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and Scientific Research
University of Diyala
College of Science
Department of Chemistry

Synthesis, Characterization and Anti-Fungal Activity of Some Heterocyclic Compounds and Their Complexes

A Thesis Submitted to the
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by

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2020 A.D

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بسم اللّه الرحمن الرحيم

﴿ يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ ﴾

صدق اللّه العظيم

(سورة المجادلة -الآية ١١)

dedication

I dedicate this humble effort to

The Holy Prophet Muhammad

(Peace be upon him on his nation) and to

My father and My mother

All my brothers and sisters

And to my fiancé

Acknowledgeme

First of all thanks to God for his entire blessing during the pursuit of my thesis. Through him, I was able to gain strength to complete this thesis.

I would like to express my gratitude and deep appreciation to my supervisos **Dr. Wasan Baqir Ali and Dr.Areej Ali Jaraullah** for their support and encouragement, their guidance and special advice to enrich throughout this work.

My special thanks to staff department of chemistry,

I am grateful to all my dear friends

Finally, thanks for everyone help me to complete this thesis

ABSTRACT

In this thesis, new compounds and complexes have successfully have been synthesized from isatin. The purity of these chemicals was confirmed by using thin layer chromatography. The chemical structure of the synthesized compounds (A_1- A_{12}) was identified by spectral methods such as [UV, FTIR, ^{1}H-NMR] Their physical properties were determined by melting points, and colors . Some compounds were used as ligands to synthesis a new complexes by their reaction with transition elements salts such as H_2 $ptCl_6$.$6H_2O$, $ZnCl_2$, Ni Cl_2.$6H_2O$ and $CoCl_2$.$6H_2O$. The new complexes were characterized by using UV, FTIR , atomic absorbtion spectroscopy, element analysis, magnetic susceptibility and conductivity measurements . The physical properties , were determined by melting points , and colors. furthermore we were studied the effect of the synthesized compounds and some complexes were examined aganist some fungal strains . The present study involved these step:

1- The reaction of isatin with 4- methyl *o*-phenylenediamine to synthesis 2- methyl -6H-indolo[2,3-b]quinoxaline[A_1], and then synthesis of [$pt(A_1)_2$].H_2O and [$Zn(A_1)_2$].$5H_2O$ complexes by using of [H_2PtCl_6.$6H_2O$], [$ZnCl_2$].

2- The reaction of isatin with 4- chloro *o*-phenylenediamine afforded 2-chloro- 6H-indolo[2,3-b]quinoxaline [A_2] .

3- The condensation of compounds [A_1, A_2] respectively with chloro acetyl chloride in the presence of triethylamine and dry benzene as solvent to gives [A_3, A_4] . Which were treated with hydrazine hydrate to give [A_5, A_6].

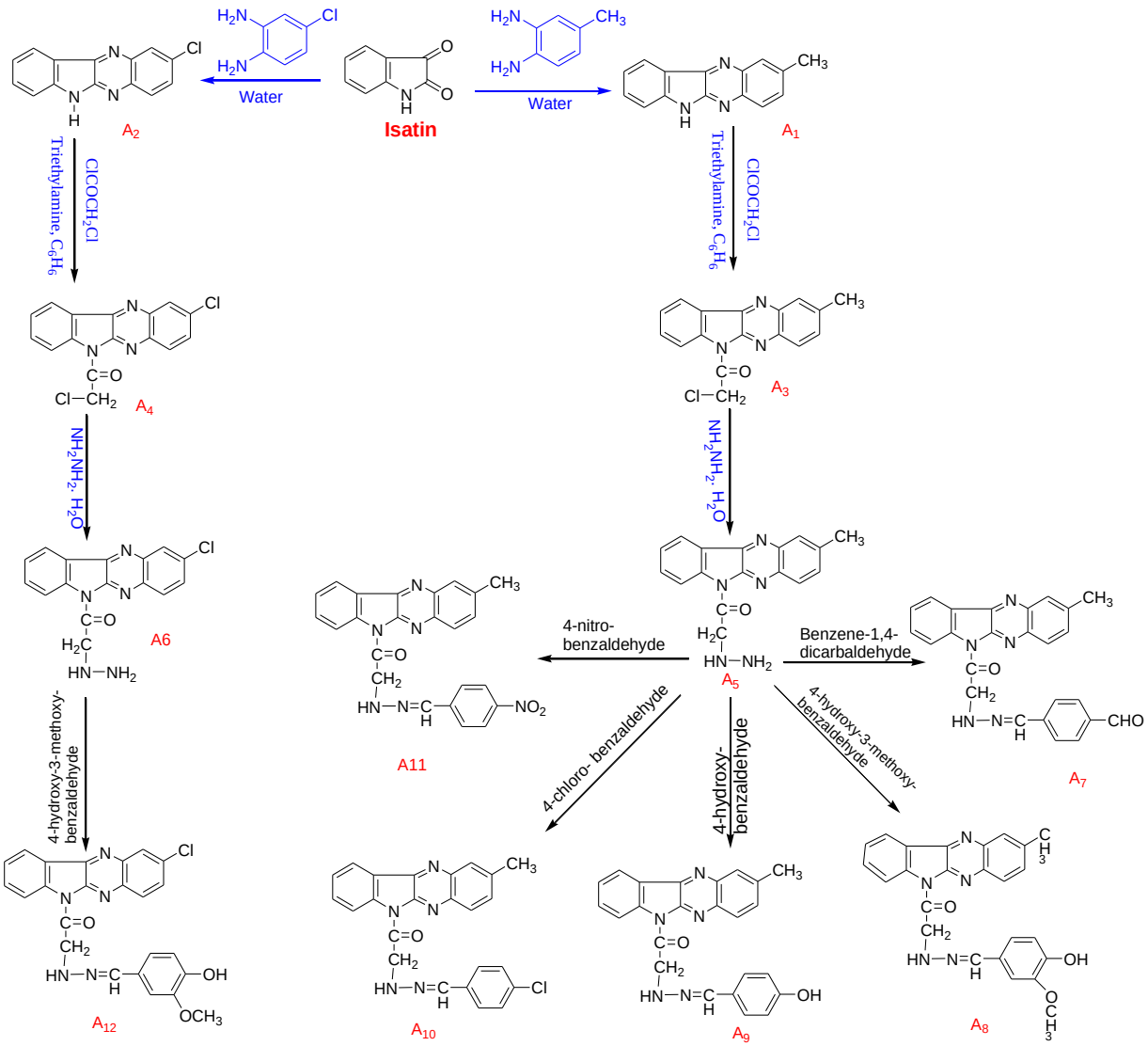
4- Synthesis of [$Ni(A_5)_2$].$6H_2O$ and [$Co(A_5)_2$].$6H_2O$ complexes by using of [$NiCl_2$.$6H_2O$] , [$CoCl_2$.$6H_2O$] .

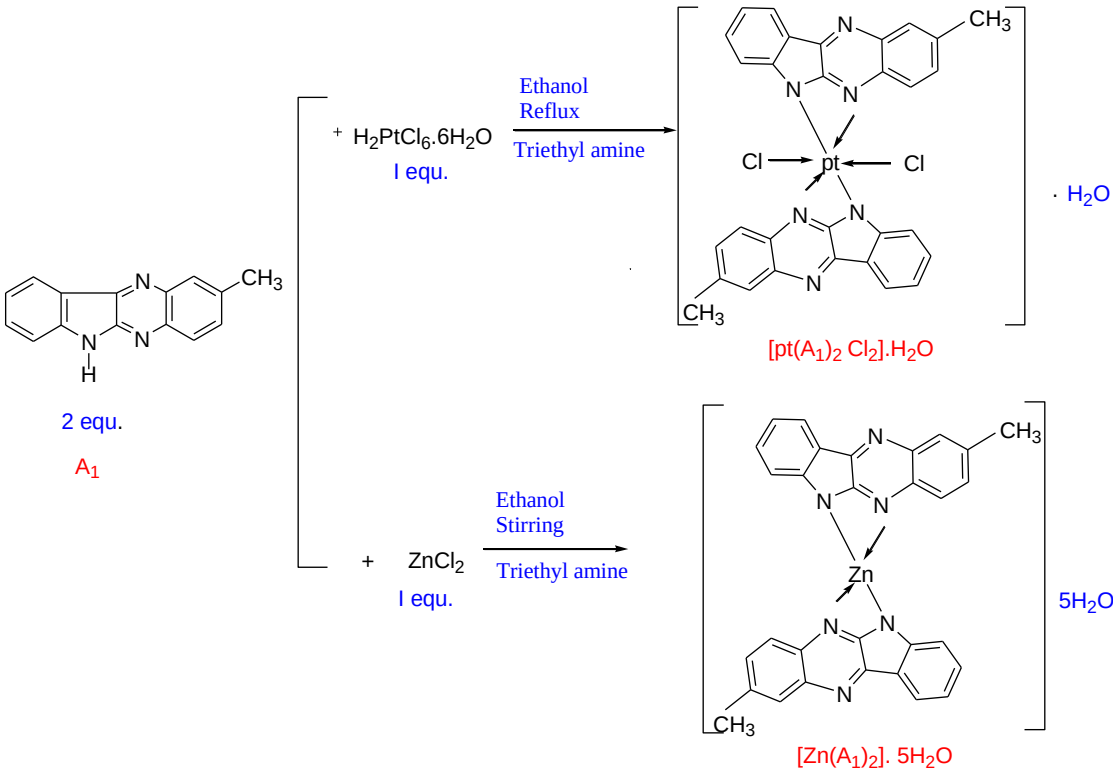
5- new Schiff bases [$A_{7.}$ $A_{8,}$ A_{9}, $A_{10,}$ $A_{11,}$ A_{12}] were synthesized through the reaction of the hydrazine derivative [$A_{5,}A_{6}$] with different aromatic aldehydes.

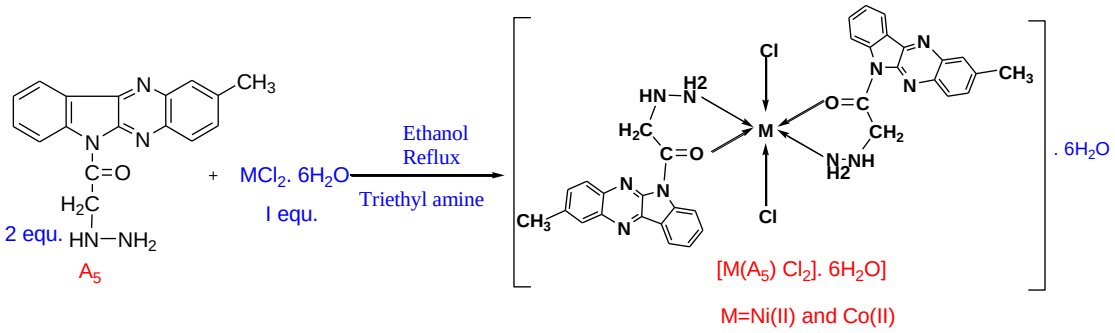
6. Synthesis of $[Ni(A_7)_2\ Cl_2].6H_2O$ and $[Ni(A_8)_2\ Cl_2].6H_2O$ complexes by using of $[NiCl_2.6H_2O]$.

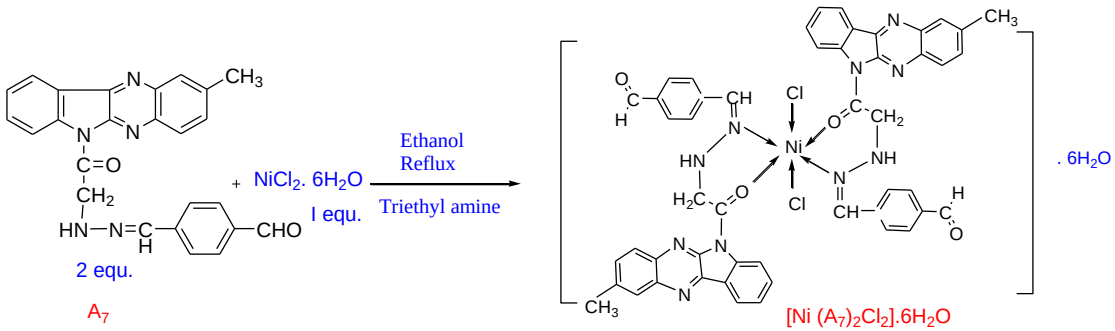
7- The antifungal activity of substituent was also evaluated . The results showed that the derivatives and complexes has promising antifungal activity toward (*Cryptococccus Neoformans, Candida Albicans, Rhodotorula rubra, Aspergilus parasiticus, Penicilium sp., Rhizopus arrhizus*).

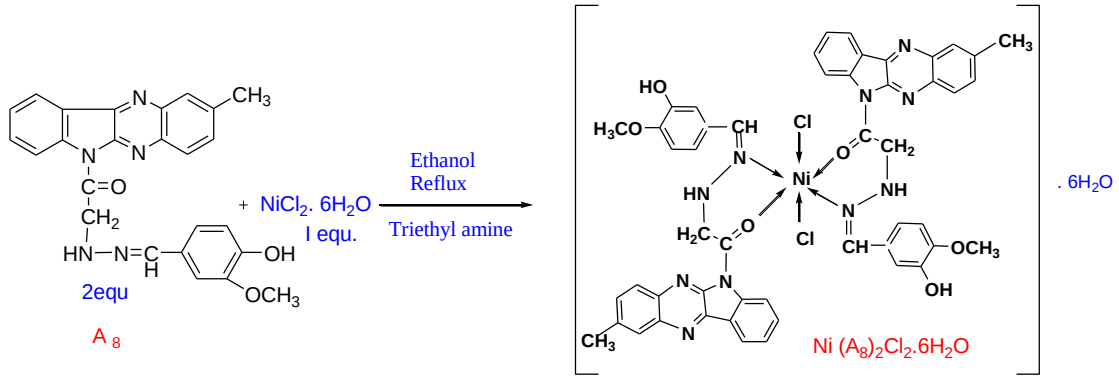
The Scheme shown illustrated synthesized compounds




2 equ.
A1
+ H2PtCl6.6H2O
I equ.
Ethanol
Reflux
Triethyl amine
[pt(A1)2 Cl2].H2O
+ ZnCl2
I equ.
Ethanol
Stirring
Triethyl amine
[Zn(A1)2]. 5H2O
5H2O


2 equ.
A5
+ MCl2. 6H2O
I equ.
Ethanol
Reflux
Triethyl amine
[M(A5) Cl2]. 6H2O
M=Ni(II) and Co(II)
. 6H2O


2 equ.
A7
+ NiCl2. 6H2O
I equ.
Ethanol
Reflux
Triethyl amine
[Ni (A7)2Cl2].6H2O
. 6H2O


2equ
A 8
+ NiCl2. 6H2O
I equ.
Ethanol
Reflux
Triethyl amine
Ni (A8)2Cl2.6H2O
. 6H2O

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Symbols and Abbreviations

Abbreviation	Meaning
H-NMR ^{1}	Proton Nuclear Magnetic Resonance
FT-IR	Fourier-transform infrared
U.V-Vis	Ultraviolet-Visible
DMSO	Dimethyl sulfoxide
M.P.	Melting point
EtOH	Ethanol
TLC	Thin layer chromatography
MWI	Microwave irradiation
&	And
^{0}C	Degree Celsius
Ar	Aromatic ring
C.H.N	Elemental-Analysis
cm	Centimeter
g	Gram
μm	Micrometer
%	Percent (per cent)
δ	Chemical shifts
h	Hour(s)
min	Minute
***M*Hz**	Megahertz
ppm	Parts per million
S	Singlet
Cal	Calculated
λ	Wave length
Cond.	Conductivity
Td	Tetrahedral
B.M	Bore Magnetone
CT	Charge Transfer
Oh	Octahedral

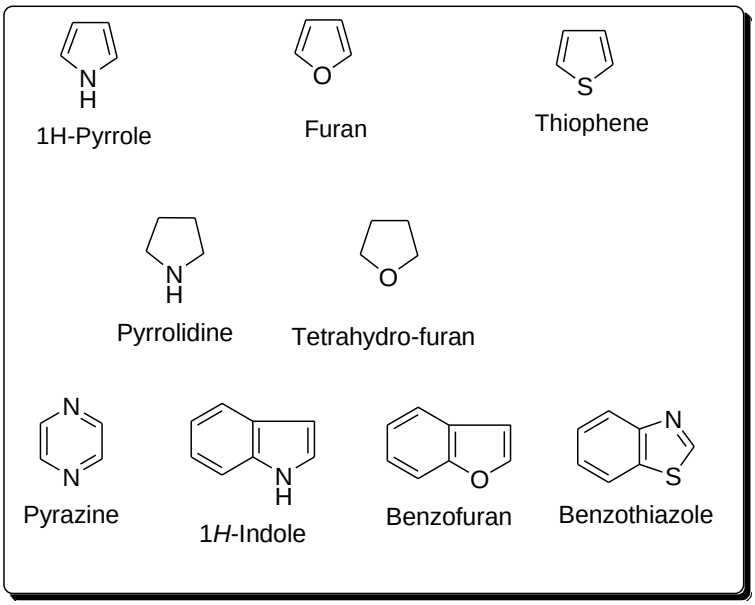
Chapter One

Introduction

1. Introduction

1.1 Heterocyclic compound

Heterocyclic chemistry is an essential field in the chemical sciences and constitutes an extensive part of the modern researches that are occurring presently through out the world [1]. Cyclic compounds in which one or more of the ring atoms are different atom other than carbon are called heterocyclic compounds which may have N, O, S and less frequently phosphorous, boron and silicon [2]. The heteroatom is a Greek word which means different [3,4]. Heterocyclic compounds can be aromatic in nature according to their chemical structure such as pyrrole, furan, and thiophene or aliphatic like pyrrolidine and tetrahydrofuran as illustrate in figure(1.1). The aromatic heterocyclic rings can be five or six-membered. They may contain one heteroatom such as pyrrole , furan, and thiophene, or two heteroatom as in imidazole which comprises of two nitrogen atom, or oxazole ring which contains nitrogen and oxygen. These heterocyclic rings could be fused with benzene ring to form one compound, for example, Indoles compounds and their derivatives [5, 6].



Figure(1.1): Simple aromatic rings and nonaromatic rings

Heterocyclic compounds containing 5- or 6-membered ring are important due to their diverse biological activities [7,8]. These are represent a large groue of heterocyclic compounds, have been extensively explored for developing pharmaceutically molecules [9]. Organic chemists have been making extensive efforts to produce these compounds are abundant in nature and great more to life because of many natural products contains many subunits in their structure such as hormones, vitamins, and antibiotics [10]. Therefore, they have attracted significant attention in the composition of many important biological molecules. Among large number of heterocycles found in nature, nitrogen heterocycles are the most abundant, especially those containing oxygen or sulphur due to their wide distribution in nucleic acid illustration and their involvement in most of the physiological processes in plants and animals [11].

1.2 Indole

The name of indole is a portmanteau of the words indigo and oleum [12], since indole was first isolated by treatment of the indigo dye with oleum [13]. Indol is an aromatic heterocyclic compound with formula C_8H_7N [14]. It is a benzopyrrol ,pyrrole rings are fused by 2- and 3-positions with the benzene ring [15] As illustrate in Figure(1.2) the Indole ring which is a well-known privileged structure scaffold occurring in numerous natural products such as alkaloids, peptides and various synthetic compounds. Because of its biodynamic properties[16].

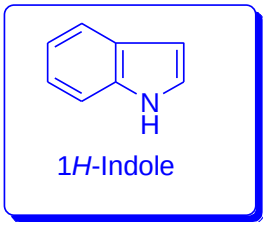
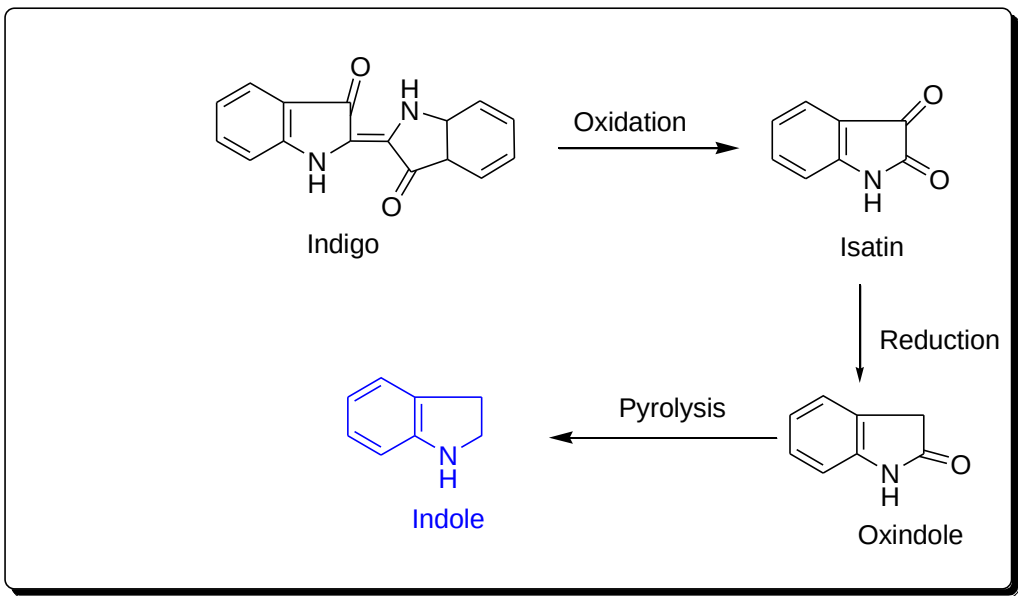


Figure (1.2) Indole ring

The interest and development in indole chemistry began in mid-nineteenth century, with intensive studies on indigo, a violet-blue dye originally derived from Indigofera species in India. In 1866, Adolf Von Baeyer discovered the conversion of oxindole into indole by a pyrolytic technique using zinc dust [17.18] as illustrate in Scheme (1.1) .



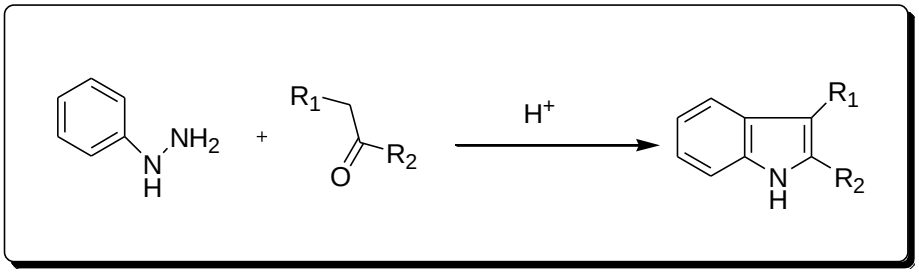
Scheme(1.1) : Preparation of Indole from Indigo.

1.2.1 Synthesis of indole

1.2.1 .1 Fischer indole synthesis

This reaction was discovered for the first time by Hermann Emil Fischer . This method involves heating phenyl hydrazine in the presence

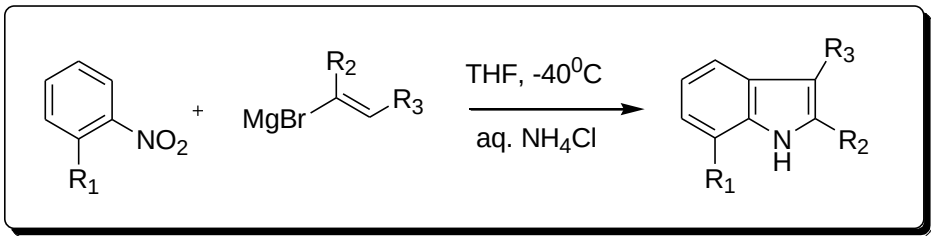
of aldehyde or ketone under acidic condition, forming phenyl hydrazone which subsequently rearranges with the loss of ammonia to give indole or 2- and 3-substituted indoles [19,20] as illustrate in Scheme (1.2) .



Scheme (1.2):Fischer indole synthesis

1.2.1.2 Bartoli indole synthesis

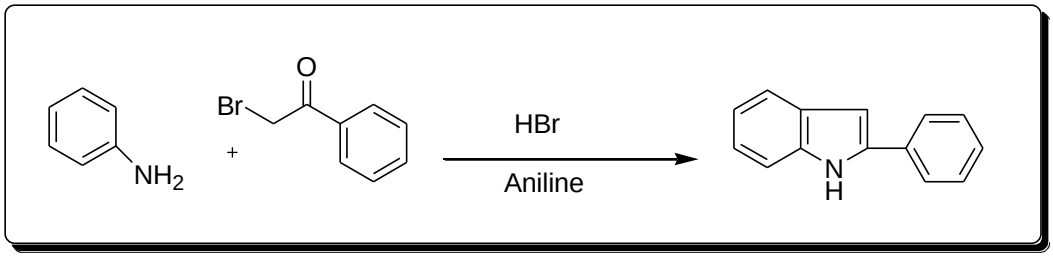
In Bartoli indole synthesis , substituted indoles are obtained by the reaction of ortho-substituted nitroarenes with vinyl Grignard reagents. In absence of ortho substitution on nitro arene [21, 22] as illustrate in Scheme (1.3).



Scheme (1.3): Bartoli indole synthesis.

1.2.1.3 Bischler Synthesis

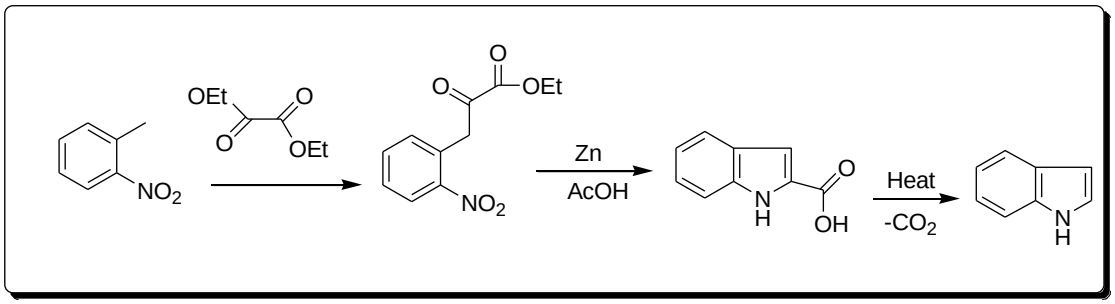
In 1892, Bischler et al, put forwarded a simple method affording a 2- aryl-indole [23] from an α-bromo-acetophenone and excess aniline as illustrate in Scheme (1.4).



Scheme (1.4): Synthesis of 2-aryl indole from α-bromo-acetophenone and excess aniline

1.2.1.4 Reissert synthesis

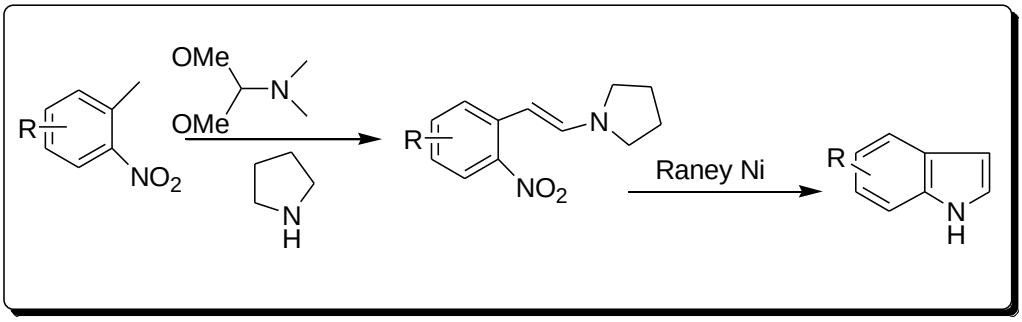
Reissert [24] reported the synthesis of indole from orthonitrotoluene and diethyl oxalate in 1897 as illustrate in Scheme (1.5) .



Scheme (1.5): Reissert synthesis of indole.

1.2.1.5 Leimgruber–Batcho synthesis

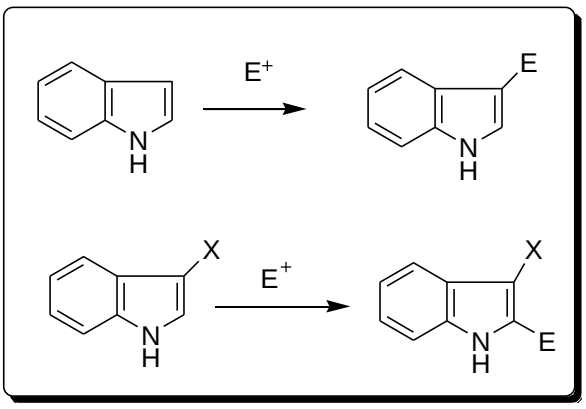
Leimgruber–Batcho Synthesis is an efficient method of indole and substituted indoles . It is generated o-nitro toluene by using N,N-dimethyl formamide dimethyl acetal and pyrrolidine which upon reductive cyclisation [25] afforded indole in the subsequent step as illustrate in scheme (1.6) .



Scheme (1.6): Leimgruber–Batchosynthesis of indole

1.2.2 Reactivity of indole

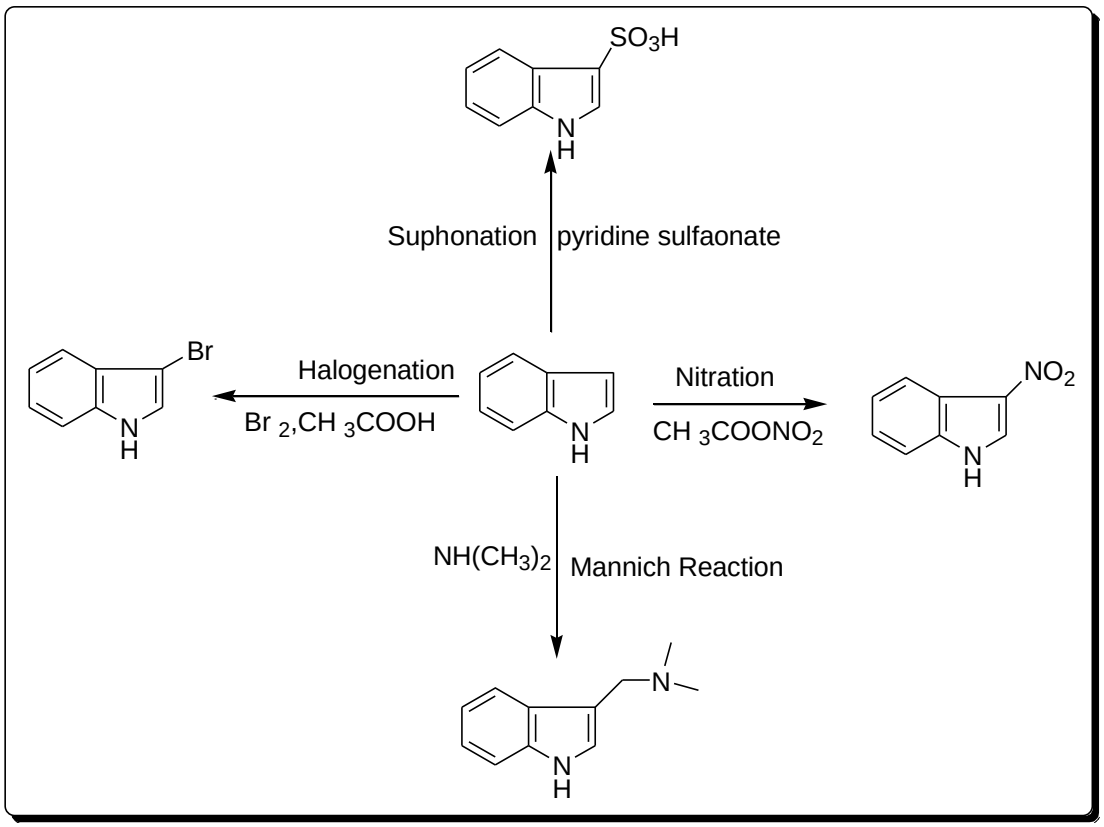
Reactivity in indole molecule is a most commonle feature. Indole undergoes electrophilic substitution mainly at position 3 of the nucleus. When position 3 of the indole nucleus is occupied by substituents other than hydrogen, position 2 is the most reactive one and when positions 2 and 3 are occupied, the electrophile occupies a position in the benzene ring as illustrate in Scheme (1.7) .



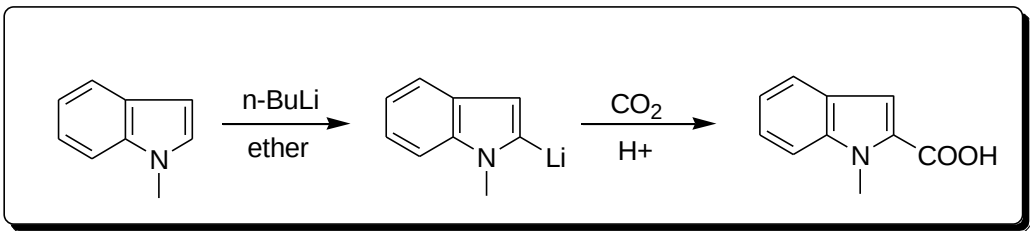
Scheme (1.7): Electrophilic substitution in indole

Indole itself is π-electron excessive system. Therefore, it undergoes electrophilic substitution reaction [26]. The attack of electrophile at position 3 generates carbocation which do not disturb the aromaticity of benzene ring whereas attack of electrophile at position 2 generates carbocation which disrupt the aromatic character by

delocalizing the positive charge over benzene ring. It also undergoes nucleophilic substitution reaction [27] as per [Scheme 1.8 and 1.9].



Scheme (1.8): Electrophilic substitution reactions of indole.



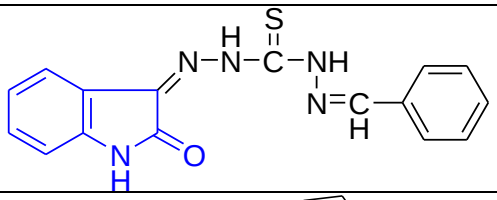
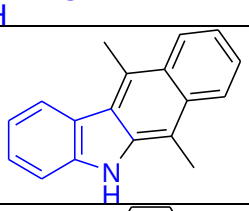
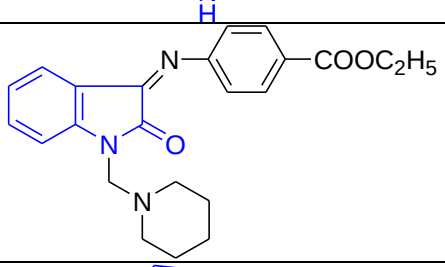
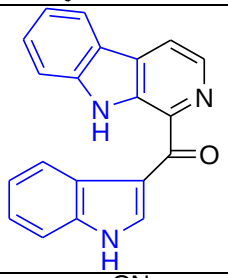
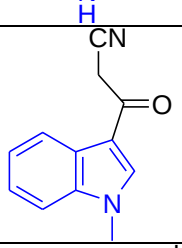
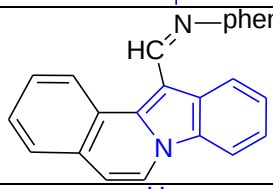
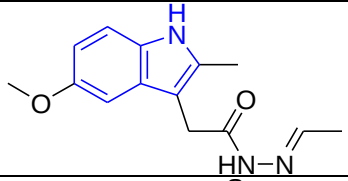
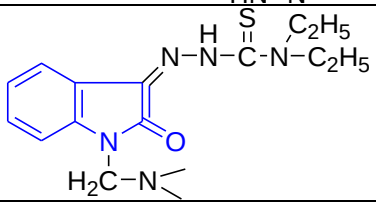
Scheme (1.9): Nucleophilic substitution reaction of indole.

1.2.3 Biological application of indole

Indole is broadly applied in pharmaceutical chemistry. The indole show promising biological activities . It can be used as Anti-diabetic, antibacterial, antifungal, antimicrobial, antioxidant, anti-inflammatory and anti-HIV . The biological activities of indole and its

derivatives are shown in (Table 1.1).

Table 1.1 : Biological activity of some Indole and derivatives.

Bioactivity	structures	References
Anti-diabetic		[28]
Anticancer		[29]
Anti-bacterial		[30]
Antifungal		[31]
Antimicrobial		[32]
Antioxidant		[33]
Anti-inflammatory		[34]
Anti-HIV		[35]

1.3 Isatin

Isatin, indoline-2,3-dione [36] or indole-1H-2,3-dione [37] is an indole derivative containing keto (C=O) group at position 2 and 3 of the ring as as illustrate in Figure(1.3) [38,39]. Isatin ring system consists of pyrrole ring fused with benzene ring [40]. which is found in many plants [41]. It has been discovered 150 years ago [42] and recenthy known as oxindole and Endogenous polyfunctional heterocyclic compounds [43]. The compound was first obtained by Erdman [44] and Laurent [45] in 1841 as a product from the oxidation of indigo dye by nitric acid and chromic acide [46,47] .

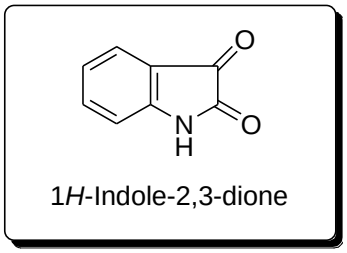


Figure (1.3): 1H-Indole-2,3-dione

Isatin group are synthetic versatile substrates, can be used for the synthesis of a wide range of heterocyclic compounds, such as indoles and quinolines [48]. Formerly, the study of isatin derivatives was connected with dye synthesis, but more recently these heterocycles are demonstrated antiprotozoal [49] , antifungal [50,51], antiviral [52,53], anticonvulsant [54], anti-inflammatory [55,56] , Anti-tubercular [57-59], antitumor [60,61] , antimicrobial [62], antimalarial [63] and antihelminthic activities. Moreover, they are influence neurodegenerative diseases, participate in metabolism, acetylcholinesterase inhibitors, and stimulate the growth of plants [64]. Drugs containing the isatin skeleton are used to treat diseases such as eplilepsy , and bulimia . Therefore the need to create novel isatin derivatives for emerging drug targets is a

promising area in medical chemistry [65]. Isatin is an endogenous compound identified in humans that possesses a wide range of biological activities [66,67]. Isatin has anticonvulsant activities and acts as a potent antagonist on a trial natriuretic peptide receptors in vitro Recently, a number of researchers have been studying the use of isatin in the fight against phytopathogens and as potential herbicides [68] .

1.3.1 Study of the reactivity of isatin

Isatin will mainly react at three different sites, N-alkylation, namely aromatic substitution at C-5, and carbonyl reactions at C-3. If the system carry electron-withdrawing groups in the benzene ring or at the nitrogen attack at C-2 can also occur as illustrate in Figure(1.4) [69] .

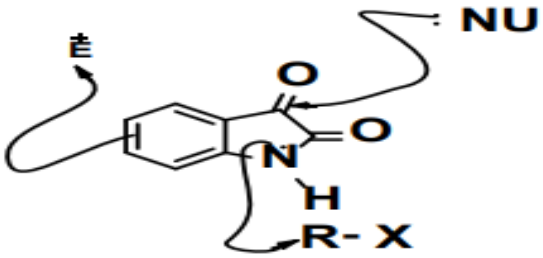


Figure (1.4): Reactivity of isatin

1.3.2 Application of Isatins in Organic Synthesis

Many synthetic [70] methodologies have been described for the conversion of isatins to other heterocyclic systems. This type of chemistry can be generalized as one of the following strategies:

- Partial or total reduction of the heterocyclic ring, leading to indoles and derivatives.

- Oxydation reaction .

- Nucleophilic addition at position C-3, which may be further followed by a cyclization process.

- Nucleophilic substitution at position C-2, leading to the opening of the heterocyclic.

1.3.3 Reactivity of the carbonyl functions of isatin

The carbonyl functions of isatin differ very much in their reactivity. The 2-carbonyl function possesses considerable amide character because of its near position to the nitrogen atom and the ability of nitrogen lone pair to deiocalize onto it reduces its electrophilicity. If such a delocalization is to appear onto the 3-carbonyl function, it would lead to loss of aromatic character of the benzene nucleus, a condition which is not favourable. This indicated, therefore, that the 3-carbonyl function would be more reactive as compared to 2-carbonyl function as illustrate in Figure(1.5) [71].

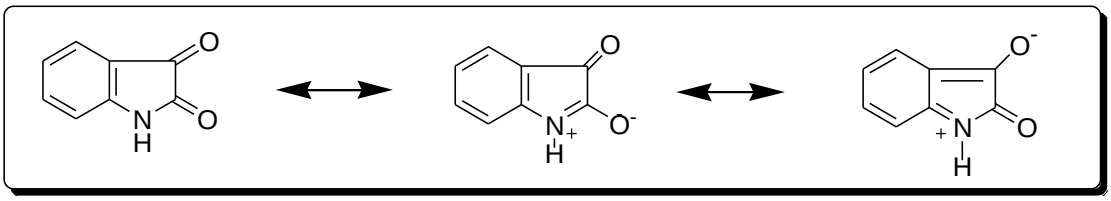
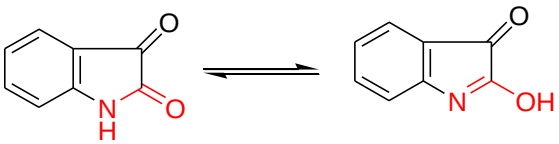


Figure (1.5): Reactivity of the carbonyl functions of isatin

1.3.4 Tautomerism of isatin

In 1882, Baeyer proposed for the first time that the isatin exists in two tautomeric forms, lactam (1) and lactim (2), in which a proton transfer between the nitrogen atom and the oxygen present at the second carbon occurs. [72,73]In the solid state, isatin predominantly exists in the lactam structure as illustrate in Figure (1.6) .



1.lactam **2.lactim**

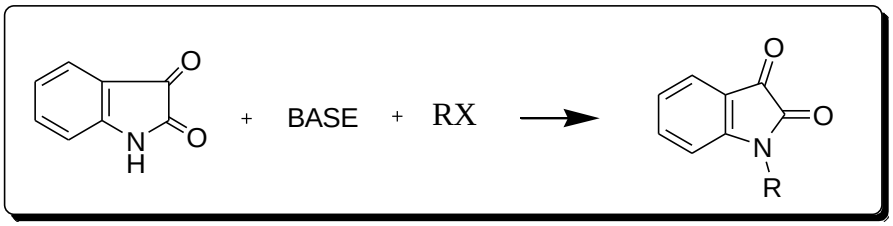
Figure (1.6): Tautomeric forms of isatin

1.3.5 General reaction of isatin

Isatin can undergo different types of reactions such as N-Alkylation, N-Arylation, N-Acylation, N-Sulphonation, Chlorination, Oxidation, Reduction, Pfitzinger reaction, Nitration and Benzylation.

1.3.5 .1 N-Alkylation

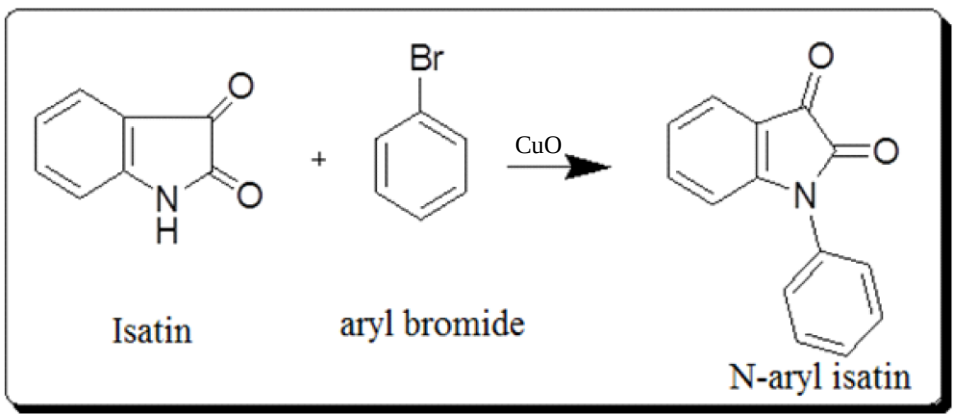
Alkylation of isatin is a synthetic viable reaction that use an alkylating agent, generally an alkyl halide, in the presence of a base . As illustrate in Scheme (1.10), the rate of reaction is depend on the reactivity of the alky halide used and so the reactions with more reactive alkyl halides require less time for completion [74,75].



Scheme (1.10): N-Alkylation of isatin

1.3.5.2 N-Arylation

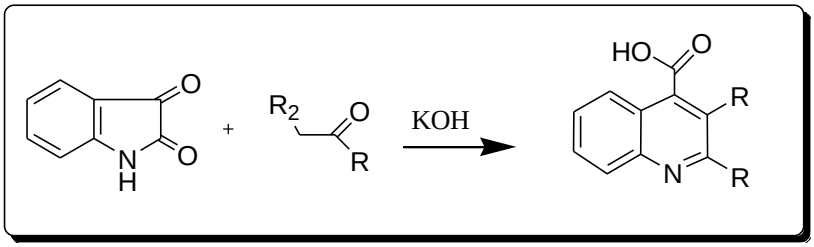
N-Arylisatin form is prepared from the reaction of isatin with isatin triphenyl bismuth actetate ($Ph_3Bi(OAc)_2$ and copper oxide (CuO) under inert atmosphere or from arylbromide and copper oxide, as illustrate in Scheme (1.11) [76].



Scheme (1.11):* N-Arylation *of isatin

1.3.5.3 Pfitzinger reaction

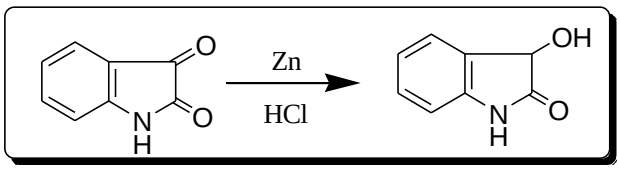
Isatin is reacted with a carbonyl compound in presence of a base givinig substituted quinoline-4- carboxylic acid [77], as illustrate in Scheme (1.12) .



Scheme (1.12): quinoline-4- carboxylic acid

1.3.5 .4 Reduction

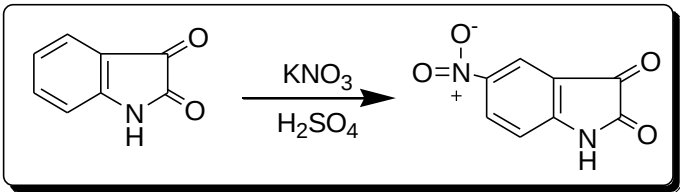
Isatin undergo reduction in presence of reducing agent such as Zn and HCl to yield 3-hydroxy-1, 3- dihydro-2H-indol-2-one , as illustrate in Scheme (1.13) [64].



Scheme (1.13): show reduction of isatin

1.3.5. 5 Nitration

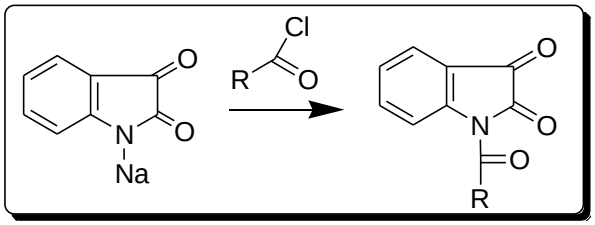
5-Nitroisatin is produced by adding KNO_3 and con. H_2SO_4 drop wise to a solution of isatin at 0-5 ^{0}C over a time period of 1 h, as illustrate in Scheme (1.14) [78].



Scheme (1.14): show nitration of isatin

1.3.5.6 N-Acylation

Many methods have been devised for the N-Acylation of isatins. These derivatives are commonly synthesized from the reaction of the sodium salt of isatin with acyl halides or sulphates, as illustrate in Scheme (1.15) [79].

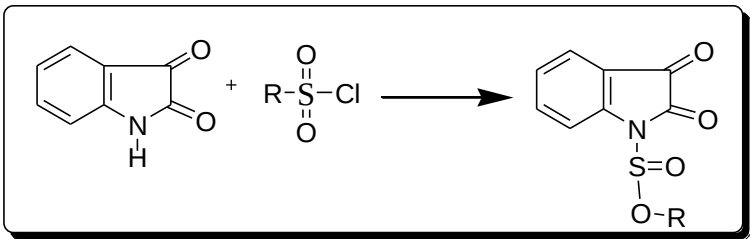


Scheme (1.15): show N-Acylation of isatin

1.3.5.7 N-Sulfonylation

The reaction between sulfonyl chloride and isatin yields N-sulphonylisatin [80] as illustrate in Scheme (1.16) .

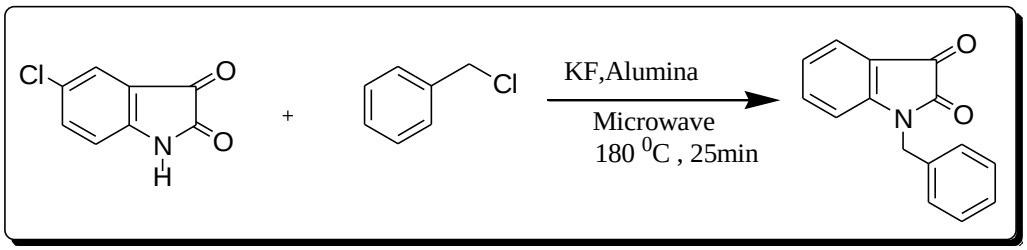
.



Scheme (1.16): show N-Sulfonylation of isatin

1.3.5.8 N-Benzylation

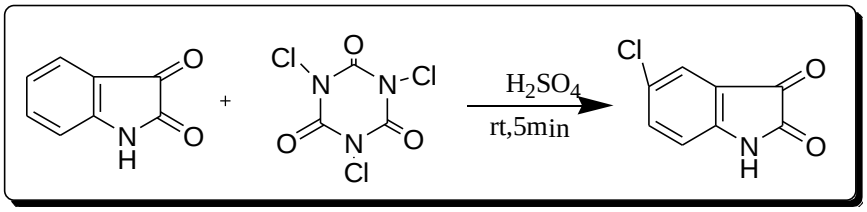
N-Benzylation reaction of isatin is achieved by the reaction of isatin with chlorobenzyl or bromobenzyl under microwave irradiation or solid support of KF/alumina [81] as illustrate in Scheme (1.17) .



Scheme (1.17): show N-Benzylation of isatin

1.3.5.9 Chlorination

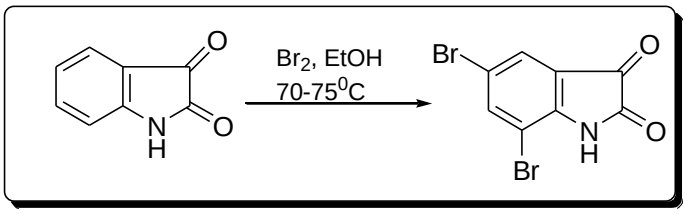
Chlorination of isatin was done by the reaction of N-Chloramide or N-Chlorimide and N-Chlorosaccharide in a heterogenous medium. It occurs at C-5 position [82] as illustrate in Scheme (1.18).



Scheme (1.18): show Chlorination of isatin

1.3.5.10 Bromination

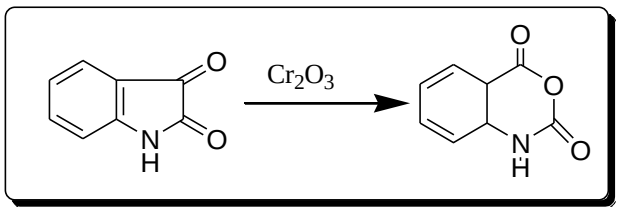
The halogenated derivatives of isatin, especially the bromosubstituted ones, are found to exhibit anti-cancer activity against the human lymphoma cell line [83]. Several synthetic methods have been reported for the mono-, di-, and tribromo substituted derivatives. **Vine et al.** have reported one such synthesis where different conditions of bromination produced different substituted bromo derivatives such as 5,7-dibromisatin as illustrate in Scheme (1.19) , 5,6-dibromo, and 5,6,7-tribromisatin [84]. The 5,7-dibromo derivative was synthesized by refluxing isatin in ethanol and adding bromine drop-wise, while maintaining the temperature at 70-75 ^{0}C [85].



Scheme (1.19): Synthesis of the 5,7-dibromisatin derivative

1.3.5.11 Oxidation

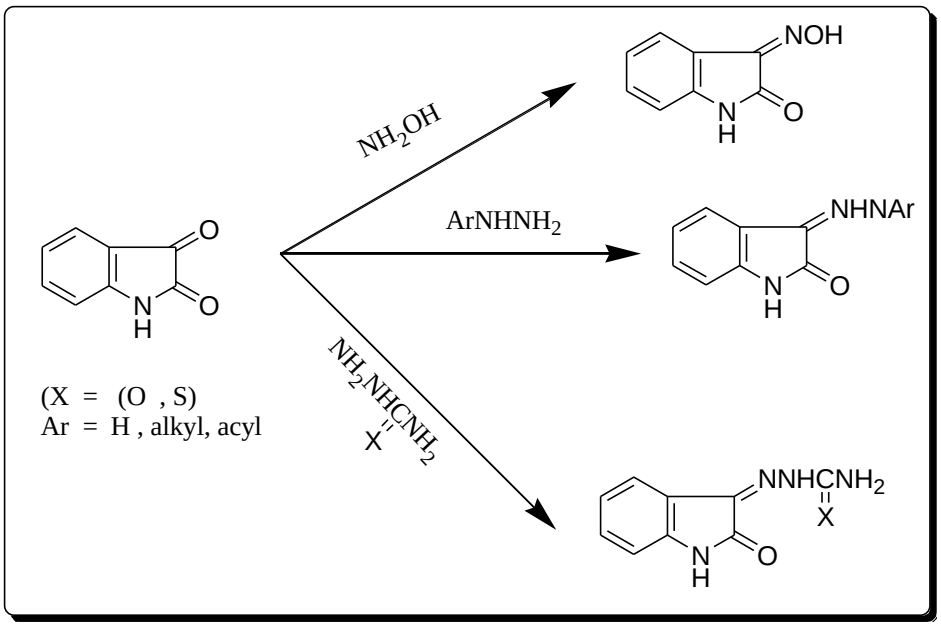
Isatin in presence of chromium trioxide is converted into isatoic anhydride, the anhydride form of isatin as illustrate in Scheme (1.20). The oxygen atom inserted between two adjacent carbonyl group is obtained from the oxidizing agent. This should not cause significant decomposition to the system [86]. Oxidation Isatoic anhydride , an abundantly employed compound in herbicide production and in medicinal chemistry.



Scheme (1.20): Organoselenium-catalyzed oxidation of isatin to isatoic anhydride.

1.3.5.12 Reactions of carbonyl groups

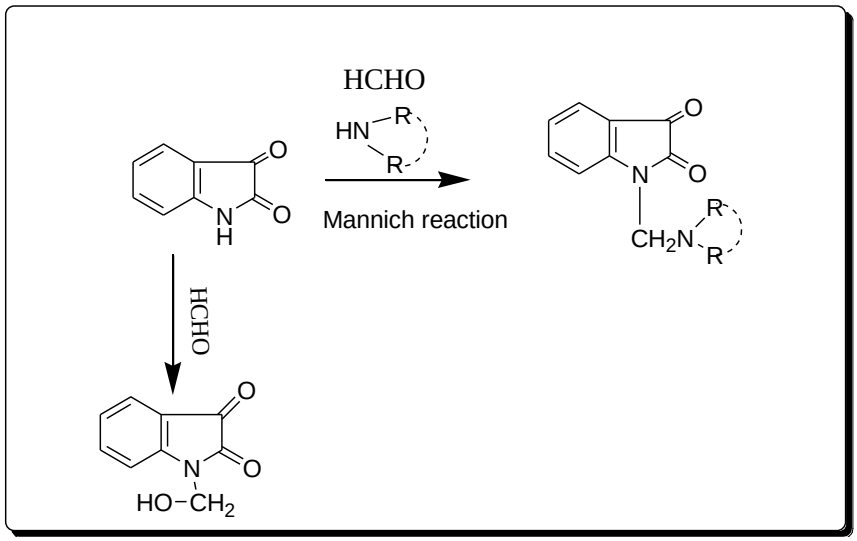
The reactive carbonyl group at the position-3 undergo typical reactions with the ketonic reagents such as hydroxylamine, phenyl hydrazine and semicarbazide as illustrate in Scheme (1.21) . The carbonyl group at position-2 is less active and has less ketonic character compared with carbonyl group at C_3 [87].



Scheme (1.21): show reactions of carbonyl groups.

1.3.5.13 Mannich reaction

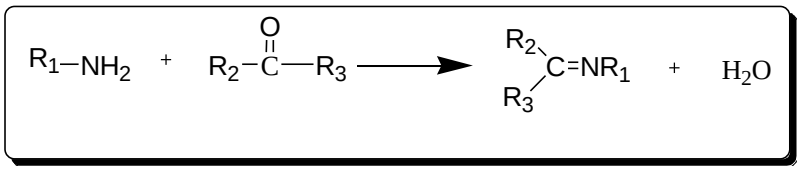
Isatin reacts with formaldehyde and a variety of amines in the Mannich reaction to produce their respective Mannich bases, in the absence of an amine, isatin and substituted isatin with formaldehyde give [88] hydroxymethyl isatins as illustrate in Scheme(1.22).



Scheme (1.22): show mannich of isatin

1.3.5.14 Schiff base

A Schiff base is usually formed by condensation of an aldehyde or ketone with a primary amine as illustrate in Scheme (1.23) [89].



Scheme (1.23) : The reaction of Schiff base

where R_1 , R_2 and R_3 are aryl, alkyl, cycloalkyl or heterocyclic groups that are of different substitutes [90] . Present day chemists still prepare diverse Schiff base ligands referred . These compounds are also know as anils, imines or azomethines. They were first reported by Hugo Schiff in 1864 [91]. Presence of aryl substituents in Schiff bases usually ease the synthesis and stability of Schiff bases while Schiff bases containing alkyl are relatively unstable. The reactivity of aldehydes are generally faster than those of the ketones in condensation reaction, there by resulting in the formation of Schiff bases with a centre that are less steric than the ketones, relatively unstable and freely polymerizable [92]. Schiff bases bonding ability depends on the nature of atoms that act as coordination site, such as N, O, and S, the electronegativity and steric factors. Schiff base acts as active ligands due to the presence of low electronegativity of nitrogen, N of the azomethine group (C=N), lone pair of electrons on the nitrogen atom, electron donating character of the double bond [93], and thus bring about stability in metals several oxidation states, regulating metal activities for variety of useful biological, catalytic conversions. Several studies showed that the presence of a lone pair of electrons in sp^2 hybridized orbital of nitrogen atom of the azomethine group is considerable chemical and biological importance [94]. They are profoundly studied due to their contribution in

developing complexes bearing significant biological activities as per their properties of synthetic flexibility, selectivity and sensitivity towards the central metal atom [95]. Schiff bases are significant class of compounds in medicinal and pharmaceutical fields as they have also been shown to exhibit wide-range of biological activities, such as antifungal [96], antibacterial [97], anti-inflammatory [98], anticancer [99], antimicrobial [100,101], antiviral [102],antiproliferative [103], analgesic [104], Antioxidants [105] .They are considered as are crystalline or oily substances, insoluble in water and soluble in organic solvents. They are weak bases, forming salts with acids in an anhydrous medium; in aqueous acid solutions, they undergo hydrolysis to yield an amine and aldehyde. The majority of Schiff bases are stable in alkaline solutions. Schiff bases are valuable intermediate products of organic synthesis, for example, in the preparation of secondary amines and various heterocyclic compounds. The Schiff bases known as azomethines dyes are used in dyeing acetate and synthetic fibers; and also used in coloring photography to reduce the photosensitivity of photographic emulsions [106].

1.3.5.14.1 Schiff Base metal complexes

Transition metal complexes derived from the Schiff base ligands with biological activity have been widely studied. Many Schiff base complexes with transition metals showed diverse biological and pharmaceutical activities. Schiff bases, having azomethine group and their metal complexes are widely used in industrial application and also reveal a wide range of biological activities. Because of the relative easiness of preparation, synthetic flexibility, and the special property of C=N group, Schiff bases are generally excellent chelating agents, form a five or six membered ring with the metal ion [107]. Schiff base ligands

are able to coordinate with varies transition metal and to stabilize them in various oxidation states. Schiff bases ligands with a variety of donor atoms exhibiting interesting coordination modes towards transition metals , and azomethine linkage is responsible for the biological activities [108]. The Schiff bases and their metal complex are also applied in biomimetic catalytic reactions, materials chemistry and industry [109]. The complexes of Schiff base have also gained attention as stereo chemical models in transition metal coordination chemistry due to their structural variety [110]. A number of transition metal schiff base complexes were studied extensively and showed variable coordination geometry and flexible oxidation states . The ions or molecules surrounding the metal are called ligands. Ligands are generally bound to a metal ion by a coordinate covalent bond by donating electrons from a lone electron pair into an empty metal orbital and thus said to be coordinated to the ion. The coordination chemistry can be classified according to the nature of the ligands [111]. The Schiff base ligands form stable complexes with different transition metal ions. The transition metal complexes are in the investigated because to their promising applications in different areas from natural sciences to material science. The mixed ligand complexes formation was important aspect in inorganic and analytical chemistry. Schiff base is common ligands in coordination chemistry. Schiff base ligands are easily prepared by the condensation between aldehydes and amines. The imine nitrogen is basic and exhibits pi-acceptor properties**.** Schiff base complexes can be classified in a different ways: Mononuclear, binuclear and Polynuclear on the basis of number of metal ions/atom present and as monodentate, bidentate and polydentate ligands. The basicity of the schiff base also play a key role in the formation and stabilization of the complexes. Development of a new chemotherapeutic Schiff bases and their metal complexes is now attracting the attention of

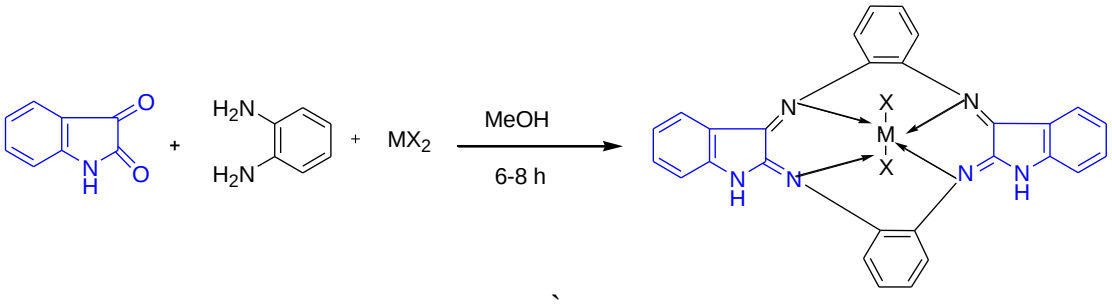
medicinal chemists [112]. The principal interaction between the inhibitor and the metal surface is chemisorption, the inhibitor molecule should have centers capable of forming bonds with electrophile and the inhibitor acts as a Lewis base. Nucleophilic centers, such as oxygen and nitrogen atoms of the protective compound have free electron pairs which are readily available for sharing together with the atoms of the benzene rings, they create multiple absorption sites for the inhibitor thus enabling stable monolayer formation . Metal complexes of Schiff bases containing heterocyclic amine rings provide molecules with larger numbers of donor atoms for coordination with metal ions[113].

1.3.5.14.2 Uses of Schiff bases complexes:

Schiff bases and their complexes are of improtant attention because of their biological activity as anti-tumor, antibacterial, fungicidal, antidepressants, antiphlogogistic, nematocide, anti-carcinogenic and catalytic activity [114, 115]. The microorganisms adsorb metal ions on their cell walls and as a result respiration processes of cells disturbed and protein synthesis is blocked which is the require for further growth of the organisms. Membrane of Gram-negative bacteria is surrounded by an outer membrane containing lipopolysaccharides. Schiff base metal complexes are able to combine with the lipophilic layer in order to enhance the membrane permeability of the Gram-negative bacteria. The lipid membrane surrounding the cell favours the passage of only lipid soluble materials; thus the lipophilicity is an important factor that controls the antimicrobial activity. The increase in lipophilicity enhances the penetration of Schiff base and its metal complexes into the lipid membranes and thus restricts growth of the organism [116].

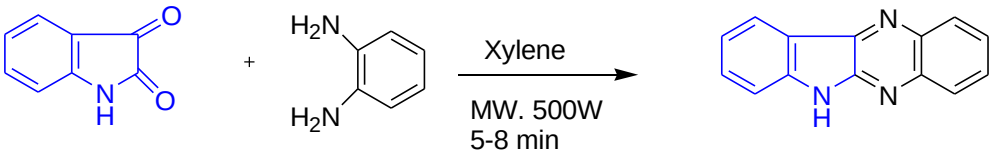
1.4 Literature review

Singh, et al [117] . synthesized novel series of complexes of the type $[M(C_{28}H_{18}N_6)X_2]$, where M=Co(II), Ni(II), Cu(II) or Zn(II) and X = Cl , NO_3 or CH_3COO, were synthesized by template condensation of isatin and 1,2-diaminobenzene in methanolic medium as illustrate in Scheme (1.24).



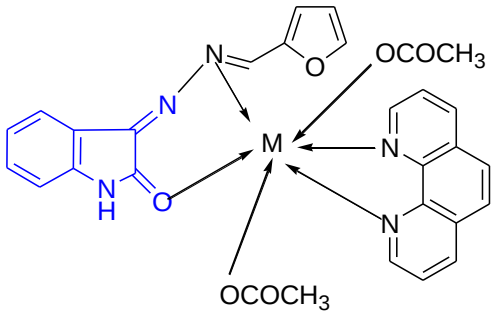
Scheme (1.24): Proposed structure of the synthesized complexes.

Bajpai, et al [118]. used isatin with o-phenylenediamine readily gives rise to quinoxaline under controlled microwave irradiation in xylene as illustrate in Scheme (1.25) .



Scheme (1.25): Synthesis of indole [2.3-b] quinoxaline

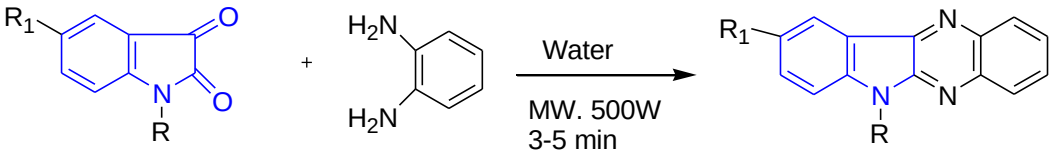
Christiea, et al [119] . synthesized a schiff bases, obtained by the condensation of isatin monohydrazone with furfuraldehyde (L_1) and its Co(II), Ni(II), Cu(II) and Zn(II) complexes as well as its mixed ligand complexes with 1,10-phenonthroline were synthesized as illustrate in Figure (1.7).



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

Figure (1.7): Synthesis of nickel,cobalt, copper and zinc and complexes of ligand

Bajpai, et al [120]. used isatin derivatives with o-phenylenediamine in water under microwave irradiation has been reported as illustrate in Scheme (1.26). The presented method is mild, environmentally friendly, inexpensive and highly effective to give the products in good to excellent yields.

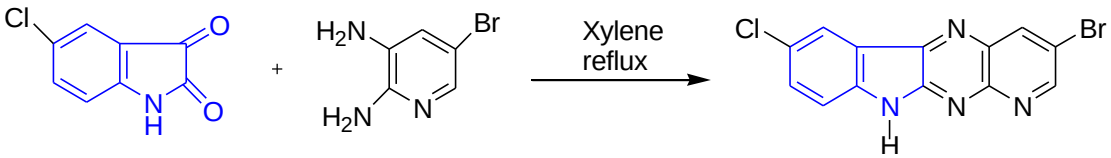


R_1= Cl, H

R=CH_2CH_2CH, CH_2Ph, $COCH_3$

Scheme(1.26): The reaction consists in the condensation of the Benzene-1,2-diamine groups on the C2 and C3 carbonyl functions of isatin.

Kaur, et al [121] . the cyclocondensation of 5-Chloro isatin derivatives by the action of diamino-5-bromo-pyridine to give heterocyclic possessing Pyrido [2,3-b] Pyrazines, in a moderate to good yield as illustrate in Scheme (1.27) .



Scheme (1.27): Synthesis of 3-Bromo-7-chloro-10H-pyrido[3,2:5,6]pyrazino[2,3-b]indole

Al-Azawi [122] . an isatin-aniline compound, namely ethyl 4-amino-N-(3-isatinyl) benzoate , was successfully synthesized in high yield 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 as illustrate in Figure (1.8) .

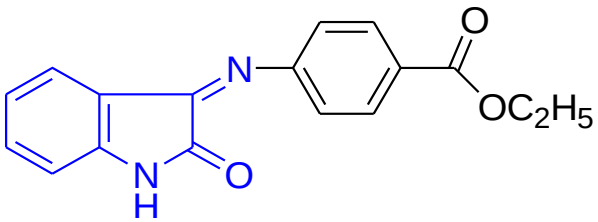


Figure (1.8): Synthesis of the inhibitor (ethyl 4-amino-N-(3- isatinyl)benzoate.

Youseftabar-Miri [123] . egg shell has been utilized as a natural, green, reusable and eco-friendly reagent for the synthesis of spiro[4H-pyran-oxindole] derivatives by one-pot multicomponent reaction of isatins, 1,3-diketones, and malononitrile/ ethyl cyanoacetate as illustrate in Figure (1.9) .

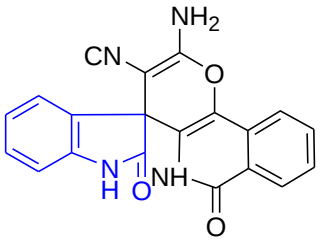
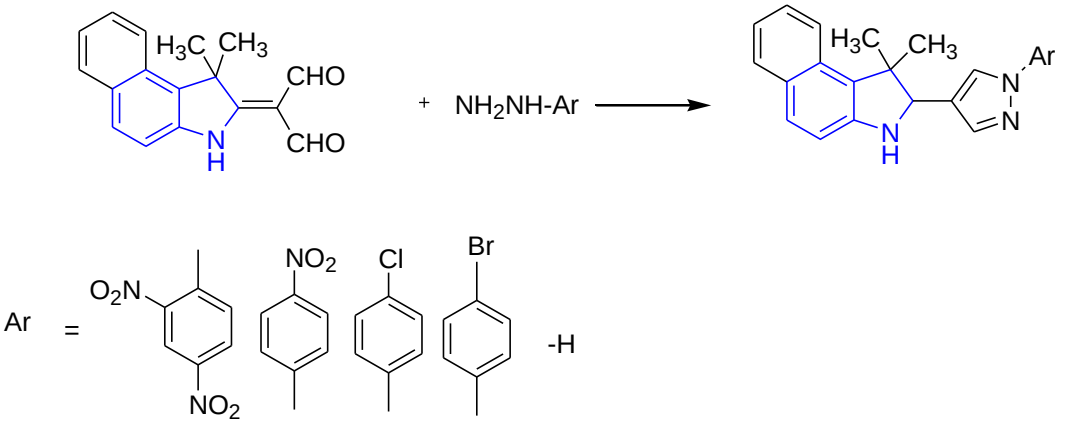


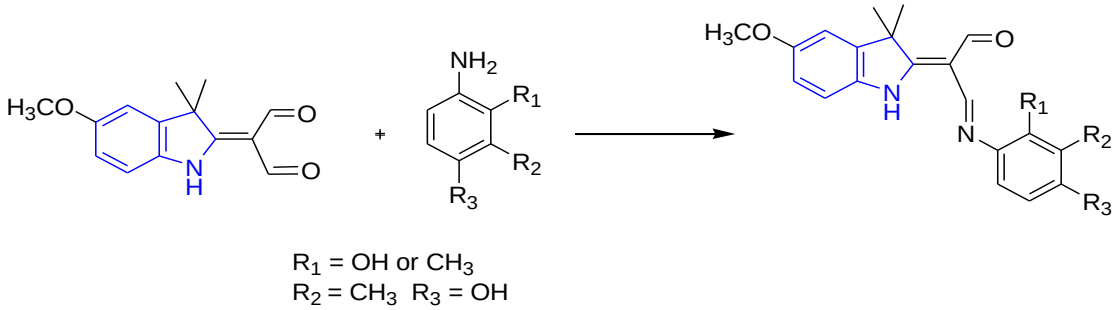
Figure (1.9): structure of spiro[4H-pyra]n-oxindole

Ali [124] . focused on synthesis of new series of pyrazole derivatives by refluxing hydrazine derivatives with 2-(1,1-Dimethyl1,3-dihydro-benzo[e]indol-2-ylidene) malonaldehydewithphosphoryl chloride in anhydrous illustrate in Scheme (1.28) .



Scheme(1.28) synthesis of series of pyrazole derivatives

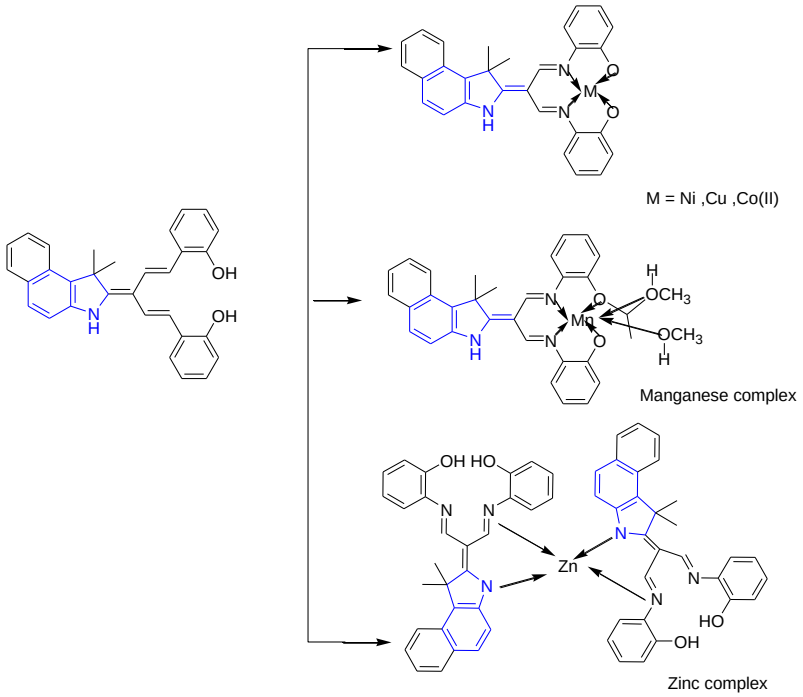
Nafia, et al [125] . synthesized three new Schiff Bases by reaction of 2-(5-methoxy-3,3-dimethyl-1,3-dihydro-indol-2- ylidene)-malonaldehyde with substituted aniline illustrate in Scheme (1.29) .



R_1 = OH or CH_3
R_2 = CH_3 R_3 = OH

Scheme (1.29): The synthetic pathway to a new Schiff bases

Hameed, et al [126]. synthesized ligand 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e] indol-2-ylidene) propane-1,3-diylidene) bis(azanylylidene) diphenol which has been synthesize by the condensation reaction of 2-hydoxy aniline with 2-(1,1-dimethyl-1,3-dihydro-2H-benzo[e]indol-2-ylidene) malonaldehyde in ratio 2:1. was 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 illustrate in Scheme (1.30) .



Scheme (1.30): Synthetic pathway to nickel, cobalt, cupper, manganese and zinc complexes

1.5 Aim of the work

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 synthesise a new chain of indole derivatives and preparing the complexes through them. In addition, investigate most of these compounds by defining the properties of the compound by melting point, TLC, spectrum UV-VIS, FT-IR and ^{1}H-NMR spectroscopy. Characterization of exterior complexes with melting point, percentage of metallic analysis using flame atomic absorption, infrared spectroscopy, visible UV spectroscopy, magnetic susceptibility, initial CHNS analysis, and electronic conductivity measurements. Finally, investigation the antifungal activity of compounds and complexes.

Chapter Two

Experimental Work

2.1 Materials

All materials and solvents used in this study were purchased from different companies, as listed in Table (2.1). These materials used as it is without any purification or modification .

Table (2.1) Chemicals and solvents used in this work and their suppliers:

NO.	Chemicals	Supplied from	Purity
1	4-chloro benzaldehyde	Aldrich	97%
2	4-chloro-o-phenylenediamine	Aldrich	97%
3	4-hydroxy benzaldehyde	CHD	99%
4	4-hydroxy-3-methoxy-benzaldehyde	Aldrich	99%
5	4-methyl-o-phenylenediamine	Fluka	98%
6	4-nitro benzaldehyde	Aldrich	98%
7	4-nitro-o-phenylenediamine	Aldrich	98%
8	Benzene	United kingdom	99.7%
9	Benzene-1,4-dicarbaldehyde	Aldrich	99%
10	Choro acetyl chloride	Aldrich	99%
11	Coblt (II) chloride hexahydrate	Riedial-Dehaen	99%
12	Dimethylsulfoxide (DMSO)	BDH	98%
13	Ethanol	Scharlu	99.9%
14	Ethyl acetate	Aldrich	99%
15	Ethyl chloroacetate	Aldrich	99%
16	Glacial Acetic acid	BDH	99.9%
17	Hexane	BDH	99%
18	Hydrazine hydrate	Merck	80%
19	Isatin	Aldrich	99%
20	Nickel (II) chloride hexahydrate	Fluka	99%
21	platinum (IV) chloride hexahydrate	Aldrich	99%
22	sodium bicarbonate	BDH	99.9%
23	Triethyl amine	Fluka	99%
24	Zinc (II) chloride	Aldrich	99.9%

2.2 Instruments

The following measurements were used to characterize the compounds and the complexes.

2.2.1 The Melting Point Measurements

The melting points of the compounds and the metal complexes was determined by open capillary tube in the stuart smpto electronic apparatus, at Department of Chemistry, College of Science, University of Diyala .

2.2.2 Antifungal Activity

Antifungal activity was tested by University of Diyala / College of Science / Department of Biology.

2.2.3 Electronic Spectra (U.V-Visible)

The electronic spectra of the some compounds and the metal complexes were obtained by using UV-Visible (V-650)/JAPAN spectrophotometer type Cary 100 at range (800-200) nm, with quartz cell of (1.0 cm) length and the concentration of ($1\times 10^{-3}mol^{-1}$), at Department of Chemistry, College of Science, University of Diyala .

2.2.4 Fourier Transform Infrared Spectroscopy (FT-IR)

Infrared spectra of the prepared compounds were recorded in (KBr) disc by using PERKIN ELMER SPEACTRUM-65 / Germany at Chemistry Department, College of Science, Diyala University (FT-IR) spectrophotometer in the range (400 - 4000) cm^{-1}. And FT-IR spectra of complexes were recoded in (CSI) disc by using PERKIN ELMER SPEACTRUM-65 / Germany at Chemistry Department, College of Science, Diyala University (FT-IR) spectrophotometer in the range (200 - 4000) cm^{-1}.

2.2.5 Nuclear Magnetic Resonance Spectrometer (NMR).

^{1}H NMR spectra were recorded on a Bruke 400 MHz spectrometer in Jordan, University of Science and Technology, College of Science, Irbid City.

2.2.6 Elemental Analysis (C.H .N)

The elemental analysis (C.H.N) of the ligand and their complexes was carried out by Eager 300 for EA1112 instrument in central Device labortoray College of science, University of Tehran.

2.2.7 Metal Analysis

The metals percentage in the complexes was measured using atomic absorption technique by Shimadzu Atomic Absorption 680 Flam Spectrophotometer for the determination of (platinum , Cobalt, Nickel and Zinc) metal ions. The measurements were carried out at the laboratories of Chemistry Department College of Science, Mustansiriyah University

2.2.8 Magnetic Susceptibility

The magnetic susceptibility in 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 , ALmustansiriyah University.

2.2.9 Conductivity Measurements

Electrical conductivity measurements (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:

$$[\Lambda_m = 1000k/c]$$

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

2.2.10 Utra Violet 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 Chemistry Department, College of Science, University of Diyala.

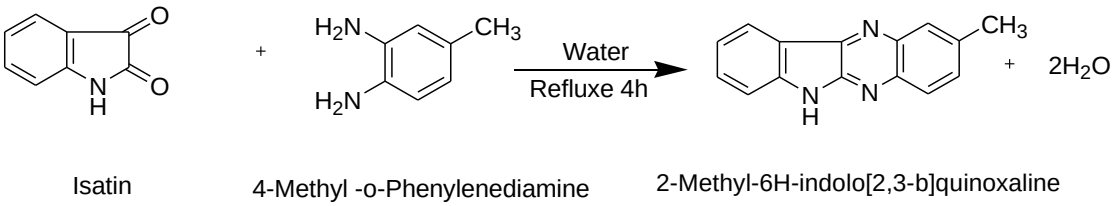
2.2.11 Rotary vacuum evaporator

The solvents were evaporated by using Heldove apparatus, Heivap, Germany at Department of Chemistry , College of Science University of Diyala.

2.3 Synthesis of heterocyclic the compounds.

2.3.1 Synthesis of 2-methyl-6H-indolo[2,3-b]quinoxaline[A_1]

Scheme (2.1) shows the chemical reaction and the operating conditions for synthesis process of 2-methyl-6H-indolo[2,3-b]quinoxaline.



Isatin 4-Methyl -o-Phenylenediamine 2-Methyl-6H-indolo[2,3-b]quinoxaline

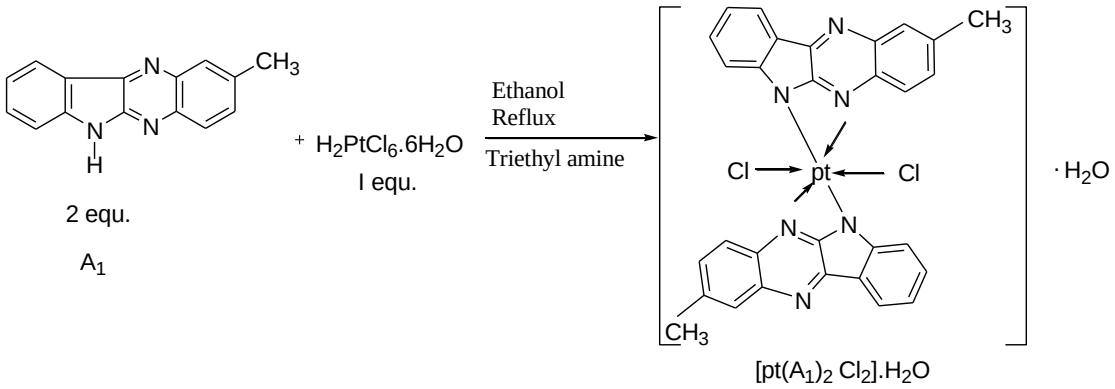
Scheme (2.1): The synthetic pathway of 2-methyl-6H-indolo[2,3-b]quinoxaline

Isatin (1.71 g, 11.6 mmol) was dissolved in refluxing aqueous sodium bicarbonate solution (2.38 g, 28.3 mmol in 160 ml water). 4-methyl-o-Phenylenediamine (1.6 g, 13.2mmol) was added and the mixture was refluxed 4 h . The completion of the reaction was checked by using T.L.C (mobile phase :ethyl acetate:hexane 1:3). After cooling to room temperature 25 ° C, the solution was acidified with acetic acid and left to stay overnight. The solution is then deposited, filtered and washed with water, the precipitate appeared was dried and recrystallized from ethanol to give pure A_1.Yield 93% ,m.p.76-78°**C.**

2.3.1.1 Synthesis of platinum (IV) complex $[pt(A_1)_2Cl_2].H_2O$

(0.11g, 0.21mmol) of $H_2PtCl_6.6H_2O$ was dissolved in (20 ml) of ethanol .The solution was then added into a solution of (A_1) ligand (0.1g, 0.42 mmol) in the same solvent(20 ml) shown in Scheme (2.2). The mixture was placed in 250 ml round bottom flask, and few drops of triethylamine were added . After that the mixture was refluxed on a water bath at 78°C. A blue precipitate was formed from Pt complex after 45 min of the reaction starting. The refluxing was continued for 2 h, then cooled to room temperature , the reaction volume was reduced to one

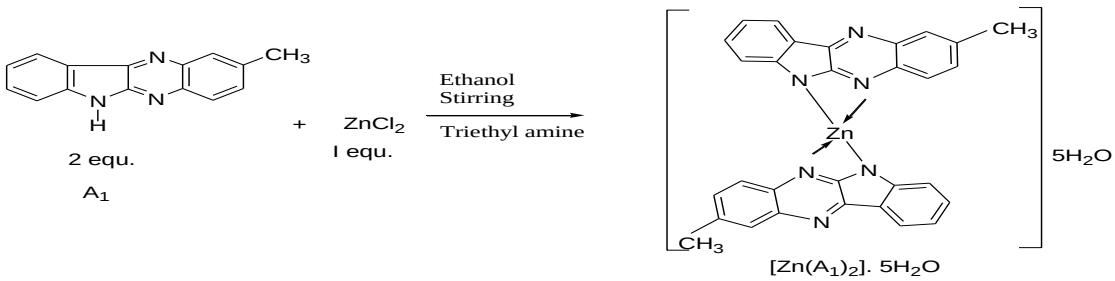
third . The precipitate was filtered, washed with water and dried in an oven at 50°C. Yield 90% , m.p 215-217°C.



Scheme (2. 2): Synthesis of platinum complexes of (A_1) ligand

2.3.1.2 Synthesis of zinc (II) complex $[Zn(A_1)_2].5H_2O$

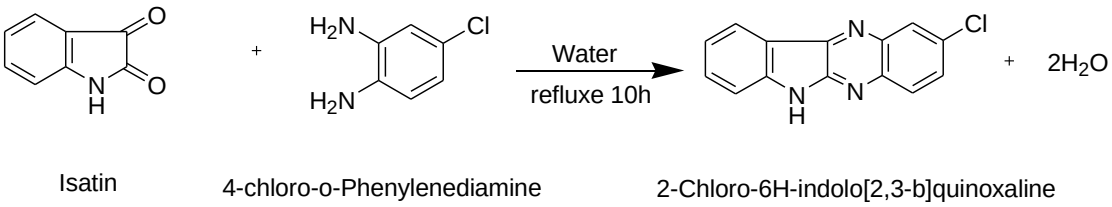
(0.028g, 0.21mmol) of $ZnCl_2$ was dissolved in (20 ml) of ethanol . The solution was then added into a solution of (A_1) ligand (0.1g, 0.429 mmol) in the same solvent(20 ml) Scheme (2.3) . The mixture was placed in 250 ml round bottom flask, and few drops of triethylamine were added and the mixture was refluxed on a water bath at 78°C.A brouwn precipitate was formed from Zn complex after 45 min of the reaction starting. The refluxing was continued for 2 h, then cooled at room temperature . The solid precipitate was filtered and washed with water and dried in an oven at 50°C. Yield 60% , m.p. 138-140°C.



Scheme (2.3): Synthesis of zinc complexes of (A_1) ligand

2.3.2 Synthesis of 2-chloro-6H-indolo[2,3-b]quinoxaline [A_2].

Scheme (2.4) shows the chemical reaction and operating conditions for synthesis process of 2-chloro-6H-indolo [2,3-b]quinoxaline that written in short as A_2 .



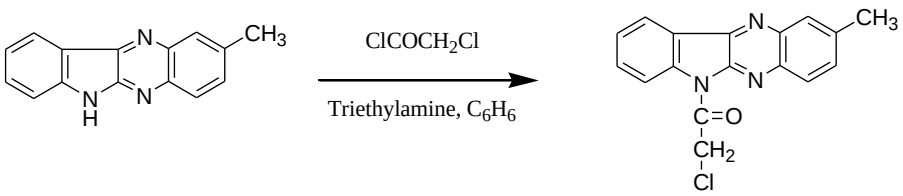
Isatin 4-chloro-o-Phenylenediamine 2-Chloro-6H-indolo[2,3-b]quinoxaline

Scheme (2.4): The synthetic pathway of 2-chloro-6H-indolo[2,3-b]quinoxaline

Isatin (1.71 g, 11.6 mmol) was dissolved in refluxing aqueous sodium bicarbonate solution (2.38 g, 28.3 mmol in 160 ml water). 4-chloro-o-phenylenediamine (1.88 g, 13.2 mmol) was added and the mixture was refluxed for 4h . The completion of the reaction was checked by using T.L.C (mobile phase :ethyl acetate:hexane 1:3). After cooling at room temperature 25 °C, the solution was acidified with acetic acid and left standing overnight. The solution is then deposited, filtered and washed with water, the precipitate appeared was dried and recrystallized from ethanol to give pure A_2.Yield 51% ,m.p. above 300 ° **C.**

2.3.3 Synthesis of 2-Chloro-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_3] .

Scheme (2.5) shows the chemical reaction and operating conditions for synthesis process of 2-Chloro-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone that written in short as A_3.



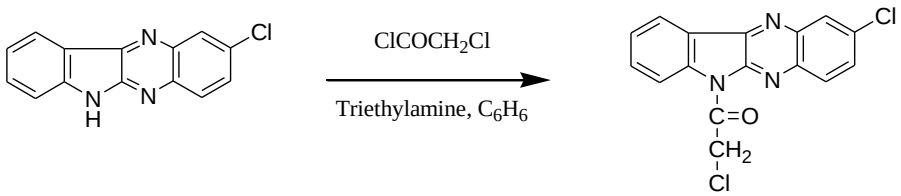
2-methyl-6H-indolo[2,3-b]quinoxaline 2-chloro-1-(2-methyl-indolo[2,3-*b*]quinoxalin-6-yl)-ethanone

Scheme (2.5): The synthetic pathway of* 2-*Chloro-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone

A mixture of 2-Methyl-6H-indolo[2,3-b]quinoxaline (0.25g,1.07 mmol) and triethylamine (0.108g,1.07 mmol) in 50 ml benzene, then add chloroacetyl chloride (0.121g,1.07 mmol) in 25 ml benzene drop by drop for about 30 min. Then the reaction mixture was stirred at room temperature for about 6 h and then refluxed for 10 h . Progress of the reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase. After the completion of reaction, the reaction mass was quenched in ice cold water and filtered, the precipitate appeared was dried and recrystallized from ethanol to give pure A_3.Yield 98% , m.p. 132-134°**C**.

2.3.4 Synthesis of 2-chloro-1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_4] **.**

Scheme (2.6) shows the chemical reaction and operating conditions for synthesis process of 2-chloro-1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-ethanone that written in short as A_4.



2-chloro-6*H*-indolo[2,3-*b*]quinoxaline

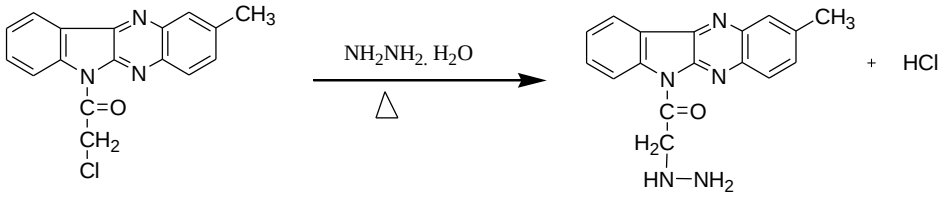
2-chloro-1-(2-chloro-indolo[2,3-*b*]quinoxalin-6-yl)-ethanone

Scheme (2.6): The synthetic pathway of-chloro-1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-ethanone

A mixture of 2-chloro-6H-indolo[2,3-b]quinoxaline (0.22g,0.867 mmol) and triethylamine (0.08g,0.867 mmol) in 50 ml benzene, chloroacetyl chloride (0.09g,0.867 mmol) in 25 ml benzene was added drop by drop for about 30 min. Then the reaction mixture was stirred at room temperature for 6 h and refluxed for 10 h . The progression of the reaction was monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase. After the completion of reaction, the reaction mass was quenched in ice cold water and filtered. The precipitate aproduced was dried and recrystallized from ethanol to give pure A_4. Yield 76% , m.p. a bove300° **C.**

2.3.5 Synthesis of 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_5]

Scheme (2.7) shows the chemical reaction and operating conditions for synthesis process of 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone that written in short as A_5.



2-chloro-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone

2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone

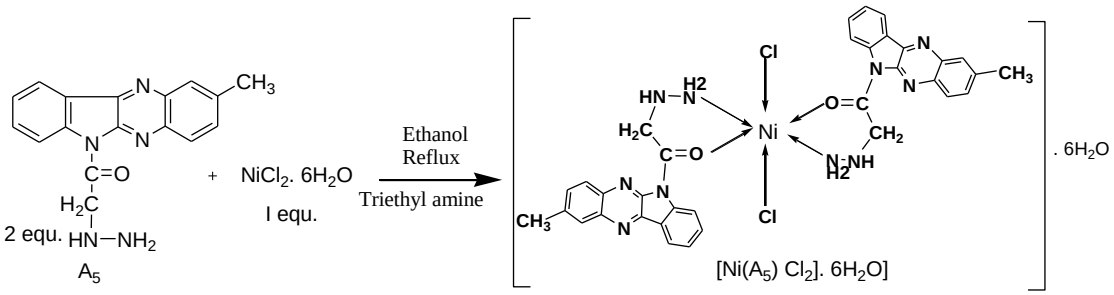
Scheme (2.7): The synthetic pathway of 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone

A mixture of 2-Chloro-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-**.** ethanone (0.5 g, 1.7mmol) in 50 ml ethanol ,hydrazine hydrate (0.15 g, 3mmol) was added with continuous stirring and the resulting mixture was refluxed on water bath for 7 h. Progress of the reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase. After cooling the mixture, precipitate was formed. The precipitate appeared was filtered, dried and recrystallized from ethanol to give A_5.Yield 83% m.p. a bove 300°**-C.**

2.3.5.1 Synthesis of nickel (II) complex $[Ni(A_5)_2Cl_2].6H_2O$

(0.1g, 0.327 mmol) of (A_5) ligand was dissolved in hot ethanol (20 ml) then a few drops of triethylamine was added into the solution

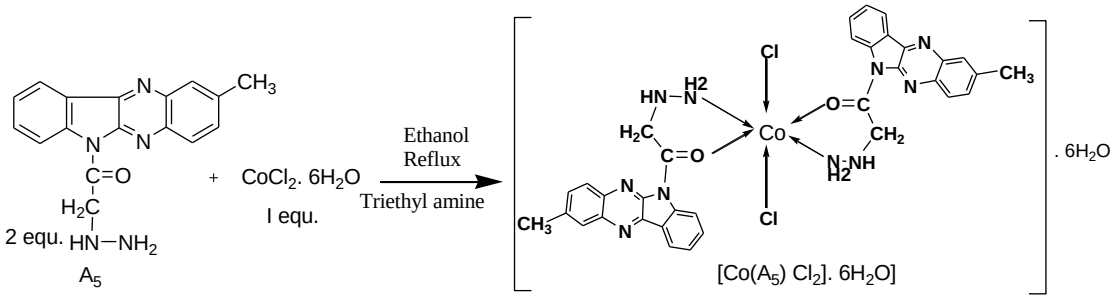
followed by the addition (0.038g,0.159mmol) of $NiCl_2.6H_2O$ was dissolved in (10 ml) of absolute ethanol shown in Scheme (2.8). The solution was refluxed for 3h where upon the solid of the product green precipitated . Then the mixture was cooled to room temperature and the precipitate was filtered off, washed with water and dried in an oven at 50°C. Yield 79% , m.p above300°C**.**



Scheme (2.8): Synthesis of nickle complex of (A_5) ligand

2.3.5.2 Synthesis of cobalt (II) complex $[Co(A_5)_2Cl_2].6H_2O$

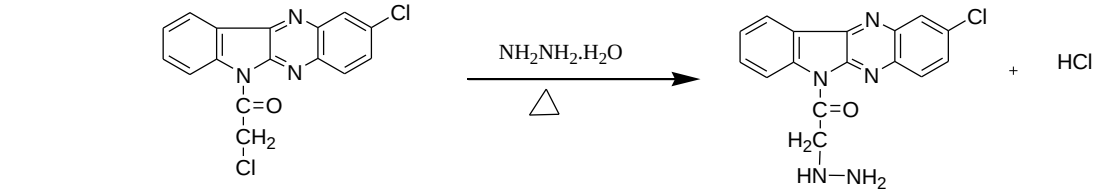
(0.039 g, 0.163 mmol) of $CoCl_2.6H_2O$ was dissolved in ethanol (10 ml). The solution was then added into a solution of ligand [A_5] (0.1 g, 0.327mmol) in the same solvent (20ml). and few drops of triethylamine was added and the mixture was refluxed for 3h Scheme (2.9) . The solvent was partially evaporated, whereupon a brownish solid precipitated. The precipitate was filtered off, washed with water and dried in oven at 50°C to give of the cobalt complex. Yield 80% , m.p above 300°C.



Scheme (2.9): Synthesis of coblt complex of (A_5) ligand

2.3.6 Synthesis of 1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-2-hydrazino-ethanone [A_6].

Scheme (2.10) shows the chemical reaction and operating conditions for synthesis process of 1-(2-Chloro-indolo[2,3-b]quinoxalin-6-yl)-2-hydrazino-ethanone that written in short as A_6.



2-chloro-1-(2-chloro-indolo[2,3-*b*]quinoxalin-6-yl)-ethanone

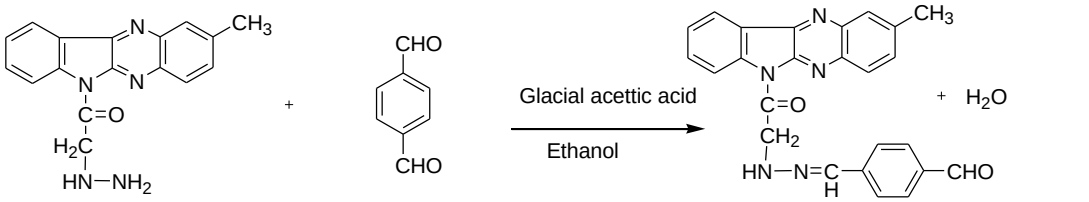
1-(2-chloro-indolo[2,3-*b*]quinoxalin-6-yl)-2-hydrazino-ethanone

Scheme (2.10): The synthetic pathway of-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-2-hydrazino-ethanone

A mixture of 2-Chloro-1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-ethanone (0.14g, 0.45mmol.) in absolute ethanol 50 ml, hydrazine hydrate (0.04g , 0.9mmol.) was added with continuous stirring and the resulting mixture was refluxed on a water bath for 10h. Progress of the reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase. After cooling the mixture, precipitate was formed. The precipitate was filtered, dried, and recrystallized from ethanol to give A_6. Yield 71%,m.p above 300°C.

2.3.7 Synthesis of 4-{[2-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-2-oxo-ethyl]-hydrazonomethyl}-benzaldehyde [A_7] .

Scheme (2.11) shows the chemical reaction and operating conditions for synthesis process of 4-{[2-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-2-oxo-ethyl]-hydrazonomethyl}-benzaldehyde that written in short as A_7 .



2-Hydrazino-1-(2-methyl-indolo[2,3-*b*]quinoxalin-6-yl)-ethanone

Benzene-1,4-dicarbaldehyde

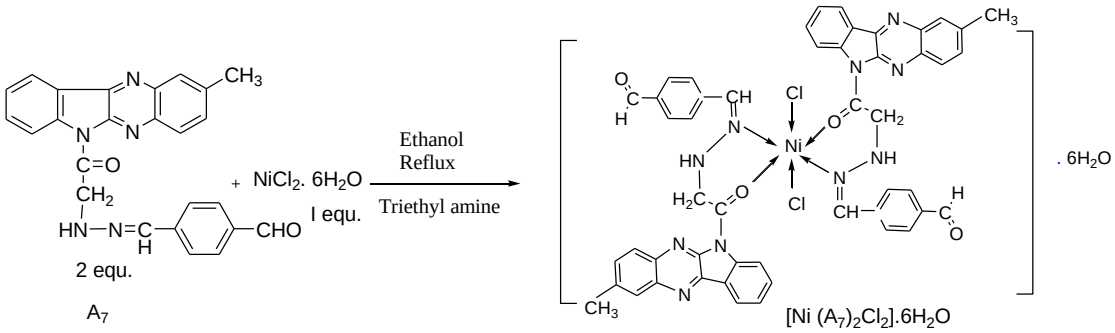
4-{[2-(2-Methyl-indolo[2,3-*b*]quinoxalin-6-yl)-2-oxo-ethyl]-hydrazonomethyl}-benzaldehyde

Scheme (2.11): The synthetic pathway of 4-{[2-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-2-oxo-ethyl]-hydrazonomethyl}-benzaldehyde

A mixture of 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone (0.2g., 0.65m mol) in ethanol 25ml. Benzene-1,4-dicarbaldehyde (0.087g.,0.65 mmol) was added with 3-4drops of glacial acetic acid. The reaction mixture was refluxed for 16 h in water bath. Progress of the reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase. Then cooled the resultant solution to room temperature. The precipitate formed, filtered, washed and recrystallized from (Ethanol/water) . Yield 94% , m.p a bove300° **C**.

2.3.7.1 Synthesis of nickel (II) complex $[Ni(A_7)_2Cl_2].6H_2O$

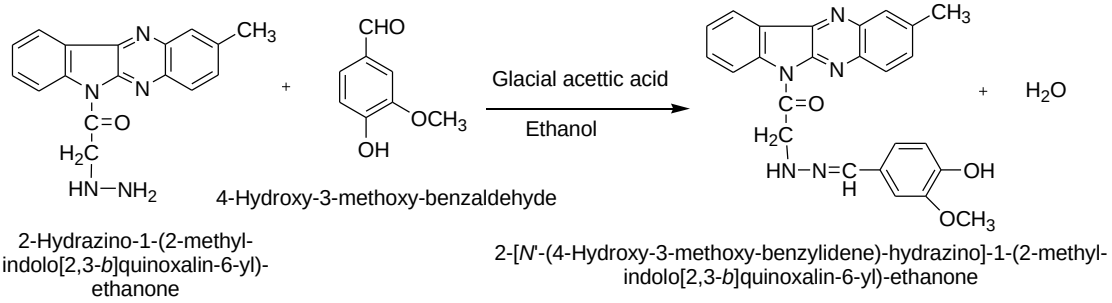
(0.1g, 0.237 mmol) of (A_7) ligand was dissolved in hot ethanol (20 ml) then a few drops of triethylamine was added into the solution followed by the adding (0.02g, 0.118mmol) of $NiCl_2.6H_2O$. The solution was then dissolved in (10 ml) of absolute ethanol Scheme (2.12). The solution was refluxed for 3h where upon the solid of the product green precipitated. Then the mixture was cooled to room temperature and the precipitate was filtered off, washed with water and dried in an oven at 50°C. Yield 91% , m.p above 300°C.



Scheme (2.12): Synthesis of nickle complex of (A_7) ligand

2.3.8 Synthesis of 2-[N'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_8]

Scheme (2.13) shows the chemical reaction and operating conditions for synthesis process of 2-[N'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone that written in short as **A_8**.

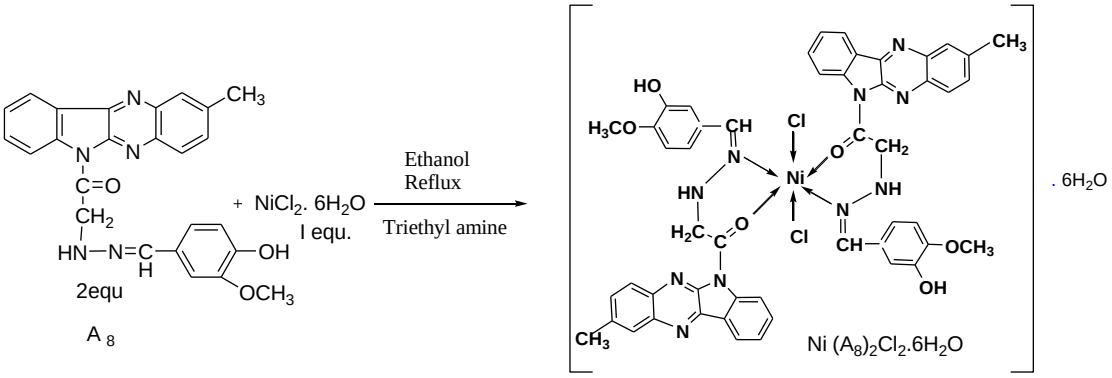


Scheme (2.13): The synthetic pathway of 2-[N'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone

A mixture of 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone (0.1g., 0.32m mol) in ethanol 20ml, then add 4-hydroxy-3-methoxy-benzaldehyde (0.049g, 0.32mmol) with 3-4drops of glacial acetic acid. The reaction mixture was refluxed for 15 h in water bath. Progress of the reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase. Then cooled the resultant solution to room temperature. The precipitate formed, filtered, washed and recrystallized from (Ethanol/water) . Yield 71% , m.p 138-140° **C**.

2.3.8.1 Synthesis of nickel (II) complex $[Ni(A_8)_2Cl_2].6H_2O$

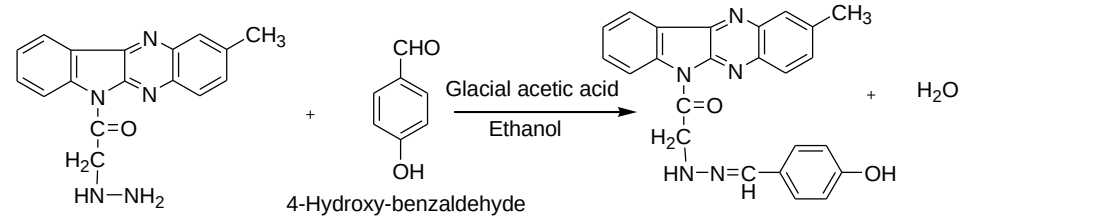
(0.1g, 0.227 mmol) of (A_8) ligand was dissolved in hot ethanol (20 ml) then a few drops of triethylamine was added into the solution followed by the addition (0.027g, 0.113mmol) of $NiCl_2.6H_2O$ was dissolved in (10 ml) of absolute ethanol Scheme (2.14) . The solution was refluxed for 3h where upon the solid of the product green precipitated. Then the mixture was cooled to room temperature and the precipitate was filtered off, washed with water and dried in an oven at 50°C. Yield 78% , m.p above 300°C.



Scheme (2. 14): Synthesis of nickle complex of (A_8) ligand

2.3.9 Synthesis of 2-[N'-(4-hydroxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_9]

Scheme (2.15) shows the chemical reaction and operating conditions for synthesis process of 2-[N'-(4-hydroxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone that written in short as **A_9**.



2-Hydrazino-1-(2-methyl-indolo[2,3-*b*]quinoxalin-6-yl)-ethanone

2-[*N*'-(4-Hydroxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-*b*]quinoxalin-6-yl)-ethanone

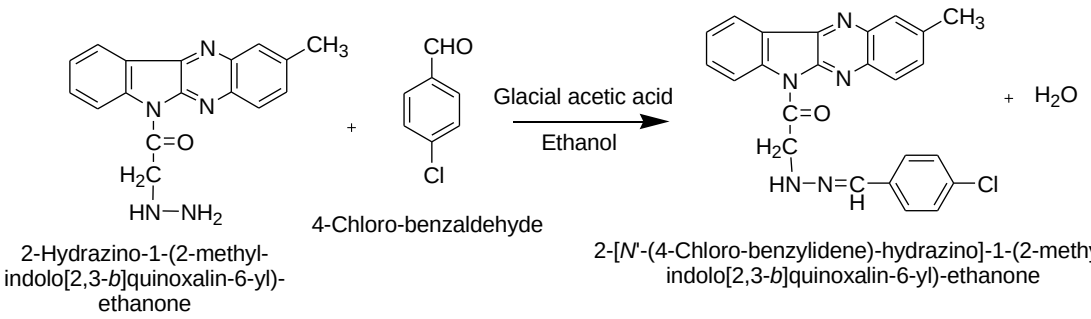
Scheme (2.15): The synthetic pathway of 2-[N'-(4-hydroxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone

A mixture of 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone (0.1g , 0.32mmol) in ethanol 25ml, 4-hydroxy-benzaldehyde (0.04g.,0.32mmol) was added with 3-4drops of glacial acetic acid. The reaction mixture was refluxed for 10 h in water bath. Progress of the reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as

mobile phase. Then cooled the resultant solution to room temperature. The precipitate formed, filtered, washed and recrystallized from (Ethanol/water). Yield-89%,m.p 236-238°**C.**

2.3.10 Synthesis of 2-[N'-(4-chloro-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_{10}]

Sheme (2.16) shows the chemical reaction and operating conditions for synthesis process of 2-[N'-(4-chloro-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone that written in short as **A_{10}**.



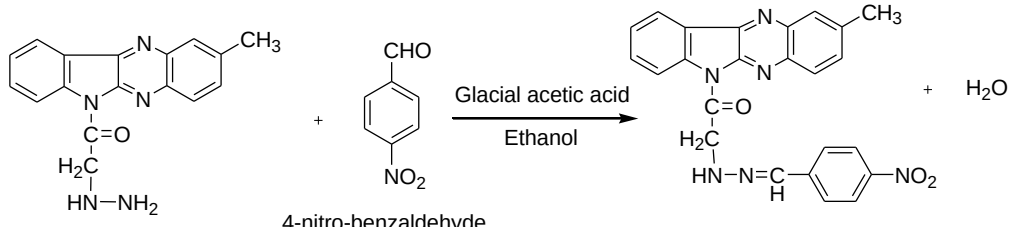
Sheme (2.16): The synthetic pathway of 2-[N'-(4-chloro-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone

A mixture of 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone (0.1g , 0.32 mmol) in ethanol 20ml., 4-Chloro-benzaldehyde (0.04g , 0.32 mmol) was added with 3-4drops of glacial acetic acid. The reaction mixture was refluxed to (70-80) °C for 12 h in water bath. Progress of reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase. Then cooled the resultant solution to

room temperature. The precipitate formed, filtered, washed and recrystallized from (Ethanol/water) . Yield 64% , m.p 260-262° **C.**

2.3.11 Synthesis of 1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-nitro-benzylidene)-hydrazino]-ethanone [A_{11}]

Scheme (2.17) shows the chemical reaction and operating conditions for synthesis process of 1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-nitro-benzylidene)-hydrazino]-ethanone that written in short as **A_{11}**.



2-hydrazino-1-(2-methyl-indolo[2,3-*b*]quinoxalin-6-yl)-ethanone

4-nitro-benzaldehyde

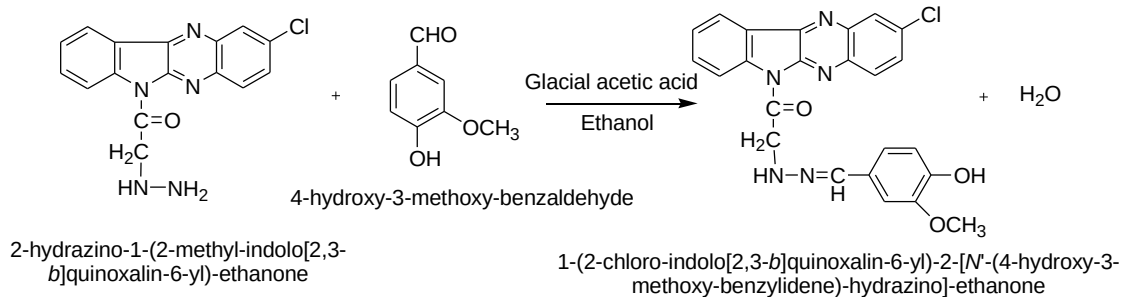
1-(2-methyl-indolo[2,3-*b*]quinoxalin-6-yl)-2-[*N*'-(4-nitro-benzylidene)-hydrazino]-ethanone

Scheme (2.17): The synthetic pathway of 1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-nitro-benzylidene)-hydrazino]-ethanone

A mixture of 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone (0.2g , 0.65 mmol) in ethanol 25ml , 4-nitro-benzaldehyde (0.09g, 0.65mmol) was added with 3-4drops of glacial acetic acid. The reaction mixture was refluxed for 6 h in water bath. Progress of the reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase. Then cooled the resultant solution to room temperature. The precipitate formed, filtered, washed and recrystallized from (Ethanol/water) . Yield 87% , m.p 180-182° **C.**

2.3.12 Synthesis of 1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-ethanone [A_{12}]

Scheme (2.18) shows the chemical reaction and operating conditions for synthesis process of 1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-ethanone that written in short as **A_{12}**.



2-hydrazino-1-(2-methyl-indolo[2,3-*b*]quinoxalin-6-yl)-ethanone

4-hydroxy-3-methoxy-benzaldehyde

1-(2-chloro-indolo[2,3-*b*]quinoxalin-6-yl)-2-[*N*'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-ethanone

Scheme (2.18): The synthetic pathway of -(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-ethanone

Amixture of 1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-2-hydrazino-ethanone (0.31 g , 0.95mmol) in ethanol 15 ml, (0.14g, 0.95 mmol) was added with 3-4 drops of glacial acetic acid .The reaction mixture was refluxed for 15 h in water bath . Progress of the reaction is monitored by TLC using 3:1 hexane:ethyl acetate mixture as mobile phase . Then cooled the resultant solution to room temperature. The precipitate formed, filtered, washed and recrystallized from (Ethanol/water). Yield 73%, m.p 254-256°**C**.

2.4 Antifungal activity testing

Antifungal susceptility testing was carried out by agar well diffusion method to detect anti fungal activity against yeasts isolate and mold (*Cryptococccus Neoformans, Candida Albicans, Rhodotorula rubra, Aspergilus parasiticus, Penicilium sp., Rhizopus arrhizus*) the moulds were grown at 25°C for 7 days . Stock solution was prepared by mixing 0.05g of compound with 1ml DMSO (solvent). The solid appeared at the petri plate which poisoned agar plates were inoculated at the centre with fungal plugs (10 mm) obtained from actively growing colony and incubated at 25°C for 7 days. Diameter of the fungal colonies was measured.

Chapter Three

Results & Discussion

3-Synthesis and characterization of compounds A_1-A_{12} and some their complexes .

The structures of the compounds (A_1-A_{12}) were identified by its melting point, TLC, UV-VIS spectrum, FT-IR, and ^{1}H-NMR spectroscopy. Identification and study of complexes were carried out by its melting point, percentage of metal analysis using flam atomic absorption, infrared spectroscopy, ultra violet-visible spectroscopy, magnetic susceptibility, elemental analysis CHNS, and electronic conductivity measurements. According to these data, the chemical formula of the prepared complexes were suggest .

3.1 Synthesis and identification of 2-Methyl-6H-indolo[2,3-b]quinoxaline[A_1] and its complexes .

Compound (**A_1**) was synthesized through the reaction of isatin with 4-methyl-o-Phenylenediamine as shown in Figure (3.1**).**

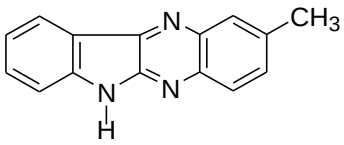
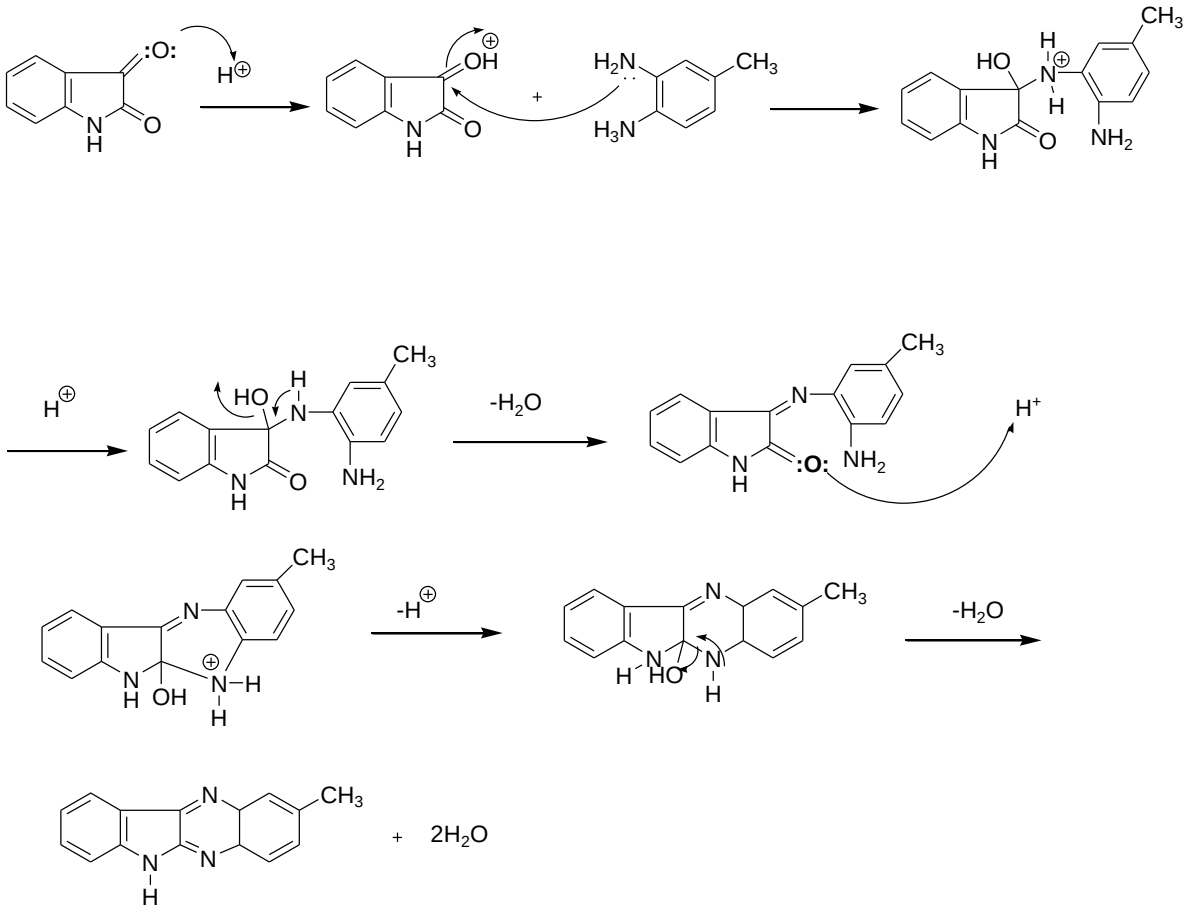


Figure (3.1): The chemical structure of compound A_1

The mechanism Suggested for the synthesis of compound A_1 is shows in Scheme (3.1) .



Scheme (3.1): The mechanism for the synthesis of (A_1)

The FT-IR spectrum of compound A_1 Figure (3.3) and Table (3.1) shows absorption bands at 3327cm^{-1} was attributed to bonding of NH group. Absorption band at 3023 cm^{-1} was due to C-H aromatic. Absorption band at 2919 cm^{-1} was due to C-H aliphatic .Bond absorption at 1610 cm^{-1} was due to C=N stretching vibartion. The bands at 1513 cm^{-1} and 1434 cm^{-1} are due to the C=C aromatic [127]. All these absorption bands are approved to the formation of this compound. The absence of the absorption bands of N-H stretching frequency from the FT-IR spectrums of $[pt(A_1)_2Cl_2].H_2O$ and $[Zn(A_1)_2]. 5H_2O$ complexes Figure (3.4and 3.5), with respect to **(A_1)** compound, and occurrence change in shape band with shifting of C=N group value from 1610 cm^{-1}, is good evidence of the coordination through the deprotonating protons of N-H and nitrogen atoms of C=N group of **(A_1)** compound to the metal

ions. In two complexes appeared bands at (3410 and 3487) cm^{-1} which referred to stretching band of H_2O uncoordination or out of sphere [128]. Table (3.1) explain FT-IR spectrum bands of A_1 compound and its complexes.

The ^{1}H-NMR spectra of the compound (A_1), Figure (3.6) 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) .

The UV-VIS spectrum of the A_1 compound Figure (3.7) and Table (3.2) showed absorption band at (245.4 nm, 40749.7 cm^{-1}) assigned to ($\pi \rightarrow \pi^*$) transition. The band observed at (290.8 nm, 34387.8 cm^{-1}) would be due to the ($n \rightarrow \pi^*$) transition. The absorption bands at (350 nm, 28571.4 cm^{-1}) and (457 nm, 21881.8 cm^{-1}) are assigned to intra ligand charge transfer ITCT transitions, the band at (457 nm, 21881.8 cm^{-1}) encroaches on the visible region and impact the ligand its color[129].

The electronic spectrum of $[pt(A_1)_2Cl_2]. H_2O$ complex Figure (3.8) and Table (3.2), explain the absorption bands due to π-π^*, n-π^* and CT transitions that observed in the spectrum of the free ligand have shifted. In addition exhibited low intensity new band at (729.4 nm, 13709.8 cm^{-1}) was assigned to d-d transition due to the coordination of the ligand with metal ion.

The ultraviolet-visible spectra of $[Zn(A_1)_2].5H_2O$ complex in Figure (3.9), show change in the bands position compared to the free ligand as listed in Table (3.2) due to charge transfer between Zn(II) and the ligand. The Zinc complex showed no absorption band for (d-d) transition because the d orbital is field (d^{10} - system).

The observed magnetic moment value for $[pt(A_1)_2Cl_2]. H_2O$ and $[Zn(A_1)_2].5H_2O$ complexes was zero, indicating diamagnetic nature. The conductivity measurements in DMSO solvent at room temperature were

(3.6) and (5.9) respectively, and this approved that the complex is non-ionic as illustrated in Table (3.2).

Elemental analysis (C.H.N.S) and metal percentage results for $[Pt(A_1)_2Cl_2].H_2O$ and $[Zn(A_1)_2].5H_2O$ complexes shows that the calculated and found percentage values of carbon, hydrogen, nitrogen and metal are in a good agreement as show in Table (3.3), Calc. for $[pt(C_{15}H_{10}N_3)_2Cl_2].H_2O$ (748.493 gm/mol): C, 48.13 ; H, 2.96; N, 11.22; pt, 26.06. Found: C, 47.98; H, 2.70; N, 11.67; pt, 26.32. And Calc. for $[Zn(C_{15}H_{10}N_3)_2].5H_2O$ (619.961): C, 58.11 ; H, 4.87; N, 13.55; Zn, 10.54. Found: C, 57.99; H, 4.83; N, 13.77; Zn, 10.39. Accordingly the following structures can be suggested:

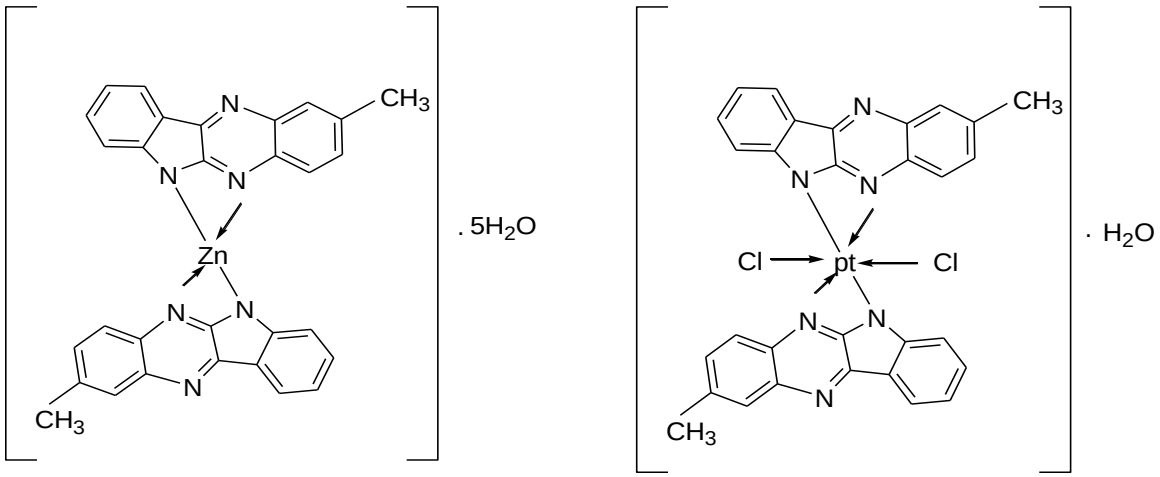
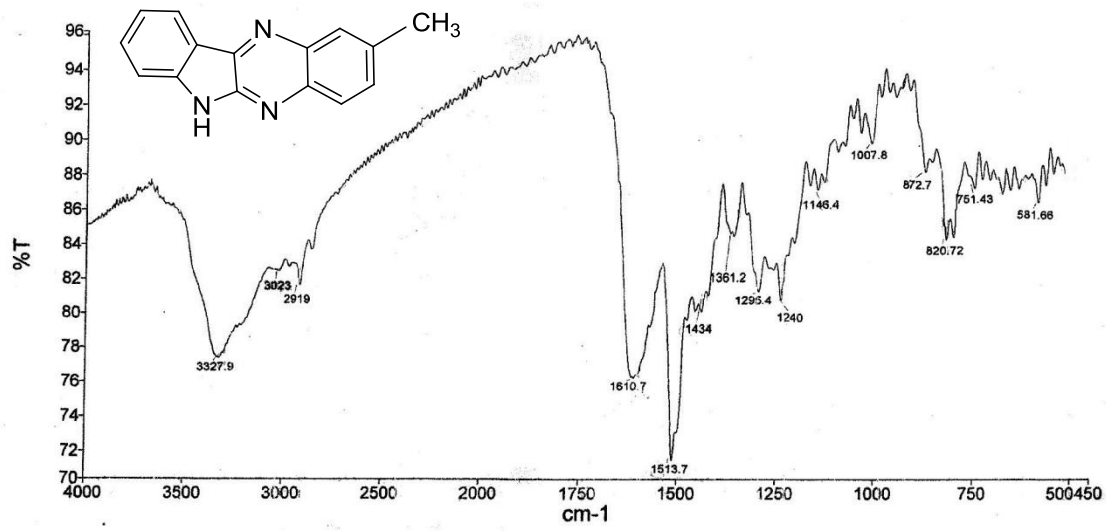


Figure (3.2): The chemical structures of$[Zn(A_1)_2].5H_2O$ and $[pt(A_1)_2Cl_2].H_2O$



Figure(3.3): FT-IR spectrum in $cm^{-1}$of (A_1) compound

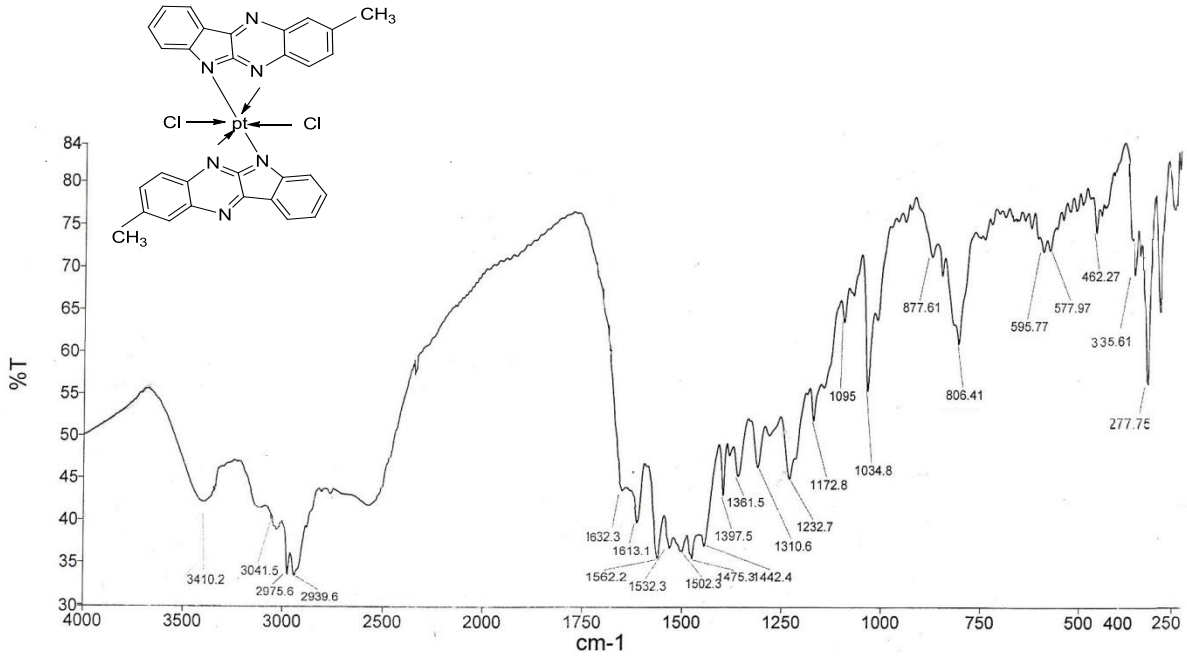


Figure (3.4): FT-IR spectrum of $[pt(A_1)_2Cl_2]. H_2O$

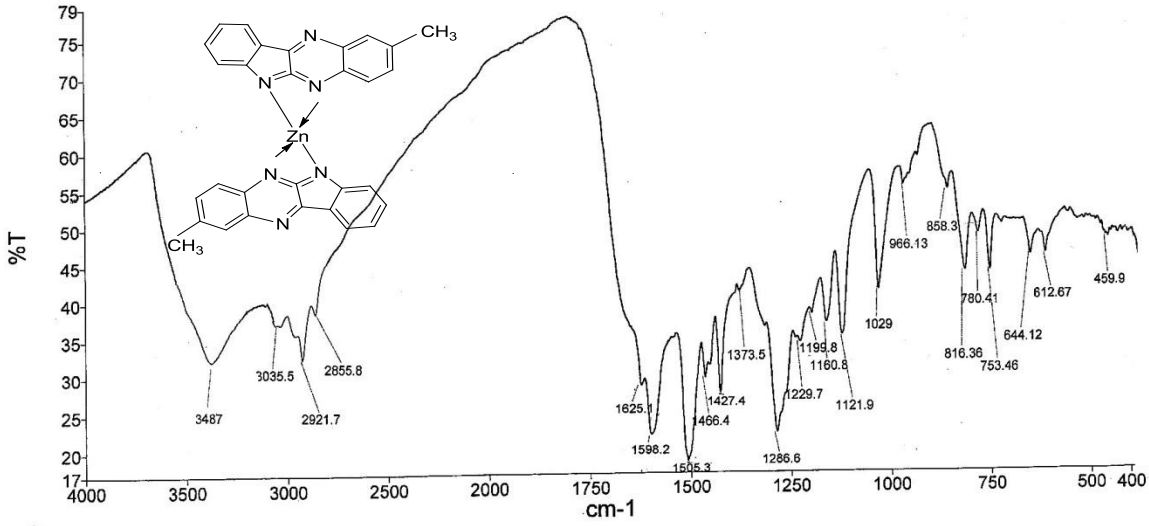


Figure (3.5): FT-IR spectrum of $[Zn(A_1)_2].5H_2O$

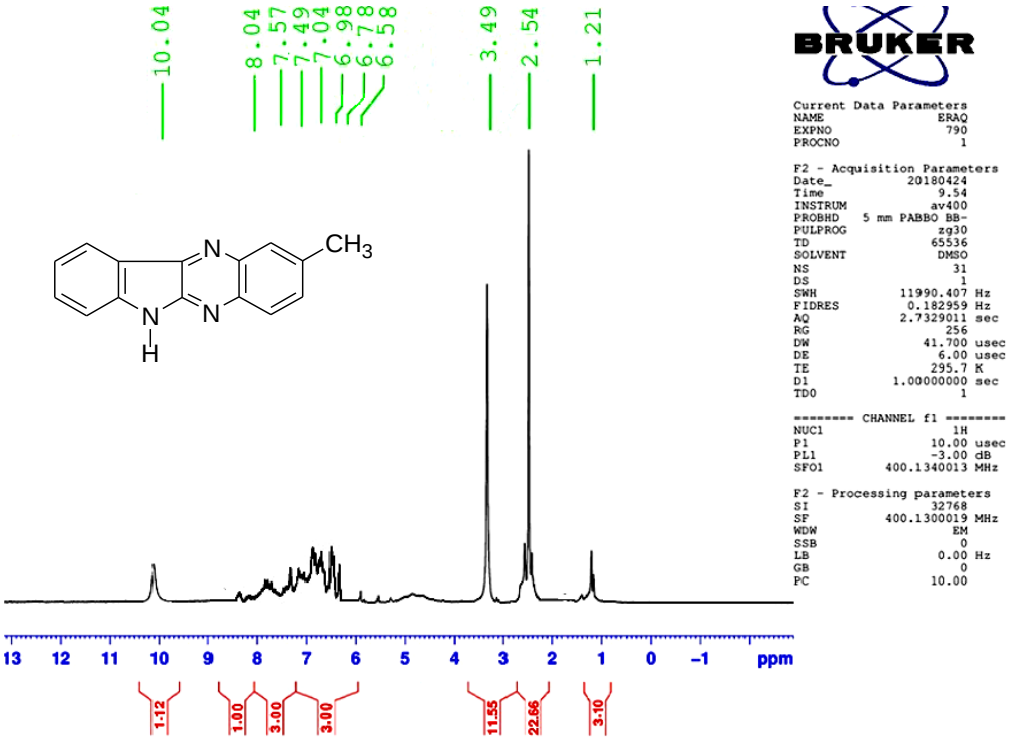


Figure (3.6): ^{1}H NMR spectrum of compound 2-methyl-6H-indolo[2,3-b]quinoxaline[A_1]

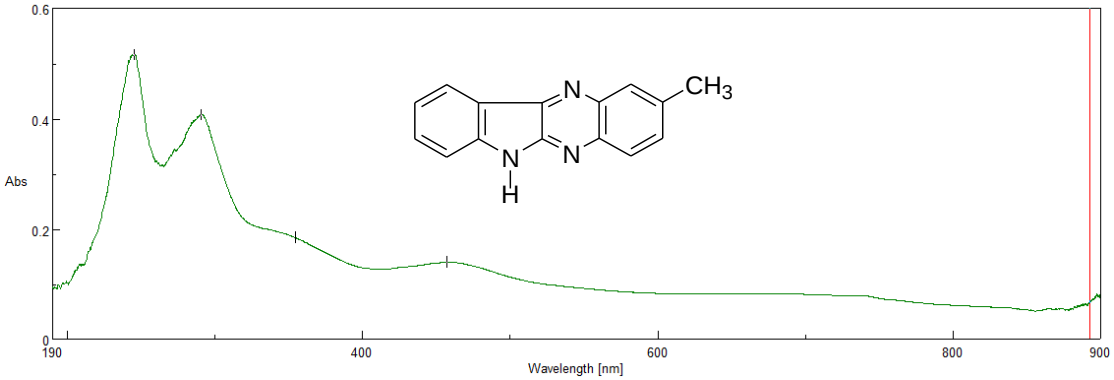


Figure (3.7): UV-VIS spectrum of A_1

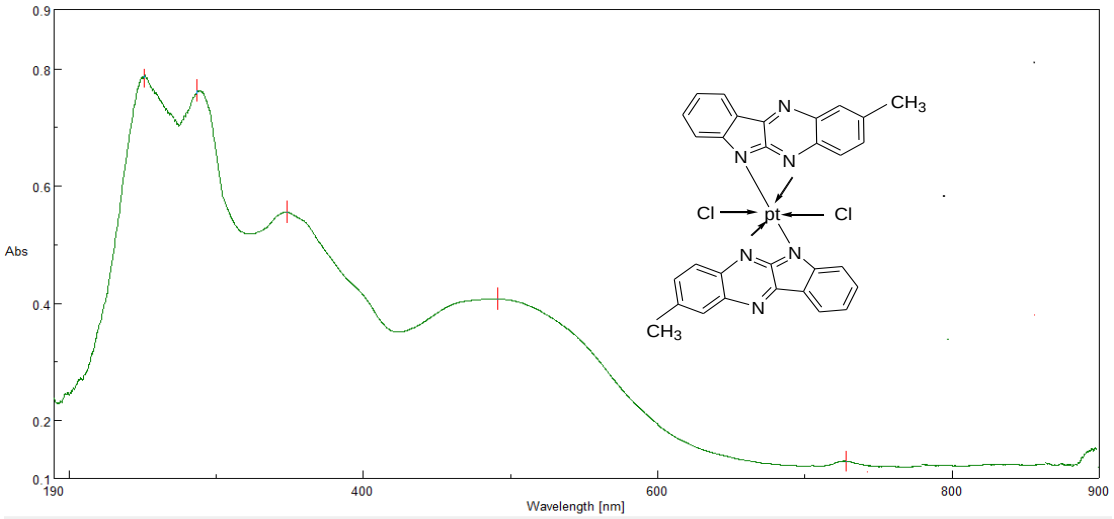


Figure (3.8): UV-VIS spectrum of $[pt(A_1)_2Cl_2]. H_2O$

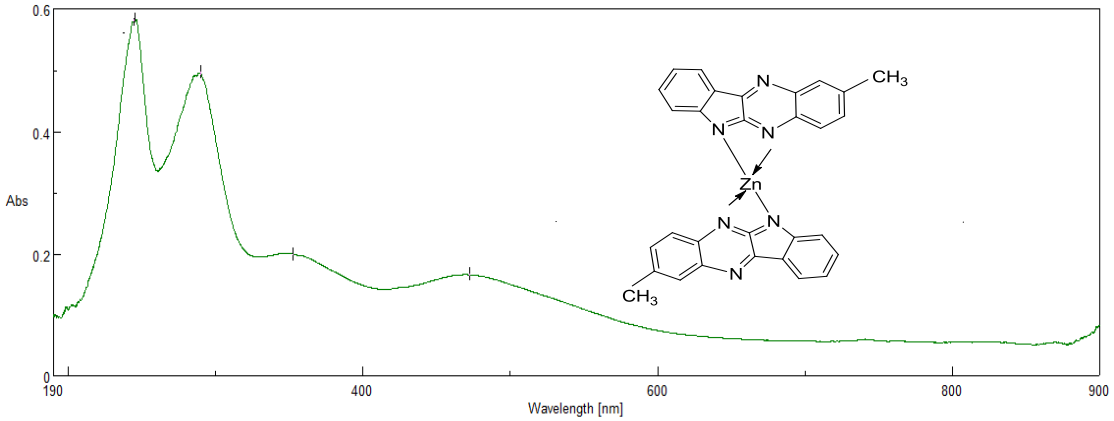


Figure (3.9): UV-VIS spectrum of $[Zn(A_1)_2].5H_2O$

3.2 Synthesis and identification of 2-Chloro-6H-indolo[2,3-b]quinoxaline[A_2] .

Compound (**A_2**) was synthesized through the reaction of isatin with 4-chloro-o-Phenylenediamine as shown in Figure (3.10**)**.

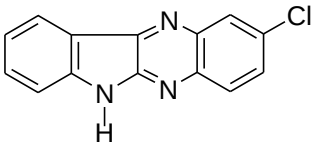


Figure (3.10): The chemical structures of compound A_2

The FT-IR spectrum of compound A_2 shows absorption Figure (3.11) and Table (3.1). The absorption bands at 3138 cm^{-1} was attributed to bonding of N-H group. Absorption band at 3027 cm^{-1} was due to C-H aromatic. Bond absorption at 1613 cm^{-1} was due to C=N stretching vibration . The bands at 1579 cm^{-1} and 1495 cm^{-1} are due to the C=C aromatic.

The ^{1}H-NMR spectrum of compound (A_2) Figure (3.12) shows the chemical shifts (DMSO-d_6, ppm): 10.10 (s, 1H, N-H) , 7.90 -8.18 (m,7H, Ar-H) .

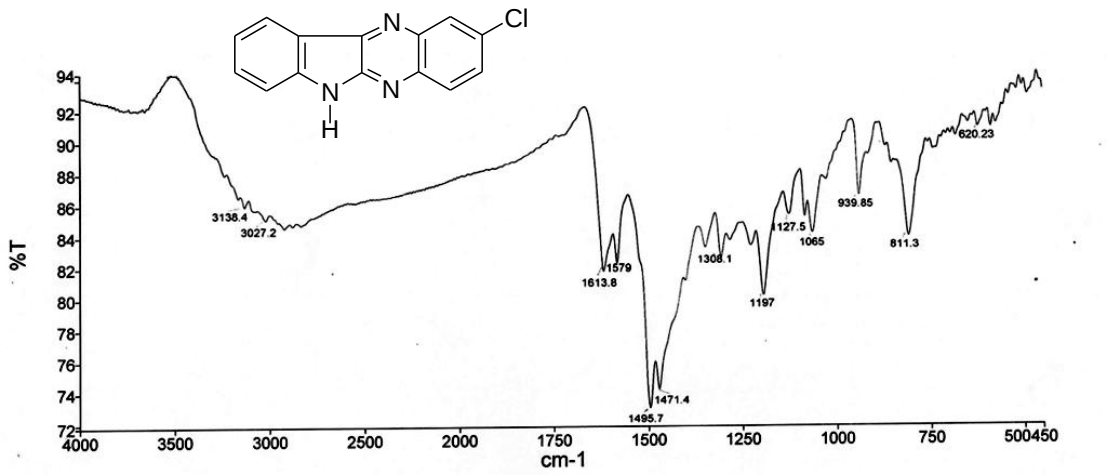


Figure (3.11): FT-IR spectrum in $cm^{-1}$of (A_2) compound

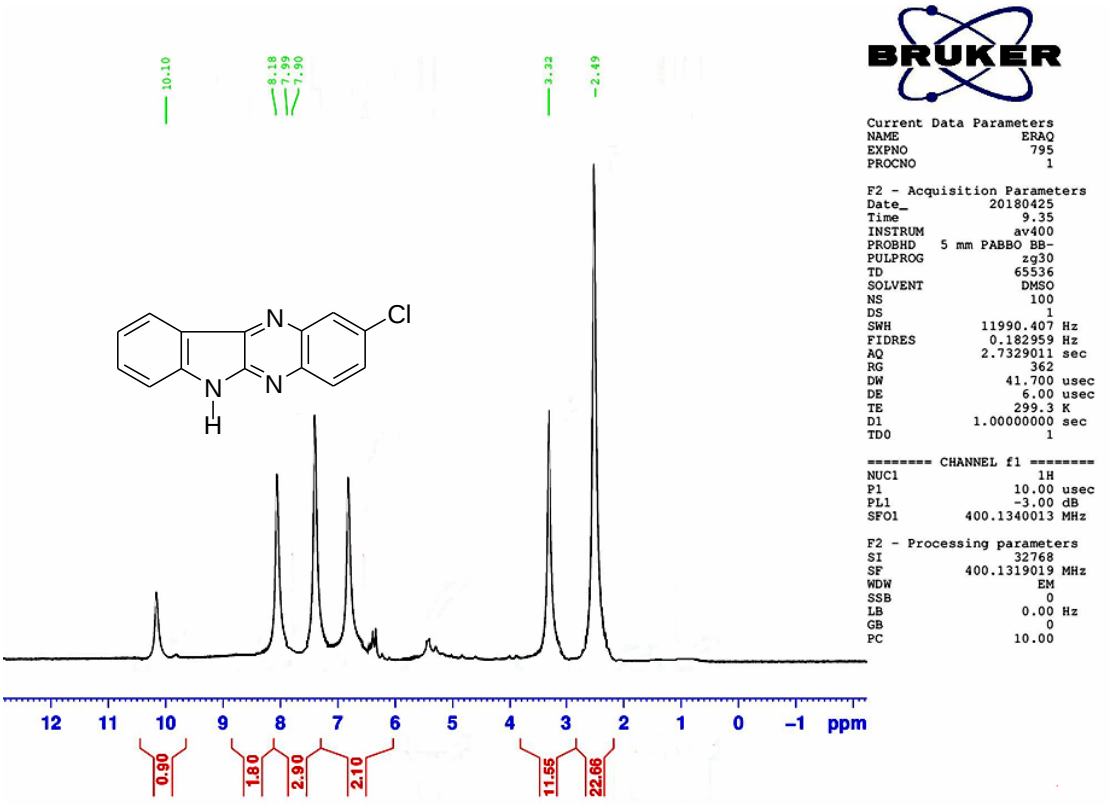


Figure (3.12): ^{1}H NMR spectrum of 2-Chloro-6H-indolo[2,3-b]quinoxaline[A_2]

3.3 Synthesis and identification of 2-Chloro-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone[A_3]

Compound (**A_3**) was synthesized through the reaction of 2-methyl-6H-indolo[2,3-b]quinoxaline with chloroacetyl chloride in presence of triethyl amine in benzene as shown in Figure (3.13**)**.

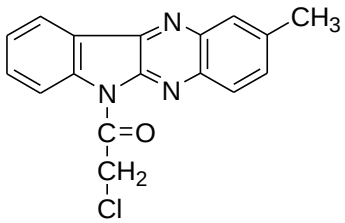
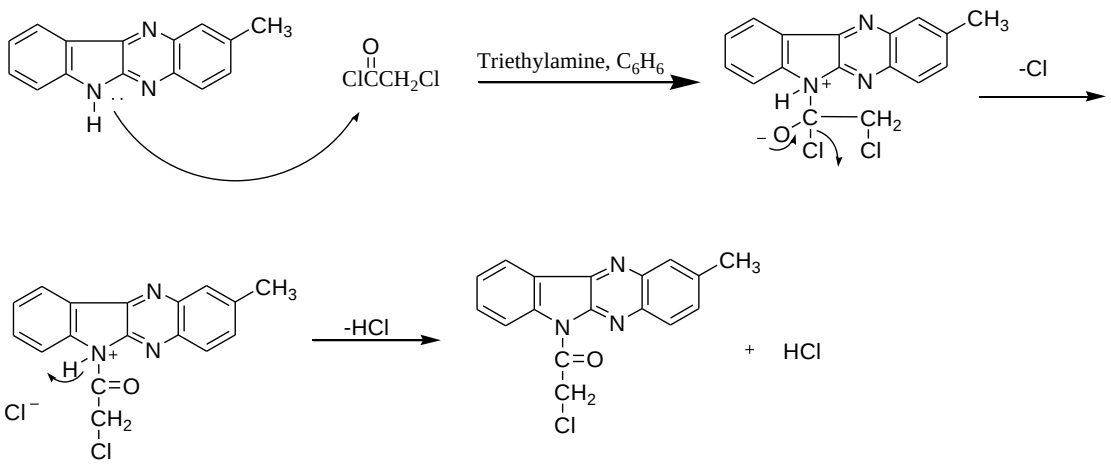


Figure (3.13): The chemical structures of compound A_3

The mechanism Suggested for the synthesis of compound A_3 is shown in Scheme (3.2).



Scheme (3.2): The mechanism for the synthesis of (A_3)

The FT-IR spectrum of compound A_3 shows absorption Figure (3.14) and Table (3.1). The absorption band at 3437 cm^{-1} was attributed to bonding of O-H (tuat.)group. Absorption band at 2930 cm^{-1} was due to C-H aliphatic. Bond absorption at 1617 cm^{-1} was due to C=N stretching vibration . Bond absorption at 1679 cm^{-1} was due to stretching vibration of C=O . The band at 1516 cm^{-1} is due to the C=C aromatic.

The ^{1}H-NMR spectrum of compound (A_3) Figure (3.15) shows the chemical shifts (DMSO-d_6, ppm): 9. 93 (s, 1H, O-H) , 7.00-7.63 (m,7H, Ar-H), 4.30 (s, 1H, CH_2) and 1.22 (s,3H, CH_3).

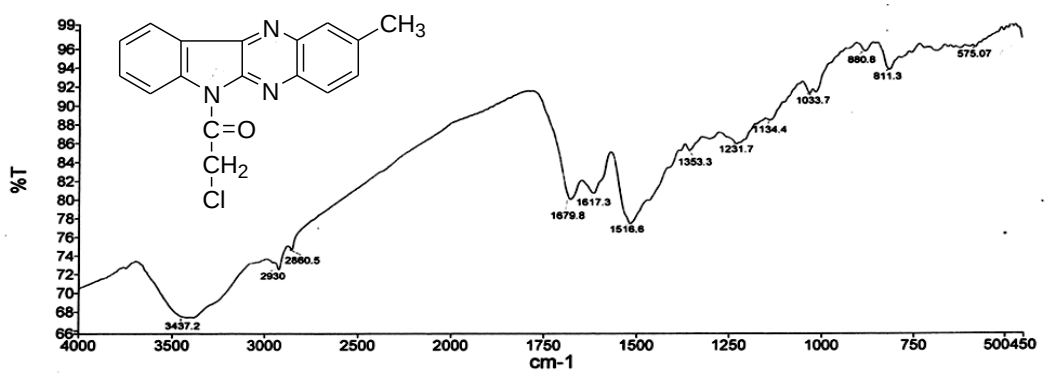


Figure (3.14): FT-IR spectrum in $cm^{-1}$of (A_3) compound

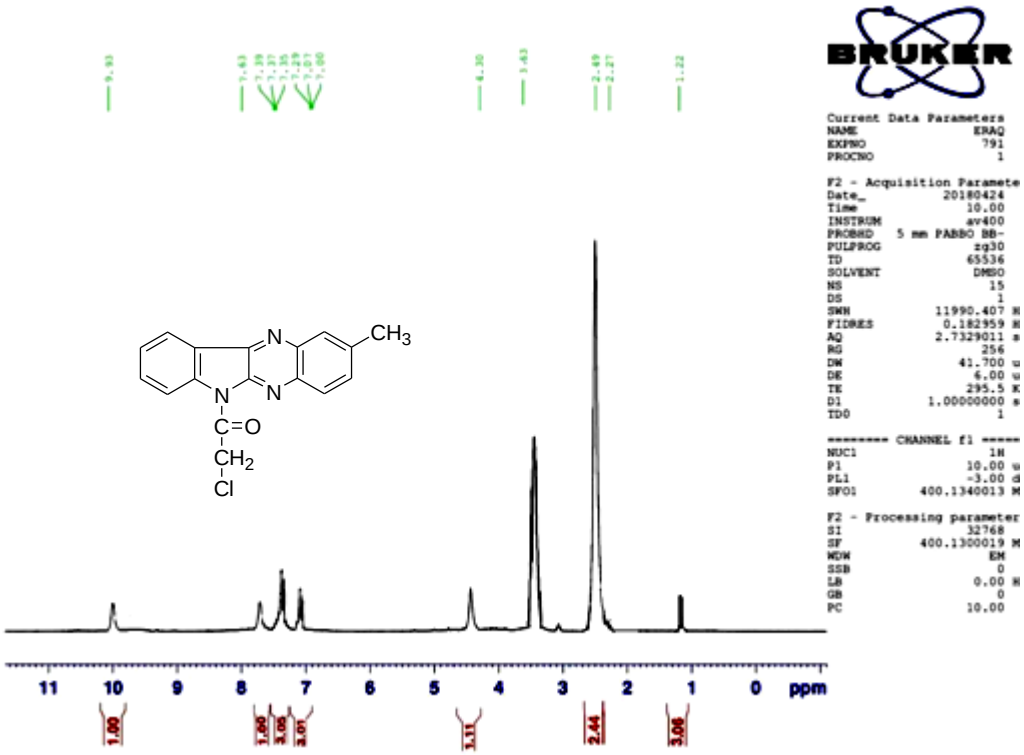


Figure (3.15): ^{1}H NMR spectrum of 2-Chloro-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone[A_3]

3.4 Synthesis and identification of 2-Chloro-1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_4].

Compound (**A_4**) was synthesized through the reaction of 2-chloro-6H-indolo[2,3-b]quinoxaline with chloroacetyl chloride in presence of triethyl amine in benzene as shown in Figure (3.16**)**.

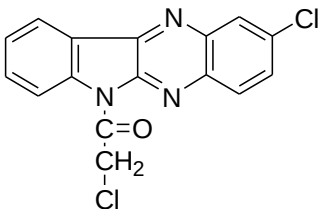


Figure (3.16): The chemical structures of compound A_4

The FT-IR spectrum of compound A_4 shows absorption Figure (3.17) and Table(3.1). The absorption bands at 3373 cm^{-1} was attributed to bonding of O-H (tuat.) group. Bond absorption at 1693 cm^{-1} was due to stretching vibration of C=O. Bond absorption at 1620 cm^{-1} was due to C=N stretching. The bands at 1523 cm^{-1} and1474 cm^{-1} are due to the C=C aromatic.

The ^{1}H-NMR spectrum of compound (A_4) Figure (3.18) shows the chemical shifts (DMSO-d6, ppm): 10.01 (s, 1H, O-H) , 7.05-7.79 (m,7H, Ar-H) and 4.3(s, 1H, CH_2).

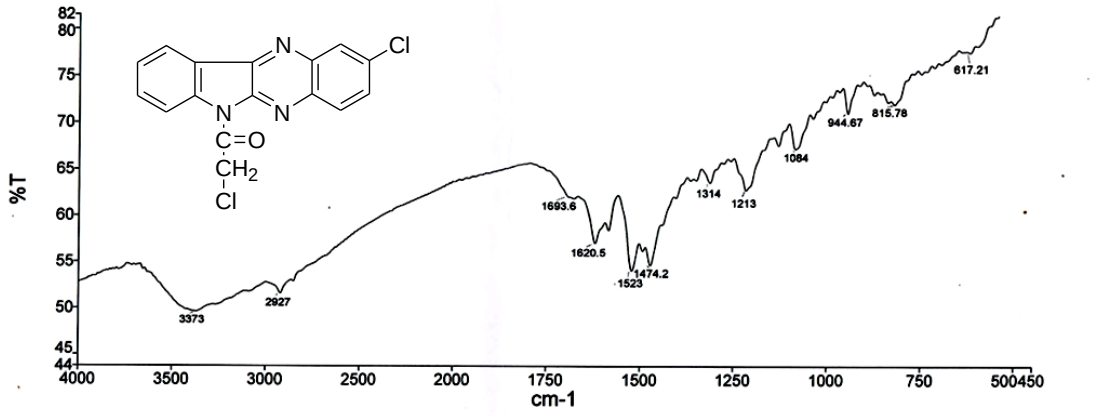


Figure (3.17): FT-IR spectrum in $cm^{-1}$of (A_4) compound

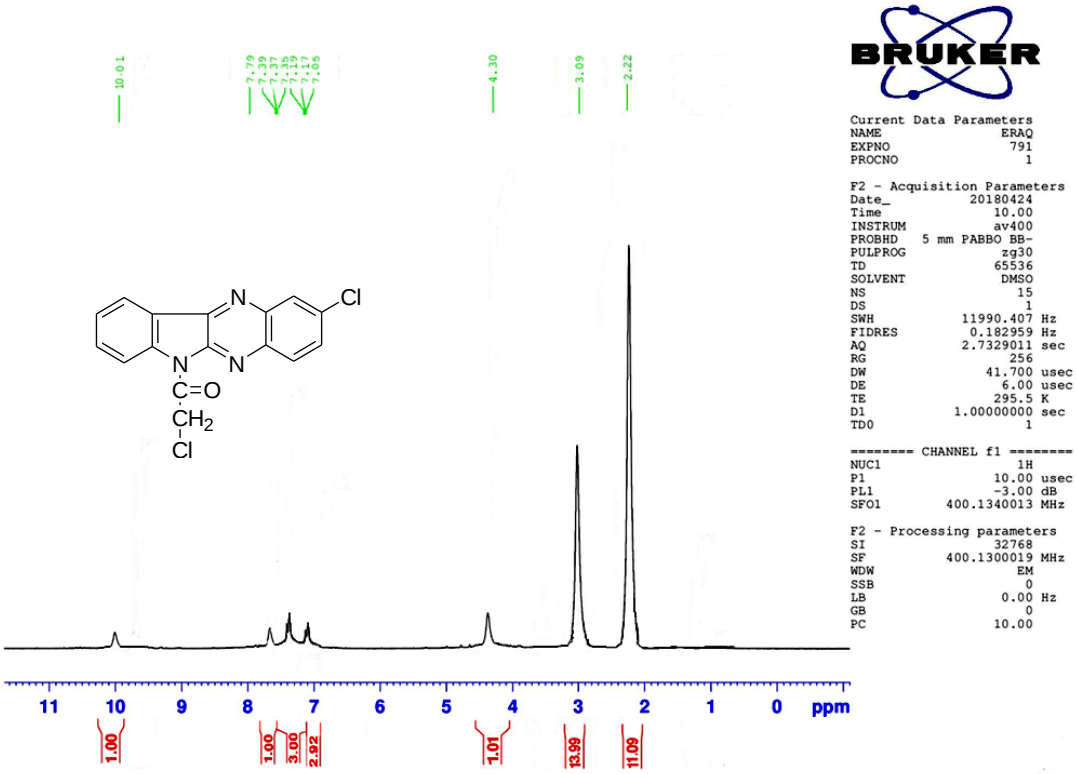


Figure (3.18): ^{1}H NMR spectrum of 2-Chloro-1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_4]

3.5 Synthesis and identification of 2-Hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_5] and its complexes

Compound (**A_5**) was synthesized through the reaction of 2-Chloro-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)- **e**thanone with hydrazine hydrate in ethanol as shown in Figure (3.19**)**.

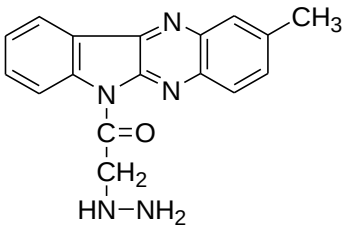
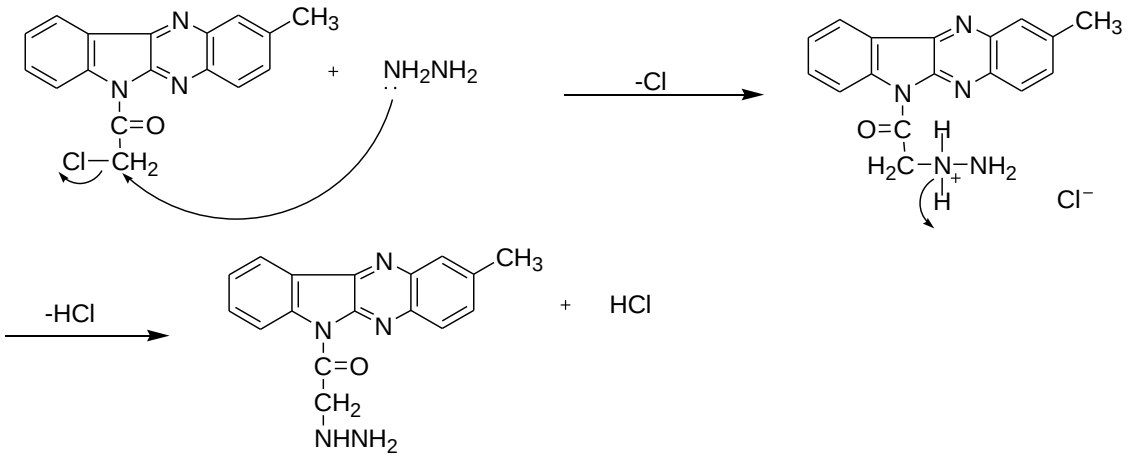


Fig (3.19): The chemical structures of compound A_5

The mechanism Suggested for the synthesis of compound A_5 is given in Scheme (3.3).



Scheme (3.3): The mechanism for the synthesis of (A_5)

The FT-IR spectrum of compound (A_5) Figure (3.21) and Table (3.1) is showing absorption bands at (3226 and 3196) cm^{-1} can attributed to bonding of NH_2 groups. Absorption bands at 3105 cm^{-1} was attributed to bonding of N-H groups, absorption band at 3034 cm^{-1} was due to C-H aromatic, absorption band at 2924 cm^{-1} was due to C-H aliphatic. Bond absorption at 1684 cm^{-1} was due to C=O stretching and bonds absorption at (1610 and 1593) cm^{-1} was due to C=N stretching vibration. Occurrence of shifting of the C=O and NH_2 stretching frequency from the FT-IR spectrums of $[Ni(A_5)_2Cl_2].6H_2O$ and $[Co(A_5)_2Cl_2].6H_2O$ complexes Figure (3.22 and 3.23) with respect to **(A_5)** compound, in the other hand appeared bands at (511 and 426) cm^{-1} which referred to stretching band of M-N, and at (603 and 582) cm^{-1} which referred to stretching band of M-O for Ni(II) and Co(II) complexes respectively, is good evidence of the coordination through the C=O and NH_2 groups of **(A_5)** compound to the metal ions. Table (3.1) explain FT-IR spectrum bands of A_5 compound and its complexes.

The ^1H -NMR spectrum of compound (A_5), Figure (3.24) shows the chemical shifts (DMSO-d_6, ppm): 9.95 (bro , 1H,N-H) [130] , 7.55-8.48

(m,7H, Ar-H) , 5.71 (bro, 2H, NH_2), 4.11(s, 2H, CH_2) and 1.22 (s,3H, CH_3) .

The UV-Visible spectra of compound A_5 Figure (3.25) shows a band at (262.4 nm, 38109.7cm^{-1}) would be due to the (n→ π*) transition .The absorption bands at (454.4 nm, 22007.04cm^{-1}) is assigned to intra ligand charge transfer ITCT transitions.

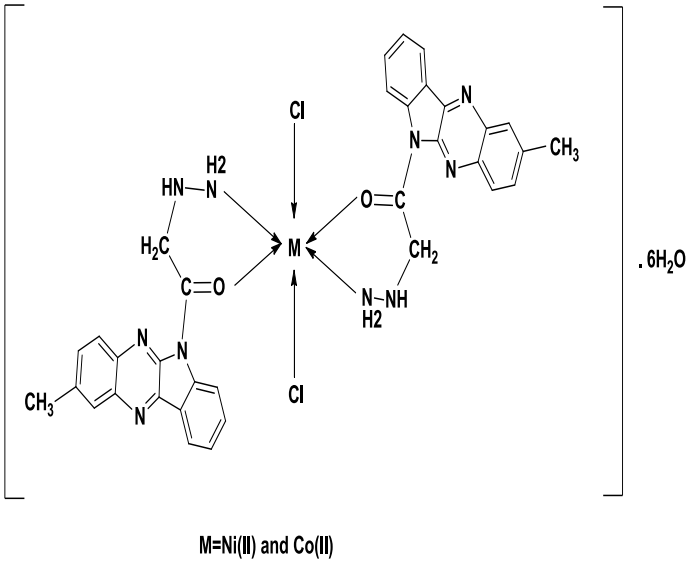
The electronic spectrum of $[Ni(A_5)_2Cl_2].6H_2O$ complex Figure (3.26) explain the absorption bands due to π-π*, n-π* and CT transitions that observed in the spectrum of the free ligand have shifted. In addition exhibited low intensity new bands at (807.8 nm, 12379.3 cm^{-1}) was assigned to d-d transition due to the coordination of the ligand with metal ion.

The electronic spectrum of $[Co(A_5)_2Cl_2].6H_2O$ complex Figure (3.27) explain the absorption bands due to π-π*, n-π* and CT transitions that observed in the spectrum of the free ligand have shifted. In addition exhibited low intensity new bands at (744 nm,13440.8 cm^{-1}) was assigned to d-d transition due to the coordination of the ligand with metal ion [131].

The observed magnetic moment value for $[Ni(A_5)_2Cl_2].6H_2O$ and $[Co(A_5)_2Cl_2].6H_2O$ complexes were (3.1) and (4.3) respectively , indicating para magnetic nature and the conductivity measurements in DMSO solvent at room temperature for Ni (II) and Co (II) complexes were (3.9) and (4.1) respectively, and this evidence that the complexes non-ionic as illustrated in Table (3.2).

Elemental analysis (C.H.N.S) and metal percentage results for$[Ni(A_5)_2Cl_2].6H_2O$ and $[Co(A_5)_2Cl_2].6H_2O$ complexes shows that the calculated and found percentage values of carbon, hydrogen, nitrogen and

metal are in a good agreement as show in Table (3.3), Calc. for $[Ni(A_5)_2Cl_2].6H_2O$ (848.325 gm/mol): C, 48.13 ; H, 4.99; N, 16.50 ; Ni, 6.91 . Found: C, 48.00; H, 5.00; N, 16.65; Ni, 7.00 . And Calc. for $[Co(A_5)_2Cl_2].6H_2O$ (848.565): C, 48.12 ; H, 4.98; N, 16.50; Co, 6.94 . Found: C, 47.99 ; H, 4.85 ; N, 16.42; Co, 6.75 . According to those data, the following structures can be suggested:



M=Ni(II) and Co(II)

Figure (3.20): The chemical structures of$[M(A_5)_2Cl_2].6H_2O$,where M=Ni(II) and Co(II)

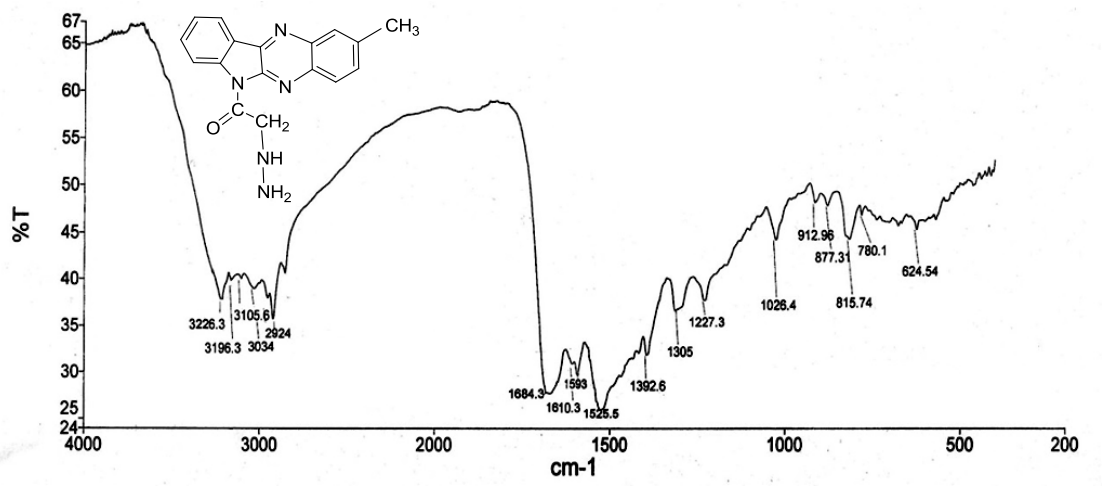


Figure (3.21): FT-IR spectrum in $cm^{-1}$of (A_5) compound

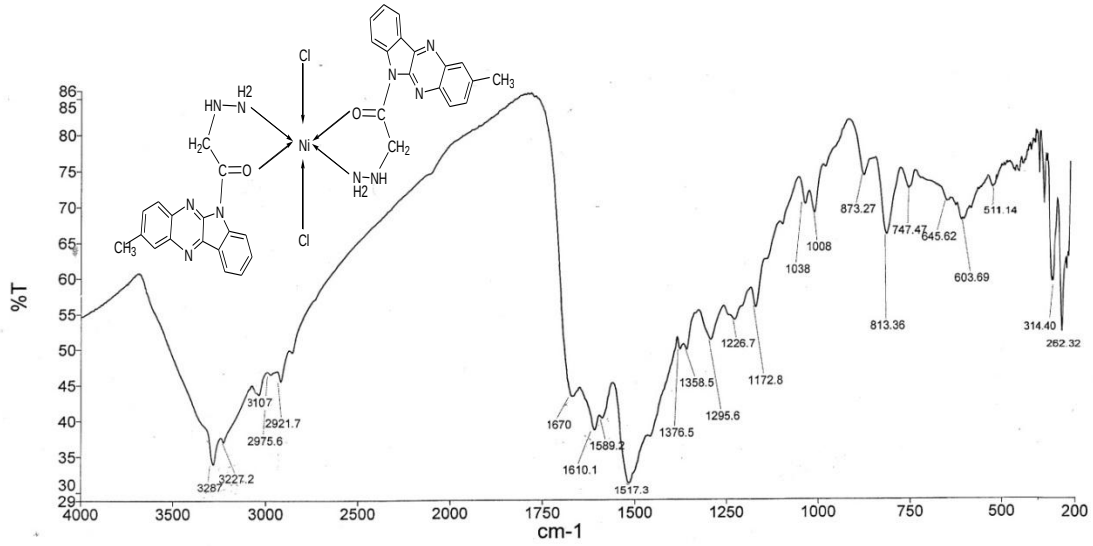


Figure (3.22): FT-IR spectrum of $[Ni(A_5)_2Cl_2].6H_2O$

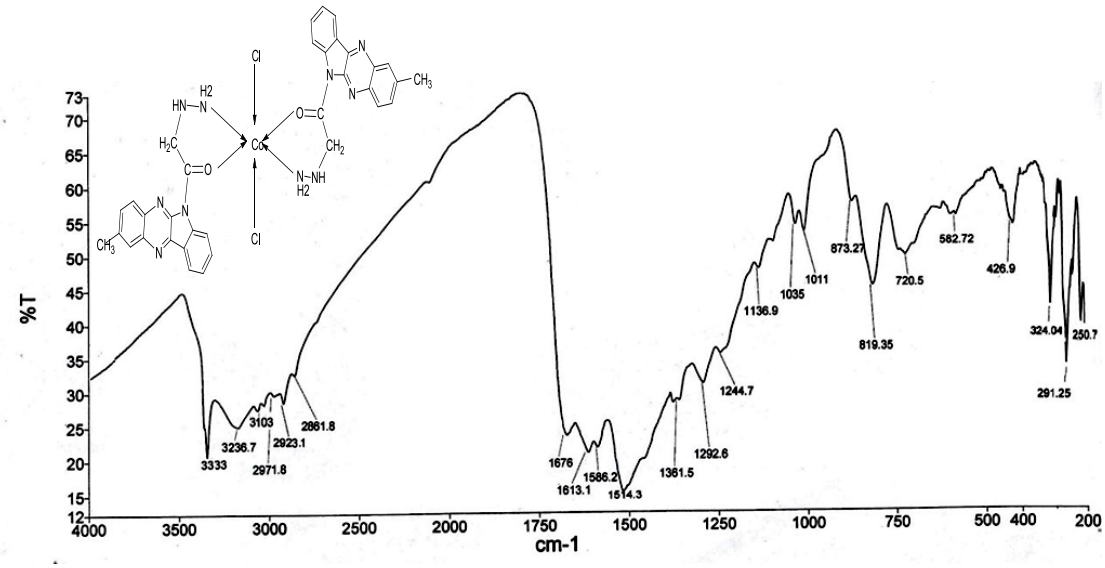


Figure (3.23): FT-IR spectrum of $[Co(A_5)_2Cl_2].6H_2O$

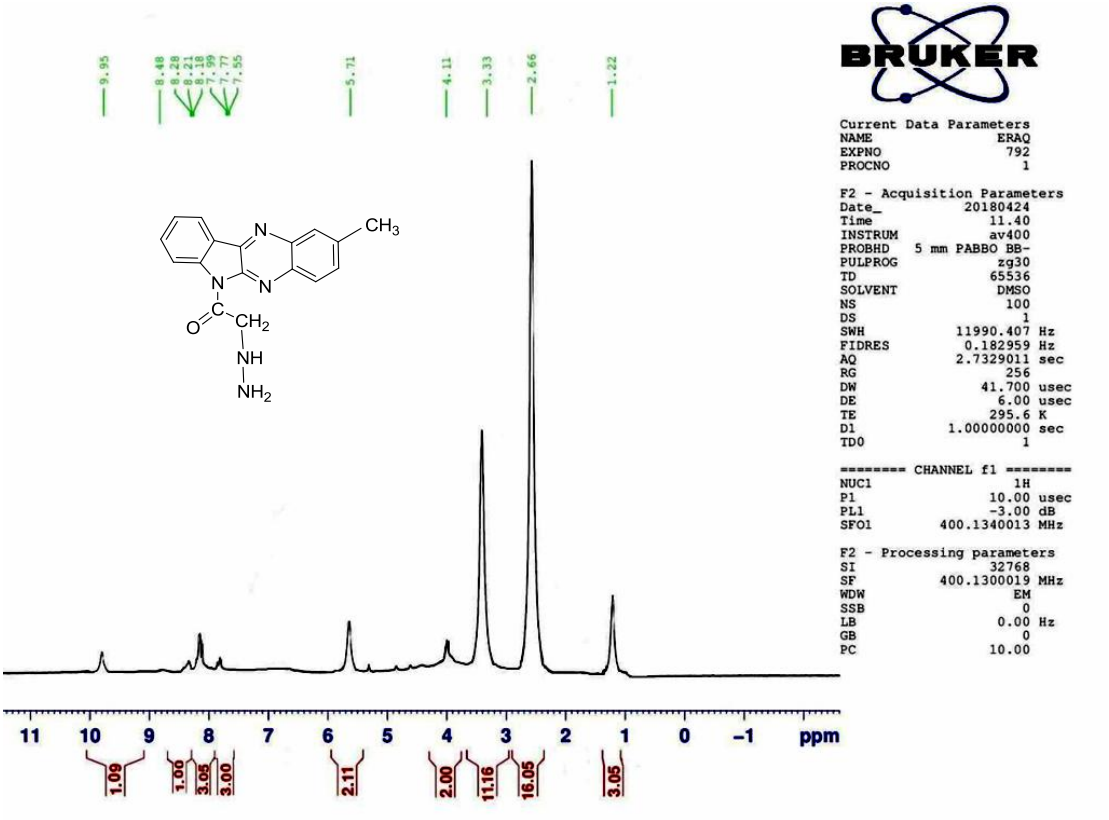


Figure (3.24): ^{1}H NMR spectrum of compound 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone[A_5]

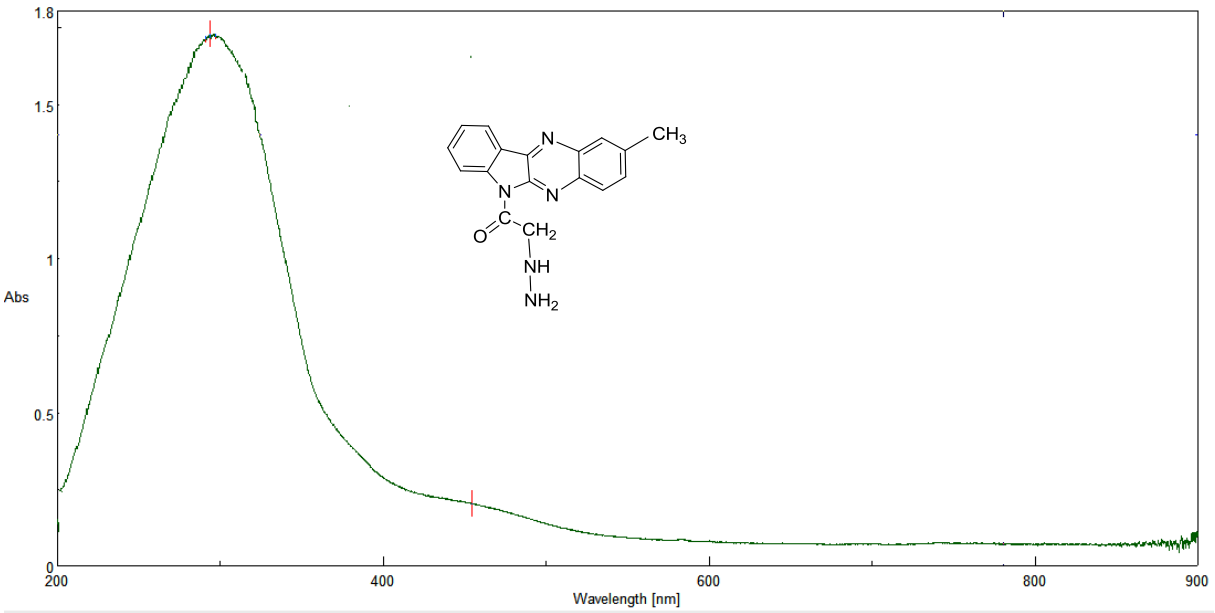


Figure (3.25): UV-VIS spectrum of A_5

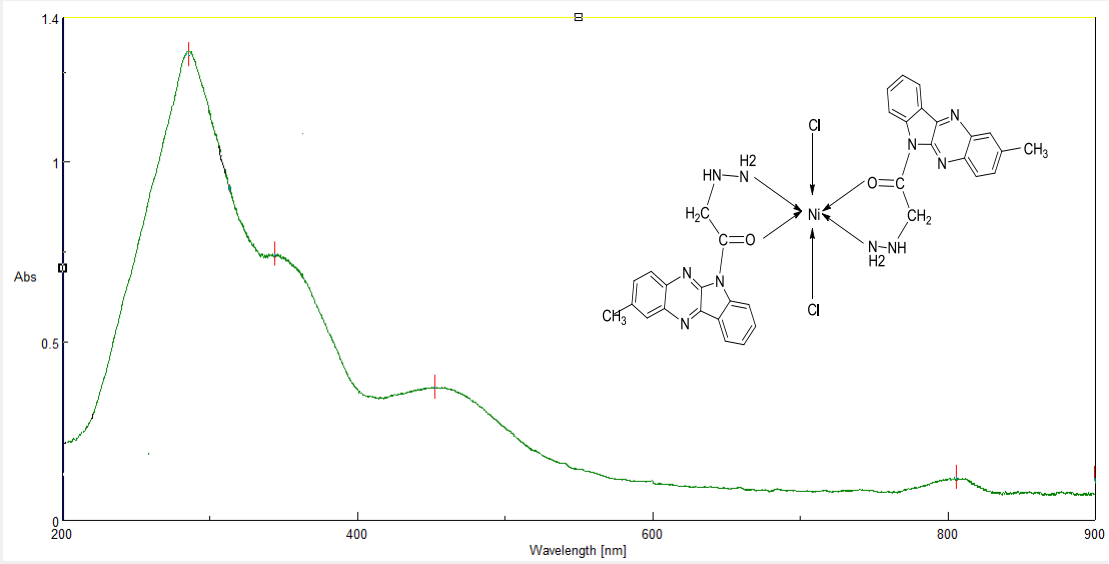
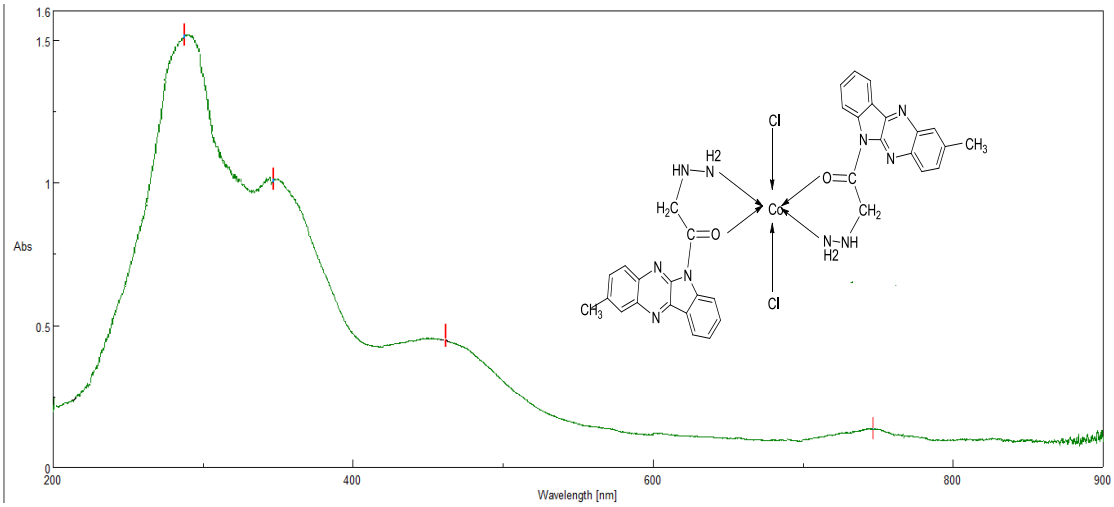


Figure (3.26): UV-VIS spectrum of $[Ni(A_5)_2Cl_2].6H_2O$ complex



Figure(3.27): UV-VIS spectrum of $[Co(A_5)_2Cl_2].6H_2O$ complex

3.6 Synthesis and identification of 1-(2-Chloro-indolo[2,3-b]quinoxalin-6-yl)-2-hydrazino-ethanone [A_6].

Compound (**A_6**) was synthesized through the reaction of 2-Chloro-1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-ethanone with hydrazine hydrate in ethanol as shown in Figure (3.28**)**.

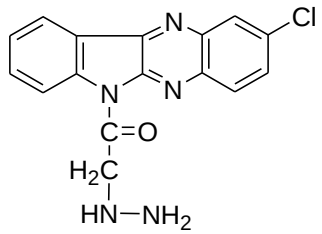


Figure (3.28): The chemical structures of compound A_6

The FT-IR spectrum of compound A_6 Figure (3.29) and Table(3.1) shows absorption bands at 3246,3205 cm^{-1} was attributed to bonding of NH_2 groups. Absorption bands at 3133 cm^{-1} was attributed to bonding of N-H group. Absorption band at 3019 cm^{-1} was due to C-H aromatic. Absorption band at 2924 cm^{-1} was due to C-H aliphatic .Bond absorption at 1676 cm^{-1} was due to stretching vibration of C=O. Bond absorption at 1619 cm^{-1} was due to C=N stretching . The sharp bands at 1583 cm^{-1} and 1496 cm^{-1} are due to the C=C aromatic.

The ^{1}H -NMR spectrum of Compound (A_6), Figure (3.30) shows the chemical shifts (DMSO-d6, ppm): 10.00 (bro,1H,N-H) , 7.05-7.79 (m,7H,Ar-H), 5.50 (bro,2H,NH_2) and 4.34 (s,2H, CH_2) .

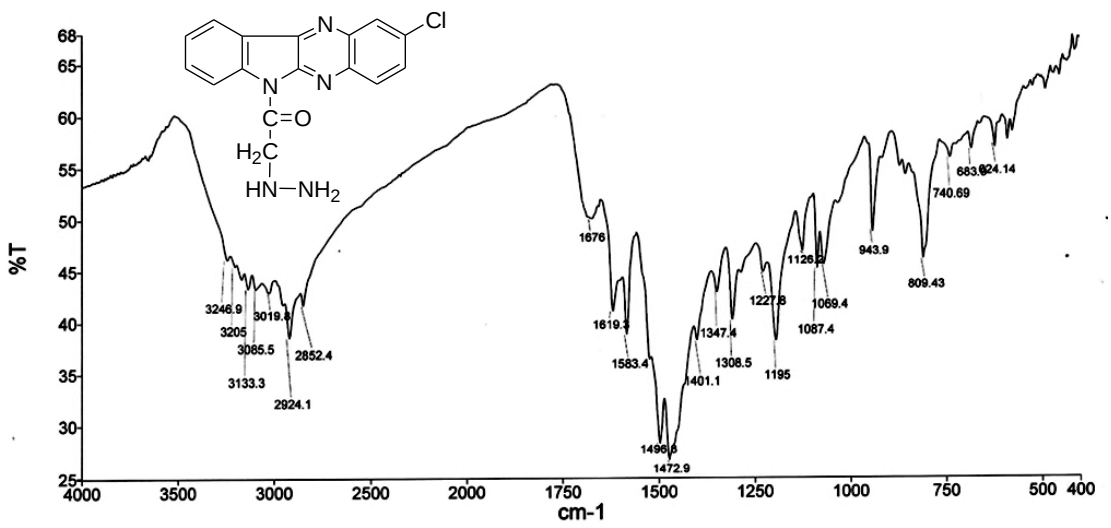


Figure (3.29): FT-IR spectrum in cm^{-1}of (A_6) compound

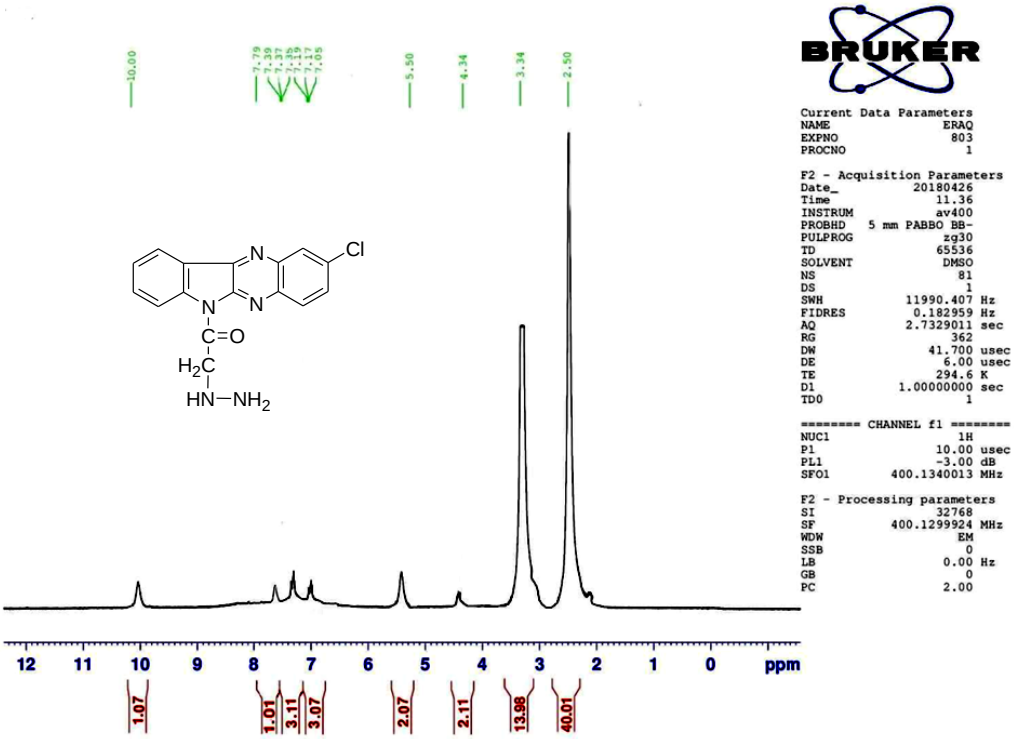


Figure (3.30): ^{1}H NMR spectrum of compound 1-(2-Chloro-indolo[2,3-b]quinoxalin-6-yl)-2-hydrazino-ethanone [A_6]

3.7 Synthesis and identification of 4-{[2-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-2-oxo-ethyl]-hydrazonomethyl}-benzaldehyde [A_7] and its complex .

Compound (A_7) was synthesized by the reaction of the compound 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone with Benzene-1,4-dicarbaldehyde in the presence of glacial acetic acid in absolute ethanol as shown in Figure (3.31).

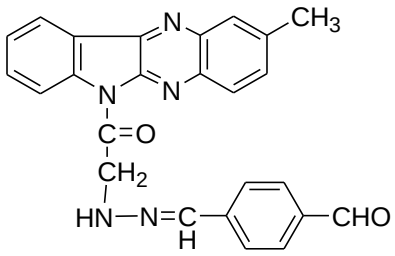
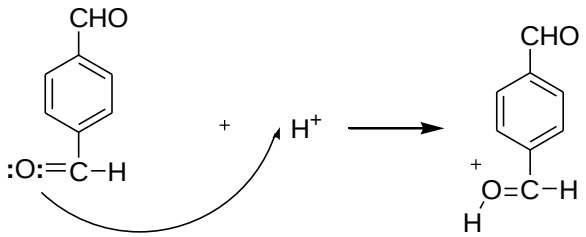


Figure (3.31): The chemical structures of compound A_7

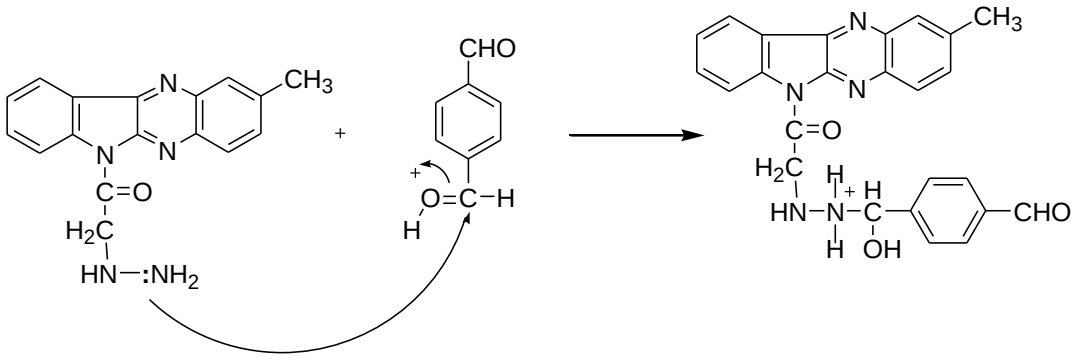
The mechanism for the synthesis of compound A_7 is given in

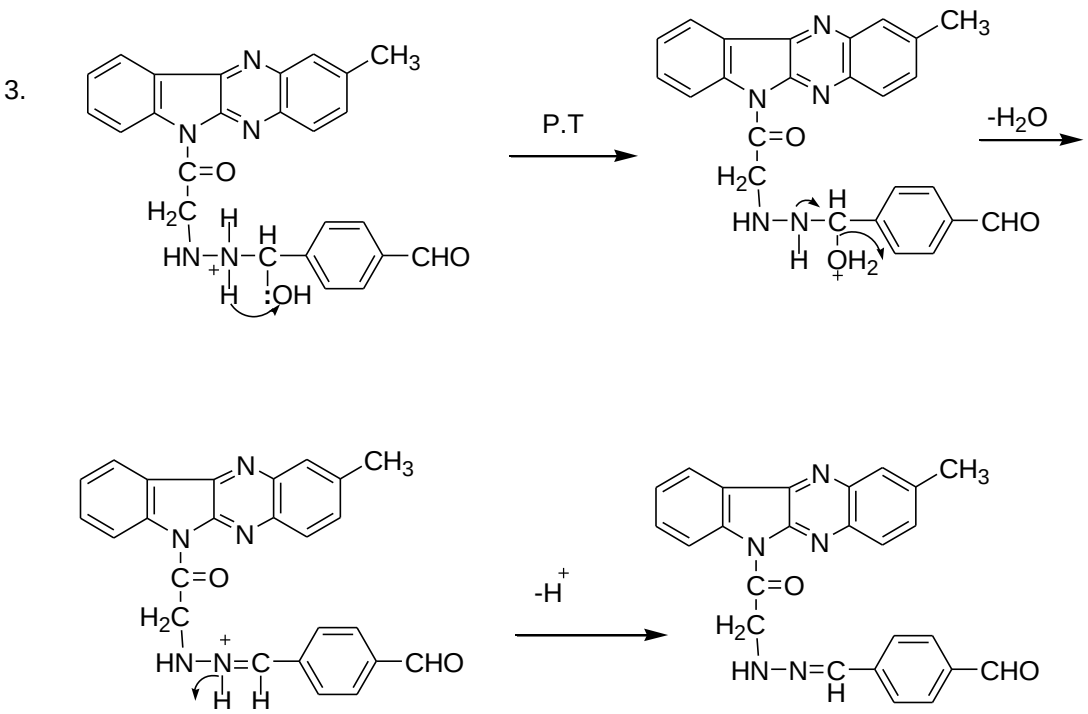
Scheme (3.4) [132] .

1.



2.





Scheme (3.4): The mechanism for the synthesis of (A_7)

The FT-IR spectrum of compound (A_7) Figure (3.33) and Table (3.1) is showing absorption bands at 3345 cm^{-1} was attributed to bonding of N-H group. Absorption band at(2998 asy,2935 sy) cm^{-1} was due to C-H aliphatic. Bond absorption at 1689 cm^{-1} was due to stretching vibration of C=O. Bond absorption at 1641 cm^{-1} was due to CH=N isomethane group stretching vibration. Occurrence of shifting of the C=O and CH=N stretching frequency from the FT-IR spectrums of $[Ni(A_7)_2Cl_2].6H_2O$ complex Figure (3.34) with respect to **(A_7)** compound, in the other hand appeared bands at (457) cm^{-1} which referred to stretching band of M-N, and at (513) cm^{-1} which referred to stretching band of M-O for Ni(II) complexe , is good evidence of the coordination through the C=O and CH=N groups of **(A_7)** compound to the metal ion. Table (3.1) explain FT-IR spectrum bands of A_7 compound and its complex.

The ^{1}H -NMR spectrum of compound (A_7), Figure (3.35) shows the chemical shifts (DMSO-d_6,ppm):10.46 (bro,1H,N-H), 9.42(s,1H,CH=O), 8.7 (s,1H,N=CH), 6.21-7.63 (m,11H,Ar-H), 4.41 (s, 2H, CH_2) and 1.15 (s,3H, CH_3) .

The UV-Visible spectra of the ligand A_7 Figure (3.36) shows two bands at (284.2 nm,35186.4 cm^{-1}) and (350.6 nm, 28522.5 cm^{-1}) which are assigned to π- π* and n-π* transition respectively.

The electronic spectrum of $[Ni(A_7)_2Cl_2].6H_2O$ complex Figure (3.37) and Table (3.2) explain the absorption bands due to π-π*, n-π* and two d-d transitions at (607.2 nm, 16469.0 cm^{-1}),(800nm, 12500 cm^{-1}) due to the coordination of the ligand with metal ion.

The observed magnetic moment value for$[Ni(A_7)_2Cl_2].6H_2O$ complex was (3.0), indicating paramagnetic nature and the conductivity measurements in DMSO solvent at room temperature for Ni (II) complex was (4.8), and this evidence that the complex non-ionic as illustrated in Table (3. 2).

Elemental analysis (C.H.N.S) and metal percentage results for $[Ni(A_7)_2Cl_2].6H_2O$ complex show that the calculated and found percentage values of carbon, hydrogen nitrogen and metal are in a good agreement as show in Table (3.3), Calc. for $[Ni(A_7)_2Cl_2].6H_2O$ (1080.547gm/mol): C, 55.57 ; H, 4.66 ; N, 12.96 ; Ni, 5.4 . Found: C, 55.63 ; H, 4.74 ; N, 13.14 ; Ni, 5.3. According to those data, the following structure can be suggested:

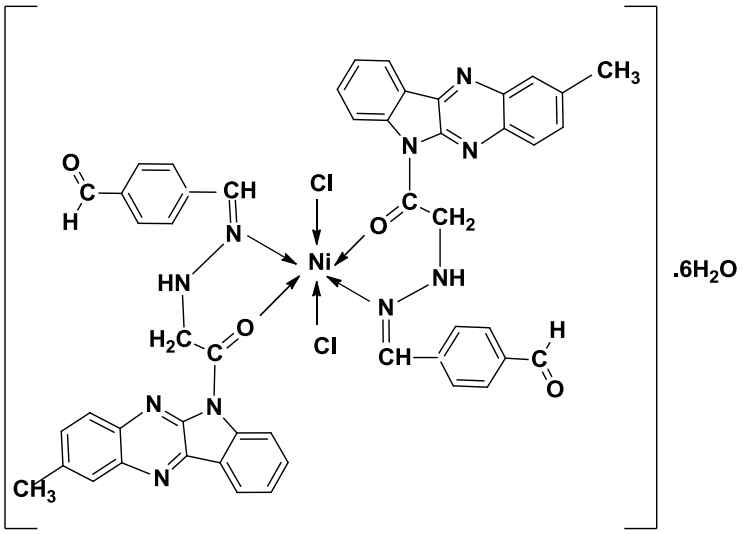


Figure (3.32): The chemical structures of[Ni $(A_7)_2Cl_2$].6H_2Ocomplex

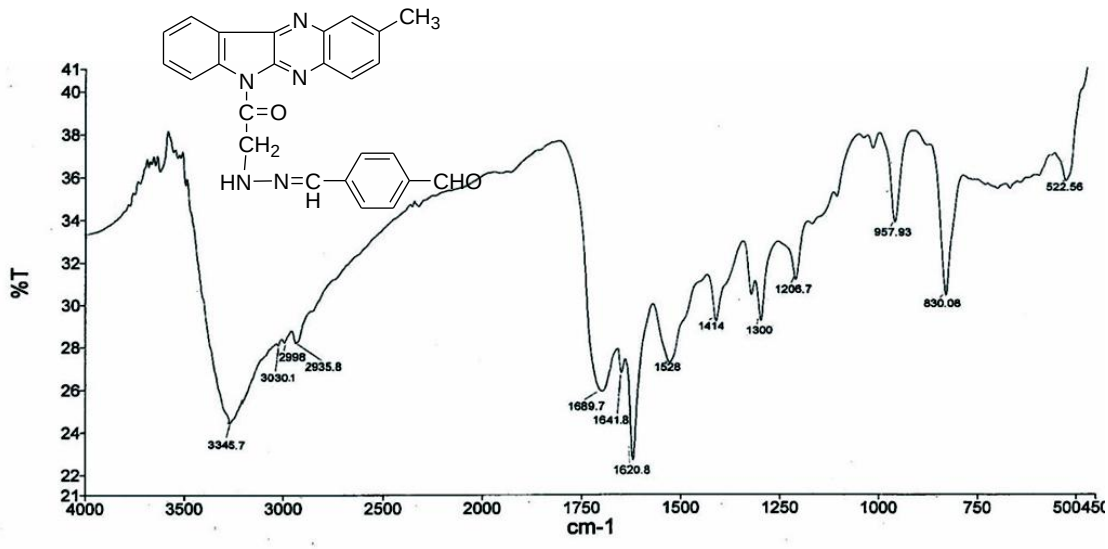


Figure (3.33): FT-IR spectrum in $cm^{-1}$of (A_7) compound

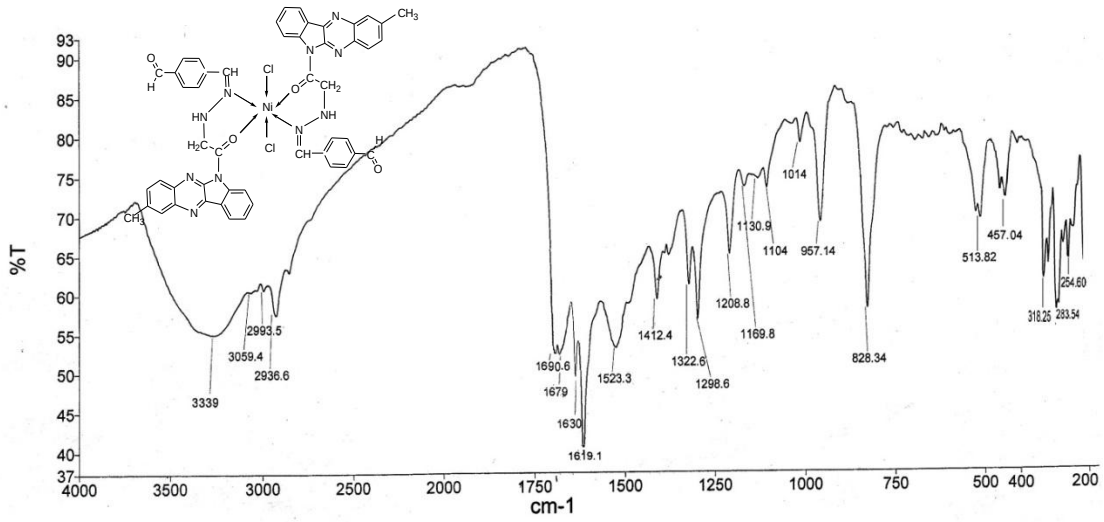


Figure (3.34) : FT-IR Spectrum of $[Ni(A_7)_2Cl_2].6H_2O$

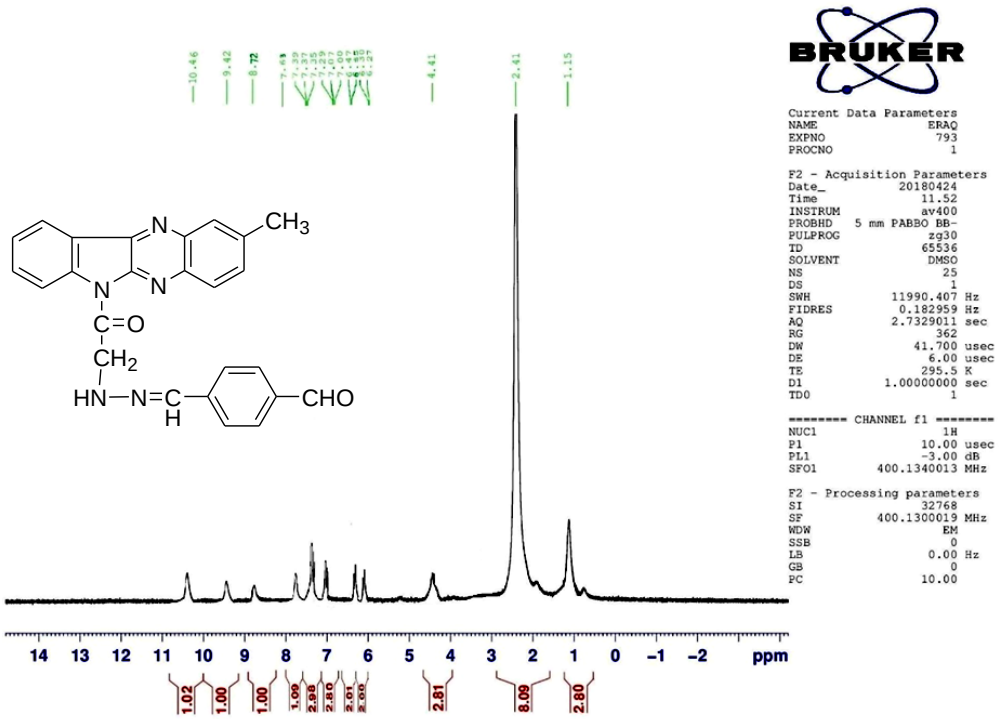


Figure (3.35): ^{1}H NMR spectrum of compound 4-{[2-(2-Methyl-indolo[2,3-b]quinoxalin-6-yl)-2-oxo-ethyl]-hydrazonomethyl}-benzaldehyde [A_7]

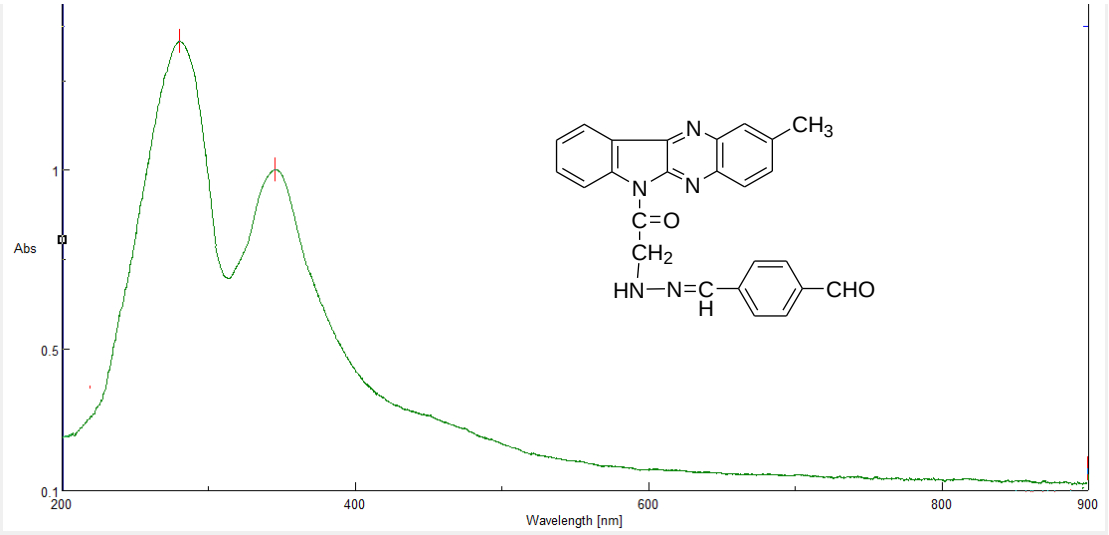


Figure (3.36): UV-VIS Spectrum of A_7

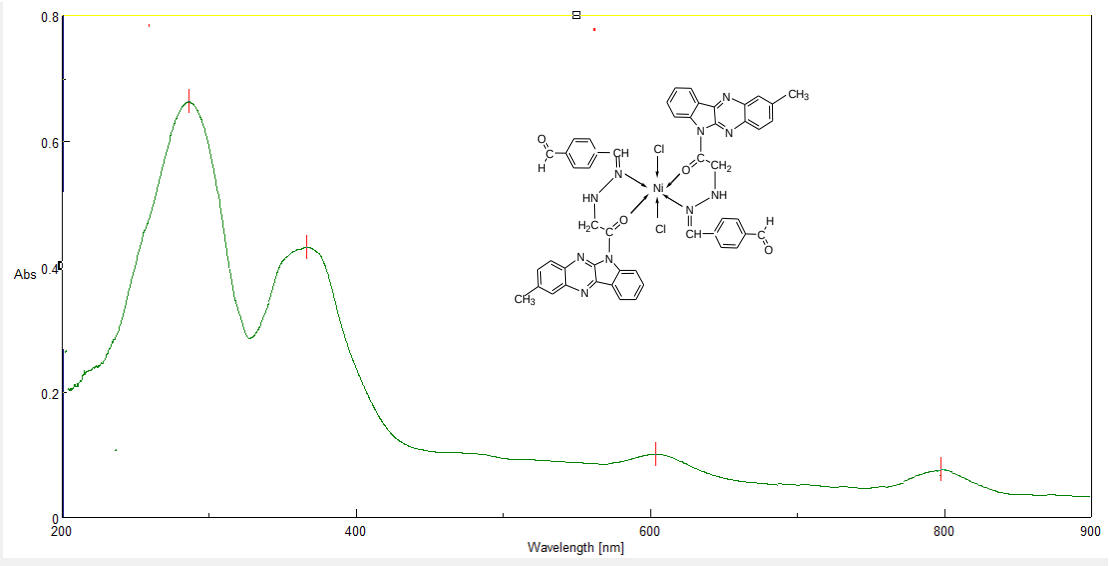


Figure (3.37) : UV-VIS spectrum of $[Ni(A_7)_2Cl_2].6H_2O$

3.8 Synthesis and identification of 2-[N'-(4-Hydroxy-3-methoxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone[A_8] and its complex .

Compound (A_8) was synthesized by the reaction of the compound 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone with 4-hydroxy-3-methoxy-benzaldehyde in the presence of glacial acetic acid in absolute ethanol as shown in Figure (3.38).

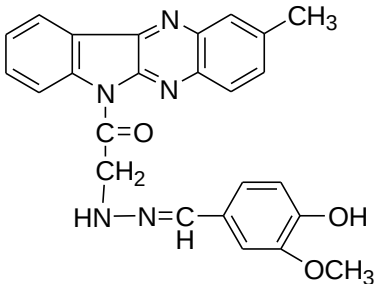


Figure (3.38): The chemical structures of compound A_8

The FT-IR spectrum of compound (A_8) Figure (3.40) and Table(3.1) is showing absorption bands at 3136 cm^{-1} was attributed to bonding of N-H group. Absorption band at 3038 cm^{-1} was due to C-H aromatic. Absorption band at 2936 cm^{-1} was due to C-H aliphatic. Bond absorption at 1662 cm^{-1} was due to stretching vibration of C=O . Bond absorption at 1640 cm^{-1} was due to CH=N isomethane group stretching Bond . Figure (3.40) shows absorption bands at 3345 cm^{-1} was attributed to bonding of N-H group. Absorption band at(2998 asy,2935 sy) cm^{-1} was due to C-H aliphatic. Occurrence of shifting of the C=O and CH=N stretching frequency from the FT-IR spectrums of $[Ni(A_8)_2Cl_2].6H_2O$ complex Figure (3.41) with respect to **(A_8)** compound, in the other hand appeared bands at (469) cm^{-1} which referred to stretching band of Ni-N, and at (573) cm^{-1} which referred to stretching band of Ni -O, is good evidence of the coordination through the C=O and CH=N groups of **(A_8)**

compound to the metal ion. Table (3.1) explain FT-IR spectrum bands of A_8 compound and its complex.

The ^{1}H -NMR spectrum of compound (**A_8**), Figure (3.42) shows the chemical shifts (DMSO-d_6, ppm): 11.05 (s,1H,O-H), 9.42 (bro,1H,N-H), 8.70 (s,1 H,N=CH), 6.36-8.19 (m,10 H, Ar-H), 4.43 (s, 2H, CH_2) 2.22 (s,3H, OCH_3), and 1.46 (s,3H, CH_3) .

The UV-Visible spectra of the compound A_8 Figure (3.43) shows two bands at (249 nm, 40160.6 cm^{-1}) and (320 nm, 31250 cm^{-1}) which are assigned to π- π* and n-π* transition respectively.

The electronic spectrum of $[Ni(A_8)_2Cl_2].6H_2O$ complex Figure (3.44) and Table (3. 2), explain the absorption bands due to π-π*, n-π* and the new band at (386, 25906.7 cm^{-1}) can be assigned to ligand-to-metal charge transfer (LMCT) transitions. In addition exhibited low intensity new bands at (569 nm, 17574.6 cm^{-1}), (793 nm,12610.3cm^{-1}) were assigned to d-d transition due to the coordination of the ligand with metal ion.

The observed magnetic moment value for $[Ni(A_8)_2Cl_2].6H_2O$ complex was (3.2), indicating paramagnetic nature and the conductivity measurements in DMSO solvent at room temperature for Ni (II) complex was (7.5) this evidence that the complex non-ionic as illustrated in Table (3.2).

Elemental analysis (C.H.N.S) and metal percentage results of $[Ni(A_8)_2Cl_2].6H_2O$ complex show that the calculated and the percentage values of carbon, hydrogen nitrogen and metal are similar as show in Table (3.3), Calc. for $[Ni(A_8)_2Cl_2].6H_2O$ (1116.577gm/mol): C, 53.78 ; H, 4.87 ; N, 12.54 ; Ni, 5.25 . Found: C, 53.60 ; H, 4.60 ; N, 12.40

; Ni ,5.16. According to those data, the following structures can be suggested:

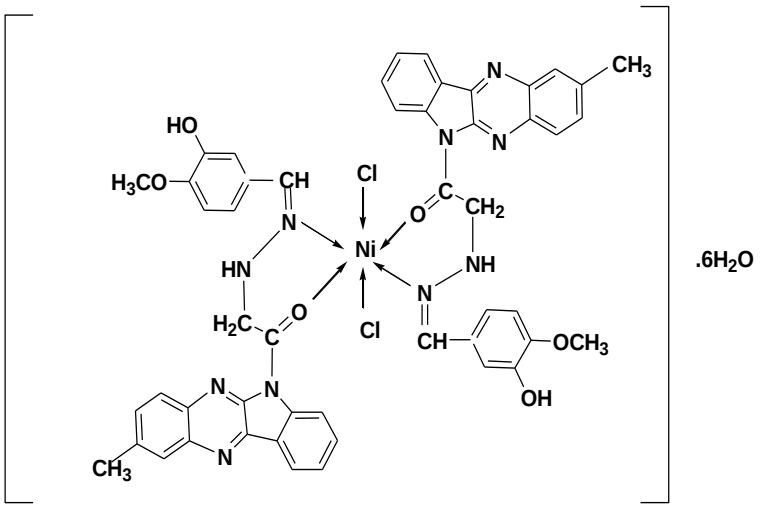


Figure (3. 39): The chemical structures of[Ni $(A_8)_2Cl_2$].6H_2O

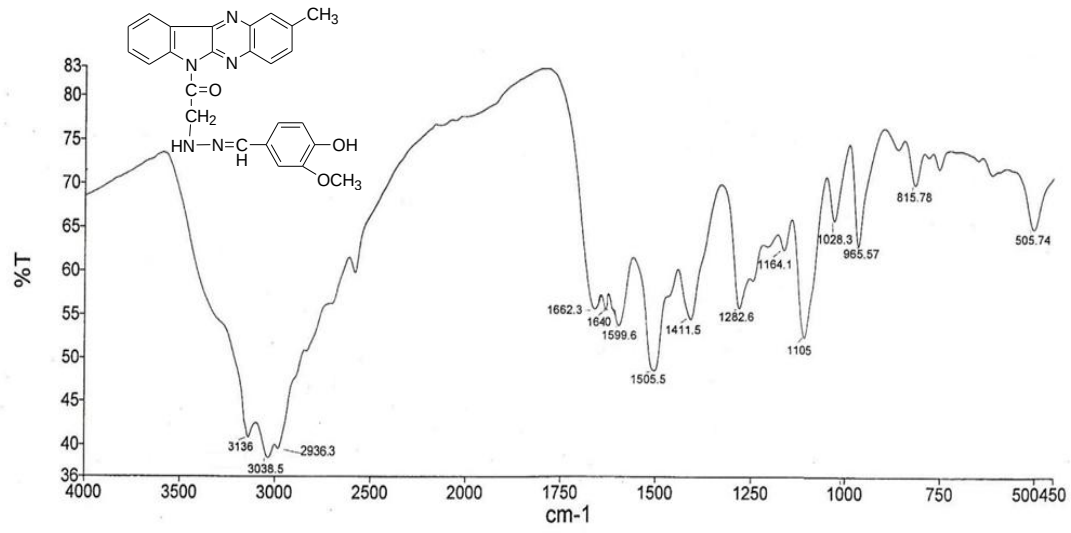


Figure (3.40): FT-IR spectrum in $cm^{-1}$of (A_8) compound

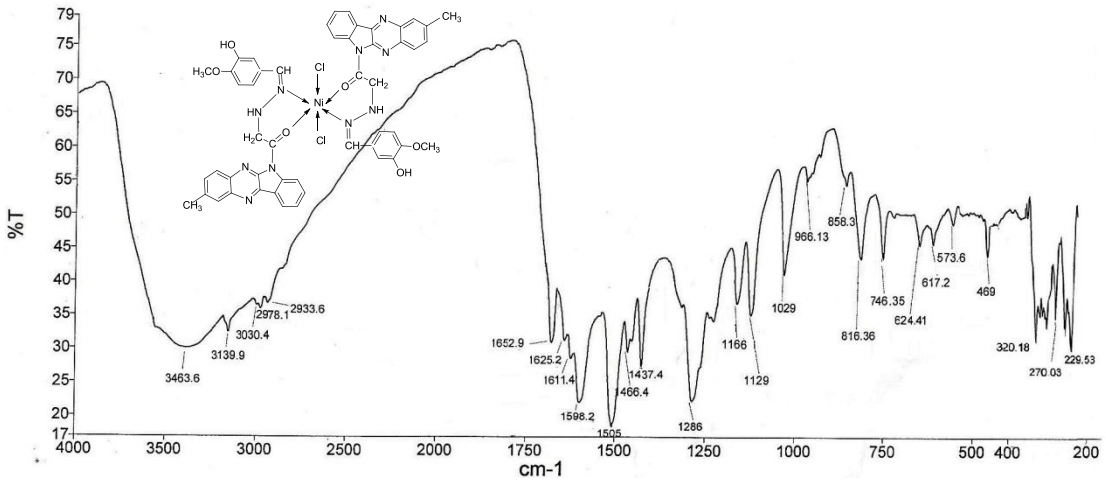


Figure (3.41) : FT-IR spectrum of $[Ni(A_8)_2Cl_2].6H_2O$ complex

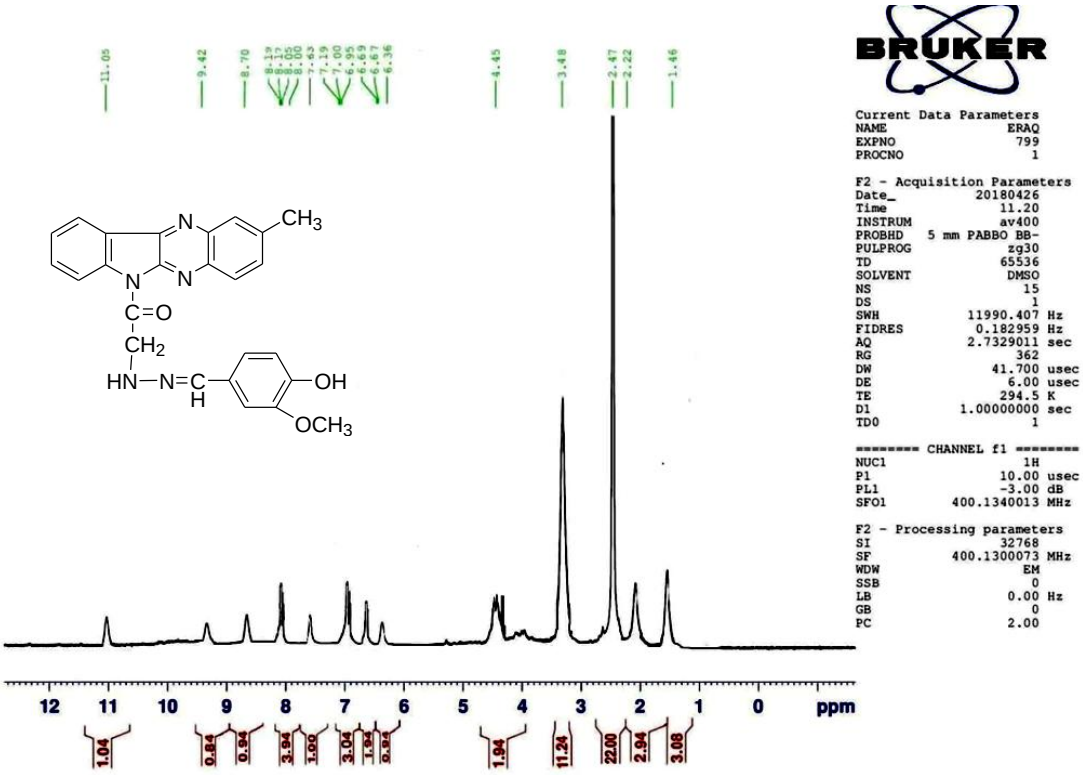


Figure (3.42): ^{1}H NMR spectrum of compound of 2-[N'-(4-Hydroxy-3-methoxy-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone[A_8].

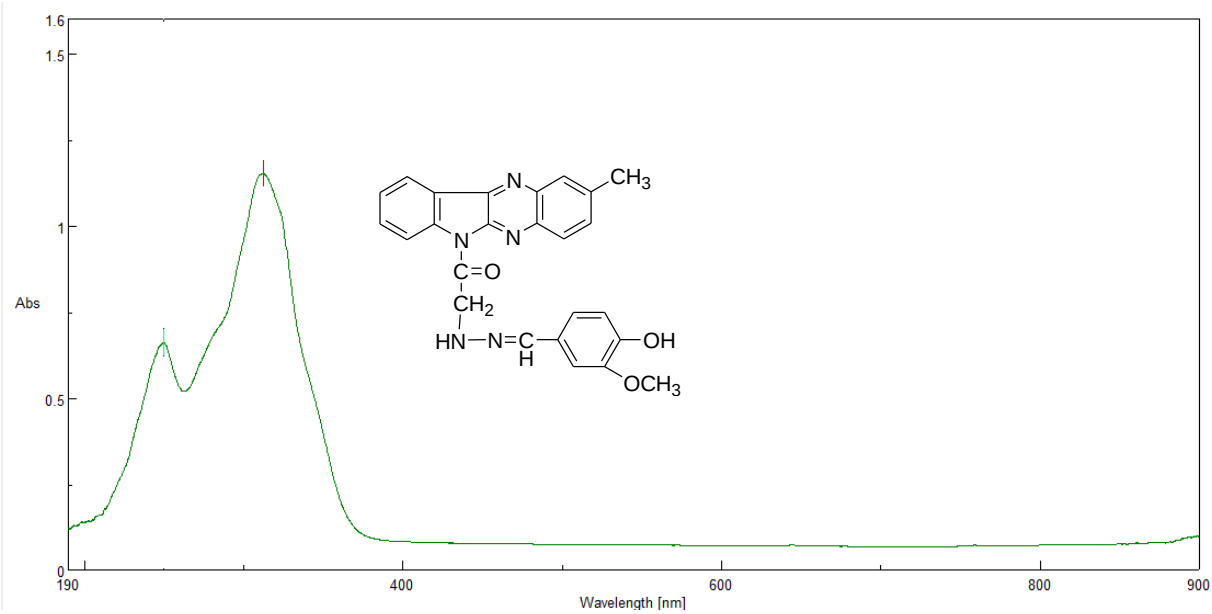


Figure (3.43): UV-VIS spectrum of A_8

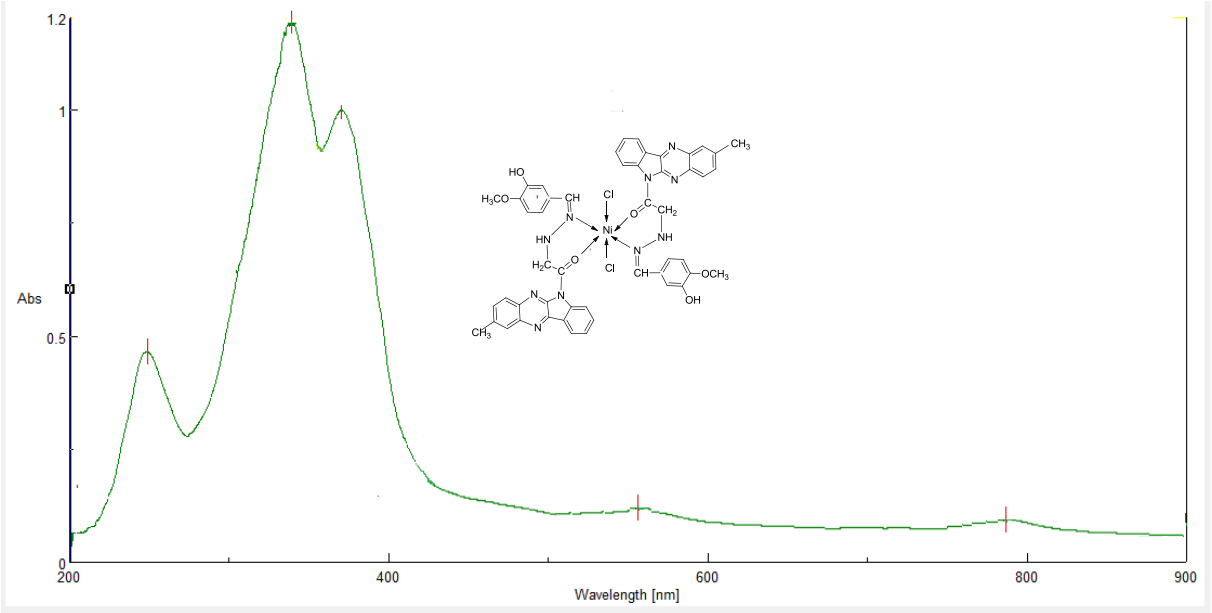


Figure (3.44): UV-VIS Spectrum of $[Ni(A_8)_2Cl_2].6H_2O$

3.9 Synthesis and identification of 2-[N'-(4-Hydroxy-benzylidene)-hydrazino]-1-(2-methylimino-3-m-tolylimino-2,3-dihydro-indol-1-yl)-ethanone [A_9] .

Compound (A_9) was synthesized by the reaction of the compound 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone with 4-hydroxy- benzaldehyde in the presence of glacial acetic acid in absolute ethanol as shown in Figure (3.45).

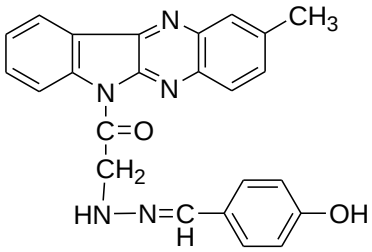


Figure (3.45): The chemical structures of compound A_9

The FT-IR spectrum of compound A_9 Figure (3.46) and Table(3.1) shows absorption bands at 3306 cm^{-1} was attributed to bonding of O-H group. absorption bands at 3195 cm^{-1} was attributed to bonding of N-H group. Bond absorption at 1654 cm^{-1} was due to stretching vibration of C=O. Bond absorption at 1601 cm^{-1} was due to C=N stretching. The bands at 1513 cm^{-1} and 1446 cm^{-1} are due to the C=C aromatic.

The ^{1}H -NMR spectrum of Compound (A_9), Figure (3.47) shows the chemical shifts (DMSO-d_6, ppm): 10.81(s,1H,O-H) 10.01 (bro, 1H,N-H), 8.48 (s,1H,N=CH), 6.27-7.79 (m,11 H,Ar-H), 3.88 (s, 2H, CH_2) and 1.22 (s,3H, CH_3) .

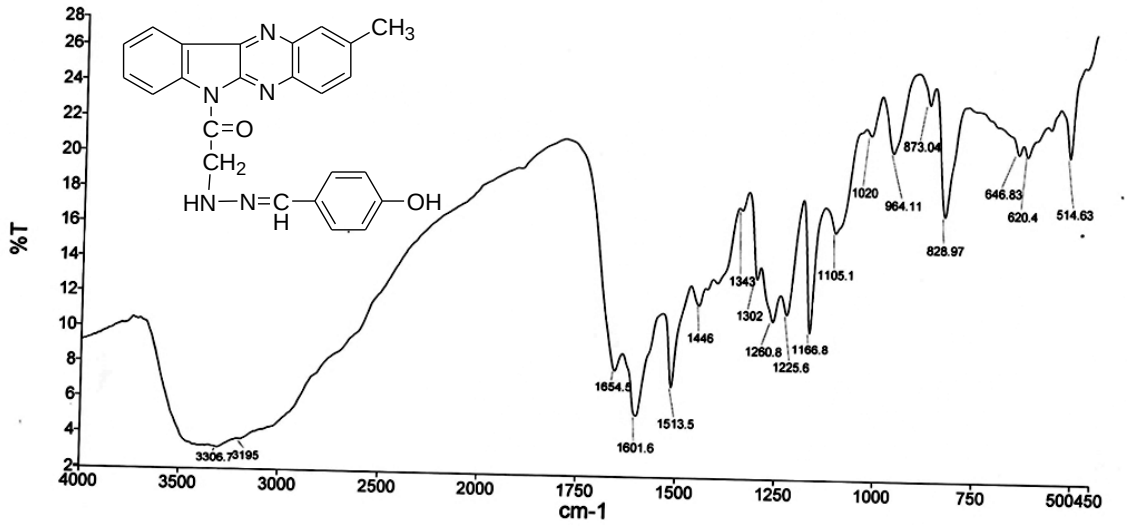


Figure (3.46): FT-IR spectrum in cm^{-1}of (A_9) compound

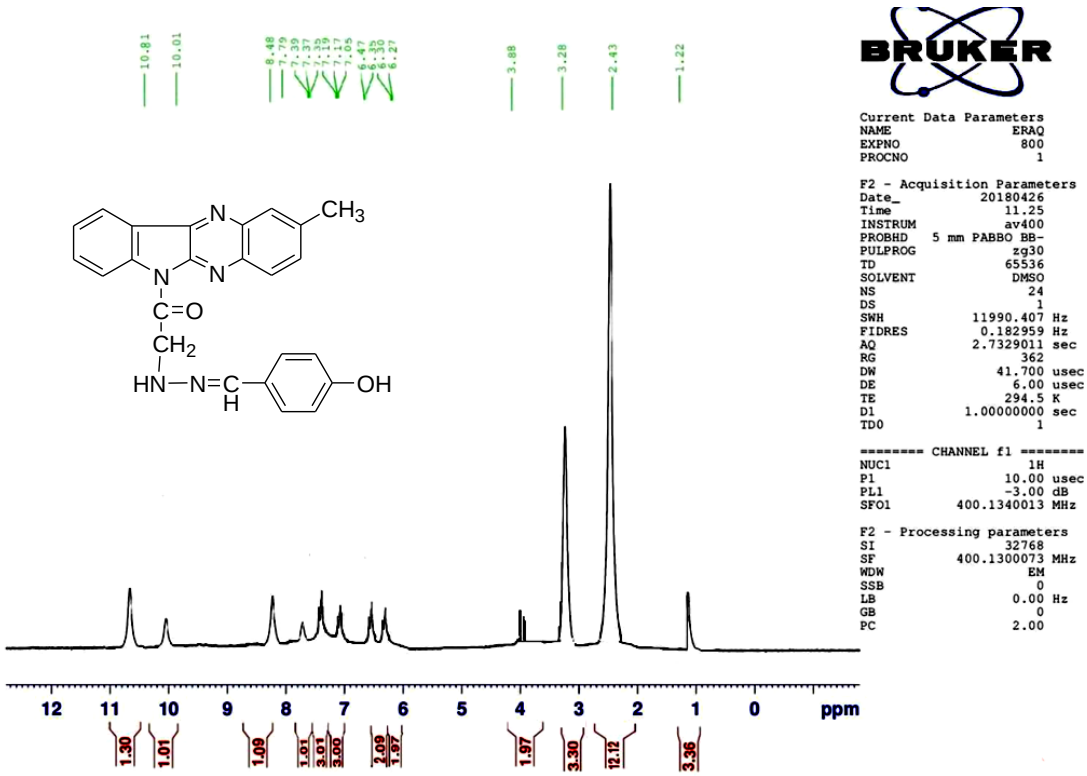


Figure (3.47): ^{1}H NMR spectrum of compound 2-[N'-(4-Hydroxy-benzylidene)-hydrazino]-1-(2-methylimino-3-m-tolylimino-2,3-dihydro-indol-1-yl)-ethanone [A_9]

3.10 Synthesis and identification of 2-[N'-(4-Chloro-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_{10}] .

Compound (A_{10}) was synthesized by the reaction of the compound 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone with 4-chloro- benzaldehyde in the presence of glacial acetic acid in absolute ethanol as shown in Figure (3.48).

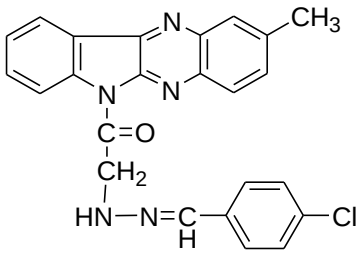


Figure (3.48): The chemical structures of compound A_{10}

The FT-IR spectrum of compound A_{10} Figure (3.49) and Table(3.1) shows absorption bands at 3378 cm^{-1} was attributed to bonding of N-H group. Absorption band at 3053 cm-1 was due to C-H aromatic. Absorption band at 2928 cm^{-1} as due to C-H aliphatic. Bond absorption at 1669 cm^{-1} was due to stretching vibration of C=O . Bond absorption at 1624 cm^{-1} was due to C=N stretching. The bands at 1528 cm^{-1} and 1486 cm^{-1} are due to the C=C aromatic.

The ^{1}H -NMR spectrum of Compound (**A_{10}**), Figure (3.50) shows the chemical shifts (DMSO-d_6, ppm): 9.90 (bro,1H,N-H), 8.72 (s, 1H,N=CH), 6.77-7.49 (m,11 H,Ar-H), 4.38 (s,2H, CH_2). and 1.85(s,3H, CH_3) .

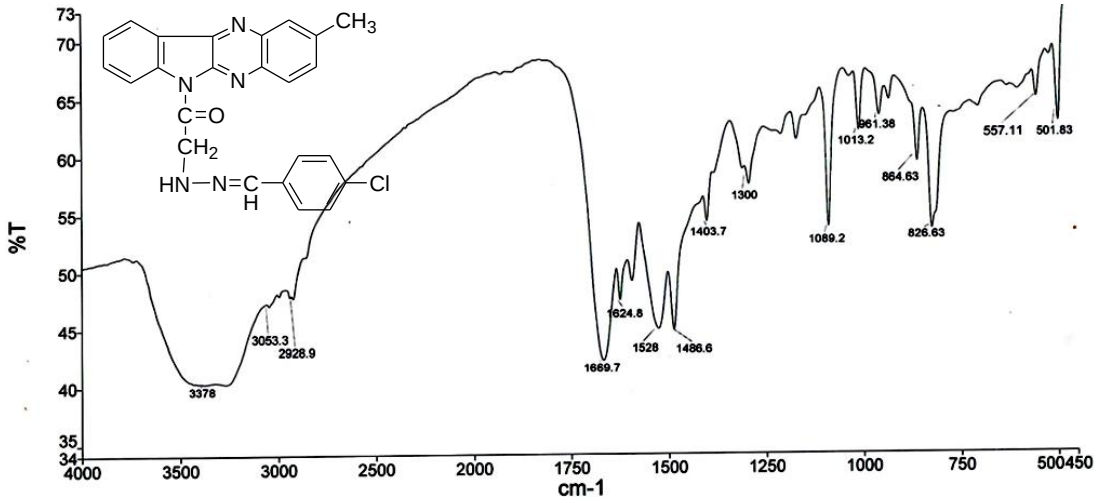


Figure (3.49): FT-IR spectrum in cm^{-1} of (A_{10}) compound

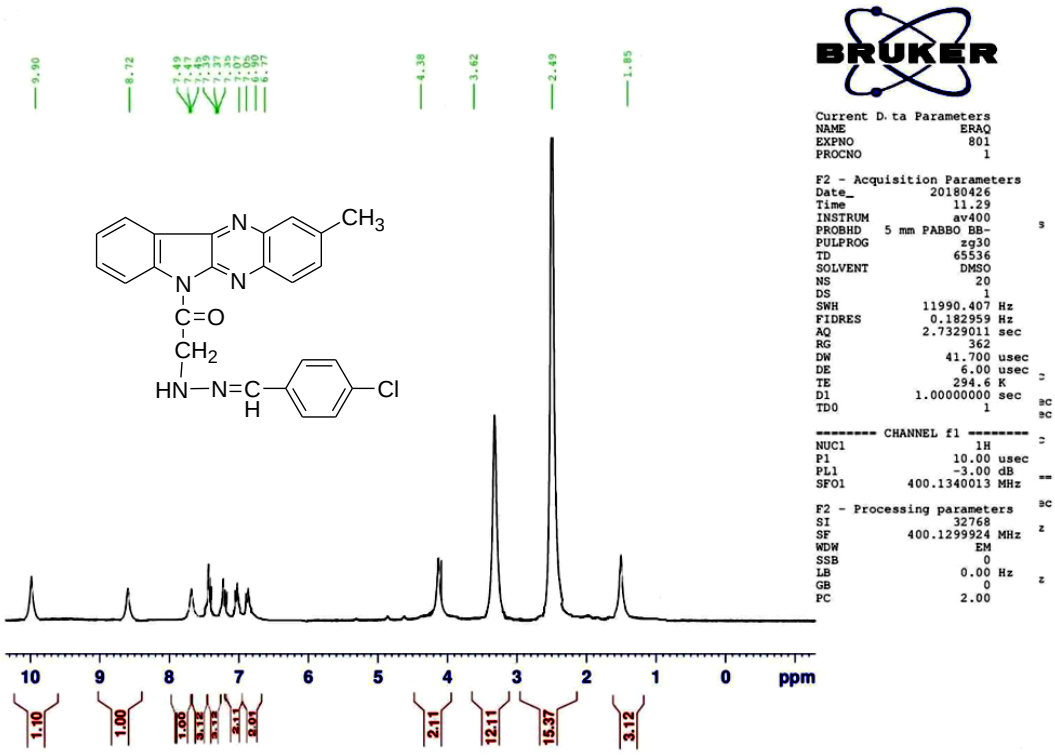


Figure (3.50): ^{1}H NMR spectrum of compound 2-[N'-(4-Chloro-benzylidene)-hydrazino]-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone [A_{10}]

3.12 Synthesis and identification of 1-(2-Methyl-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-nitro-benzylidene)-hydrazino]-ethanone [A_{11}] .

Compound (A_{11}) was synthesized by the reaction of the compound 2-hydrazino-1-(2-methyl-indolo[2,3-b]quinoxalin-6-yl)-ethanone with 4-nitro- benzaldehyde in the presence of glacial acetic acid in absolute ethanol as shown in Figure (3.51).

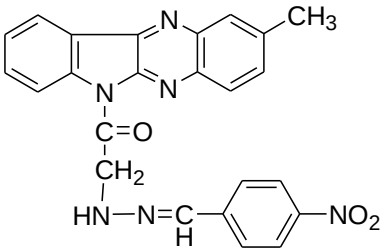


Fig (3.51): The chemical structures of compound A_{11}

The FT-IR spectrum of compound A_{11} Figure (3.52) and Table(3.1) shows absorption bands at 3175 cm^{-1} was attributed to bonding of N-H group. Bond absorption at 1664 cm^{-1} was due to stretching vibration of C=O . Bond absorption at 1628 cm^{-1} was due to C=N stretching. The bands at 1404 cm^{-1} is due to the C=C aromatic .The sharp bands at 1347 cm^{-1} and 1526 cm^{-1} are due to the NO_2.

The ^{1}H -NMR spectrum of Compound (A_{11}), Figure (3.53) shows the chemical shifts (DMSO-d_6, ppm): 9.64 (bro,1H,N–H) , 8.83 (s, 1H,N=CH), 7.1-8.3 (m,11 H,Ar-H) , 4.33 (s, 2H,CH_2) and 1.22(s,3H, CH_3) .

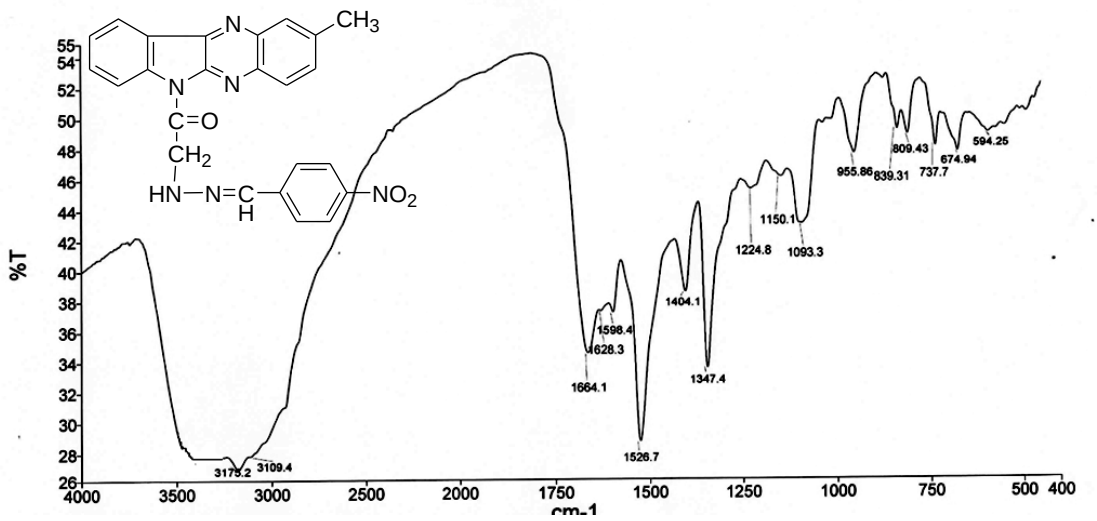


Figure (3.52): FT-IR spectrum in cm^{-1} of (A_{11}) compound

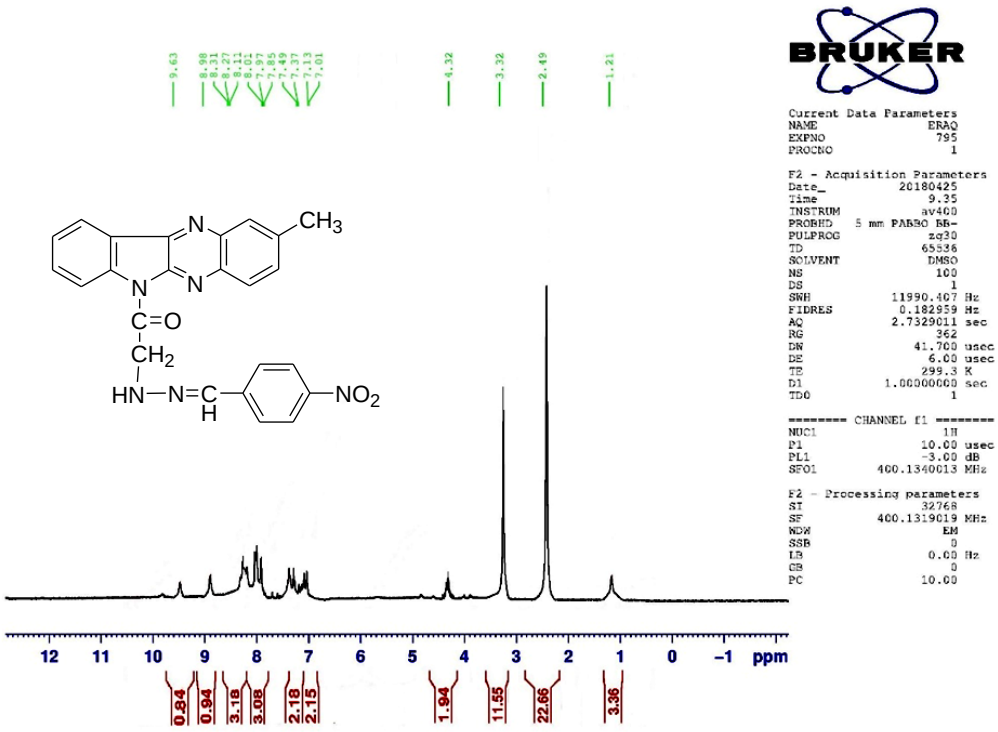


Figure (3.53) ^{1}H NMR spectrum of compound 1-(2-Methyl-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-nitro-benzylidene)-hydrazino]-ethanone [A_{11}]

3.12 Synthesis and identification of 1-(2-Chloro-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-ethanone[A_{12}] .

Compound (A_{12}) was synthesized by the reaction of the compound 1-(2-chloro-indolo[2,3-b]quinoxalin-6-yl)-2-hydrazino-ethanone and 4-hydroxy-3-methoxy-benzaldehyde in the presence of glacial acetic acid in absolute ethanol as shown in Figure (3.54).

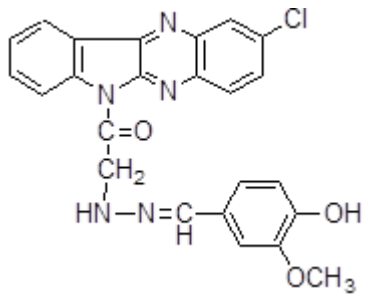


Figure (3.54): The chemical structures of compound A_{12}

The FT-IR spectrum of compound A_{12} Figure (3.55) and Table (3.1) shows absorption bands at 3353 cm^{-1} was attributed to bonding of O-H group. Absorption bands at 3142 cm^{-1} was attributed to bonding of N-H group. Absorption band at 2942 cm^{-1} was due to C-H aliphatic. Bond absorption at 1669 cm^{-1} was due to stretching vibration of C=O. Bond absorption at 1616 cm^{-1} was due to C=N stretching. The sharp bands at 1587 cm^{-1} and1513 cm^{-1} are due to the C=C aromatic.

The ^{1}H -NMR spectrum of Compound (A_{12}), Figure (3.56) shows the chemical shifts (DMSO-d_6, ppm): 10.22 (s,1H,O-H) 9.74 (bro,1H,N-H), 8.5 (s, 1H,N=CH), 6.36-8.2 (m,10 H,Ar-H) , 4.43 (s,2H, CH_2) and 2.26 (s,1H,OCH_3).

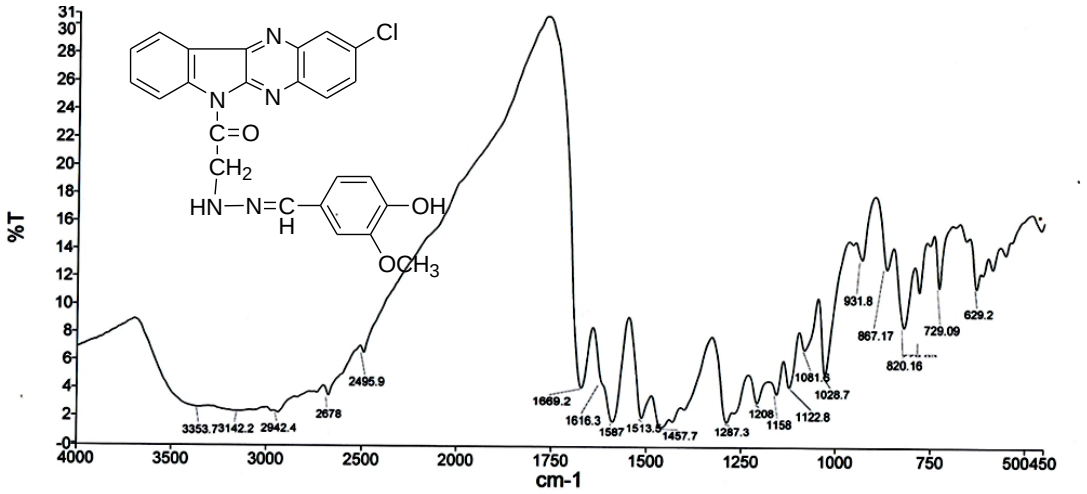


Figure (3.55): FT-IR spectrum in cm^{-1}of (A_{12}) compound

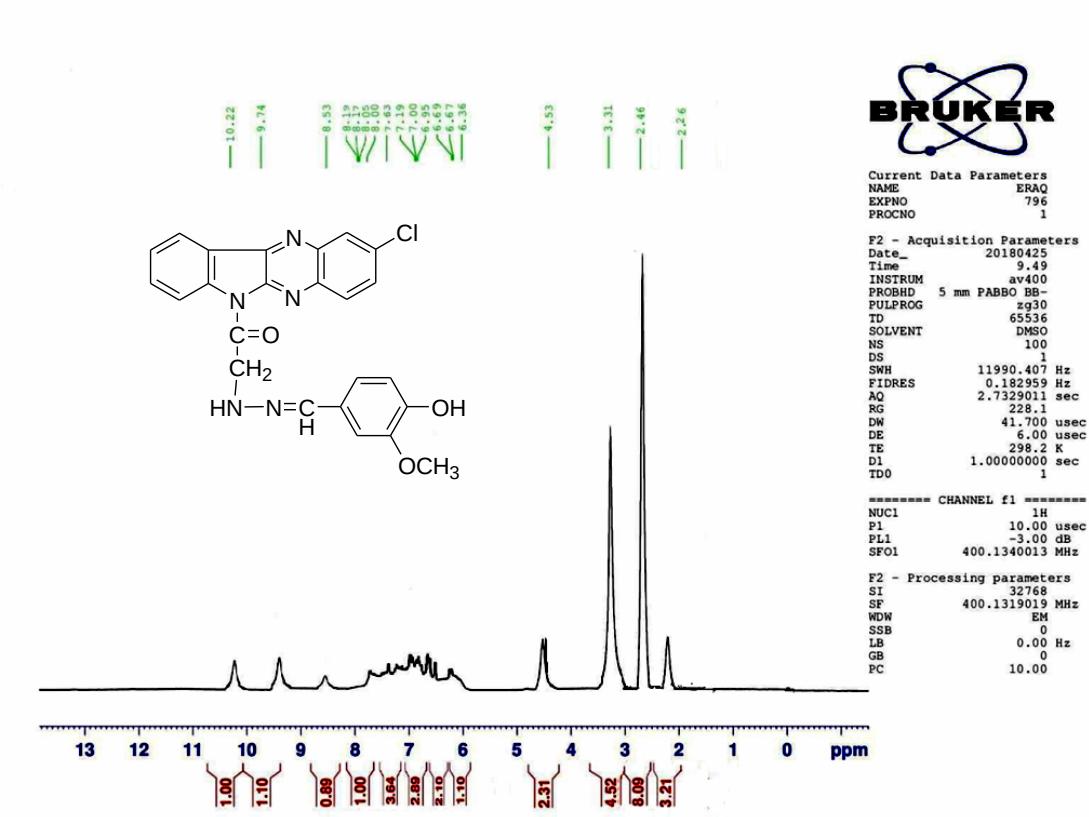


Figure (3.56): ^{1}H NMR spectrum of compound 1-(2-Chloro-indolo[2,3-b]quinoxalin-6-yl)-2-[N'-(4-hydroxy-3-methoxy-benzylidene)-hydrazino]-ethanone[A_{12}]

Table (3.1):The most diagnostic FT-IR bands of the compounds and some their metal complexes in (cm^{-1}).

Comp. symbol	ν N-H	ν C-H aromatic	ν C-H aliphatic	ν C=O	ν C=N	ν M-N	ν M-O	ν M-Cl	Others
A_1	3327	3023	2919	---	1610	---	---	---	ν ($C=C_{aromatic}$) 1434-1513
$[pt(A_1)_2Cl_2].H_2O$	---	3041	2975 2939	---	1632 1613	462	---	335	ν OH(H_2O hydrate) 3410
$[Zn(A_1)_2].5H_2O$	----	3035	2921 2855	---	1625 1598	459	---	---	ν OH(H_2O hydrate) 3487
A_2	3138	3027	---	---	1613	---	---	---	ν ($C=C_{aromatic}$)= 1495, 1579
A_3	---		2930	1679	1617	---	---	---	3437(OH) tuat. ν ($C=C_{aromatic}$) 1516
A_4	---		2927	1693	1620	---	---	---	3373(OH) tuat. ν ($C=C_{aromatic}$) 1474, 1523
A_5	3105	3034	2972 2924	1684	1610 1593	---	---	---	Broad band (H_2O hydrate) ν (NH_2 group) 3226, 3196 ν ($C=C_{aromatic}$) 1525
$[Ni(A_5)_2Cl_2].6H_2O$	3107	----	2975 2921	1670	1610 1589	511	603	314	Broad band (H_2O hydrate) ν NH(NH_2 group) 3287, 3227
$[Co(A_5)_2Cl_2].6H_2O$	3103	---	2971 2923	1676	1613 1586	426	582	324	Broad band (H_2O hydrate) ν (NH_2 group) 3333, 3236
A_6	3133	3019	2924 2852	1676	1619	---	---	---	Broad band (H_2O hydrate) ν (NH_2 group)

									3246,3205 ν (C=C $_{aromatic}$) 1496
A_7	3345	3030	2998 2935	1689	1641 1624	---	---	---	ν (C=C $_{aromatic}$) 1414-1528
$[Ni(A_7)_2 Cl_2]6H_2O$	3339	3059	2993 2936	1690 1679	1630 1619	457	513	318	Broad band (H_2O hydrate)
A_8	3136	3038	2936	1662	1640 1599	---	---	---	ν OH(phenol) broad band
$[Ni(A_8)_2 Cl_2]6H_2O$	3139	3030	2978 2933	1652	1625 1611 1598	469	573	320	Broad band (H_2O hydrate) ν OH(phenol) 3463
A_9	3195			1654	1601				ν OH(phenol) 3306 ν (C=C $_{aromatic}$) 1446-1513
A_{10}	3378	3053	2928	1669	1624				ν (C=C $_{aromatic}$) 1486-1528
A_{11}	3175	3109	2923	1664	1628 1598				NO_2 1347-sym. 1526-asym. ν (C=C $_{aromatic}$) 1404
A_{12}	3142		2942	1669	1616	---	---	---	ν OH(phenol) 3353 ν (C=C $_{aromatic}$) 1587,1513

Table(3.2):Electronic spectra ,conductance in DMSO solvent and magnetic moment(B.M) for the prepared ligand and there metal complexes.

Comp.	**Absorption Band (nm, Cm^{-1})**	**Assignments**	***M*eff (B.M)**	**Mol.Cond. $Cm^2.ohm^{-1}$. mol**	**Suggested Geometry**
A_1	(245.4, 40749.7) (290.8, 34387.8) (350, 28571.4) (457, 21881.8)	π → π* n →π* ILCT ILCT	--------	--------	--------

[pt(A_1)$_2$ Cl_2].H_2O	(251.2,39808.9) (281.8, 35486.1) (348.2,28719.1) (491.2, 20358.3) (729.4,13709.8)	ILCT ILCT ILCT ILCT $^1A_1g \rightarrow {}^1T_1g$	Dia	3.6	Oh
[Zn(A_1)$_2$]].5H_2O	(248.4, 40257.6) (289.8, 34506.5) (352.4, 28376.8) (472.2, 21177.4)	ILCT	Dia	5.9	Td
A_5	(262.4, 38109.7) (454.4, 22007.04)	$\pi \rightarrow \pi^*$ ILCT	-------	-------	-------
[Ni(A_5)$_2$$Cl_2$].6$H_2O$	(294.4, 36469.7) (343.8, 28669.7) (452.2, 22114.1) (807.8, 12379.3)	ILCT LMCT ILCT $^3A_2g \rightarrow {}^3T_2g$	3.1	3.9	Oh
[Co(A_5)$_2$$Cl_2$].6$H_2O$	(274.2, 36469.7) (347.6, 28768.6) (452.2,22114.1) (744,13440.8)	ILCT LMCT ILCT $^4T_1g \rightarrow {}^4A_2g$	4.3	4.1	Oh
A_7	(284.2,35186.4) (350.6, 28522.5)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	-------	-------	-------
[Ni(A_7)$_2$$Cl_2$].6$H_2O$	(290.2, 34458.9) (379.4, 26357.4) (607.2, 16469.0) (800, 12500)	ILCT ILCT $^3A_2g \rightarrow {}^3T_1g_{(F)}$ $^3A_2g \rightarrow {}^3T_2g$	3	4.8	Oh
A_8	(249, 40160.6) (320, 31250)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	-------	-------	-------
[Ni(A_8)$_2$$Cl_2$].6$H_2O$	(254, 39370) (345, 28985.5) (386, 25906.7) (569, 17574.6) (793,12610.3)	ILCT ILCT LMCT $^3A_2g \rightarrow {}^3T_1g_{(F)}$ $^3A_2g \rightarrow {}^3T_2g$	3.2	7.5	Oh

Table (3.3): C.H.N and metal percentage results for complexes

Comp.	Chemical formula	M.W g/mol	Elemental analysis *Found (calc.)*			Metal Percentage *Found (calc.)*
			C	H	N	
A_1	$C_{15}H_{11}N_3$	233.256	--------	--------	--------	--------
$[pt(A_1)_2\ Cl_2].\ H_2O$	$[pt(C_{15}H_{10}N_3)_2Cl_2].\ H_2O$	748.493	47.98 (48.13)	2.70 (2.96)	11.67 (11.22)	26.32 (26.06)
$[Zn(A_1)_2]\ ].5H_2O$	$[Zn(_{15}H_{10}N_3)_2].5H_2O$	691.961	57.99 (58.11)	4.83 (4.87)	13.77 (13.55	10.39 (10.54)
A_5	$C_{17}H_{15}N_5O$	305.319	--------	--------	--------	--------
$[Ni(A_5)_2Cl_2].6H_2O$	$[Ni(C_{17}H_{15}N_5O)_2Cl_2].6H_2O$	848.325	48.00 (48.13)	5.00 (4.99)	16.65 (16.50)	7.00 (6.91)
$[Co(A_5)_2Cl_2].6H_2O$	$[Co(C_{17}H_{15}N_5O)_2Cl_2].6H_2O$	848.565	47.99 (48.12)	4.85 (4.98)	16.42 (16.50)	6.75 (6.94)
A_7	$C_{25}H_{19}N_5O_2$	421.43	--------	--------	--------	--------
$[Ni(A_7)_2Cl_2].6H_2O$	$[Ni(C_{25}H_{19}N_5O_2)_2Cl_2].6H_2O$	1080.547	55.63 (55.57)	4.74 (4.66)	13.14 (12.96)	5.3 (5.4)
A_8	$C_{25}H_{21}N_5O_3$	439.445	--------	--------	--------	--------
$[Ni(A_8)_2Cl_2].6H_2O$	$[Ni(C_{25}H_{21}N_5O_3)_2Cl_2].6H_2O$	1116.577	53.60 (53.78)	4.60 (4.87)	12.40 12.54)	5.16 (5.25)

Table(3.4): Physical data for new compounds and metals complexes.

Comp. symbol	*Molecular Formula*	*M. Wt (g.mol $^{-1}$)*	*M.P. ° C*	*Yield %*
A_1	$C_{15}H_{11}N_3$	*233.3*	76-78	93
$[pt(A_1)_2\ Cl_2]\ H_2O$	$[pt(C_{15}H_{10}N_3)_2Cl_2].H_2O$	748.49	Above300	90
$[zn(A_1)_2]\ 5H_2O$	$[Zn(C_{15}H_{10}N_3)_2].5H_2O$	691.961	130-132	60
A_2	$C_{14}H_8N_3Cl$	253.7	Above300	51
A_3	$C_{17}H_{12}N_3OCl$	309.7	132-134	98
A_4	$C_{16}H_9N_3OCl_2$	230.2	Above300	76
A_5	$C_{17}H_{15}N_5O$	305.2	Above300	83
$[Ni(A_5)_2\ Cl_2]\ 6H_2O$	$[Ni(C_{17}H_{15}N_5O)_2Cl_2]\ .6H_2O$	848.325	Above300	79
$[Co(A_5)_2\ Cl_2]\ 6H_2O$	$[Co(C_{17}H_{15}N_5O)_2Cl_2].6H_2O$	848.565	Above300	80
A_6	$C_{16}H_{12}N_5OCl$	325.8	Above300	71
A_7	$C_{25}H_{19}N_5O_2$	421.5	Above300	94
$[Ni(A_7)_2\ Cl_2]\ 6H_2O$	$[Ni(C_{25}H_{19}N_5O_2)_2Cl_2].6H_2O$	1080.547	Above300	91
A_8	$C_{25}H_{22}N_5O_3$	439.2	138-140	71
$[Ni(A_8)_2\ Cl_2]\ 6H_2O$	$[Ni(C_{25}H_{21}N_5O_3)_2Cl_2].6H_2O$	1116.577	Above300	78
A_9	$C_{24}H_{19}O_2N_5$	409.4	236-238	89
A_{10}	$C_{24}H_{18}N_5OCl$	427.9	260-262	64
A_{11}	$C_{24}H_{18}N_6O_3$	438.4	180-182	87
A_{12}	$C_{24}H_{18}N_5O_3Cl$	459.9	254-256	73

3.13 Antifungal activity testing

The antifungal activity of the synthesized ligands and the complexes were evaluated against *(Cryptococccus neoforman, Candida albicans, Rhodotorula rubra, Aspergilus parasiticus, Penicilium sp, Rhizopus arrhizus*) by the agar plate technique . DMSO was chosen as a solvent. The results of the synthesized compounds in are shown in Table (3.5) . The complex $[Co(A_5)_2Cl_2].6H_2O$ was showed high activity. Also complex $[pt(A_1)_2Cl_2].H_2O$ exhibits good activity. Remaining compounds showed good, moderate to poor activity against the fungal strains. In conclusion, shown complexes exhibit higher antifungaul activity than the corresponding free ligands due to chelation process which reduces the polarity of metal ions [133].

Table (3.5): The* anti fungal test *results of the synthesizde compounds and their complexes .

Compound	No	*Cryptococccs neoformans*	*Candida albicans*	*Rhodotorula rubra*	*Aspergilus parasiticus*	*Penicilim sp.*	*Rhizops arrhizus*
		Inhibition zone diameter (mm)					
A_1	7	21	16	24	22	0	0
$[pt(A_1)_2Cl_2].H_2O$	1	26	24	25	15	15	23
A_2	2	30	16	25	0	0	0
A_3	4	25	15	18	0	20	25
A_5	3	24	21	1-25	16	20	22
$[Co(A_5)_2Cl_2].6H_2O$	8	32	27	26	20	24	26
A_{11}	6	11	18	30	0	17	0

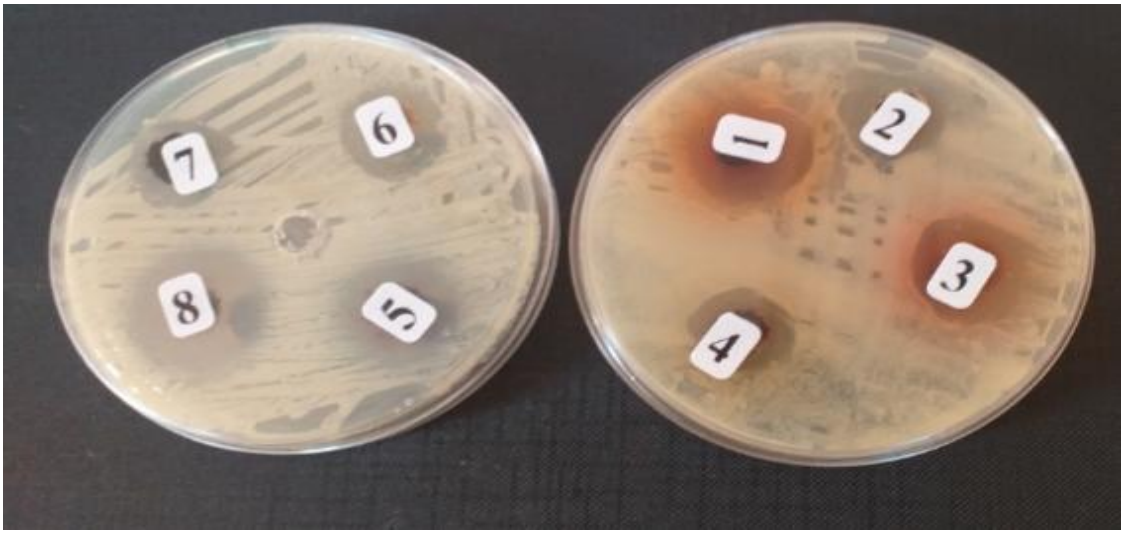


Figure (3.57): Antifungal activity against Candida albicans

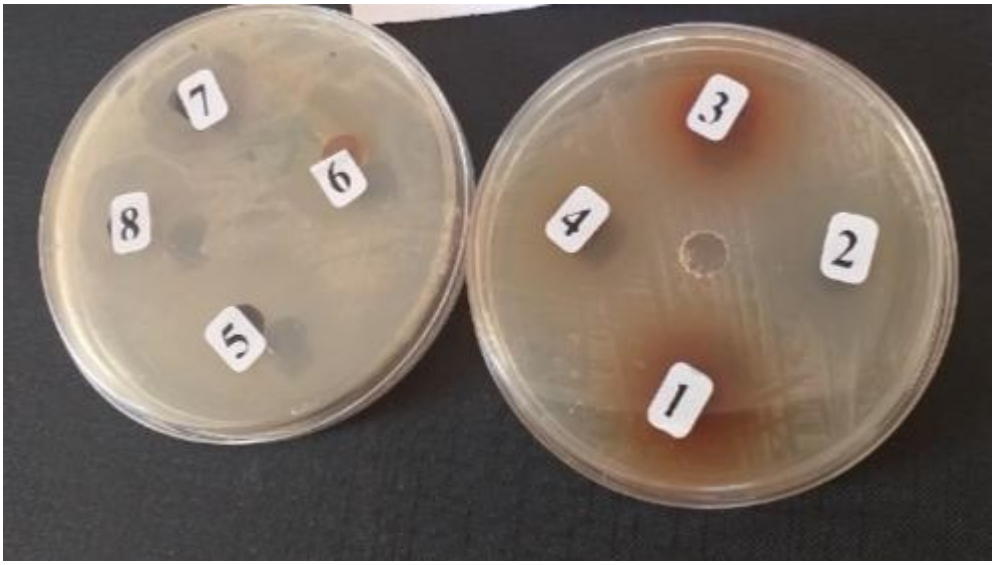
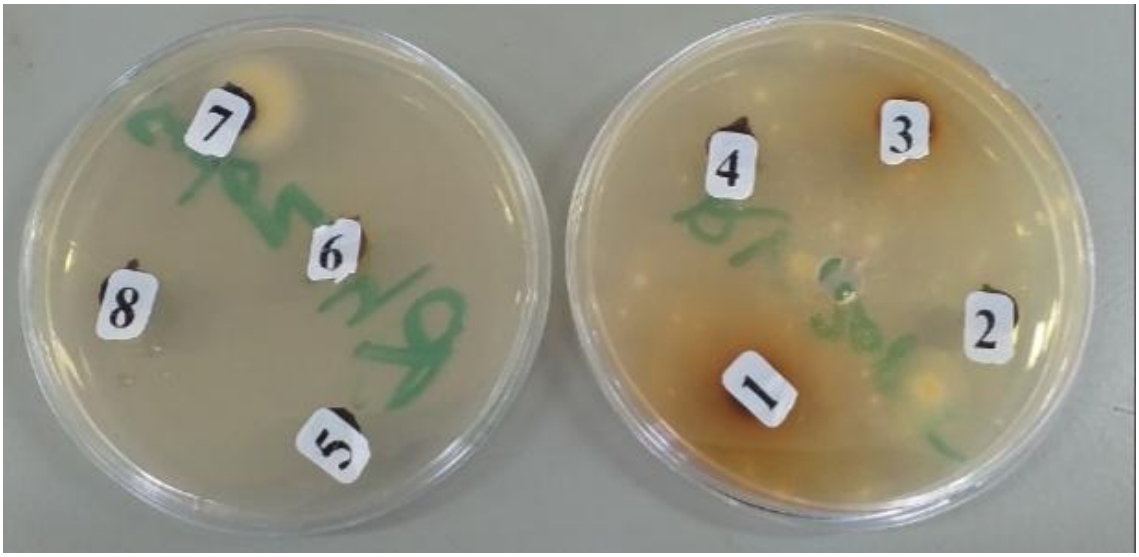


Figure (3.58): Antifungal activity against Rhodotorula rubra



Figure(3.59): Antifungal activity against Rhizopus arrhizus.

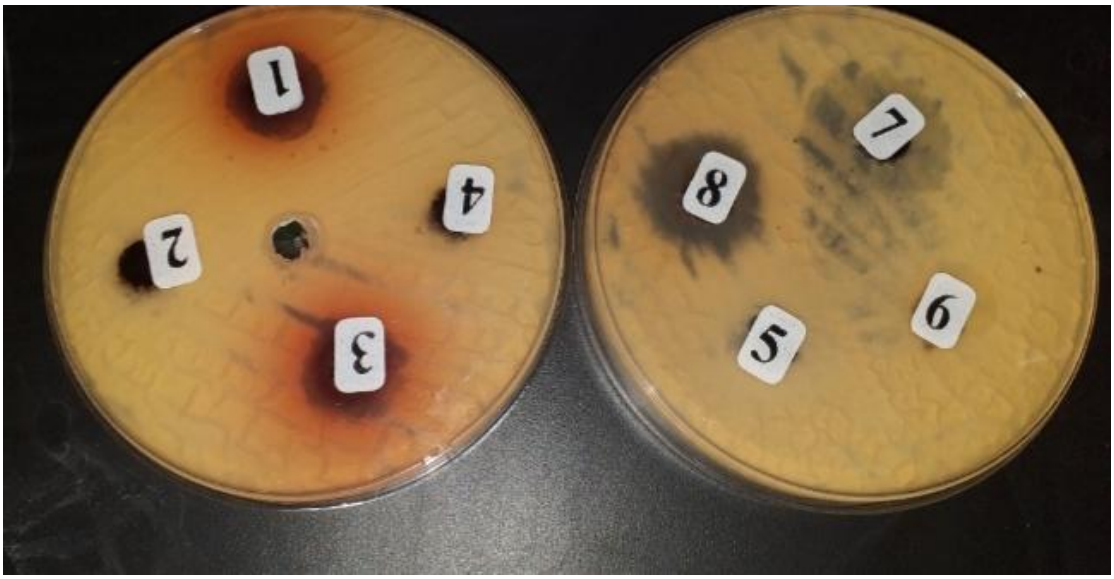


Figure (3.60): Antifungal activity against Aspergilus parasiticus

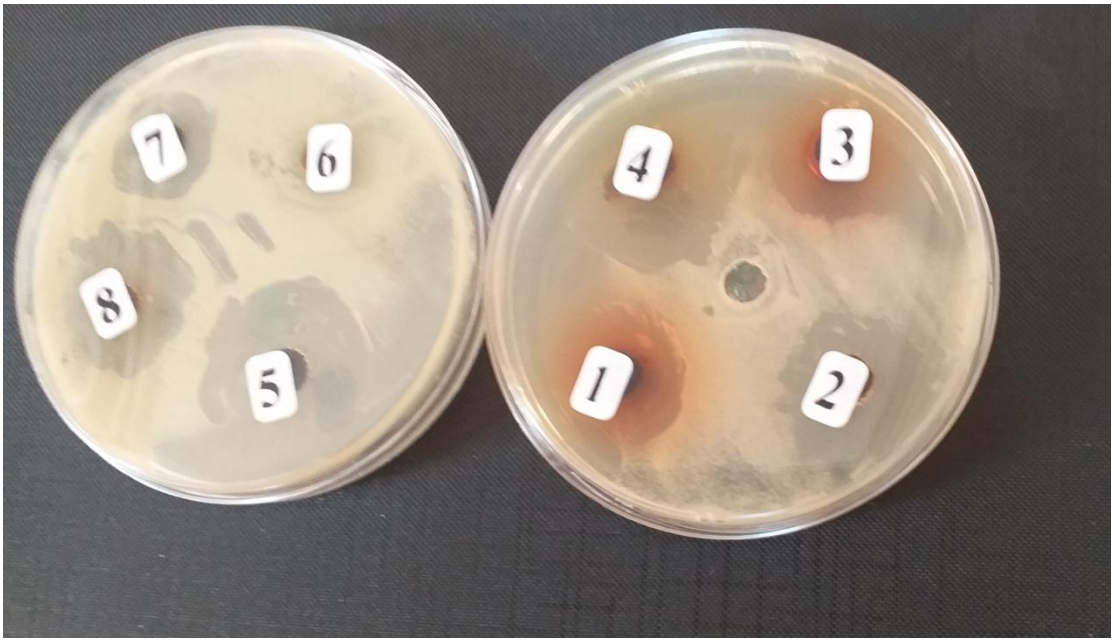


Figure (3.61): Antifungal activity against Cryptococccus neoformans

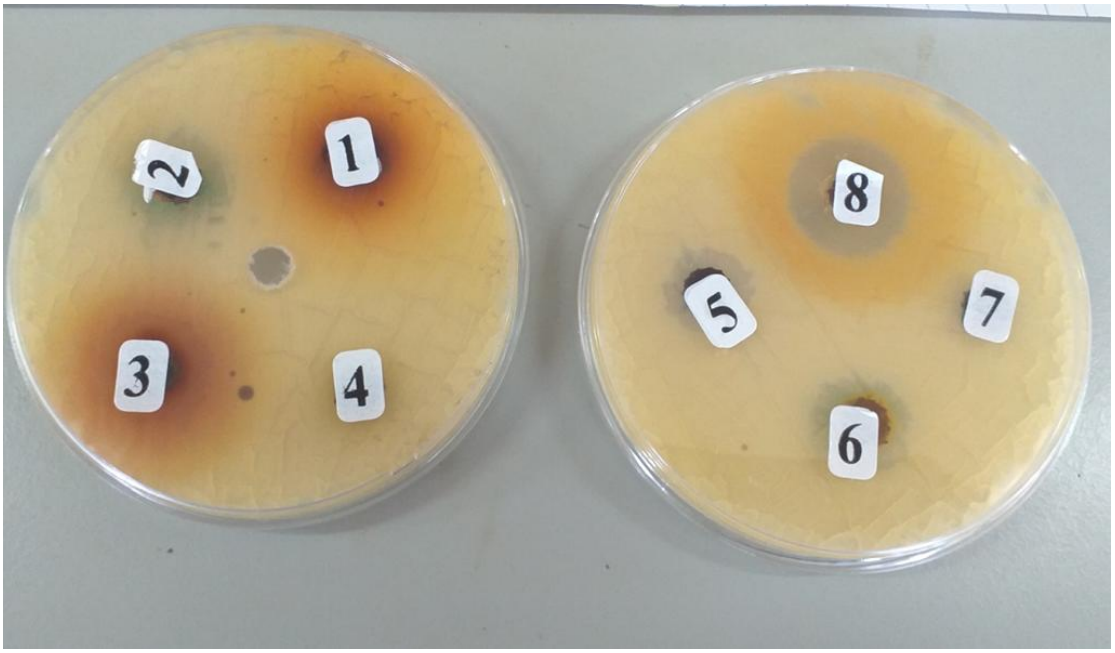


Figure (3.62): Antifungal activity against Penicilium sp.

CONCLUSION

Conclusion

New compounds of indole were synthesized (A_1-A_{12}) and identified by melting point, TLC, UV-VIS spectrum, FT-IR, and ^{1}H-NMR spectroscopy techniques. Identification and study of complexes were carried out by melting point, percentage of metal analysis using flam atomic absorption, infrared spectroscopy, ultra violet-visible spectroscopy, magnetic susceptibility, elemental analysis CHNS, and electronic conductivity measurements. Conductivity measurements showed that all the synthesized complexes were non-ionic and all their complexes were octahedral geometry around metal ions expect complex $[Zn(A_1)_2Cl_2].5H_2O$ was tetrahedral geometry . Most of the synthesized compounds were tested for in vitro against several fungi including *Cryptococccus neoforman, Candida albicans, Rhodotorula rubra, Aspergilus parasiticus, Penicilium sp, Rhizopus arrhizus* the agar plate technique. The results showed that, the complex $[Co(A_5)_2Cl_2]6H_2O$ exhibited high activity. Also complex $[pt(A_1)_2Cl_2]H_2O$ exhibited high activity. The other compounds showed high, moderate to poor activity against the fungal strains compared to the metal complexes, ligands have shown poor activity.

Suggestions for future work:

1. Synthesize a series of new complexes for synthesized compounds (A_2 ,A_6 ,A_9 ,A_{10} ,A_{11} ,A_{12}) with different transition metal ions and evaluate their biological activities.
2. Synthesis of new Schiff bases from the reaction of the compounds (A_5-A_6) with different aldehydes .

3. Study of biological activity of the derivatives and their complexes against other types of fungi and bacteria .
4. Investigate of some industrial applications of these derivatives and their complexes.

References

REFERENCES

1. Ahmed, S. K . (2019). Synthesis and characterization of 1،2،4-triazol derivatives and study their activities as corrosion inhibitors of low carbon steel in acidic media. M.Sc. thesis, College of Science, University of Diyala, Iraq.

2. Mane, D., Azeem, S., Pande, S., Malpani, O., and Kharat, J . (2018) . Synthesis of some flavone and pyrazoline derivative and their antimicrobial and physicochemical study. *Current Engineering and Scientific Research*, (5): 489- 493.

3. Hassan, A. H. (2019). Synthesis, characterizations and evaluation of biological activity of some new pyrazoles derived from substituted indol-2-ylidene. M.Sc. thesis, College of Science, University of Diyala, Iraq.

4. Mishra, G., Singh, A. K., and Jyoti, K. (2011). Review article on 1,3,4-thiadiazole derivatives and its pharmacological activities. *International Journal of ChemTech Research*, *3*(3): 1380-1393.

5.Joule, J. A., and Mills, K. (2012). Heterocyclic chemistry at a glance. 2nd ed. John Wiley and Sons. USA, 354-357.

6. Mohammed , A. M. (2018) . Synthesis and characterization of some new benzimidazole derivatives and their biological activity study. M.Sc. thesis, College of Science, University of Diyala, Iraq.

7. Alsubari, A., Bouhfid, R., and Essassi, E. M. (2009). Synthesis of new oxindole derivatives containing an oxazolidin-2-one. *Online Journal of Organic Chemistry*, *10* (7): 337-346 .

8. Makarem, S., Mirza, B., Mohammad Darvish, Z., Amiri Notash, N., and Ashrafi, S. (2019). Organic electrosynthesis: Apromising alternative methodology for the synthesis of nanosized particles of pyrans. *Analytical and Bioanalytical Chemistry Research*, *6*(1): 231-240.

9. Zou, S., Wang, S., and Xi, C. (2018). Rotf-induced annulation of heteroatom reagents and unsaturated substrates leading to cyclic compounds. *Royal Society open science*, *5*(11): 181389.

10. Khan. A. and Asiri A. M . (2012) . Synthesis , characterization , and in vitro antibacterial activities of macromolecules derived from bis chalcone. *J. Heterocycl. Chem* . 49: 1434–1439.

11. Asireddy, S. R., Avuti, A., Boggula, N., Bakshi, V., and Kyatham, R. (2018). Synthesis, characterization and pharmacological evaluation of novel indole derivatives. *The Pharma Innovation Journal , 7*(9): 355-361

12. Patil, S. S., and Dandagvhal, K. R. (2016). Indole an interesting scaffold in drug discovery. *Int. J. Res. Pharm. Chem*, *6*(2): 301-311.

13. Patole, S., and Rajput, S. (2018). Microwave assisted synthesis characterization and microbial evaluation of 4-tetrahydro-2Hpyrrolo [2, 3-c: 5, 4-c'] dipyrazole-2, 5 (7H)-dicarboxamide derivatives. *Asian Journal of Research in Chemistry, 11(1):* 77-83

14. Faraj, F. L. (2015). Metal coordination behaviour and biological activities of indole and quinazoline derivatives (Doctoral dissertation, Jabatan Kimia, Fakulti Sains, University Malaya) .

15. Nafia, R . A. (2019). Synthesis, characterizations and biological activity of new schiff bases derived from 2-(5-Methoxy-3,3- dimethyl-1,3-dihydro-indol-2-ylidene)-malonaldehyde with Substituted Aniline . M.Sc. thesis, College of Science, University of Diyala, Iraq.

16. Knepper, K., Vanderheiden, S., and Bräse, S. (2012). Synthesis of diverse indole libraries on polystyrene resin–scope and limitations of an organometallic reaction on solid supports. *Beilstein J ournal of Organic Chemistry*, *8*(1): 1191-1199.

17. Kerzarea, D. R., and Khedekar, P. B. (2016). Indole derivatives acting on central nervous system–review. *J. Pharm Sci Bioscientific*, *6*(1):144-156 .

18. Naim, M. J., Alam, O., Alam, J., Bano, F., Alam, P., and Shrivastava, N. (2016). Recent review on indole: a privileged structure scaffold. *Int. J. Pharm. Sci. Res*, *7*: 51-62.

19. Sajjadifar, S., Vahedi, H., Massoudi, A., and Louie, O. (2010). New 3H-indole synthesis by fischer's method. Part I. *Molecules*, *15*(4): 2491-2498.

20. Inman, M., and Moody, C. J. (2013). Indole synthesis–something old, something new. *Chemical Science*, *4*(1): 29-41.

21. Bartoli, G., Dalpozzo, R., and Nardi, M. (2014). Applications of bartoli indole synthesis. *Chemical Society Reviews*, *43*(13): 4728-4750.

22. Shaikh, S., Shaikh, N., Zamir, M., Salunke, S., and Baseer, M. (2013). Synthesis of new 2-substituted phenyl-1H-indoles via Fischer indole reaction. *Chemical Science Transactions*, *2*(2): 584-588.

23.Vaitla, J., Bayer, A., and Hopmann, K. H. (2017). Synthesis of indoles and pyrroles utilizing iridium carbenes generated from sulfoxonium ylides. *Angewandte Chemie International Edition*, *56*(15): 4277-4281.

24. Campeau, L. C., and Fagnou, K. (2006). Palladium-catalyzed direct arylation of simple arenes in synthesis of biaryl molecules. *Chemical Communications*, 12: 1253-1264.

25. Gribble, G. W. (2016). Indole ring synthesis: from natural products to drug discovery. *Current Organic Synthesis*, *15*: 152-153 .

26. Shelke, G. M. (2016). Development of synthetic methods for selected indole based heterocyclic compounds from indole isatin and indoline 2 thione. Doctoral dissertation institute of technology and Science pilani (rajasthan) India .

27. Bansal, R. K. (2009). *Laboratory manual of organic chemistry*. New Age International.

28 . Tejasree, C., Kiran, G., Rajyalakshmi, G., and Reddy, A. R. N. (2014). Idiaabetic activity of 1-(4-(dimethylamino) benzylidene)-5-(2-oxoindolin-3-.ene) iocarbohydrazonein rats. *International Journal of Pharmaceutical Sciences and Research*, *5*(7): 2738.

29. Miller, C. M., O'Sullivan, E. C., and McCarthy, F. O. (2019). Novel 11-substituted ellipticines as potent anticancer agents with divergent activity against cancer cells. *Pharmaceuticals*, *12*(2): 90 .

30. Dileepan, A. B., Prakash, T. D., Kumar, A. G., Rajam, P. S., Dhayabaran, V. V., and Rajaram, R. (2018). Isatin based macrocyclic Schiff base ligands as novel candidates for antimicrobial and antioxidant drug design: In vitro DNA binding and biological studies. *Journal of Photochemistry and Photobiology B: Biology*, *(183*): 191-200 .

31. Yuan, M. X., Qiu, Y., Ran, Y. Q., Feng, G. K., Deng, R., Zhu, X. F., .and Li, H. J. (2019). Exploration of indole alkaloids from marine fungus pseudallescheria boydii F44-1 using an amino acid-directed dtrategy. *Marine Drugs*, *17*(2): 77.

32. Chodvadiya, V. D., Pambhar, K. D., Parmar, N. D., Dhamsaniya, A. P., Chhatbar, P. V., Ram, H. N., and Patel, P. K. (2019). Synthesis and characterization of N-methyl indole derivatives via desulfitative displacement by various amines and its antimicrobial activity. *World Scientific News*, *120*(2): 181-191.

33. Dixit, A., Pathak, D., and Sharma, G. K. (2019). Synthesis, antibacterial and antioxidant activity of novel 12-(N-arylmethaniminyl) indolo [1, 2-c] quinazolines. *Marmara Pharmaceutical Journal, 23(3):* 584-595.

34. Bhat, M., Al-Omar, M., Raish, M., Ansari, M., Abuelizz, H., Bakheit, A., and Naglah, A. (2018). Indole derivatives as cyclooxygenase inhibitors: synthesis, biological evaluation and docking studies. *Molecules*, *23*(6): 1250.

35. Aljamali, N. M., and Al-Husseini, Z. N. O . (2018). Formation, characterization, chromatographic and microbial behavior of (inamine-imine-isatin) reagents . *Referred International Journal ,3(2):* 92-104.

36. Kobelev, A. I., Stepanova, E. E., Dmitriev, M. V., and Maslivets, A. N. (2019). Annulation of 1H-pyrrole-2, 3-diones by thioacetamide: an approach to 5-azaisatins. *Beilstein Journal of Organic Chemistry*, *15*(1): 364-370.

37. Guksu, Z., Palabıyık, O., Karaca, A., Süt, N., and Vardar, S. A. (2019). Effect of isatin on ischemia and reperfusion injury: an experimental study in the isolated rat heart. *Koşuyolu Heart Journal*, *22*(1): 57-62.

38. Alkam, H. H. (2017). Synthesis and characterization of new bidentate schiff base ligand type (NO) donor atoms derived from isatin and 3-amino benzoic acid and its complexes with Co (II), Cu (II), Cd (II) and Hg (II) ions. *Ibn AL-Haitham Journal For Pure and Applied Science*, *30*(3): 158-169.

39. Vandana, K., Marathakam, A., Thushara, B. S., and Rajitha, K. (2017). A review on isatin derivatives with diverse biologigal activities. *World Journal of Pharmaceutical Researc, 6(16):* 318-332 .

40. Grewal, A. S. (2014). Isatin derivatives with several biological activities. *International Journal of Pharmaceutical Research*, *6*(1): 1-7.

41. Baluja, S., Bhalodia, R., Bhatt, M., Vekariya, N., and Gajera, R. (2013). Solubility of a pharmacological intermediate drug isatin in different solvents at various temperatures. *International Letters of Chemistry, Physics and Astronomy*, *12*: 36-46 .

42. Mathur, G., and Nain, S. (2014). Recent advancement in synthesis of isatin as anticonvulsant agents: a review. *Med. Chem*, *4*(4): 417-427.

43. Chandra, P. M., and Venkateshwar, J. (2014). Biological evaluation of Schiff bases of new isatin derivatives for anti alzheimer's activity. *Asian J . Pharm Clin Res*, *7*(2): 114-7.

44. Moradi, R., Ziarani, G. M., and Lashgari, N. (2017). Recent applications of isatin in the synthesis of organic compounds. *Arkivoc*, *2017*(1): 148-201.

45. Khan, F. A., and Maalik, A. (2015). Advances in pharmacology of isatin and its derivatives: A review. *Tropical Journal of Pharmaceutical Research*, *14(10):* 1937-1942.

46. Birolli, W. G., Ferrreira, I. M., Jimenez, D. E., Silva, B. N., Silva, B. V., Pinto, A. C., and Porto, A. L. (2017). First asymmetric reduction of isatin by marine-derived fungi. *Journal of the Brazilian Chemical Society*, *28*(6): 1023-1029.

47. Asif, M. (2017). A mini review on synthesis and biological activities of isatin derivatives. *Universal Journal of Chemistry*, *1*(1): 17-26.

48. Chittethu, A. B., Asha, J., Balasubramanian, R., Saranya, T. S., and Manakadan, A. A. (2017). Utility of isatin semicarbazones in mammary

carcinoma cells-A proof of concept study. *Journal of Young Pharmacists*, *9*(2): 218 .

49. Banerjee, B. (2017). Recent developments on ultrasound-assisted one-pot multicomponent synthesis of biologically relevant heterocycles. *Ultrasonics sonochemistry*, *35*: 15-35 .

50. Xie, Z., Wang, G., Wang, J., Chen, M., Peng, Y., Li, L., and Li, W. (2017). Synthesis, biological evaluation, and molecular docking studies of novel isatin-thiazole derivatives as α-glucosidase inhibitors. *Molecules*, *22*(4): 659 .

51. Dogan , İ. S., Bolek, G. G., and Kahveci, B. (2019) . Synthesis of Some New Isatin Derivatives and Identification of Their Structures. *Süleyman Demirel Üniversitesi Fen Bilimleri Enstitüsü Dergisi*, *23*: 67-70.

52. Yurttaş, L., Ertaş, M., Cankılıç, M. Y., and Demirayak, Ş. (2017). Synthesis and antimycobacterial activity evaluation of isatin-derived 3-[(4-aryl-2-thiazolyl]) hydrazone]-1H-indol-2, 3-diones. *Acta Pharmaceutica Sciencia*, *55(1):* 1307-2080 .

53. Jayabalakrishnan, C., and Natarajan, K. (2001). Synthesis, characterization, and biological activities of ruthenium (II) carbonyl complexes containing bifunctional tridentate Schiff bases. *Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry*, *31*(6): 983-995.

54. Fernandes, I. P., Silva, B. V., Silva, B. N., Pinto, A. C., Oliveira, S. C. B., and Oliveira-Brett, A. M. (2018). Isatin 1-morpholinomethyl, 1-hydroxymethyl, 1-methyl, and their halogenated derivatives, redox behaviour. *Journal of Electroanalytical Chemistry*, *812*: 143-152.

55. Meenakshi, K., Gopal, N., and Sarangapani, M. (2014). Synthesis, characterization and antimicrobial activity of some novel Schiff and Mannich bases of isatin. *Int. J. pharm sci*., *6*(6): 318-322.

56. Haghighi, M., and Nikoofar, K. (2016). Nano TiO2/SiO2: an efficient and reusable catalyst for the synthesis of oxindole derivatives. *Journal of Saudi Chemical Society*, *20*(1): 101-106.

57. Mishra, K. N., Sengupta, S. K., Pandey, O. P., and Goswami, S. (2017). Synthesis, physicoanalytical characterization and biological activity of Isatin Thiosemicarbazones derivatives of Dichloro bis (cyclopentadienyl) hafnium (IV)(Cp_2HfCl_2). *Research Journal of Pharmaceutical Biolgical and Chemical Sciences*, *8*(3): 1779-1785 .

58. Birolli, W. G., Ferrreira, I. M., Jimenez, D. E., Silva, B. N., Silva, B. V., Pinto, A. C., and Porto, A. L. (2017). First asymmetric reduction of isatin by marine-derived fungi. *Journal of the Brazilian Chemical Society*, *28(6):* 1023-1029.

59. Tisovský, P., Šandrik, R., Horváth, M., Donovalová, J., Jakusová, K., Cigáň, M., and Filo, J. (2017). Effect of structure on charge distribution in the isatin Anions in aprotic environment: Spectral study. *Molecules*, *22(11):* 1961.

60. Divar, M., Khalafi-Nezhad, A., Zomorodian, K., Sabet, R., Faghih, Z., Jamali, M., and Khabnadideh, S. (2017). Synthesis of some novel semicarbazone and thiosemicarbazone derivatives of isatin as possible biologically active agents. *British Journal of Pharmaceutical Research*, *17*(6):1-13 .

61. Ziarani, G. M., Moradi, R., and Lashgari, N. (2016). Synthesis of spiro-fused heterocyclic scaffolds through multicomponent reactions

involving isatin. *ARKIVOC: Online Journal of Organic Chemistry*, (i): 1-81 .

62. Makarem, S., Mirza, B., Mohammad Darvish, Z., Amiri Notash, N., & Ashrafi, S. (2019). Organic electrosynthesis: apromising alternative methodology for the synthesis of nanosized particles of pyrans. *analytical and bioanalytical Chemistry Research*, *6*(1): 231-240.

63. Kumar, R., and Kumar, M. (2018). Synthesis of 3-[4-(2-Amino-6 (substituted phenyl)-pyrimidin-4-yl)-phenylimino]-5-chloro-1, 3-dihydro-indol-2-one derivatives of 5-chloroisatin as potential antimicrobial agents. *Journal of Pharmaceutical, Chemical and Biological Sciences*, *5*(4): 399-404 .

64. Da Silva, J. F., Garden, S. J., and Pinto, A. C. (2001). The chemistry of isatins: a review from 1975 to 1999. *Journal of the Brazilian Chemical Society*, *12*(3): 273-324.

65. Aboul-Fadl, T., Bin-Jubair, F. A., and Aboul-Wafa, O. (2010). Schiff bases of indoline-2, 3-dione (isatin) derivatives and nalidixic acid carbohydrazide, synthesis, antitubercular activity and pharmacophoric model building. *European journal of medicinal chemistry*, *45*(10): 4578-4586.

66. Zlatković, M. Z., Troter, D. Z., Stanojević, J. S., Todorović, Z. B., Cakić, V. S., and Konstantinović, S. S. (2018). Antibacterial activity and photolytic stability of synthesized 5-chloroisatin-3-hydrazone. *Advanced Technologies*, *7*(1): 41-46.

67. Yılmaz, F., Karaali, N., and Şaşmaz, S. (2017). Microwave-assisted synthesis of some nitro-benzimidazoles and their salicyl and isatin Schiff bases. *Bulletin of the Chemical Society of Ethiopia*, *31*(2): 351-359.

68. Meeran, M. N., and Hussain, A. Z. (2017). Synthesis, Characterization and DPPH scavenging assay of isatin related spiroheterocyclic compounds. *Indian Journal of Pharmaceutical Sciences*, *79*(4): 641-645.

69. Khaleel, A. M. (2008). Synthesis and characterization of new schiff bases and amides derived from N(1) substituted isatin with 2-aminobenzothiazole, 2-aminopyrimidine and dithiooxamide and some of their metal complexes. (Doctoral thesis , College of Science, University of Baghdad , Iraq) .

70. Al Maamari, K. A. (2013). Isatin drivatives: synthesis, reactivity and anti corrosion properties. (Doctoral thesis , College of Rabat faculty , University of mohammed V) .

71. Ramzan , M. (2009). Synthesis and biological studies of some isatins-derived thiosemicarbazones and their transition metal complexes (Doctoral thesis , bahauddin zakariya university multan, pakistan) .

72. Sumpter, W. C. (1944). The chemistry of isatin. *Chemical reviews*, *34*(3): 393-434.

73. Jiang, K. M., Luesakul, U., Zhao, S. Y., An, K., Muangsin, N., Neamati, N and Lin, J. (2017). Tautomeric-dependent lactam cycloaddition with nitrile oxide: facile synthesis of 1, 2, 4-oxadiazole [4, 5-a] indolone derivatives. *ACS omega*, *2*(7): 3123-3134.

74. Vine, K. L., Locke, J. M., Ranson, M., Pyne, S. G., and Bremner, J. B. (2007). An investigation into the cytotoxicity and mode of action of some novel N-alkyl-substituted isatins. *Journal of Medicinal Chemistry*, *50*(21): 5109-5117.

75. Clay, C. M. (2011). Synthesis of isatin derivatives used for the inhibition of pro-apoptotic jurkat t cells. M.Sc. thesis, College of Science, University of Wright State .

76. Pinto, A. C., da Silva, F. S. Q., and Da Silva, R. B. (1994). Reduction of N-acylisatins with [BH_3. THF] complex. *Tetrahedron letters*, *35*(48): 8923-8926 .

77. Saha, T. (2004). Synthesis of some spiro heterocyclic derivatives of subtituted isatins . M.Sc thesis, Bangladesh university of engineering and technology, dhaka, Bangladesh .

78. Kadam, A., Zhang, Z., and Zhang, W. (2011). Microwave-assisted fluorous multicomponent reactions-A combinatorial chemistry approach for green organic synthesis. *Current Organic Synthesis*, *8*(2): 295-309.

79. Black, D. S. C., Bowyer, M. C., Catalano, M. M., Ivory, A. J., Keller, P. A., Kumar, N., and Nugent, S. J. (1994). Substitution, oxidation and addition reactions at C-7 of activated indoles. *Tetrahedron*, *50*(35): 10497-10508.

80. Berti, C., Greci, L., Andruzzi, R., and Trazza, A. (1982). New aspects in the chlorination of indoles with 1-chlorobenzotriazole and 1-chloroisatin. *The Journal of Organic Chemistry*, *47*(25): 4895-4899.

81. Hajare, R. A., Gaurkhede, R. M., Chinchole, P. P., Chandewar, A. V., Wandhare, A. S., and Karki, S. S. (2009). Synthesis, structure and spectral charectarization of friedal craft N-Benzylation of isatin and their novel schiff's bases. *Asian J. Research Chem*, *2*(3): 289-291.

82. Bridges, T. M., Marlo, J. E., Niswender, C. M., Jones, C. K., Jadhav, S. B., Gentry, P. R., and Lindsley, C. W. (2009). Discovery of the first highly M5-preferring muscarinic acetylcholine receptor ligand, an M_5

positive allosteric modulator derived from a series of 5-trifluoromethoxy N-benzyl isatins. *Journal of Medicinal Chemistry*, *52*(11): 3445-3448 .

83. Westley, C. B., Vine, K. L., and Benkendorff, K. (2006). A proposed functional role for indole derivatives in reproduction and defense of the muricidae (Neogastropoda: Mollusca). *Indirubin, the Red Shade of Indigo*, 31-44.

84. Vine, K. L., Locke, J. M., Ranson, M., Pyne, S. G., and Bremner, J. B. (2007). In vitro cytotoxicity evaluation of some substituted isatin derivatives. *Bioorganic & Medicinal Chemistry*, *15*(2): 931-938.

85. Krishnegowda, G., Gowda, A. P., Tagaram, H. R. S., Staveley-O'Carroll, K. F., Irby, R. B., Sharma, A. K., and Amin, S. (2011). Synthesis and biological evaluation of a novel class of isatin analogs as dual inhibitors of tubulin polymerization and Akt pathway. *Bioorganic & Medicinal Chemistry*, *19*(20): 6006-6014.

86. Deligeorgiev, T., Vasilev, A., Vaquero, J. J., and Alvarez-Builla, J. (2007). A green synthesis of isatoic anhydrides from isatins with urea–hydrogen peroxide complex and ultrasound. *Ultrasonics sonochemistry*, *14*(5): 497-501.

87. Lakshmi, G. (2011). Synthesis and Biological Evaluation of 3-[(2-Phenyl Methylidene) Hydrazono]-1, 3-Dihydro-2h-Benzo [G] Indol-2-One Derivatives (Doctoral dissertation, JKK Nattraja College of Pharmacy, Komarapalayam) .

88. Lempert, K., and Gyulai, P. (1970). uber die reaktion von alkalisalzen der isatinsaure mit phenylisocyanat und phenylisothiocyanat. *Periodica Polytechnica Chemical Engineering*, *14*(1): 13-31.

89. Utreja, D., and K Dhillon, N. (2014). Synthesis of metal complexes of schiff bases and their nematicidal activity against root knot nematode meloidogyne incognita. *Letters in Organic Chemistry*, *11*(2): 116-125.

90. Ashraf, M. A., Mahmood, K., Wajid, A., Maah, M. J., and Yusoff, I. (2011). Synthesis, characterization and biological activity of schiff bases. *Ipcbee*, *10*: 1-7.

91. Hossain, S., Zakaria, C. M., and Kudrat-E-Zahan, M. (2017). Structural and biological activity studies on metal complexes containing thiosemicarbzone and isatin based schiff base: A review. *Asian Journal of Research in Chemistry*, *10*(1): 6-13.

92. Sadi, A. H., Idris, M. I., and Bashir, S. S. (2017). Synthesis, characterization and antimicrobial studies of Ru (II) complexes with Schiff base co-ligand derived from 5, 6-diamino-1, 10-phenanthroline and benzene-1, 4-dicarbaldehyde. *Bayero Journal of Pure and Applied Sciences*, *10*(1): 468-476.

93. Ejidike, I. P. (2016). Synthesis, characterization and In Vitro biological studies of metal schiff bases (Doctoral dissertation, University of Fort Hare).

94. Shebl, M. (2014). Synthesis, spectroscopic characterization and antimicrobial activity of binuclear metal complexes of a new asymmetrical Schiff base ligand: DNA binding affinity of copper (II) complexes. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *117*: 127-137.

95. Kaur, G. (2016). Synthesis of metal complexes of Schiff bases of halogenated anilines and their antifungal activity (Doctoral dissertation, Punjab Agricultural University, Ludhiana).

96. Karem, L. K. A., Waddai, F. Y., and Karam, N. H. (2018). Schiff base complexes of some drug substances. *Journal of Pharmaceutical Sciences and Research*, *10*(8): 1912-1917.

97. Zakir, H. M., Ali, M. M., and Jesmin, M. (2016). Antibacterial activities of benzoin thiosemicarbazone and its complexes with Co (II) and Ni (II). *Asian Journal of Medical and Pharmaceutical Researches*, *6*(4): 32-40.

98. Al-Azawi, K., AL-Duhaidahawi, D. L., Al-Amiery, A., Kadhum, A. A. H., and Amir, A. (2019). Synthesis of schiff base metal complexes with motivating scavenging potential studies. *Free Radicals and Antioxidants*, *9*(1): 1-4 .

99. Ali, S. M., Zakir, H. M., Shahriar, S. S., Sarkar, M. H., Dey, A. K., Nur, H. P., and Jesmin, M. (2015). In vivo anticancer activities of Ni (II)-Benzoin thiosemicarbazone complex [Ni $(BTSC)_{2'}$] against ehrlich ascites carcinoma cells. *Journal of Bio-Science*, *23*: 77-88.

100. Rajamma, D. B., Iyer, G. C. R., Madar, I. H., and Karunakar, P. (2019). Identification of (1E, 3E)-1, 3-bis [(2-hydroxy-1-naphthyl) methylene] urea as mutated MAP Kinase P38 inhibitor through reverse pharmacophore mapping approach: green synthesis, characterisation and in silico docking analysis. *Indian Journal of PharamceutIcal Education and Research*, *53*(2): 276-285 .

101. Matar, S. A., Talib, W. H., Mustafa, M. S., Mubarak, M. S., and Al-Damen, M. A. (2015). Synthesis, characterization, and antimicrobial activity of Schiff bases derived from benzaldehydes and 3, 3′-diaminodipropylamine. *Arabian Journal of Chemistry*, *8*(6): 850-857.

102. Zakir, H. M., Mondol, M. M. H., Shahriar, S. M. S., Hossain, M. A., Rahim, M. A., Dey, A. K., and Khanam, J. (2019). Benzoin

thiosemicarbazone inhibits growth and triggers apoptosis in earlich ascites carcinoma cells through an intrinsic pathway. *American Journal of Cancer*, *7*(1): 1-9.

103. Aliyu, H. N. (2018). Schiff bases and their transition metal complexes: the drugs for the next generation. Bayero University Press.

104. Mumtaz, A., Mahmud, T., Elsegood, M. R., and Weaver, G. W. (2016). Synthesis and characterization of new schiff base transition metal complexes derived from drug together with biological potential study. *J Nucl Med Radiat Ther*, *7*(6): 2155-9619.

105. Mumtaz, A., Mahmud, T., Elsegood, M. R. J., Weaver, G. W., Qazi, J. I., and Deeba, F. (2019). Synthesis, characterization and in vitro biologicl studies of novel schif base and its transition metal complexes derived from sulphadoxine. *Farmacia*, *67*(1): 107-110.

106. Mahapatra, D. K., Das, D., and Shivhare, R. S. (2017). Substituted thiazole linked murrayanine-Schiff's base derivatives as potential anti-breast cancer candidates: Future EGFR Kinase inhibitors. *Int J Pharm Sci Drug Res*, *9*(3): 139-144.

107. Mishra, N., Poonia, K., and Kumar, D. (2013). An overview of biological aspects of schiff base metal complexes. *International Journal of Advancements in Research & Technology*, *2*(8): 52-66.

108. Mohamed, G. G. (2006). Synthesis, characterization and biological activity of bis (phenylimine) schiff base ligands and their metal complexes. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *64*(1): 188-195.

109. Çelik, C., Tümer, M., and Serin, S. (2002). Complexes of tetradentate schiff base ligands with divalent transition

metals. *Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry*, *32*(10): 1839-1854.

110. Biswas, C., Drew, M. G., Figuerola, A., Gómez-Coca, S., Ruiz, E., Tangoulis, V., and Ghosh, A. (2010). Magnetic coupling in trinuclear partial cubane copper (II) complexes with a hydroxo bridging core and peripheral phenoxo bridges from NNO donor Schiff base ligands. *Inorganica Chimica Acta*, *363*(5): 846-854 .

111. Ding, C. X., Ni, J., Yang, Y. H., Ng, S. W., Wang, B. W., and Xie, Y. S. (2012). Mono-, Tetra-and octanuclear transition metal complexes of in situ generated schiff base ligands containing up to 12 coordinating atoms: syntheses, structures and magnetism. *Cryst .Eng .Comm*., *14*(21): 7312-7319 .

112. Rodríguez-Argüelles, M. C., López-Silva, E. C., Sanmartín, J., Pelagatti, P., and Zani, F. (2005). Copper complexes of imidazole-2-, pyrrole-2-and indol-3-carbaldehyde thiosemicarbazones: inhibitory activity against fungi and bacteria. *Journal of Inorganic Biochemistry*, *99*(11): 2231-2239.

113. Ahmed, N. K . (2011). Synthesis, characterization and study of antibacterial activities of ligands type (OS and NOS) and their Complexes with some divalent metal ions . M.Sc. thesis, College of Science, University of Baghdad, Iraq.

114. Ren, S., Wang, R., Komatsu, K., Bonaz-Krause, P., Zyrianov, Y., McKenna, C. E., and Lien, E. J. (2002). Synthesis, biological evaluation, and quantitative structure− activity relationship analysis of new Schiff bases of hydroxysemicarbazide as potential antitumor agents. *Journal of medicinal chemistry*, *45*(2): 410-419.

115. Kannan, S., Ramesh, R., and Liu, Y. (2007). Ruthenium (III) mediated C–H activation of azonaphthol: Synthesis, structural characterization and transfer hydrogenation of ketones. *Journal of Organometallic Chemistry*, *692*(16): 3380-3391.

116. Nair, M. S., and Arish, D. (2011). Synthesis, characterization and biological studies of Co (II), Ni (II), Cu (II) and Zn (II) complexes involving a potentially tetradentate schiff base ligand. *Transactions of the Indian Institute of Metals*, *64*(3): 287-292 .

117. Singh, D. P., Grover, V. I. D. H. I., Kumar, K. R. I. S. H. A. N., and Jain, K. (2011). Synthesis and characterization of divalent metal complexes of the macrocyclic ligand derived from isatin and 1, 2-diaminobenzene. *Serbian Chemical Society. Journal*, *76*(3): 385-393 .

118. Bajpai, S., Singh, S., and Srivastava, V. (2013). Simple and efficient microwave-assisted synthesis of quinoxaline and spiro-indole derivatives in xylene. *Int. J. Innov. Res. Sci. Eng. Technol*, *2*(9): 4830-4838 .

119. Christiea, C. A., Shijub, C., and Rejia, T. A. F. (2016). Synthesis, spectroscopic characterization and biological activities of Co (ii). Ni (ii), Cu (ii) and Zn (ii) complexes of schiff base derived from isatin monohydrazone and furfuraldehyde*" Ejpmr, 3(20):* 238-244.

120. Bajpai, S., Gajaganti, S., Srivastava, V., and Singh, S. (2017). Development of greener approach: microwave assisted syntheSsis of quinoxaline derivatives in water. *Journal of Scientific Research*, *(61)*: 173-177.

121. Kaur, J., Utreja, D., Jain, N., and Sharma, S. (2019). Recent Developments in the Synthesis and Antimicrobial Activity of Indole and its Derivatives. *Current Organic Synthesis*, *16*(1): 17-37.

122. Al-Azawi, K. F. (2018). Corrosions inhibitions of milds steelsin hydrochloricsacid solutionsby an isatinaniline compound. *Engineering and Technology Journal*, *36*(2 Part (B) Engineering): 98-103.

123. Youseftabar-Miri, L. (2019). A clean and efficient synthesis of spiro [4H-pyran-oxindole] derivatives catalyzed by egg shell. *Iranian Chemical Communication*, *7*(2): 142-152.

124. Ali, W. B. (2018). Synthesis, Characterization and Theoretical Study of Some Pyrazole Compounds Derived From 1, 1, 2-Trimethylbenz [e] Indole. *Diyala Journal For Pure Science*, *14*(03): 206-219.

125. Nafia, R. A., and Faraj, F. L. (2019). Synthesis and characterization of new indole schiff bases and study effect of the compounds on lymphatic cell in metaphase in human blood. *Journal of Pharmaceutical Sciences and Research*, *11*(4): 1319-1326.

126. Hameed, R. F., Jarullah, A. A., and Faraj, F. L. (2019). Synthesis and evaluation of cytotoxicity effect of new ligand (LBe) and it's complexes on a cervical cancer. *Oriental Journal of Chemistry*, *35*(3): 1208-1214.

127. Silverstein R. M., Webster F. X. and Kiemle D.J. (2005). Spectrometric identification of organic compounds. 7th ed., John wiley and Sons Inc., New York.

128. Hashim C. S. and. Alias M. F. (2012). Synthesis and studying new complexes of some transition metals ions on RD cell line. M.Sc. thesis, College of Science for Women,University of Baghdad, Iraq.

129. Al-Shaalan, N. H. (2011). Synthesis, characterization and biological activities of Cu (II), Co (II), Mn (II), Fe (II), and UO2 (VI) complexes

with a new schiff base hydrazone: O-Hydroxyacetophenone-7-chloro-4-quinoline hydrazone. *Molecules*, *16*(10): 8629-8645.

130. Ali, M. N., and Al-Majidi, S. M. (2010). Synthesis of some new N-substituted -1,2,3,4-tetrahydrocarbazole derivatives and study their biologicalactivity. *Journal of Al-Nahrain University-Science*, *13*(1): 26-35.

131. Lever A. B. P. (1968), Inorganic Electronic spectroscopy, Elsevier publishing Company, New York, London.

132. Abid, O. H., Muslim, R. F., and Mohammed, K. M. (2016). Synthesis and characterization of novel 1, 3-oxazepin-4-ones derivatives via Schiff bases reactions with phthalide. *Journal of University of Anbar for Pure Science*, *10*(2): 1-9 .

133. Devi, J., Yadav, M., Kumar, D., Naik, L. S., and Jindal, D. K. (2019). Some divalent metal (II) complexes of salicylaldehyde-derived schiff bases: synthesis, spectroscopic characterization, antimicrobial and in vitro anticancer studies. *Applied Organometallic Chemistry*, *33*(2): e4693 .

الخلاصة

في هذه الرسالة حضرت بنجاح مركبات جديدة من إيساتين ، وأكدت نقاوتها بأستخدام كروموتوغرافيا الطبقة الرقيقة. تم تحديد التركيب الكيميائي للمركبات المحضرة [A_1- A_{12}] بواسطة الطرق الطيفية (طيف الاشعة تحت الحمراء، طيف الاشعة فوق البنفسجية والمرئية ، وطيف الرنين النووي المغناطيسي) بالإضافة الى تحديد الخواص الفيزيائية بواسطة درجة الانصهار والألوان. ومن جانب أخر استخدمت بعض المركبات كليكاندات لتحضير معقدات جديدة من خلال تفاعلها مع بعض املاح العناصر الانتقالية مثل حامض كلوريد البلاتين الرباعي سداسي الماء، كلوريد الخارصين الثنائي ، كلوريد النيكل الثنائي سداسي الماء ،وكلوريد الكوبلت سداسي الماء . شخصت المعقدات المحضرة باستخدام طيف الاشعة تحت الحمراء، طيف الاشعة فوق البنفسجية والمرئية ، طيف الامتصاص الذري ، التحليل الدقيق لعناصر ، الحساسية المغناطيسية وقياسات التوصيلية فضلا عن تقدير الخواص الفيزيائية بواسطة درجات الانصهار والألوان علاوة على ذلك تم دراسة تأثير المركبات والمعقدات على بعض سلالات الفطريات.

وشملت هذه الدراسة هذه الخطوات التالية :

١- تفاعل ايساتين مع ٤- ميثيل o- فينيلين ثنائي امين لتحضير ٢- ميثيل -٦ هيدروجين- إندولو [٢،٣-ب] كينوكسالين [A_1] ، ثم تحضير المعقدات $[pt(A_1)_2\ Cl_2].\ H_2O$ ، $[Zn(A_1)_2].\ 5H_2O$ باستخدام $[H_2PtCl_6.6H_2O$، $ZnCl_2]$.

٢- - تفاعل ايساتين مع ٤- كلورو أو فينيلين ثنائي امين لتحضير ٢- كلورو- ٦ الهيدروجين- إندولو [٢،٣-ب] كينوكسالين [A_2].

٣- تكثيف المركبات [A_1، A_2] على التوالي مع كلورو أسيتيل كلوريد في وجود ثلاثي إيثيلين والبنزين الجاف كمذيب ليعطي [A_3, A_4]. التي تم معاملتها مع هيدرازين هيدرات لإعطاء [A_5 ، A_6].

٤- تحضير المعقدات $[Ni\ (A_5)_2\ Cl_2].\ 6H_2O$ ، $[Co\ (A_5)_2\ Cl_2].\ 6H_2O$ باستخدام املاح النيكل الثنائي $NiCl_2.6H_2O$ ، وباستخدام الكوبلت الثنائي $CoCl_2.6H_2O$.

٥- بالإضافة الى ذلك ، تم تحضير قواعد شيف الجديدة [A_7,A_8,A_9,A_{10},A_{11},A_{12}] من خلال تفاعل مشتق الهيدرازين [A_5، A_6] مع الديهايدات عطرية مختلفة.

٦. تحضير المعقدات $[Ni\ (A_8)_2\ Cl_2].\ 6H_2O$, $[Ni\ (A_7)_2\ Cl_2].\ 6H_2O$ باستخدام ملح النيكل الثنائي(II) $[NiCl_2.6H_2O]$.

٧- قمنا بتقييم آثار البدائل على النشاط المضاد للفطريات ، وأظهرت معظم المشتقات والمعقدات نشاط جيد إلى متوسط نحو (*Cryptococccus Neoformans* ،*Candida Albicans* ، *Rhodotorula rubra* ،*Aspergilus parasiticus* ،*Penicilium sp.* ،*Rhizopus arrhizus).*

وزارة التّعليم العالي والبحث العلمي
جامعة ديالى
قسم الكيمياء/كلّية العلوم

تحضير وتشخيص والنشاط المضاد للفطريات لبعض المركبات الحلقية غير المتجانسة ومعقداتها

رسالة مقدمة إلى

مجلس كلية العلوم - جامعة ديالى

وهي جزء من متطلبات نيل شهادة ماجستير في علوم الكيمياء

ختام عبدالكريم اسماعيل

(بكالوريوس في علوم كيمياء- عام 2016 كلية العلوم جامعة ديالى)

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