CHAPTER I

INTRODUCTION
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The development of the chemistry of binuclear complexes has been stimulated by a desire to synthesize model systems that may "mimic" the active sites of metallobiomolecules, may bind and activate small molecules, and may be used to investigate the mutual influence of two metal centers in terms of cooperative effect on the electronic, magnetic and redox properties of such systems. Consequent to this, the design and synthesis of ligands that would bind two metal ions, either the same or different, in the isovalent or heterovalent states have been the focus of extensive studies.

A large section of coordination chemistry is now being dominated by organic thioderivatives of hydrazine, viz., thiohydrazides, thiosemicarbazides, thiosemicarbazones and thiohydrazones. The coordination behaviour of both the ligands and metal chelates are influenced by the presence of a sulphur atom in the hydrazine moiety. Furthermore, these thio ligands may sometime provide metal chelates possessing very interesting structures.

The organic molecules having the general formula (1) are known to act as chelating ligands for transition metal ions [1]. Among these potential ligands, thiosemicarbazides and thiosemicarbazones have played a key role in synthesizing varieties of transition and nontransition metal complexes.
Metal complexes of sulphur-nitrogen chelating agents have attracted considerable attention because of their physico-chemical properties and pronounced biological activities [2-4]. Although a vast amount of research work on metal complexes of bi-, tri- and tetradentate sulphur-nitrogen chelating agents have been reported; pentadentate ligands and their metal complexes have been less well investigated.

Thiosermicarbazones are obtained by condensing thiosemicarbazide with suitable aldehyde or ketone compound. Thiosermicarbazones exist in the thioketo form in the solid state. In solution, however thiosemicarbazones can exist in the thioketo (2) and thioenol (3) form. These reagents act as good chelating agents and form complexes with various metal ions, bonding through thioketo sulphur atom and hydrazine nitrogen atom, although in few cases, they behave as monodentate ligands bonding through sulphur atom only [5].

\[
\begin{align*}
R - & \text{C=N} - N - C - \text{NH}_2 \\
& \text{S} \\
R' & - \text{C=N} - N - C - \text{NH}_2
\end{align*}
\]

Thiosermicarbazones find several applications [6] as sensitive and selective reagents in the detection and determination of various metal ions. These findings are based exclusively on the ability of these compounds to form highly coloured stable complexes with transition metal ion. Thiosermicarbazones are important because of their potentially beneficial biological activity [7]. The first compound to be examined for biological activity, 2-formylpyridine thiosemicarbazone, was shown to possess mild antileukemic activity against L-1210 tumour in mice [8, 9]. The biological function of these compounds is not clear, but presumably additional chemical insight into the nature of the compounds will contribute to the solution of the problem. Complexes where the donor atoms are nitrogen and sulphur may be expected to possess unusual electronic structures, since complexes with sulfur donor atoms have exhibited a
variety of oxidation states, and four-coordinated planar nitrogen complexes are known to have highly delocalized electronic structures.

The stereochemistries adopted by thiosemicarbazone ligands while interacting with transition metal ions depend essentially upon the presence of an additional coordination center in the ligand moiety and charge on the ligand, which, in turn, is influenced by the thione ⇔ thiol equilibrium. For example, benzaldehyde thiosemicarbazone is generally found to act as a neutral bidentate ligand, depending upon the pH of the synthetic medium, yielding complexes of the type [ML$_2$X$_2$] (where M = Co(II), Ni(II), Cu(II), or Fe(II); L = the ligand in thione form and X = the monoanionic ligand), whereas salicylaldehyde thiosemicarbazone is found to act as a tridentate uninegative ligand yielding compounds of type ML$_2$, which may be spin-free or spin-paired. As a result of the above considerations, the most common stereochemistries encountered in thiosemicarbazone complexes are octahedral and square planar. On rare occasions five-coordinate structures are also obtained, as in the cases of Co(II), Fe(II), Ni(II) and VO(IV) complexes and Fe(III) complex of 2-acetylpyridine thiosemicarbazone [10]. Since some of these five-coordinate complexes possess biological activity, e.g., antimalarial and antitumor activity [11], more studies of synthesis and structure are required for this class of complexes.

HSAB considerations dictate that the oxidation state of the metal affects the degree of its “softness” character, and this is found to be stronger for transition metals in low oxidation states. Thus the low-spin d$^8$ and d$^{10}$ ions exhibit higher stability constants with this class of sulfur ligands because of the formation of strong σ-bonds as well as d-$d^*$ bonds by donation of a pair of electrons to ligands.

Exhaustive literature survey has revealed that recently large amount of work has been done on transition metal complexes with thiosemicarbazones as revealed by a large number of publications on this subject. In this chapter, recent work on thiosemicarbazones with various metal ions is discussed.
There are some interesting reports on oxovanadium(IV) complexes of semicarbazone and thiosemicarbazone ligands. Jain et al. [12] have described dimeric vanadyl(IV) complexes of α-pyridyl thiosemicarbazone of the type \([L\text{VO}(\mu-X)_2\text{VOL}]X'_2\) (L = the ligand, X, X' = OH, Cl or CN). The vanadyl ions have square pyramidal geometry with oxygen at the apex, and with the bidentate ligand coordinating via the pyridine nitrogen and the thione sulfur atoms. The nonparticipation of the hydrazino nitrogen atom, however, implies that sterically it is unavailable for coordination. On the other hand, Pino and co-workers [13] have shown that it is the pyridine nitrogen atom that either moves in or out of coordination making the ligand α-pyridyl thiosemicarbazone either tridentate or bidentate, respectively. Furthermore, it has been pointed out [14] that such dimeric oxovanadium(IV) complexes have room-temperature magnetic moments well below 1.68-1.78 BM.

Recently Gerbeleu and co-workers [15] showed that alkylation of the thiocarbonyl sulfur of thiosemicarbazone derivatives induces not only complexation through the terminal amino group but also enough acidic character for it to function as a monoacidic ligand. In the presence of various metal salts e.g., Cu(II), Ni(II) and VO(IV) thiosemicarbazone ligands are capable of condensing at the terminal amino nitrogen atom through another aldehyde or ketone to yield quadridentate ligand of type (4). Using such template reactions as shown in (5), Gerbeleu and Zhovmir [16] claimed to have isolated thiosemicarbazone complexes without sulfur coordination.

\begin{center}
\includegraphics[width=0.5\textwidth]{diagram.png}
\end{center}
There is a solitary report [17] on the synthesis of Mn(III) complexes with some bidentate and tridentate Schiff base ligands, viz., 1-salicyl-4-benzyl-amido thiosemicarbazone and 1-phenyl-4-benzylamido thiosemicarbazone, respectively. The former yields an octahedral complex of the type \([ML_2]^+\), while the latter leads to pseudooctahedral compounds of the type \([ML_2(OH)_2]^+\). The structures are supported by IR data, electronic spectral data, and magnetic moments (4.54-4.87 BM).

\[
\begin{array}{c}
\text{L} \quad \text{M}^{2+} \quad \text{OH} \quad \text{L} \\
\text{O} \quad \text{CHO} \quad \text{H}_2\text{N.NH.CS.NH}_2 \\
\end{array}
\]

\[
\begin{array}{c}
\text{M}^{2+} \quad \text{OH} \quad \text{L} \\
\text{O} \quad \text{CHO} \quad \text{H}_2\text{N.NH.CS.NH}_2 \\
\end{array}
\]

\[
(M = \text{VO}^{2+}, \text{Ni}^{2+} \text{or} \text{Cu}^{2+}; R = \text{H}, \text{NH}_4, \text{Na} \text{or} \text{K})
\]

There are some interesting reports on the metal complexes of isothiosemicarbazones, where sulfur is not involved in coordination. For example, Co(II), Cr(III), Mn(III) and Fe(III) form a series of complexes with S-substituted N\(^1\), N\(^4\)-di(salicylidene) isothiosemicarbazone (H\(_2\)LRR') (L) [18-20]. The composition and magnetic properties of these complexes are found to be dependent on the groups R and R'.

Yampol’skaya et al. [21] have shown that the reaction of S-substituted salicylaldehyde isothiosemicarbazone (H\(_2\)L). (H\(_2\)L=o-HOC\(_6\)H\(_4\)CH=N=N=C(-SR)-NH\(_2\); R = CH\(_3\), C\(_2\)H\(_5\), CH\(_2\)-CH=CH\(_2\)) with zinc acetate afforded compounds of the type Zn\(_2\)(CH\(_3\)COO)_6(HL). The crystal structure analysis of the compound
with R = C₂H₅ indicate that the compound is a coordination polymer and is made up of dimers in which five-coordinate zinc ions are joined by three bridges—the phenol oxygen of HL⁻ and terdentate μ₃-bridging acetate groups.

Recently, the use of thiosemicarbazones for the rapid spectrophotometric determination of various metals has been reported, e.g., 4-salicyl-amido-1-diacetylmonoxime-3-thiosemicarbazone [22] and 2,4-dihydroxybenzophenone thiosemicarbazone [23] have been used for the determination of Pd(II) and Cu(II) with a very good limit of sensitivity range.

**Aim of Research**

Thiosemicarbazone, a versatile organic reagent, has a remarkable chelating ability, and possesses a wide spectrum of analytical applications, biological activity like antibacterial, antitumour etc. and has medicinal properties. Large number of thiosemicarbazone ligands have been derived by simply condensing aliphatic, aromatic or heterocyclic aldehydes or ketones with thiosemicarbazides. Many of the compounds possess a wide spectrum of medicinal properties. Molecular models essential for medicinal or biological activities must be ascertained by designing new molecular models of thiosemicarbazones. The strategies for modifying the thiosemicarbazone ligand are namely,
1) Changing the point of attachment of the thiosemicarbazone moiety in the parent aldehyde or ketone
2) Substitution on the terminal \( ^{14} \)N position
3) Variation of parent aldehyde or ketone.

Although the stereochemical investigation of metal complexes of a variety of thiosemicarbazides and thiosemicarbazones have been the subject of intensive research, those of \( ^{14} \)N substituted thiosemicarbazones have received little attention.

An important development in the field of coordination chemistry has been the design and synthesis of ligands capable of binding two or more metal ions. Much of the interest in multimetal complexes originates from their potential as models for metalloproteins. In particular, the binuclear metal complexes are of interest because, it is known or believed that many of the biological functions performed by certain metalloproteins are consequences of the metal centers occurring in pairs [24-34].

These facts created interest in us to design and synthesize the new compartmental ligands capable of binding two metal ions. The ligands 2,6-diformyl-p-cresol bis(phenyl-thiosemicarbazone) and substituted thiosemicarbazones (7) were prepared. 

\[ 
\text{CH}_3 \\
\text{HN} \\
\text{N} \\
\text{OH} \\
\text{HN} \\
\text{N} \\
\text{NH} \\
\text{S} = \text{C} - \text{N} \\
\text{R} \\
\text{7} \\
\text{R} \\
\]

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The newly synthesized thiosemicarbazones have three interesting features,

1] The ligands contain SNONS donor sequences possessing five potential coordinating sites.

2] The ligand can bind two metal ions leading to oxobridged binuclear complex.

3] The ligand can behave as monobasic, dibasic or tribasic depending on reaction condition and nature of metal ions.

Keeping in view, the present trends in the field of modern coordination chemistry, a modest attempt has been made to synthesize and characterize VO(IV), Mn(III) and Zn(II) complexes using the above ligands and to test the biological activities of these compounds.
REFERENCES