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.

ANN ARBOR, MICHIGAN RECEIVED SEPTEMBER 17, 1947

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

Hydroxyalkylamides of 4-Arsonophenoxy- and 4-Arsonoanilinoacetic Acids

BY C. K. BANKS, D. F. WALKER, JOHN CONTROULIS, E. W. TILLITSON[1] AND L. A. SWEET

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	$C_6H_8AsN_2O_3$	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	$C_{16}H_{28}AsN_2O_{11}$	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

(1) Present address: Department of Chemical Engineering, Wayne Univ., Detroit, Michigan.

(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.

TABLE II

ARSENOUS ACIDS,[a] R—C$_6$H$_3$—As(OH)$_2$

R	Yield, %	Empirical formula	Arsenic, %[b] Calcd.	Found
—NCN	46	$C_7H_7AsN_2O_2$	33.13	32.81
—NHNH$_2$	32	$C_6H_9AsN_2O_2$	34.60	34.52
—NHCH$_2$SO$_3$Na	86	$C_7H_9AsNNaO_5S$	23.60	23.20
—NHCH$_2$CONHCH$_2$CH$_2$OH	64	$C_{10}H_{15}AsN_2O_4$	24.77	24.67
—NHCH$_2$CON(CH$_2$CH$_2$OH)$_2$	72	$C_{12}H_{19}AsN_2O_5$	21.62	21.38
—OCH$_2$CONHCH$_2$CH$_2$OH	73[c]	$C_{10}H_{14}AsNO_5$	24.71	24.78
—OCH$_2$CON(CH$_2$CH$_2$OH)$_2$	62	$C_{12}H_{18}AsNO_6$	21.54	21.37
—OCH$_2$CONHC(CH$_2$OH)$_3$	55	$C_{12}H_{18}AsNO_7$	20.63	20.55

[a] All compounds are colorless. [b] Determined by the method of Banks and Sultzaberger, THIS JOURNAL, **69**, 1 (1947). [c] The same compound was also obtained from methyl 4-arsonosophenoxyacetate and ethanolamine, yield 92%.

methylol group was formed on the amide nitrogen and one on the arylamino nitrogen in the last two instances. The position of the methylol group on nitrogen rather than on the benzene ring was proved by hydrolysis to 4-arsonophenoxyacetic acid and N-4-arsonophenylglycine.

4-Aminobenzenearsonous acid reacted with sodium formaldehyde bisulfite to yield a sulfomethyl derivative. 4-Cyano- and 4-hydrazinobenzenearsonous acid[9,10] were obtained by reduction of the corresponding arsonic acids.

Experimental

Acetamides.—The methyl ester of 4-arsonophenoxyacetic acid or 4-arsonophenylglycine (0.1 mole) was dissolved in an excess of the amine (100 ml.) and heated to 80° for two hours. On adding the reaction mixture to an excess of alcohol (2 l.), the amine salt of the hydroxyalkylacetamide crystallized. It was filtered off and dried *in vacuo*. The free arsonic acids were liberated when the amine salts were dissolved in a small amount of water and made strongly acid to congo red paper with hydrochloric acid. The arsonic acids were recrystallized from water.

Arsonous Acids.—The arsonous acids were prepared from the corresponding arsonic acids by previously published methods.[11]

Methylol Amides.—The arsono-substituted acetamide (0.1 mole) or urea was dissolved in water (25 ml.) by the addition of sodium hydroxide to *p*H 7, or the sodium salt was dissolved in water, and 37% aqueous formaldehyde (1 ml. per gram) added. The mixture was heated to 80° for two hours, then concentrated *in vacuo* to a solid. The residue was dissolved in a minimum of water, filtered and the sodium salt crystallized upon the addition of alcohol and ether. The free arsonic acids could be obtained by carefully acidifying cold aqueous solutions of the salts.

Acetone 4-Arsonophenylhydrazone.—4-Hydrazinobenzenearsonic acid[10] (5.8 g.) was warmed with 25 ml. of acetone and 5 ml. of water until solution occurred. On chilling, a mass of pale red crystals was obtained. After two recrystallizations from water–acetone (1:2), a nearly white crystalline product was obtained. Unlike the initial material, the product did not give a silver mirror test with ammoniacal silver nitrate.

Summary

1. Four new N-hydroxyalkyl derivatives of 4-arsonoanilinoacetic acid and five corresponding derivatives of 4-arsonophenoxyacetic acid are reported. Representative salts are described.

2. The arsonic acids were reduced to the corresponding arsonous acids.

3. Several miscellaneous related arsenicals are also reported.

DETROIT 32, MICH. RECEIVED AUGUST 27, 1947

(9) Banks, Controulis and Holcomb, THIS JOURNAL, **68**, 2102 (1946).

(10) U. S. Patent 2,390,529 (1945).

(11) Banks, Gruhzit, Tillitson, Controulis, Walker and Sultzaberger, THIS JOURNAL, **66**, 1771 (1944); **69**, 5 (1947).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

C-Alkylation and O-Alkylation in the Synthesis of Substituted Furoic Acids

BY CHARLES D. HURD AND KENNETH WILKINSON

In the alkylation of ethyl sodio-oxaloacetate with ethyl bromopyruvate Sutter[1] claimed to have prepared 2,3,5-furantricarboxylic acid. That is to say, he assumed that C-alkylation had occurred followed by ring closure and the elimination of water. However, Reichstein[2] prepared the same tricarboxylic acid by partially decarboxylating furantetracarboxylic acid, and since pyrolysis of such acids causes preferential decarboxylation in the *alpha* position he contended that Sutter had experienced O-alkylation and had obtained 2,3,4-furantricarboxylic acid. Archer and Pratt[3] demonstrated that O-alkylation was the course followed in the analogous condensation between ethyl bromopyruvate and ethyl sodio-β-ketosuberate, since subsequent ring closure yielded 5-(3,4-dicarboxyfuryl)-valeric acid.

Similar interaction of acetoacetic ester and chloroacetone should produce 2,5-dimethyl-3-furoic acid (I) by C-alkylation, and 2,4-dimethyl-3-furoic acid (II) by O-alkylation. On the basis of

(1) Sutter, *Ann.*, **499**, 56 (1932).

(2) Reichstein, *Helv. Chim. Acta*, **16**, 276 (1933).

(3) Archer and Pratt, THIS JOURNAL, **66**, 1656 (1944).