ADDIS ABABA UNIVERSITY
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STUDIES ON Ni (II) COMPLEX DERIVED FROM NINHYDRIN DI-SEMICARBAZONE

BY
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By

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List of abbreviations and symbols

DMSO	Dimethylsulfoxide
DMF	Dimethylformamide
NDSC	Ninhydrin-2,3-disemicarbazone
PLTSC	Pyridoxalthiosemicarbazone
PLITSC	Pyridoxalisosemicarbazone
PLSC	Pyridoxalsemicarbazone
TLC	Thin layer chromatography
TMS	Tetramethylsilane
BS	Benzaldehyde semicarbazone
Uv-Vis	Ultraviolet-visible
B.M.	Bohr magneton
δ	Bending vibration
ν	Stretching vibration

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Gizaw G/Selassie

Abstract

The disemicarbazone derivative of ninhydrin (NDSC) was synthesized by the 1:2 condensations between ninhydrin and semicarbazide hydrochloride in ethanolic medium. It was characterized on the basis of mass spectrum, ^{1}H-NMR, ^{13}C-NMR, IR, UV-vis and analytical data. The Ni (II) complex of NDSC was successfully synthesized in better yield from template procedure. The complex was characterized by analytical, conductance, IR, UV-vis and magnetic susceptibility data. The results suggest that the complex with the molecular formula [Ni-NDSC(H_2O)Cl]Cl has octahedral geometry with the ligand behaving as a neutral ONNO donor.

1. Introduction

General

Metal Complex with Schiff–Bases

Schiff base ligands are considered ‘privileged ligands’ (advantaged) because they are easily prepared by condensation between aldehydes and imines [1]. Stereogenic centres or other elements of chirality (planes, axes) can be introduced in the synthetic design. Schiff base ligands are able to coordinate many different metals, and to stabilize them in various oxidation states, enabling the use of Schiff base metal complexes for a large variety of catalytic transformations [1]. They are able to transmit chiral information to produce non-racemic products through a catalytic process: chiral aldehydes or chiral amines can be used. Schiff base ligands are able to coordinate metals through imine nitrogen and another group, usually linked to the aldehyde [1].

Schiff bases are prepared by condensation of aldehyde bearing coordinating group with amines, amino acids and peptides. For example the so-called Salen ligands with four coordinating sites and two axial sites open to ancillary ligands are formed by combination of two equivalents of salicylaldehyde with a diamine (1,2-diamine) [1]. Although the term Salen was used originally only to describe the tetradentate Schiff bases derived from ethylenediamine, the more general term Salen type is used to describe the class of

[ONNO] tetradentate bis-Schiff base ligands (Fig.1)

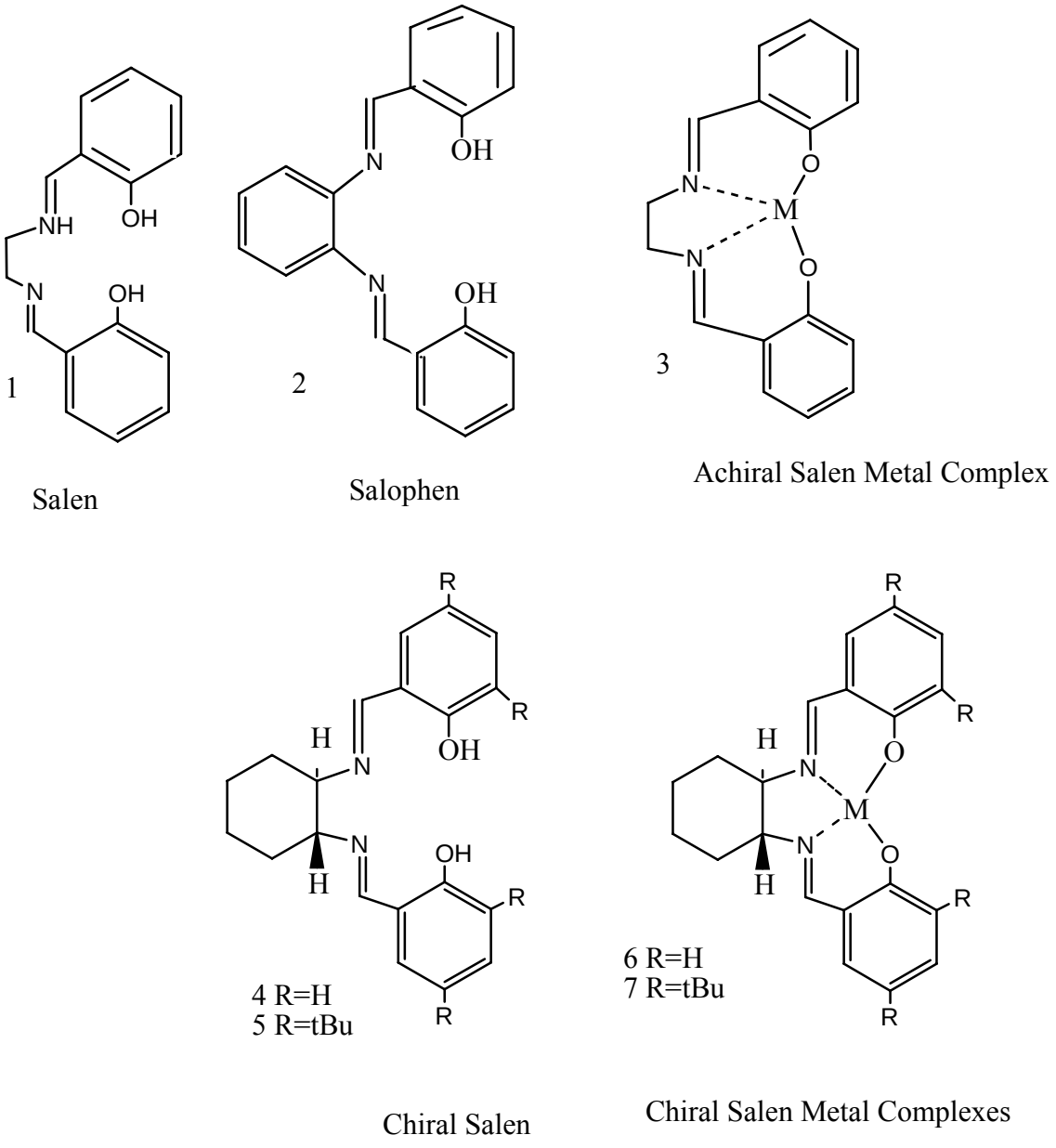
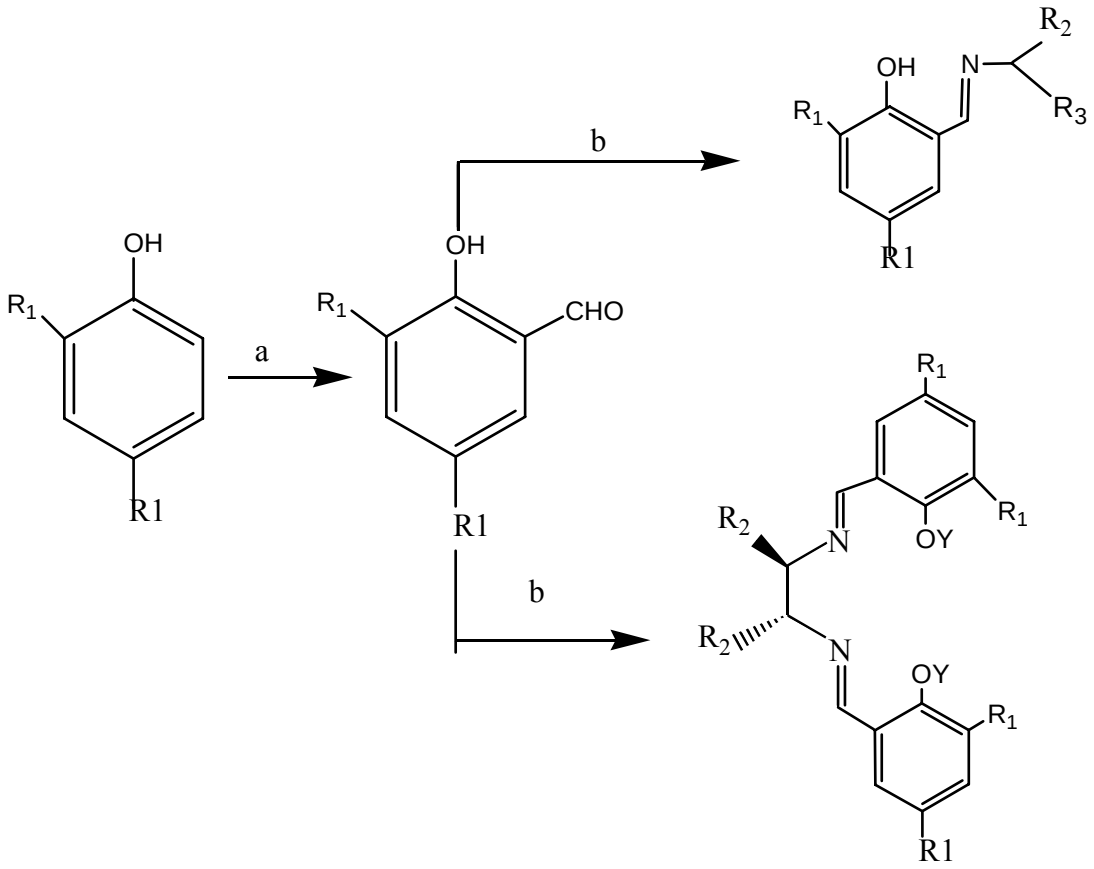


Figure 1 Different Salen Ligands and M (Salen) complexes

Preparation of Schiff Bases:-Condensation between aldehydes and amines is realized under different reaction conditions and in different solvents. The presence of dehydrating agents normally favors the formation of Schiff bases. For example, the condensation of salicylaldehyde or salicylaldehyde derivatives with 1, 2-diamines leads to the formation of one extremely important class of ligands, generally known as Salens(Fig1).



Scheme 1: Preparation of Schiff bases

Schiff bases are suitable ligands for the preparation of libraries of ligands due to the easy reaction conditions and the variety of chiral amines and aldehydes used as precursors. Amino acids and peptides are particularly suitable for the creation of effective catalysts [1].

The Complexation Steps: Different Routes[1]: In many catalytic applications Schiff base metal complexes are prepared ***in situ*** by producing a reaction between the Schiff base and available and well-defined metal complexes. Essentially, five different synthetic routes can be identified for the preparation of Schiff base metal complexes (scheme 2 shows preparation of metal complexes of Schiff base derived from salicylaldehyde and ethylenediamine). The routes involve the use of:

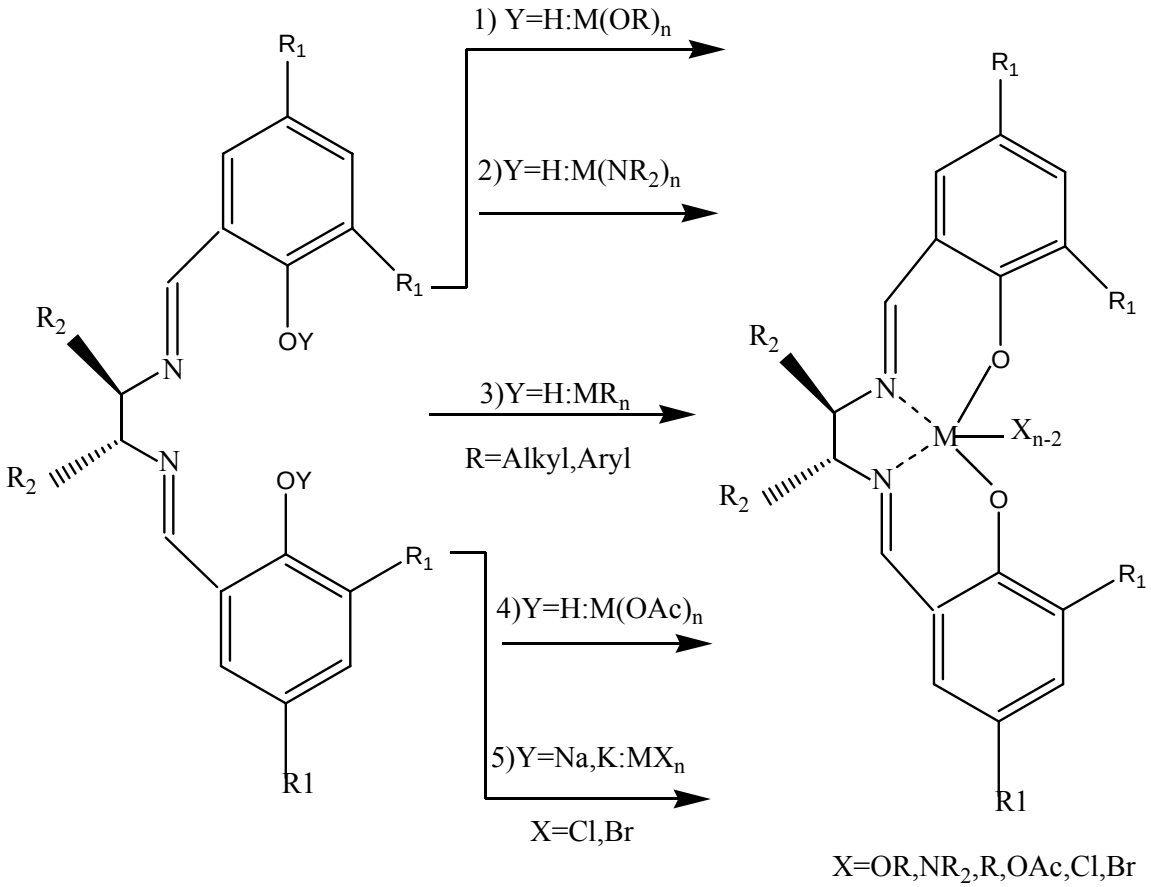
1/metal alkoxides, M (OR)n, for early transition metals M=Ti,Zr

2/ metal amides $(NMe_2)_4$, for early transition metals M=Ti, Zr, e.g $Ti(NMe_2)_4$,$Zr(NMe_2)_4$

3/metal alkyl complexes, MR_n, e.g. $AlMe_3$, $GaMe_3$, $InMe_3$ etc

4/metal acetates, $M(OAc)_2$ (M=Ni, Cu, Co)

5/ metal halides, MX_n

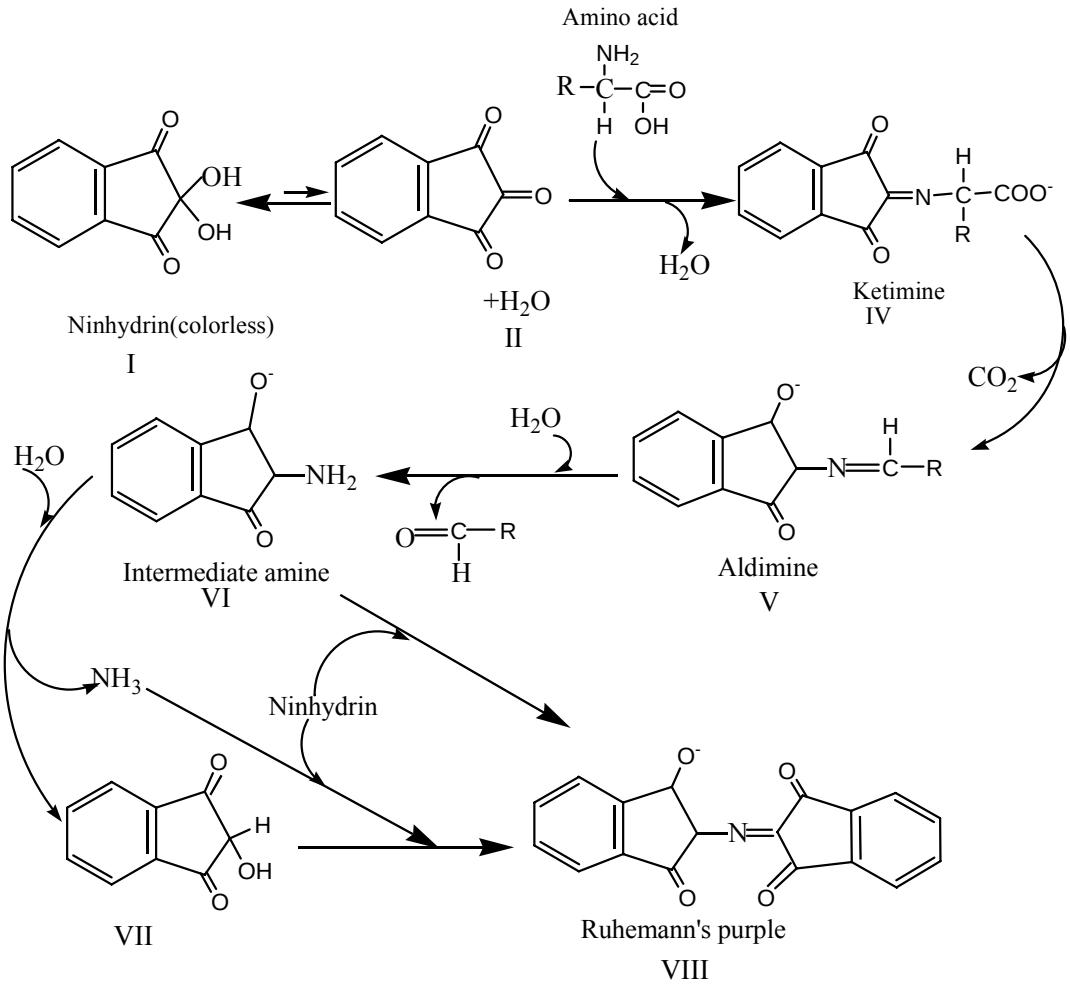


Scheme 2: Preparation of Schiff base Complexes

Deprotonation of acidic phenolic hydrogen can be realized using lithium bases (MeLi, BuLi). However, since lithium alkyls can attack the imine group of the Schiff base; it is advisable to perform the deprotonation step with NaH or KH in coordinating solvents [1].

The condensation of ninhydrin (1,2,3-triketohydrindene hydrate or 2,2-dihydroxy-1,3-indandione) with α-amino acids and amines in the presence of metal ions can also result in the formation of Schiff base metal complexes. Ninhydrin (1,2,3-triketohydrindene

hydrate or 2,2-dihydroxy-1,3-indandione;I and II, scheme 3) reacts with α-amino acids to yield a characteristically blue/purple colored compound commonly known as Ruhemann's purple VIII [2], after Siegfried Ruhemann who first observed the color reaction [2].The blue compound, VIII, maximally absorbs at 570 nm and this forms the basis for the spectrophotometric quantitative determination of amino acids that can detect as little as one microgram of material [2]. The mechanism of the reaction is not certain. However, a simplified form of the mechanism proposed by Filippovich and McCaldin is shown in scheme 3 [2] below.



Scheme 3. The reaction of ninhydrin with α-amino acids [2].

It has a condensation step that leads to a Schiff base formation followed by decarboxylation, hydrolysis, and finally further condensation with another ninhydrin molecule to give the final product, Ruhemann's purple [2]. If a metal ion is present before the reaction commences, the reaction doesn't proceed to the final product, but stops at the first step, the metal ion forming a highly stable colored complex with the Schiff base [3]. It is anticipated that this can form a basis for studying the reaction between ninhydrin and a variety of amino acids in the presence of metal ions, particularly transition metals. Schiff bases are good ligands for metal ions [2].The ketimine IV, is therefore, a potential ligand for metal ions that can act as a tridentate ligand forming two stable five membered rings on complexation. The Schiff base can have metal binding sites as shown in figure 2 [2].

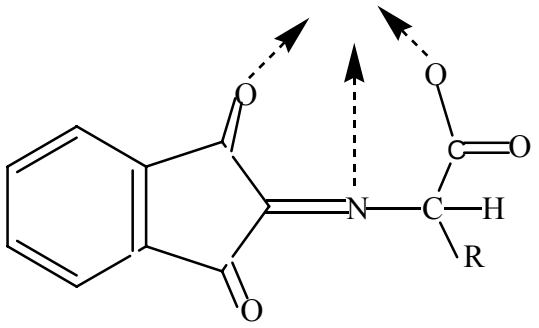


Figure 2 possible metal binding centers of a Schiff base derived from nihydrin and an amino acid.

In accordance with this proposal, Rao and Reddy synthesized and characterized Co (II), Ni (II), and Zn (II) complexes of a Schiff base derived from ninhydrin glycine (indae-1, 3-dione-2-imine-N-acetate, IDLA).

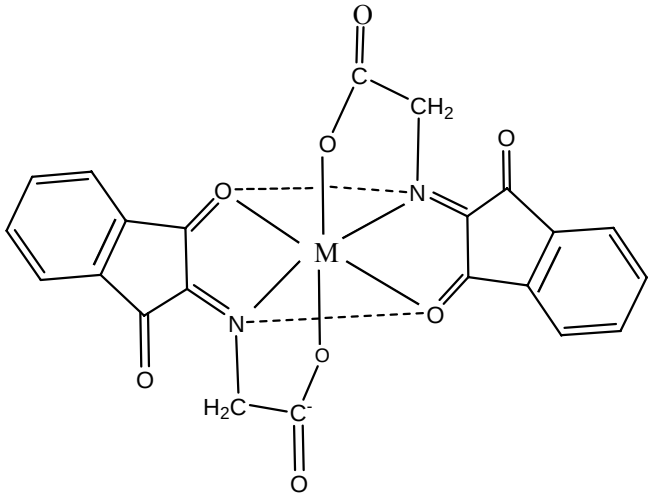


Figure 3: Metal Complexes of IDLA,[M=Co(II),Ni(II), and Zn(II)]

Ninhydrin exhibits strong antibacterial and antiviral activities [2]. It has also shown that physiological activity of organic compounds is much more enhanced on coordination to metals; particularly, Schiff bases and their metal complexes have been shown to exhibit enhanced activities [3]. Thus Schiff bases and their metal complexes have attracted a great deal of attention in biochemistry due their vast applications as anticancer, antitubercular, anticonvulsant and insecticidal, antibacterial etc agents.

Semi-, thiosemi-, and isothiosemicarbazones, (SC, TSC, ITSC, respectively) (Fig. 4), as well as their metal complexes have been the subject of great interest of many researchers for a number of years. Like the majority of similar Schiff bases, semicarbazones, thiosemicarbazones and isothiosemicarbazones are mainly obtained in good yield by the condensation reaction of alcoholic solutions of an aldehyde or a ketone and the corresponding semicarbazide derivative [4]. Depending on the form (neutral, protonated) of the ligand precusor, *i.e.*, of the presence of a proton acceptor (CO_3^{2-}, OAc^-), it is possible to obtain either neutral or protonated forms of the ligands [4].

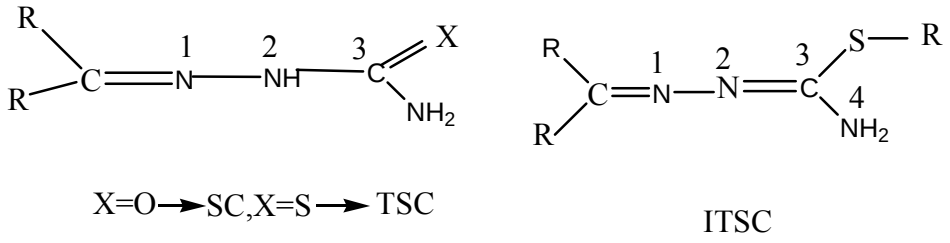


Figure 4: General structural formulas of semi- thiosemi- and isothiosemicarbazones [4].

The largest group of metal complexes with Schiff bases which have been synthesized and characterized up to now, represent complexes with PLTSC while the peparative coordination chemistry of PLSC and PLITSC ligands is of a much more recent date [4].

From the point of view of the metals with which complexes with all three ligands have been prepared and investigated, the most numerous are copper and iron complexes [4]. With respect of their composition, a common feature of all of these complexes is that they belong to the type of mono (Schiff-base)-ligand complexes.

The significance of these compounds, apart from their diverse chemical and structural characteristics, stems not only from their potential but also their proved application as biologically active molecules a wide spectrum of activity. This is especially related to thiosemicarbazones and their metal complexes [5]. Furthermore, bearing in mind that many semi- and thiosemicarazones form stable colored metal complexes, some of them have been proposed as analytical reagents [5]

The coordination chemistry of semi-, thiosemi- and isotiosemicarbazones appeared to be very interesting from the point of view of both the number of metals forming complexes with them and the diversity of the ligand systems themselves (among them being also macro cyclic ones) *i.e.*, their denticity, set of donor atoms, stabilization of various (less common) oxidation states of metals, reactions of coordinated ligands, etc [5].

For instance, the investigation of metal complexes with Schiff bases derived from pyridoxal (PL), *e.g.*, 3-hydroxy-5-hydroxymethyl-2-methylpyridine-4-carboxaldehyde (one of the forms of vitamin B_6), and amines, and/or amino acids, can serve as models for studying a wide range of biological reactions which are catalyzed by enzymes, in which

pyridoxal phosphate (PLP), as the physiologically active form of pyridoxal, appears as an essential component [5] It has been shown that in the presence of metal ions, free pyridoxal can catalyze a variety of metabolic reactions, *e.g.,* of amino acids (transmination, decarboxylation, racemization and carbon–carbon bond cleavage), in which PLP acts as a co-enzyme [5]. On the other hand, some recent pharmacological studies of Schiff bases of pyridoxal and aminoguanidine enabled researchers to set up the hypothesis that this Schiff base is more effective than aminoguanidine, which is known as a good inhibitor of the formation of advanced glycation end products, and is considered to be promising for the treatment of diabetic complications. Pyridoxal semi-, thiosemi- and isothiosemicarbazones (PLSC, PLTSC and PLITSC, respectively) (Fig.5) form a special group of these ligands.

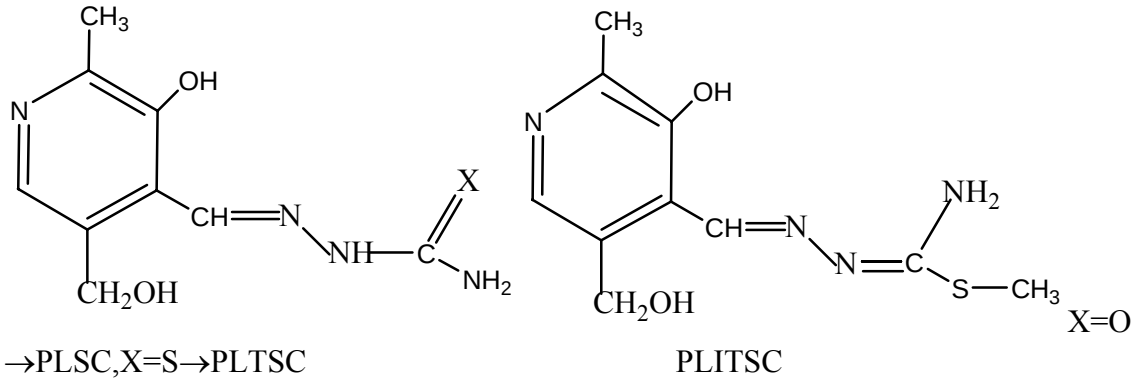


Figure 5: Structural formulas of pyridoxal semi- (PLSC), thiosemi-(PLTSC) and isothiosemicarbazone (PLITSC).

All three ligands (PLSC, PLTSC, and PLITSC) are yellowish substances, sparingly soluble in water and organic solvents, whereby the protonated forms exibit somewhat higher solubility [5]. On heating, especially in the presence of metal ions, due to complexation, their solubility shows a dramatic increase. The molar conductivity of aqueous solutions of the protonated forms of these ligands corresponds to 1:1 type of electrolytes. Both ligand forms (neutral and protonated) are characterized by enhanced thermal stability and they melt in the range from 212 ^{o}C (PLITSC.H_2O) to 245^{0}C (PLSC.HCl.H_2O) [5].

Coordination Mode [5]

The common coordination mode of these ligands (pyridoxal semi-, thiosemi-, and isothiosemicarbazones) is presented in Fig. 6. As can be seen, of seven potential ligator atoms of all three ligands, three are engaged in coordination, two of them being identical for all three ligands. Namely, the identical ligators are the phenolic oxygen and hydrazine N_1 nitrogen. In the case of PLSC and PLTSC, the third ligator atom is the oxygen or sulfur atom of the amide, *i.e.*, thioamide group (Fig. 6 a,b,c). In the case of PLITSC, the third ligator atom is the N_4 nitrogen of the isothioamide group (Fig.6d, e, f).

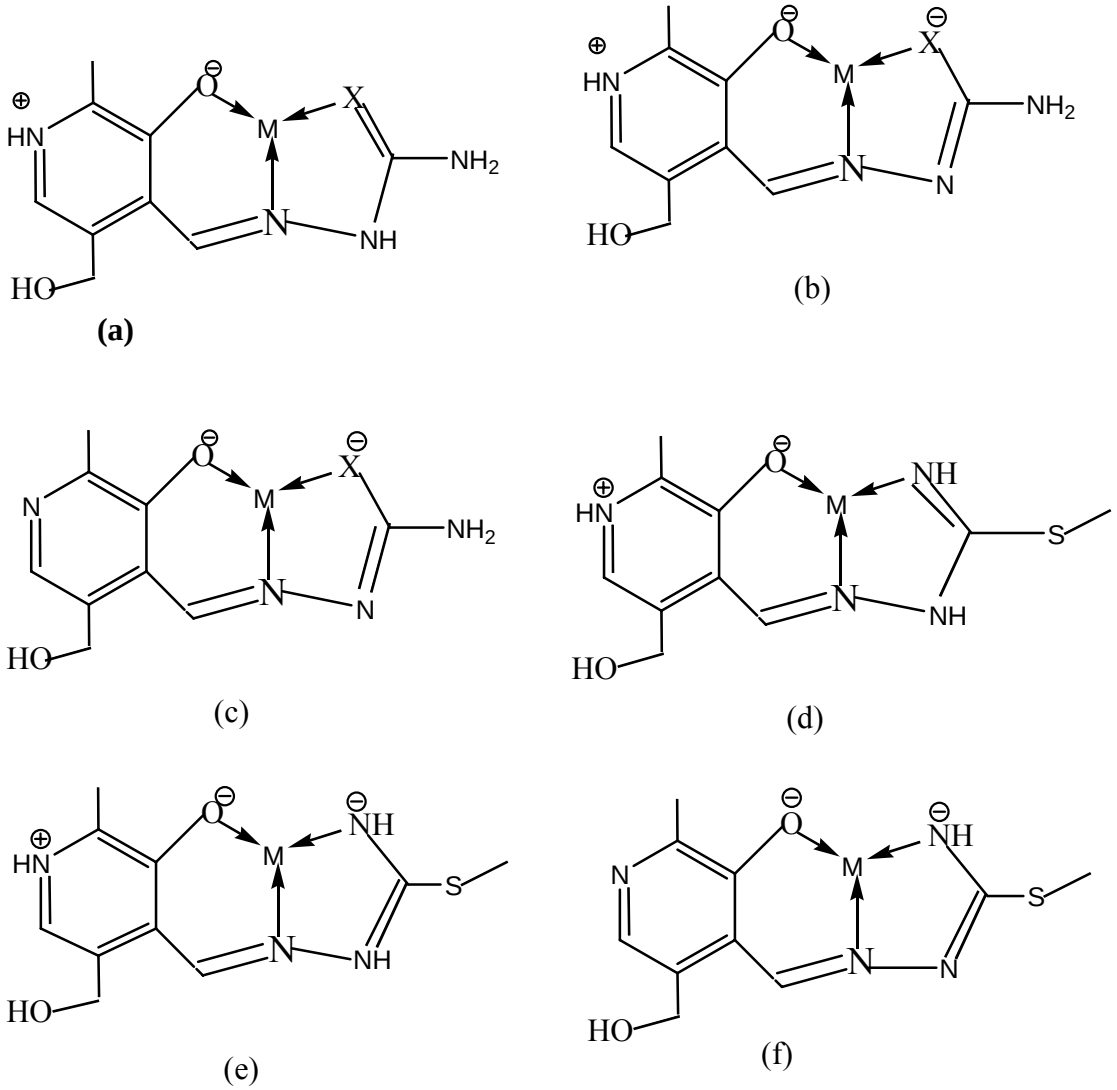


Figure 6: Coordination modes and ligand forms of PLSC, PLTSC (a, b, c) and PLITSC (d, e, f).

In all cases, two metallocycles are formed: one six-membered (pyridoxilydene) and one five-membered (semicarbazide derivative). Furthermore all three ligands can be coordinated either in neutral, monoanionic or dianionic forms. The monoanionic forms of PLSC and PLTSC are formed by deprotonation of the enol/thiol forms (Fig. 6b), and in the case of PLITSC, by deprotonation of the hydrazine nitrogen atom (Fig. 6e), *i.e.*, of the imido form of the isothiosemicarbazide residue. The dianionic forms of all three ligands are formed by the additional deprotonation of the pyridine nitrogen (Fig. 6c, f), *i.e.*, of the Zwitter ion, the existence of which is explained by the migration of the hydrogen atom from the phenolic OH group to the heterocyclic nitrogen atom. It should be pointed out that this proton transfer is characteristic not only of coordinated but also of non-coordinated pyridoxal derivatives.

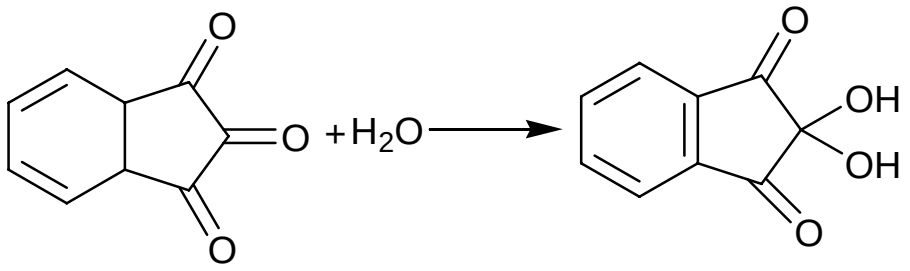
The form of the coordinated ligand will depend primarily on the pH and then on the nature of the metal ion. Namely, the presence of proton acceptors (NH_3, OAc^-, Py, *etc.*) will facilitate the formation of complexes with the anionic forms of the ligand. Thus, for example, with Zn $(NO_3)_2$ and Ni $(NO_3)_2$, PLTSC give [Zn (PLTSC) $(NO_3)_2$].H_2O and [Ni (PLTSC-H) NO_3].$2H_2O$, whereas with M (OAc) .H_2O, (M = Zn, Ni), it forms Zn (PLTSC H) OAc .H_2O and [Ni (PLTSC-2H)].$2H_2O$.

By comparing the deprotonation of these three ligands, *i.e.,* the deprotonation of the residue of the semicarbazide derivative, it can be concluded that thiosemicarbazide is most readily deprotonated and that deprotonation of isothiosemicarbazide is the most difficult.

The present investigation was, therefore, undertaken to synthesis and characterize nickel (II) complex of ninhydrin-2, 3-disemicarbazone, which is a condensation product of ninhydrin and semicarbazide hydrochloride.

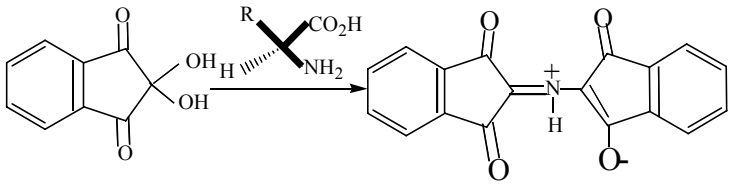
1.1 Ninhydrin

The best-known triketone derivative of 1, 2, 3-indanetrione is ninhydrin, the monohydrate of indan-l, 2, 3-trione [6]. 1, 2, 3-Triketohydrindane forms a stable hydrate known as ninhydrin [7]. Ninhydrin is the 2-hydrate of indane-1, 2, 3-trione.



Scheme 4 Conversion of 1, 2, 3-indantrione to ninhydrin (2, 2-dihydroxy-1, 3-indanedione)

It reacts with α-amino acids to yield highly colored product. This compound was first synthesized in 1910 by Siegfried Ruhemann**,** who also investigated its reaction with amines and amino acids to form a colored compound known as Ruhemann's Purple (RP) [9].



Ninhydrin

Or 2,2-Dihydroxy-1,3-indanedione

Ruhemann's Purple(RP)

Scheme 5 Formation of Ruhemann's Purple

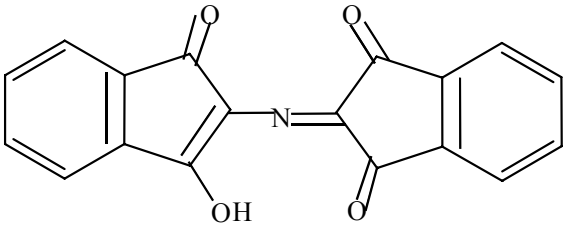
In contact with the skin, it produces a rather long-lasting purple discoloration.

It is a valuable reagent for the calorimetric detection and estimation of α-amino acids [9].

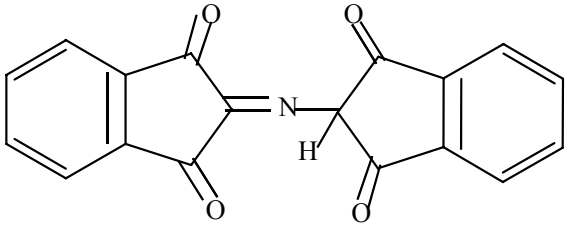
In this reaction the Schiff base initially formed decomposes and hydrolyses to give α-amino -1, 3-diketohydrindene, an aldehyde and carbon dioxide.

The color-forming reaction is interesting because most α-amino acids give the same color irrespective of their structure.

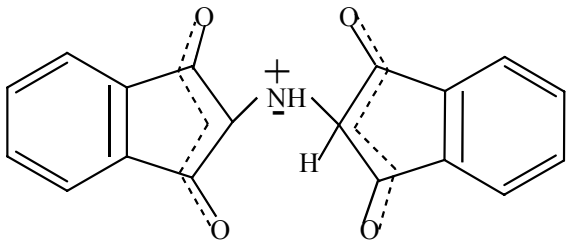
There are three different isomers for Ruhemann's purple [9]. The most brightly colored version of Ruhemann's purple is anionic version of isomer 1, where the proton is missing from the hydroxide group. Isomer 1 may very well be the protonated version of the colored anion, as their electronic structures and spectra are similar[9].



Ruhemann's Purple Isomer 1



Ruhemann's Purple Isomer 2



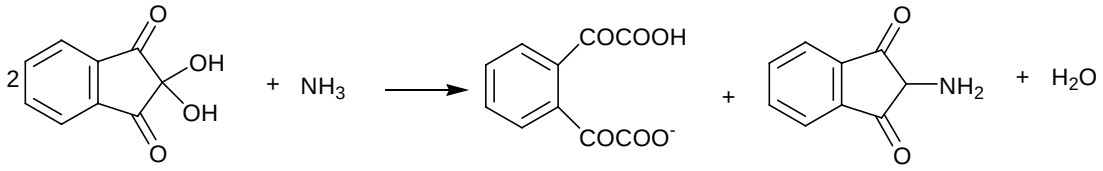
Ruhemann's Purple Isomer 3

Figure 7 Different isomers of Ruhemann's purple

The formation of Ruhemann's purple can be understood as taking place in three general stages [9]. (1)The first and rate determining step is the amino acid attack on ninhydrin or its analogue. As carbon dioxide and an aldehyde are ultimately produced, this stage is recognized as a special case of the Strecker degradation. (2) The second stage involves the production of several intermediates from principal dehydration. (3) Finally, in the third stage some of the intermediates become involved in the side reactions and some go on to form Ruhemann's purple.

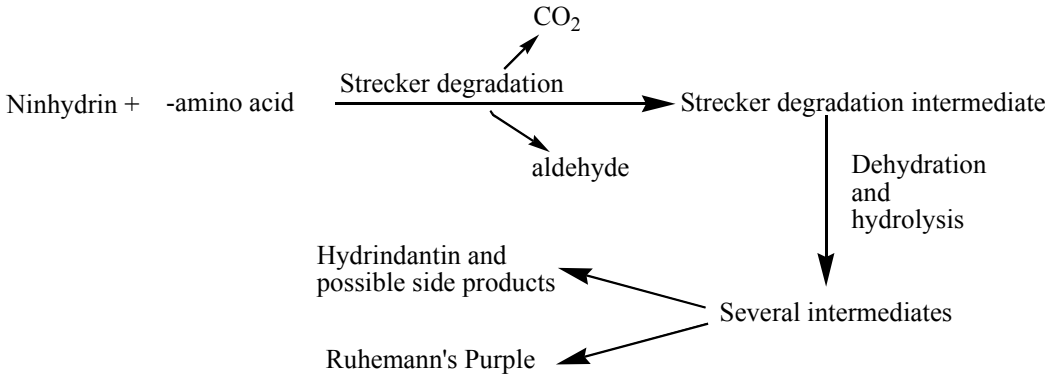
Ninhydrin is used as spraying reagent in the identification and quantitative estimation of α-amino acids. All α-amino acids give the same blue product, proline and hydroxy proline, however, give a yellow product.

In the ninhydrin reaction, α-amino acids, proteins or their degradation products that contain a free carboxyl group having an α-amino group, give a blue color when treated in dilute solution with triketohydrindene hydrate (ninhydrin) [10, 11]. Ammonium salts, dilute ammonia solutions, and certain amines also give a blue color under certain conditions, apparently because of an intermolecular oxidation and reduction of the ninhydrin in the presence of ammonia [10].



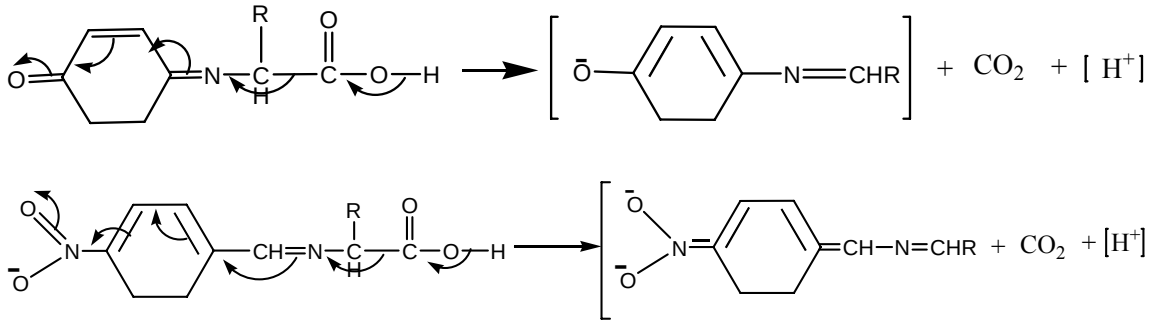
Scheme 6 Intramolecular redox reaction of ninhydrin in the presence of ammonia

The ninhydrin reaction is a special case of the more general Strecker degradation in which any compound containing an aldehyde, or keto group in conjugation with another carbonyl group or a nitro group reacts with an α-amino acids to give an aldehyde and carbon dioxide [9, 10, 11, 12].



Generally speaking the Strecker degradation is a mechanism which explains the formation of CO_2 and an aldehyde after hydrolysis of a conjugated carbonyl or carbonyl-nitro group. The ready loss of carbon dioxide is dependent on the ability of the second

carbonyl group or the nitro group to accommodate the pair of electrons that binds the carbonyl group [10].



Scheme 7 Mechanisms of Strecker degradation.

In acid, most aldehydes form nonisolable hydrates (gem-diols). Two exceptions are the stable chloral hydrate, $Cl_3CCH(OH)_2$,and ninhydrin [13-16]

The exceptional properties are due to the strong electron withdrawing groups on α carbon atom destabilize an adjacent carbonyl group because of repulsion of adjacent positive charges. Hydrate formation overcomes the forces of repulsion [13-15]. Therefore, the hydrate of the middle carbonyl group of ninhydrin removes both pairs of repulsions [13-16]. The stability of the diols is probably due to unfavorable dipole-dipole repulsion in the parent carbonyl compounds [13-16].

Ninhydrin is one of the most widely used reagents for chemical development of fingerprints on porous surfaces such as paper, wood, and walls [17]. The detection is based on the reaction of ninhydrin with a monoacidic component of the fingerprint (the amino acid secreted from the ecrine gland) to form an intensively colored compound named Ruhemann's Purple (RP) [17]. It is a useful reagent for latent prints visualization [17]. Although the relative amount of amino acids in a fingerprint residue is low compared to the amount of salts and fatty acids, they form a unique, lasting picture of an individual. The study of the formation of Ruhemann's purple from ninhydrin and amino acids is significant from a forensic science point of view because of the strong interest in

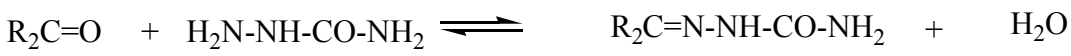
the forensic chemistry and law enforcement communities in developing alternatives to the current generation of ninhydrin like chemicals for the detection and development of latent fingerprints [17]. Information about the mechanism of reaction between ninhydrin and amino acids can ultimately help to design compounds with stronger chromo-fluorogenic properties in aid of detecting fingerprints at crime scenes [17].

Ninhydrin and modified ninhydrins were the best reagents for use on paper. Therefore, it is also possible to enhance the properties of ninhydrin via structural modifications to create a superior print development reagent which would be useful to professionals involved in identification of latent fingerprints [17].

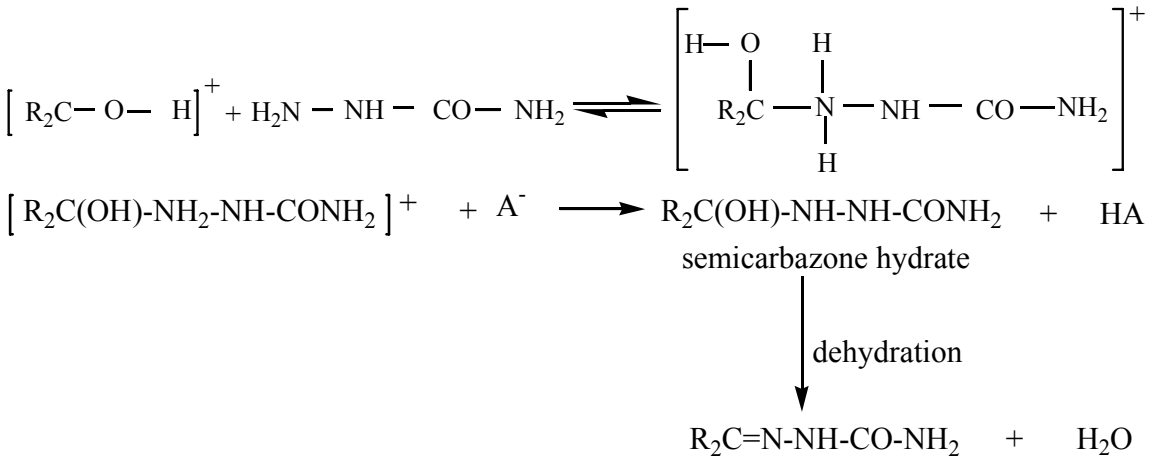
In addition to primary amino groups, imines such as pipecolic acid and proline, the guanidino group of arginine, the amide groups of asparagine, the indole ring of tryptophan, the sulfhydryl group of cysteine, amino groups of cytosine and guanine, and cyanide ions also react with ninhydrin to form various chromophores of analytical interest [17]. Since its discovery, extensive efforts have been made to apply manual and automated ninhydrin reactions as well as ninhydrin spray reagents to the detection, isolation, and analysis of numerous compounds of interest across a broad spectrum of disciplines [17]. These include agricultural, biochemical, clinical, environmental, food, forensic, histochemical, microbiological, medical, nutritional, plant, and protein sciences [17]. This reaction is unique among chromogenic reactions in that at pH 5.5 it results in the formation of the same soluble chromophore by all primary amines which react, be they amines, amino acids, peptides, proteins, and even ammonia [17]. Because the chromophore is not chemically bound to the protein or other insoluble material, it is not lost when the insoluble substrate is removed by centrifugation or filtration after the reaction is completed. The visible color of the chromophore is distinctive and is generally not affected by the yellow colors present in many foods, plant, and tissue extracts. Adaptations of the classical ninhydrin reaction to specialized needs in analytical chemistry and biochemistry include the use of acid, alkaline, and fluorogenic ninhydrin reagents. A better understanding of the multifaceted ninhydrin reactions provides a scientific basis for further improvements of this important analytical technique [17].

1.2 Formation of Semicarbazones

The semicarbazone formation is a general acid catalyzed reaction of ketones or aldehydes with semicarbazide complicated by the basic properties of semicarbazide [13].



The mechanism of the semicarbazone reaction [18]:-Since the nitrogen linkage in the semicarbazone is formed by an electron pair contributed by the semicarbazide, the catalysis must depend up on an attack by the acid on the carbonyl compound. Such an attack by an acid must decrease the electron density on the carbonyl carbon and favor the formation of the carbon nitrogen-bond; an attack on the semicarbazide would decrease the electron density on the nitrogen, which is unfavorable to reaction.



The semicarbazone formation is reversible and comes to an equilibrium, the composition of which is markedly affected by the acidity of the solution because semicarbazide and the semicarbazone are both bases.

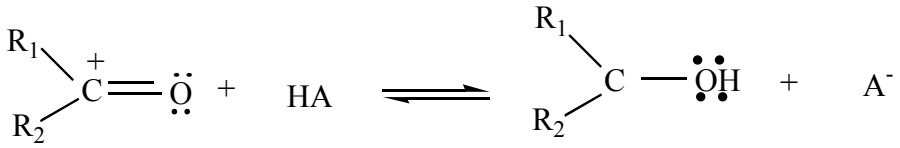
In important respects the formation of semicarbazones is probably typical of the formation of hydrazones, aryl hydrazones, and oximes [19]. Semicarbazide is a base that is half converted into the corresponding of ammonium ion at pH 3.7. At progressively lower pH values the reactive semicarbazide is increasingly converted at equilibrium into unreactive ion, and both the equilibrium and the rate becomes unfavorable to

semicarbazone formation. On the other hand, the formation of semicarbazones is subjected to general acid catalysis, and hence solutions of high pH are also unfavorable to the rate of the reaction [19]. The most favorable rates are obtained in the solutions of pH close to that of half neutralized semicarbazide and in the presence of moderate concentrations of organic acids [19].

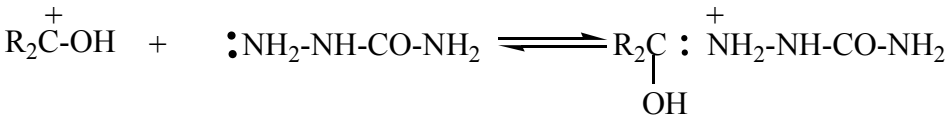
With varying degrees of acidity of the medium, semicarbazone formation passes through a steep maximum at a definite pH (varying with the nature of the carbonyl compound but usually between 4 and 5) [20]. In practice the acetic acid-sodium acetate buffer is usually employed as the medium [20].

The course of the (reversible) reaction can best be represented as follows [20]:

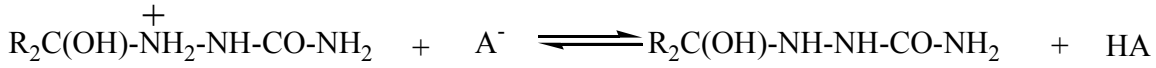
a/ Addition of a proton from the acid catalyst (HA) to the carbonyl compound with the formation of the conjugated acid.



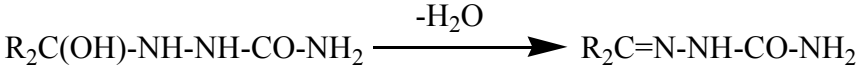
b/ A nucleophilic reaction on carbon with the lone pair of electrons on the NH_2-group of the semicarbazide;



c/ Reaction of this positive ion with the anion A^- of the catalyst;

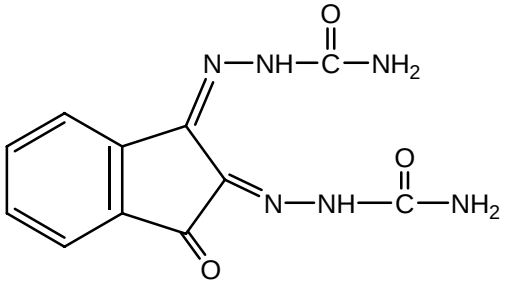


d/ Elimination of water



The position of the equilibrium in the formation of semicarbazone is, of course, also dependent on the pH, the quantity of the semicarbazone eventually formed doesn't pass through a maximum, but is greater at high pH [20].

However, when an ethanolic solutions semicarbazide hydrochloride and ninhydrin are mixed together in 2:1 molar ratio and refluxed for a few minutes two of the three carbonyl groups of ninhydrin undergo condensation reaction to give a new compound ninhydrin-2, 3-disemicarbazone whose structure is confirmed by ^{1}H-NMR, ^{13}C-NMR, and IR spectral analysis.



Ninhydrin-2, 3-disemicarbazone

Figure 8 Structure of ninhydrin-2,3-disemicarbazone

Uses of Semicarbazones

The convulsions of approximately 25% of epileptics are inadequately controlled by currently available medication; therefore the preparation of new antiepileptic drugs is of great interest. Aryl semicarbazones can be considered a new class of compounds presenting anticonvulsant activity [21]. In addition, they can be orally administered and are more active as anticonvulsants than mephenytoin or phenobarbital. However, one disadvantage of these compounds is their low water solubility [21].

It was deduced recently that the requirement for anticonvulsant activity includes [21]

1. An aryl hydrophobic binding site with halo substituent preferably in the *para* position.
2. A semicarbazone system containing 2-electron donor system and a hydrogen bonding domain.
3. Another hydrophobic-hydrophilic site controlling the pharmacokinetic properties of the anticonvulsant.

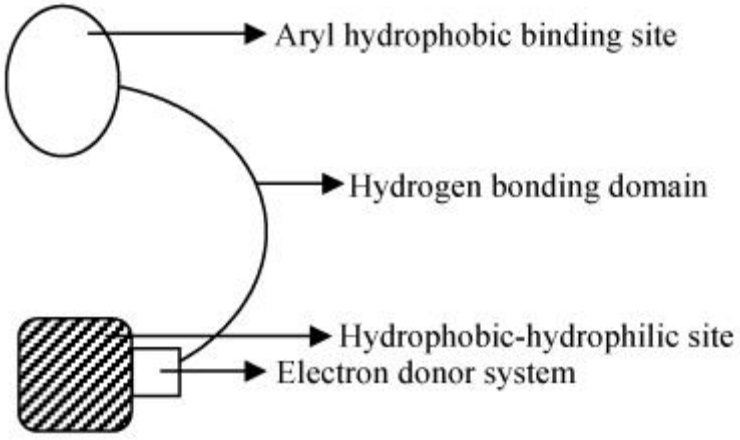


Figure 9 Structural requirements for semicarbazones displaying anticonvulsant activity

1.3. Nickel (II) Complexes

Nickel (II) forms a large number of complexes the main structural types being octahedral, tetrahedral, and square-planar [22].

Octahedral complexes: Octahedral nickel (II) complexes having $^3A_{2g}$ ground state are expected to have three spin-allowed transitions [17]. $^3A_{2g}\rightarrow{}^3T_{2g}$, $^3A_{2g}\rightarrow{}^3T_{1g}$ (P) and $^3A_{2g}\rightarrow{}^3T_{1g}$ (F) in the ranges of 7000-13000, 11000-20000 and 19000-27000 cm^{-1} respectively [22]. Two spin forbidden transitions are also possible, $^3A_{2g}\rightarrow{}^1E_g$ and $^3A_{2g}\rightarrow{}^1T_{2g.}$

Magnetically, octahedral nickel (II) complexes have a relatively simple behavior. They all should have two unpaired electrons and thus posses' magnetic moments ranging from 2.9 to 3.4 B.M. depending on the orbital angular momentum contribution [22].

Tetrahedral complexes: For regular or nearly regular tetrahedral complexes there are characteristic spectral and magnetic properties. Naturally the more the irregular geometry of a paramagnetic nickel (II) complex, the less likely it is to conform to these specifications [22].The tetrahedral nickel (II) complexes with $^3T_1$ (F) ground state generally exhibit four transitions [22].$^3T_1\rightarrow{}^3A_2$, $^3T_1\rightarrow{}^1E$, $^3T_1\rightarrow{}^3T_1$ (P) and $^3T_2\rightarrow{}^1T_1$.The

band $^3T_1 \rightarrow {}^3T_1$ (P) is a strong band of high intensity when compared with others. The transition from the ground $^3T_1$ (F) state to the $^3T_1$ (P) state occurs in the visible region (~15,000 cm^{-1}) and is relatively strong ($\varepsilon \approx 10^2$) compared to the corresponding $^3A_{2g} \rightarrow {}^3T_{1g}$ transition in octahedral complexes. Thus tetrahedral complexes are generally strongly colored and tend to be blue or green unless the ligands also have absorption bands in the visible region [22]. Because the ground state $^3T_1$ (F) has much inherent orbital angular momentum, the magnetic moments of truly tetrahedral Ni (II) should be about 4.2 B.M. at room temperature. However, even slight distortions reduces this markedly (by splitting the orbital degeneracy).Thus fairly regular tetrahedral complexes have moments of 3.5 to 4.0 B.M.; for the more distorted ones the moments are 3.0 to 3.5 B.M. (i.e., in the same range as six coordinated complexes) [22] .

Square planar complexes: For the vast majority of four coordinated nickel (II) complexes, square planar geometry is preferred. This is a natural consequence of the d^8 configuration, since the square planar ligand set causes one of the d orbitals (d_{x2-y2}) to be uniquely high in energy and the eight electrons can occupy the other four d orbitals but leave this strongly antibonding one vacant [22]. In tetrahedral coordination, on the other hand, occupation of antibonding orbitals is unavoidable. Square Planar complexes of nickel (II) are thus invariably diamagnetic [22]. They are frequently red, yellow or brown owing to the presence the absorption band of medium intensity ($\varepsilon \approx 60$) in the range 450-600 nm, but other colors do occur when additional absorption bands are present [17]. Square planar nickel (II) complexes don't have any absorption band below 10000 cm^{-1}, due to large crystal field splitting [22]. Hence they can be clearly distinguished from octahedral and tetrahedral complexes.

1.4. Methods and Instrumentation

With respect to the applied methods and synthesis conditions of metal complex bearing this ligand (ninhydrin-2, 3-disemicarbazone), it can be said that practically the complex was obtained by the simple template method, *i.e.*, by the reaction of hot ethanolic solution of ninhydrin, semcarbazide hydrochloride and nickel (II) chloride in warm ethanol in one

pot as well as by the reaction of the ligand ninhydrin-2, 3-disemicarbazone with nickrel (II) chloride.

The salt used was $NiCl_2.6H_2O$ (Riedel-deHaen), Ninhydrin (Pharmacos),
Semicarbazide hydrochloride, other reagent and solvents used in this investigation were silver nitrate (BDH), nitric acid, ammonia solution, dimethylglyoxime, potassiumferocyanate, and sodium hydroxide. Absolute ethanol was used as the solvent throughout the investigation. Solvents like DMSO, DMF, acetonitrile, dichloroethane, chloroform, methanol, carbon tetrachloride, THF, acetic acid diethylether, and distilled water were used.

Melting/decomposition temperatures were determined with SMP3, Digital Melting point apparatus. Electronic spectra of the complexes were recorded using SPECTRONIC GENESYS 2PC Uv-Visible spectrometer with a 1cm cell in DMSO at room temperature. Infrared spectra (KBr pellet) were recorded on Perkin Elmer Spectrum BX FT-IR spectrometer in the range of 4000-400 cm^{-1}. Molar conductivities of the complexes were measured at room temperature with freshly prepared 0.95mM solutions in DMSO using a JENWAY 4330 conductivity and pH meter.

Chloride ions were determined as AgCl by using concentrated nitric acid and silver nitrate. The metal content was estimated by using BUCK SCIENTIFIC ATOMIC ABSORPTION SPECTROPHOTMETER MODEL 210 VGB. The ^{1}H and ^{13}C NMR spectra for the ligand were recorded using BRUKER 400 Ultra-Shield NMR Instrument.
Magnetic susceptibility measurements of the complexes were performed at $23^{o}C$ on a MSB-AUTO Magnetic balance (Sherwood Scientific).
The mass spectra of the ligand were recorded on Therm Finnigan flight temperature insertion probe. The sample was ramped from RT to 300 ^{o}C.
The purity of the complex was tested by thin layer chromatography.

1.5 Aim and scope of the Investigation

A search through literature reveals that a lot of work has been done on different metal complexes of Schiff bases derived from ninhydrin and α-amino acids or amines, which have O and N donor sites. It is also well-known from the literature that much work has been done on the synthesis and characterization of semicarbazones and their metal complexes. However, the synthesis and characterization of ninhydrin-2, 3-semicarbazone and its metal complex has not been yet reported. The present study aimed to synthesize and characterize the new ligand ninhydrin-2, 3-disemicarbazone and to investigate the reaction of this tetradentate ninhydrin-2, 3-disemicarbazone derived from the condensation of ninhydrin with semicarbarbazide hydrochloride with nickel (II) ions. The prepared ligands and complexes were characterized by atomic absorption, molar conductivity measurements, mass spectrometer, and infrared and electronic spectral data. The ligand was further identified using ^{1}H-NMR spectra and ^{13}C-NMR.

The ligand has two nitrogen and two oxygen donor sites, which can effectively coordinate to a metal ion in a tetradentate fashion. This tetradentate ligand forms a 1:1 complex with nickel (II) ion. It coordinates with the metal (II) ion in a tetradentate manner through the two oxygen carbonyl groups of the two amide groups and the two azomethine nitrogen atoms of the of the ninhydrin-2,3-disemicarbazone.

In view of the wide range of potential applications of semicarbazones and their metal complexes in agriculture (as herbicides), pharmaceuticals (as anticonvulsant) and analytical field, it has been aimed to synthesize and study the structure of 2, 3-disemicarbazone and its Ni (II) complex.

This project presents the synthesis and characterization of ninhydrin-2, 3-disemicarbazone and its metal complex containing Ni (II).

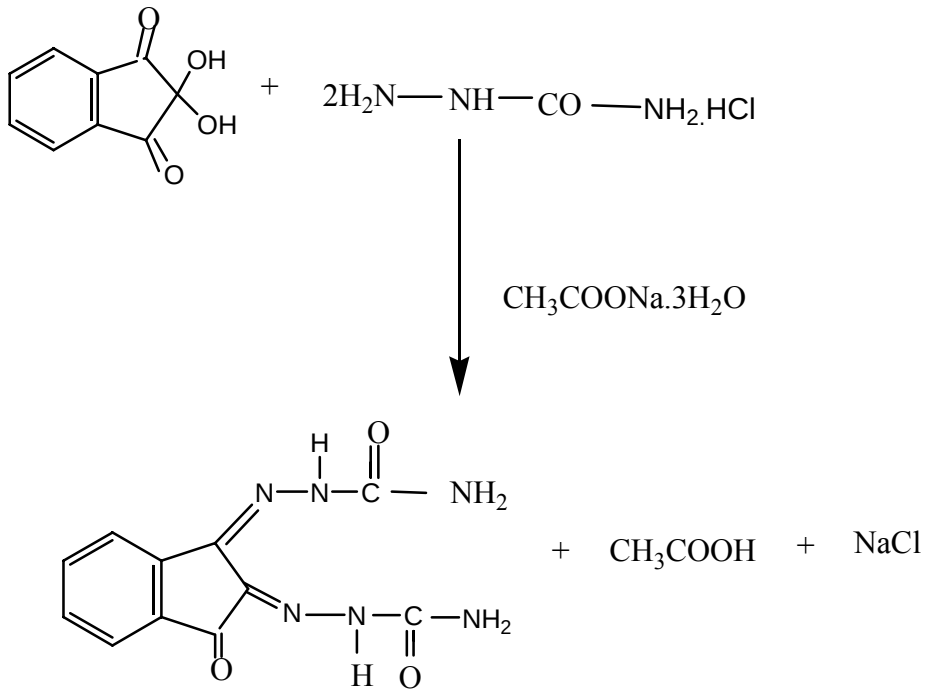
2. Synthesis

2.1. Synthesis of Ninhydrin-2, 3-disemicarbazone (NDSC)

Procedure: The ligand was synthesized by condensation of ninhydrin and semicarbazide hydrochloride (1:3 molar ratios) dissolved in hot ethanol (20ml each). Ninhydrin (0.178g, 0.999 mmol) dissolved in 20ml of ethanol was mixed with hot ethanolic solution (20ml) containing semicarbazide hydrochloride (0.34, 2.99 mmol) and sodium acetate (0.41g, 2.99mmol). The resulting reaction mixture was refluxed for 15 minutes. The yellow solid precipitate formed was filtered by suction filtration, washed with absolute ethanol, air dried and finally preserved in a desiccator. It melts/decomposes at about 244^0C.

The structure of the ligand was characterized by elemental analysis, IR, UV-vis and NMR studies. Yield was 161 mg (41%).

^{1}H-NMR (DMSO):δ 12.19 (s, NH), 10.63 (s, NH), 7.02 (br.NH_2), 7.57(t), 7.76 (dd),and 8.13 ppm (d) are aromatic H): ^{13}C-NMR (DMSO): δ 186.77(C=O on ninhydrin), 156.57,and 154.33 ppm (C=O of the amide group), 121.82, 124., 130.72, 133.72, 136.57,and 144.32 ppm (arom.C),134.06 and 134.88 ppm(C=N).



2.2. Synthesis of Ni (II)-NDSC Complex

Procedure: The complex of nickel (II) was synthesized using a general procedure. The complex was prepared by mixing ninhydrin and semicarbazide hydrochloride in the presence of the metal ion. Ninhydrin (0.18g, 0.999 mmol) dissolved in 20ml and a metal salt (0.24g, 0.999 mmol) dissolved in 20ml of ethanol were mixed together (1:1 molar ratio) and the resulting mixture was refluxed on water bath for two hours, followed by addition of 2.99 mmol (0.34g) of semicarbazide hydrochloride dissolved in ethanol (20ml) to the hot mixture (1:1:2 molar ratio) and refluxed further for two hours. The resulting blue precipitate was then filtered off by suction, washed with cold absolute ethanol. The product was then dried in open air and stored in desiccator. The purity of the complex was checked by TLC, IR spectra, and melting point. Yield: 45%

The complex of Ni (II) was also prepared by mixing a hot ethanolic solution of nickel (II) chloride (0.24g, 0.99mmol) with a hot ethanolic solution of the ligand ninhydrin-2, 3-disemicarbazone (0.27g, 0.999 mmol) (in 1:1 molar ratio). The reaction mixture was refluxed on water bath for about 2 hours. The blue colored complex was precipitated out. The precipitate was filtered by suction, washed with cold ethanol; air dried and kept in desicator. Yield: 15%.

3. Results and discussion

3.1 Characterization of the Ligand

3.1.1 General Characteristics

Ninhydrin-2, 3-disemicarbazone has a yellowish color and is insoluble in water and organic solvents, while it is soluble in DMF and DMSO. On heating, especially in the presence of metal ions, due to complexation, their solubility shows a dramatic increase. This ligand melt/decomposes in the range from 226-244^{o}C.

3.1.2 IR Spectrum

From the structure of the semicarbazones, RR'CN-NH-$CONH_2$, a number of characteristic vibrational modes would be expected, e.g., υ(NH), υ (C=O), δ(NH), and υ C=N). Of these, all but the υ(C=N) are common to amides, which are known to give rise to υ(NH), an amide I band [υ(C=O)] at about 1695 cm^{-1} and amide II band at about 1600 cm^{-1}) [17]. The semicarbazone grouping gives characteristic absorptions at about 3460, 3370-2800 cm^{-1} and 767 cm^{-1} which are assigned to the NH stretching and rocking modes[18]. There is a complex series of bands between 3370 and 3000 cm^{-1} which is similar to the broad υ(OH) absorption of carboxylic acids and is assigned to bonded υ (NH) modes. υ (C=N) occurs at 1600 cm^{-1} and its intensity varies widely. The semicarbazone has absorptions in the l230-1030 $cm.^{-1}$ region which are probably due to υ(C-N) [18].

Ninhydrin shows three bands in the C=O stretching region: 1768, 1754, and 1720 cm^{-1} [22]. The 1754 and 1720 cm^{-1} bands are characteristic of its 1,3-dicarbonyl functional group and the 1768 cm^{-1} band is characteristic of the intermediate carbonyl in the tricarbonyl species, which is in equilibrium with the dihydroxy species [22]. In the ninhydrin-2, 3-disemicarbazone there is one carbonyl stretching peaks at decreased frequency (1717 cm^{-1}), which shows the derivatization of the higher frequency (1768 and 1754 cm^{-1}) carbonyl groups of ninhydrin.

Ninhydrin-2,3-disemicarbazone shows its characteristic absorption bands in the 3350-3100, 1697, 1665-1500 cm^{-1} and 1230-1030 cm^{-1} regions, assignable to N–H, C=O (amide I band), C=N and C–N stretching vibrations respectively. The breadth of the υ(NH) band indicates the presence of hydrogen bonds. The strong absorption at 1717 cm^{-1} corresponds the stretching vibration of C=O that would remain intact on ninhydrin. The bands in the 1500-1430 cm^{-1} are assigned to C=C stretching vibrations of the aromatic ring. One characteristic peak at 1681 cm^{-1} indicates N-H bending (amide II band). The band(s) at 1653 and 1598 cm^{-1} are due to the two C=N (imino group) groups of the ligand ninhydrin-2, 3-disemicarbazone

3.1.3 ^{1}H NMR and ^{13}C NMR

The formation of ninhydrin semicarbazone was confirmed by ^{1}H-NMR and ^{13}C-NMR studies. The ^{1}H-NMR spectrum of the ninhydrin-2, 3-disemicarbazone ligand shows that the four aromatic ring protons of ninhydrin produce characteristic signals at 7.57, 7.76, and 8.11 ppm. The $–NH_2$ protons produce a broad signal at 7.02 ppm and the NH protons of the two NH groups give their characteristic signals at 10.63 and 12.19 ppm. This difference in the environments of NH protons may be due to the involvement of one of the semicarbazone functions in hydrogen bonding with the carbonyl oxygen as shown in figure below:

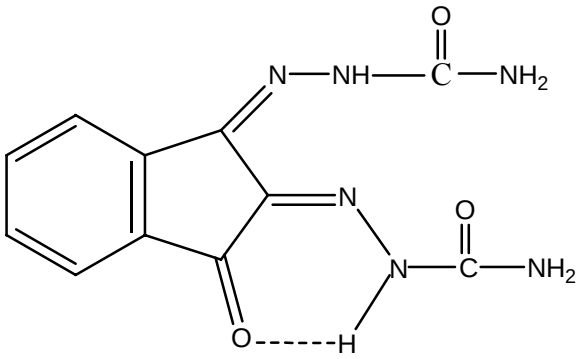


Figure 10 Hydrogen bonding scheme in NDSC

The ^{13}C-NMR spectra of the ligand were recorded by employing TMS as internal reference and DMSO as solvent at ambient temperature. The numbers of signals of sharp peaks represent the number of carbons of the compound, which are chemically non-equivalent. There are eleven nonequivalent carbon atoms. The spectra exhibit the imino, C=N carbon at 134.88 and 134.06 ppm which implies that the two C=N are nonequivalent and carbonyl carbon, C=O on the ring at 186 ppm. The chemical shifts of aromatic carbons appear at 144, 136, 133, 124, and 121 ppm. The chemical shifts of carbons of the amide group are at 156 and 154 ppm. The chemical shift of the quaternary carbon of the aromatic carbon adjacent to the C=O of the ring occurs at 144 ppm. The ^{13}C-NMR spectra indicate that all the carbon atoms in this compound are nonequivalent. In the DEPT spectra there are only four carbon atoms, which imply that there are seven quaternary carbons in the molecule. The ^{13}C-NMR also the supports the hydrogen bonding as deduced from ^{1}H-NMR spectrum. Due to the intramolecular hydrogen bonding, the azomethine and amide carbons appear as distinctly separate signals.

3.1.4 UV-vis spectrum

The electronic spectra for the ligand were measured in the DMSO solutions. The ligand spectrum consists of a maximum at ~323 nm which can be assigned to the $\pi \rightarrow \pi^*$ transition of the carbonyl groups and the other band at 384 nm can be tentatively assigned to $n \rightarrow \pi^*$ transitions.

3.1.5 Mass spectrum

The mass spectrum of ninhdrin-2,3-disemicarbazone shows no molecular ion peak at the expected m/z 274 which is diagnostically very important. However, it shows peak at m/z 259(due to loss of NH) and m/z 241(due to loss of NH and H_2O).

3.2 Ni (II)-NDSC Complex

The interaction of nickel (II) metal chlorides with ninhydrin and semicarbazide hydrochloride resulted in the formation of a complex nickel (II) ninhydrin-2,3-disemicarbazone. The complex is blue solid. The complex does not have a sharp melting point / but decomposes above 226^0C. This complex is generally insoluble in common organic solvents. However, it is soluble in DMSO, DMF.

3.2.1 Analytical Data

The complex was analyzed for metal and chloride ions. The data show a metal to ligand ratio of 1:1 in Ni (II) complex with additional water and chloride ions. The amount of chloride ions calculated under this experimental condition was 16.47%, which suggests that there would be two chloride ions in the complex. Since the complex is a 1:1 electrolyte one of the determined chloride ions must be in the inner coordination sphere. Therefore the following formulation is suggested for the complex:[NiNDSC(H_2O)Cl]Cl, where NDSC is ninhydrin-2,3-disemicarbazone. The molar conductance data show that Ni (II) complex of ninhydrin-2, 3-disemicarbazone a 1:1 electrolyte.

Qualitative Metal Ion Test: The presence nickel (II) ion in the complex was tested by using dimethylglyoxime. When the nickel complex dissolved in nitric acid is treated with dimethylglyoxime solution, it forms a red precipitate.

Quantitative Determination of Nickel: As the data from atomic absorption spectrophotometer indicate the amount of nickel (II) ion present in the compound is 13.38%, which is in close agreement with the theoretically estimated value from the structure of the complex. This percentage nickel in the complex confirms that the ligand to metal ratio is 1:1

Quantitative determination of chloride ion: The amount of chloride ion present in the complex was determined by treating with silver nitrate and the quantity of chloride ion present in the complex is 16.47%, which is nearly same as the theoretically estimated value.

Table1: Analytical and conductance data for Ni (II) complex of NDSC

Complex	%Metal found(calc)	%Chloride found (calc.)	Λ(S cm^2mol^{-1})
[NiNDSC(H_2O)Cl]Cl	13.38(13.88)	16.47(16.86)	97

3.2.2 Molar conductivity

The molar conductance values (97Scm^2mol^{-1}) of this complex measured in DMSO indicate that it is a 1:1 type of electrolyte. This implies that one the chloride ions is in the coordination sphere, while the other one is in ionization sphere:[NiLCl(H_2O)]Cl, where L= Ninhydrin-2,3-disemicarbazone

3.2.3 Magnetic Susceptibility

Magnetic behavior of octahedral nickel (II) complexes is relatively simple. Nickel (II) has the electronic configuration $3d^8$ and should exhibit a magnetic moment higher than expected for two unpaired electrons in octahedral (2.8–3.2 B.M.) and tetrahedral (3.4–4.2 B.M.) complexes whereas its square planar complexes would be diamagnetic.

Therefore, the paramagnetism observed for nickel (II) ninhydrin-2, 3-disemicarbazone complex is 2.99 B.M. which is in the ranges from 2.6–3.2 B.M. is consistent with the octahedral stereochemistry of the complex. Further data from spectral studies will provide support for this conclusion.

3.2.4 IR Spectrum

The ligand ninhydrin-2, 3-disemicarbazone and its nickel (II) complex of have been characterized by recording their IR spectra. A common feature of both the ligand NDSC and Ni (II) complex spectra is that in the high-energy range, *i.e.*, between 3500 and 3100 cm^{-1} they possess several bands which are attributed to the ν(OH) vibration of H_2O and

υ(NH) respectively. The *ν*(NH) band, which in the spectra of free NDSC is observed at about 3328 cm^{-1} is remained unchanged in the complex. In nickel (II) complex, the stretching frequency in the 3400-3300 cm^{-1} region is attributed to *ν*(OH). The –OH absorption bands appear in this region in the complex, clearly indicating that the –OH group of H_2O does take part in coordination. Furthermore, the spectral changes observed around 770 cm^{-1} and 880 cm^{-1} indicate the wagging and rocking modes of coordinated water. The very strong *ν*(C=O) band in NDSC ligand at 1697 cm^{-1}, *i.e.*, around the value characteristic for the majority of semicarbazones [24] is shifted to lower energies in the complex. A number of bands in the range 1655- 1400 cm^{-1} in the spectra of both ligand and complex are attributed to the aromatic ring vibrations, as well as to the *ν*(C=N) and δ(NH_2) of the chain. In the complex the spectral change observed in the 1665 - 1400 cm^{-1} region indicate coordination through the two imino nitrogens.

The band(s) at 1653 and 1598 cm^{-1} are due to the two C=N (imino group) groups of the ligand ninhydrin-2, 3-disemicarbazone. These bands under went a shift to lower frequency (1642 and 1576 cm^{-1}) after complexation, indicating the coordination of the two imino nitrogen to the metal atom and this can be explained by the donation of electrons from nitrogen to the empty d-orbitals of the metal atom. In the spectra of the complex, the broad band at 3389 cm^{-1}, together with new band at 1128 cm^{-1} indicating the presence of coordinated water. The nature of metal–ligand bonding is confirmed by the change in the spectra of the complex in the region 619-441 cm^{-1}. The band at 552 cm^{-1} (in the ranges 610-220 cm^{-1}) which is the part of the broad band in the region 660-440 cm^{-1} indicates the υ(M-Cl) stretching vibration. The broadening of the band may be due to the presence of the different naturally occurring isotopes of chlorine. The υ(M-O) stretching vibration which is in the range 450-350 cm^{-1} and the υ(M-N) stretching vibration which occurs in the range 535-275 cm^{-1} are also hided in this broad spectral region.

The complex shows one strong band in the carbonyl stretching region at 1717 cm^{-1} which is characteristic of the one carbonyl functionality and one other strong band at 1638 cm^{-1} characteristic of amide I band (C=O). The 1720 cm^{-1} band remain unchanged while the

position of amide I shift from 1698 to 1638 cm^{-1} which indicates the involvement of two of the amide carbonyl groups in coordination. That is, in the metal complex, the azomethine group is shifted to lower frequency region, which indicates that coordination takes place through the azomethine group. The 1768 and 1754 cm^{-1} C=O stretching band of ninhydrin are lost, along with the loss (decrease of the amide C=O group and imino C=N group) of the semicarbazone shows coordination through the two oxygens of amide group, and the two nitrogen's of the imino group of the ninhydrin-2,3-disemicarbazone with the metal ions.

Ninhydrin semicarbazone is expected to act as tetradentate one, the possible coordination sites being nitrogen's of the two imino groups, and oxygen's of the two amide group. A comparison of the IR spectra of ninhydrin semicarbazone and its nickel (II) complex imply that the ligand ninhydrin-2, 3-disemicarbazone is tetradentate in nature with two amide group oxygen and two imino-nitrogen as four coordination sites.

In conclusion the IR data clearly showed that in the complexes the ninhydrin-2,3-disemicarbazone behaves as a tetradentate ONNO donor ligand involving the two imino group nitrogen ,and two carbonyl oxygen of the amide group.

These studies indicate that the semicarbazone serve as tetradentate ligands, coordinating through the carbonyl-oxygen atoms of the two amide groups, and the two azomethine nitrogens-N atoms.

Table 2: Infrared spectral data of the metal complexes of ninhydrin semicarbazone(KBr pellets)

Compound	υ_{OH}	υ_{NH}	$\upsilon_{C=O}$ (ninhydrin)	$\upsilon_{C=O}$ (amideI)	$\upsilon_{C=N}$	δ_{NH} (amideII)	M-O	M-N	M-Cl
Ninhydrin			1768 1754 1720						
Ninhydrin-2,3-disemicarbazone		3318 3254 3065 2880	1720	1697	1653 1598	1681			
Nickel(II) Complex	3388	3389 3328	1720	1638	1642 1576	1681	450	480	552

3.2. 5 Electronic Spectra

Nickel (II)-NDSC Complex

The electronic spectra measurements were very useful for assigning the stereochemistry of the metal ion in the complex based on the position and number of d-d transition peaks. The electronic absorption spectra of ninhydrin-2, 3-disemicarbazone and its Ni (II) complex were recorded at room temperature using DMSO as the solvent. The nickel (II) complex shows bands at 24509 cm^{-1} due to $n\rightarrow\pi^*$ transition and also bands at 21551 cm^{-1} in the complex are due to $\pi\rightarrow\pi^*$ transition.

However, the expected d-d transition for the octahedral complex which consists of three bands one at 10 000 cm^{-1} due to $^3A_{2g}\rightarrow{}^3T_{2g}$, 16 000 cm^{-1} due to $^3A_{2g}\rightarrow{}^3T_{1g}$ (F), and 25 000 cm^{-1} for $^3A_{2g}\rightarrow{}^3T_{1g}$ (P) transitions have not been resolved under the experimental condition and due to the low solubility of the complex in many solvents. However, the

geometry of the complex has been concluded on the basis of analytical, conductance, IR and magnetic susceptibility data.

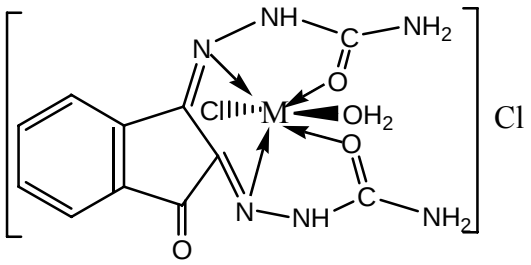


Figure11. Proposed Structure of Nickel (II) Complex of Ninhydrin-2, 3-disemicarbazone ([Ni-NDSC(H_2O)Cl]Cl)

4. Conclusions

On the basis of analytical, conductance, magnetic susceptibility and spectral studies, it can concluded that the ligand ninhydrin-2,3-disemicarbazone(NDSC),behaves as a neutral tetradentate ONNO donor ligand toward Ni(II) ion and form an octahedral complex with the formula [Ni-NDSC(H_2O)Cl]Cl.

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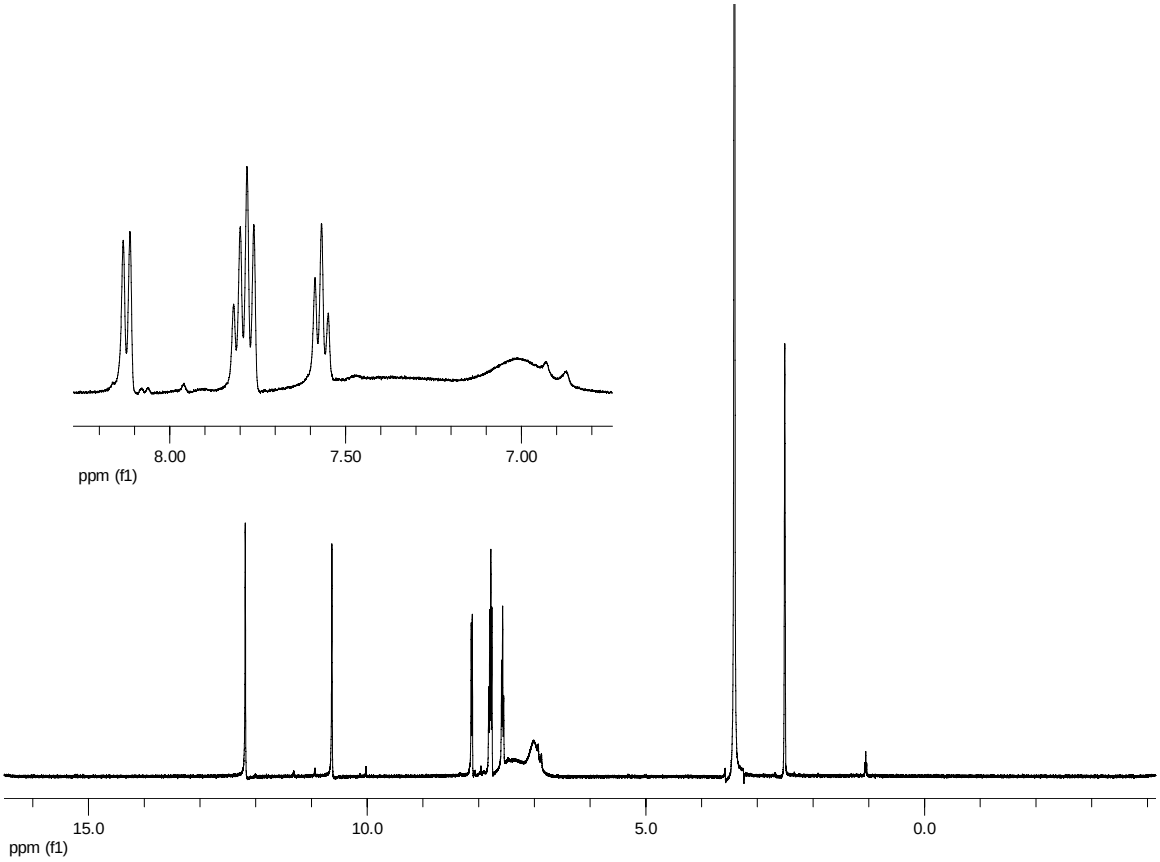
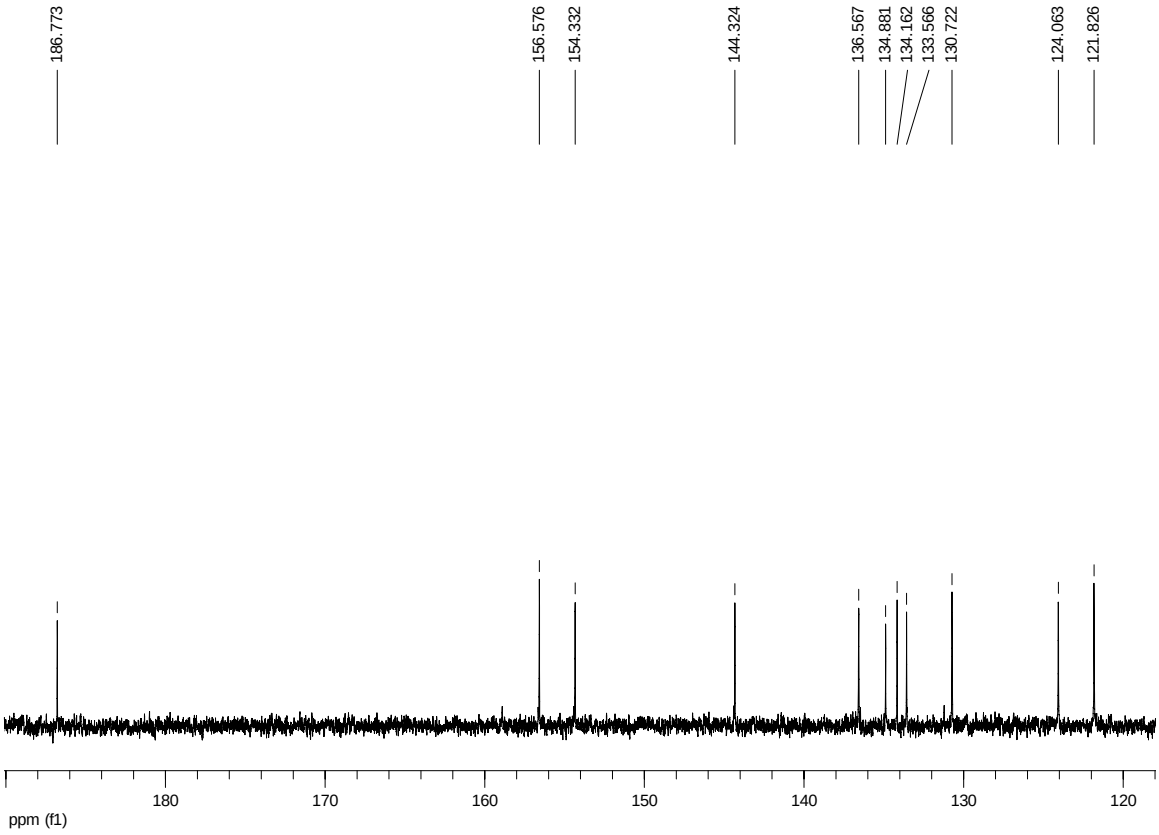
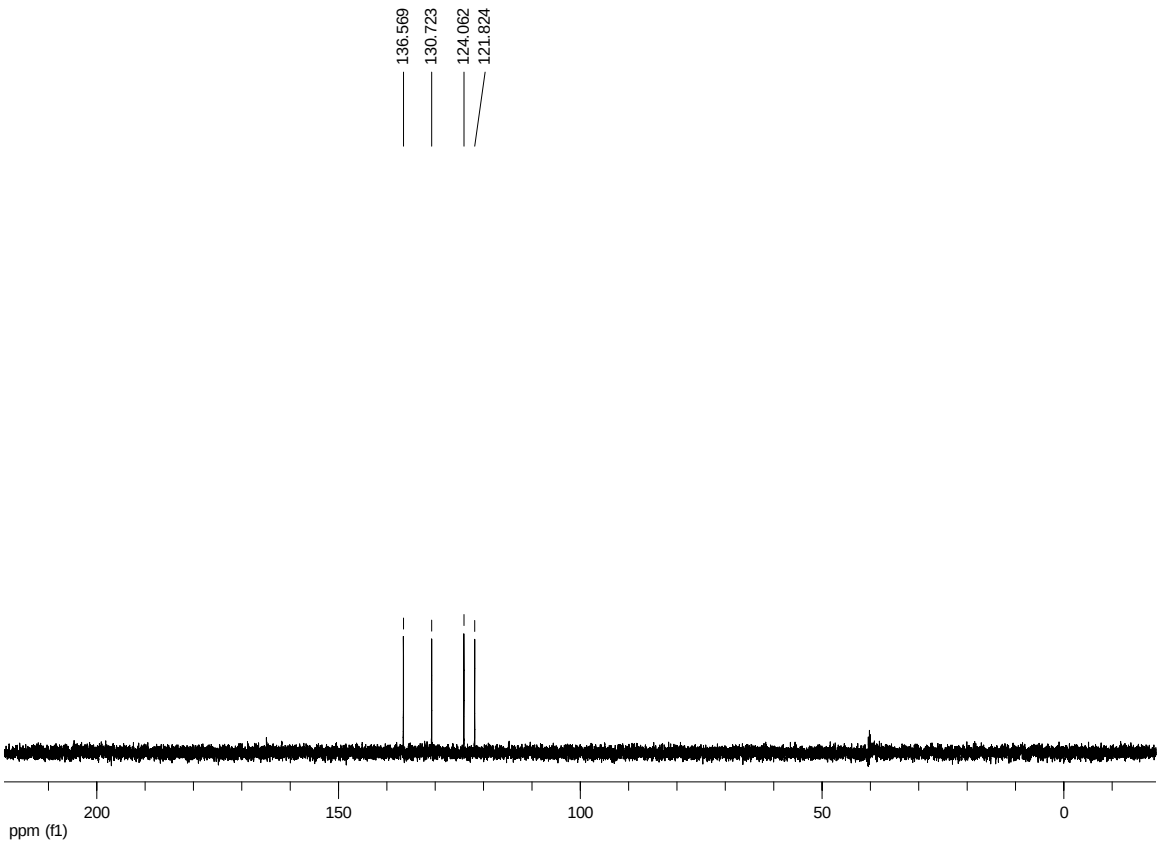
Appendix 1: ^{1}H-NMR of the ligand (ninhydrin-2, 3-semicarbazone



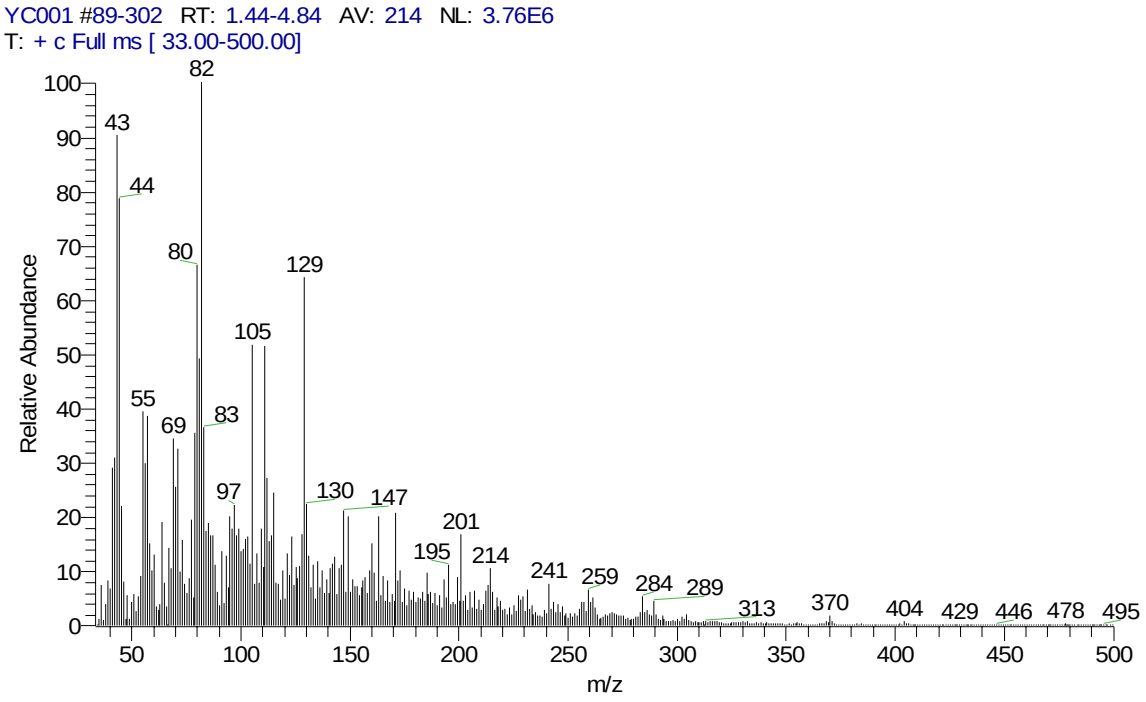
Appendix 2: ^{13}C-NMR of the ligand (ninhydrin-2, 3-disemicarbazone)



Appendix 3: DEPT ^{13}C-NMR of the ligand (ninhydrin-2, 3-disemicarbazone



Appendix 4: Mass spectrum of ligand



August 7, 2007

Declaration

I the undersigned confirm the results reported in this work were obtained by research carried out by me under the supervision of my Advisor in the Faculty of Science, Department of Chemistry, Addis Ababa University in the academic year 2006-2007. No part of this work shall be published in scientific journals or reported in the media or presented at a conference without the knowledge and consent of my Advisor, who is the principal scientist responsible for any publication. Furthermore if the work is published the institutional address given should be that of the Chemistry Department, AAU.

Name: _____ Signature: _____

This project work has been submitted for examination with my approval as a university advisor.

Advisor: _____

Signature: _____

Place and date of submission: School of Graduate Studies
Addis Ababa University