[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Sulfides and Sulfones Derived from *p*-Mercaptophenylarsonic Acid[1]

BY JACK F. MORGAN AND CLIFF S. HAMILTON

Although numerous ethers derived from *p*-hydroxyphenylarsonic acid have been described in the literature, very little is known of the corresponding thioethers or sulfides derived from *p*-mercaptophenylarsonic acid. Only four such compounds, *p*-methyl-,[2a,b] *p*-ethyl-,[3] *p*-benzylmercaptophenylarsonic acid[4] and *p*-arsonophenylmercaptoacetic acid,[2] are described in the literature. In each case they were prepared by means of the Bart[5] or Scheller[6] reactions. *p*-Arsonophenylmercaptoacetic acid has also been produced from diazotized arsanilic acid by treatment with potassium xanthate followed by basic hydrolysis and reaction with monochloroacetic acid.[7]

In the present work one sulfide, *p*-β-hydroxyethylmercaptophenylarsonic acid, was prepared by means of the Bart reaction. Several other sulfides containing substituted aliphatic, heterocyclic and aromatic groups attached to the sulfur atom of *p*-mercaptophenylarsonic acid were synthesized by a more convenient method. *p*-Thiocyanophenylarsonic acid was obtained in 30–45% yields by the method of Barber.[8] Basic hydrolysis of the thiocyano derivative gave an intermediate acid. This intermediate was readily condensed with active aliphatic, heterocyclic and aromatic halides in basic solution to form the desired sulfides. The intermediate is apparently either composed principally of *p*-mercaptophenylarsonic acid or readily yields this arsonic acid when dissolved in alkaline solution.

In general, sulfones are obtained readily from organic sulfides by oxidation with hydrogen peroxide. In this manner both *p*-methyl-[2a] and *p*-ethylsulfonylphenylarsonic acid[3] have been prepared. In addition *p*-methylsulfonylphenylarsonic acid has been synthesized by means of the Bart reaction on *p*-aminophenylmethylsulfone.[9] No other mention is made in the literature of sulfones derived from *p*-sulfophenylarsonic acid.

Ten sulfides derived from *p*-mercaptophenylarsonic acid were, with one exception, readily converted to the corresponding sulfones by treatment with hydrogen peroxide. 2′-Amino-4′-pyrimidyl-4-arsonophenylsulfide decomposed when warmed in perhydrol.

Experimental

_p_-Aminophenyl-β-hydroxyethylsulfide (I).—*p*-Nitrophenyl-β-hydroxyethylsulfide was prepared by the method of Waldron and Reid.[10] By means of hydrogen and Raney nickel, 100 g. of the nitro compound was reduced in acetone solution. Removal of the acetone yielded (I) (84 g., 99%), m. p. 43–44°, b. p. 232–235° (38 mm.) (dec.). The product consisted of a light tan wax-like crystalline mass, soluble in the usual organic solvents and hot water, but almost insoluble in cold water. For analysis a sample of the amine was converted to its hydrochloride.

_p_-Aminophenyl-β-hydroxyethylsulfide Hydrochloride (II).—An ether solution of (I) was treated with dry hydrogen chloride. The precipitated hydrochloride (II) was removed by filtration, washed with ether and recrystallized from ethanol–petroleum ether, m. p. 170°.

Anal. Calcd. for $C_8H_{12}ClNOS$: N, 6.81; Cl, 17.24. Found: N, 6.61; Cl, 16.92.

_p_-β-Hydroxyethylmercaptophenylarsonic Acid (III).—This arsonic acid was readily prepared in yields of 46–48% from the corresponding amine by the method of Bart.[5] The compound was purified by two recrystallizations from water. The white dimorphous solid may be obtained either as leaflets melting at 120.5–121° or as needles melting at 132–133°. Either crystalline form could be obtained from aqueous solution by seeding with the appropriate crystals.

Anal. Calcd. for $C_8H_{11}AsO_4S$: As, 26.93. Found: needles, As, 26.93; leaflets, As, 26.90.

_p_-Thiocyanophenylarsonic acid was prepared by the method of Barber[8] in 30–45% yields.

Intermediate Acid (IV).—A solution of *p*-thiocyanophenylarsonic acid (50 g.) in 500 ml. of 10% sodium hydroxide was refluxed for six hours, cooled and slowly treated with 4 *N* hydrochloric acid. The small amount of red gum, which first separated, was removed and the acidification continued (congo red) to obtain a nearly white precipitate of (IV); yield, 35 g. (78% calcd. as *p*-mercaptophenylarsonic acid). This product does not melt below 250°, is insoluble in boiling water but readily dissolves in dilute sodium hydroxide.

Sulfides Derived from (IV).—The intermediate acid (IV) (11.7 g., 0.05 mole calcd. as *p*-mercaptophenylarsonic acid) and dissolved in an aqueous or dilute alcohol solution of sodium hydroxide (6 g., 0.15 mole) and treated with the appropriate halide (0.1 mole). The mixture was refluxed for a period of four to sixty hours depending on the reactivity of the halide. The crude product which separated on acidification (congo red) was purified by two recrystallizations from water, the hot solution being treated with activated charcoal.

Dilute ethanol (25–30%) was used as solvent when halides of low solubility were employed, *i. e.*, ethyl chloroacetate, *p*-nitrochlorobenzene or 2-amino-4-chloropyrimidine. Because *p*-[β-(β′-hydroxyethoxy)-ethylmercapto]-phenylarsonic acid existed as an oil it was isolated as its sodium salt from ethanol solution.

Sulfones.—The appropriate sulfide (2 g.) was treated with 10 ml. of 27.5% hydrogen peroxide solution and warmed a short time. The resulting solution was allowed to stand overnight and cooled in the refrigerator for several hours. The white crystalline sulfone was removed by filtration, washed with a small amount of water and dried. In a few cases no solid separated and the compounds were isolated by slow evaporation of the peroxide solutions at room temperature. Some of the sulfones were further purified by recrystallization from water.

---

(1) Original manuscript received October 16, 1943.

(2) (a) Doak, Steinman and Eagle, THIS JOURNAL, **62**, 3012 (1940); (b) Streitwolf, Fehrle, Herrmann and Hilmer, German Patent, 536,996 (1930) [*Chem. Zentr.*, **103**, [I] 254 (1932)].

(3) Cherline and Iacoubovitch, *Bull. soc. chim.*, [5] **1**, 1367 (1934).

(4) Takahashi, *J. Pharm. Soc.* Japan, **55**, 875 (1935); *Chem. Abs.*, **30**, 721 (1936).

(5) Bart, *Ann.*, **429**, 55 (1922).

(6) Scheller, British Patent, 261,026 (1925); German Patent, 522,892 (1926).

(7) Lucius and Bruning, German Patent, 216,270 (1908); British Patent, 4246 (1908) [*Chem. Zentr.*, **80** [IV] 2105 (1909)].

(8) Barber, *J. Chem. Soc.*, 2727 (1930).

(9) Barber, *ibid.*, 2047 (1930).

(10) Waldron and Reid, THIS JOURNAL, **45**, 2399 (1923).

TABLE I

SULFIDES

	Name	Yield, %	M. p., °C.	Formula	As analyses, %[11] Calcd.	As analyses, %[11] Found
1	*p*-β-Hydroxyethylmercaptophenylarsonic acid[a] (III)	46–48	120.5–121 132 –133	$C_8H_{11}AsO_4S$	26.93	26.90 26.93
2	*p*-γ-Hydroxypropylmercaptophenylarsonic acid	31	116.3–117.5	$C_9H_{13}AsO_4S$	25.64	25.74
3	*p*-β-Ethoxyethylmercaptophenylarsonic acid	52	121 –122	$C_{10}H_{15}AsO_4S$	24.47	24.65
4	Sodium *p*[-β-(β′-hydroxyethoxy)-ethylmercapto]-phenylarsonate	54	>250	$C_{10}H_{14}AsNaO_5S$	21.77	21.67
5	*p*-Acetonylmercaptophenylarsonic acid	18	172.5	$C_9H_{11}AsO_4S$	25.82	26.05
6	*p*-Arsonophenylmercaptoacetic acid[b]	55	192	$C_8H_9AsO_5S$	25.64	25.65
7	Ethyl *p*-arsonophenylmercaptoacetate[c]	19	123	$C_{10}H_{13}AsO_5S$	23.40	23.56
8	2′-Amino-4′-pyrimidyl-4-arsonophenylsulfide	39	131.5–132	$C_{10}H_{10}AsN_3O_3S$	22.90	22.87
9	4′-Nitro-4-arsonodiphenylsulfide	52	183	$C_{12}H_{10}AsNO_5S$	21.09	21.17
10	4′-Amino-4-arsonodiphenylsulfide[d]	31	211.5 (dec.)	$C_{12}H_{21}AsNO_3S$	23.04	23.07

[a] Prepared by the Bart reaction (specific preparation is given). [b] Previously reported as melting at 187° (ref. 7) and 248–250° (ref. 2b). [c] Also isolate a 27% yield of *p*-arsonophenylmercaptoacetic acid (6) melting at 192°. [d] Prepared by the reduction of (9) with hydrogen and Raney nickel in aqueous sodium bicarbonate.

TABLE II

SULFONES

	Name	Yield, %	M. p., ° C.	Formula	As analyses, % Calcd.	As analyses, % Found
1	*p*-β-Hydroxyethylsulfonylphenylarsonic acid	59	177	$C_8H_{11}AsO_6S$	24.15	24.30
2	*p*-γ-Hydroxypropylsulfonylphenylarsonic acid	78	160.5	$C_9H_{13}AsO_6S$	23.11	23.33
3	*p*-β-Ethoxyethylsulfonylphenylarsonic acid	89	182.5–184.5	$C_{10}H_{15}AsO_6S$	22.15	22.36
4	Sodium *p*-[β-(β′-hydroxyethoxy)-ethylsulfonyl]-[a] phenyl arsonate	83	180.5	$C_{10}H_{14}AsNaO_7S$	19.91	20.00
5	*p*-Acetonylsulfonylphenylarsonic acid	30	202.5–203.5	$C_9H_{11}AsO_6S$	23.25	23.70
6	*p*-Arsonophenylsulfonylacetic acid[a]	91	188 –189	$C_8H_9AsO_7S$	23.11	22.91
7	Ethyl *p*-arsonophenylsulfonylacetate	59	165 –166	$C_{10}H_{13}AsO_7S$	21.27	21.47
8	4′-Nitro-4-arsonodiphenylsulfone	40	>250	$C_{12}H_{10}AsNO_7S$	19.35	19.25
9	4′-Amino-4-arsonodiphenylsulfone[b]	52	229–230 (dec.)	$C_{12}H_{12}AsNO_5S$	20.97	21.00

[a] Isolated by evaporation because of high solubility. [b] Prepared by reduction of (8) with hydrogen and Raney nickel in aqueous sodium bicarbonate.

Melting Point Determination.—Organic arsonic acids normally are converted to their anhydrides by heat; the temperature and time required to complete the dehydration depends on the acid involved and may be a function of the relative acidity of that acid. The dehydration is illustrated by the equation

$$RAsO_3H_2 \xrightarrow{\Delta} RAsO_2 + H_2O$$

If an arsonic acid is heated slowly to its normal melting point, any of three observations may be made depending on the ease of dehydration of the compound. These observations will be: for no dehydration, the normal melting point; partial dehydration, lowered melting point or partial melting; complete dehydration, no melting until melting point of anhydride is reached. In general the anhydrides melt at considerably higher temperatures than the corresponding arsonic acids and frequently decompose at temperatures above 250° without melting.

Melting points of the compounds described in this paper were accurately determined by inserting a sample in a preheated bath at a temperature which was 0–5° below the melting point and slowly raising the temperature of the bath. The shortened time allowed for dehydration allows the observation of melting points which otherwise might be overlooked.

A Bureau of Standards certified thermometer was used in all melting point determinations and stem corrections were calculated to obtain corrected readings.

Summary

1. Two general methods were used to synthesize a number of new sulfides derived from *p*-mercaptophenylarsonic acid.

2. *p* - β - Hydroxyethylmercaptophenylarsonic acid was prepared from the corresponding amine by means of the Bart reaction.

3. *p*-Thiocyanophenylarsonic acid was hydrolyzed in alkaline solution to yield an intermediate acid. This intermediate was readily condensed with substituted aliphatic, heterocyclic and aromatic halides to yield sulfides derived from *p*-mercaptophenylarsonic acid.

4. Sulfides derived from *p*-mercaptophenylarsonic acid were oxidized with hydrogen peroxide to obtain eight new sulfones.

LINCOLN, NEBRASKA

RECEIVED MARCH 16, 1944

---

[11] Cislak and Hamilton, THIS JOURNAL, **52**, 638 (1930).