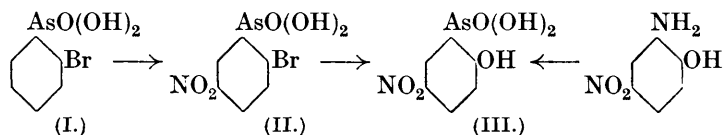


CCCX.—*Nitration of Halogenophenylarsinic Acids.*

By HARRY JAMES BARBER.

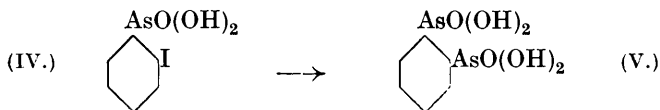
FOR the preparation of certain diphenylaminearsinic acids (this vol., p. 471) halogenonitrophenylarsinic acids having the halogen in the ortho- or para-position with respect to the nitro-group were required: 4-chloro-3-nitro- (D.R.-P. 245,836), 3-chloro-4-nitro-, 3-chloro-6-nitro- (Balaban, J., 1928, 809), and 2-chloro-5-nitro-phenylarsinic acids (D.R.-P. 286,547) have been described. The greater reactivity to be expected of their halogen atoms made the preparation of the corresponding bromo- and iodo-compounds desirable. 2-Halogeno-3-nitro- and 3-halogeno-2-nitro-phenylarsinic acids could not be obtained by nitration of the corresponding halogenophenylarsinic acids.

2-Bromophenylarsinic acid (I), prepared from *o*-bromoaniline in 42% yield by the Bart reaction, gave on nitration 2-bromo-5-nitrophenylarsinic acid (II), identical with the product obtained from 2-bromo-5-nitroaniline by the Bart reaction. Its identity was further confirmed by its hydrolysis with alkali to 5-nitro-2-hydroxyphenylarsinic acid (III).



On attempting to prepare 2-iodophenylarsinic acid (IV) from *o*-iodoaniline small yields were obtained, partly owing to the interaction of the iodophenylarsinic acid formed and the excess of

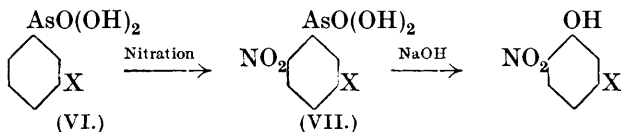
sodium arsenite in presence of copper arsenite to give *o*-phenylenediarsinic acid (V).



This explanation was confirmed by the conversion of 2-iodophenylarsinic acid, prepared from 2-aminophenylarsinic acid by the Sandmeyer reaction, into *o*-phenylenediarsinic acid by boiling with aqueous sodium arsenite in presence of copper arsenite. The only previously recorded instance of the ready replacement of a nuclear halogen by the arsenic acid group is that of *o*-bromobenzoic acid giving *o*-carboxyphenylarsinic acid (Rosenmund, *Ber.*, 1921, **54**, 438): failure to effect the replacement occurs in numerous cases of active halogen compounds (Balaban, *J.*, 1926, 569). Such reaction is indicative of a high degree of activity of the iodine atom ortho to the arsenic acid group. With copper powder, sodium 2-iodophenylarsinate in boiling aqueous solution lost iodine completely, giving a mixture of phenylarsinic acid, 2-hydroxyphenylarsinic acid, and a trace of diphenyl-2:2'-diarsinic acid (?). It thus differs from 2-iodobenzenesulphonic acid, which under similar conditions gives mainly the diphenyldisulphonic acid (Barber and Smiles, *J.*, 1928, 1142). As with the corresponding sulphonic acids, 3- and 4-iodophenylarsinic acids did not lose iodine on treatment with copper powder under those conditions.

Nitration of 2-iodophenylarsinic acid gave 2-iodo-5-nitrophenylarsinic acid, which was oriented by its hydrolysis with alkali to 5-nitro-2-hydroxyphenylarsinic acid (III).

The 3-halogenophenylarsinic acids (VI) were all prepared from 3-chloro-, 3-bromo-, and 3-iodo-aniline by the Bart reaction. Each on nitration gave the 3-halogeno-6-nitrophenylarsinic acid (VII) as the sole product. The orientation of these acids involves a new mode of dearsenication. The arsenic acid group with a nitro-group in the ortho-position is readily eliminated by aqueous alkali, being replaced by a hydroxyl group. 3-Chloro-6-nitrophenylarsinic acid thus gave 3-chloro-6-nitrophenol (and not *p*-nitrophenol as stated by Balaban, *loc. cit.*). The other 3-halogeno-6-nitrophenylarsinic acids behaved similarly.



This behaviour is analogous to the replacement of one nitro-group

in *o*-dinitrobenzene derivatives by hydroxyl, the case corresponding to the above being that of 4-chloro-1:2-dinitrobenzene (*Ber.*, 1876, **9**, 768).

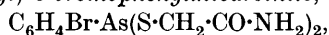
Although there is a close analogy throughout between the behaviour of the nitro- and of the arsenic acid group, *o*-phenylenediarsinic acid is not affected by boiling alkali.

No instance of dinitration was experienced in this series.

The thiolacetamide derivatives (thioarsinites; this vol., p. 1024) were used frequently as a means of identifying the arsenic acids and are described in a number of instances.

EXPERIMENTAL.

Di(carbamylmethyl) o-bromophenylthioarsinite,



the thiolacetamide derivative of 2-bromophenylarsinic acid, has m. p. 137—138° (Found: *M*, by iodine titration, 407. $\text{C}_{10}\text{H}_{12}\text{O}_2\text{N}_2\text{BrS}_2\text{As}$ requires *M*, 411).

2-Bromo-5-nitrophenylarsinic Acid (II).—(a) 2-Bromo-5-nitroaniline (m. p. 137—139°) was submitted to the Bart reaction and gave the required acid (yield, 25%). The *thiolacetamide* derivative has m. p. 171—172° (Found: *M*, 460. $\text{C}_{10}\text{H}_{11}\text{O}_4\text{N}_3\text{BrS}_2\text{As}$ requires *M*, 456). The orientation of the 2-bromo-5-nitroaniline was confirmed by de-amination to give 4-nitrobromobenzene. (b) 2-Bromophenylarsinic acid (28 g.) was dissolved in concentrated sulphuric acid (60 c.c.), nitric acid (*d* 1.52; 7.5 c.c.) added, and the mixture heated on a boiling water-bath for 1—2 hours. The cooled mixture was poured into cold water (500 c.c.), and the crude product removed (31 g.; 95%). This was apparently homogeneous, as successive fractions from 50% acetic acid gave a thiolacetamide, m. p. 171—172°, not depressed on admixture with that from (a).

The *arsinic acid* crystallised from 50% acetic acid in prisms which were either anhydrous or monohydrated (Found: As, 22.4; H_2O , 4.9; and As, 23.1, 23.4; H_2O , 0. $\text{C}_6\text{H}_5\text{O}_5\text{NBrAs}\cdot\text{H}_2\text{O}$ requires As, 21.8; H_2O , 5.2%. $\text{C}_6\text{H}_5\text{O}_5\text{NBrAs}$ requires As, 23.0%). When boiled for 1 hour with 25% sodium hydroxide solution, it gave 5-nitro-2-hydroxyphenylarsinic acid, identified by its *thiolacetamide*, m. p. 194—195° (Found: *M*, 400. $\text{C}_{10}\text{H}_{12}\text{O}_5\text{N}_3\text{S}_2\text{As}$ requires *M*, 393). The m. p. was not depressed by admixture with the thiolacetamide from the arsenic acid derived from 4-nitro-2-aminophenol.

2-Iodophenylarsinic Acid (IV).—The Bart reaction on 2-iodoaniline, if carried out normally, gave *o*-phenylenediarsinic acid (yield, 20%) (Found: As, 46.1. Calc.: As, 46.0%); but when the reaction was carried out at room temperature, some *2-iodophenylarsinic acid* was isolated. The two products were separable by

glacial acetic acid, the iodo-acid being readily soluble and the diarsinic acid insoluble. The Sandmeyer reaction on 2-aminophenylarsinic acid gave the required acid (yield, 50%). It formed hexagonal plates from 50% acetic acid and long prisms from water, both monohydrated (Found: As, 21.8; H₂O, 5.2, 5.4. C₆H₆O₃IAs₂H₂O requires As, 21.7; H₂O, 5.2%).

2-Iodophenylarsinic acid (3.3 g.), dissolved in *N*-sodium hydroxide (20 c.c.) containing arsenious oxide (1.0 g.) and boiled for 1 hour in presence of a trace of copper sulphate, gave *o*-phenylenediarsinic acid (1.3 g.; 40%).

2-Iodophenylarsinic acid (33 g.) was dissolved in 2*N*-sodium hydroxide (50 c.c.) and boiled under reflux with "Naturkupfer C" (17 g.) for 4 hours. The solution was diluted with water (100 c.c.), filtered from copper and cuprous iodide (28.2 g.; theoretical, 29.7 g.), and made acid to Congo-red with hydrochloric acid. After a day a small crop (*ca.* 0.5 g.) of crystalline material was removed. This was sparingly soluble in water and contained no iodine. It crystallised from 50% acetic acid in prisms (Found: As, 36.0. C₁₂H₁₂O₆As₂ requires As, 37.2%). Sufficient material was not available for further analysis). The mother-liquor gave on concentration a mixture of phenylarsinic acid and 2-hydroxyphenylarsinic acid. The former, being the less soluble, was obtained pure, m. p. 167—170° (thiolacetamide, m. p. 128—130°). The presence of the 2-hydroxyphenylarsinic acid was shown by the characteristic purple colour produced with ferric chloride.

2-Iodo-5-nitrophenylarsinic acid was obtained by nitration of 2-iodophenylarsinic acid as described for the bromo-compound. No evidence of the formation of isomerides was obtained. It formed rhombic plates from 50% acetic acid (1 g.; 30 c.c.) (Found: As, 20.2. C₆H₅O₅NIAs requires As, 20.1%). The *thiolacetamide* had m. p. 158—160° (Found: *M*, 515. C₁₀H₁₁O₄N₃IS₂As requires *M*, 503).

With alkali the acid gave 5-nitro-2-hydroxyphenylarsinic acid (thiolacetamide, m. p. 194—195°) as in the case of the bromo-compound. Like 2-iodophenylarsinic acid, it lost iodine completely on treatment with copper powder. It has not been found possible to separate the products; the hydroxy-compound was formed, as shown by the red colour with ferric chloride characteristic of 5-nitro-2-hydroxyphenylarsinic acid.

3-Chlorophenylarsinic acid, obtained from 3-chloroaniline by the Bart reaction (yield, 45%), gave on nitration 3-chloro-6-nitrophenylarsinic acid (Found: As, 26.4. Calc.: As, 26.7%), the *thiolacetamide* of which had m. p. 172—173° (Found: *M*, 402. C₁₀H₁₁O₄N₃ClS₂As requires *M*, 411.5). (The direct titration of the thiolacetamides of *o*-nitrophenylarsinic acids is unsatisfactory owing

to the slowness of the oxidation. It is necessary to add excess of standard iodine solution, keep the mixture for 5 minutes, and then titrate the excess of iodine.) The nitro-acid, which was identical with that obtained from 3-chloro-6-nitroaniline (Balaban, *loc. cit.*), when boiled (1 g.) for 1 hour with 25% sodium hydroxide solution (10 c.c.) gave 3-chloro-6-nitrophenol (yield, 35%), m. p. 38—40°, which was isolated either directly as its sodium salt or by acidification and steam distillation of the reaction mixture. A sample of 3-chloro-6-nitrophenol prepared from 3-chloroaniline by the action of nitrous fumes (*Centr.*, 1924, II, 2268) did not depress the above m. p.

2-Nitrophenylarsinic acid similarly gave *o*-nitrophenol (yield, 30%) with alkali.

3-Bromophenylarsinic acid was obtained from 3-bromoaniline by the Bart reaction (yield, 35%). It formed long slender prisms from 2*N*-acetic acid (Found : As, 26.6. $C_6H_6O_3BrAs$ requires As, 26.7%). The thiolacetamide had m. p. 131—132° (Found : *M*, 417. $C_{10}H_{12}O_2N_2BrS_2As$ requires *M*, 411).

3-Bromo-6-nitrophenylarsinic acid, obtained by nitration as in the case of the chloro-compound, crystallised in plates from 50% acetic acid (Found : As, 22.1; H_2O , 4.6. $C_6H_5O_5NBrAs, H_2O$ requires As, 21.8; H_2O , 5.2%). With alkali, 3-bromo-6-nitrophenol (yield, 35%), m. p. 42—45°, is formed.

3-Iodophenylarsinic acid, from 3-iodoaniline (yield, 24%), formed slender prisms (Found : As, 23.2. $C_6H_6O_3IAs$ requires As, 22.9%). The thiolacetamide had m. p. 138—139° (Found : *M*, 463. $C_{10}H_{12}O_2N_2IS_2As$ requires *M*, 458). Nitration of the acid gave 3-iodo-6-nitrophenylarsinic acid (yield, 75%), which crystallised from 50% acetic acid (1 g.; 40 c.c.) in slender prisms (Found : As, 20.2. $C_6H_5O_5NIAs$ requires As, 20.1%). With alkali, 3-iodo-6-nitrophenol, m. p. 92—94°, is obtained.

4-Bromo-3-nitrophenylarsinic acid (Found : As, 23.5. $C_6H_5O_5NBrAs$ requires As, 23.0%) was obtained by nitration of 4-bromophenylarsinic acid. It formed rectangular plates from hot water.

4-Iodo-3-nitrophenylarsinic acid (Found : As, 19.9. $C_6H_5O_5NIAs$ requires As, 20.1%), from 4-iodophenylarsinic acid, formed leaflets from hot water.

Both 4-bromo-3-nitro- and 4-iodo-3-nitro-phenylarsinic acids gave 3-nitro-4-hydroxyphenylarsinic acid with alkali.

My thanks are due to Dr. A. J. Ewins for his criticism of this paper, and to Mr. R. H. Klein, F.I.C., for the analyses.