Synthesis and Reactivity of Indium(III) and Thallium(I) Imine Complexes

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ABSTRACT

The coordination behaviour of thiosemicarbazone (L^1H) and semicarbazone (L^2H) ligands having the donor systems N, O or N, S towards indium(III) and thallium(I) has been studied. The unimolar, bimolar and trimolar reactions of indium isopropoxide and unimolar reactions of TlCl with monobasic bidentate ligands result in the formation of coloured solids, which have been characterized by elemental analysis and molecular weight determinations. The UV, IR and ^1H NMR spectral studies of indium(III) complexes indicated pentacoordinated structure for 1:1 complex, hexacoordinated for 1:2 and 1:3 complexes. Thallium(I) complexes exhibited bicoordinated geometries. Both the ligands and their complexes have been screened for their fungicidal and bactericidal activity.

INTRODUCTION

Non-transition metal compounds are currently attracting attention because of their importance as synthetic intermediates /1/. Non-transition metal chelates with imines are a source of important pharmacodynamics significance. It has been observed that chelation apparently plays a definite role in the enhanced activity /2/ Thiosemicarbazones are used as analytical reagents /3-7/. Further, the metal complexes formed with these reagents are of great medical value in the treatment of diseases like influenza, protozoa and smallpox, and also certain kinds of tumors /8/. In the treatment of cancer, the active species is the metal chelate of thiosemicarbazone. Metal chelates of these reagents are also used as pesticides and fungicides in agriculture.

There has been no sufficient work on the corresponding thallium(I) and indium(III) complexes with these ligands. The group thirteen elements form tetra- /9/, penta- /10/ and hexa- /11/ coordinated complexes. Radio-thallium is used in monitoring cardiac function. This metal ion is rapidly and almost completely absorbed following ingestion, inhalation or skin contact /12,13/. Determination of thallium is of interest due

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to its clinical, environmental and industrial applications /14/. Thallium is used as a probe for K^+ in biological systems /15/.

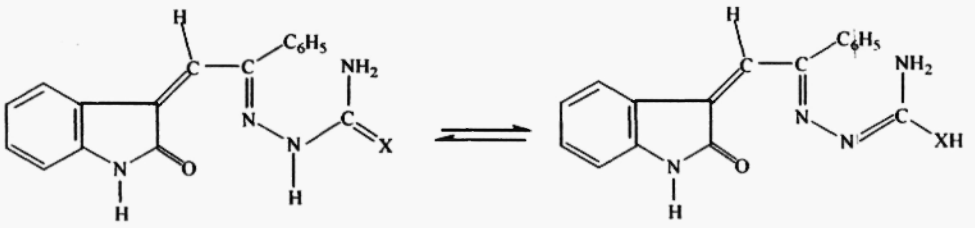
There has been considerable interest in the metal [indium(III)] complexes of semicarbazones due to their uses as antitumor agents /16/, analgesics, sedatives /17/, antimicrobials /18/, antineoplastic agents /19/ and for the treatment of chronic high altitude hypoxia /20/. Indium plays an important role in the biochemical and medicinal processes /21/ and in calcific tumors /22/. Keeping these facts in view, we have synthesized, characterized and screened the thallium(I) and indium(III) complexes of two biologically active semi- and thiosemicarbazone ligands.

MATERIALS AND METHODS

All the chemicals used were of A.R. grade and the reactions were carried out under strictly anhydrous conditions. All the solvents and reagents were dried and distilled before use. Thallous chloride was used as such and for the preparation of indium isopropoxide anhydrous indium(III) chloride was dissolved in a mixture of benzene and isopropanol and refluxed till dissolution. Sodium metal was dissolved separately by refluxing in a mixture of benzene and isopropanol. This solution was added, while hot, to the previous solution and reaction mixture was refluxed for ~ 4 h. The precipitation of sodium chloride was filtered out and the filtrate was concentrated by distillation. Indium isopropoxide was obtained by leaving the concentrated solution overnight. The white crystals, thus obtained, were dried *in vacuo*.

Preparation of the Ligands

The ligands L^1H and L^2H were prepared by the condensation of isatin and acetophenone in equimolar ratio. The resulting mixture was then condensed with hydrazinecarbothioamide and hydrazinecarboxamide (in the presence of sodium acetate) in 1:1 molar ratio in alcohol. The reaction mixture was then refluxed over a water bath for 3-4 h and allowed to stand overnight. The resulting products were recrystallized from ethanol and dried under vacuum. They exist in two tautomeric forms (see Fig. 1).



where X = S (L^1H) and O (L^2H)

Fig. 1: Tautomerisation in ligands.

Preparation of the Complexes

1. *Preparation of Indium(III) Complexes*

Indium isopropoxide and ligands were dissolved in dry benzene in 1:1, 1:2 and 1:3 ratios. The resulting mixture was refluxed for 16-24 h. The progress of the reaction was checked by measuring the amount of isopropanol in the azeotrope. After completion of the reaction the excess of the solvent was removed under reduced pressure and dried *in vacuo*. The physical and analytical data of these complexes are listed in Table I.

2. *Preparation of Thallium(I) Complexes*

Thallous chloride was dissolved in sodium salt of the ligands in 1:1:1 ratio. Sodium salt of the ligand is prepared in methanol. The resulting mixture was refluxed for 16 – 24 h. After completion of the reaction the excess of the solvent was removed under reduced pressure and dried *in vacuo*. The physical and analytical data of these complexes are listed in Table I.

Table I

Physicochemical and Analytical Data for L^1H, L^2H and their Complexes.

Compound	Colour and state	Yield %	M.pts. (°C)	Found (Calcd.) %			Mol. Wt. Found (Calcd.)
				M	N	S	
L^1H	Yellow	-	208	-	17.56 (17.40)	10.05 (9.96)	325 (322)
L^2H	Yellow	-	219	-	18.50 (18.31)	-	302 (306)
$Tl(L^1)$	Yeloowish brown	76	218	38.42 (38.86)	10.34 (10.65)	6.01 (6.10)	529 (526)
$Tl(L^2)$	Brick red	79	228	39.91 (40.08)	11.12 (10.99)	-	513 (510)
$In(OPr^i)_2(L^1)$	Light brown	82	242	20.82 (20.71)	10.30 (10.10)	5.86 (5.78)	1101 (1109)
$In(OPr^i)(L^1)_2$	Mustard yellow	85	256	12.94 (13.28)	11.32 (12.96)	7.33 (7.42)	1601 (1729)
$In(L^1)_3$	Yellowish brown	84	264	10.46 (10.64)	15.43 (15.58)	9.10 (8.91)	1071 (1079)
$In(OPr^i)_2(L^2)$	Yellow	86	245	21.22 (21.32)	10.58 (10.40)	-	1068 (1077)
$In(OPr^i)(L^2)_2$	Dim yellow	88	260	13.22 (13.79)	13.11 (13.46)	-	1620 (1665)
$In(L^2)_3$	Dim yellow	87	268	11.27 (11.14)	16.22 (16.30)	-	1027 (1031)

Nitrogen and sulfur were estimated by Kjeldahl's and Messenger's methods, respectively /23/. The isopropanol in the azeotrope was estimated by dichromate oxidation method. Molecular weights were determined by the Rast Camphor method and conductivity was measured with a Systronics conductivity bridge (type 304). IR spectra were recorded on a Perkin-Elmer 577 Grating spectrophotometer. ^{1}H NMR spectra were recorded on a JEOL AL 300 FT NMR in DMSO-d6 using TMS as an internal standard.

RESULTS AND DISCUSSION

The reactions of TlCl with L^1H and L^2H have been carried out in unimolar ratio in methanol. The replacement of chloride resulted in the formation of Tl(N⌒X) type of compounds.

$$TlCl + N\frown Xna \longrightarrow Tl(N\frown X) + NaCl$$

In the case of indium isopropoxide the reactions have been carried out in 1:1, 1:2 and 1:3 molar ratios in dry benzene. The successive replacement of the isopropoxy moiety in the form of isopropanol takes place as follows

$$In(OPr^i)_3 + N\frown XH \xrightarrow{MeOH} In(OPr^i)_2(N\frown X) + Pr^iOH \quad (i)$$

$$In(OPr^i)_3 + 2N\frown XH \xrightarrow{MeOH} In(OPr^i)(N\frown X)_2 + 2Pr^iOH \quad (ii)$$

$$In(OPr^i)_3 + 3N\frown XH \xrightarrow{MeOH} In(N\frown X)_3 + 3Pr^iOH \quad (iii)$$

where N⌒X is the donor system of the ligand and X = oxygen or sulfur.

These reactions proceed easily and the resulting compounds are coloured solids and soluble in methanol, DMF, THF and DMSO. All the reactions could be completed within 16-24 h.

SPECTRAL STUDIES

IR Spectra

The IR spectra of the ligands show broad bands in the regions 3200 – 3120 cm^{-1} (L^1H) and 3140-3100 cm^{-1} (L^2H) due to νNH vibrations, which disappear in the spectra of the complexes, indicating the loss of a proton on chelation with the metal atom /27/. On the basis of the shift observed for the ν >C=N vibrations

from 1590cm^{-1} (L^1H) and 1615 cm^{-1} (L^2H) to higher wave number in the metal complexes, it can be deduced that the imine nitrogen is involved in the coordination to the metal atom. The bands at 1052 cm^{-1} (L^1H) and 1685 cm^{-1} (L^2H), due to ν >C=S and >C=O vibrations respectively, were observed in the spectra of the ligands /28/. The absence of these bands in the spectra of the complexes supports the coordination of the sulfur and oxygen to the metal atom. The In complexes show new bands in the far infra red region 520 ± 10 cm^{-1}, 480 – 350 cm^{-1} and 320 – 280 cm^{-1}, due to the different vibrational modes of ν In-O, ν In←N and ν In-S respectively, which support the coordination pattern. The free ligands display two sharp bands at 3448 cm^{-1} and 3321 due to ν_{asym} and ν_{sym} NH_2 groups, respectively. These bands are observed at almost the same positions in the spectra of the metal complexes, suggesting the non-involvement of this amino group in chelation. The T1 complexes exhibit two bands at ~ 440 cm^{-1} and 425 cm^{-1}, which may be attributed to the different vibrational modes of Tl – O and Tl←N, respectively.

U.V. Spectra

The electronic spectra of the ligands exhibit two maxima at 280 and 310 nm, assignable to π-π* electronic transitions, that remain almost unchanged in the spectra of the metal complexes. The spectra of the ligands also show a broad band at ca ~ 365 nm, attributable to n-π* transitions of the azomethine (>C=N) group. However, in the spectra of the complexes, this band shifts to a lower wavelength due to the coordination of the azomethine nitrogen to the metal atom, indicating the delocalization of electronic charge within the chelate ring and thereby stabilizing the resulting complexes /29/.

^{1}H NMR Spectra

The ^{1}H NMR spectra of the free ligands, thallium(I) complexes and indium(III) complexes have been recorded in DMSO-d_6. The free ligands (L^1H and L^2H) exhibit singlets at δ11.38 and δ11.56 ppm due to the –NH proton. The absence of these signals in the complexes suggests that this proton has been lost via thioenolization and ketoenolization of >C=S and >C=O groups and coordination of the sulfur and oxygen atoms to the metal atom, respectively. The complexes show a multiplet in the region δ7.04 – 8.35 ppm due to the aromatic protons and a singlet due to $-NH_2$ group appears at δ3.39 and 3.46 ppm in the free ligands. These resonance signals remain unchanged in the spectra of the complexes, suggesting their non-involvement in chelation (Table II).

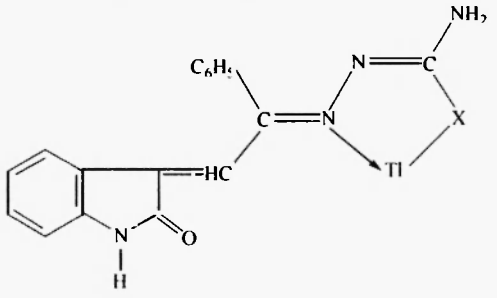
On the basis of the above discussions, a bicoordinated structure has been proposed for thallium(I) complexes and a pentacoordinated environment may be proposed for the 1:1 indium(III) complexes and hexacoordinated structure for 1:2 and 1:3 complexes (Fig. 2).

Table II

^{1}H NMR spectral data of ligands and their metal complexes.

Compound	-NH ring (bs)	-NH Free (bs)	-NH_2 (bs)	Aromatic protons (m)	Isoprpoxy groups	
					Gem. dimethyl (d)	Methine (Septet).
L^1H	11.96	11.38	3.43	7.04 – 8.27	-	-
L^2H	11.94	11.40	3.40	7.07 – 8.30	-	-
$Tl(L^1)$	11.92	-	3.45	7.10 – 8.35	-	-
$Tl(L^2)$	11.95	-	3.44	7.12 – 8.30	-	-
$In(OPr^i)_2(L^1)$	11.93	-	3.42	7.08 – 8.31	1.02 (terminal) 1.23 (bridging)	4.07 (terminal) 4.20 (bridging)
$In(OPr^i)(L^1)_2$	11.96	-	3.29	7.06 – 8.28	1.22 (bridging)	4.49 (bridging)
$In(L^1)_3$	11.92	-	3.44	7.14 – 8.32	-	-
$In(OPr^i)_2(L^2)$	11.94	-	3.44	7.14 – 8.32	1.03 (terminal) 1.21 (bridging)	4.10 (terminal) 4.45 (bridging)
$In(OPr^i)(L^2)_2$	11.93	-	3.46	7.11 – 8.26	1.26 (bridging)	4.51 (bridging)
$In(L^2)_3$	11.96	-	3.45	7.05 – 8.27	-	-

bs = broad singlet, d = doublet, m = multiplet



1:1 Complex

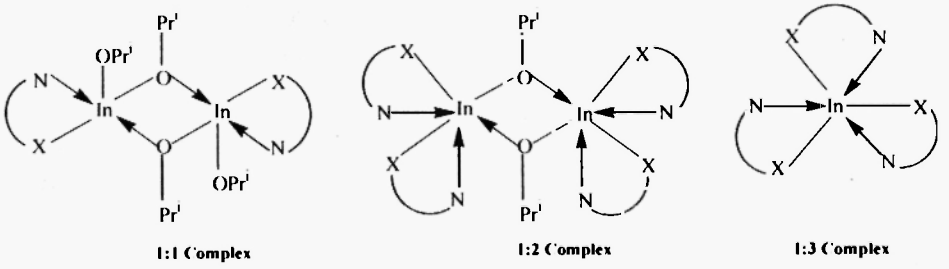


Fig. 2: Proposed structure of the complexes.

ANTIMICROBIAL SCREENING

Antifungal Activity (in vitro)

The antifungal activity was evaluated by the Radial Growth method using Czapek's agar medium having the composition, glucose 20 gm, starch 20 gm, agar-agar 20 gm and distilled water 1000 ml. To this, medium was added requisite amount of the compound after being dissolved in methanol to obtain certain final concentrations (50, 100 and 200 ppm). The organisms used in these investigations included *Alternaria alternata* and *Rhizoctonia bataticola*. The linear growth of the fungus was obtained by measuring the diameter of the colony in petriplate after 96 h at 28 ± 2°C and percentage inhibition calculated as 100 (C-T) / C, where C and T are the diameter of the fungus colony in the control and test plates, respectively /24/. (Table III)

Antibacterial activity (in vitro)

The activity against bacteria was evaluated by the Inhibition Zone technique (Paper-disc plate method). The nutrient agar medium (peptone 5 gm, beef extract 5 gm, NaCl 5 gm, agar-agar 20 gm. and distilled water 1000 ml) and 5 mm diameter paper disc of Whatman No.1 were used. The compounds were dissolved in methanol in 250, 500 and 1000 ppm concentrations. The filter paper discs were soaked in different concentration of the compounds and then placed in the petriplates previously seeded with the test organisms (*Staphylococcus aureus* and *Escherichia coli*). The plates were incubated for 20-30 h at 28 ± 2°C and the inhibition zone around each disc was measured /25,26/ (Table IV).

Table III

Fungicidal Screening Data for the Ligands and their Complexes [Inhibition after 96 h (%) (Conc. in ppm)]

Compounds	*Alternaria alternata*			*Rhizoctonia batatica*		
	50	100	200	50	100	200
L^1H	39	47	54	38	47	53
L^2H	33	40	46	34	38	44
$Tl(L^1)$	44	57	68	42	54	67
$Tl(L^2)$	41	52	61	40	49	58
$In(OPri)_2(L^1)$	59	65	72	57	65	71
$In(OPri)(L^1)_2$	56	61	70	55	62	68
$In(L^1)_3$	54	58	66	52	60	65
$In(OPri)_2(L^2)$	57	64	69	56	63	68
$In(OPri)(L^2)_2$	54	59	67	51	58	62
$In(L^2)_3$	51	56	65	48	57	61
Standard (Bavistin)	94	100	100	86	98	100

Table IV

Antibacterial Screening Data for the Ligands and their Complexes [Diameter of Inhibition Zone (mm) (Conc. in ppm)]

Compounds	*Staphylococcus aureus*			*Escherichia coli*		
	250	500	1000	250	500	1000
L^1H	6	8	10	4	6	8
L^2H	5	6	9	3	5	7
$Tl(L^1)$	8	10	12	7	8	10
$Tl(L^2)$	7	9	11	6	7	9
$In(OPri)_2(L^1)$	11	12	13	9	10	12
$In(OPri)(L^1)_2$	10	11	12	8	9	11
$In(L^1)_3$	8	10	11	6	7	9
$In(OPri)_2(L^2)$	10	11	12	7	9	10
$In(OPri)(L^2)_2$	9	10	11	6	8	9
$In(L^2)_3$	8	9	10	5	6	7
Standard (Streptomycin)	15	17	18	14	16	17

ANTIFUNGAL AND ANTIBACTERIAL ACTIVITIES

The antifungal and antibacterial activities of the ligands and their corresponding complexes against various fungi and bacteria have been recorded in Tables III and IV. The results of testing show that almost all the compounds are more active than the parent ligands against all the organisms used. All the compounds are inhibiting the growth of the fungi and bacteria to a great extent as the concentration is increased. In the case of indium(III) complexes, the biochemical properties of the molecules are greater if the isopropoxy group is replaced by a ligand moiety. It may be inferred that the compounds having three ligand moieties are more active than compounds having two or one ligand moieties. The studies indicated that compounds having a semicarbazone moiety are less potent than the compounds having a thiosemicarbazone, i.e. sulfur moiety.

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