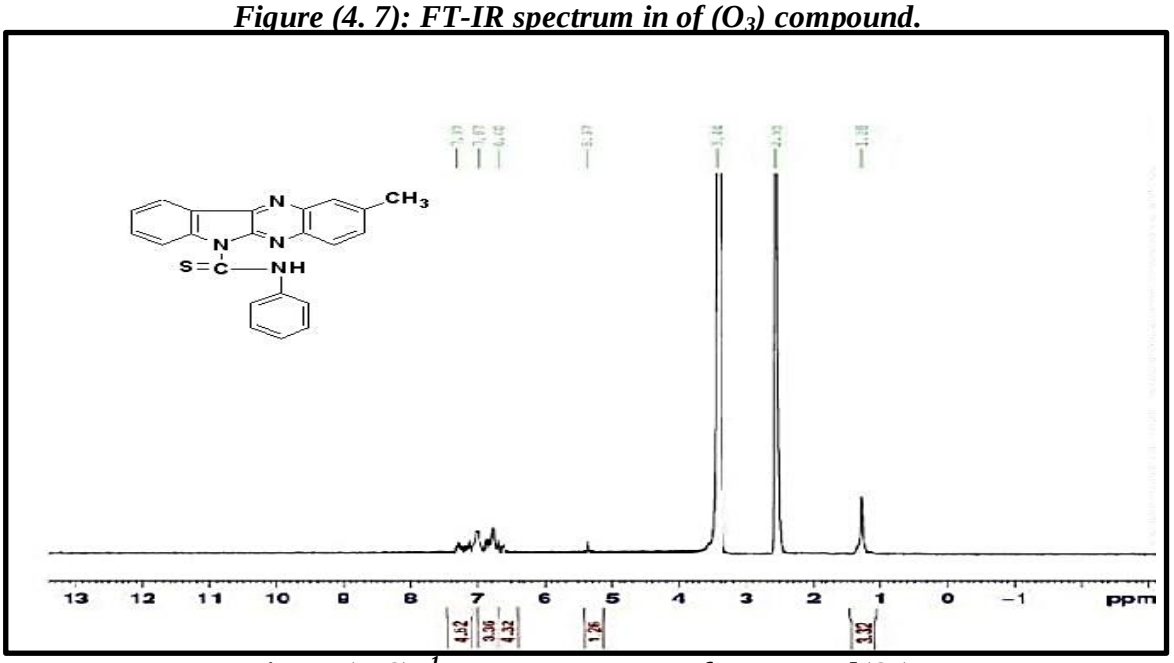


Figure (4. 8): ^{1}H NMR spectrum of compound(O_3).

4. 4 Synthesis and identification of 6-benzyl-2-methyl-6H-indolo[2,3-b] quinoxaline [O_4]

Compound (O_4) was synthesized through the reaction of compound (O_2) with benzyl chloride with a structure appears in ***Figure (4. 9)***.

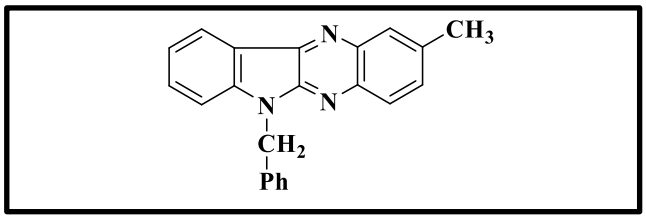


Figure (4. 9): The chemical structure of compound(O_4).

The FT-IR spectrum of compound (O_4) ***Figure (4. 10)*** and ***Table (4. 1)*** shows absorption band at 3027 cm^{-1} was due to C-H aromatic and absorption band at 2919-2847 cm^{-1} was due to C-H aliphatic. Bond absorption at 1607 cm^{-1} was due to (C=N) stretching vibration .The bands at 1510 cm^{-1} and 1495cm^{-1} are due to the C=C aromatic.

The ^{1}H-NMR spectrum of compound (O_4) ***Figure (4. 11)*** shows the chemical shifts (DMSO-d_6, ppm): 6.74-7.88(m,12H, Ar-H),4.38(s,2H,CH_2)and 1.27 (s,3H, CH_3).

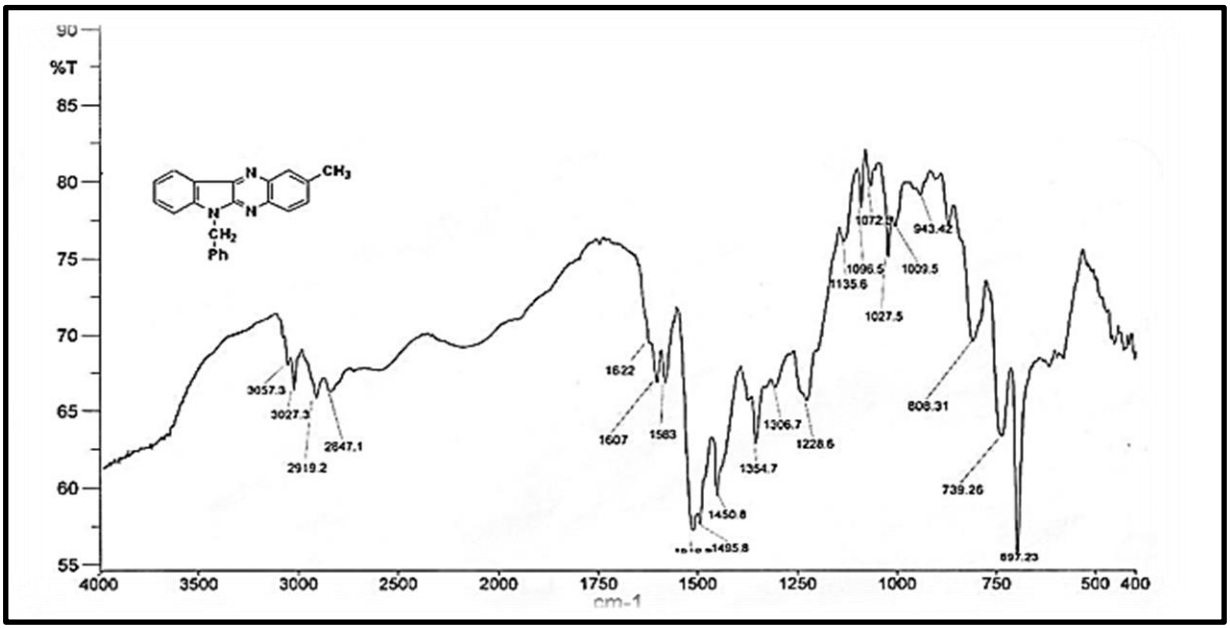


Figure (4. 10): FT-IR spectrum in of (O_4) compound.

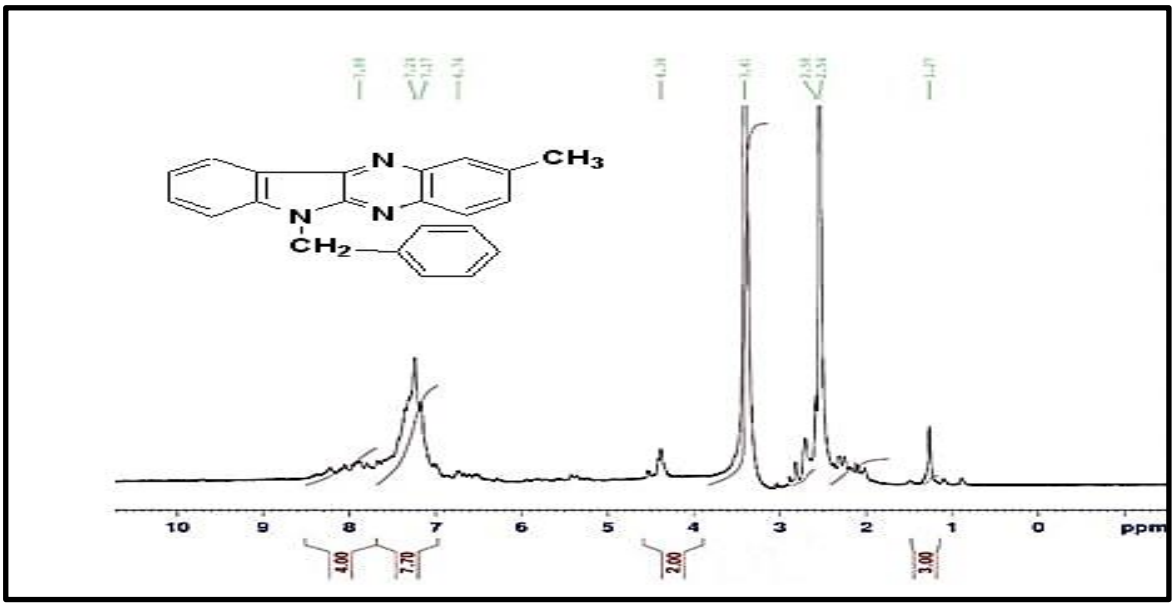


Figure (4. 11): ^{1}H NMR spectrum of 6-benzyl-2-methyl-6H-indolo[2,3-b]quinoxaline (O_4).

4. 5 Synthesis and identification of the compounds $O_5 – O_8$

The compounds (O_5 - O_8) were synthesized by the reaction of the isatin and the corresponding alkyl halide with a structure appears in ***Figure (4. 12).***

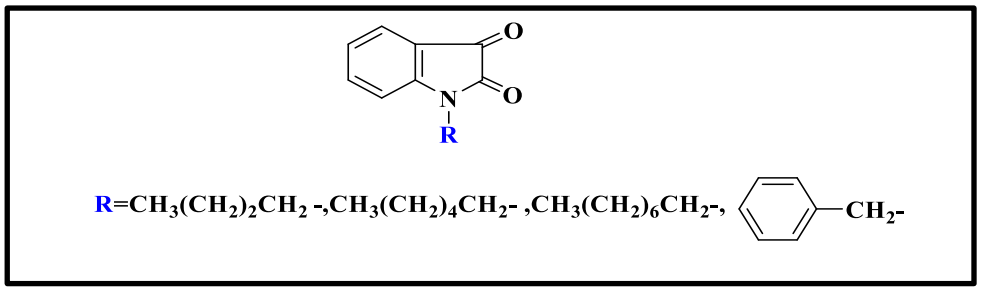


Figure (4.12): The structures of compounds O_5-O_8

The structure of the compounds (O_5-O_8) was characterized by using FT-IR and^{1}H-NMR spectroscopy. FT-IR spectrum of compound O_5 ***Figure (4. 13)*** showed the band at 3081cm^{-1}was assigned to C-H aromatic .Whereas stretching bands of aliphatic C-H appeared at 2961-2871. The bands at 1715 cm^{-1} was referred to stretching vibration of C=O ,The bands at 1519 cm^{-1}

and 1453 cm^{-1} are due to the C=C aromatic .The FT-IR spectral data of compounds O_5-O_8 listed in ***Table(4. 1)***

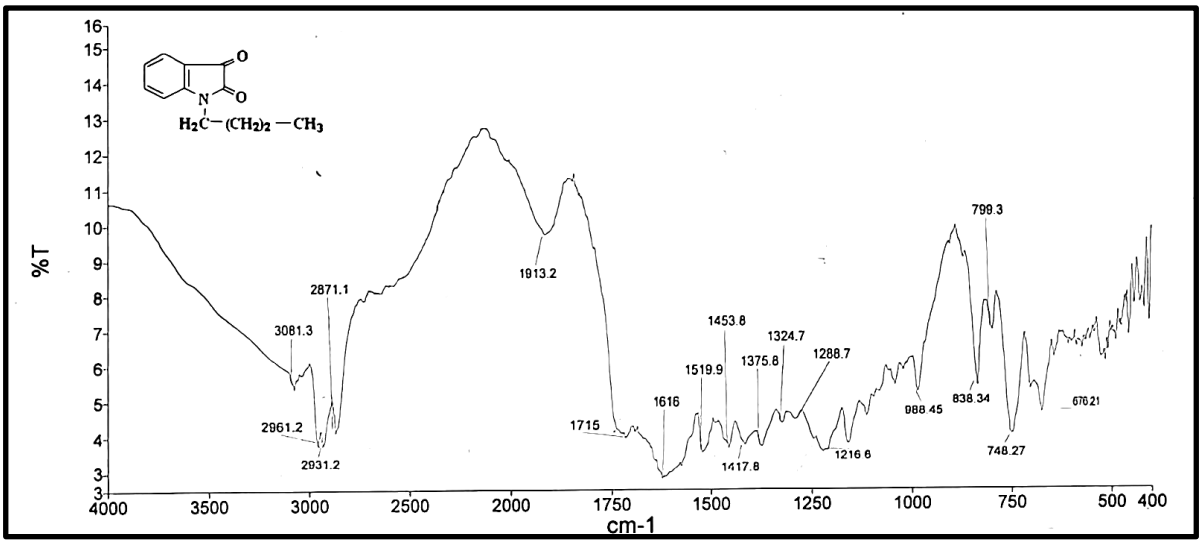


Figure (4. 13): FT-IR spectrum in of (O_5) compound.

^{1}H-NMR spectra of the compound (O_5), ***(Figure 4. 14)*** showed the following chemical shifts (DMSO-d_6, ppm): 6.49-7.59 (m, 4H, Ar-H), 3.15(t,2H,CH_2) , 1.28-1.56(m,4H,2CH_2) and 0.85(t,3H, CH_3)

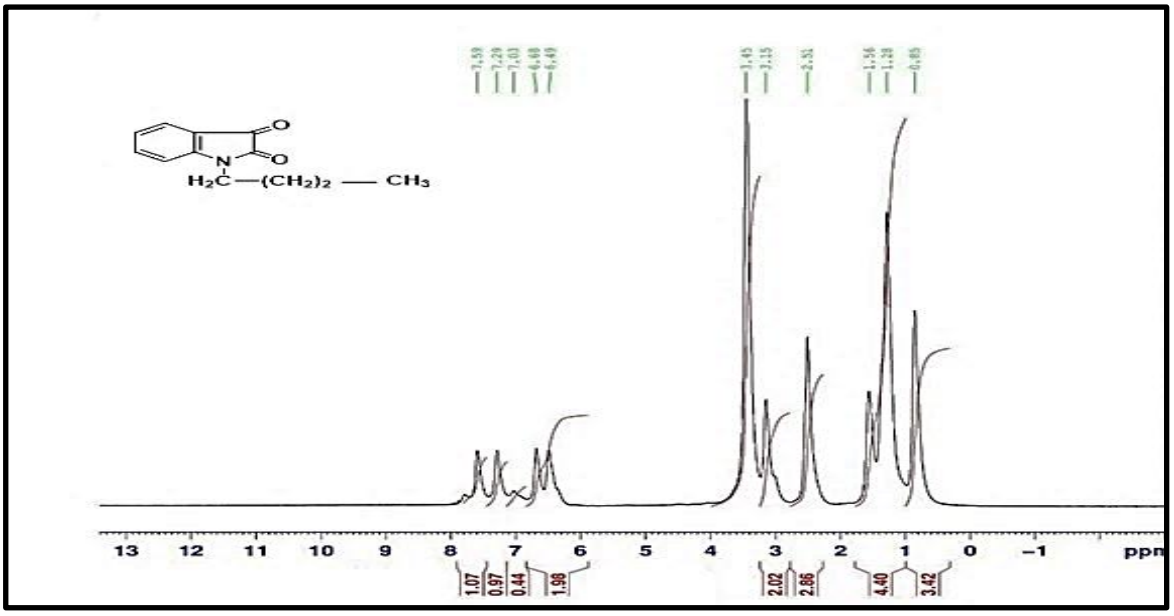


Figure (4. 14): ^{1}H NMR spectrum of compound 1-Butyl-1H-indole-2,3-

dione(O_5).

4. 6 Synthesis and identification of the compounds O_9 - O_{12} .

The compounds (O_9-O_{12}) were prepared by the reaction of theO_5 - O_8 with 3,4-diamino benzoic acid, with a structure appears in ***Figure (4. 15).***

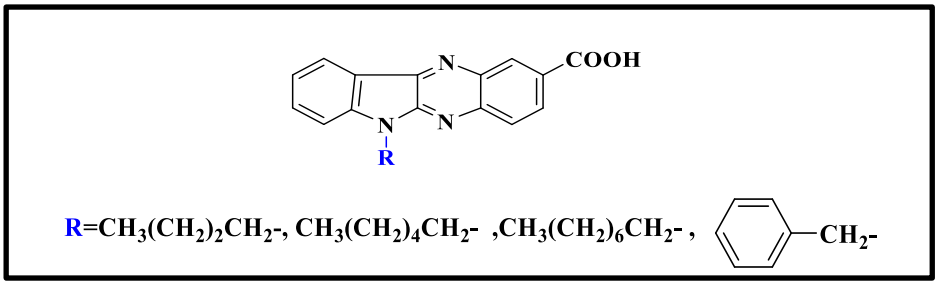


Figure (4. 15): The Chemical structure of compounds (O_9-O_{12}).

The structure of the compounds (O_9 - O_{12}) were characterized by using FT-IR and ^{1}H-NMR spectroscopy. FT-IR spectra of compound O_{10} ***Figure 4.16*** showed the appearance absorption band in range between (3471-٢٥٠٠cm^{-1}) was due to O-H. The band at 3081cm^{-1} was due to C-H aromatic. Whereas stretching bands of aliphatic CH appeared at (2958,2856). The bands at 1779 cm^{-1}due to the stretching vibration of C=O (carboxylic acid). Band absorption at 1636 cm^{-1} was assigned to stretching vibration C=N. The FT-IR spectral data of compounds O_9 - O_{12} are listed in ***Table(4. 1).***

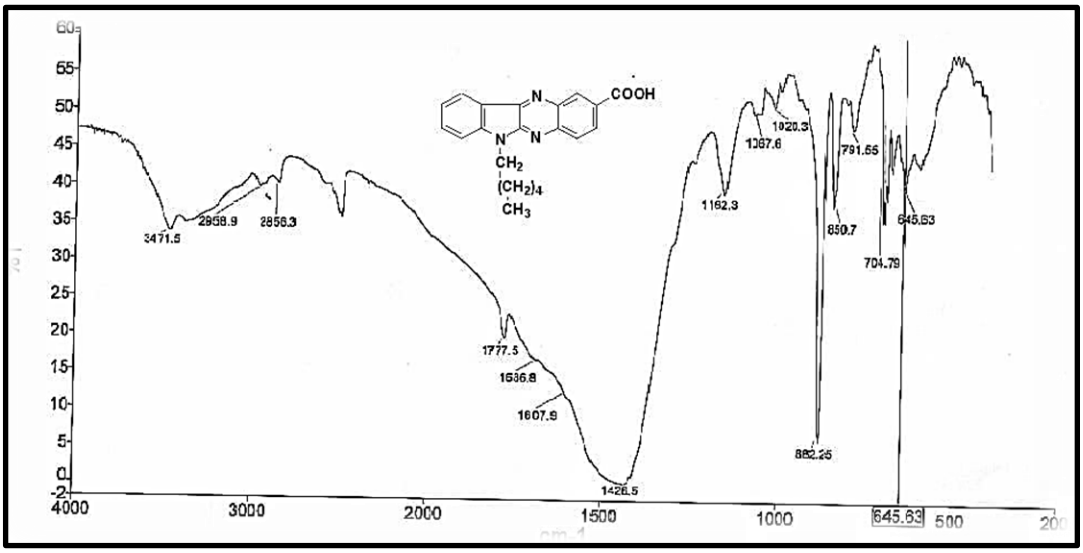


Figure (4. 16): FT-IR spectrum in of (O_{10}) compound.

^{1}H-NMR spectrum of compound (O_{10}) ***(Figure 4.17)***showed the following chemical shifts (DMSO-d_6, ppm): 9.19 (s,1H, COOH), 6.42-7.18 (m,7 H, Ar-H), 4.55 (t, 2H, N-CH_2) , 2.02 (m,8H,4CH_2), and 1.29 (t,3H, CH_3).

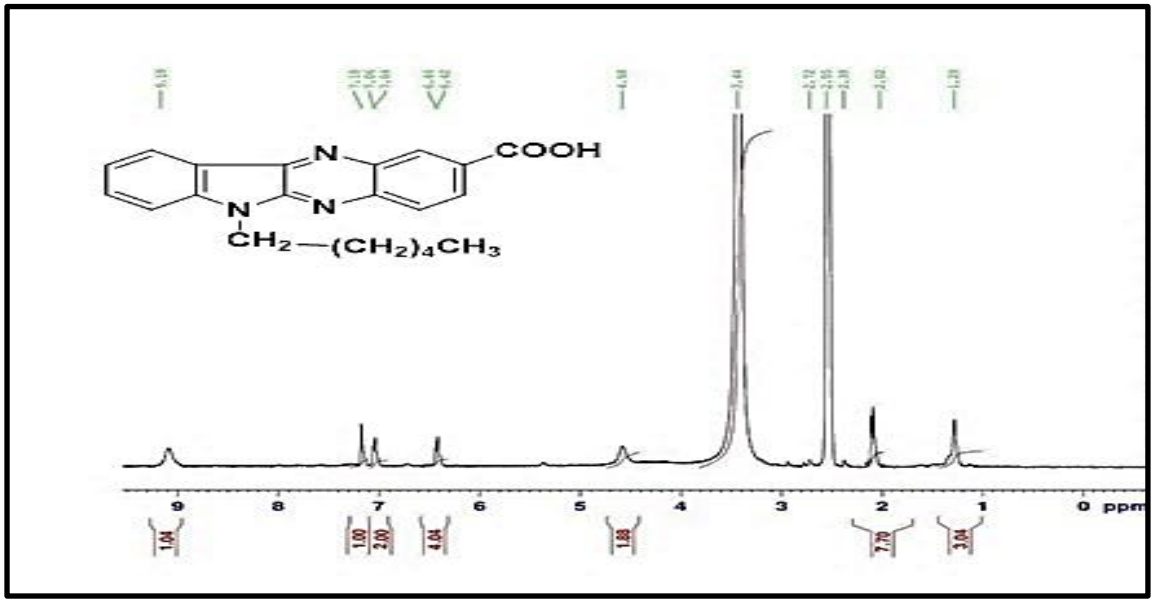


Figure (4. 17): ^{1}H NMR spectrum of compound 6-Hexyl-6H-indolo[2,3-b] quionxaline-2-Carboxylic acid (O_{10}).

4. 7 Synthesis and identification of Schiff base 2-(3,4 di aminophenyl (phenyl) methylene-amino phenol [O_{13}]

compound (O_{13}) was synthesized through the reaction of o-amino phenol with 3,4-diamino benzophenon, with a structure appears in ***Figure (4. 18).***

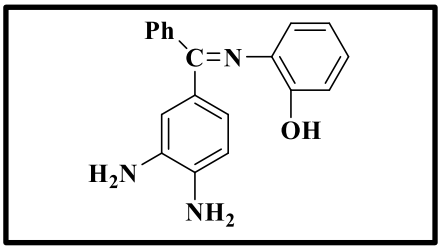


Figure (4. 18): The chemical structures of compound (O_{13}).

The FT-IR spectrum of compound (O_{13}) ***Figure (4. 19)*** and ***Table (4. 1)*** shows absorption bands at 3373cm^{-1} was attributed to bonding of OH group. Absorption band at 3302cm^{-1}and 3291 was attributed to symmetric and asymmetric stretching vibration of NH_2 group. Absorption band at 3065cm^{-1}due to C-H aromatic. Band absorption at 1623 cm^{-1} was due to C=N stretching vibration [٩3].

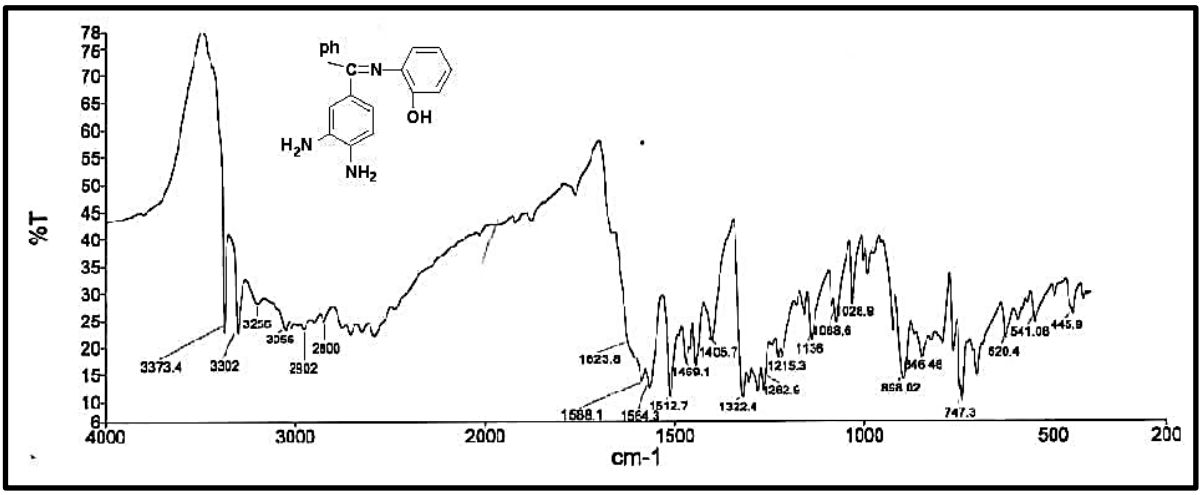


Figure (4. 19): FT-IR spectrum in of (O_{13}) compound.

4. 8 *Synthesis and identification of Z-2(1-6H-Iindol[2,3-b]quinoxaline-2yl) ethylidene amino phenol [O_{14}].*

Compound (O_{14}) was synthesized through the reaction of isatin with 2-(3,4-di

amino phenyl)(phenyl)methylene-amino phenol [O_{13}] , with a structure appears in ***Figure (4. 20).***

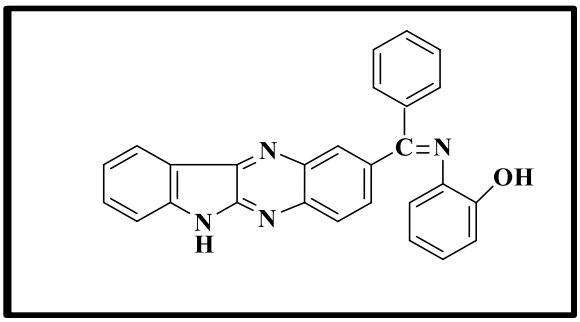


Figure (4. 20): The chemical structures of compound (O_{14}).

The FT-IR spectrum of compound (O_{14}) ***Figure (4. 21)*** indicated the disappearance stretching frequency of $NH_2$and appearance absorption bands at 3352 $cm^{-1}$was attributed to N-H group. Absorption band at (3477)was due to bonding of OH group. Absorption band at3026cm^{-1}due to C-H aromatic. Bond absorption at 1641 cm^{-1} was due to C=N stretching vibration. as listed in ***Table (4. 1)***.

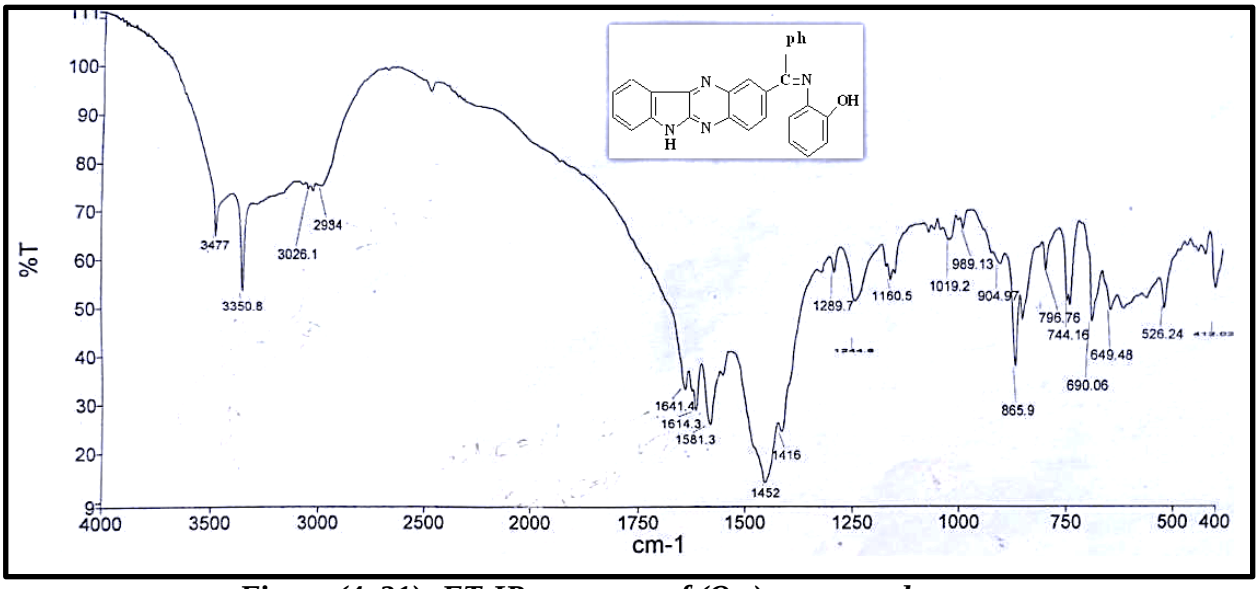


Figure (4. 21): FT-IR spectrum of (O_{14}) compound.

The 1H-NMR spectra of the compound (O_{14}), ***Figure (4. 22)*** shows the following chemical shifts.(DMSO-d_6, ppm): 12.32 (s,1H,NH), 7.11-8.12 (m, 16H, Ar-H) and 4.35 (s,1H,OH),

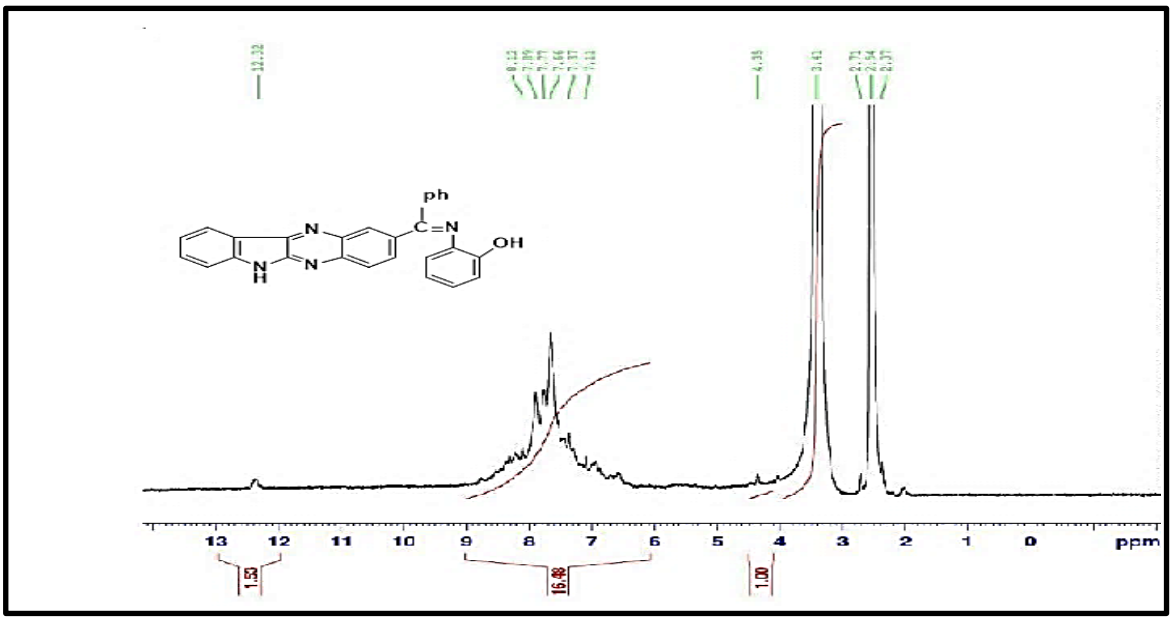


***Figure (4. 22): ^{1}H NMR spectrum of compoundd*-2-((1-(6H-indolo[2,3-b]quinoxalin-2-yl)ethylidene) amino) phenol (O_{14}).**

4. 9 Synthesis of 3-(2-Amino-5-B-Benzoyl-Phenylimino)-1,3di Hydro-Indol-2-One [O_{15}] and its complexes .

Compound (O_{15}) was synthesized through the reaction of isatin with 3,4-diamino benzophenon with water and sodium bicarbonate, with a structure appears in ***Figure (4. 23).***

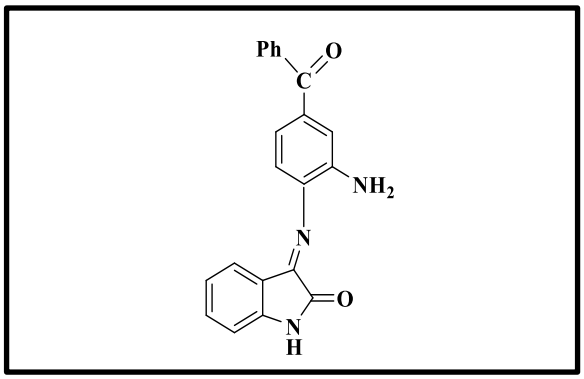
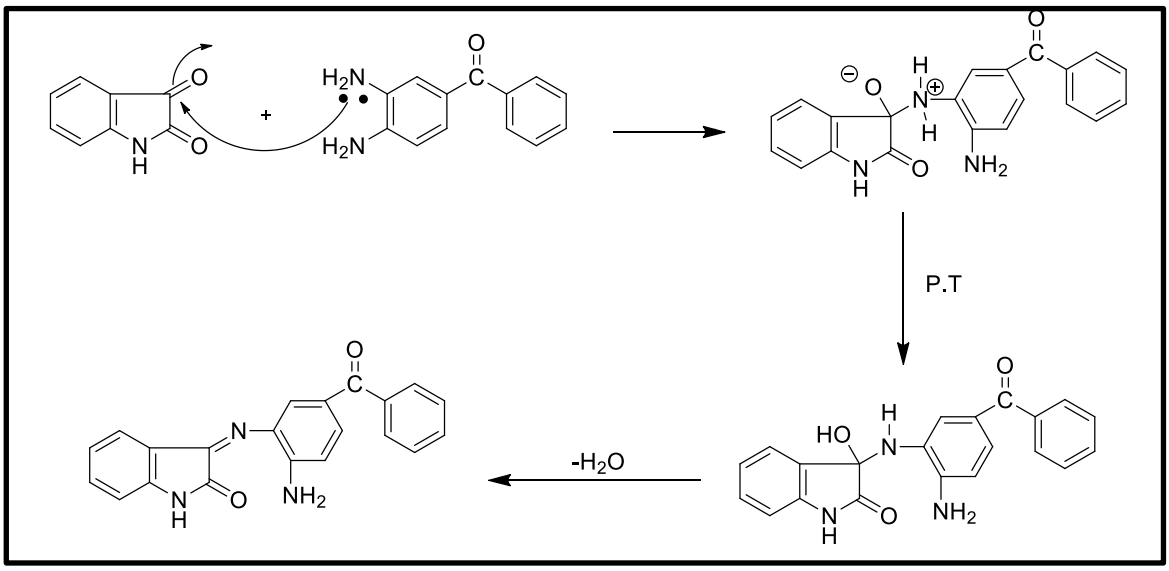


Figure (4. 23): The chemical structure of compound (O_{15}).

The suggested mechanism for the synthesis of compound O_{15} as appears in Scheme (4. 3).



Scheme (4. 3): The mechanism for the synthesis of (O_{15}).

Then, this compound used as ligand to syntheize complexes from reaction of the ligand with metal chloride such as cobalt chloride hexahydrate, nickel chloride hexahydrate, copper chloride dihydrate, and anhydrous zinc chloride, with a structure appears in ***Figure (4. 24).***

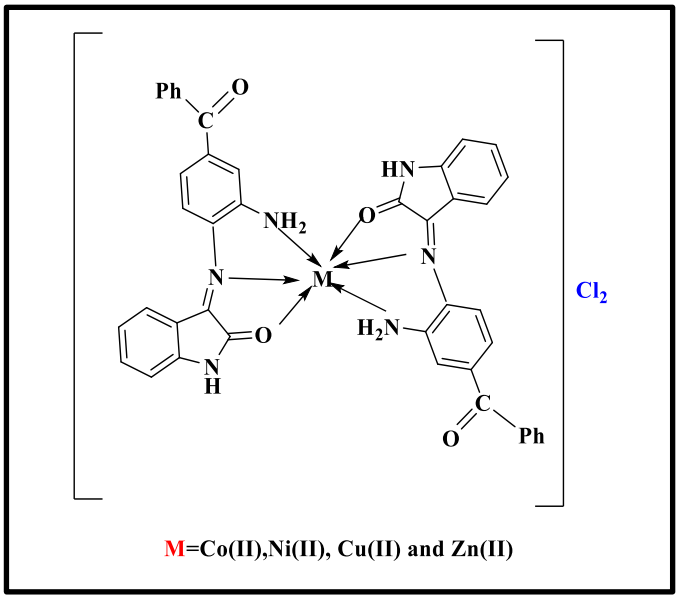


Figure (4. 24): The chemical structure of $[M(C_{21}H_{15}N_3O_2)_2]Cl_2$ complexes.

4. 10 Identification of 3-(2-Amino-5-B-Benzoyl-Phenylimino)-1,3diHydro-Indol-2-One [O_{15}] and its complexes .

The ^{1}H-NMR spectra of the compound (O_{15}), ***Figure (4. 25)*** shows the following chemical shifts (DMSO-d_6, ppm): 6.56-7.59 (m, 12H, Ar-H), 5.52(s,1H, N-H) and 4.74 (s, 2H,NH_2) .

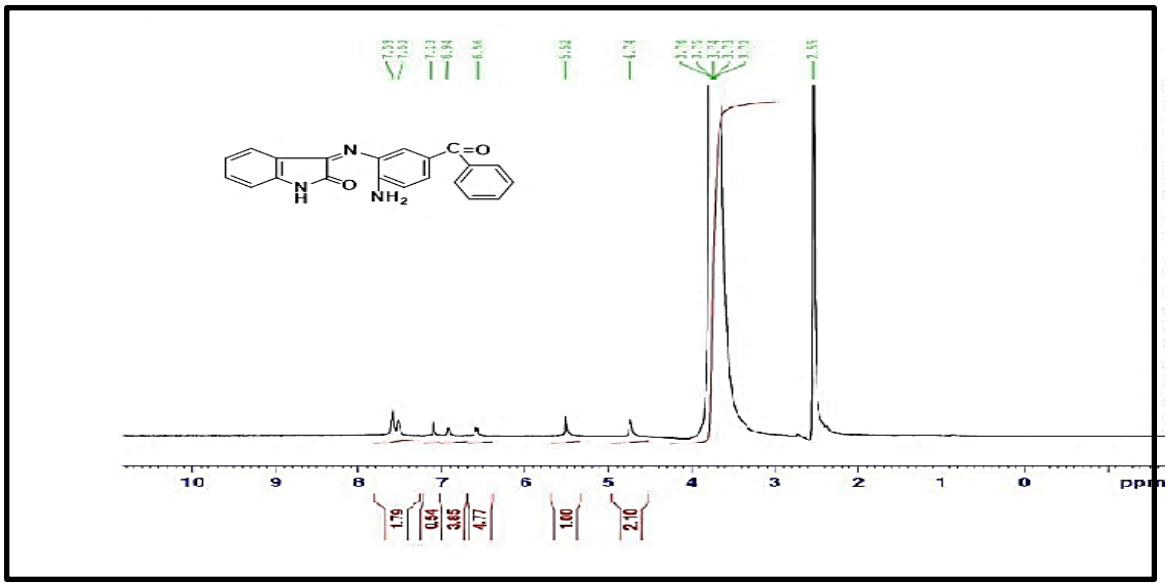


Figure (4. 25): ^{1}H NMR spectrum of compound3-(2-amino-5-b-benzoyl phenylimino)-1,3dihydro-indol-2-one (O_{15}).

4. 10. 1 FT-IR of Ligand (O_{15}) *and its Complexes.*

The FT-IR spectra of compound (O_{15}) ***Figure (4. 26)*** show absorption bands at 3374 cm^{-1} and 3188 cm^{-1} assigned to the stretching vibration of N –H bond for NH_2 group [94] and NH indole ring respectively. The sharp absorption band at 1662 cm^{-1} which was attributed to stretching vibration of carbonyl group. Also appearance absorption band at 1599 cm^{-1} which attributed to azomethine group CH=N [95], All these absorption bands an evidence to the formation of this compound (O_{15}). ***Table (4. 2)***explain the FT-IR spectra data of compound (O_{15}).

The FT-IR spectrum of cobalt, nickel, copper, and zinc complexes ***Figures (4. 27.) – (4. 30)*** exhibited occurrence shifting in stretching vibration of the

amine NH_2, carbonyl C=O and azomethine C=N groups values with respect to free ligand, was good evidence of the coordination through the nitrogen atoms of an azomethine group, nitrogen atoms of amine group and oxygen atoms of carbonyl groups of (O_{15})compound to the metal ion, in the other hand appeared new bands of weak intensity at (508, 512, 528, and 529) cm^{-1}

which indicates stretching vibration of M-N, and at (435, 422, 432, and 418) cm^{-1}which refers to stretching vibration of M-O for Co^{II}, Ni^{II}, Cu^{II}, and Zn^{II} complexes respectively [96 and 97]. The FT-IR spectra data of ligand and its complexes were listed in ***Table (4. 2)***.

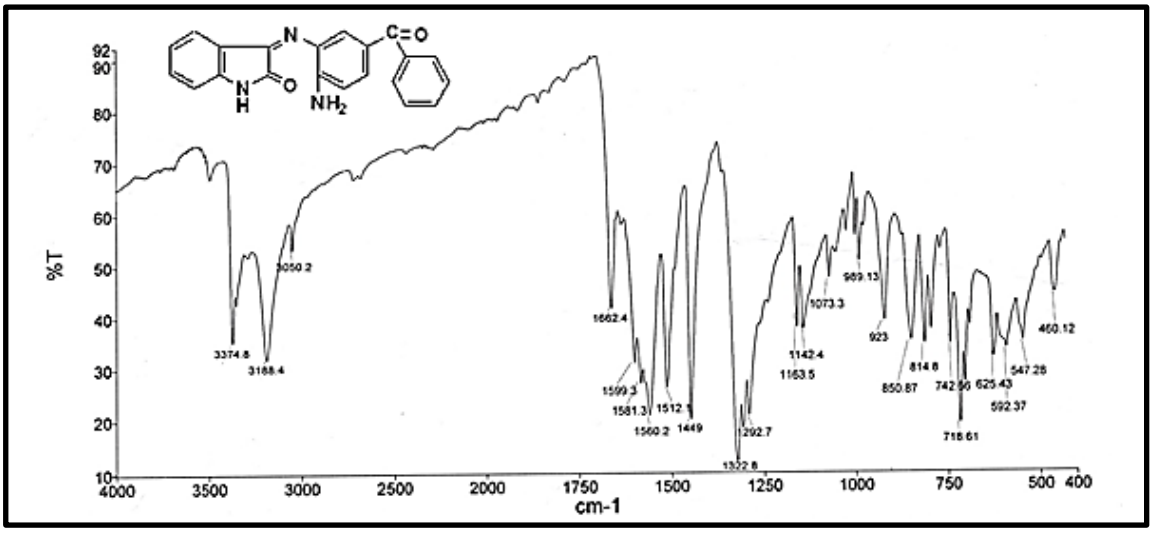


Figure (4. 26): FT-IR spectrum of (O_{15}) compound.

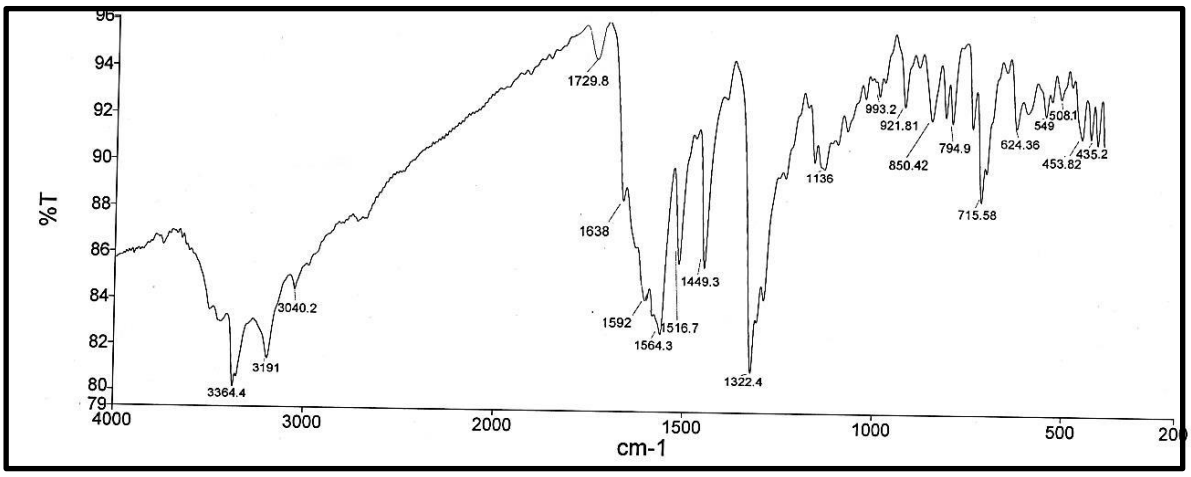


Figure (4.27): FT-IR spectrum of $[Co(C_{21}H_{15}N_3O_2)_2]Cl_2$.

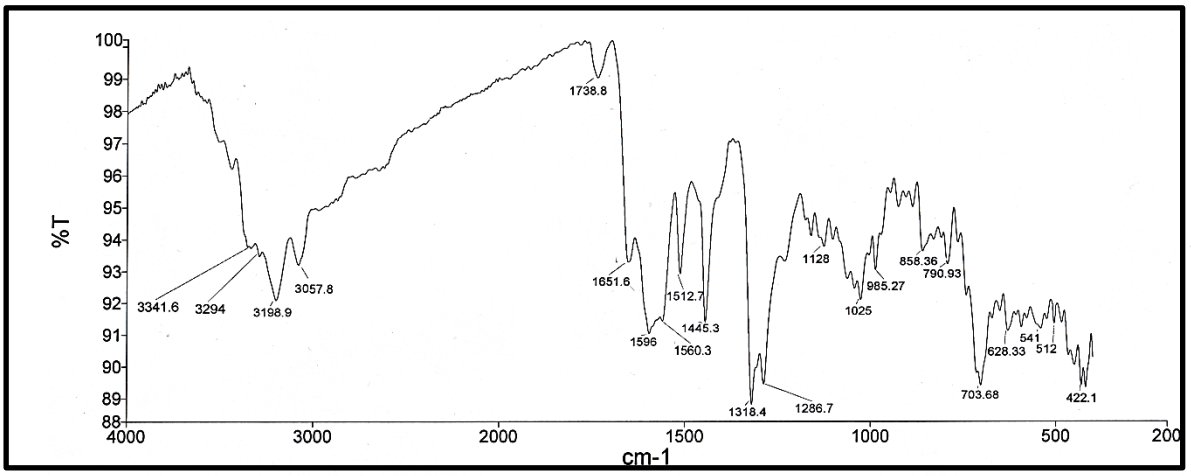


Figure (4.28): FT-IR spectrum of $[Ni(C_{21}H_{15}N_3O_2)_2]Cl_2$.

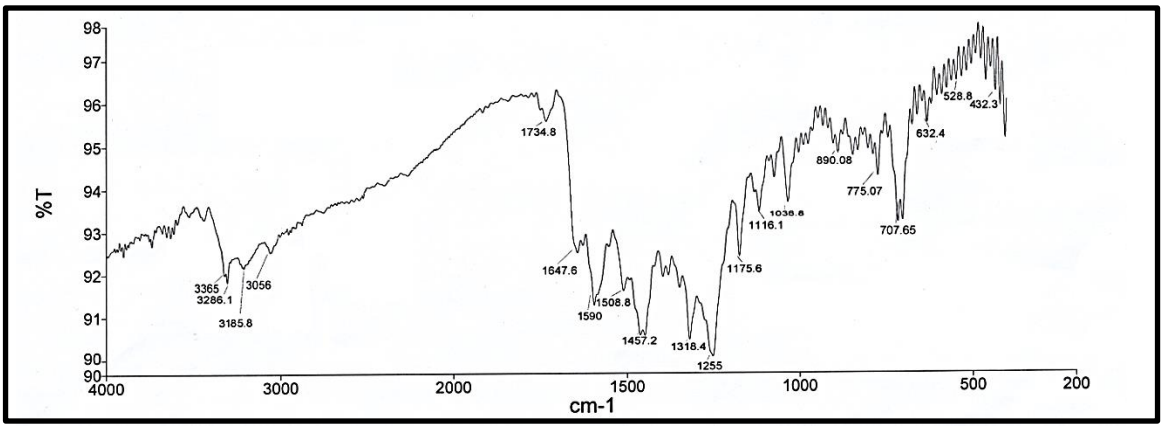


Figure (4.29): FT-IR spectrum of $[Cu(C_{21}H_{15}N_3O_2)_2]Cl_2$

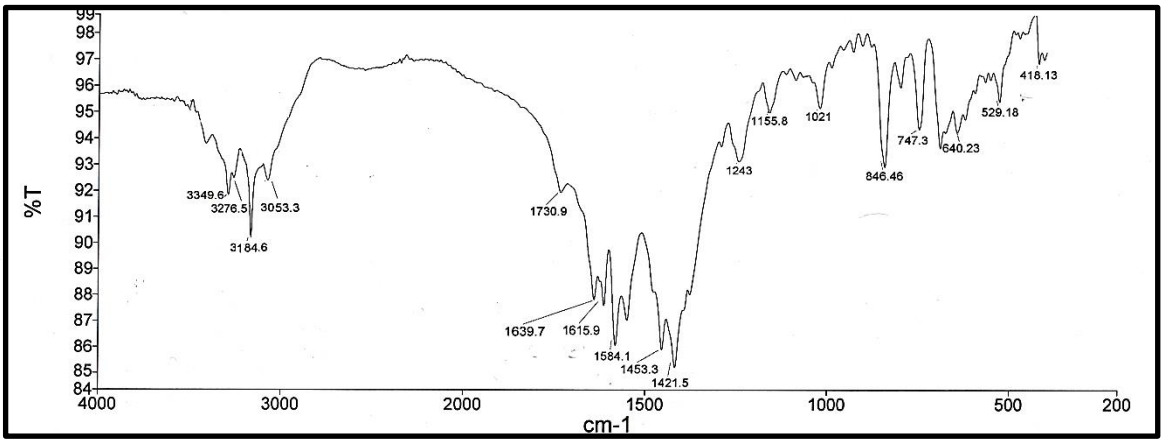


Figure (4.30): FT-IR spectrum of $[Zn(C_{21}H_{15}N_3O_2)_2]Cl_2$.

4. 10. 2 The electronic spectrum and magnetic susceptibility of complexes.

The electronic spectrum of ligand $C_{21}H_{15}N_3O_2$ in (UV-Vis) region in dimethyl sulfoxide solvent exhibited three bands as shown in ***Figure (4. 31) and Table (4.3)***. The first and second absorption bands attributed to $\pi \rightarrow \pi^*$ electronic transition which appeared at (260.8 nm, 38343 cm^{-1} and 312.6 nm, 31989 cm^{-1}), and third absorption band at (370.2 nm, 27012 cm^{-1}) assigned to $n \rightarrow \pi^*$ transition[98 and 99].

The electronic spectrum of$[Co(C_{21}H_{15}N_3O_2)_2]Cl_2$ complex ***Figure (4.32)*** exhibited a high intensity absorption band at (285.4, 303.6 and 366.8) nm, (35038, 32938 and 27262) cm^{-1}which were assigned to intra ligand transitions. In addition that the complex was showed two low intensity bands at (502 and 763.6) nm(19920 and 13095) cm^{-1} which were assigned to d-d transitions $^4T_1 g_{(F)} \rightarrow {}^4T_1 g_{(P)}$ and $^4T_1 g_{(F)} \rightarrow {}^4A_2 g_{(F)}$ respectively [100 and 101]

The observed magnetic moment value for this complex was (μ_{eff}= 4.06 B.M),indicating paramagnetic nature and was characteristic of high spin octrahedral cobalt ion species d^7.

The electronic spectrum of $[Ni(C_{21}H_{15}N_3O_2)_2]Cl_2$ complex ***Figure (3. 33)*** was appeared three high intensity absorption bands at (271.8, 310.6 and 372)nm (36791,32195 and 26881) cm^{-1} were refers to intra ligand transitions, also the low

intensity bands were showed at (475.6 and 733.6) nm (21026 and 13631) cm^{-1} assigned to d-d transitions $^3A_2g_{(F)} \rightarrow {}^3T_1g_{(P)}$ and $^3A_2g_{(F)} \rightarrow {}^3T_1g_{(F)}$ respectively [100 **and** 101]. The observed magnetic moment value for this complex was (μ_{eff}= 2.89 B.M), indicating paramagnetic nature and octahedral geometry.

In the present work, the electronic spectrum of $[Cu(C_{21}H_{15}N_3O_2)_2]Cl_2$ complex ***Figure (3. 34)*** gave two bands at (257 and 351) nm (38789 and 28473) cm^{-1}were assigned to intra ligand transitions. As well as the complex shows one broad band at (543) nm (18416) cm^{-1} attributed to electronic transition $^2Eg_{(D)} \rightarrow {}^2T_2g_{(D)}$, which is in conformity with the octahedral configuration around the copper ion[99 and 100]. The value of (μ_{eff}) that measured for this complex is (1.74 B.M), indicating paramagnetic nature and octahedral geometry.

The ultra violet-visible spectra of $[Zn(C_{21}H_{15}N_3O_2)_2]Cl_2$ complex in ***Figure (4. 35)*** show no absorption band at (400-900) nm, That is indicates no (d-d) electronic transition happened d^{10} system in the visible region and relative change in the bands position compared to that of the free ligand evidence for the coordination between Zn and ligand. The prepared complex was diamagnetic which was expected for d^{10} ion [102 and 103].

Table (4. 3) explain the magnetic susceptibility and Uv-Vis bands of the complexes with their assigned transitions.

4. 10. 3 Molar conductance of complexes $[M(C_{21}H_{15}N_3O_2)_2]Cl_2$

The molar conductance of all synthesized complexes were measured in DMSO at room temperature. The values obtained in the range (70-80) .

[$Cm^2 .ohm^{-1} .mol^{-1}$] ,this indicates that the synthesized complexes are ionic with (1: 2) ratio (complex ion **:** chloride ions) [104].This means that the two chloride

ions in the complexes were lying outside the coordination sphere. The molar conductance values of all synthesized complexes were listed in ***Table(4. 3)***.

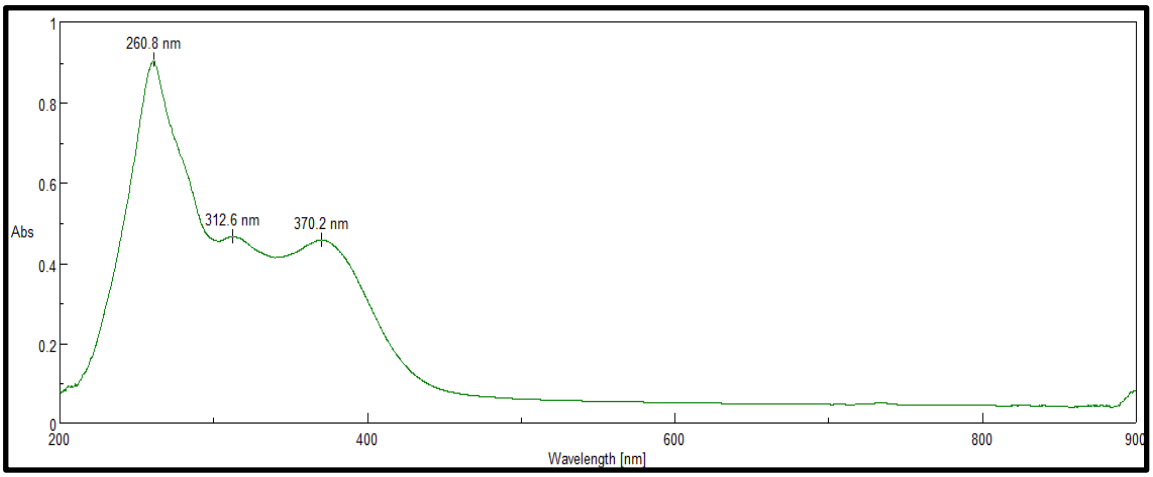


Figure (4. 31): Electronic Spectrum of ligand (O_{15}).

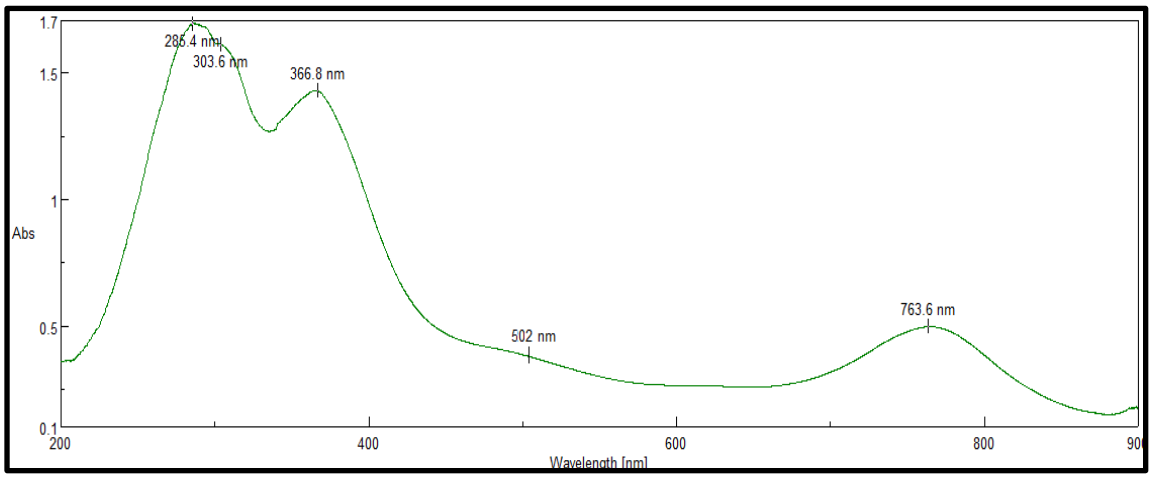


Figure (4. 32): Electronic Spectrum of $[Co(C_{21}H_{15}N_3O_2)_2]Cl_2$.

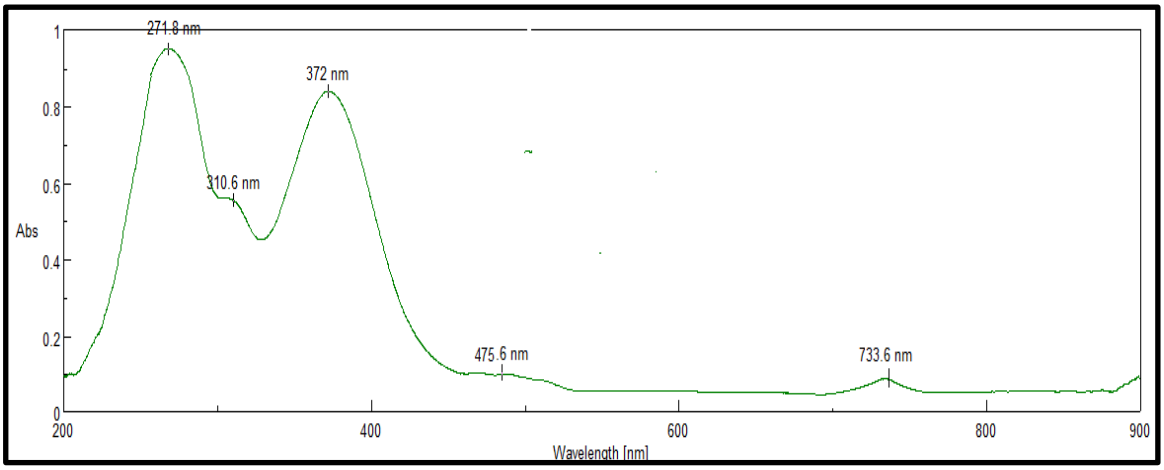


Figure (4. 33): Electronic Spectrum of $[Ni(C_{21}H_{15}N_3O_2)_2]Cl_2$.

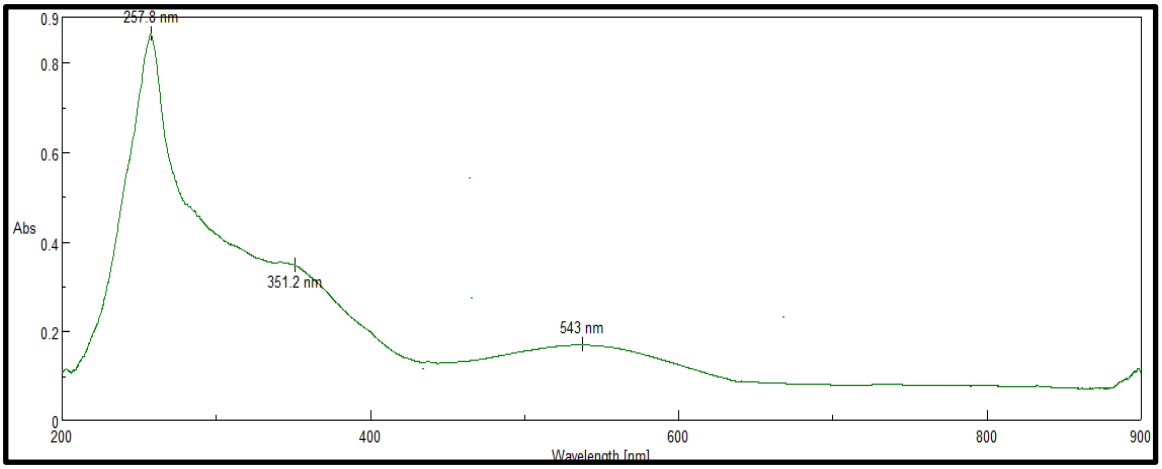


Figure (4.34): Electronic Spectrum of $[Cu(C_{21}H_{15}N_3O_2)_2]Cl_2$.

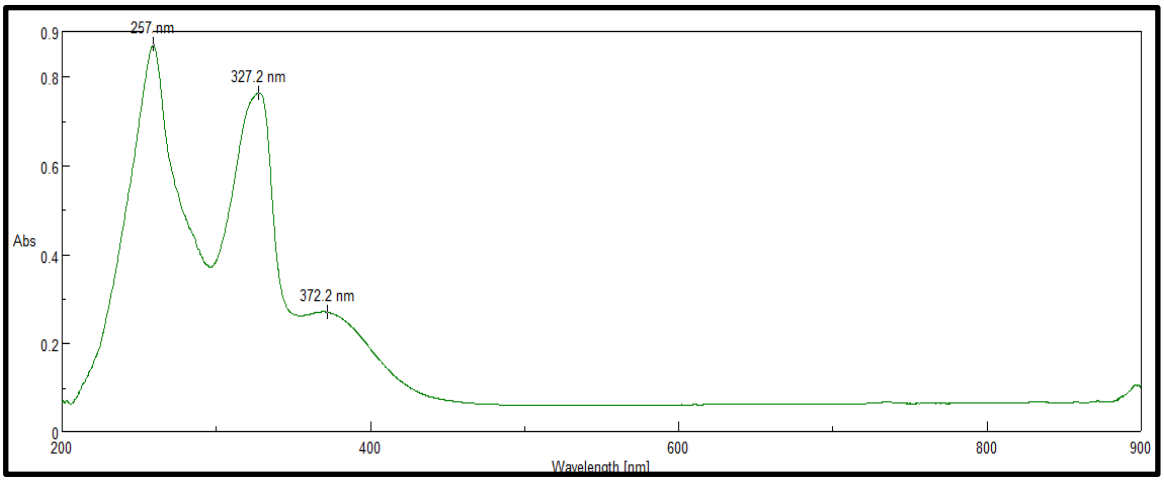


Figure (4. 35): Electronic Spectrum of $[Zn(C_{21}H_{15}N_3O_2)_2]Cl_2$.

4. 10. 4 Elemental analysis, atomic absorption and physical properties of the complexes.

Elemental analysis (C.H.N.) and metal percentage of prepared complexes showed the calculated and found percentage values of carbon, hydrogen, nitrogen, and metal were in good agreement and were consistent with the structure of the synthesized compounds. The analysis data and physical properties for each complexes were given in ***Table (4. 5)***.

Table (4. 1):The most diagnostic FT-IR bands of the compounds (O_1- O_{14}) in (cm^{-1}).

Comp.No.	ν OH	ν C-H aromatic	ν C-H aliphatic	ν C=O	ν C=N	ν C=C aromatic	Others
O_1	3365	3041	----	1667	1564	1401	
O_2	----	302٩	2919	----	161٥	1513-1434	ν (NH) 332١
O_3	----	3027	2981	----	1655	1527-1442	ν (NH) 3211 ν (S=C) 1191
O_4	----	3027	2919,2847	----	1607	1510-1495	
O_5	----	3081	2961,2871	1715	----	1519,1453	
O_6	----	3077	2927,2864	1714	----	1521,1458	
O_7	----	3٠٧٧	29٢٧-28٥٦	17 ٤٢	----	15٢١-146٦	
O_8	----	30٤٨	2921	1699	----	1504-1405	
O_9	3471	3068	2972-28٦٨	1695	1632	1596,1452	
O_{10}	3471	3081	2958-2856	1779	1636	1426	
O_{11}	3341	3055	2929	1734	1667	1457	
O_{12}	3435	3152	2982	1706	1643	1552,1414	
O_{13}	3373	3056	2902-2800	----	1623	1588,1564	ν (NH_2) 3302, 3250
O_{14}	3477	3026	2934	----	16٤١	1581,1452	ν(NH) 33٥٠

Table (4. 2): Absorption bands of stretching vibration for the ligand (O_{15}) and its metal complexes in (cm^{-1}).

Compound	NH_2	N-H	C-H aromatic	C=O	C=O indole	C=N	M-N	M-O
$C_{21}H_{15}N_3O_2$	3374	3188	3050	-----	1662	1599	-----	-----
$[Co(C_{21}H_{15}N_3O_2)_2]Cl_2$	3364	3191	3040	1729	1638	1592	508	435
$[Ni(C_{21}H_{15}N_3O_2)_2]Cl_2$	3341 3294	3198	3057	1738	1651	1596	512	422
$[Cu(C_{21}H_{15}N_3O_2)_2]Cl_2$	3365 3286	3185	3056	1734	1647	1590	528	432
$[Zn(C_{21}H_{15}N_3O_2)_2]Cl_2$	3349 3276	3184	3053	1730	1639	1615	529	418

Table(4. 3):Electronic spectra ,conductance in DMSO solvent and magnetic moment(B.M) forlig and O_{15} and its metal complexes.

Compounds	Absorption Bands **nm**	Absorption Bands **Cm^{-1}**	Assignments	M_{eff} *B.M*	Mol. Cond. $Cm^2.ohm^{-1}.mol^{-1}$	Suggested Geometry
$C_{21}H_{15}N_3O_2$	**260.8** **312.6** **370.2**	**38343** **31989** **27012**	**$\pi \rightarrow \pi^*$** **$\pi \rightarrow \pi^*$** **$n \rightarrow \pi^*$**	-------	--------	--------
$[Co\ (C_{21}H_{15}N_3O_2)_2]Cl_2$	**285.4** **303.6** **366.8** **502** **763.6**	**35038** **32938** **27262** **19920** **13095**	Intra ligand Intra ligand Intra ligand $^{.4}T_1g._{(F)} \rightarrow {}^{.4}T_1g_{(p)}$ $^{.4}T_1g._{(F)} \rightarrow {}^{4}A_2g_{(F)}$	**4.06**	**80**	**Oh**
$[Ni(C_{21}H_{15}N_3O_2)_2]Cl_2$	**271.8** **310.6** **372** **475.6** **733.6**	**36791** **32195** **26881** **21026** **13631**	Intra ligand Intra ligand Intra ligand $^{.3}A_2g_{(F)} \rightarrow {}^{.3}T_1g_{(p)}$ $^{.3}A_2g_{(F)} \rightarrow {}^{3}T_1g_{(F')}$	**2.89**	**70**	**Oh**
$[Cu(C_{21}H_{15}N_3O_2)_2]Cl_2$	**257** **351** **543**	**38789** **28473** **18416**	Intra ligand Intra ligand Intra ligand $^{2}Eg_{(D)} \rightarrow {}^{2}T_2g_{(D)}$	**1.74**	**78**	**Oh**
$[Zn(C_{21}H_{15}N_3O_2)_2]Cl_2$	**257** **327.2** **372.2**	**38910** **30562** **26867**	Intra ligand	**0.00**	**79**	**Oh**

Table (4. 4): Physical Properties of –new compounds O_1 toO_{15}

Comp. Symbol	*Molecular Formula*	*M. Wt (g.mol^{-1})*	*Color*	*M.P. ° C*	*Yield %*
O_1	$C_{15}H_9N_3O_2$	*263.3*	Brown	167	*93*
O_2	$C_{15}H_{11}N_3$	*233.3*	Brown-dark	79	*90*
O_3	$C_{22}H_{16}N_4S$	*268.5*	light brown	151	*81*
O_4	$C_{22}H_{17}N_3$	*323.4*	brown –black	180	*90*
O_5	$C_{12}H_{13}NO_2$	*203.2*	Orange	38	*62*
O_6	$C_{14}H_{17}NO_2$	*231.3*	Light Green	68	*64*
O_7	$C_{16}H_{21}NO_2$	*259.3*	Brown	77	*60*
O_8	$C_{15}H_{11}NO_2$	*237.1*	Green	130	*69*
O_9	$C_{19}H_{17}N_3O_2$	*319.4*	Light Brown	104	*78*
O_{10}	$C_{21}H_{21}N_3O_2$	*347.4*	Brown	193	*60*
O_{11}	$C_{23}H_{25}N_3O_2$	*375.5*	Brown	118	*72*
O_{12}	$C_{22}H_{15}N_3O_2$	*353.4*	Red	157	*78*
O_{13}	$C_{19}H_{17}N_3O$	*303.1*	Brown yellow	179	*92*
O_{14}	$C_{27}H_{18}N_4O$	*414.4*	Brown	227	*91*
O_{15}	$C_{21}H_{15}N_3O_2$	*341.4*	Bright yellow	182	*81*

Table (4.5): Physical properties, elemental analysis and atomic absorption data for new prepared metal complexes

Complexes	**Color**	**m.p. °C**	**Yield %**	**M.Wt g.mol^{-1}**	**elemental analysis % found (Calc.)**			**Metal Percentage % Found (Calc.)**
					C	**H**	**N**	
$[Co(C_{21}H_{15}N_3O_2)_2]Cl_2$	**Black**	**298**	**78**	**812.529**	**61.00 (62.08)**	**4.32 (3.72)**	**9.68 (10.34)**	**8.35 (7.25)**
$[Ni(C_{21}H_{15}N_3O_2)_2]Cl_2$	**Green**	**Above300 Dec**	**75**	**812.289**	**61.11 (62.09)**	**4.59 (3.72)**	**9.60 (10.34)**	**7.81 (7.22)**
$[Cu(C_{21}H_{15}N_3O_2)_2]Cl_2$	**Brouwn**	**Above300 Dec**	**83**	**817.136**	**61.53 (61.73)**	**4.53 (3.70)**	**9.34 (10.28)**	**7.42 (7.77)**
$[Zn(C_{21}H_{15}N_3O_2)_2]Cl_2$	**Orange**	**Above300 Dec**	**62**	**819.006**	**60.57 (61.58)**	**4.06 (3.69)**	**9.18 (10.26)**	**6.93 (7.98)**

4. 11 Biological activity

Most of the target compounds were evaluated for their antibacterial activity against one gram-negative organism such as ***(E.coli,)*** and one gram-positive organism such as ***(S. aureus)*** by the disk diffusion method. The test compounds were dissolved in DMSO. Two standard antibiotics (STREPTOMTCIN) were used as a reference standard for comparison. Zones of inhibition ***Figures (4. ٣٦)*** caused by the compounds were measured in (mm). The results of the antibacterial activity of the synthesized compounds are listed in ***Table (4. 6)***. The antibacterial activities of the test compounds are shown briefly below

- The compounds (O_{12},O_{15}), [Co(O_{15})]Cl_2 and [Zn (O_{15})]Cl_2showed high activity against ***S. aureus*** bacteria, the compounds (O_{10}), [Ni (O_{15})]Cl_2 and[Cu(O_{15})]Cl_2 showed moderate activity against the same type of bacteria, whereas compound (O_3) showed low activity against this type of bacteria, and from the other hand the compound (O_{14}) don't appear activity against **S. aureus** bacteria. The compounds (O_{10},O_{12},O_{14},O_{15}) and[Zn (O_{15})]Cl_2 showed good activity against **E. coli** bacteria. Whereas compounds (O_3),[Co(O_{15})]Cl_2 and [Ni (O_{15})]Cl_2 showed moderate activity, whereas compound [Cu(O_{15})]Cl_2 showed no activity against this type of bacteria.

Table 4. 6 : The inhibition zones of the compounds

Comp. No.	Concentration (mg / ml)	Zone of inhibition (inmm)	
		Gram-positive(*S.aureus*)	Gram-negative(*E.coli*)
O_3	200	*5*	*16*
O_{10}	200	*14*	*33*
O_{12}	200	*25*	*26*
O_{14}	200	*----*	*27*
O_{15}	200	*36*	*23*
[Co(O_{15})]Cl_2	200	*24*	*19*
[Ni(O_{15})]Cl_2	200	*15*	*13*
[Cu(O_{15})]Cl_2	200	*18*	*----*
[Zn(O_{15})]Cl_2	200	*23*	*23*

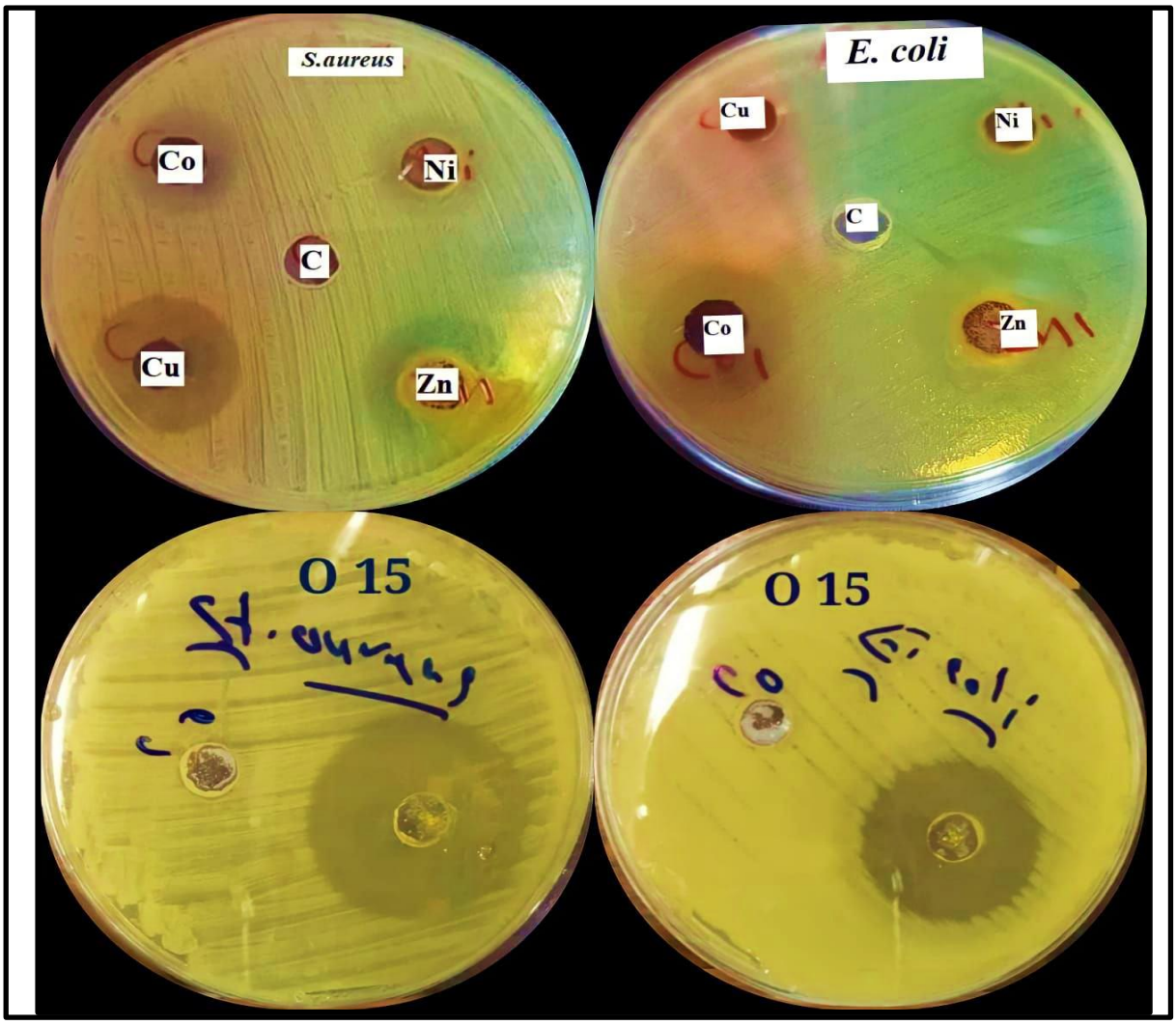


Figure (4- 3 ٦): Effects of the tested ligand (O_{15}) and complex against S. aureus and E.coli.

Conclusion

The present study concluded the following:

1. *Synthesis of fifteen new indole derivatives (O_1-O_{15}) from the reaction of isatin, they identified by FT-IR, and ^{1}HNMR spectroscopy techniques.*

2. *Synthesis new complexes of (O_{15}) ligand and characterize them by using conventional techniques (FT-IR,UV-Vis, C.H.N. , metal analysis, magnetic susceptibility and molar conductivity).*

3. *The ligand (O_{15}) act like a tridentate ligand through coordination with nitrogen atoms of an azomethine group, nitrogen atoms of amine group and oxygen atoms of carbonyl groups with (Co (II), Ni (II),Cu (II), and Zn (II)) ions.*
4. *Conductivity measurements showed that all the synthesized complexes were ionic in nature with (1:2) ratio.*
5. *According to the data obtained the proposal structures for complexes were octahedral geometry.*
6. *Some of The synthesized compounds were examined for their antibacterial activities toward two strains of bacteria (**E.colias**) and (**S. Aureus**). The result indicated that the activity against **S. aureus** bacteria was high for (O_{12}, O_{15}), [Co(O_{15})]Cl_2 and [Zn (O_{15})]Cl_2, moderate for (O_{10}), [Ni (O_{15})]Cl_2, and [Cu(O_{15})]Cl_2, low for compound (O_3) and no apparent activity for (O_{14}), Also the data proved the activity against (**E.colias**) bacteria for compounds (O_{10}, O_{12}, O_{14}, O_{15}) and [Zn (O_{15})]Cl_2 was highest than (O_3), [Co(O_{15})]Cl_2 and [Ni (O_{15})]Cl_2, whereas compound [Cu(O_{15})]Cl_2 showed no activity against this type of bacteria.*

Suggestions for future work:

1. *Synthesis a chain of new derivatives of substituted isatin and substituted amines and determined their biological activities and industrial applications.*
2. *Synthesis a series of new complexes for synthesized compounds with different transition metal ions and evaluate their biological activities.*
3. *Study of biological activity of the derivatives and their complexes against other types of bacteria.*
4. *Investigate some industrial applications of these derivatives and their complexes.*

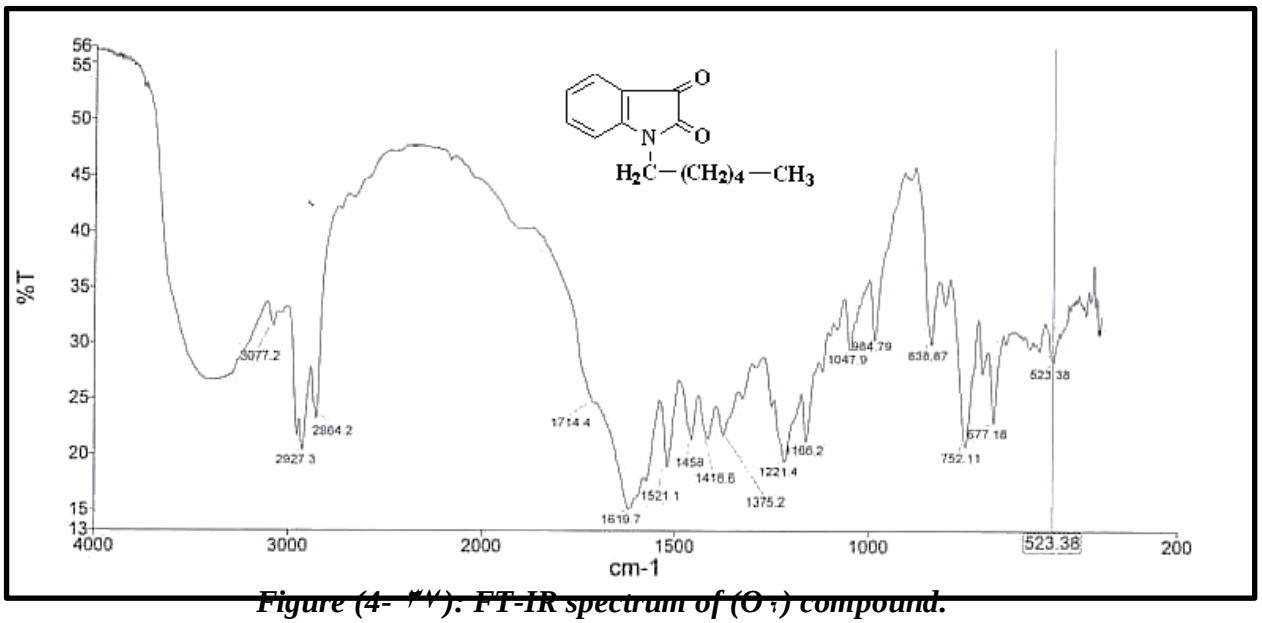


Figure (4- ٣٧): FT-IR spectrum of (O_7) compound.

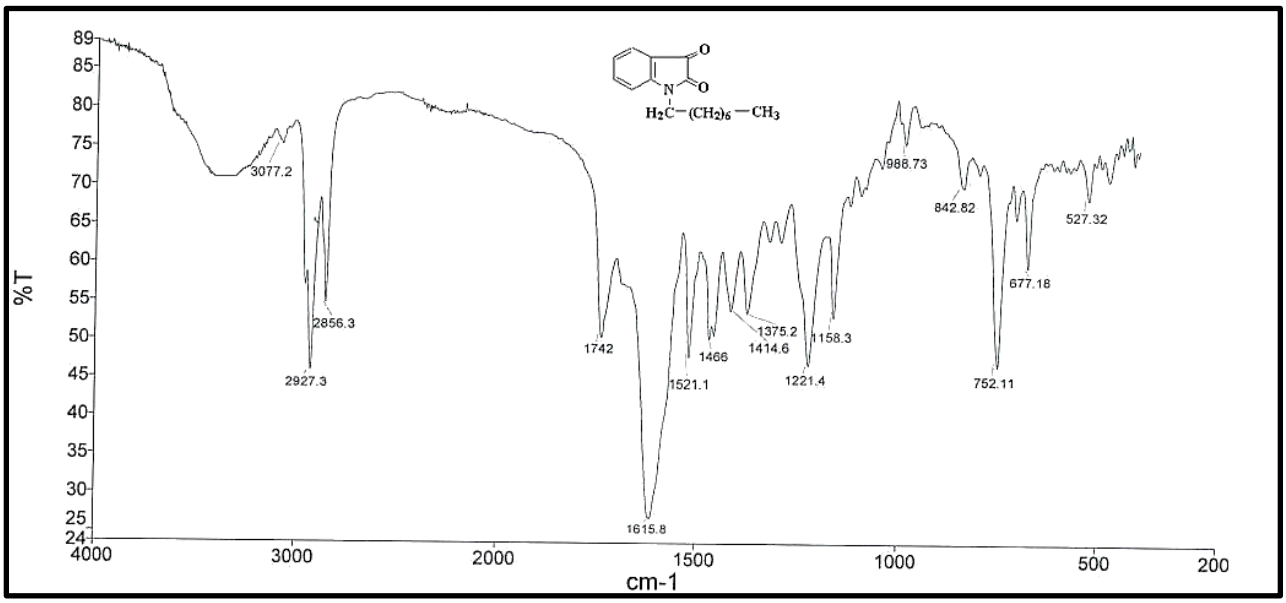


Figure (4- ٣٨): FT-IR spectrum of (O_8) compound.

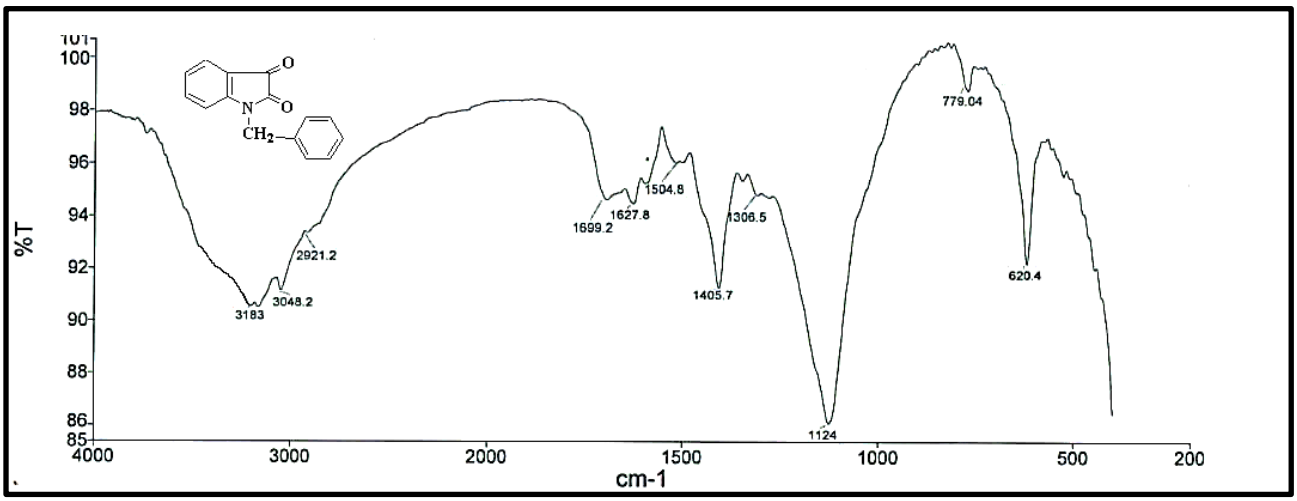


Figure (4- ٣٩): FT-IR spectrum of (O_9) compound.

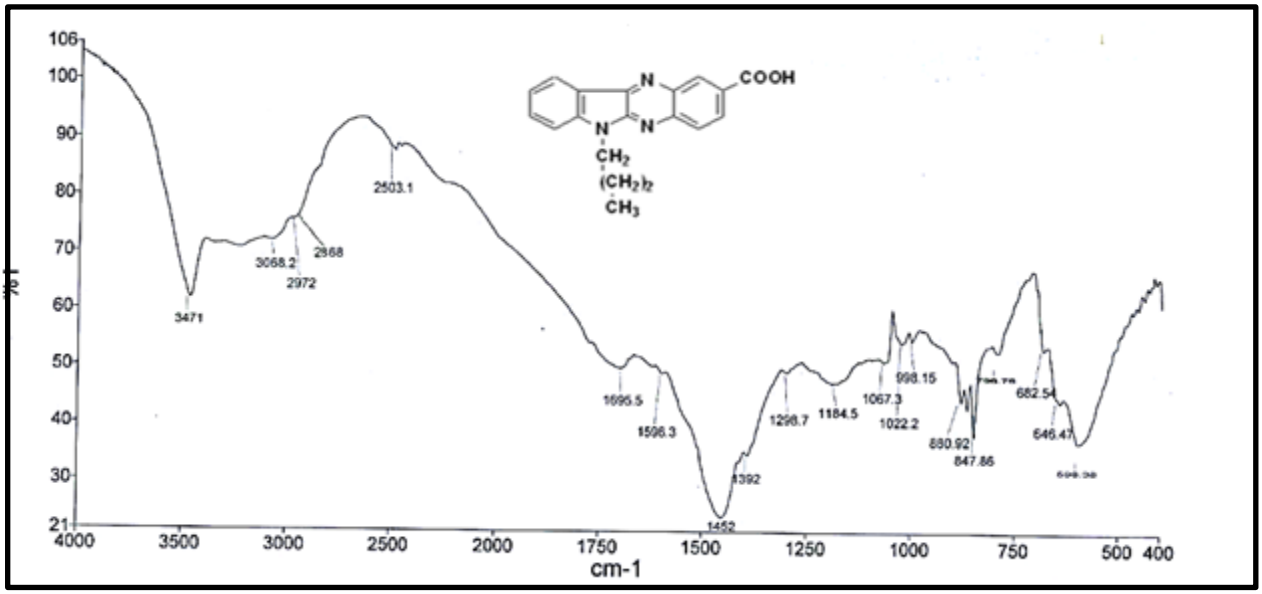


Figure (4- ٤٠): FT-IR spectrum of (O_1) compound.

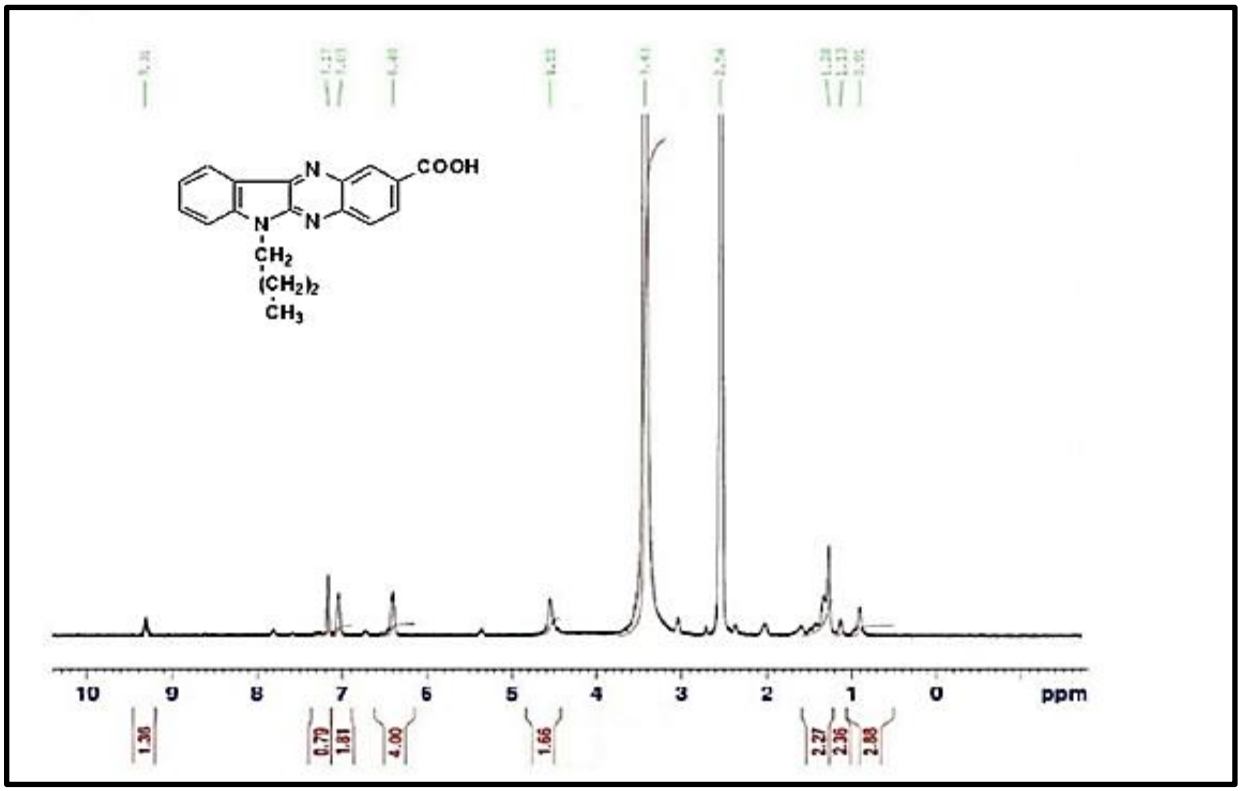


Figure (4- ٤١): ^1H NMR tspectrumo of compound6-Butyl-6H-indolo[2,3-b]quionxaline-2-carboxylic acid(O_1).

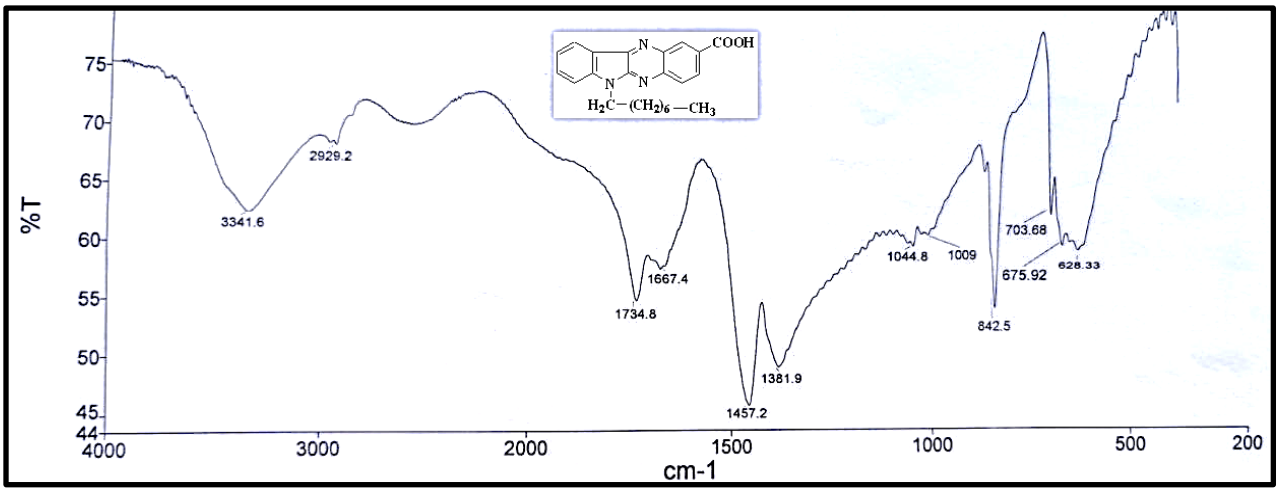


Figure (4- ٤٢): FT-IR spectrum of (O_{1}) compound.

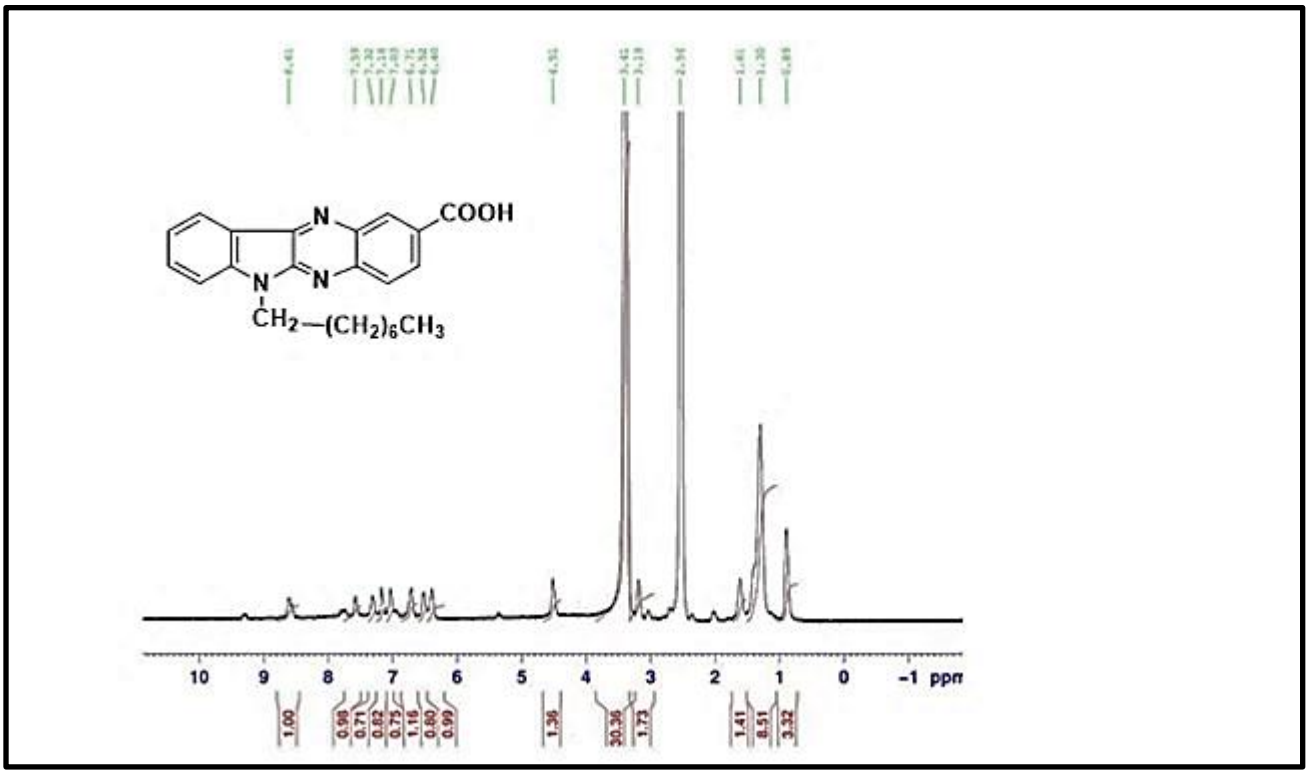


Figure (4- ٤٣): ^{1}H NMR tspectrumo of compound 6-Octyl-6H-indolo[2,3-b]quionxaline-2-carboxylic acid (O_{11}).

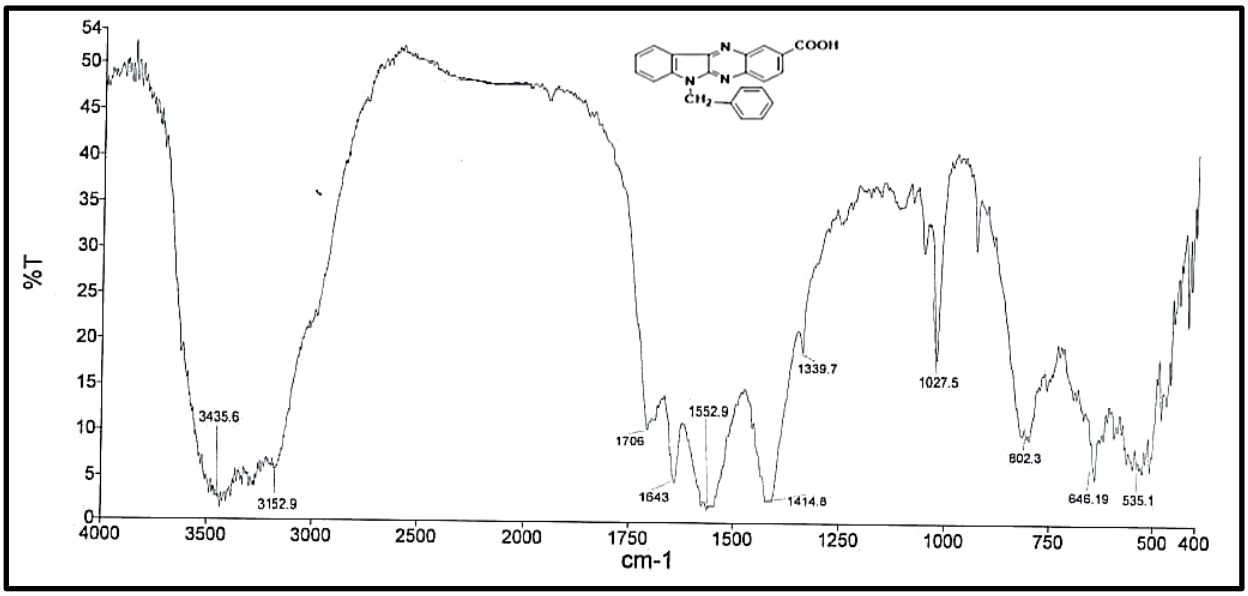


Figure (4- ٤٤): FT-IR spectrum of (O١٢) compound.

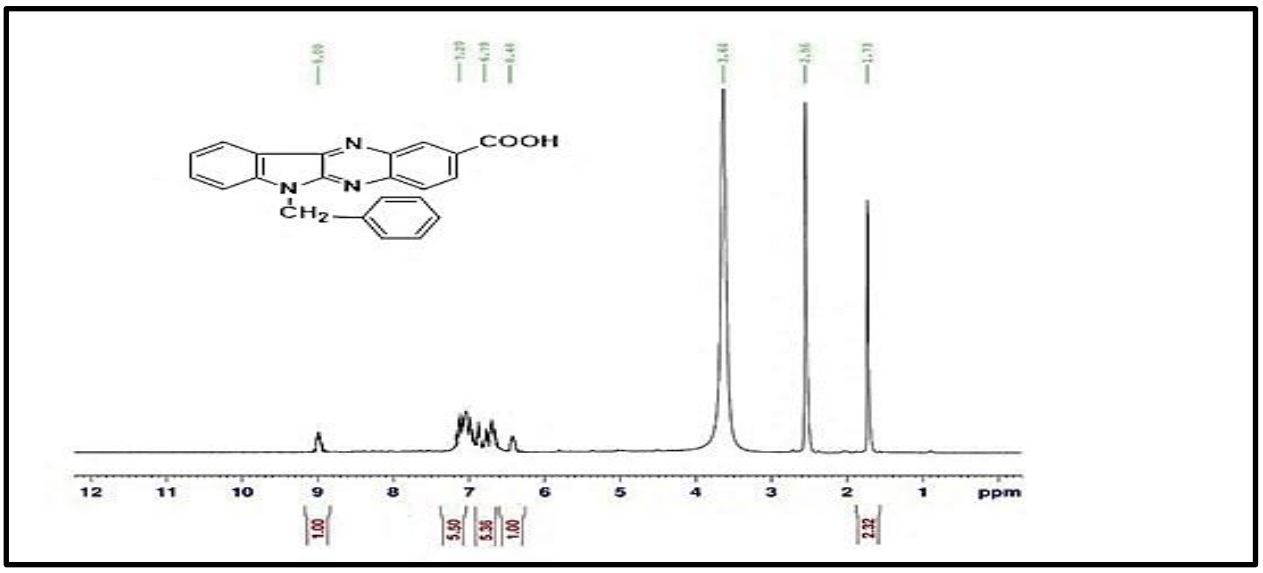


Figure (4- ٤٥): ^{1}H NMR tspectrumo of compound6- **Benzyl** *-6H-indolo[2,3-b]quionxaline-2- carboxylic acid (O_{12})*

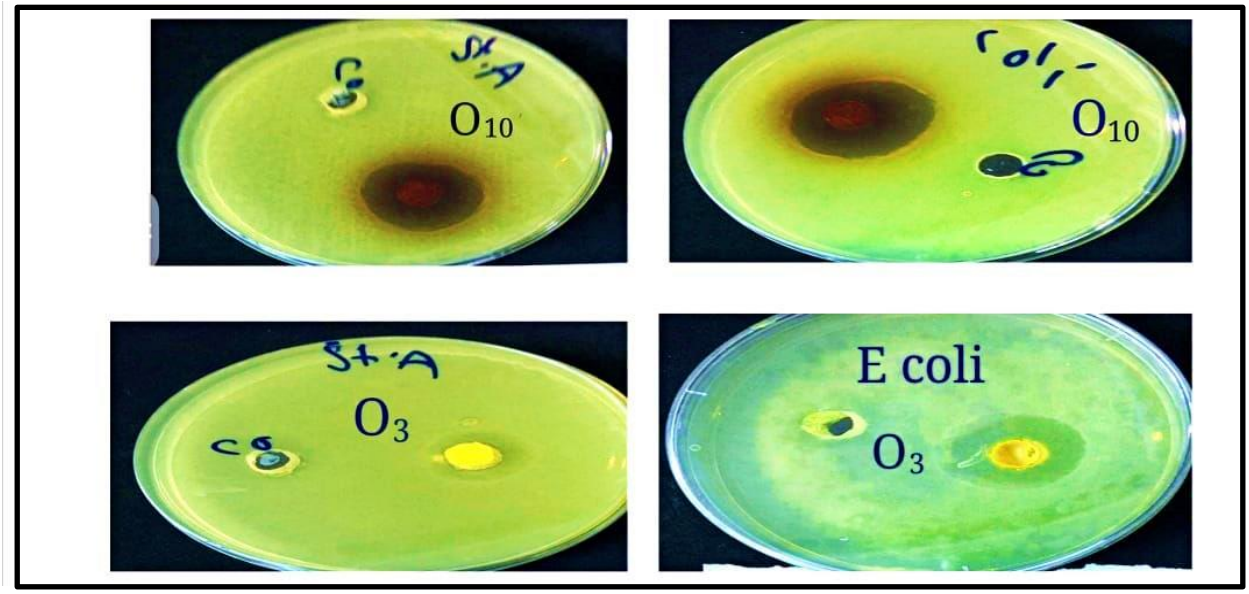


Figure (4- ٤٦): Effects of the tested compounds on S. aureus and E.coli to (O_{10},O_3)

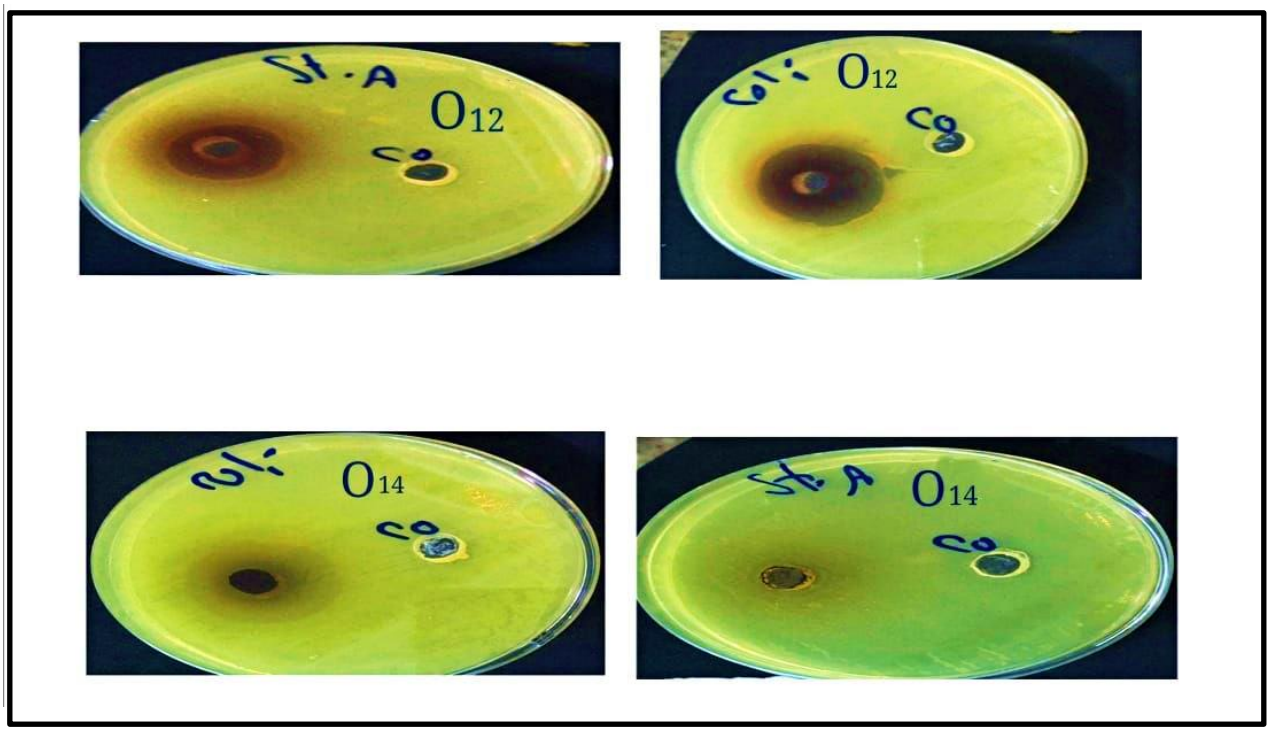


Figure (4- ٤٧): Effects of the tested compounds on S. aureus and E.coli to (O_{12},O_{14})

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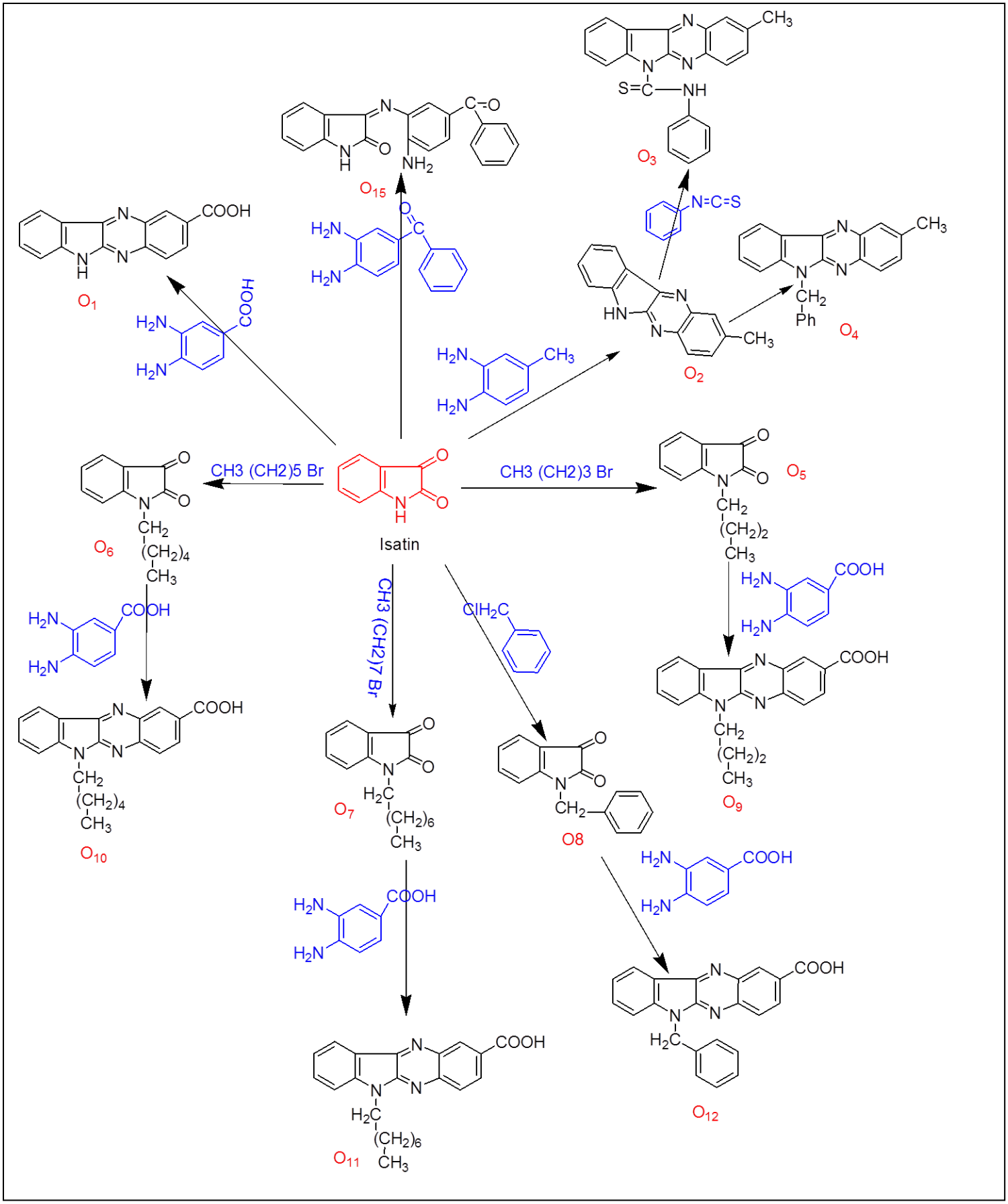
الخلاصة

تم في هذا البحث، تحضير مركبات جديدة من الايساتين بنجاح وتم تأكيد نقاوتها باستخدام كروموتوغرافيا الطبقة الرقيقة. شخصت التراكيب الكيميائية للمركبات المحضرة (O_1-O_{15}) باستخدام بعض التقنيات الطيفية مثل طيف الاشعة تحت الحمراء و طيف الرنين النووي المغناطيسي. استخدم المركب O_{15} كليكاند لتحضير معقدات جديدة من خلال تفاعله مع أملاح العناصر الانتقالية مثل كلوريد الكوبلت سداسي الماء وكلوريد النيكل سداسي الماء وكلوريد النحاس ثنائي الماء وكلوريد الخارصين اللامائي. شخصت المعقدات الجديدة باستخدام طيف الاشعة فوق البنفسجية والمرئية و طيف الاشعة تحت الحمراء وطيف الامتصاص الذري وتحليل العناصر والحساسية المغناطيسية وقياسات التوصيلية. تم تحديد الخصائص الفيزيائية للمركبات والمعقدات المحضرة من خلال درجات الانصهار والألوان. تضمنت الدراسة الحالية الخطوات التالية:

١. تحضير مركب جديد ٦-هيدرو اندولو [٣,٢- ب] كينوكسالين -٢- كاربوكسلك اسد (O_1) من خلال تفاعل الايساتين مع ٤,٣ - ثنائي امينو بنزوك اسد.
٢. تحضير ٢- مثيل -٦-هيدرو اندولو[٣,٢- ب] كينوكسالين (O_2) بواسطة تفاعل الايساتين مع ٤- مثيل اورثو فنيلين ثنائي الامين ثم تفاعل ٢- مثيل -٦-هيدرو اندولو[٣,٢- ب] كينوكسالين (O_2) مع فنيل ايزوثايو سيانيد لتحضير ٢ مثيل –اندولو [٣,٢- ب] كينوكسالين -٦-كاربو ثايوكاسد فثايل اميد(O_3) كما أنه يتفاعل ٢- مثيل -٦-هيدرو اندولو[٣,٢- ب] كينوكسالين (O_2) مع كلوريد البنزيل لتحضير ٦-بنزيل -٢- مثيل -٦هيدرو – اندولو [٣,٢-ب] كينوكسالين(O_4).
٣. تحضير مركبات N- الكيل ايساتين [O_5 - O_8] من خلال تفاعل الايساتين مع هاليدات الالكيل المختلفة.
٤. تحضير المركبات [O_9-O_{12}] بواسطه تفاعل ٤,٣- ثنائي امينو بنزوك اسد مع مركبات N- الكيل ايساتين للحصول على مركبات بديلة جديدة وفعالة.
٥. تحضير قاعدتين شيف جديدتين بخطوتين م
٦. ن خلال تفاعل ٣، ٤- ثنائي امينو بنزوفينون مع اورثو امينو فينول لإنتاج المركب[O_{13}] ، ثم تفاعل قاعدة شيف [O_{13}] مع الايساتين لإنتاج المركب [O_{14}]
٧. تفاعل الايساتين مع ٤،٣- ثنائي امينو بنزوفينون لتحضير المركب الجديد٣- (٢ -امينو ٥-ب- بنزيل فنيل امينو)١-٣،ثنائي هيدرو اندول ٢-اون[O_{15}] ومعقداته [Cl_2[$Co(O_{15})_2$، Ni] $(O_{15})_2]Cl_2$، $[Cu(O_{15})_2]Cl_2$ ، $[Zn(O_{15})_2]$.

٨. كذلك تم تقييم الفعالية البايولوجية لبعض المركبات المحضرة ضد نوعين من البكتيريا (E.colias) و (S. Aureus). أظهرت معظم هذه المركبات نشاطًا مضادًا للبكتيريا جيدًا إلى مقبول ضد السلالتين من البكتيريا المستخدمة.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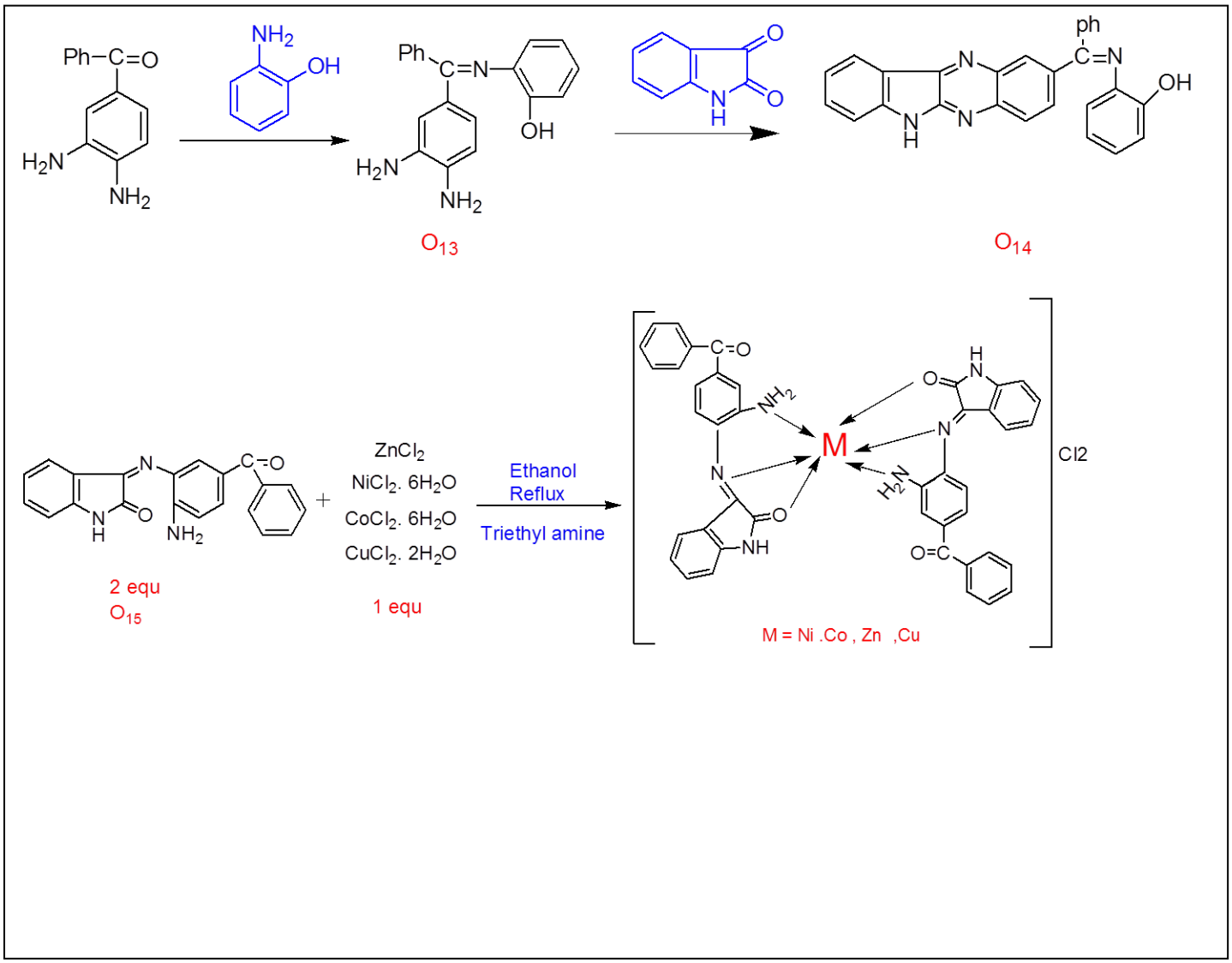
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CoCl2. 6H2O
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Triethyl amine
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O=C
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M = Ni .Co , Zn ,Cu

وزارة التّعليم العالي والبحث العلمي جامعة ديالى

كلّية العلوم /قسم الكيمياء

تحضير وتشخيص سلسلة جديدة من مشتقات الايزاتين مع بعض المعقدات

رسالة مقدمة إلى

مجلس كلية العلوم – جامعة ديالى

وهي جزء من متطلبات نيل شهادة الماجستير في علوم الكيمياء

امنية وائل محمد

(بكالوريوس في علوم الكيمياء عام ٢٠١٥ - كلية العلوم جامعة ديالى)

بإشراف

أ. م.د. وسن باقر علي

أ.م.د.اريج علي جارالله

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