TABLE V

Number	EVK	1	2	3	4	5	6	7	8	9	MIK
% MIK in monomer mixture	0	10.47	20.49	29.37	39.91	50.25	60.24	70.41	80.50	89.43	100
$n^{20}D$	1.4182	1.4189	1.4195	1.4200	1.4204	1.4210	1.4214	1.4220	1.4225	1.4230	1.4233
d^{20}_{20}	0.8497	0.8498	0.8504	0.8503	0.8508	0.8522	0.8524	0.8532	0.8537	0.8539	0.8541
Days to form solid polymer	1	1	1	2	3	2	4	4	5	6	6
Degree of yellow color (relative)	1	1	2	3	4	5	4	3	2	1	1
Rockwell hardness (15X)		Too soft to test			69.7	82.5	90.0	92.1	92.8	93.0	94.5

set aside at Dry Ice temperature overnight. A considerable quantity of a white, crystalline solid separated; a portion, crystallized from absolute ethanol, melted at 56.3–56.7°. The mixed melting point value was 56.0–56.7°.

Polymerization.—A series of mixtures of the two authentic monomers was prepared for refractive index and density determinations. To 10 ml. of each mixture was added 0.1 ml. of a commercial 30% solution of acetyl peroxide in dimethyl phthalate. The reactions were run in sealed ampoules at 40°. The results are presented in Table V.

Summary

The syntheses of authentic ethyl vinyl ketone and methyl isopropenyl ketone by independent routes have been described.

By comparison of the properties of these products with those of the purified materials isolated from the catalytic vapor phase reaction of methyl ethyl ketone and formaldehyde, it has been established that the vapor-phase reaction leads to the formation of both ketones.

The physical properties of the ketones and of some of their derivatives have been described.

KINGSPORT, TENNESSEE RECEIVED FEBRUARY 16, 1948

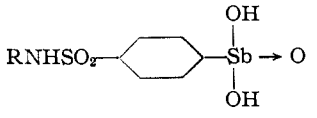
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF COLORADO]

The Preparation of Aromatic Stibonic Acids of Certain Benzenesulfonamides

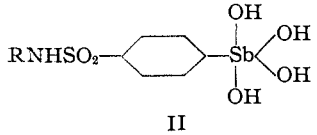
BY ROBERT D. ENGLERT[1] AND ORVILLE J. SWEETING

In connection with work in this Laboratory on the chemotherapy of Schistosomiasis it was of interest to prepare for test pure samples of stibonic acids derived from certain sulfonamides: sulfanilamide, sulfathiazole, sulfapyridine, and sulfadiazine. For the tests of biological activity, it was necessary to obtain the stibonic acids free from extraneous toxic antimony compounds such as the oxides.

The structure of these compounds in the solid state, all of which melt at high temperatures, has been explained in terms of polymers associated through hydrogen bonding,[2] but for simplicity these compounds may be formulated as follows, I representing the acid and II the corresponding hydrated form, in which R represents hydrogen or the 2-thiazolyl, 2-pyridyl, or 2-pyrimidyl radical.



I



II

Two methods of synthesis have been used, with concordant results: decomposition of the aryldiazonium fluoborate salts in a manner similar to that used for preparing aromatic arsonic acids,[3] and a modified Scheller reaction.[4]

In many cases it has been found that different preparations of the same stibonic acid give inconsistent analyses when purified by double precipitation methods from alkaline solution by addition of strong acid; it was for this reason that the pyridinium arylchloroantimonates,[5] $[ArSbCl_5]^-[C_5H_5NH]^+$, were recrystallized from a solvent of mixed hydrochloric acid and ethanol. This procedure gave quite pure aromatic stibonic acids except with the product from sulfapyridine. The latter acid was purified only with difficulty, since the pyridine nucleus of the stibonic acid no doubt retains some antimony.

Experimental Part

Melting points were observed with a Fisher–Johns melting point apparatus and are uncorrected unless otherwise stated. Analyses for antimony were done by a micro titration with standard potassium bromate solution and for chloride by the micro Volhard method, using 5- to 10-mg. samples of the stibonic acid.

Preparation of an Aromatic Stibonic Acid *via* the Diazonium Fluoborate.—Diazonium fluoborates have not been extensively used for the preparation of organic arsenical and antimonial compounds. In many instances, however, the fluoborates are advantageous to use instead of other diazonium compounds since their stability toward heat results in diminished tendency to form undesirable products.[6] It was therefore thought advisable to investi-

(1) Fellow in Chemistry at the Chemical Foundation Laboratory, by grant from the U. S. Public Health Service.

(2) Doak, THIS JOURNAL, **68**, 1991 (1946).

(3) Ruddy, Starkey and Hartung, *ibid.*, **64**, 828 (1942); Hamilton and Morgan in "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 419.

(4) Scheller, British Patent 261,026 (1925) [*C. A.*, **21**, 3371 (1927)]; French Patent 624,028 [*Chem. Zentr.*, **98**, II, 2229 (1927)]; Doak, THIS JOURNAL, **62**, 167 (1940).

(5) Doak and Steinman, *ibid.*, **68**, 1987 (1946).

(6) See Hamilton and Morgan, ref. 3.

gate the use of the fluoborates in the preparation of aromatic stibonic acids.

A mixture of 51.6 g. (0.30 mole) of sulfanilamide, 31.0 ml. of concentrated hydrochloric acid, and 100 ml. of water was heated in an 800-ml. beaker on a steam-bath until solution was complete. The mixture, cooled in an ice-bath, was treated with 20.7 g. of sodium nitrite in about 30 ml. of water; the temperature remained below 5° during diazotization. When all of the sodium nitrite had been added, 70 ml. of cold fluoboric acid solution (40%) was added gradually. The temperature increased only slightly and the mass became firm enough to stop a mechanical stirrer. The rest of the fluoboric acid solution was added at temperatures below 10°, while stirring was continued manually for fifteen minutes. The filtered diazonium fluoborate was washed successively with 100 ml. of ice water, 65 ml. of methanol, and 40 ml. of ether, and sucked as dry as possible after each washing. The product amounted to 59.0 g. after it had been air-dried overnight, 74% of the theoretical yield. The decomposition temperature was 111°.

To a mixture of 13.5 g. (0.050 mole) of *p*-sulfonamidobenzenediazonium fluoborate and 11.4 g. (0.050 mole) of antimony trichloride in 60 ml. of 95% ethanol, 0.5 g. of cuprous chloride was added in several small portions. The mixture was stirred while a vigorous and steady reaction occurred and, after the reaction had moderated, was placed on a steam-bath and heated to about 45°. The mass dissolved to give a red solution which was heated at 60° for fifteen minutes. The solution was treated with 60 ml. of concentrated hydrochloric acid followed by 25 ml. of pyridine reagent (20 ml. of concentrated hydrochloric acid and 5 ml. of pyridine). Crystals of the pyridinium salt of the stibonic acid began to form almost immediately and 10 ml. of concentrated hydrochloric acid was then added. After cooling, the precipitate was filtered and washed with concentrated acid until the washings became colorless. The crystals were dissolved in 120 ml. of a 1:1 mixture of ethanol and concentrated hydrochloric acid and as soon as crystals appeared, 20 ml. more of the acid was added. On cooling, the crystalline pyridinium salt was obtained and the filtrate was reworked to recover further product. The pyridinium salt, very slightly pink in color, melted at 216° (cor.) after drying for thirty-six hours.

Anal. Calcd. for $C_{11}H_{12}O_2N_2Cl_5SSb$: Sb, 22.8; Cl, 33.2. Found: Sb, 23.2; Cl, 33.1.

The pyridinium salt was decomposed in 1% aqueous sodium carbonate, decolorized with activated charcoal, and filtered. Dropwise addition of hydrochloric acid to the filtrate, with rapid stirring, precipitated the stibonic acid. This was collected on a buchner funnel and washed with large amounts of water, slightly acidified with hydrochloric acid. The stibonic acid was redissolved in carbonate solution and reprecipitated. It was left over sodium hydroxide overnight, followed by drying at 90° under reduced pressure. The acid was exposed to air for twenty-four hours before analysis. The yield of *p*-sulfonamidobenzenestibonic acid monohydrate was 7.8 g. (45%) from 0.050 mole of the diazonium fluoborate, or an over-all yield of 33% based on the original amine.

Anal. Calcd. for $C_6H_8O_5NSSb \cdot H_2O$: Sb, 35.20. Found: Sb, 35.7.

Preparation of Aromatic Stibonic Acids by a Modified Scheller Reaction.—Diazotization of the amine, introduction of antimony and purification of the resulting stibonic acid were accomplished in essentially the manner described by Doak and Steinman.[5] Decomposition of the diazo-antimony trichloride complex was effected, however, by 2 g. of cuprous chloride for each 0.1 mole of amine and the nitrogen was allowed to evolve spontaneously for twenty-four hours before the action was brought to completion by heating to 60°. The mixture was then diluted with three times its volume of cold water and the precipitated crude stibonic acid was removed by filtration. The impure acid was washed with water, pressed dry, dissolved in a 1:1 mixture of ethanol and concentrated hydrochloric acid, and treated with a mixture of pyridine in hydrochloric acid to form the pyridinium salt. The precipitated salt was collected on a sintered glass filter and washed with concentrated hydrochloric acid, followed by recrystallization from ethanol–hydrochloric acid mixture.

The sulfathiazole and sulfadiazine derivatives in the pyridinium salt form were best recrystallized by dissolving in alcohol containing a small amount of acid, followed by addition of more hydrochloric acid to a faint turbidity. Cooling then gave well-defined crystals.

The pyridinium salts were decomposed in 1% aqueous sodium carbonate and treated further as already described.

By an alternative method of purification, the crude stibonic acid was dissolved in alcohol, hydrochloric acid, and excess pyridine, followed by pouring with stirring into concentrated hydrochloric acid. After having been collected and washed with concentrated hydrochloric acid on a sintered glass filter, the crystals were decomposed by carbonate and treated as described.

Decomposition of the pyridinium salts gave stibonic acids as white powders in every case. *p*-Sulfonamidobenzenestibonic acid has been reported in the literature previously, prepared by procedures different from those used in the present work. Mingoia and Perego[7] obtained the compound as a brick red solid in the anhydrous form. Several patents[8] also describe the preparation of the compound.

***p*-Sulfonamidobenzenestibonic Acid.**—A yield of 15.6 g. (45%) of a white compound was obtained from 0.1 mole of sulfanilamide. This stibonic acid evidently comes to equilibrium as a monohydrate upon standing in air at the usual temperatures and prevailing relative humidity (about 45%). Various samples analyzed immediately after removal from the desiccator gave 36.7% of antimony, whereas samples which had been left in air and analyzed at times varying from twenty-four hours to more than one month gave 35.2% of antimony. It will be seen that these values agree satisfactorily with the values for the anhydrous and monohydrated stibonic acid, respectively.

Anal. Calcd. for $C_6H_8O_5NSSb$: Sb, 37.13; for $C_6H_8O_5NSSb \cdot H_2O$: Sb, 35.20.

***p*-N-(2-Thiazolyl)-sulfonamidobenzenestibonic Acid.**—A yield of 14.4 g. (35%) was obtained from 0.1 mole of sulfathiazole.

Anal. Calcd. for $C_9H_9O_5N_2S_2Sb$: Sb, 29.62. Found: Sb, 29.5.

***p*-N-(2-Pyridyl)-sulfonamidobenzenestibonic Acid.**—A yield of 10.4 g. (26%) was obtained from 0.1 mole of sulfapyridine. This compound was exceedingly difficult to obtain in the pure state, as has been explained.

Anal. Calcd. for $C_{11}H_{11}O_5N_2SSb$: Sb, 30.06. Found: Sb, 31.4.

***p*-N-(2-Pyrimidyl)-sulfonamidobenzenestibonic Acid.**—A 7.2-g. (18%) yield was obtained from 0.1 mole of sulfadiazine by the usual method of isolation. This was increased to 38%, however, by using the alternative isolation procedure described above.

Anal. Calcd. for $C_{10}H_{10}O_5N_3SSb$: Sb, 29.99. Found: Sb, 30.1.

p-Sulfonamidobenzenestibonic acid has been tested for therapeutic effect against *Schistosoma mansoni* in the mouse. As the sodium salt, it has proved to be more effective than one of the drugs in current use, tartar emetic, but not quite so effective as fouadin. Comparison of fouadin and the stibonic acid sodium salt, A, is given in Table I.[9] It is evident that the efficacy depends upon the

(7) Mingoia and Perego, *Arquiv. biol.* (São Paulo), **28**, 137 (1944). These authors also mention preparation of the stibonic acids derived from sulfathiazole, sulfapyridine and sulfadiazine, but the method employed does not give stibonic acids sufficiently pure for the purposes of the present work.

(8) I. G. Farbenindustrie A.-G., British Patent 487,233 [*C. A.*, **32**, 9403 (1938)]; Schmidt, U. S. Patent 2,215,430 [*C. A.*, **35**, 857 (1941)]; Ida, Japanese Patent 130,481 [*C. A.*, **35**, 5133 (1941)]; Schmidt, German Patent 728,803 [*C. A.*, **38**, 377 (1944)].

(9) Private communication from Lt. (j. g.) J. H. Killough (MCR) USNR, Naval Medical Research Institute, Bethesda, Maryland.

individual schedule used. It is believed that the optimum schedule for A may increase the total possible antimony dosage.

TABLE I

Schedule[a]	Fouadin	A[b]
1/2 LD_{50} 1x/day × 14 days[c]	0.2 worms/mouse[d]	1.4 worms/mouse
1/2 LD_{50} 2x/day × 14 days	0.3 worms/mouse	0.0 worms/mouse
1/2 LD_{50} 2x/day × 7 days	4.5 worms/mouse	14.0 worms/mouse

[a] Drugs administered by intraperitoneal injection. [b] A has twice the efficacy of tartar emetic. [c] LD_{50}/20 g. mouse: fouadin, 18.1 mg.; A, 1.66 mg.; tartar emetic, 0.92 mg. [d] Average number of worms per mouse on autopsy two weeks after therapy; controls had approximately 50 worms per mouse.

Summary

Aromatic stibonic acids have been prepared in pure form from several of the sulfonamides. One of these, *p*-sulfonamidobenzenestibonic acid, displays biological activity against *Schistosoma mansoni* in the mouse.

BOULDER, COLORADO RECEIVED MARCH 26, 1948

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE OHIO STATE UNIVERSITY]

The Molecular Structure of the Two Dimethylhydrazines by Electron Diffraction

BY WILLIAM H. BEAMER[1]

Introduction

The N–N internuclear distance in which the two atoms are bound together by a single covalent bond has been measured for hydrazine by Giguere and Schomaker.[1a] This distance was used by Schomaker and Stevenson,[2] along with the O–O[1a] and F–F[3] distances, as an example of the inadequateness of the simple additivity rule of covalent radii proposed by Pauling.[4] Schomaker and Stevenson suggested that in compounds between atoms differing greatly in electronegativity there is appreciable resonance between ionic and covalent structures (as is known from other considerations) and this resonance leads to shorter interatomic distances. In those bonds which involve like atoms this resonance is at a minimum value. It has been considered worthwhile to extend the results to include a measurement of the N–N single covalent bond distance in the dimethylhydrazines.

By combining the results of the hydrazine investigation with those of dimethylamine[5] one might expect to predict the parameters of asymmetric dimethylhydrazine. The values so predicted were found to fit the observed data well. It was also desired to determine the effects, if any, of the methyl substitution.

The symmetric dimethylhydrazine is of interest because the orientation of the two methyl groups in respect to each other has been a point of discussion. West and Killingsworth[6] determined the electric moment to be 1.35*D*. This would suggest that the *trans* form, which would have no moment, could not be predominant. Penney and Sutherland[7] found hydrazine also to have a dipole moment. They showed that as a result chiefly of the hindrance of rotation about the N–N bond by the interaction of the unsymmetrical wave functions of the two nitrogen atoms the most stable arrangement of hydrazine is that in which the bond angles H–N–H are about 110° and in which one amino group is twisted in respect to the other 90° from the *cis* position. Assuming this same structure for the symmetric dimethylhydrazine West and Killingsworth show that by adding the bond moments for the different bonds of the molecule an electric moment is found which agrees fairly well with the measured value. They also found a Raman spectrum for symmetric dimethylhydrazine which had no strong vibration near 1,000 $cm.^{-1}$, the position at which a symmetrical vibration of the two halves of the molecule along the N–N bond would be expected to fall. This led those investigators to choose for symmetric dimethylhydrazine the structure suggested by Penney and Sutherland.

Boersch[8] investigated the structure of azomethane but was unable to decide between the *cis* and *trans* orientations for the two methyl groups. His work did allow him to exclude the linear model.

It was hoped that an electron diffraction study of symmetric dimethylhydrazine would throw some light on the relative position of the two methyl groups despite the small contribution of the C–C scattering to the total molecular scattering.

Experimental

The asymmetric dimethylhydrazine was prepared by the method of Hatt[9] as the hydrochloride. The melting point of 82.0° indicated high purity. The free dimethylhydrazine was obtained by distillation from a strongly alkaline solution. The product was redistilled at atmospheric pressure. After standing a few hours over pow-

(1) Present address: Spectroscopy Laboratory, The Dow Chemical Company, Midland, Michigan.

(1a) Paul A. Giguere and V. Schomaker, THIS JOURNAL, **65**, 2025 (1943).

(2) V. Schomaker and D. P. Stevenson, *ibid.*, **63**, 37 (1942).

(3) Max T. Rogers, V. Schomaker and D. P. Stevenson, *ibid.*, **63**, 2610 (1941).

(4) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1940.

(5) S. H. Bauer, THIS JOURNAL, **60**, 524 (1938).

(6) W. West and R. B. Killingsworth, *ibid.*, **60**, 1 (1938).

(7) W. G. Penney and G. B. B. M. Sutherland, *Trans. Faraday Soc.*, **30**, 898 (1934); *J. Chem. Phys.*, **2**, 492 (1934).

(8) H. Boersch, *Monatsh.*, **65**, 311 (1935).

(9) H. H. Hatt, "Organic Syntheses," **16**, 22 (1936).