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The Preparation of Stibonic Acids by the Scheller Reaction

BY G. O. DOAK AND HARRY G. STEINMAN

The Scheller reaction[1] has been used extensively in this Laboratory for the preparation of arylarsonic acids.[2] We have now extended this study to the preparation of the analogous antimony compounds. The reaction was found to be applicable to aniline and its meta and para substituted derivatives, but with ortho substituted anilines the yields were poor.

Arylstibonic acids prepared by either the customary diazo reaction or the Scheller reaction contain antimony trioxide as an impurity. With the latter reaction this cannot be prevented by using an excess of the diazonium compounds. The methods for purification reported in the literature, such as repeated precipitation from alkaline solution[3a] or purification through the ammonium or pyridinium arylchloroantimonates,[3b,c] were not entirely satisfactory in that different lots of the same compound often gave different analytical results. A few stibonic acids were successfully purified by recrystallization from organic solvents but this method was of only limited application.

We have found that arylstibonic acids can be purified by recrystallization of the corresponding pyridinium arylchloroantimonates $[(ArSbCl_5)^-(C_5H_5NH)^+]$, using as a solvent a mixture of hydrochloric acid and an alcohol (methyl, ethyl or isopropyl).[4] In addition, the recrystallized pyridinium salts gave reproducible melting points which could be used to characterize and identify the individual stibonic acids.

The pyridinium salts were usually prepared by dissolving the stibonic acid in hot concentrated hydrochloric acid and adding a solution of pyridine hydrochloride in hydrochloric acid, whereupon the crystalline pyridinium salt precipitated. Certain stibonic acids, which were only slightly soluble in hydrochloric acid, *e.g.*, *p*-nitrobenzenestibonic acid, and stibonic acids which contained groups subject to acid hydrolysis, *e.g.*, the esters of stibonobenzoic acids described in the following paper, were dissolved in methanol- or ethanol-hydrochloric acid and the pyridinium salts precipitated from these solutions. We were unable to obtain satisfactory pyridinium salts with certain ortho substituted stibonic acids, which underwent disproportionation, and with stibonic acids substituted by amide or similar groups which were hydrolyzed under the experimental conditions. The pyridinium salts obtained from stibonic acids containing free carboxyl groups could not be recrystallized from methanol- or ethanol-hydrochloric acid, as the carboxyl group was esterified under these conditions. With *m*-stibonobenzoic acid, but not the para isomer, the pyridinium salt was successfully recrystallized from isopropyl alcohol-hydrochloric acid. The methods used for purifying those stibonic acids which failed to yield satisfactory pyridinium salts are described in the experimental part.

(1) Scheller, French Patent 624,028; *Chem. Zentr.*, **98**, II, 229 (1927).

(2) Doak, THIS JOURNAL, **62**, 167 (1940); Doak, Steinman and Eagle, *ibid.*, **62**, 3012 (1940); **64**, 1064 (1942); **66**, 194, 197 (1944); Steinman, Doak and Eagle, *ibid.*, **66**, 192 (1944).

(3) (a) Mistry and Guha, *J. Indian Inst. Sci.*, **15A**, 25 (1932); (b) Schmidt, *Ann.*, **421**, 174 (1920); (c) Schmidt, *ibid.*, **429**, 144 (1922).

(4) Pfeiffer and Schmidt, *J. prakt. Chem.*, **152**, 27 (1939), recrystallized pyridinium bromo-β-naphthylantimonate from acetone. With the compounds described in the present paper neither acetone, methanol nor ethanol were satisfactory as solvents.

Experimental

Procedure

The amine (0.2 mole) was dissolved or suspended in 500 ml. of absolute alcohol[5] in a 3-liter beaker which was surrounded by an ice-bath equipped with an efficient stirring device. Sulfuric acid (20 g.) and antimony trichloride (55.6 g., 0.2 mole) were added. When the latter had completely dissolved, diazotization was effected with 14 g. of sodium nitrite dissolved in 20 ml. of water. In several reactions the antimony trichloride was added after diazotization without affecting the results. The thick mixture was stirred for one-half hour, when 4 g. of cuprous bromide was added and the ice-bath removed. Nitrogen was evolved spontaneously as the mixture warmed. With *p*-nitroaniline, *p*-aminobenzoic acid and similar amines the evolution of nitrogen was complete in from one-half to two hours. With amines such as *m*- and *p*-toluidine as long as twenty-four hours were required. Warming the reaction mixture to 60° facilitated the evolution of nitrogen in these cases with no apparent decrease in yield. When the evolution of nitrogen was complete, the reaction mixture was steam distilled to remove the alcohol, and the crude stibonic acid separated by filtration, washed with water, and finally pressed as dry as possible. It was then dissolved either in concentrated hydrochloric acid or a mixture of hydrochloric acid and methanol or ethanol (1:1), depending on the particular stibonic acid, and 100 ml. of pyridine reagent added. The latter was prepared by diluting 80 ml. of concentrated hydrochloric acid to 100 ml. with technical pyridine. After cooling to room temperature, the precipitated pyridinium salt was removed by filtration through a sintered glass filter and washed several times with concentrated hydrochloric acid. It was then dissolved in dilute sodium carbonate solution (about 6 liters of approximately a 1% solution was usually required), filtered if necessary, and the filtrate stirred with 5 g. of activated charcoal and again filtered. The free acid was obtained from the filtrate by the dropwise addition of dilute hydrochloric acid, while stirring rapidly. It was transferred to a large Büchner funnel and thoroughly washed with water acidified with a few drops of dilute hydrochloric acid. Use of this acid wash water largely prevented the amorphous stibonic acids from peptizing and passing through the filter. After drying to constant weight in the air, the resulting stibonic acids were usually sufficiently pure for use in the preparation of various derivatives. In order to obtain analytically pure compounds they were dissolved in hydrochloric acid

(5) Isopropyl alcohol, 99.4%, obtained from the Carbon and Carbide Chemicals Corporation, was used in several reactions.

TABLE I

STIBONIC ACIDS AND THE CORRESPONDING PYRIDINIUM ARYLCHLOROANTIMONATES

Stibonic acid	Yield, %[a]	Formula[b]	Sb analyses, % Calcd.	Sb analyses, % Found	Pyridinium arylchloroantimonate formula	M. p., °C.[c]	Sb analyses, % Calcd.	Sb analyses, % Found	Cl analyses, %[d] Calcd.	Cl analyses, %[d] Found
Benzene-	39, 16[e]	$C_6H_7O_3Sb$	49.0	49.0 48.8[o]	$C_{11}H_{11}Cl_5NSb$	139	26.7	26.7	38.9	39.2
o-Toluene-	2, 37[f]	$C_7H_9O_3Sb$	46.3	46.3	$C_{12}H_{13}Cl_5NSb$	172.6	25.9	25.9	37.7	38.3
m-Toluene-	24	$C_7H_9O_3Sb$	46.3	46.3	$C_{12}H_{13}Cl_5NSb$	203.6	25.9	25.6	37.7	37.5
p-Toluene-	47	$C_7H_9O_3Sb$	46.3	46.3 46.2[o]	$C_{12}H_{13}Cl_5NSb$	180	25.9	25.9	37.7	37.9
o-Bromobenzene-	1, 2[f]	$C_6H_6BrO_3Sb$	37.2	37.1	$C_{11}H_{10}BrCl_5NSb$	164	22.8	22.8	33.2	33.2
p-Bromobenzene-	40	$C_6H_6BrO_3Sb$	37.2	37.1	$C_{11}H_{10}BrCl_5NSb$	154	22.8	22.7	33.2	33.1
p-Chlorobenzene-	78	$C_6H_6ClO_3Sb\cdot H_2O$	40.4	40.2	$C_{11}H_{10}Cl_6NSb$	160	24.8	24.8	36.3	36.2
o-Nitrobenzene-	16	$C_6H_6NO_5Sb\cdot H_2O$[g]	39.1	39.3	[m]					
m-Nitrobenzene-	46	$C_6H_6NO_5Sb\cdot H_2O$[h]	39.1	39.4	$C_{11}H_{10}Cl_5N_2O_2Sb$	187	24.3	24.2	35.4	35.3
p-Nitrobenzene-	53, 37.5[e]	$C_6H_6NO_5Sb\cdot H_2O$[i]	39.1	38.7	$C_{11}H_{10}Cl_5N_2O_2Sb$	168.5	24.3	24.1	35.4	36.0
p-Carbamylbenzene-	49	$C_7H_8NO_4Sb\cdot H_2O$[j]	39.3	39.1	[m]					
o-Stibonobenzoic	0, 83[f]	$C_7H_7O_5Sb\cdot H_2O$	39.2	38.9	[m]					
m-Stibonobenzoic	72[e]	$C_7H_7O_5Sb$	41.6	41.5	$C_{12}H_{11}Cl_5NO_2Sb$	293	24.4	24.5	35.6	35.6
p-Stibonobenzoic	68, 72[e]	$C_7H_7O_5Sb\cdot H_2O$	39.2	39.2	$C_{12}H_{11}Cl_5NO_2Sb$[n]	252	24.4	24.6	35.6	35.6
p-Stibonophenoxy-acetic	26	$C_8H_9O_6Sb$	37.7	37.6	$C_{13}H_{13}Cl_5NO_3Sb$[n]	114	23.0	22.9	33.5	33.2
6-Nitro-*o*-toluene-	30	$C_7H_8NO_5Sb$[k]	39.6	38.9	[m]					
3-Nitro-*p*-toluene-	27	$C_7H_8NO_5Sb$[l]	39.6	39.6	$C_{12}H_{12}Cl_5N_2O_2Sb$	191	23.6	23.6	34.4	34.0

[a] The majority of the stibonic acids described have been prepared three or more times in quantities of from 0.1 to 1 mole, with remarkably consistent yields. In these cases, the percentage yields given are the average. [b] Schmidt (ref. 3b) regards arylstibonic acids in the solid state as trimers, with variable degrees of hydration. Evidence will be presented in a following paper which throws considerable doubt on such a structure. [c] For the method used for melting points, see THIS JOURNAL, **66**, 192 (1944). [d] Ionizable chlorine. [e] Isopropyl alcohol was used in the Scheller reaction. [f] Prepared by the customery diazo procedure in aqueous alkaline reaction. [g] N Calcd.: 4.49. Found: 4.48. [h] N Calcd.: 4.49. Found: 4.52. [i] N Calcd.: 4.49. Found: 4.55. [j] N Calcd.: 4.52. Found: 4.62. [k] N Calcd.: 4.55. Found: 4.56. [l] N Calcd.: 4.55. Found: 4.51. [m] Pyridinium salts of these compounds could not be prepared. [n] The analyses are for the unrecrystallized pyridinium salts, as these compounds are esterified by recrystallization from methanol- or ethanol-hydrochloric acid. [o] Prepared by hydrolysis of the tetrachloride.

and the pyridinium salt again precipitated. These salts were then recrystallized from methanol- or ethanol-hydrochloric acid (1:1). Alternatively, the pyridinium salts from the original precipitation were recrystallized one or more times from the same solvents, the crystals washed with hydrochloric acid, dissolved in sodium carbonate solution and the free acid obtained as previously described.[6] A second precipitation from sodium carbonate solution gave a pure white compound in every case.[7]

With several compounds it was found necessary to modify the general procedure described above. In the preparation of *p*-carbamylbenzenestibonic acid, steam distillation was omitted and the crude acid precipitated from the reaction mixture by pouring into water. The precipitate was washed with water and then triturated with concentrated hydrochloric acid to remove any *p*-stibonobenzoic acid formed by hydrolysis of the amide group. The insoluble residue was then hydrolyzed with cold water, washed and dried.

The pyridinium salt of *o*-nitrobenzenestibonic acid could not be prepared. When this acid was warmed with concentrated hydrochloric acid it underwent disproportionation. The fraction insoluble in hydrochloric acid, after treatment with water, analyzed as *o,o'*-dinitrodiphenylstibinic acid.

Anal. Calcd. for $C_{12}H_9N_2O_6Sb\cdot H_2O$: Sb, 29.2; N, 6.72. Found: Sb, 29.8; N, 6.67.

From the hydrochloric acid solution antimonic acid was obtained on dilution with water. *o*-Nitrobenzenestibonic acid was therefore purified by trituration with ice-cold concentrated hydrochloric acid. The insoluble residue was dissolved in dilute sodium carbonate solution and the free acid obtained by acidification. It was again triturated with hydrochloric acid and the process repeated. The desired compound was obtained as a colorless powder.

The preparation of *o*-bromobenzenestibonic acid, *o*-toluenestibonic acid and *o*-stibonobenzoic acid by the Scheller reaction was unsatisfactory. They were prepared by the customary diazo procedure, but in the case of *o*-bromobenzenestibonic acid the yields were still poor.

Benzene- and *o*-bromobenzenestibonic acid, and *o*-, *m*- and *p*-toluenestibonic acids were successfully recrystallized from acetic acid. The amorphous stibonic acids were dissolved in the hot solvent, filtered and the solvent allowed to evaporate spontaneously. The crystalline precipitates were dried over sodium hydroxide *in vacuo* at 100°, and then exposed to air for twenty-four hours prior to analysis. Benzene- and *o*-bromobenzenestibonic acids were obtained as needles; *m*- and *p*-toluenestibonic acids as diamond-shaped plates. Analyses of the recrystallized acids were in agreement with those from the amorphous compounds.

Benzene- and *p*-toluenestibonic acids were converted to the corresponding tetrachlorides by treatment with cold concentrated hydrochloric acid, and then hydrolyzed back to the stibonic acids. Analyses of the resulting compounds agreed with those of the original acids, before such treatment. This is in contrast to the findings of Schmidt,[3b] who obtained acids with lower antimony values by hydrolysis of the tetrachlorides.

Table I lists the stibonic acids prepared together with the corresponding pyridinium salts. *o*- and *m*-toluene-, 6-nitro-*o*-toluene- and 3-nitro-*p*-toluenestibonic acids, *o*-bromo- and *p*-carbamylbenzenestibonic acids, and *o*-

(6) While the loss from recrystallization was usually slight, a further yield of crude stibonic acid could be obtained by treating the mother liquors with sufficient water to precipitate any dissolved compound.

(7) *p*-Nitrobenzenestibonic acid, previously reported as colored (Charrier, *Gazz. chim. ital.*, **52**, II, 16 (1922)) was obtained as a white powder by this procedure.

and *p*-stibonobenzoic acids have not been previously described. *p*-Stibonophenoxyacetic acid has been reported by Brahmachari,[8] but no analyses were given. *m*-Stibonobenzoic acid apparently has been prepared by Dyson,[9] but the method of preparation was not mentioned nor were analyses given. The other stibonic acids listed have been prepared by other workers using the customary diazo procedure. Antimony was determined by titration with standard potassium bromate solution and the results reported are the average of two or more determinations.

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(8) Brahmachari, *Indian J. Med. Research*, **10**, 492 (1922).

(9) Dyson, *Rec. trav. chim.*, **57**, 1016 (1938).

Summary

A number of arylstibonic acids have been prepared by the Scheller reaction. Satisfactory results were obtained with aniline and its derivatives substituted in meta and para position, but not with derivatives substituted in ortho position. The majority of the stibonic acids prepared were purified by recrystallization of the corresponding pyridinium arylchloroantimonates. The latter compounds were found to give definite melting points which served to characterize the individual stibonic acids.

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Some Reactions of Arylstibonic Acids

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The present communication describes the preparation of stibonic acids by reactions such as oxidation, esterification and ammonolysis, using as starting materials the stibonic acids prepared by the Scheller reaction and described in a previous paper.[1]

While such reactions have been used successfully for the preparation of arsonic acids, the metal–carbon bond is considerably weaker in the arylstibonic acids. In consequence, the resulting compounds are usually high in antimony, presumably due to rupture of the antimony–carbon bond during the reaction with the formation of inorganic antimony compounds. While many of these compounds could be purified by recrystallization of the corresponding pyridinium salts, this procedure was limited to compounds which did not disproportionate or hydrolyze under the conditions necessary for recrystallization, and was not applicable to many ortho substituted stibonic acids or compounds containing amide groups. Compounds in the latter class, prepared by ammonolysis of the corresponding esters, usually gave nitrogen analyses slightly lower than theoretical, presumably due to slight hydrolysis of the ester. No general method for purifying these compounds has been discovered. Where the pyridinium salts could be prepared and recrystallized, their melting points served to identify the individual stibonic acids and particularly to confirm the synthesis of the same compound by two or more different procedures.

Experimental

3-Nitro-*p*-toluenestibonic Acid.—*p*-Toluenestibonic acid (26.4 g., 0.1 mole), dissolved in 125 ml. of sulfuric acid was nitrated at 0–5° with a mixture of 7 ml. of sulfuric acid and 7 ml. of nitric acid (d. 1.14). The nitration mixture was poured onto ice and the resulting precipitate washed with water and purified through the pyridinium salt. The latter compound, when recrystallized from ethanol–hydrochloric acid (1:1), was identical (melting point, mixed melting point and analyses) with the pyridinium salt from the 3-nitro-*p*-toluenestibonic acid prepared by the Scheller reaction.

(1) Doak and Steinman, THIS JOURNAL, **68**, 1987 (1946).

Oxidation of Toluenestibonic Acids

***p*-Stibonobenzoic Acid.**—*p*-Toluenestibonic acid (26.4 g., 0.1 mole), was suspended in 500 ml. of hot water and 100 ml. of *N* potassium hydroxide, and oxidized at 80° with 35 g. of powdered potassium permanganate. The reaction was complete in two hours, when excess permanganate was destroyed with alcohol, the manganese dioxide removed by filtration and thoroughly washed with hot water. The impure *p*-stibonobenzoic acid, obtained by acidification of the combined filtrate and washings, was purified through the pyridinium salt. The latter compound was identical with the pyridinium salt from the *p*-stibonobenzoic acid prepared by the Scheller reaction.

2-Nitro-4-stibonobenzoic acid was prepared in a similar manner. The pyridinium salt was recrystallized without esterification from ethanol–hydrochloric acid.

The oxidation of *o*-toluene- and 6-nitro-*o*-toluenestibonic acids yielded principally antimony pentoxide.

The Esterification of Stibonobenzoic Acids

Methyl and Ethyl *p*-Stibonobenzoate.—The corresponding acids (20 g.) were suspended in 200 ml. of dry methanol at 0° and a stream of dry hydrogen chloride passed in for six hours. The resulting clear solutions were allowed to stand overnight at room temperature and then added to 3 liters of cold water to precipitate the esters. **Methyl *m*-stibonobenzoate** was prepared from *m*-stibonobenzoic acid (10 g.) by refluxing in methanol solution (100 ml.) for fifteen minutes, using sulfuric acid (10 g.) as a catalyst. The ester was precipitated from solution by the addition of water. The purification of all three esters described above was effected through the corresponding pyridinium salts.

A third method for preparing carboxy esters of stibonic acids has been found which is simple and of general applicability. The pyridinium salt of the corresponding stibonobenzoic acid was dissolved in warm methanol– or ethanol–hydrochloric acid mixture. The pyridinium salt of the ester separated from solution on cooling, and was readily converted to the desired ester stibonic acid by hydrolysis. The methyl and ethyl esters of both *m*- and *p*-stibonobenzoic acids have been prepared in this manner.