[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

Diarsyls. VII. 4,4″-Dihydroxy- and 3,3′,3″,3‴-Tetra-(hydroxyphenyl)-diarsyl. Reaction between 4-Hydroxy- and 4-Aminophenylarsine and Tetraphenylarsyl Oxide[1]

BY F. F. BLICKE AND J. F. ONETO

In order to obtain 4-nitrodiphenylarsinic acid, phenylarsine oxide was allowed to react with diazotized 4-nitroaniline. The nitro acid was reduced to the corresponding amino acid and the latter converted into 4-hydroxydiphenylarsinic acid by the diazo reaction. Treatment of the latter compound with hypophosphorous acid yielded 4,4″-dihydroxytetraphenyldiarsyl.

The diarsyl dissolved readily in sodium hydroxide solution and precipitated unchanged upon the addition of acid. It reacted with oxygen in the manner characteristic of diarsyls.

Preparation of 3,3′,3″,3‴-tetra-(hydroxyphenyl)-diarsyl was effected through the following series of reactions: nitration of diphenylarsinic acid to 3,3′-dinitrodiphenylarsinic acid and reduction of the latter to the corresponding diamino acid; the amino acid was converted into 3,3′-dihydroxydiphenylarsinic acid by means of the diazo reaction; the diarsyl was formed through interaction of the acid with hypophosphorous acid.

It was also found that the tetrahydroxydiarsyl is formed by the interaction of 3,3′,3″,3‴-tetra-(hydroxyphenyl)-arsyl oxide and diphenylarsine in accordance with the following equation.

$$(HOC_6H_4)_2As—O—As(C_6H_4OH)_2 + 2HAs(C_6H_5)_2 = (HOC_6H_4)_2As—As(C_6H_4OH)_2 + (C_6H_5)_2As—As(C_6H_5)_2 + H_2O$$

Separation of the two diarsyls was attained by treatment of the mixture with sodium hydroxide solution; the hydroxydiarsyl dissolved in the alkaline layer.

The behavior of the oxide and arsine mentioned above is in accordance with that of other oxides and arsines. Thus 3,3′,3″,3‴-tetraaminotetraphenylarsyl oxide and diphenylarsine, as well as tetraphenylarsyl oxide and 3,3′-diaminodiphenylarsine, yield a mixture of 3,3′, 3″, 3‴-tetraaminotetraphenyldiarsyl and tetraphenyldiarsyl.[2] In no instance has evidence been obtained which indicates that a mixed diarsyl, such as $(HOC_6H_4)_2As—As(C_6H_5)_2$ or $(NH_2C_6H_4)_2As—As(C_6H_5)_2$ is formed.

It was now of interest to determine whether primary arsines, 4-hydroxy- and 4-aminophenylarsine, reacted in an analogous manner with an arsyl oxide, tetraphenyldiarsyl, for example. It was shown that the above-mentioned primary arsines react in accordance with formulation A and not according to B (X = OH or NH_2)

$$\text{A}\quad 2(C_6H_5)_2As—O—As(C_6H_5)_2 + 2H_2AsC_6H_4X = 2(C_6H_5)_2As—As(C_6H_5)_2 + XC_6H_4As{=}AsC_6H_4X$$

$$\text{B}\quad (C_6H_5)_2As—O—As(C_6H_5)_2 + H_2AsC_6H_4X = (C_6H_5)_2As_2AsC_6H_4X$$

Thus from 4-hydroxyphenylarsine, tetraphenyldiarsyl and 4,4′-dihydroxyarsenobenzene were formed while 4-aminophenylarsine yielded tetraphenyldiarsyl and 4,4′-diaminoarsenobenzene.

Experimental Part

4-Nitrodiphenylarsinic Acid.—This unknown acid was prepared by the method of Sakellarios;[3] m. p. 177–179°.

Anal. Calcd. for $C_{12}H_{10}O_4NAs$: As, 24.41. Found: As, 24.33.

4-Aminodiphenylarsinic Acid.—To a vigorously stirred solution of 425 g. of ferrous sulfate in 1200 cc. of water there was added 182 g. of flake sodium hydroxide in 700 cc. of water, then 75 g. of 4-nitrodiphenylarsinic acid, dissolved in 60 g. of sodium hydroxide and 750 cc. of water. After twenty-four hours the mixture was filtered, the filtrate acidified to congo red paper, boiled with charcoal, filtered, cooled and made alkaline. After concentration to one-third its volume the solution was made barely acidic and the precipitated amino acid recrystallized from 50% alcohol; m. p. 215–216°.

Anal. Calcd. for $C_{12}H_{12}O_2NAs$: As, 27.05. Found: As, 26.89.

4-Hydroxydiphenylarsinic Acid.—A mixture of 13.8 g. of 4-aminodiphenylarsinic acid, 10 cc of concd. sulfuric acid, 80 cc. of water and 200 g. of ice was treated with 7.6 g. of sodium nitrite. After twelve hours it was filtered, the filtrate boiled for a few minutes, filtered again, and treated with charcoal. From the cold solution there separated 8 g. of the hydroxy acid; m. p. 202–203°.

Anal. Calcd. for $C_{12}H_{11}O_3As$: As, 26.95. Found: As, 26.88.

4,4″-Dihydroxytetraphenyldiarsyl.—A mixture of 5 g. of 4-hydroxydiphenylarsinic acid, 40 cc. of 50% hypophosphorous acid, two drops of hydriodic acid and 15 cc. of acetic acid was heated in a radical bulb[4] for two hours at 70°; 100 cc. of water was added, the precipitate filtered

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(1) This investigation was made possible by a grant from the Faculty Research Fund.

(2) Blicke, Oakdale and Oneto, THIS JOURNAL, **56**, 141 (1934).

(3) Sakellarios, *Ber.*, **57**, 1514 (1924).

(4) See Fig. 2, Blicke, Oakdale and Oneto, THIS JOURNAL, **56**, 142 (1934).

and washed thoroughly. The precipitate was dissolved in hot acetic acid, transferred to an ordinary radical bulb, most of the acid removed and the precipitated diarsyl treated with 10 cc. of benzene and 15 cc. of petroleum ether to dissolve a yellow by-product. The solvents were decanted and the diarsyl washed with petroleum ether; m. p. 161–163° in a sealed tube filled with nitrogen.

Anal. Calcd. for $C_{24}H_{20}O_2As_2$: As, 30.59. Found: As, 30.38.

Dissolved in acetophenone 0.950 g. of the diarsyl absorbed 38 cc. (N. T. P.) of oxygen in two minutes; calcd. 42 cc.

3,3′-Dihydroxy- and 3,3′-Dimethoxydiphenylarsinic Acid.—A vigorously stirred mixture of 58 g. of 3,3′-diaminodiphenylarsinic acid, 800 cc. of water, 33 cc. of concd. sulfuric acid and ice was treated, at 0°, with 28 g. of sodium nitrite. After twelve hours the mixture was heated to 45–50° to expel nitrogen, filtered, the filtrate thoroughly cooled and the precipitated dihydroxy acid removed. The mother liquor was made slightly alkaline, concentrated and acidified, whereupon more acid was obtained; yield 30–35 g.; when heated the acid darkens at about 202°.

Anal. Calcd. for $C_{12}H_{11}O_4As$: As, 25.49. Found: As, 25.01.

Methylation of 9 g. of the dihydroxy acid with 20 cc. of dimethyl sulfate, 20 g. of sodium hydroxide and 100 cc. of water and acidification of the mixture yielded the dimethoxy acid; m. p. 151–153° after recrystallization from 50% alcohol.

Anal. Calcd. for $C_{14}H_{15}O_4As$: As, 23.27. Found: As, 22.93.

3,3′-Dihydroxydiphenylbromo- and 3,3′-Dihydroxydiphenyliodoarsine.—A mixture of 5 g. of the dihydroxy acid, 4 cc. of acetic acid, 8 cc. of constant boiling hydrobromic acid and a drop of hydriodic acid was saturated with sulfur dioxide; when cooled the bromide precipitated; m. p. 131–133° after recrystallization from benzene.

Anal. Calcd. for $C_{12}H_{10}O_2AsBr$: As, 21.98; Br, 23.43. Found: As, 22.28; Br, 23.42.

A cooled solution of 5 g. of the dihydroxy acid in 5 cc. of acetic and 8 cc. of hydriodic acids (sp. gr. 1.70) was treated with sulfur dioxide. The precipitated iodide is obtained as orange crystals after recrystallization from acetic acid or benzene; m. p. 130–131°.

Anal. Calcd. for $C_{12}H_{10}O_2AsI$: As, 19.32; I, 32.71. Found: As, 19.73; I, 32.88.

3,3′,3″,3‴-Tetra-(hydroxyphenyl)-diarsyl. **(a) From 3,3′-Dihydroxydiphenylarsinic Acid and Hypophosphorous Acid.**—A mixture of 5.8 g. of 3,3′-dihydroxydiphenylarsinic acid, 10 cc. of alcohol, 20 cc. of 50% hypophosphorous acid and two drops of hydriodic acid was heated in a "radical" bulb for three hours at 70°. The diarsyl was precipitated by the addition of 100 cc. of water, the liquid decanted, the material washed thoroughly with water and dried; m. p. 207–208° in a sealed tube under nitrogen; yield about 3 g.

Anal Calcd. for $C_{24}H_{20}O_4As_2$: As, 28.72. Found: As, 28.79.

Dissolved in acetophenone 0.9913 g. of the diarsyl absorbed 41 cc. (N. T. P.) of oxygen in less than one minute; calcd. 40 cc.

The diarsyl is soluble in ether, alcohol and acetone and insoluble in benzene, chloroform and carbon tetrachloride; it dissolves in 10% sodium hydroxide solution and precipitates unchanged upon the addition of acid. The diarsyl in ether decolorized iodine instantly to form 3,3′-dihydroxydiphenyliodoarsine; m. p. 131–132°.

(b) From 3,3′,3″,3‴-Tetra-(hydroxyphenyl)-arsyl Oxide and Diphenylarsine.—To obtain the arsyl oxide 3,3′-dihydroxydiphenylbromoarsine was heated with 10% sodium hydroxide solution and the gummy oxide, obtained by neutralization of the cold solution with dilute sulfuric acid, extracted with ether.

Crystals, principally tetraphenyldiarsyl, separated rapidly when 1.7 cc. of diphenylarsine, in 10 cc. of alcohol, was added to 2.7 g. of the gummy arsyl oxide, in 30 cc. of alcohol, in a "radical" bulb. After forty-eight hours the alcohol layer was decanted into bulb 2; the crystalline residue was shaken with a mixture of 20 cc. of 10% sodium hydroxide solution and 30 cc. of benzene and filtered through a plug of cotton into bulb 3. The benzene layer was decanted into a fourth bulb, and the solvent removed; 1.2 g. of tetraphenyldiarsyl was obtained; m. p. 125–127° under nitrogen. Reaction of the diarsyl with iodine yielded diphenyliodoarsine; mixed m. p. 42–43°.

The solvent was removed from the alcoholic solution in bulb 2, the residue shaken with a mixture of 8 cc. of 10% sodium hydroxide solution, 25 cc. of water and 20 cc. of benzene, the mixture filtered through a plug of cotton into another bulb and the alkaline layer decanted into a bulb of special type.[4] The tetrahydroxydiarsyl was precipitated by neutralization of the solution, filtered, washed with water, dissolved from the filter plate with 40 cc. of alcohol, the solution transferred to an ordinary "radical" bulb and the solvent removed. The tetrahydroxydiarsyl melted at 203–205° and decolorized iodine with the formation of 3,3′-dihydroxydiphenyliodoarsine; m. p. 130–131°.

4-Hydroxyphenylarsine and Tetraphenylarsyl Oxide.—A yellow-brown precipitate of 4,4′-dihydroxyarsenobenzene formed at once when 1.4 g. of 4-hydroxyphenylarsine[5] in 12 cc. of benzene was added to 3.9 g. of the arsyl oxide in 25 cc. of benzene in a "radical" bulb. After forty-eight hours the benzene layer was decanted into another bulb and the solvent removed; 2 g. of tetraphenyldiarsyl was obtained which melted at 126–128° in a sealed tube under nitrogen and yielded diphenyliodoarsine, m. p. 42–43°, when treated with iodine.

A second procedure, which in some respects is more satisfactory, consists in removal of the hydroxy arseno compound by extraction of the reaction mixture with 30 cc. of 5% sodium hydroxide solution.

4-Aminophenylarsine and Tetraphenylarsyl Oxide.—A mixture of 7.1 g. of tetraphenylarsyl oxide in 85 cc. of benzene and 2.5 g. of 4-aminophenylarsine in 15 cc. of benzene was shaken for twenty-four hours in a "radical" bulb. The mixture was filtered from the yellow precipi-

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(5) Modifications of the procedures for the preparation of 4-hydroxy- and 4-aminophenylarsine (German Patents 251,571 and 275,216) which we used will be described later.

tate of 4,4′-diaminoarsenobenzene through a plug of cotton into a second bulb, the benzene solution washed with dilute hydrochloric acid, with water and the solvent then removed; 5.2 g. of tetraphenyldiarsyl was obtained; m. p. 123–126° in a sealed tube under nitrogen; when treated with iodine diphenyliodoarsine was formed; m. p. 42–44°.

Summary

4,4″-Dihydroxytetraphenyldiarsyl has been obtained by the action of hypophosphorous acid on 4-hydroxydiphenylarsinic acid.

3,3′,3″,3‴-Tetra-(hydroxyphenyl)-diarsyl was prepared from 3,3′-dihydroxydiphenylarsinic acid and hypophosphorous acid and also by interaction of 3,3′,3″,3‴ - tetra - (hydroxyphenyl) - arsyl oxide and diphenylarsine.

4-Hydroxyphenylarsine and tetraphenylarsyl oxide yield 4,4′ - dihydroxyarsenobenzene and tetraphenyldiarsyl; from 4-aminophenylarsine and tetraphenylarsyl oxide there was obtained 4,4′ - diaminoarsenobenzene and tetraphenyldiarsyl.

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

The Reversible Addition of Aromatic Compounds to Benzalacetophenones

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The addition of benzene and chlorobenzene to benzalquinaldines and to nuclear halocinnamic acids in the presence of aluminum chloride and hydrogen chloride appears to take place reversibly.[1] It was to be expected that this type of behavior would be general for α,β-unsaturated carbonyl compounds;[2] and in the hope of simplifying the experimental work the investigation has been extended to the benzalacetophenones.

The results obtained with this system have furnished some new types of evidence in support of the theory of reversibility previously outlined. Substituted benzalacetophenones of the class represented by I react with benzene in the presence of aluminum chloride and hydrogen chloride to give β,β-diphenylpropiophenone (II). This reaction has been effected with benzalacetophenones in which X = Cl (*o*, *m* and *p*), Br (*m* and *p*) and CH_3 (*p*).

$$\underset{\mathrm{I}}{\mathrm{XC_6H_4CH{=}CHCOC_6H_5}}\ \left\{\begin{array}{ll} + \mathrm{C_6H_6} \rightleftharpoons \mathrm{(C_6H_5)_2CHCH_2COC_6H_5} & \mathrm{II} \\ \qquad\qquad\quad \uparrow \mathrm{C_6H_6} & \\ + \mathrm{C_6H_5Cl} \rightleftharpoons \mathrm{((\mathit{p})ClC_6H_4)_2\,CHCH_2COC_6H_5} & \mathrm{III} \end{array}\right.$$

The replacement of the tolyl group by the phenyl radical is noteworthy as an indication that such replacements are not due primarily to differences in the radicals involved, since in this instance these differences are slight.

The condensation of chlorobenzene with benzalacetophenones of the type under investigation (I) gives β,β-di-(*p*-chlorophenyl) - propiophenone (III).[3] When X is a halogen atom this product is obtained regardless of the position or nature of the halogen atom involved. This type of reaction has been observed in cases in which X = Cl (*o* and *p*) and Br (*m*). The last-named is the first example of a replacement of one halophenyl group by another and, like the replacement already referred to of the tolyl group by the phenyl radical, suggests that any aromatic radical (if the orientation of substituents is disregarded) may under suitable conditions replace any other aromatic radical. This is a necessary consequence of the assumption that the reaction is reversible.

The most striking result obtained in this series is the conversion of one β,β-diarylpropiophenone into another. When the dichloro ketone (III) is treated with benzene under the usual conditions it is transformed into the corresponding chlorine-free ketone (II). This substitution of one aryl radical for another in a β,β-diarylpropiophenone is a realization of one of the steps previously postulated to explain the replacement which occurs when I is converted into II or into III.

Experimental

***m*-Chlorobenzalacetophenone.**—This compound was

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(1) Hoffman, Farlow and Fuson, THIS JOURNAL, **55**, 2000 (1933); Fuson, Kozacik and Eaton, *ibid.*, **55**, 3799 (1933).

(2) It should be mentioned that it has frequently been demonstrated that the addition of aromatic hydrocarbons to olefins is reversible. (For a good example, see Boedtker and Halse, *Bull. soc. chim.*, [4] **19**, 444 (1916).) To what extent the behavior of the conjugated systems under consideration resembles that of simple olefins is not yet clear.

(3) The structure of the dichloro compound was established by oxidation which gave *p,p′*-dichlorobenzophenone.