

Role of Thiosemicarbazide and its Derivatives as N,S Donor Ligand

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Date of Submission: 7th March, 2016

Date of Acceptance: 30th March, 2016

Abstract

Bidentate ligands with nitrogen and sulphur as potential site for coordination have vast effect on coordination chemistry. Nitrogen as having 'border line' property can coordinate with both hard and soft transition metal ions whereas sulphur prefers to bind with soft metal ions. So thiosemicarbazides and their derivatives, having three nitrogen centres and one sulphur donor centre, would bind with all most all metal ions. Several research works have been carried out using thiosemicarbazides and their derivative as ligand to study the mode of coordination of the ligand and to study geometry, spectroscopic behavior, magnetic properties and antibacterial and antitumor activities of the prepared complexes with various transition metals. The present article is to review and summarize such major research works in this area.

Key words: Thiosemicarbazide, Metal complexes, N S donor ligand, Antibacterial activity.

1. Introduction

Ligands having nitrogen as site for coordination has versatile characteristics. It can be considered as a 'border line' base in the hard-soft concept. As it is of smaller size and high electron density, can coordinate with 'hard acid' metal ions e.g. beryllium(II), calcium(II), chromium(III), iron(III) etc. Besides that the lone pair of electron on nitrogen has considerable extent of polarisability. On the other hand the transition metal ions with nearly filled d- orbital viz. nickel(II), palladium(II), platinum(II) etc. have high deformability. These facts lead to greater interpenetration of orbitals of ligand and metal ions. As a result nitrogen also has high affinity towards 'soft' transition metal ions. So it can be concluded that nitrogen can coordinate with metal ion of both class 'a' and class 'b'.

Therefore it is evident that ligand with donor site nitrogen would prefer hard or border line metal ions. Again as sulphur contains low lying vacant 3d orbital of suitable energy, metal to ligand back donation is possible from transition metal ions having filled or almost filled d-orbital to sulphur containing ligands. That is why sulphur as donor atom would prefer bonding to 'soft' or class 'b' metal ions. So a bidentate or multidentate ligand containing nitrogen and sulphur would bind to almost all transition metal ions. Therefore such ligands would have a versatile coordinating behaviour to transition metals¹.

From above discussion it is clear that ligands containing both sulphur and nitrogen as possible site for coordination are of high interest and study worthy. Another point of interest for

sulphur containing ligand is that sulphur can act as bridging ligand and polymeric complex may be formed through bridging by such sulphur center.

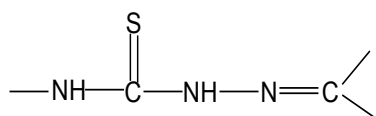
2. Thiosemicarbazides and their derivatives as ligand

Thiosemicarbazide (tscH) can have following two structures:-

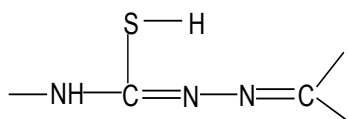


So it can act as neutral ligand as per first structure or it can lose the thiol proton to behave as mononegative bidentate ligand.

Structure of thiosemicarbazone can be represented as:-



In solution thiosemicarbazone probably also exists in thiol form along with the above mentioned thione form,



So they can also behave both like neutral bidentate and charged bidentate ligand depending upon preparative conditions. Furthermore it is interesting that it is possible to isolate complexes having both tautomeric forms of the ligand.

A neutral chelate of cobalt with molecular formula $[\text{Co}(\text{Hnqtsc})(\text{nqtsc})]\cdot\text{H}_2\text{O}^2$ had been prepared [H_2nqtsc = 2-hydroxy-1,4-naphthaquinone-1-thiosemicarbazone] and according to magnetic and spectral data the compound appeared to contain both tautomers of the ligand.

Thiosemicarbazides and thiosemicarbazones are of great biological importance due to their antifungal, antibacterial³ and antitumor⁴ action. 1-Acyl-4-aryl-thiosemicarbazides⁵ showed tuberculostatic activity and different transition metal complexes with these ligands were prepared to exploit such biological activities.

Thiosemicarbazides, thiosemicarbazones and their corresponding transition metal complexes had been studied in detail and reviewed adequately by Livingstone⁶, Akbar ali & Livingstone⁷, Campbell⁸ and Subhas Padhye & G.B.Kauffman². The present discussion will be confined about some notable and representative studies which have been reported since 1980 onwards.

Copper(II), cobalt(II), nickel(II) and mercury(II) complexes of 1,4-diphenyl thiosemicarbazide (dptsc) had been reported⁹. The composition of these complexes were found as $[\text{Cu}(\text{Hdptsc})\text{X}\cdot\text{H}_2\text{O}] \cdot n\text{H}_2\text{O}$ where X= Cl, Br or CH_3COO ; n=0 or 1; $[\text{M}((\text{Hdptsc})_2 \cdot y\text{H}_2\text{O})]$ where M= Co^{II} , or Ni^{II} , y=0 or 1; $[\text{Hg}(\text{dptsc})\text{Cl}_2] \cdot 2\text{H}_2\text{O}$ and $[\text{Cu}(\text{dptsc})_2\cdot\text{SO}_4] \cdot \text{H}_2\text{O}$. The stereochemistry of the complexes were studied with the help of magnetic and electronic measurements. The anomalous

magnetic moments observed had been explained. Infrared spectral studies had been used to determine the bonding sites in the complexes.

The preparation and properties of a series of transition metal complexes $M(\text{spts}) n\text{H}_2\text{O}$ [$M=\text{Co}(\text{II}), \text{Ni}(\text{II}), \text{Cu}(\text{II}), \text{Zn}(\text{II})$ and $\text{Cd}(\text{II})$, spts is the deprotonated form of 1-succinyl bis(4-phenyl-thiosemicarbazide) i.e H_2spts and $n=0-2$] were reported¹⁰. Analytical, spectral (electronic, infrared and nmr), conductometric and magnetic data showed that the cobalt(II) and copper(II) complexes had tetrahedral and octahedral structures respectively whereas the nickel(II) complex had a mixed stereochemistry of tetrahedral and square planar isomers. The ligand behaved as a dibasic quadridentate {NSSN} donor. The stoichiometry and stability constants of cobalt(II), nickel(II) and copper(II) complexes were determined spectrophotometrically. The electrical properties were also investigated and activation energies were calculated. The values obtained for cobalt(II), nickel(II) and copper(II) complexes were similar to that of narrow band semiconductor materials.

Ligational, corrosion inhibition and antimicrobial properties of 4-phenyl-1-benzenesulfonyl-3-thiosemicarbazide [pbst] with complexes of the type $[\text{Co}(\text{pbst})(\text{OAc})(\text{H}_2\text{O})_2]$, $[\text{Co}(\text{pbst})_2\text{H}_2\text{O}]$, $[\text{Ni}(\text{pbst})(\text{OAc})]2\text{H}_2\text{O}$, $M(\text{pbst})_2$ where $M = \text{nickel}$ and zinc ; $[\text{Cu}(\text{pbst})(\text{H}_2\text{O})_2]$ were described¹¹. The complexes were characterized by elemental analyses, molar conductivity measurements, NMR, infrared and reflectance spectral studies and by magnetic moment measurements. The infrared spectra showed that the ligand behaved as mononegative, bidentate, coordinating via NH and C-S groups. Thioenolisation had been confirmed by pH titration of Hpbst and its metal complexes against 0.01 M NaOH solution. The antibacterial and antifungal activities of the ligand and corresponding complexes were studied. It was observed that the ligand possessed greater anti microbial activities than its complexes. The corrosion inhibitory property was studied on aluminium in CCl_3COOH using Hpbst by weight loss and corrosion potential measurements. It was found that the effectiveness depends upon its concentration.

Chelating behavior of substituted 1-benzoyl-4-phenyl thiosemicarbazide¹² were explored by complex formation of the ligand(LH) with cobalt, nickel, copper, zinc and cadmium. The reaction products were studied by elemental analyses, molar conductivity, magnetic susceptibility measurements, reflectance and infrared spectral studies. The infrared spectra showed that LH coordinated via nitrogen and sulphur or via nitrogen and oxygen. The $\text{ML}_2, n\text{H}_2\text{O}$ ($M=\text{Cu}, \text{Ni}; n=0-2$) complexes had square planar stereochemistry where as CoL_2 had octahedral and tetrahedral structures. The influence of substitution in the benzene ring on the stereochemistry was studied.

The ligand 1,4-dibenzoyl-3-thiosemicarbazide (dbtsc)¹³ formed complexes of the type $[\text{M}(\text{Hdbtsc})(\text{SCN})]$ ($M=\text{Mn}(\text{II}), \text{Co}(\text{II})$ and $\text{Zn}(\text{II})$), $[\text{M}(\text{Hdbtsc})(\text{SCN})(\text{H}_2\text{O})]$ ($M=\text{Ni}(\text{II}), \text{Cu}(\text{II})$) $[\text{M}(\text{Hdbtsc})\text{Cl}]$ ($M=\text{Co}(\text{II}), \text{Ni}(\text{II}), \text{Cu}(\text{II})$ and $\text{Zn}(\text{II})$) $[\text{Mn}(\text{dbtsc})\text{Cl}_2]$. They had been characterized by elemental analyses, magnetic susceptibility measurements, uv-vis, infra red, ^1H and ^{13}C NMR and FAB mass spectral data. Room temperature ESR spectra of the manganese(II) and copper(II) complexes showed characteristics of tetrahedral and square planar complexes respectively. The ligand and its soluble complexes were screened against several bacteria, fungi and tumour cell lines. It was found that all thiocyanato and chloro complexes inhibited the growth of *Pseudomonas flauracences*. Copper complexes exhibited excellent antifungal activity against *Aspergillus flavus* and *Aspergillus niger*. The ligand exhibited better antitumour activity than copper(II) complexes against Jurket and Daltons *Lymphoma cell lines*.

Complexes of N-substituted thiosemicarbazide with ruthenium(II)-2,2' bipyridyl were prepared and characterized by infrared, uv-vis and ^1H NMR spectroscopy in addition to their elemental analyses¹⁴.

The complexes were tested for anti cancer activity against *Ehrlich Ascites Carcinoma*. Their effects on the hematological profile of the tumour hosts had also been studied. The complexes were found to possess antibacterial activity against both Gram +ve and Gram –ve stains of bacteria.

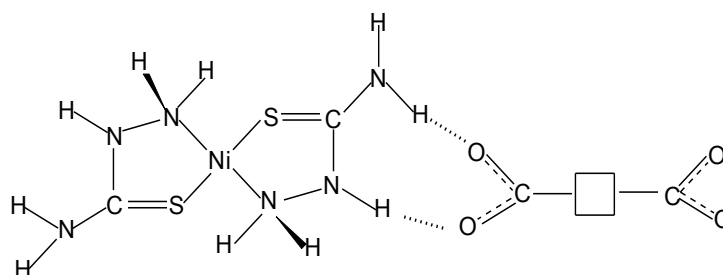
Bis(thiosemicarbazide) nickel(II) dicarboxylate and the substitution products with different hydrogen bonding groups in the complex had been used for structural manipulation to explore the supramolecular structures of bis(thiosemicarbazidato) nickel(II) i.e. neutral complexes¹⁵. The carboxylate group can act as a base and a neutral complex can be generated. The crystal structures of different substituted products showed that only thioamide hydrogen atom was responsible for hydrogen bond formation.

Recently a new class of platinum blues have been isolated and characterized¹⁶. This blue complexes of platinum(II) have the composition of PtL_2 where LH= 1-phenyl thiosemicarbazide, 4-phenyl thiosemicarbazide, 1,4-diphenyl thiosemicarbazide and 4-(2-pyridyl)- thiosemicarbazide. Electronic spectra of all the complexes showed a metal to ligand charge transfer band in the 650 to 750 nm region in different solvents. Infrared spectra indicated bonding through sulphur and nitrogen while ¹H NMR spectra suggested bonding through hydrazinic nitrogen atom.

Thiosemicarbazide reacts with butane 2,3-dione oxime to give a schiff base product via the selective reaction of hydrazine nitrogen atom. Ligating property of the ligand with palladium(II) was investigated¹⁷. It was found that palladium(II) was bound in a trimodal, *cis* arrangement to oxime nitrogen, hydrazine nitrogen and sulphur atom. Crystal structure revealed that oxime thiosemicarbazide had reacted with $PdCl_2(PhCN)_2$ presumably via the elimination of HCl, in the thiol rather than thione form. The hydrogen bonding interaction of the oxime hydrogen that caused the ligand to be a dimer in the solid state was lost on complexation with palladium(II) giving the complex a monomeric structure.

$Pd(DMSO)_2Cl_2$ was taken as starting material to prepare complexes of the composition PdL_2Cl_2 where L is nitrogen, sulphur donor ligands derived from S-methyl dithio carbazate, S-benzyl dithiocarbazate, and thiosemicarbazide¹⁸. The complexes had been characterized by elemental analyses, infrared, electronic spectra, nmr and thermogravimetry. Based on the above experiments the ligands were found to coordinate via thione sulphur and azomethine nitrogen atom. The antiamoebic action of the complexes was also evaluated against *Entamoeba histolytica* (strain HK-9).

Red green crystals of $[Ni(tscH)_2]^{+2}[tere]^{-2}$ were isolated by mixing equimolar aqueous solution of $[Ni(tscH)_2]NO_3$ and disodium salt of terephthalic acid¹⁹. It was found that the ligand molecules had been coordinated by thione sulphur and terminal NH_2 group of the ligand. The complex formed polymeric chain by hydrogen bond through the dicarboxylate anion as :-



Redox behavior of bis(2,2'-bipy)-ruthenium(II) complexes containing thiosemicarbazide ligands were reported²⁰. The prepared complexes were of two types. In $[\text{Ru}(\text{bipy})_2\{\text{N-S}\}]^{+2}$ type of complexes the 4-aryl thiosemicarbazide ligand chelated in the keto form through hydrazinic nitrogen and thione sulphur. On the other hand in $[\text{Ru}(\text{bipy})_2\{\text{N-S}\}]^{+1}$, the thiosemicarbazide moiety remained chelated to ruthenium(II) through hydrazinic nitrogen and deprotonated thiolato sulphur atom.

Kinetics of interaction of thiosemicarbazide with $\text{cis-}[\text{Ru}(\text{bipy})_2(\text{H}_2\text{O})_2]^{+2}$ was studied²¹ spectrophotometrically at pH 4.8. It was concluded that the reaction proceeded via outer sphere association complex formation followed by two slow consecutive steps. The first step was conversion of the complex into inner sphere complex whereas second step was the entrance of thiosemicarbazide molecule in the coordination zone of the ruthenium(II). In each step an aqua ligand was displaced. The equilibrium constant for outer sphere complex formation had been evaluated together with rate constant.

Bis(1,10 phenanthroline)ruthenium(II) or Bis(2,2' bipy)ruthenium(II) complexes with benzoin thiosemicarbazide ligand was tested *in-vivo* for anticancer activity against transplantable murine tumour cell line, *Ehrlich's Ascitic Carcinoma* (EAC)²². It was observed that the complexes increased life span of the EAC-bearing mice, decreased their tumour size and viable ascitic cell count. Clinical tests showed improved Hb, RBC and WBC counts. It was also observed that ruthenium(II) complexes protected red blood cells from 2,2' azo-bis(2 methyl propionamide) dihydrochloride (AAPH) induced hemolysis. Inhibitory effect was found to be dose dependent at a concentration range of 20-120 $\mu\text{g/ml}$.

Reaction of $\text{Ru}(\text{bipy})\text{Cl}_4$ with different thiosemicarbazides(L) in methanol produced $\text{Ru}(\text{L})(\text{bipy})\text{Cl}_2$ type of complex where the ligand had been coordinated in the thione form²³. The complexes were characterized by elemental analyses, magnetic moment measurement and spectroscopic techniques. The redox behavior was studied by cyclic voltammetry.

Nickel(II) and palladium(II) were found to form complexes with thiosemicarbazide(tsc), 1-phenyl thiosemicarbazide(1-ptsc) and 4-phenyl thiosemicarbazide(4-ptsc) with composition MLCl_2 and ML_2Cl_2 . Electronic spectra of them suggested distorted octahedral symmetry for $\text{Ni}(\text{tsc})\text{Cl}_2$, $\text{Ni}(\text{tsc})_2\text{Cl}_2$, $\text{Ni}(4\text{-ptsc})\text{Cl}_2$, $\text{Ni}(4\text{-ptsc})_2\text{Cl}_2$ whereas the complex $\text{Ni}(1\text{-ptsc})_2\text{Cl}_2$ was weakly paramagnetic suggesting square planar geometry²⁴.

Structure of $\text{Ni}(\text{CN})_2(\text{tsc})\cdot\text{H}_2\text{O}$ was elucidated by X-Ray diffraction study²⁵. It was found that the compound has square planar geometry with two adjacent cyano carbon atoms. Nitrogen and sulphur atoms from thiosemicarbazide ligand were linked to the nickel(II). Ni-S distance was 2.169 Å and that for Ni-N was 1.923 Å. Water molecule did not enter the inner coordination sphere, but was hydrogen bonded to the ligand units of the complex and seemed to play a very important role in the crystal structure.

Crystal structure²⁶ of diaqua bis (1,1,4-trimethyl thiosemicarbazide) nickel(II) dinitrate revealed a distorted octahedral geometry around nickel atom. The two water molecules occupied the axial positions of that geometry. Thiosemicarbazide NH group and water remained in hydrogen bonded form with nitrate anion.

Reaction of aromatic thiosemicarbazides with palladium(II) cation produced complexes with composition $\text{Pd}(\text{H}_2\text{L})\text{Cl}_2$, $\text{Pd}(\text{HL})_2$ and $\text{Pd}(\text{L})$. Infrared spectra showed that the ligand behaved as

neutral, mononegative or binegative species. It was found that the ligand coordinated in a bidentate or bridging tetra dentate way²⁷.

Ruthenium and palladium complexes of 1-phenylacetyl -4- phenyl-3- thiosemicarbazide ($H_2p_1p_2$) and 1-phenoxyacetyl -4- phenyl - 3 -thiosemicarbazide ($H_2p_xp_2$) were characterized by infrared, electronic and 1H nmr spectra, conductometric titration and thermal analyses²⁸. Composition of the complexes were found to be $Ru(HL)_2(H_2O)_2$ and $Pd(Hp_1p_2)(bipy)^+$. The Ru complexes were efficient catalyst for oxidation of primary alcohol to aldehyde and acid, secondary alcohol to ketone and aryl halide to aldehydes and acids in presence of $NaIO_4$ as cooxidant.

Complexes of thiophene-2-carboxaldehyde thiosemicarbazone with ruthenium(III), rhodium(III), iridium(III) and platinum(IV) were octahedral in structure²⁹. Analytical data suggested formation of three types of complex $M(HL)_2X_n$, ML_3 and $[PtL_3]Cl$ ($X = Cl, Br$ or $1/2SO_4$, $n = 3$ for Ru, Rh and Ir, $n = 4$ for Pt). Complexes of rhodium(III), platinum(IV) and iridium(III) were diamagnetic whereas that of ruthenium had magnetic moment in the range of 1.75-1.80 BM. at room temperature. Molar conductance measurements in 10^{-3} M MeOH solution at $25^\circ C$ showed that the complexes of general formula $M(HL)_2X_3$, $M(HL)_2X_4$ and ML_3 were 1:1, 1:2 and non electrolytes respectively. Molar conductivity and spectroscopic (uv and infrared) data suggested that the compounds had octahedral structure.

2-Acetyl pyridine thiosemicarbazone can act as a tridentate ligand³⁰. Its ligating property was explored for palladium(II) complexes with neutral(LH) and deprotonated ligand(L). $[Pd(HL)_2]X_2$ and PdL_2 (where $X = Cl, Br$) type of complexes were studied by elemental analyses, conductivity measurement and spectroscopic studies. Crystal structure of $PdLBr$ showed that the complex had a square planar geometry with NNS donor sites, and a planar tricyclic ligating system had been formed. The protonation constants of the ligand were also determined spectrophotometrically.

Interestingly thiosemicarbazones could also behave as bridging ligand. The X-ray crystal structure of palladium(II) complex of 2-hydroxyacetophenone N(4)-ethylthiosemicarbazone showed it to be an approximately symmetric, triangular, trinuclear complex with bridging thiosemicarbazonato sulphur atoms³¹. The three bridging ligands had same formal charge and bonding pattern. The species could be formed from the monomer on dissolution in dimethyl formamide or directly from $LiPdCl_4$ and thiosemicarbazone in methanol ammonia solution.

Similarly 2-hydroxy-4-methoxyacetophenone N(4)-dimethylthiosemicarbazone ($4MeOAp_4Me_2$) also formed triangular trinuclear complex with palladium(II). The X-ray crystallographic structure determination of $[Pd(4MeOAp_4Me_2)]_3.DMSO$ showed it to contain a chair type hexagon of alternating palladium and sulphur atoms with the shape of a molecular bowl³².

A series of ruthenium(II) complexes of the NNS donor ligands, methyl 2-pyridyl ketone 4-(4-tolyl)thiosemicarbazone (HL) had been synthesized³³ using $RuCl_3.xH_2O$ and $Ru(PPh_3)_3Cl_2$. Chemical and electrochemical studies had been carried out. Structures of two of the prepared complexes were confirmed by single crystal X-Ray diffraction. The thione form of the ligand was coordinated to the ruthenium atom through the pyridine nitrogen, imine nitrogen and the thione sulphur atom. The existence of a new unstable ligand methyl(2-pyridyl)-methyleneimine (mpi) was confirmed from crystal structure study. The complex $[Ru(HL)(PPh_3)(mpi)]Cl_2$ produced through reductive cleavage of the hydrazinic N-N bond of the thiosemicarbazone ligand.

Nickel(II), copper(I) and copper(II) complexes of thiosemicarbazone derived from 3- and 4-formyl pyridine and from 3- and 4- acetyl pyridine had been characterized³⁴ on the basis of micro analyses, molar conductivity, magnetic moment measurements and infrared, nmr spectral data. 3- and 4- formyl pyridine coordinated nickel(II) as M:L= 1:2 with one protonated and one deprotonated ligand with composition $[M(LH)L]ClO_4^-$. Tetrahedral geometry was suggested with the first ligand while the second one formed square planar structure. Octahedral nickel(II) complexes of composition $[Ni(LH)_2L]ClO_4^-$ were formed with the ligands 3- and 4- acetyl pyridine thiosemicarbazone. Here also two ligands were neutral while the third was anionic.

Neutral 2-acetyl pyridine-(2-methyl thiosemicarbazone), 2-acetyl pyridine-(4-methyl thiosemicarbazone), 2-acetyl pyridine-(4-phenyl thiosemicarbazone) were used to prepare complexes of the type $M(HL)_2Cl_2$ [M= palladium and platinum] and $M(HL)_2Cl_3$ [M= ruthenium, rhodium and Iridium]. It was found for palladium(II) and platinum(II) the ligands behaved as neutral bidentate, whereas for ruthenium(III), rhodium(III) and iridium(III) they were neutral tridentate. These results were based on elemental analyses, molar conductivity, magnetic moment measurements and infrared, uv-vis, raman and ¹H, ¹³C nmr spectral data³⁵. Various ligand field and nephelauxetic parameters had also been calculated. The ligands and their platinum metal-group complexes were found to exhibit potent cytotoxic activity against *Ehrlich ascites* tumour cells *in vitro*.

Ten mixed ligand thiosemicarbazone complexes of composition $[M(bipy)_2(bztsc-R)]ClO_4$ [M=Ru, Os, bipy = 2,2' bipyridine, Hbztsc-R= benzaldehyde thiosemicarbazone] and two complexes of composition $[M(bipy)_2(actsc)]ClO_4$ where Hactsc= acetone thiosemicarbazone were shown to be diamagnetic³⁶. They all showed several intense metal to ligand charge transfer (MLCT) band in visible region of electronic spectra in acetonitrile solvent. Structure of $[Ru(bipy)_2(bztsc-NO_2)]ClO_4$ and $[Ru(bipy)_2(actsc)]ClO_4$ had been determined by X-ray crystallography. Benzaldehyde thiosemicarbazone exist in thione form with phenyl group *trans* to hydrazinic nitrogen atom. It was found to coordinate to the metal through hydrazinic nitrogen and sulphur forming four membered chelate rings. On the other hand 'actsc' coordinated through imine nitrogen and sulphur forming five membered chelate rings. The difference in coordination modes of two types of ligands appeared to result from the difference in steric bulk. In acetonitrile solution they all showed reversible M(II)-M(III) oxidation in the range 0.18 v and 0.58 v vs SCE followed by irreversible oxidation in the range 1.11 v to 1.60 v vs SCE. Two successive one electron reductions of the coordinated bipyridine were also observed in the range -1.53 volt to -1.96 volt vs SCE.

Isatin-β-thiosemicarbazone(H₂L) complexes of manganese, iron, cobalt, nickel, copper and zinc were studied³⁷. X-ray structure of $[Ni(HL)_2]EtOH$ and $[Ni(HL)_2].2DMF$ revealed distorted octahedral coordination with monodeprotonated ligand that behaved as ONS terdentate. Biological studies carried out *in vitro* on human leukaemic cell lines U937. The result showed that the free ligand and copper(II) complex were more active in the inhibition of cell proliferation than the nickel(II) complex. No compound was able to induce apoptosis.

Reaction of ring substituted 4-phenyl thiosemicarbazones of salicylaldehyde and o-hydroxyacetophenone(LH) with $[Ru(PPh_3)_3]Cl_2$ in refluxing MeOH produced $[Ru(PPh_3)_2(LH)]Cl$ where the ligand acted as monoanionic tridentate ONS donor. The ligands coordinated to ruthenium(II) through deprotonated phenolic oxygen, thione sulphur and azomethine nitrogen³⁸.

Thiosemicarbazone derivative of vitamin K₃ were synthesized to form complexes with manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II)³⁹. The complexes were studied by uv-visible, infrared spectroscopy and thermal analyses. They exhibited strong inhibitory action against

Gram(+) *staphylococcus aureus* and Gram(-) *Hay bacillus*, *E.Coli*. The antibacterial activity of the complexes was stronger than that of the ligand.

Reaction of 4-formylantipyrine with thiosemicarbazide, N(3)-methyl thiosemicarbazide and N(3)-ethyl thiosemicarbazide produced the expected thiosemicarbazones. The reactions of them with K_2PdCl_4 produced $Pd\{N-S\}_2$ complexes with coordination through the imine nitrogen and thiolate sulphur of anionic thiosemicarbazone moiety⁴⁰. Such results were based on spectral studies i.e. infrared, uv-vis, 1H and ^{13}C nmr spectroscopy and electrochemical techniques. Crystal structure of one of the complexes showed *trans* arrangement of the two bidentate ligands.

Mixed ligand complexes of thiosemicarbazone derived from thiophen-2-carboxaldehyde and cyclooctadiene with ruthenium(II)⁴¹ showed significant antiamebic property and they were more effective than metronidazole against HK-9 strain of *Entamoeba histolytica* *in vitro*. Similar thiosemicarbazone complexes of ruthenium(II) and palladium(II) were prepared where thiosemicarbazone derived from 5-nitrophen-2-carboxaldehyde and cycloalkyl amino thiocarbonyl hydrazines were used as ligands. According to spectral studies the ligands behaved as bidentate, coordinating through thionic sulphur atom and azomethine nitrogen. Microdilution method was used for assessment of antiamebic activity against HK-9 strain of *Entamoeba histolytica*. Enhancement of such activity was resulted by introducing palladium(II) and ruthenium(II) in thiosemicarbazone moiety⁴².

Recently two complexes of dioxovanadium(V) with salicylaldehyde thiosemicarbazone (SALTSC), of the coordination formulas $[VO_2(SALTSC-H)] \cdot H_2O$ (1) and $NH_4[VO_2(SALTSC-2H)]$ (2), were synthesized and characterized by elemental analysis, conductometric measurements, IR and UV-Vis spectroscopy and X-ray analysis. The complexes were obtained in the reaction of an aqueous ammoniacal solution of NH_4VO_3 and SALTSC. The results of the characterization showed that SALTSC was coordinated in the usual ONS tridentate mode as monoanion in complex 1 and dianion in complex 2. In both complexes, the vanadium atom was present in a deformed square-pyramidal environment and being slightly shifted towards the apical oxo-ligand ($\approx 0.52 \text{ \AA}$)⁴³.

The reaction of 1:1 mixture of 4-R-benzaldehyde thiosemicarbazone [denoted in general as **HL-R**; where H stands for the dissociable acidic proton and R (R = OCH₃, CH₃, H, Cl and NO₂) for the substituent] and 1-nitroso-2-naphthol (abbreviated as **Hnn**), with an equivalent quantity of $Na_2[PdCl_4]$ in ethanolic medium resulted into formation of mixed-ligand complexes of the type $[Pd(L-R)(nn)]$. A similar reaction of a mixture of **HL-R** and quinolin-8-ol (**Hq**) with $Na_2[PdCl_4]$ produced another family of mixed-ligand complexes of the type $[Pd(L-R)(q)]$. Crystal structures of $[Pd(L-Cl)(nn)]$, $[Pd(L-CH_3)(q)]$ and $[Pd(L-Cl)(q)]$ had been studied. In all the complexes the thiosemicarbazones found to be coordinated to the metal center, *via* dissociation of the acidic proton, as monoanionic bidentate N,S-donors having five-membered chelate rings. In the $[Pd(L-R)(nn)]$ complexes, the 1-nitroso-2-naphtholate anion was coordinated as a N,O-donor forming a five-membered chelate ring. Similarly in the $[Pd(L-R)(q)]$ complexes, the quinolin-8-olate anion was bound to the metal center in the N,O-mode forming a five-membered chelate ring. All the $[Pd(L-R)(nn)]$ and $[Pd(L-R)(q)]$ complexes shown characteristic 1H NMR signals, and in dichloromethane solution they all exhibited intense absorptions in the visible and ultraviolet regions. Catalytic activities of the $[Pd(L-R)(nn)]$ and $[Pd(L-R)(q)]$ complexes had also been studied towards some C-C and C-N coupling reactions, where both were found to show notable catalytic efficiency⁴⁴.

3. Conclusion

From the above discussion it is clear that thiosemicarbazides, thiosemicarbazones and their derivatives can coordinate with metal ions in various ways and their complexes have enhanced antibacterial and antifungal activities compared to that of free ligands. Some of the complexes also reported to have interesting catalytic activity.

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