[Contribution from the Lilly Research Laboratories]

THE REACTION OF ARYL MERCAPTANS WITH INORGANIC TRIVALENT ANTIMONY COMPOUNDS

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Received January 25, 1951

The preparation of aliphatic thioantimonites of the type $(RS)_3Sb$ has been reported frequently (1, 2, 3). Such compounds have usually been prepared according to equations A and B.

$$\text{A.}\quad 3\ RSH + SbCl_3 \longrightarrow (RS)_3Sb + 3\ HCl$$

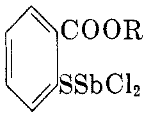
$$\text{B.}\quad 3\ RSNa + SbCl_3 \longrightarrow (RS)_3Sb + 3\ NaCl$$

$$R = \text{aralkyl or alkyl}$$

However, aromatic compounds of a similar type are not well known. Five such compounds of structure I have been reported.

$(ArS)_3Sb$

I



II

a. R = H

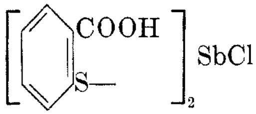
b. R = CH_3

c. R = C_2H_5

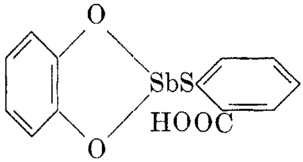
d. R = $CH_3CH_2CH_2$

e. R = $(CH_3)_2CH$

f. R = n-C_4H_9



III



IV

In these cases the aryl group was phenyl (4), *p*-tolyl (4), *p*-acetaminophenyl (5), sodium *o*-carboxyphenyl (6), and *o*-carbomethoxyphenyl (7). Other compounds reported in which an aryl residue is linked through sulfur to antimony are IIa and III (5) and IV (8). All of these compounds were prepared by the above two reactions or by similar ones using antimony trioxide. In view of the paucity of data on tri-(arylmercapto)-S-antimonous acids it was decided to undertake an investigation of the means of making such compounds.

In the present series of experiments fifteen thiophenols were used. These were thiosalicylic acid, methyl thiosalicylate, ethyl thiosalicylate, propyl thiosalicylate, isopropyl thiosalicylate, butyl thiosalicylate, *m*-mercaptobenzoic acid, methyl *m*-mercaptobenzoate, ethyl *m*-mercaptobenzoate, *p*-mercaptobenzoic acid, methyl *p*-mercaptobenzoate, thiophenol *p*-sulfonic acid, *o*-nitrothiophenol, *p*-nitrothiophenol, and *p*-methoxythiophenol. These mercaptans were chosen primarily because of accessibility and are predominantly compounds containing electron-attracting groups. Most of the experiments were carried out by boiling a solution of a thiophenol and antimony trichloride using a 1:1 or 3:1 molar ratio of mercaptan to antimony compound. Solvents used were carbon tetrachloride, ether, acetic acid, and 10% hydrochloric acid. Some of the thiophenols were heated in a sodium carbonate solution with antimony trioxide using a 6:1 molar ratio of mercaptan to antimony compound. The reactions were run for periods of two to forty hours. Attempts were made to cause thiosalicylic acid to react with antimony trichloride at a temperature of 160° using no solvent. The reaction of the sodium salt of methyl thiosalicylate with antimony trichloride was also tried. Most of the experiments were unsuccessful. The only exceptions were those using *p*-nitrothiophenol and thiosalicylic acid and its esters.

Esters of thiosalicylic acid reacted with equimolecular amounts of antimony trichloride to give IIb, IIc, IId, IIe, and IIf in good yields for the most part. The products were light yellow solids forming needle-like crystals upon crystallization from carbon tetrachloride. Recrystallizations from the same solvent caused slight decomposition. These antimony compounds were unstable in alcoholic and aqueous solution and on long standing. Alcoholysis or hydrolysis gave a water-insoluble antimony compound and chloride ion. The structure IIb was assigned to the product of the reaction of methyl thiosalicylate with antimony trichloride from a consideration of its great reactivity and from analytical data. The structures of IIc, IId, IIe, and IIf were assigned from analytical data and from their similarity to IIb in method of synthesis. Attempted replacement of the two chlorine atoms in IIb by groups such as RS- was unsuccessful.

Klement and May (5) have reported that the reaction of thiosalicylic acid with antimony trichloride gave IIa and III. Several attempts to repeat these workers' results were not entirely successful. Two compounds in addition to thiosalicylic acid were isolated by fractional crystallization of the reaction mixture. The lower-melting fraction (m.p. 80–104°) had a carbon-hydrogen content approaching that of III while the higher-melting fraction gave analytical data approximating the theoretical analysis for IIa. Purification of these two fractions resulted in compounds melting at 76–81° and 113–115°. The analytical data for both of these compounds indicated that they had structure IIa although neither set of data were in complete accord with this structure. The higher-melting fraction isolated in a later experiment had a sulfur analysis much closer to structure IIa but the antimony analysis was not as close. When the high-melting and low-melting fractions were mixed, the melting point of the mixture was intermediate between that of the two fractions. It is probable that compound V of Klement and May (5) has structure IIa.

The reaction of *p*-nitrothiophenol with antimony trichloride in carbon tetrachloride gave tri-(*p*-nitrophenylmercapto)-S-antimonous acid (I when aryl is *p*-nitrophenyl) in poor yield. The product was a bright yellow solid which was recrystallized from acetone. This compound was quite stable to water and alcohol. The structure assigned to this compound was deduced from analyses and method of synthesis.

The ready replacement of only one chlorine atom in antimony trichloride by a thiosalicylic acid or ester residue is difficult to explain since the other mercaptans used did not undergo such a reaction. Methyl *p*-mercaptobenzoate would be expected to react more readily than the *ortho* isomer as no steric hindrance would be present. German Patent 552,447 (7) describes the reaction of methyl thiosalicylate with antimony trioxide at about 160° in a hydrogen or carbon dioxide atmosphere to give a product presumably having structure I in which the aryl group is *o*-carbomethoxyphenyl. Attempted repetition of this work was unsuccessful. It is possible that others of the thiophenols studied gave reactions similar to that of *p*-nitrothiophenol, and that a combination of poor yield and a complex reaction mixture prevented isolation of such products.

The thiophenols used were either commercial products or were prepared by well-known reactions. However, repetition of a number of published methods for synthesis of *m*-mercaptobenzoic acid led to the conclusion that these methods were impractical for synthetic work. Consequently a modification of the method of Schwarzenbach and Rudin (9) has been developed to give fair yields of *m*- and *p*-mercaptobenzoic acids. This method is quite reliable.

I am indebted to Messrs. W. L. Brown and H. L. Hunter for the microanalyses reported in this paper and to Dr. H. L. Breunig and Mrs. Marilyn Creedon for portions of the experimental work.

EXPERIMENTAL

General. The experimental conditions used in the preparation of tri-(*p*-nitrophenylmercapto)-S-antimonous acid were quite similar to those used in most of the runs made in this series of experiments. In some cases the molar ratio of mercaptan to antimony trichloride was 3:1. When antimony oxide was used the experiments were run in water using a mercaptan: sodium carbonate: antimony trioxide molar ratio of $1:1:\frac{1}{6}$.

Thiophenols. Thiosalicylic acid and *thiophenol p-sulfonic acid* were commercial products. *o-Nitrothiophenol* was prepared according to the method of Lecher and Simon (10). *p-Nitrothiophenol* was prepared according to the method of Price and Stacy (11). *p-Methoxythiophenol* was prepared as described by Suter and Hauser (12). *Esters* of *thiosalicylic* acid were prepared by Fischer esterification of thiosalicylic acid.

Methyl m-mercaptobenzoate. A mixture of 34.2 g. (0.25 mole) of *m*-aminobenzoic acid, 48.5 cc. of concentrated hydrochloric acid, and 108 g. of ice was stirred at a temperature below 10° while 17.2 g. (0.25 mole) of sodium nitrite dissolved in 108 cc. of water was added slowly.

A solution of 40 g. (0.25 mole) of potassium ethyl xanthate in 50 cc. of water was added to 32.4 g. (0.3 mole) of sodium carbonate in 216 cc. of water. The resulting solution was stirred at 60–70° while the cold diazonium solution was added and then the stirring was continued at the same temperature for one hour after addition was complete. The reaction mixture was boiled for two hours with 40 g. (1.0 mole) of sodium hydroxide in 108 cc. of water. The alkaline solution was acidified slowly with concentrated hydrochloric acid. Alkaline hydrolysis and acidification were carried out under nitrogen. The solid product was dried for 18 hours in a vacuum desiccator.

The still damp solid was stirred with 500 cc. of boiling methanol while the methanol was saturated with dry hydrogen chloride. The cooled reaction mixture was filtered, and the solvent was removed from the filtrate by evaporation on the steam-bath under reduced pressure. The residue was distilled *in vacuo*. The fraction boiling at 120–135°/11 mm. was retained and redistilled. The second distillation gave 13.9 g. (33%) of methyl *m*-mercaptobenzoate, b.p. 126–131°/11 mm.

Ethyl m-mercaptobenzoate. This ester was prepared as was the methyl ester. The yield of ethyl *m*-mercaptobenzoate, b.p. 147–149°/11 mm., was 6.8 g. (15%).

Methyl p-mercaptobenzoate. The experimental conditions used were the same as those for methyl *m*-mercaptobenzoate except that *p*-aminobenzoic acid was the starting material. In the first distillation a fraction boiling at 134–150°/11 mm. was retained. Methyl *p*-mercaptobenzoate, b.p. 139–144°/11 mm., m.p. 45–47°, was obtained in a yield of 12.1 g. (29%).

m-Mercaptobenzoic acid. A solution of 50.4 g. (0.3 mole) of methyl *m*-mercaptobenzoate in 300 cc. of water containing 30 g. (0.75 mole) of sodium hydroxide was refluxed in a nitrogen atmosphere for two hours. The cooled reaction mixture was acidified with 75 cc. of concentrated hydrochloric acid by adding the acid slowly under nitrogen with stirring and cooling. The precipitate was removed, washed thoroughly with water, and dried to constant weight in a vacuum desiccator. Recrystallization from a mixture of alcohol and water gave 44.7 g. (96%) of *m*-mercaptobenzoic acid, m.p. 142–145°.

p-Mercaptobenzoic acid. Methyl *p*-mercaptobenzoate was hydrolyzed to *p*-mercaptobenzoic acid as was the *meta*-isomer. The final product was recrystallized from alcohol instead of alcohol-water. The yield of *p*-mercaptobenzoic acid, m.p. 216–219°, was 11.3 g. (36%).

Dichloro-(2-carboxyphenyl)thioantimonite (IIa). A solution of 10 g. (0.044 mole) of freshly distilled antimony trichloride in 100 cc. of dry benzene was added as rapidly as possible to a well-stirred mixture of 22 g. (0.14 mole) of thiosalicylic acid and 160 cc. of dry benzene. No visible reaction occurred. The reaction mixture was stirred for seven hours with constant refluxing. There was some evolution of hydrogen chloride. The hot solution was filtered to remove 0.5 g. of insoluble material, and the filtrate was allowed to stand until a copious precipitate had formed. The precipitate was dried. It proved to be 18.1 g. of thiosalicylic acid, m.p. 158–164°. The filtrate was again allowed to stand until a precipitate had formed. This solid weighed 3.6 g. and melted at 80–104°. It was designated fraction A.

Anal. Calc'd for $C_7H_5Cl_2O_2SSb$: C, 24.27; H, 1.44; S, 9.27.
Calc'd for $C_{14}H_{10}ClO_4S_2Sb$: C, 36.30; H, 2.14.
Found: C, 33.43; H, 2.34.

Three recrystallizations of fraction A from dry benzene gave a white solid, m.p. 76–81°.

Anal. Found: C, 25.47; H, 1.80; S, 9.00.

The filtrate from fraction A was evaporated until nearly all of the benzene was removed. The cooled residue was filtered and the solid thus obtained was dried, m.p. 98–105°. This was designated fraction B.

Anal. Calc'd for $C_7H_5Cl_2O_2SSb$: C, 24.27; H, 1.44; S, 9.27; Sb, 35.16.
Found: C, 24.13; H, 1.77; S, 7.69.

One recrystallization of fraction B from chloroform gave a white solid melting at 113–115°.

Anal. Found: C, 24.18; H, 1.64; S, 10.18; Sb, 35.03.

The mixture melting point of fraction A and B was 108–111°.

Dichloro-(2-carbomethoxyphenyl)thioantimonite (IIb). A mixture of 8.4 g. (0.05 mole) of methyl thiosalicylate, 11.4 g. (0.05 mole) of antimony trichloride, and 200 cc. of dry carbon tetrachloride was refluxed for 16 hours. After a few hours of refluxing a clear solution formed but crystals began to appear again as the refluxing proceeded. The reaction mixture was cooled and filtered, giving 16.2 g. (90%) of light yellow needle-like crystals, m.p. 131–133°. Repeated recrystallization from carbon tetrachloride caused no rise in the melting point.

Anal. Calc'd for $C_8H_7Cl_2O_2SSb$: C, 26.69; H, 1.96; S, 8.90; Sb, 33.83.
Found: C, 26.68; H, 2.07; S, 8.57; Sb, 33.20.

Dichloro-(2-carbethoxyphenyl)thioantimonite (IIc). The procedure described for IIb was used with 139.4 g. (0.76 mole) of ethyl thiosalicylate and 175 g. (0.76 mole) of antimony trichloride. The yield of product, m.p. 114–115°, was 120 g. (42.3%).

Anal. Calc'd for $C_9H_9Cl_2O_2SSb$: C, 28.92; H, 2.43.
Found: C, 28.90; H, 2.59.

Dichloro-(2-carbopropoxyphenyl)thioantimonite (IId). The procedure used was very similar to that described for IIb. There was used 156.6 g. (0.8 mole) of propyl thiosalicylate and 175 g. (0.76 mole) of antimony trichloride. The hot reaction mixture was concentrated to one-half its volume before cooling. The yield of antimony compound melting at 96–97° was 163.8 g. (52.8%).

Anal. Calc'd for $C_{10}H_{11}Cl_2O_2SSb$: C, 30.96; H, 2.84.
Found: C, 31.11; H, 3.16.

Dichloro-(2-carboisopropoxyphenyl)thioantimonite (IIe). This procedure was similar to that described for IId using 162.2 g. (0.83 mole) of isopropyl thiosalicylate and 190 g. (0.83 mole) of antimony trichloride; yield, 200.6 g. (62.6%), m.p. 133–134°.

Anal. Calc'd for $C_{10}H_{11}Cl_2O_2SSb$: C, 30.96; H, 2.84.
Found: C, 30.41; H, 2.94.

Dichloro-(2-carbobutoxyphenyl)thioantimonite (IIf). This procedure was very similar to those described above using 210.3 g. (1.0 mole) of butyl thiosalicylate and 228.1 g. (1.0 mole) of antimony trichloride. After the reaction was complete solvent was removed by reduced pressure evaporation. Most of the residue was dissolved in a mixture of carbon tetrachloride and petroleum ether. The solution was removed by decantation and concentrated by evaporation under reduced pressure. After the residue had stood for several days it became partially solid, was filtered, and the solid was pressed dry on filter paper giving a crystalline product, m.p. 55–56°.

Anal. Calc'd for $C_{11}H_{13}Cl_2O_2SSb$: C, 32.87; H, 3.26.
Found: C, 33.37; H, 3.40.

Tri-(p-nitrophenylmercapto)-S-antimonous acid. A mixture of 91 g. (0.587 mole) of *p*-nitrothiophenol, 133 g. (0.587 mole) of antimony trichloride, and 3.3 l. of dry carbon tetrachloride was stirred and refluxed for 24 hours. The solvent was removed by evaporation. The hot residue was diluted with 115 cc. of acetone and allowed to stand overnight. The crystalline precipitate was washed thoroughly with acetone. The acetone washings were allowed to stand at room temperature for four hours and were filtered again. The solid obtained was boiled with 225 cc. of acetone, and the mixture was filtered. The cooled filtrate deposited 11.7 g. of yellow fluffy crystals, m.p. 182–184°. The yield was 10%.

Anal. Calc'd for $C_{18}H_{12}N_3O_6S_3Sb$: C, 37.35; H, 2.06; N, 7.19; S, 16.44; Sb, 20.83.
Found: C, 36.88; H, 2.26; N, 7.23; S, 16.29; Sb, 21.03.

SUMMARY

The reaction of thiophenols with antimony trichloride and trioxide has been investigated.

Six new products of such reactions were prepared.

A reliable method for the preparation of *m*-mercapto- and *p*-mercapto-benzoic acids has been developed.

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