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

Tetraphenylphosphonium and Tetraphenylstibonium Chloride

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Tetraphenylarsonium chloride[2,3] has been found to have unique and very valuable analytical applications[4] inasmuch as it can be used satisfactorily for the determination of perchlorate, periodate, perrhenate, mercury, cadmium, tin and zinc.

In the hope that a substance might be found which would be equally useful as an analytical reagent, but available at a lower cost, we have studied the preparation and properties of tetraphenylphosphonium and tetraphenylstibonium chloride.

Tetraphenylphosphonium chloride had been prepared by Dodonov and Medox[5] by interaction of triphenylphosphine, phenylmagnesium bromide and oxygen, conversion of the tetraphenylphosphonium bromide produced into the phosphonium hydroxide, and treatment of the latter substance with hydrochloric acid. We found that tetraphenylphosphonium chloride could be obtained by successive recrystallizations of the corresponding bromide from saturated sodium chloride solutions. However, a far more advantageous process was elution of the bromide through a chloride-charged resin; Amberlite IR-4-B[6] proved to be satisfactory for this purpose.

In order to obtain the required tetraphenylphosphonium bromide it is not necessary to prepare and isolate triphenylphosphine since the phosphonium bromide can be obtained in one operation, and in good yield, from phosphorus trichloride merely by allowing the latter substance to react with phenylmagnesium bromide, and then passing oxygen into the mixture.[7]

The only tetraphenylstibonium salt known hitherto is the stibonium bromide which had been synthesized by Chatt and Mann[8] from triphenylstibine, bromobenzene and aluminum chloride. We prepared the bromide by interaction of triphenylstibine dichloride with phenylmagnesium bromide. The stibonium bromide was converted into the chloride by elution through chloride-charged Amberlite resin.

(1) This paper represents part of a dissertation presented to the Horace H. Rackham School of Graduate Studies by L. R. Perkins in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

(2) Blicke and Marzano, THIS JOURNAL, **55**, 3056 (1933); Blicke and Monroe, *ibid.*, **57**, 720 (1935); Blicke, Willard and Taras, *ibid.*, **61**, 88 (1939).

(3) This product can be purchased from the Standard Sample Company, Ames, Iowa.

(4) Lamprey, Doctoral Dissertation, University of Michigan, 1935; Willard and Smith, *J. Ind. Eng. Chem., Anal. Ed.*, **11**, 186, 269, 305 (1939).

(5) Dodonov and Medox, *Ber.*, **61**, 907 (1928).

(6) This resin can be obtained from the Resinous Products Chemical Company, Philadelphia, Pa.

(7) The analytical applications of tetraphenylphosphonium chloride will be described soon by Willard and Perkins.

(8) Chatt and Mann, *J. Chem. Soc.*, 1192 (1940).

Experimental Part

Tetraphenylphosphonium Chloride.—In order to obtain tetraphenylphosphonium bromide, a solution of phenylmagnesium bromide was prepared from 160 g. (1.02 moles) of bromobenzene, 20.9 g. (0.86 mole) of magnesium and 600 ml. of ether in an atmosphere of nitrogen. The solution was cooled with ice, stirred rapidly, and 18 g. (0.13 mole) of phosphorus trichloride, dissolved in 50 ml. of ether, was added slowly. The material was stirred and refluxed for one hour. Dry oxygen, at the rate of about 250 ml. per minute, was then passed into the mixture while it was stirred and cooled; the gas was passed through a sintered glass disc in order to obtain fine bubbles. After the mixture had been treated with 250 g. of ice and 80 ml. of concentrated hydrochloric acid, the ether layer was separated and discarded. To the product, which had separated as an oil, and the aqueous layer, water was added until the total volume was 1 liter; the mixture was then heated until practically all of the oil had dissolved. After treatment with Norite, the mixture was filtered, and 250 g. of sodium chloride was added to the hot filtrate. The solution was cooled with ice, the precipitated crystalline bromide filtered, dried and washed with ether. The crude bromide weighed 50.0 g. (91%).

Fifty grams of the crude bromide was dissolved in 2 liters of boiling water, the solution cooled to room temperature, and then passed, successively, through two tubes; each tube was 25 mm. in diameter and 120 cm. long, and each contained 250 g. of the chloride-charged anion-exchange resin (Amberlite IR-4-B). The effluent solution was concentrated to a volume of 500 ml., 150 g. of sodium chloride was added, the precipitated phosphonium chloride filtered and dried. It was then dissolved in 50 ml. of hot ethanol, the mixture filtered, and the filtrate concentrated to a volume of 15 ml. The product was precipitated by addition of 500 ml. of dry ether; yield 39 g. or 79% based on the phosphorus trichloride used; m. p. 265–267°.[9]

Tetraphenylstibonium Chloride.—Crude triphenylstibine[10] (23.0 g.), dissolved in 35 ml. of carbon tetrachloride, was treated with chlorine until the solution became yellow; most of the solvent and excess chlorine were then removed on a steam-bath. The triphenylstibine dichloride (40.3 g., 94%), which separated from the cold, concentrated solution, melted at 142–144°.[11]

Phenylmagnesium bromide was prepared from 30.0 g. (0.19 mole) of bromobenzene, 4.4 g. (0.18 mole) of magnesium and 200 ml. of ether in a flask provided with a stirrer. After the addition of 25.4 g. (0.06 mole) of triphenylstibine dichloride, dissolved in a mixture of 30 ml. of dry benzene and 270 ml. of dry ether, the material was stirred occasionally, and allowed to remain at room temperature for at least three days. The mixture was treated with 30 g. of ice and 20 ml. of 48% hydrobromic acid, the ether–benzene layer separated, and the aqueous layer extracted four times with 100 ml. portions of ether. The combined ether–benzene layer and the extracts were heated on a steam-bath until the solvents had been removed; the viscous, brown, oily residue solidified when cooled. It was dissolved in 1 liter of boiling water, the solution filtered through glass wool, the filtrate concentrated to a volume of 250 ml., and 25 g. of sodium bromide was added to the hot solution. The stibonium bromide, which pre-

(9) The reported m. p. is 165° (ref. 5).

(10) The stibine was obtained by the method described by Morgan and Mickelthwaite (*J. Chem. Soc.*, **99**, 2290 (1911)). For our purpose it was merely necessary to remove the ether from the solution of the crude product.

(11) Pfeiffer (*Ber.*, **37**, 4621 (1904)) reported 141.5°.

cipitated from the cold solution, was washed with 5 ml. of water; yield 28.0 g.; m. p. 210–215°[12].

Anal. Calcd. for $C_{24}H_{20}SbBr$: Br^-, 15.7. Found: Br^-, 15.6.

The bromide (50 g.) was converted into the chloride by one passage through the anion-exchange resin in the manner which has been described; yield 40 g. (87%); m. p. 202–205°.

Anal. Calcd. for $C_{24}H_{20}SbCl$: Cl^-, 7.62. Found: Cl^-, 7.65.

The stibonium chloride can be recrystallized from water or ethyl acetate. It is only slightly soluble in ether or benzene.

(12) The reported m. p. is 210–218° (ref. 8).

Summary

New procedures have been developed for the preparation of tetraphenylphosphonium and tetraphenylstibonium chloride and bromide. The analytical applications of tetraphenylphosphonium chloride will be described in an early publication.

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF PARKE, DAVIS AND CO.]

Hydroxyalkylamides of 4-Arsonophenoxy- and 4-Arsonoanilinoacetic Acids

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Study of the derivatives of 4-amino- and 4-hydroxybenzenearsonic acid has indicated that certain of them are of greater interest for therapeutic purposes than the parent arsenicals. 4-Arsonophenylurea (carbarsone-U.S.P.),[2] 4-arsonophenylglycineamide (tryparsamide-U.S.P.)[3] and others have become accepted therapeutic agents. Investigations of two types of derivatives, the carbamylmethyl[3,4] and the hydroxyalkyl,[5,6] have led to a number of interesting compounds. In order to determine the effect of incorporating both the hydroxyalkyl and carbamido functions in the same molecule, the hydroxyalkylamides of 4-arsonophenoxyacetic and 4-arsonophenylglycine were prepared.

4-Arsonophenoxyacetic acid[7] and 4-arsonophenylglycine[8] were converted to their methyl esters.[3,4] Reaction of these esters with hydroxyalkylamines yielded the desired amides. The substituted arsonic acids were reduced to the corresponding arsonous acids.

TABLE I

ARSONIC ACIDS[a] R–C$_6$H$_4$–R′

R	R′	Yield, %	Empirical formula	Arsenic, %[b] Calcd.	Found
$-AsO_3H_2$	$-NHCH_2CONHCH_2CH_2OH$	61	$C_{10}H_{15}AsN_2O_5$	23.54	23.35
$-AsO_3H_2$	$-NHCH_2CON(CH_2CH_2OH)_2$	76	$C_{12}H_{19}AsN_2O_6$	20.67	20.80
$-AsO_3HNa$	$-N(CH_2OH)CONHCH_2OH$	52	$C_9H_{12}AsN_2NaO_6$	21.89	21.89
$-AsO_3HNa$	$-N(CH_2OH)CH_2CONHCH_2OH$	95	$C_{10}H_{14}AsN_2NaO_6$	21.04	21.25
$-AsO_3H_2$[c]	$-NHNH_2$	50	$C_6H_9AsN_2O_3$	32.30	31.98
$-AsO_3H_2$[d]	$-NHN{=}C(CH_3)_2$	42	$C_9H_{13}AsN_2O_3$	27.53	27.80
$-AsO_3H_2$	$-OCH_2CONHCH_2CH_2OH$	50	$C_{10}H_{14}AsNO_6$	23.48	23.85
$-AsO_3HNa$	$-OCH_2CONHCH_2CH_2OH$	89	$C_{10}H_{13}AsNNaO_6$	21.96	22.12
$-AsO_3H\cdot H_3NCH_2CH_2OH$	$-OCH_2CONHCH_2CH_2OH$	94	$C_{12}H_{21}AsN_2O_7$	19.67	19.72
$-AsO_3H\cdot H_3NCH_2CHOHCH_3$	$-OCH_2CONHCH_2CHOHCH_3$	97	$C_{14}H_{25}AsN_2O_7$	18.35	18.54
$-AsO_3H_2$	$-OCH_2CONHC(CH_2OH)_3$	82	$C_{12}H_{18}AsNO_7$	20.62	20.55
$-AsO_3H\cdot H_3NC(CH_2OH)_3$	$-OCH_2CONHC(CH_2OH)_3$	78	$C_{16}H_{29}AsN_2O_{11}$	14.97	15.00
$-AsO_3H_2$	$-OCH_2CONHCH_2OH$	32	$C_9H_{12}AsNO_6$	24.55	24.48
$-AsO_3HNa$	$-OCH_2CONHCH_2OH$	85	$C_9H_{11}AsNNaO_6$	22.90	22.90
$-AsO_3H_2$	$-OCH_2CON(CH_2CH_2)_2O$	43	$C_{12}H_{16}AsNO_6$	21.75	21.79

[a] All compounds are colorless unless otherwise noted. [b] Arsenic determined by a modification of the method of Cislak and Hamilton, THIS JOURNAL, 52, 638 (1930). [c] Light brown. [d] Yellow.

Methylolamides could not be prepared by the above procedure but it was found that formaldehyde would condense with the unsubstituted amides to yield the desired products. 4-Arsonophenoxyacetamide gave a monomethylol compound while 4-arsonophenylurea and 4-arsonophenylglycineamide lead to dimethylol derivatives. It would appear from these data that one

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(2) German Patent 213,155.

(3) Jacobs and Heidelberger, THIS JOURNAL, 41, 1587 (1919).

(4) Jacobs and Heidelberger, *ibid.*, 41, 1440, 1581, 1600, 1610, 1809, 1822, 1826, 1834 (1919).

(5) Hamilton, *ibid.*, 45, 275 (1923).

(6) Sweet and Hamilton, *ibid.*, 56, 2409 (1934).

(7) Palmer and Kester, "Org. Syn.," 8, 4 (1928).

(8) German Patent 204,664.