

alkyl or alkylene halide at 140° to 155° for 4 hours, in the dark. The reaction product was extracted with hot alcohol, to remove tarry impurities and unchanged base, and then washed with cold alcohol upon a Büchner funnel.

They are moderately soluble in hot water and hot alcohol, slightly soluble in cold alcohol and in water, and practically insoluble in other common organic solvents. With the exception of the *isopropyl* and *isobutyl* iodides, all of these compounds gave a yellow aqueous solution under neutral or acid conditions, but these solutions were changed by the addition of alkalies to a fuchsin-red color.

Derivative.	Reaction Temp. °C.	Color.	M. p. (corr.) °C.	Analyses.			
				Subs. G.	N. Cc.	N. Calc.	Found.
Ethiodide	140°	brick red	231	0.6040	19.2 (27°, 754 mm.)	3.23	3.50
<i>iso</i> -Propyl iodide	140	light tan	266	0.6186	19.4 (29°, 756 mm.)	3.13	3.43
Propyl iodide	150-5	bright vermilion	221	0.6104	19.0 (28°, 751 mm.)	3.13	3.40
<i>iso</i> -Butyl iodide	150-5	orange-red	259	0.6000	18.0 (29°, 756 mm.)	3.04	3.28
Butyl iodide	155-60	deep orange	219	0.6647	17.9 (27°, 751 mm.)	3.04	2.96
<i>iso</i> -Amyl iodide	155	orange	185	0.6545	18.2 (30°, 748 mm.)	2.95	2.99
Allyl-bromide	150	bright orange	237	0.6147	19.3 (29°, 748 mm.)	3.52	3.40

### Summary.

The addition of straight chain alkyl iodides and allyl bromide to the nitrogen atom of 2(4-hydroxy-3-methoxy-styryl)quinoline, gave compounds having the properties of indicators, but no difference in shades or colors of these compounds was observed when aqueous solutions were used as indicators. It was found, however, that with the exception of the *iso*amyl compound, which behaved like the straight chain compounds, except the compounds of the branch chain alkyls did not have this property of an indicator except to a very slight degree.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE COLLEGE OF LIBERAL ARTS, NORTHWESTERN UNIVERSITY.]

### SOME DERIVATIVES OF PHENOXARSIN.<sup>1</sup>

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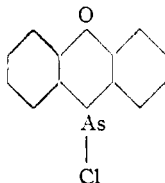
The following study was undertaken to determine whether certain derivatives of phenoxarsin possessed therapeutic properties, and in general to study the effect of linkage between the rings in secondary aromatic arsines.

A comparison of diphenyl chloro-arsine, (C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>AsCl, with the three condensation products of arsenic chloride with each diphenyl amine,<sup>2</sup>

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<sup>2</sup> A. Contardi. *Giorn. chim. applicata* 2, 100-12 (1920); *C. A.* 14, 2628 (1920).

diphenyl ether, and phenyl- $\alpha$ -naphthylamine, shows noteworthy variations in physical, chemical, and physiological properties. The first, an oil boiling at 333°, melts at 37–38° when pure, and is irritating and toxic. 6-Chloro-phenarsazine, a yellow solid melting at 193°, has still more marked physiological properties. The heterocyclic three-ringed compound, 6-chloro-phenoxarsin,  $O(C_6H_4)_2AsCl$ , exists as crystalline



needles melting at 124° and is notably less irritating to the eyes, nose, and skin, than either of the foregoing compounds. Its derivatives tend toward higher melting solids in comparison with the similar derivatives of diphenyl chloro-arsine. In its general chemical reactions, however, as reflected in the following compounds, it closely resembles the analogous reactions of diphenyl chloro-arsine. Chloro-phenyl- $\alpha$ -naphthyl arsazine,  $HN(C_6H_5)(C_{10}H_6)AsCl$ , is a yellow solid melting at 228° (uncorr.) and is markedly less irritating to the mucous surfaces than is 6-chloro-phenarsazine.

### Experimental.

**6-Chloro-phenoxarsin.**—Sir William Pope in a Chemical Warfare Communication gave the following directions for preparing 6-chloro-phenoxarsin. "A mixture of diphenyl-ether 34 g. and arsenic trichloride 36 g., boils at 170° under a reflux condenser, without the evolution of hydrochloric acid. On adding aluminum chloride, 2 g., the liquid becomes deep red, hydrogen chloride is evolved, and the boiling temperature rises to 200° within 2.5 hours. The product partially solidifies on cooling, and is distilled under 15–20 mm. The main portion comes over at 210–230° under 15 mm. pressure and solidifies on cooling. The substance crystallizes well from light petroleum and melts at 125°."

Pope gave no yield, but following his method we have obtained 20 g., 36% of the calculated amount, of pure product melting at 124° (uncorr.). Better yields result by refluxing equivalent quantities of diphenyl ether and redistilled arsenic trichloride with small quantities of aluminum chloride (moisture being carefully excluded) until the temperature reaches 200°. Instead of distilling under reduced pressure as directed by Pope, which decomposes some of the product, the mixture is allowed to cool slowly, the liquid is poured from the crystals which are best recrystallized from alcohol, ether, or glacial acetic acid, and the liquor further refluxed for more product. By this modification a yield of 46% has been obtained.

6-Chloro-phenoxarsine is quite soluble in benzene, acetone, and chloroform, moderately soluble in alcohol, ether, and glacial acetic, and but slightly soluble in light petroleum ether. It is stable toward boiling water and 10% aqueous sodium hydroxide, and irritating toward the mucous membrane, especially in solution with volatile solvents.

All analyses were conducted by Ewins' method<sup>1</sup> or by titration with iodine in acetic acid solution. In the latter method 0.1 to 0.2 g. of the sample is dissolved in 50 cc. of glacial acetic acid and water added until a cloud forms. Sufficient acetic acid is then added to clear the solution and the whole titrated with 0.1 *N* iodine solution and starch.

Subs., 0.2449, 0.2480: 17.25, 17.70 cc., 0.1022 *N* I. Calc. for  $C_{12}H_5OClAs$ : As, 26.9%. Found: 26.98, 27.33.

**6-Iodo-phenoxarsin**,  $O(C_6H_4)_2AsI$ .—A solution of 25 g. of 6-chloro-phenoxarsin in 800 cc. of methyl alcohol is poured into a solution of 23 g. of potassium iodide, 1.5 times the calculated quantity, dissolved in 200 cc. of methyl alcohol. Yellow needles of the iodide form at once, the yield being 27 g., or 88%. The substance recrystallizes from ethyl alcohol in fine bright yellow needles, melting at 144° (uncorr.). It is slightly soluble in methyl and ethyl alcohol, and easily soluble in benzene.

Subs., 0.3949, 0.1547: 20.61, 8.19 cc. 0.1022 *N* I. Calc. for  $C_{12}H_5OIAs$ : As, 20.3. Found: 20.0, 20.3.

Molecular wt., calc.: 370. Found: 378.

**6-Bromo-phenoxarsin**,  $O(C_6H_4)_2AsBr$ .—A solution of 25 g. of 6-chloro-phenoxarsin in 800 cc. of methyl alcohol is poured into a solution of 13 g. of sodium bromide, 1.5 the calculated amount, both solutions being warm. Crystals of the bromo compound soon appear with the sodium chloride. Recrystallization from ethyl alcohol gave finally 17 g., a yield of 58%, of dull yellow crystals occurring in radiating aggregates belonging to the monoclinic system. Much better yields result if 6-phenoxarsin oxide is refluxed for 3 hours with an excess of conc. hydrobromic acid. The compound crystallizes from alcohol with one molecule of hydrogen bromide, which may be removed by repeated washing with very dilute alkali. The crystals are distinctly yellow and melt sharply at 128° (uncorr.).

Subs., 0.2408, 0.2510: 30.95, 32.80 cc. I. Calc. for  $C_{12}H_5OBrAs.HBr$ : As, 18.6. Found: 18.5, 18.8.

**6-Phenoxarsin oxide**,  $O(C_6H_4)_2As-O-As(C_6H_4)_2O$ .—This compound may be prepared by the addition of alkalis, sodium methylate or ethylate, or the introduction of ammonia gas into alcoholic or benzene solutions of 6-chloro-phenoxarsin. It comes out quantitatively as a heavy white precipitate, on addition of conc. ammonia to a warm solution of 20 g. of 6-chloro-phenoxarsin in 800 cc. of ethyl alcohol, the filtrate from

<sup>1</sup> Ewins, *Trans. Chem. Soc.*, 109, 1355 (1916).

the first crop of crystals being diluted with water. Recrystallization from alcohol gives needle-like fibers, melting at  $182^{\circ}$  (uncorr.). The product is soluble in all common organic solvents but insoluble in alkali solutions or water. Haloid acids reconvert it readily into the corresponding halogen arsine. From hot benzene it appears as large diamond-shaped crystals.

Subs., 0.2492, 0.2582: 49.20, 50.65 cc., 0.04018 *N I*. Calc. for  $C_{24}H_{16}O_8As_2$ : As, 29.9%. Found: 29.7, 29.5.

**6-Phenoxarsin sulfide**,  $O(C_6H_4)_2As-S-As(C_6H_4)_2O$ .—Twenty g. of 6-chloro-phenoxarsin is dissolved in 700 cc. of absolute ethyl alcohol and hydrogen sulfide is bubbled through the solution. A heavy deposit of small gray needles appears at once. These are insoluble in all common solvents save glacial acetic acid. From this, small, faintly straw colored needles melting at  $161^{\circ}$  (uncorr.) are obtained. Yield 18 g., practically quantitative.

Subs., 0.1611, 0.2178: 11.86, 16.09 cc., 0.1022 *N I*. Calc. for  $C_{24}H_{16}O_2SAs_2$ : As, 28.9. Found: 28.2, 28.3.

**6-Thiocyano-phenoxarsin**,  $O(C_6H_4)_2AsCNS$ .—Twenty g. of 6-chloro-phenoxarsin is dissolved in 800 cc. of ethyl alcohol and 10 g. of potassium thiocyanate, 1.5 times the calculated amount, dissolved in 80 cc. of ethyl alcohol, slowly added. The potassium chloride comes out at once and on concentrating the filtrate the product appears. Recrystallization from alcohol gives short prisms of the monoclinic system, bright yellow and melting at  $129^{\circ}$  (uncorr.). Yield 15 g., or 89%.

Subs., 0.0992, 0.1119: 6.47, 7.37 cc., 0.1022 *N I*. Calc. for  $C_{12}H_8OAsCNS$ : As, 24.89. Found 25.00, 25.20.

**Phenoxy-cacodyl or 6,6-Bisphenoxarsin**,  $O(C_6H_4)_2As-As(C_6H_4)_2O$ .—The method of Michaelis<sup>1</sup> was followed. Eight g. of 6-phenoxarsin oxide is dissolved in 150 cc. of absolute alcohol, and to the boiling solution is added in small portions 9 cc. of phosphorous acid, sp. gr. 1.12. After the solution is heated for a half hour bright yellow needles appear, and the heating is continued for one hour longer. The solution is filtered hot and the filtrate further refluxed for more product. The yield is 4.8 g., or 62%.

Phenoxy-cacodyl melts at  $159^{\circ}$  (uncorr.) and is insoluble in hot or cold water or alcohol, ether, boiling dil. alkali or hydrochloric acid, and is unaffected by these latter. It is soluble in benzene, chloroform, hot acetic acid, and slightly soluble in light petroleum ether. It is, however, impossible to recrystallize the compound from its solvents as it rapidly goes over to phenoxarsinic acid. Exposed to the air the crystals slowly go over to a mixture of the oxide and the acid. The crystals are best purified by shaking with water and washing on the filter with water and alcohol.

<sup>1</sup> Michaelis, *Ber.*, 15, 1954 (1882).

Subs., 0.2426, 0.2372: 49.75, 48.35 cc. 0.04018 *N* I. Calc. for  $C_{24}H_{16}O_2As_2$ : As, 30.8. Found: 30.9, 30.7.

**Phenoxarsinic Acid**,  $O(C_6H_4)_2AsOOH$ .—A modification of Michaelis' method<sup>1</sup> for the preparation of an arsenic acid from a secondary chloroarsine was applied, using bromine in place of chlorine. The latter method is inapplicable here as it gives chlorinated products in part, when chlorine is passed through an aqueous suspension of 6-chloro-phenoxarsin. 33.5 g. of 6-chloro-phenoxarsin is suspended in 100 cc. of water and the calculated amount of bromine, 19.2 g., added with constant stirring. A liter of water is added and the whole boiled for two hours. Solution is gradually effected and after filtering hot the arsenic acid comes out on standing, as glistening white needles. The yield is 17 g., or 51%.

By oxidation of 6-chloro-phenoxarsin with hydrogen peroxide in glacial acetic acid a yield of 65% is obtained.

Phenoxarsinic acid melts at 219°, is soluble in chloroform, hot water, and alcohol. The last is the best solvent for recrystallization.

Subs., 0.2484, 0.2440: 17.30, 17.05 cc. 0.1022 *N* I. Calc. for  $C_{17}H_9O_3AsH$ : As, 27.2. Found: 26.7, 26.8.

To prepare the sodium salt of phenoxarsinic acid, 18 g. is dissolved in 250 cc. of alcohol with heating, and to the warm solution is added a solution of 1.7 g., 10% excess of the calculated amount, of sodium in absolute alcohol. On adding ether to cloudiness, clearing with a trace of alcohol and allowing to stand, white crystals of the sodium salt as uniform hexagonal plates separate. The yield was 15.7 g. or 78%. The salt does not melt nor char up to 250°, and is quite soluble in water and alcohol.

Subs., 0.2400, 0.2499: 13.4, 13.8 cc., 0.1022 *N* I. Calc. for  $C_{17}H_9O_3AsNa \cdot 3H_2O$ : As, 21.3. Found: 21.4, 21.2.

Loss on heating to constant weight at a 105°. Calc. for  $3H_2O$ : 15.4. Found: 15.2.

**6-Ethyl-phenoxarsin**,  $O(C_6H_4)_2AsC_2H_5$ .—The Grignard reagent is prepared in the usual manner from 2 g. of magnesium and 8 g. of ethyl iodide in 50 cc. of absolute ether. To this is added very slowly, 23 g. of 6-chloro-phenoxarsin dissolved in 500 cc. of absolute ether. A solid separates at first and dissolves later, forming two layers. After standing overnight the mixture is poured onto ice. The solid product which separates is filtered off and the ether concentrated for further material. The product is soluble in alcohol, ether, and benzene, from any of which it crystallizes as white needles melting at 218° (uncorr.). The yield is 18 g. or 60%.

Subs., 0.2486, 0.2420: 45.75, 44.55 cc. *N* I. Calc. for  $C_{14}H_{13}OAs$ : As, 27.6. Found: 27.7, 27.7.

Attempts to prepare the 6-phenyl-phenoxarsin resulted in the formation of 6-phenoxarsin oxide.

<sup>1</sup> Michaelis, *Ber.*, 9, 1566 (1876).

By refluxing 6-ethyl-phenoxarsin with the calculated amount of ethyl iodide for 6 hours, the di-ethyl phenox-arsonium iodide is formed. Pure white translucent needles, not melting below 300°, are obtained by refluxing the reaction mixture with hot water. An aqueous solution of these crystals gives a test for ionic iodine. With silver oxide the arsonium hydroxide apparently results.

Work upon the condensation product of arsenic chloride with mixed and ring substituted amines, diphenyl hydrazine, diphenyl methane, diphenyl sulfide, and similar compounds is being continued.

#### Summary.

1. Diphenyl chloro-arsine and the condensation products of arsenic chloride with diphenyl ether, diphenyl amine and phenyl- $\alpha$ -naphthylamine are briefly contrasted.

2. Derivatives of 6-chloro-phenoxarsin are described and the close resemblance between the chemical properties of this compound and diphenyl chloro-arsine indicated.

3. Properties and directions for preparing the following compounds are submitted: 6-chloro-phenoxarsin, 6-iodo-phenoxarsin, 6-bromo-phenoxarsin, 6-phenoxarsin oxide, 6-phenoxarsin sulfide, 6-thiocyano-phenoxarsin, phenox-cacodyl, phenoxarsinic acid, sodium phenoxarsinate, 6-ethyl-phenoxarsin, and di-ethyl phenoxarsonium iodide and hydroxide.

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## THE PREPARATION OF PARA-DIPHENYL-PROPIOLIC ACID; AND NEW REACTIONS OF DIPHENYL AND ITS DERIVATIVES.<sup>1</sup>

BY CHESTER L. KNOWLES.

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In connection with a study of some reactions of the propiolic acids, it became desirable to prepare *p*-diphenyl-propiolic acid. Before the synthesis of *p*-diphenyl propiolic acid described below was developed, attempts were made to condense both the acid and ester of *p*-diazo-cinnamic and hydrocinnamic with benzene by Molau and Berger's synthesis.<sup>2</sup> It was noted that no condensation took place due to the long side chain or acid radical on the benzene ring carrying the diazo radical. The above mentioned authors state this fact in a later communication.

On attempting to condense *p*-diazo-cinnamic acid and benzene by means of aluminum chloride  $\beta,\beta'$ -diphenyl-propionic acid is formed; m. p. 149°. This compound was first thought to be *p*-diphenyl-acrylic

<sup>1</sup> Summary of a thesis submitted by Chester L. Knowles to the Faculty of Brown University in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

<sup>2</sup> Ber., 26, 1198 (1893).