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Synthesis, characterization and antimicrobial studies of Sb(III) complexes of substituted thioimines

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Some antimony complexes of a new class of substituted thioimines have been prepared by reacting Ph_3Sb (III) with [1-(2-naphthyl) ethyledene] hydrazinecarbodithioic acid phenyl methyl ester (L^1H), [1-(2-thienyl) ethyledene] hydrazinecarbodithioic acid phenyl methyl ester (L^2H), [1-(2-pyridine) ethyledene] hydrazinecarbodithioic acid phenyl methyl ester (L^3H) and [1-(2-furanyl)ethyledene] hydrazinecarbodithioic acid phenyl methyl ester (L^4H), in unimolar and bimolar ratios using thermal as well as microwave method. All the new complexes have been characterized by elemental analyses, molecular weight determinations and spectral studies including electronic, IR, ^1H and ^{13}C NMR spectra. The spectral data are consistent with the tetra-coordinated and penta-coordinated environments around Sb(III). The bidentate ligands coordinate through the nitrogen and sulfur atoms. Free ligands and their metal complexes have been screened for their antimicrobial activity on different species of pathogenic fungi and bacteria and their biological activity is discussed briefly.

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Microwave irradiations, can be used for a variety of applications including organic synthesis, wherein chemical reactors are accelerated because of selective absorption of MW energy by the polar molecules[1]. The use of microwave energy instead of conventional heating often results in good yields in a short time as compared to reduction in classical synthetic methods[2]. During the last one and a half decades, the chemistry of organoantimony(III) derivatives with nitrogen and sulphur donor ligands has attracted attention due to their uses as potential antimicrobials[3]. Antimony had quite widespread use in pharmacology for the treatment of syphilis, fever, melancholy, pneumonia, epilepsy, and inflammatory conditions[4]. Organic antimony salts are used medically to treat some tropical diseases, especially in the treatment of all forms of leishmenasis[5]. Organoantimony compounds also exhibit significant antispermatogenic[6] as well as antitumor activities[7], which is associated with cytostatic activity[8] similar to that for cisplatin. The chemistry of the metal complexes of main group elements with various nitrogen and oxygen donor ligands is the subject of increasing interest due to the striking structural features exhibited by this class of compounds and also on account of their biological significance[9]. The number and diversity of nitrogen and sulphur chelating agents used to prepare new coordination and organometallic compounds has increased rapidly during the past few years[10]. Studies on metal complexes of hydrazine carbodithioic acid [dithiocarbazate (NH_2NHCS_2-)] have been thoroughly studied and reported by a number of workers[11-13]. Despite extensive preparative and spectroscopic investigations on organoderivatives of boron[14], tin, silicon[15], germanium[16] and titanium[17] with Schiff bases containing N^O donor system, comparatively, fewer studies have been made on the organoantimony(III)[18-20] derivatives. There are only a few reports on the Schiff base complexes of antimony adducts with (V) oxidation state[21]. So, there is a considerable scope for undertaking systematic studies of coordination compounds of organoantimony(III) with a variety of chelating agents. We report herein the bidentate (N^S) Schiff bases, derived from the condensation of S-benzyldithiocarbazate with heterocyclic ketones and their antimony (III) complexes, using thermal as well as microwave irradiations[22]. The present course of study was initiated with the preparation, characterization and biological screening of antimony(III) derivatives with some substituted S-benzyl dithiocarbazates.

Material and Methods

All the chemicals and solvents used were dried and purified by the standard methods and moisture was excluded from the glass apparatus using fused $CaCl_2$ guard tubes. The chemicals used were of reagent grade. Triphenylantimony (Merck) was used as such without further purification. The ligands were synthesized by the condensation reaction of heterocyclic ketones with S-benzyldithiocarbazate. Ligands and their complexes were characterized by elemental analysis and spectral [IR, NMR (^{1}H and ^{13}C)] studies. Electronic spectra of the complexes were recorded in chloroform on a UV-160A Shimadzu spectrophotometer in the range 200-600 nm.^{1}H NMR spectra were recorded on a JEOL-AL-300 FT NMR spectrometer in $CDCl_3$ and DMSO-d_6 using TMS as the internal standard. Sulphur was estimated gravimetrically by the Messenger's method[23] as $BaSO_4$. Nitrogen and antimony were estimated by the Kjeldahl's method and Iodometric method, respectively[23]. Molecular weight determinations were carried out by the Rast Camphor method[24]. The physical properties and analytical data of these complexes are given in Table 1.

Synthesis of the ligands

A mixture of hydrazine hydrate (5 g) and potassium hydroxide (5.7g) in 90% ethanol (35 mL) was cooled down to 0°C in an ice-salt bath. Carbon disulphide (7.6 g) was added dropwise with constant stirring over a period of an hour. During this time, two layers were formed. The yellow oil in the lower layer was then separated using a separating funnel and dissolved in previously cooled 40% ethanol (30 mL). The mixture was kept in an ice-bath and benzyl

Table 1 — Analytical data and physical properties of the ligands and complexes

Comp.[a]	Colour	M.pt. (°C)	Found (Calc.) (%)			Mol. wt.
			N	S	Sb	Found (Calc.)
L^1H	Yellow	118	9.28 (9.65)	21.78 (22.08)	-	307 (290)
L^2H	Brown	102	9.52 (9.14)	31.17 (31.39)	-	338 (306)
L^3H	Yellow	148	13.78 (13.94)	21.01 (21.27)	-	271 (301)
L^4H	Brown	140	8.30 (7.99)	18.11 (18.30)	-	346 (351)
$[Ph_2Sb(L^1)]$	Yellow	145	4.32 (4.51)	9.97 (10.24)	19.68 (19.45)	619 (626)
$[PhSb(L^1)_2]$	Orange	130	6.21 (6.28)	14.21 (14.28)	13.13 (13.56)	879 (898)
$[Ph_2Sb(L^2)]$	Dark brown	110	4.80 (4.86)	16.50 (16.56)	20.04 (20.96)	567 (581)
$[PhSb(L^2)_2]$	Dark brown	115	6.89 (6.97)	23.69 (23.75)	14.78 (15.03)	801 (810)
$[Ph_2Sb(L^3)]$	Dark green	170	7.32 (7.35)	11.03 (11.13)	20.84 (21.13)	562 (576)
$[PhSb(L^3)_2]$	Greenish brown	178	10.48 (10.58)	15.99 (16.03)	14.89 (15.22)	794 (800)
$[Ph_2Sb(L^4)]$	Light yellow	160	4.84 (4.99)	11.24 (11.35)	20.02 (21.54)	558 (565)
$[PhSb(L^4)_2]$	Light orange	175	7.21 (7.26)	16.45 (16.50)	14.15 (15.67)	765 (777)

[a]All were solids

chloride was then added dropwise with continuous stirring for 6-7 h. Ultimately, S-benzyldithiocarbazate precipitated as white amorphous material at the bottom of the flask. This was separated by filtration and washed with distilled water. Finally, the synthesis was completed by air drying of the product (M.pt. =118°C), and recrystallization was done by using benzene.

Monobasic bidentate phenyl methyl ester (S-benzyl) derivatives of hydrazine carbodithioic acid (dithiocarbazate) derived from heterocyclic ketone were prepared by refluxing an equimolar amount of ketone with phenylmethyl ester of hydrazine carbodithioic acid in ethanol along with two drops of hydrochloric acid. On cooling, crystals of ligands separated out, which were washed with ice cold ethanol. They were recrystallised from benzene, analysed and characterized. Tautomeric structures of the ligands are shown in Scheme 1.

Synthesis of the diorganoantimony(III) complexes

***Conventional method*[25]**

About 25 mL of benzene solution of Ph_3Sb (starting material) was added to a benzene suspension (15 mL) of the ligand [L^1H, L^2H, L^3H and L^4H]. The solution was refluxed for 6-8 h and excess of the solvent was removed under reduced pressure. For purification, the compound was dissolved in a small amount of benzene (15 mL) and then petroleum ether (b.pt. 40-60°C) was added slowly till compound began to separate. Compound was finally dried under reduced pressure. All the complexes were prepared by adopting similar procedure.

***Microwave method*[26]**

In microwave assisted synthesis the reactions of Ph_3Sb with various substituted S-benzyldithiocarbazate ligands were carried out in 1:1 and 1:2 molar ratios, using 2-3 mL of dry benzene as a solvent. The reaction mixture was taken in open beaker and then irradiated inside a microwave oven till the completion of the reaction. The resulting product was washed and dried *in vacuo*. The purity of the compounds was checked by TLC.

Antifungal/antibacterial screening

The antifungal and antibacterial activity of the parent ligands and their complexes was tested *in vitro* for the growth inhibiting potential against various fungal and bacterial strains using Radial Growth Method[27] and Paper Disc Technique[27], respectively. Fungal strains *Fusarium oxysporum* and *Colletotrichum capsici* and bacterial strains *Escherichia coli* and *Klebsiella aerogenous* were used. The biocidal activity has been compared with the conventional fungicide *Bavistin,* and the conventional bactericide *Streptomycin.* The concentrations of respective ligands and their complexes were 50, 100 and 200 ppm in case of antifungal screening as well as these were 500 and 1000 ppm in case of antibacterial screening. Methanol was used as solvent for preparing solutions.

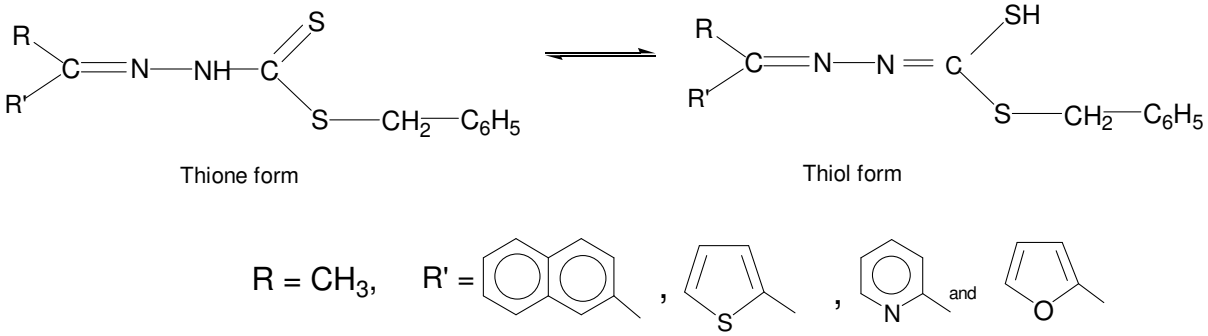
Results and Discussion

Reactions of triphenylantimony(III) with the monobasic bidentate ligands having N^S donor set in 1:1 and 1:2 molar ratios proceed with the cleavage of the antimony carbon bond[25] of Ph_3Sb and yield the monosubstituted derivatives.

$$Ph_3Sb + N^{\frown}S\,H \longrightarrow Ph_2Sb(N^{\frown}S) + C_6H_6$$

$$Ph_3Sb + 2NS^{\frown}H \longrightarrow PhSb(N^{\frown}S)_2 + 2C_6H_6$$

After removing the solvent under reduced pressure, coloured solid compounds were obtained, which were found to be sparingly soluble in CH_2Cl_2, $CHCl_3$ and CCl_4 and highly soluble in benzene. The molecular



Scheme 1

weight determination shows the resulting derivatives as monomers. A drastic reduction in reaction time was observed due to the rapid heating capability of microwaves.

UV spectra

The electronic spectra of free ligands and their complexes show bands at *ca*. 285 and 320 nm assigned to π-π* electronic transitions within the benzene ring. An additional band arising from >C=N chromophore at *ca.* 370 nm shift to a lower wavelength for metal complexes due to coordination of azomethine nitrogen to the metal atom, indicating delocalization of the electronic charge within the chelate ring[28].

IR spectra

The infrared spectra of the ligands show a strong band in the region 3450-3180 cm^{-1} attributable to ν(NH), and this disappears in the spectra of the corresponding metal complexes. In the deprotonated form, these act as potentially bidentate ligands coordinating through the azomethine nitrogen and thiolo sulphur forming a five membered chelate ring. This is evidenced by the absence of ν(NH) as well as ν (>C=S) vibrations in the corresponding complexes.

A strong and sharp band around 1600 cm^{-1} may be attributed to ν (>C=N) vibrations[29]. This band undergoes considerable shift towards the lower frequency by 10-15 cm^{-1} compared to the free ligand value, indicating that Sb^{+3} is a strong acceptor. This is in keeping with the fact that Sb^{+3} have high effective nuclear charge with appreciable acidic property. Another strong band in the spectra of the ligands appears at ~1050 cm^{-1} which may be tentatively assigned to ν(C=S) which show that in the solid state the ligand exists in thione form (Scheme 1). This band disappears in the spectra of the complexes indicating the coordination of the ligand through sulphur. In the spectra of the ligands a doublet at around 2900 and 2960 cm^{-1} attributed to symmetric and asymmetric vibrations of –CH of S-CH_2-C_6H_5 grouping, reduced to a weak doublet in the spectra of the complexes[30].

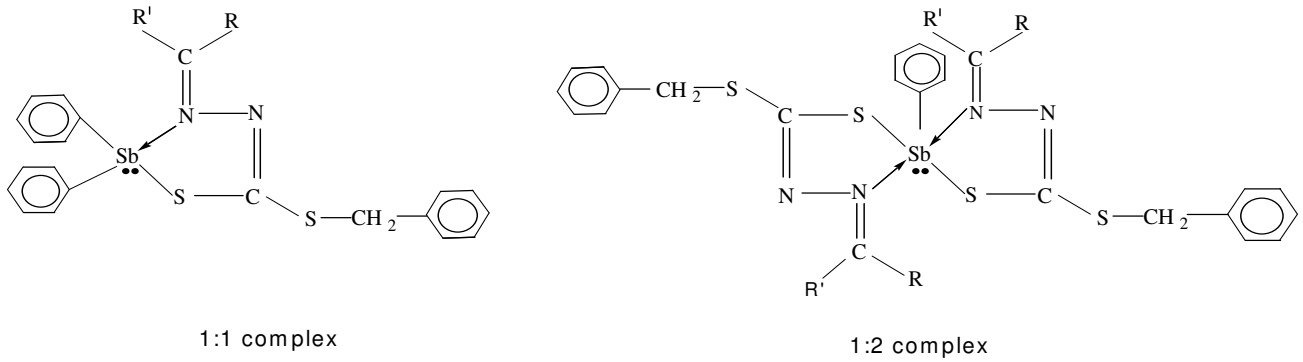
^{1}H NMR spectra

The above bonding patterns are further supported by the proton magnetic resonance spectral studies of the ligands and their corresponding complexes. The ^{1}H NMR spectra of the ligands exhibit the –CH_2- protons signal in the range of δ1.26-1.78 ppm. Aromatic proton signals appear in the range of δ 7.10-8.38 ppm and these remain at the same position in the spectra of the metal complexes. The protons of NH and SH groups of the ligands give signal in the range of δ 9.8-10.28 and 3.9-4.40 ppm, respectively. The NH signal disappears in the spectra of the metal complexes indicating the chelation of the ligand moiety to antimony through the nitrogen atom, whereas the disappearance of SH signal indicates the bonding of the ligand to antimony through sulphur atom. The signals in the range of δ 2.44-2.82 ppm observed in the ligand assigned to the methyl protons $H_3C-\overset{|}{C}=N$ attached with the azomethine group, shifted downfield in the spectra of the corresponding antimony complexes on account of its dieshielding which is attributed to the donation of the lone pair of electron of the azomethine nitrogen to the antimony atom.

^{13}C NMR spectra

To support the proposed structures, ^{13}C NMR spectra of the ligands and their corresponding complexes were recorded in $CDCl_3$ and DMSO-d_6. A comparison of ^{13}C NMR spectra of the organoantimony (III) derivatives with those of the ligands (L^1H – L^4H) provides very useful information about the mode of bonding. The signal for >C=N (azomethine) carbon appears at δ150.82 ppm in ligand and this signal shifts to δ 140.12 - 145.7 ppm in complexes, which confirms the complexation. The >C=S (thiolo) group signal also shows a shift in its position as compared to ligand (δ 177.75 ppm) and appears at δ 162.42 – 167.34 ppm. This indicates the participation of thiolo group in bonding. Thus, considerable shifts in carbon attached to S and N indicate the involvement of sulphur and nitrogen atom in coordination with antimony atom. The carbon of the phenyl group (Sb-Ph) is observed at position comparable to other similar compounds. The signals for phenyl carbons attached to antimony are observed in the range of δ142-132 ppm. Further, only one set of signals to central antimony atom has been observed which indicate that the two phenyl groups are chemically equivalent[31].

Thus, on the basis of the above spectral evidences, tetra-coordinated and penta-coordinated structures may be proposed for the resulting organoantimony (III) as well as monoorganoantimony(III) complexes as shown in Scheme 2.



Scheme 2

Antifungal and antibacterial activities

The experimental results showded that there is an increase in the toxicity of the complexes as compared to the parent ligands. The results recorded from the biological activity were also further compared with the standard fungicide Bavistin and conventional bactericide Streptomycin. The results are quite promising. It is clear from the antifungal screening data, that the metal complexes are more fungitoxic than the chelating agent itself[32]. The enhanced activity of the metal complexes may be ascribed to the increased lipophilic nature of these complexes arising due to the chelation[33]. It was also noted that the toxicity of the metal chelates increases on increasing the concentration. The observed toxicity can be explained on the basis of the Tweedy's chelation theory[34]. It has also been observed that dithiocarbazates of antimony (III) compounds are toxic for various microbes[35,36].

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