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# FUNGICIDAL ACTIVITY OF μ-OXY BIS(TRIPHENYLORGANOANTIMONY) COMPOUNDS

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***Abstract:*** μ-oxy bis(triphenylantimony)(III) dichloride $(C_6H_5SbCl)_2O$ and μ-oxy bis(triphenylantimony)(III) chloro carboxylate of the general formula Ph3Sb(L)-O-Sb(L)Ph3 &Ph3SbCl-O-Sb(L)Ph3 respectively have been synthesized by the metathetical reaction where L is the different carboxylate such as 2-Pyrazine, p-methoxymendalate, aminosuccinate, mendalate, salicylate, benzilate.The newly synthesized compounds have been formulated and characterized on the basis of elemental analysis, biological activity, molecular weights, solid state IR, and $^1H$, $^{13}C$ NMR data.

**Keywords:** Organoantimony, bis(triphenylantimony)(III) dichloride, μ-oxy bis(triphenylorganoantimony) compounds & Fungal Strain.

## I.Introduction:

The role of organometallic compounds in all aspects of biological studies has been substantial, both historically and currently. While a vast literature has appeared and like other areas of chemistry proliferated in recent years, it has been widely scattered and dispersed. Likewise, research activity has been erratic. Some compounds receive very intense attention, others considerably less and most none. Attempts to correlate, compare and predict have been equally irregular. Certainly, the research reported, substantial and worthwhile as it is little more than an opening wedge.

The advances in synthetic techniques, structural investigation and mechanistic knowledge certainly indicate that many organic derivatives of boron, silicon, phosphorus, arsenic and even germanium or tin may have medicinal uses but not yet realized. Earlier in this century Salvarsan was often used in conjunction with compounds of antimony or bismuth because such combinations enhanced its effectiveness. Some other combinations may also be found regarding this.

Organometals provide valuable approaches to metabolic studies. Already they have provided useful information about oxidative phosphorylation, transmethylation, and the principles of chemotherapy. Compounds of silicon, phosphorus, and boron would seem to be most promising here and perhaps also tellurium this last especially as there is a growing interest in the role of selenium. The use of certain organometals as biocides adds a further dimension here.

Arsenic and mercury compounds have featured prominently in the concern about man's environment and lead to only a slightly lesser degree. Almost certainly this will continue. The need for continuing biocides, balanced against the need to avoid contamination by long-lived, toxic materials, will enhance the development of organotin compounds and probably those of certain other metals.

Certainly, a tremendous amount remains to be done. Biological applications have already abetted the growth of organometallic chemistry, but the best seems yet to come.

## II.Biological effects of organoantimony &organobismuth compounds:

Metal containing compounds may offer advantages over price. Organic compounds in drug therapy termed as 'Metallotherapy', first developed by Paul Ehrlich in 1865.Metal may coordinate to organic molecules and could alter metabolic pathway.Slow release/delivery of organic molecule to affected site *i.e.* it could act as Prodrug. Metal containing compounds are frequently used as: Antimony (antiprotozoal), bismuth (antiulcer), gold (antiarthritic), iron (antimalarial), platinum (anticancer), silver (antimicrobial).Synergic administration could reduce toxicity (*e.g.* Bismuth compounds could reduce the toxicity of cis-platin $[(NH_3)_2Cl_2Pt]$.

In context of above antimicrobial, antitumor, antileishmanisis potential of organobismuth compounds is not full developed despite apparent nexus between Helicobacter pylori – peptic ulcer, gastric cancer and bismuth-based drugs.

Group 15 elements, As, Sb and Bi is used clinically, basically in the treatment of *Syphilis, Leishmaniasis* and in acute hepatic and peptic ulcers. These metals/metalloids containing organic compounds (metal-carbon bond) may offer certain advantages in drug therapy *e.g.* the coordination of an organic molecule to a metal Centre may alter the normal metabolic pathway of the body and may lead to a slow release mechanism for delivery of organic molecules. The discovery of a synthetic arsenical, Salvarsan in 1910, was an effective cure for syphilis led to an extensive investigation on the synthesis and biological studies of organo arsenic and antimony compounds in the subsequent years.

Organoantimony and organobismuth compounds proved potent not only against infection caused by *Trypanosomes* but also active against *Leishmanial* organisms [1-4]. However, the main drawback in metal therapy is the associated toxicity of the respective metal. Nevertheless, the importance of organometallic compounds in medicine is undisputed and could be judged by the use of antimony as antiprotozoal, bismuth as antiulcers, gold as antiarthritic, iron as antimalarial, and platinum as anticancer and silver as antimicrobial agents in the treatment of various diseases. Some reports on biological activity of organoantimony compounds [5] have stated that most of

them are toxic when injected in patients but do not have a reputation as potential hazards to those preparing them and tested in the pharmaceutical industry as potential drugs. The organoantimony iminodiacetates can be used as insecticides [6]. The phenylantimony and bismuth pyrimidine derivatives also show antifungal activity [7-8]. Not only as antimicrobial and insecticidal agents but organoantimony compounds also exhibit antitumor activity more prominently. Thus, a series of organoantimony (III) compounds isolated with polydentate carboxylate has been investigated for their antitumor activity against different kinds of cancer cell line *in vitro* [9-10]. Tetraarylstibonium complexes have been reported by Prem Raj *et al.* [11] to exhibit significant biological activity. Triarylantimony(V) derivatives of various amides and carboxylates and some unsymmetrical organoantimony compounds have also been reported to possess antibacterial, antifungal, antiviral and insecticidal activity, by Kiran Singhal *et al.* [12-13]. However, there is much work remains to be done on biological activity and bio-chemical aspects of organoantimony compounds. Our recent findings have shown that unsymmetrical triorganoantimony and pentafluorophenyl antimony(III) and antimony(V) halides and carboxylate, cyclohexyl and α-naphthyl antimony compounds to be quite effective against several fungal and bacterial strains alongwith insects, pests, mites (*Spodoptera litura* and *Tebanychus urticae*) which was a major outcome in the field of biomedicinal importance or organo-antimony compounds [14].

A substantial literature is reported on biological effects of organoantimony compounds and to a lesser extent of organobismuth compounds. Much of the work is older as it was generated by the research for analogs of Salvarsan. The therapeutical uses of antimony have been reviewed by Christiansen [15], those of Bismuth by Gilman and Yale [16] along with some recent work has been included in the review by Sijkesteijn *et al*. [17].

The two main features distinguish these compounds from those of other heavy metals, as far as biological activity concerned: both can exist in two different oxidation states *i.e.* +3 and +5 (trivalent and pentavalent), but only the trivalent state compounds show important effects (because of Lewis acidity) and the aromatic compounds also show higher efficacy. The less stable aliphatic derivatives of antimony and bismuth have received little attention till date. Apparently, it is well found that the organobismuth compounds are less toxic towards mammals than those of antimony just the reverse of the tin-lead pair [18].

Early work on organoantimony compounds centralized on their similarity to Salvarsan and related arsenicals which proved against infections caused by *Trypanosome* and *Leishmania*, especially, where those organisms resisted arsenicals. Organobismuth compounds were likewise more effective but apparently much of their efficacy depended on the ability of organic compounds to generate metallic bismuth *in situ* [16].

Some recent research has been reported that organoantimony iminodiacetates can be used as insecticides [19] captostibone (*o*-carboxymethylthiobenzene stibonic acid) acts effectively against *Trypanosoma evansi* in rodents and has a chemotherapeutic agent index of 3.4 [20]. A *p*-aminobenzenestibonic acid derivative provide full protection to panies for ninety days against *T. evansi* at a level of 50 mg/kg [21]. Phenylantimony and phenylbismuth pyrimidine derivatives exhibit potent antifungal activity [22]. The phenylbismuth bis(2-thiopyridine-N-oxide) has been proposed as a bactericidal and fungicidal additive in soap formation [23]**.**

In view of the large spectrum of biological activity shown by organoantimony compounds, coupled with our research group's interest on antimicrobial, insecticidal and antitumor activity for such derivatives, especially carboxylates which exhibit both hydrophilic and lipophilic character, the author considered it worth to investigate antimicrobial activity of representative carboxylates together with pseudohalides having aromatic and fused aromatic rings bound to antimony. Tetrachloropyridyl containing antimony derivatives were considered to be better candidate because of the presence of tetrachloro substituted pyridine and their hydrolytic stability. Similar Sb-O-Sb arrangement sodium stibiogluconate [24] which has been found extremely effective against *Leishmaniasis* were also assayed for anti-microbial activity.

The first organometallic fungicide, "Upsulun" an organomercurial was introduced by Bayer in 1915 (Ulfvarson, 1969) [25] while some different organomercuric compounds and formulations have also been used as fungicides. Beiter and Leebrick (1963) [26-28] examined the fungicidal activity of a series of tri and pentavalent organoantimony and organobismuth compounds. It was found that the compounds were moderately fungitoxic, and organoantimonials being more effective in comparison to organobismuth compounds.

**III.Experimental**

Because of the complex interactions that may occur when an organic solvent is used as a carrier in fungicidal effect. The fungal isolated *Fusarium oxysporum, Drechlera oxyzae* with 100 µg/ml. All control and experimental plates were taken in replicates of five and colony diameters were measured after 96 h incubation at 37ºC. The percentage inhibition of fungal growth on medium supplemented with range of DMSO concentration was calculated also by growth on control plates. The net fungicidal effect was derived from the data of inhibition of growth of the test compound plus DMSO with respect to the fungal growth in the corresponding solvent control plates.

**IV.Fungicidal Effect of Experimental Compounds**

The test compounds listed in the Table 1&2 were dissolved in DMSO forming stock solution which was added as 100 µg/ml volume of plant pathogenic and beneficial fungal strains. The concentrations used were 10, 20, 50, 100 µg/ml. All the plates were incubated at 37ºC temperature on BOD incubator at which good growth was obtained for all the test cultures. Percent inhibition was determined after 96 h of incubation with respect to growth on medium containing only 100 µg/ml DMSO.

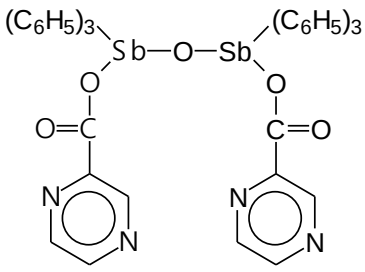
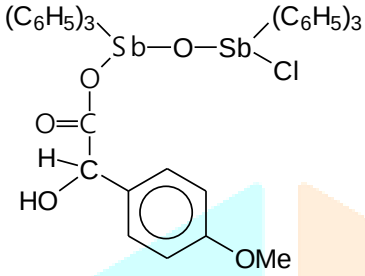
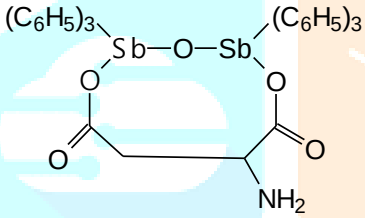
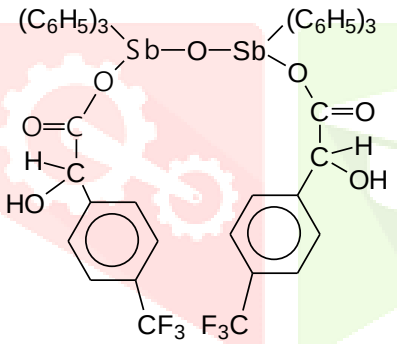
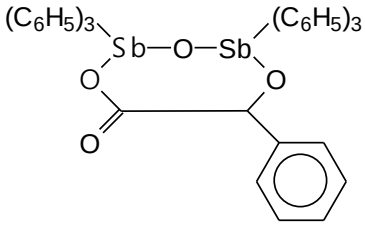
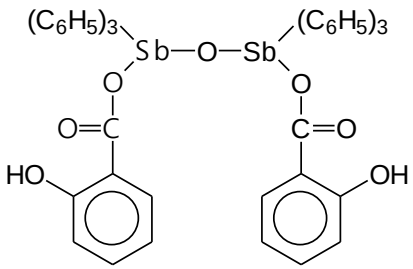
**V.Results and discussion:**

The interaction data from experiments with DMSO and µ-oxy bis (triarylantimony) for *Fusarium oxysporum, Drechlera oxyzae, Sclerotium rolfsii, Sclerotinia sclerotiorum, Trichodrema,* respectively (Table 1&2). It is found that DMSO was taken as the (–) control and antifungal, antibiotic *cyclohexamide* was taken as the positive control. All possible interactions between the solvent and the test compound were observed against the five fungal strains. An additive response occurred with *Drechlera oryzae*. This was concluded since there was no statistically significant difference found in the net fungicidal activity. Percent inhibition values are summarized in Table 1&2.

These interaction responses were observed in the study of solvent fungicide combinations reported by Burrell and Corke and Goel (1980) [8]. In all the assays, which ware performed, additive response between the test compound and the solvent was considered appropriate for studies of biofungicide of organo antimony compounds. Organoantimony compounds for the test fungi are summarized in Table 6. µ-oxy bis(triphenylantimony)(III) dichloride $(C_6H_5SbCl)_2O$ and µ-oxy bis(triphenylantimony) [2-pyrazine carboxylate] had $EC_{50}$ value 6.4 µg/ml against *F. oxysporum*.

The compounds were non-effective against the tested soil born fungi. This shows that the compounds do not interfere with soil fungal flora. They show compatibility with the beneficial bio-fungicide. *Trichoderma* at least up to 100 µg/ml.

**Table 1: Fungicidal Effect of organoantimony compounds determined for four fungi grown on different plant pathogenic**

| S.No. | Compounds | Radial growth of fungi on 100 µg/ml after one week | | | | |
|---|---|---|---|---|---|---|
| | | ***Fusarium oxysporum*** | ***Drechlera oryzae*** | ***Sclerotinia rolfeii*** | ***Sclerotinia sclerotiorum*** | ***Trichoderma*** |
| 1. | $(C_6H_5SbCl)_2O$ | 4.2 | 3.6 | 40 | 40 | 40 |
| 2. |  | 6.4 | 6.3 | 40 | 40 | 40 |
| 3. |  | 5.6 | 6.9 | 40 | 40 | 40 |
| 4. |  | 4.6 | 8.1 | 40 | 40 | 40 |
| 5. |  | 2.8 | 9 | 40 | 40 | 40 |
| 6. |  | 2.4 | 7.8 | 40 | 40 | 40 |
| 7. |  | 2.8 | 9 | 40 | 40 | 40 |

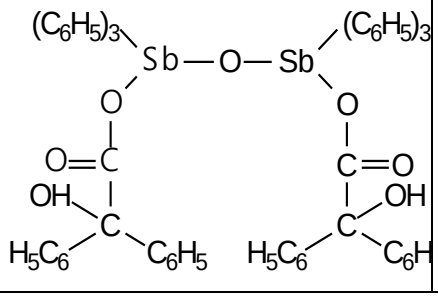
| S.No. | Compounds | Radial growth of fungi on 100 µg/ml after one week | | | | |
|---|---|---|---|---|---|---|
| | | *Fusarium oxysporum* | *Drechlera oryzae* | *Sclerotinia rolfeii* | *Sclerotinia sclerotiorum* | *Trichoderma* |
| (–) Control |  | 3.2 | 10.5 | 40 | 40 | 40 |

**Table 2: Radial growth of fungi on 100 µg/ml concentration after one week is given below**

| S. No. | Compound | *Fusarium oxysporum* | | *Drechlera oryzae* | | *Sclerotinia rolfeii* | | *Sclerotinia sclerotiorum* | |
|---|---|---|---|---|---|---|---|---|---|
| | | 3rd day | 7th day | 3rd day | 7th day | 2nd day | 7th day | 2nd day | 7th day |
| 1. | µ-oxy bis(triphenylantimony)(V) dichloride | 2.1 | 4.2 | 1.2 | 3.6 | 1 | 40 | 2.7 | 40 |
| 2. | µ-oxy bis(triphenylantimony) [2-pyrazine carboxylate] | 3.2 | 6.4 | 2.1 | 6.3 | 1.4 | 40 | 2.3 | 40 |
| 3. | Triphenylantimony(V) *p*-methoxy mendalate µ-oxytriphenyl antimony (V) chloride | 2.8 | 5.6 | 2.3 | 6.9 | 1.2 | 40 | 2.5 | 40 |
| 4. | µ-oxy bis(triphenylantimony)(V) aminosuccinate | 2.3 | 4.6 | 2.7 | 8.1 | 1.2 | 40 | 2.6 | 40 |
| 5. | µ-oxy bis(triphenylantimony)(V) triparafluoromethyl mendalate | 1.4 | 2.8 | 3 | 9 | 1.2 | 40 | 2.9 | 40 |
| 6. | µ-oxy bis(triphenylantimony)(V) mendalate | 1.2 | 2.4 | 2.6 | 7.8 | 1.5 | 40 | 2.4 | 40 |
| 7. | µ-oxy bis(triphenylantimony)(V) salicylate | 1.4 | 2.8 | 3 | 9 | 1.4 | 40 | 2.5 | 40 |
| (-) Control | µ-oxy bis(triphenylantimony)(V) benzilate | 1.6 | 3.2 | 3.5 | 10.5 | 1.2 | 40 | 2.5 | 40 |

**Figure 1: Antifungal activity of μ-oxy bis [triphenylantimony (V)] against *Trichoderma***

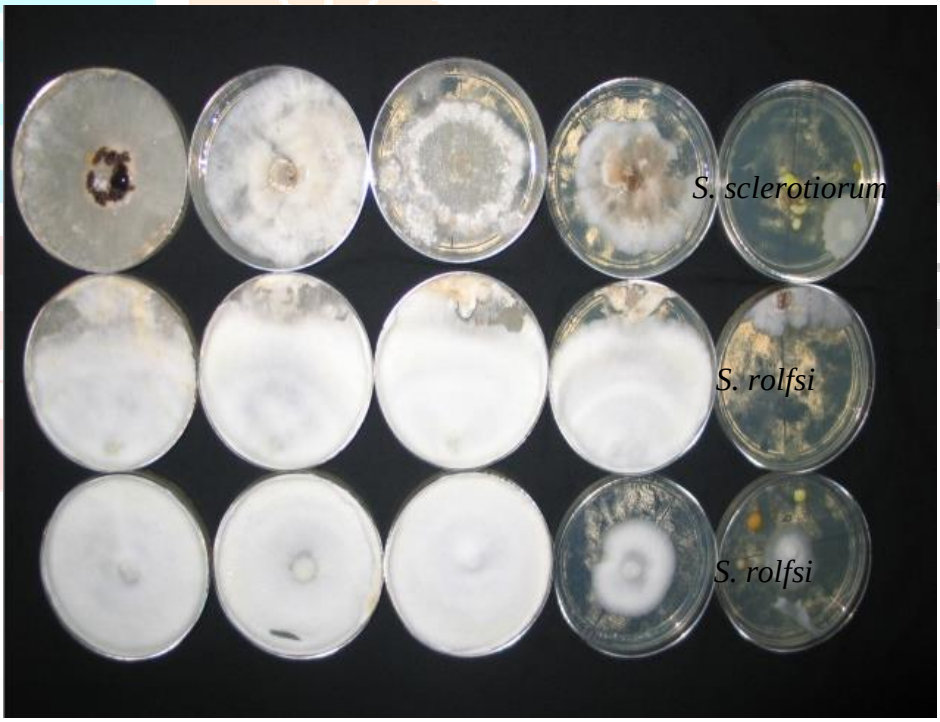



**Figure 2: Fungicidal effect of different (*S. Sclerotiorum*, *S. rolfsi*) fungi**

**Figure 3: *Sclerotinia sclerotiorum*: Growth inhibition of the fungi after 3 days of compounds 1-5**

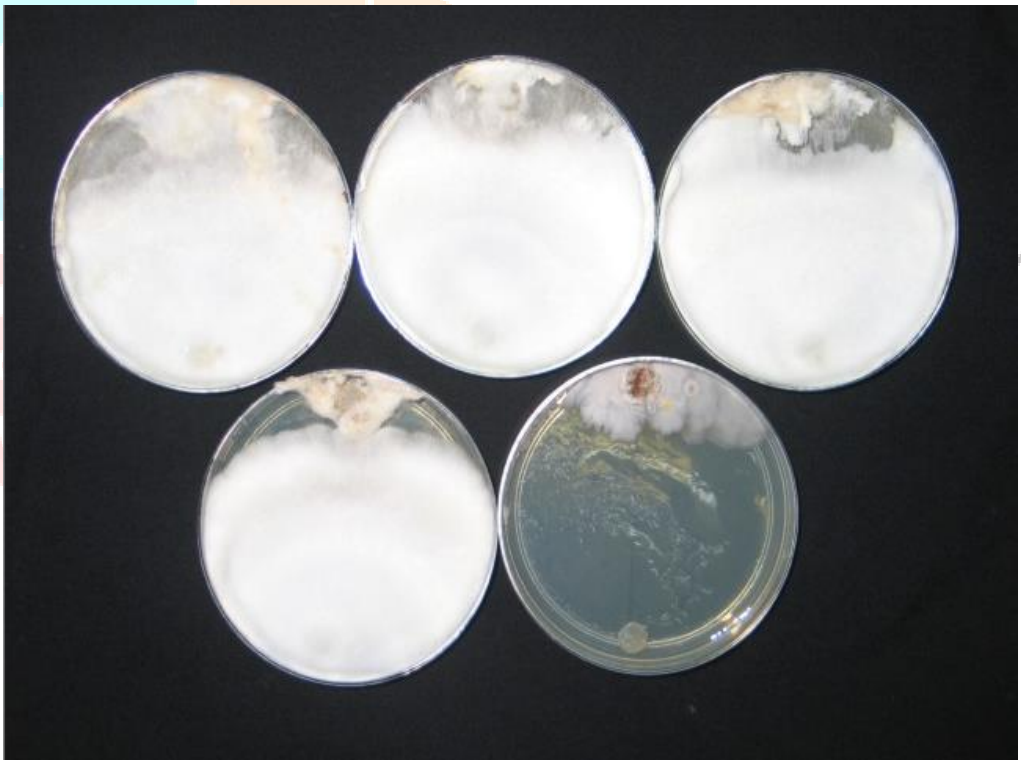


**Figure 4: *Trichoderma*: Growth inhibition of the fungi after 7 days In compounds 1-5**

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