through a minimum and in solutions more alkaline than 0.3 M sodium hydroxide the velocity constant is a linear function of the hydroxyl-ion concentration.

3. The results are interpreted in terms of a mechanism involving chlorination of enol and enolate ion by hypochlorous acid and hypochlorite ion.

4. The rates of reaction increase in the order pinacolone, acetone, acetophenone; both the rate of this reaction and the dependence of the rate on the hydroxyl-ion concentration vary much more with the structure of the ketone than does the rate of enolization in an acid medium.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NEBRASKA]

Arsenated Phenoxyethanols

BY MELVIN R. STEVINSON[1] AND CLIFF S. HAMILTON

Several arsenated phenylglycol ethers have been reported in the literature[2] and some of these, notably β-2-amino-4-arsonophenoxyethanol, possess rather remarkable trypanocidal action. The present investigation deals with a series of arsenated phenoxyethanols formed by condensing propylene chlorohydrin with 4-hydroxyphenylarsonic acid in alkaline solution.

When α-methyl-β-4-arsonophenoxyethanol was nitrated at 0° for approximately twenty minutes with one molecular portion of nitric acid (sp. gr. 1.49–1.50) the corresponding nitrate was obtained. If the reaction was carried out with two molecular proportions of nitric acid at the same temperature and for three hours the nitro ester resulted.

α-Methyl-β-2-nitro-4-arsonophenoxyethyl nitrate was hydrolyzed by refluxing with 3 N hydrochloric acid or 3 N sulfuric acid to yield α-methyl-β-2-nitro-4-arsonophenoxyethanol and this was reduced catalytically to the amine. From 4-β-hydroxy-*n*-propoxyphenylarsonic acid the corresponding oxide was prepared by reduction with sulfurous acid, employing hydriodic acid as a catalyst.

Several arseno derivatives were obtained from the corresponding arsonic acids by reduction with hypophosphorous acid.

Experimental

α-Methyl-β-4-arsonophenoxyethanol and its Sodium Salt.—A solution of 218 g. of 4-hydroxyphenylarsonic acid in 750 cc. of 6 N sodium hydroxide was cooled to 20° and 170 cc. (2 mol. eq.) of propylene chlorohydrin was added cautiously. The mixture was refluxed gently as long as two separate layers could be observed; time, eight to ten hours. The solution was then poured into a beaker surrounded by ice and the arsonic acid was precipitated by the addition of 12 N hydrochloric acid until the mixture was distinctly acid to Congo red paper. The acid was purified by recrystallization from water.

When the acid was dissolved in enough 2 N sodium hydroxide to yield a solution neutral to litmus paper and was filtered into absolute ethanol, the monosodium salt separated as small granular crystals.

α-Methyl-β-2-nitro-4-arsonophenoxyethyl Nitrate.—α-Methyl-β-4-arsonophenoxyethanol (40 g.) was stirred with 80 cc. of nitric acid (sp. gr. 1.50) for three hours at 0°. The product was precipitated by pouring into cold water.

α-Methyl-β-2-nitro-4-arsonophenoxyethanol.—α-Methyl-β-2-nitro-4-arsonophenoxyethyl nitrate (40 g.) was hydrolyzed by refluxing for two hours with 144 cc. of 3 N sulfuric acid. During this time the ester passed into solution and brown fumes of oxides of nitrogen were evolved. By filtering the hot solution and cooling it to 0°, α-methyl-β-2-nitro-4-arsonophenoxyethanol was obtained as a pale yellow, crystalline product. It was purified by recrystallization from water.

α-Methyl-β-2-amino-4-arsonophenoxyethanol and its Acetyl Derivative and Sodium and Potassium Salts.—To a suspension of 32 g. (0.10 mole) of very pure α-methyl-β-2-nitro-4-arsonophenoxyethanol in 200 cc. of water was added 50 cc. of 2 N sodium hydroxide and 10 g. of Raney[3] nickel catalyst. The container was placed on a shaking apparatus and hydrogen gas was introduced under a pressure of 2 atm. Shaking was begun and continued until the solution became colorless and the pressure gage indicated the addition of the required amount of hydrogen. The mixture was filtered free of catalyst and placed in a cooled flask. Sufficient 6 N hydrochloric acid was added to make the solution neutral to Congo red paper, and the flask was stoppered and set away in a refrigerator. Overnight the amino derivative crystallized as slender needles. If further purification was necessary, it was recrystallized from 200 cc. of water. The product was quite sensitive to air oxidation, especially in warm aqueous solutions. When the amine was dried for two and one-half hours at 70° in a vacuum oven, it was obtained anhydrous. Upon standing in contact with air at room temperature it formed the monohydrate. Drying the product for prolonged

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(1) Parke, Davis and Company Fellow.

(2) Benda and Sievers, German Patent 552,267 (1932); L. Cassella and Co., British Patent 373,071 (1932); Sweet and Hamilton, THIS JOURNAL, **56**, 2409 (1934).

(3) Covert and Adkins, *ibid.*, **54**, 4116 (1932).

TABLE I

	Name	Crystal form	Yield, %	M. p., °C.	Formula	As analyses,[c] %	
						Calcd.	Found
1	α-Methyl-β-4-arsonophenoxyethanol	Colorless needles[a]	55-62	132	$C_9H_{13}O_5As$	27.15	27.16
2	Sodium salt of 1	Colorless granules	93	. . .	$C_9H_{12}O_5AsNa$	25.14	25.16
3	4-β-Hydroxy-*n*-propoxyphenylarsenious oxide	Colorless powder	76	>250	$C_9H_{11}O_3As$	30.96	30.94
4	α-Methyl-β-4-arsonophenoxyethyl nitrate	Colorless rhomboids[a]	86	158–159	$C_9H_{12}O_7NAs$	23.34	23.34
5	α-Methyl-β-2-nitro-4-arsonophenoxyethyl nitrate	Colorless rhomboids[a]	79	183 (dec.)	$C_9H_{11}O_9N_2As$	20.47	20.56
6	α-Methyl-β-2-nitro-4-arsonophenoxyethanol	Large colorless rods[a]	94	175	$C_9H_{12}O_7NAs$	23.34	23.32
7	α-Methyl-β-2-amino-4-arsonophenoxyethanol	Colorless needles[a]	52	87[b]	$C_9H_{14}O_5NAs.H_2O$	24.24	24.30
8	Arsono anhydride of 7	. . . .	100	200 (dec.)	$C_9H_{12}O_4NAs$	27.33	27.28
9	Sodium salt of 7	Colorless needles	90	. . .	$C_9H_{13}O_5NAsNa$	23.65	23.64
10	Potassium salt of 7	Colorless needles	93	. . .	$C_9H_{13}O_5NAsK$	22.76	22.74
11	α-Methyl-β-2-acetylamino-4-arsonophenoxyethanol	Colorless rhomboids[a]	67	153	$C_{11}H_{16}O_6NAs.H_2O$	21.34	21.38
12	Arseno-4,4′-di-α-methyl-β-phenoxyethanol	Orange powder	85	170–175 (dec.)	$C_{18}H_{22}O_4As_2$	33.15	33.14
13	Arseno-3,3′-dinitro-4,4′-di-α-methyl-β-phenoxyethanol	Yellow powder	86	200–205 (dec.)	$C_{18}H_{20}O_8N_2As_2$	27.64	27.52
14	Arseno-3,3′-dinitro-4,4′-di-α-methyl-β-phenoxyethyl nitrate	Yellow powder	87	158–160 (dec.)	$C_{18}H_{18}O_{12}N_4As_2$	23.69	23.58
15	Arseno-3,3′-diamino-4,4′-di-α-methyl-β-phenoxyethanol	Yellow powder	97	156–158 (dec.)	$C_{18}H_{24}O_4N_2As_2$	31.08	30.90

[a] By recrystallization from water. [b] Without water of crystallization, m. p. 137°. [c] See Cislak and Hamilton, THIS JOURNAL, **52**, 638 (1930).

periods at 70° in the vacuum oven or for shorter periods at higher temperatures resulted in the loss of the water of hydration and an additional molecule of water, the latter presumably from the arsonic acid group.

A neutral solution was made by dissolving 10 g. of the pure amine and 1.8 g. of anhydrous sodium carbonate in 10 cc. of water. When this was poured into a cold mixture of 200 cc. of absolute ethanol and 150 cc. of dry acetone, the monosodium salt was obtained. Substituting the equivalent amount of potassium carbonate produced the potassium salt which seemed more stable than the sodium salt.

Reaction of either of the above salts with acetic anhydride produced α-methyl-β-2-acetylamino-4-arsonophenoxyethanol which crystallized from water with one molecule of water of crystallization.

4 - β - Hydroxy - *n* - propoxyphenylarsenious Oxide.—Twelve grams of α-methyl-β-4-arsonophenoxyethanol was dissolved in 66 cc. of 1 *N* hydrochloric acid containing 0.3 g. of potassium iodide. This solution was saturated with sulfur dioxide gas and the oxide separated as an amorphous substance. It was purified by dissolving in 3 *N* sodium hydroxide and reprecipitating with 1 *N* hydrochloric acid.

Summary

1. 4-Hydroxyphenylarsonic acid was condensed with propylene chlorohydrin to form α-methyl-β-4-arsonophenoxyethanol.

2. Nitration of α-methyl-β-4-arsonophenoxyethanol with nitric acid (sp. gr. 1.50) gave two different products depending upon experimental conditions.

3. α-Methyl-β-2-nitro-4-arsonophenoxyethyl nitrate was hydrolyzed in 3 *N* hydrochloric acid or 3 *N* sulfuric acid solution to give the mononitro compound.

4. The α-methyl-β-2-amino-4-arsonophenoxyethanol was obtained by reducing the corresponding nitro compound with molecular hydrogen in the presence of Raney nickel catalyst. Various derivatives were made from the free acid.

5. Arseno-4,4′-di-α-methyl-β-phenoxyethanol, arseno-3,3′ - dinitro - 4,4′ - di - α - methyl-β-phenoxyethanol, arseno - 3,3′ - dinitro - 4,4′ - di-α-methyl-β-phenoxyethyl nitrate and arseno-3,3′ - diamino - 4,4′ - di - α - methyl - β - phenoxyethanol were prepared from the corresponding arsonic acids by reduction with hypophosphorous acid.

6. 4-β-Hydroxy-*n*-propoxyphenylarsenious oxide was prepared from the corresponding arsonic acid by reduction with sulfur dioxide using hydriodic acid as the catalyst.

LINCOLN, NEBRASKA

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