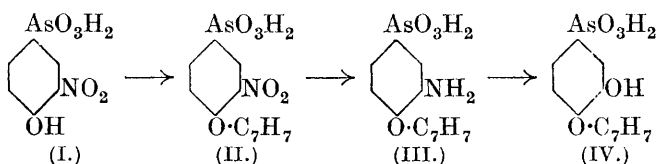


CCCXXXVIII.—*Some Benzyloxyphenylarsonic Acids.*

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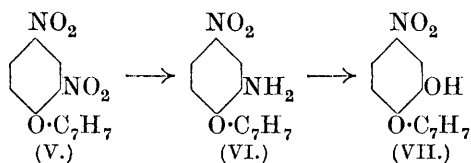
IN continuation of work (Balaban, J., 1928, 809; 1929, 1088) on new methods for the preparation of 3:4-dihydroxyphenylarsonic acid, the scheme undertaken was to prepare its 4-benzyl ether (IV) and examine the hydrolysis of this acid to the dihydroxy-compound. Since the syntheses carried out have not led to the formation of this ether, an account is now given of the results obtained.

The following series of reactions illustrates the first method employed :



3-Nitro-4-hydroxyphenylarsonic acid (I) is readily converted by benzyl chloride and sodium hydroxide in alcoholic solution into 3-nitro-4-benzyloxyphenylarsonic acid (II), whereas 4-benzyloxyphenylarsonic acid, which can be similarly prepared, failed to give any crystalline substance on nitration. Reduction of (II) gave the corresponding amino-acid (III), in which the amino-group could not be replaced by hydroxyl. With chloroacetamide, (III) yields 4-benzyloxyphenylarsonic acid 3-glycineamide, which could not be converted into a benzisoxazine derivative.

Attention was next directed to 4-nitropyrocatechol 1-benzyl ether (VII), which on reduction and application of the Bart-Schmidt reaction should give the compound (IV). In all, three methods of preparation were tried, but without success.



2:4-Dinitrochlorobenzene was converted into 2:4-dinitrophenyl benzyl ether (V) and this was reduced in very poor yield to 4-nitro-2-aminophenyl benzyl ether (VI) by ammonium sulphide : reduction with aluminium amalgam or by West's method was unsuccessful (Spiegel and Sabbath, *Ber.*, 1901, **34**, 1944, could not reduce 4-nitrophenyl benzyl ether with tin or stannous chloride and hydrochloric

acid, or with alcoholic ammonium sulphide, but succeeded with iron and 1% acetic acid). Sufficient of compound (VI) has not been obtained to continue the synthesis. In repeated attempts to convert 4-nitropyrocatechol methylene ether into (VII) by means of sodium benzyloxide (compare Robinson and Robinson, J., 1917, **111**, 929), benzoic acid was the only substance isolated. Finally, 2-chloro-5-nitrophenol (Meldola, Woolcott, and Wray, J., 1896, **69**, 1326), when treated with benzyl alcohol and potassium hydroxide in alcohol, gave a small yield of a substance, m. p. 175° , which is possibly 2-chloro-5-hydroxylaminophenol.

3-Amino-4-hydroxyphenylarsonic acid gives an olive-green colour with aqueous ferric chloride. Of about forty arsonic acids tested by this reaction, those containing an *o*-hydroxy- or *o*-amino-phenyl group usually gave a colour; the diamino- and triamino-phenylarsonic acids behaved similarly. The test may prove of value in helping to identify these acids.

EXPERIMENTAL.

2 : 4-Dinitrophenyl Benzyl Ether (V).—This ether was readily obtained in 70% yield by heating together 2 : 4-dinitrochlorobenzene (20.25 g.), benzyl chloride (20 c.c.), and potassium hydroxide (5.6 g.) in water (20 c.c.) on the water-bath for 1 hour. When the oil obtained after treatment of the reaction mixture with water and concentrated hydrochloric acid was stirred with 95% alcohol, the required ether (19.3 g.) separated. It crystallised from acetone (charcoal) in pale yellow, stout, hexagonal prisms, m. p. 154° with previous softening (Kumpf, *Annalen*, 1884, **224**, 128, gives m. p. 150°).

4-Nitro-2-aminophenyl Benzyl Ether (VI).—The above dinitro-compound (13.7 g.), suspended in boiling 95% alcohol (500 c.c.), was treated with ammonium sulphide (75 c.c.) in small amounts. After 3 hours, the solution was filtered hot, 8.5 g. of unchanged dinitro-compound being recovered. The mother-liquor after removal of solvent was diluted with water and extracted with ether. The crude base (2.0 g.) had m. p. 92° . The *hydrochloride* crystallised from 2*N*-hydrochloric acid, in which it was sparingly soluble, in almost colourless laminæ, m. p. 220° (efferv.) (Found : N, 10.3. $C_{13}H_{12}O_3N_2 \cdot HCl$ requires N, 10.0%).

4-Benzoyloxyphenylarsonic Acid.—A mixture of 4-hydroxyphenylarsonic acid (21.8 g.), benzyl chloride (12.65 c.c.; 1 mol.), sodium hydroxide (8.0 g.; 2 mols.), alcohol (80 c.c.), and water (20 c.c.) was heated under reflux on the water-bath for 15 hours. After removal of alcohol the solution was acidified with hydrochloric acid (Congo-paper), 15.4 g. (yield, 50%) of the *acid* being obtained. It crystal-

lised from 95% alcohol in anhydrous colourless needles, unmelted at 300° (Found : As, 24·5. $C_{13}H_{13}O_4As$ requires As, 24·3%). It is very sparingly soluble in boiling acetic acid and almost insoluble in boiling water. The barium salt crystallises in glistening laminae.

3-Nitro-4-benzyloxyphenylarsonic acid (II), similarly prepared (yield, 36%) from 3-nitro-4-hydroxyphenylarsonic acid (heating, 20 hours), crystallised from boiling water, in which it was very sparingly soluble, in anhydrous colourless needles (Found : As, 21·4; N, 4·3. $C_{13}H_{12}O_6NAs$ requires As, 21·2; N, 4·0%). It is readily soluble in hot acetic acid but insoluble in alcohol. The barium salt forms irregular plates.

3-Amino-4-benzyloxyphenylarsonic acid (III).—The above acid was reduced at 80–90° with ferrous hydroxide, the *amino-acid* (yield, 73·6%) being obtained only by repeated extraction of the iron residues with 0·2*N*-sodium hydroxide. It separated from 50% alcohol in anhydrous, colourless, elongated, hexagonal plates which blacken at *ca.* 220° (Found : As, 23·1; N, 4·1. $C_{13}H_{14}O_4NAs$ requires As, 23·2; N, 4·3%). It is readily soluble in dilute hydrochloric acid, in hot acetic acid and warm 95% alcohol, but sparingly soluble in water. The *acetamido*-derivative crystallises from water (charcoal) in anhydrous, fine, colourless needles (Found : As, 20·3; N, 4·2. $C_{15}H_{16}O_5NAs$ requires As, 20·5; N, 3·8%).

4-Benzyloxyphenylarsonic Acid 3-Glycineamide.—This acid, obtained in 55% yield by the usual method, crystallised from 66% acetic acid (charcoal) in anhydrous, almost colourless, hexagonal plates, m. p. 215° (efferv.) (Found : As, 19·8; N, 7·1. $C_{15}H_{17}O_5N_2As$ requires As, 19·7; N, 7·4%).

Action of Alcoholic Potassium Hydroxide on 2-Chloro-5-nitrophenol.—19·3 G. of the chloronitrophenol, 12·4 g. of potassium hydroxide, 35 c.c. of water, and 12·5 c.c. of benzyl alcohol were heated under reflux for 21 hours on the steam-bath. After acidification and removal of solvent an oil was obtained from which 1·2 g., m. p. 175°, were separated. The *substance* crystallised from 95% alcohol, in which it was fairly readily soluble, in yellow hair-like needles (Found : N, 9·1, 8·8, 9·1; Cl, 22·2. $C_6H_6O_2NCl$ requires N, 8·8; Cl, 22·2%), very sparingly soluble in boiling water.

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