CCCCXIV.—*Heterocyclic Compounds of Arsenic. Part V. Benziminazolearsinic Acids.*

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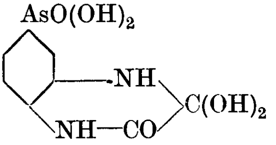
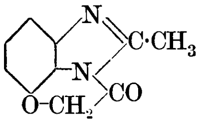
IT has previously been shown (Phillips, this vol., pp. 172, 2393) that 2-substituted benziminazoles can readily be obtained from mono- and di-acyl-*o*-diamines by the action of boiling dilute mineral acids and from *o*-diamines by the action of organic acids in the presence of boiling dilute mineral acids. It is now shown that these reactions may be employed for the synthesis of benziminazolearsinic acids. 3 : 4-Diaminophenylarsinic acid gives with formic, acetic, propionic, and lactic acids, respectively, benziminazole-5(6)-arsinic acid, 2-methyl-, 2-*ethyl*-, and 2-α-*hydroxyethyl-benziminazole*-5(6)-*arsinic acids*. Similarly, 2-*methyl*- and 2-α-*hydroxyethyl-benziminazole*-4(7)-*arsinic acids* and *benziminazole*-4(7)-*arsinic acid* were obtained from 2 : 3-diaminophenylarsinic acid. 3 : 4-Diacetamidophenylarsinic acid, on treatment with boiling dilute hydrochloric acid, gave 2-methylbenziminazole-5(6)-arsinic acid, which was also obtained by the application of the Bart reaction to 5-amino-2-methylbenziminazole. In no case except that of 2-α-hydroxyethylbenziminazole-5(6)-arsinic acid was the cyclic compound obtained in the absence of the catalyst.

The action of dibasic acids on the above diaminophenylarsinic acids calls for special note (compare Phillips, this vol., p. 2397). Malonic acid and 3 : 4-diaminophenylarsinic acid in the presence of boiling dilute hydrochloric acid gave an amorphous compound which appeared to be malon-*o*-phenyleneamide-4-arsinic acid, identical with the substance obtained by Lewis and Bent (*J. Amer. Chem. Soc.*, 1926, **48**, 949) from 3 : 4-diaminophenylarsinic acid and malonic ester. Oxalic acid under the same conditions gave a quantitative yield of 2 : 3-*dihydroxyquinoxaline*-6(7)-*arsinic acid* identical with the product obtained in this laboratory by the reduction of 3-nitro-4-oxalylaminophenylarsinic acid and by the action of oxalyl chloride on 3 : 4-diaminophenylarsinic acid. In all cases it was obtained as a monohydrate which did not lose water at 100°. It is possibly, therefore, a dihydroxy-derivative of formula (I).

(I.)





(II.)

The arseno-derivative obtained by reduction of compound (I) was insoluble in alkalis and dilute mineral acids; the isomeric 2-carboxybenziminazolearsinic acid formula is therefore untenable (compare Phillips, this vol., p. 2398).

2 : 3-Diaminophenylarsinic acid condensed similarly with oxalic acid under the above conditions, giving a good yield of 2 : 3-*dihydroxyquinoxaline*-5(8)-*arsinic acid*, which was also obtained as a monohydrate stable at 100°.

The action of succinic or benzoic acid and derivatives of the latter on 3 : 4-diaminophenylarsinic acid gave no crystalline product.

Although 5-amino-3-hydroxy-1 : 4-benz*iso*oxazine and its 6-arsinic acid (Newbery and Phillips, this vol., p. 3048; Newbery, Phillips, and Stickings, *ibid.*, p. 3057) behave similarly to *o*-aminoacetanilide towards nitrous acid, forming triazoles, complex benziminazoles of the type (II) could not be obtained from them by the action of acetic anhydride and boiling dilute hydrochloric acid or from their acetyl derivatives by treatment with boiling dilute mineral acids.

Attempts to nitrate 2-methylbenziminazole-5(6)-arsinic acid under a variety of conditions gave either unchanged material or mixtures from which no crystalline substance could be obtained; similar results were recorded for 3 : 4-diacetamidophenylarsinic acid.

EXPERIMENTAL.

3 : 4-Diacetamidophenylarsinic acid could not be obtained by acetylation of 3 : 4-diaminophenylarsinic acid (compare Baxter and Fargher, J., 1919, **115**, 1372), but was prepared in 50% yield by decomposing a diazotised solution of 4-amino-1 : 2-diacetamidobenzene (Phillips, this vol., p. 175) (8 g.; 60 c.c. of ice-water; 8 c.c. of hydrochloric acid, *d* 1·16; 2·8 g. of sodium nitrite) at 50° with a copper arsenite suspension (5 g. of arsenious oxide; 6 g. of sodium hydroxide in 50 c.c. of water; 8 c.c. of 2*N*-copper sulphate). The solution was then acidified to litmus, filtered from amorphous material, acidified to Congo-red, and concentrated to 50 c.c. The arsinic acid obtained crystallised from concentrated aqueous solution in colourless needles, m. p. 320° (decomp.), readily soluble in cold water (Found : As, 24·0; N, 9·0. Calc.: As, 23·7; N, 8·9%).

2-Methylbenziminazole-5(6)-arsinic acid, obtained by Baxter and Fargher (*loc. cit.*) by treatment of the above arsinic acid with water in a sealed tube, was best prepared (*a*) by refluxing the above acid (4 g.) with 5*N*-hydrochloric acid (20 c.c.) for 40 minutes and neutralising the filtered solution to Congo-red; yield, 2·5 g. (78%). It was also obtained (*b*) by boiling under reflux 3 : 4-diaminophenylarsinic acid (4 g.; Bertheim, *Ber.*, 1911, **44**, 3095) with 5*N*-hydrochloric acid (30 c.c.) and acetic acid or anhydride (2 c.c.) for 40 minutes and neutralising the filtered solution to Congo-red; yield, 2 g. (40%). (*c*) A diazotised solution of 5-amino-2-methylbenziminazole dihydrochloride (22 g.; water, 100 c.c.; sodium nitrite, 7 g.) was decomposed at 50° with copper arsenite (arsenious oxide, 15 g.; sodium hydroxide, 15 g.; 2*N*-copper sulphate, 6 c.c.; water, 100 c.c.); yield, 30%.

2-Methylbenziminazole-5(6)-arsinic acid (m. p. 275°, decomp., when anhydrous) was obtained in all cases as a monohydrate (Found: As, 27·3; N, 10·0. Calc.: As, 27·4; N, 10·2%), which lost half its water at 100° and the rest only slowly at 120° (Found in anhydrous substance: As, 29·4; N, 10·8. Calc.: As, 29·3; N, 10·9%). It consists of colourless prisms, sparingly soluble in cold water, but readily soluble in mineral acids and in alkalis. The calcium and magnesium salts are amorphous. The acid contains no free amino-group as shown by the diazo-alkaline β-naphthol test. The *nitrate* (Found : As, 24·0. N, 13·45. $C_8H_9O_3N_2As,HNO_3$ requires As, 23·5; N, 13·2%) was obtained in white needles in quantitative yield by the action of boiling 10% nitric acid on the arsinic acid.

2 : 2'-*Dimethyl*-5 : 5'-*arsenobenziminazole*, obtained in 60% yield by hyposulphite reduction of the above arsinic acid, was a deep yellow, amorphous solid, insoluble in water and alkalis, soluble in dilute mineral acids. It contains no free amino-group as shown by the diazo-alkaline β-naphthol test. On desiccation in a vacuum it retained 4 molecules of water, one of which was removed with difficulty at 90° (Found : As, 32·0; N, 11·85; H_2O lost at 90°, 3·9. $C_{16}H_{14}N_4As_2,4H_2O$ requires As, 31·0; N, 11·6; $1H_2O$, 3·95%).

The following three acids were obtained by refluxing 3 : 4-diaminophenylarsinic acid with 5*N*-hydrochloric acid and formic, propionic, or *l*-lactic acid for 1 hour, treating the solution with charcoal, and neutralising it to Congo-red or litmus.

Benziminazole-5(6)-arsinic acid crystallised from water in diamond-shaped plates, identical with the material obtained by Baxter and Fargher's method (*loc. cit.*) (Found : As, 31·2; N, 11·6. Calc. : As, 31·0; N, 11·6%). On reduction with sodium hyposulphite, it gave 5 : 5'-*arsenobenziminazole* in 60% yield as a yellow amorphous solid, insoluble in water, alkalis, and organic solvents, soluble in dilute mineral acids, and containing no free amino-group (Found : As, 38·6; N, 14·4. $C_{14}H_{10}N_4As_2$ requires As, 39·0; N, 14·6%).

2-*Ethylbenziminazole*-5(6)-*arsinic acid* was purified by the method suggested by Christiansen (*J. Amer. Chem. Soc.*, 1920, **42**, 2403) for 3-amino-4-hydroxyphenylarsinic acid. It formed clusters of needles, moderately easily soluble in cold water and alcohol, readily soluble in alkalis and dilute mineral acids. The calcium salt separates from a hot aqueous solution in clusters of prisms, soluble in cold water; the magnesium salt is amorphous (Found : As, 27·5; N, 10·5. $C_9H_{11}O_3N_2As$ requires As, 27·8; N, 10·4%).

2-α-*Hydroxyethylbenziminazole*-5(6)-*arsinic acid*, purified by acidification of its alkaline solution, formed colourless needles, insoluble in cold water and sparingly soluble in boiling water. It forms an amorphous magnesium salt (Found : As, 26·4; N, 10·0. $C_9H_{11}O_4N_2As$ requires As, 26·2; N, 9·8%). The acid was also obtained (yield, 1 g. or 40%) when 3 : 4-diaminophenylarsinic acid (2 g.) was heated in a boiling water-bath for 1 hour with *l*-lactic acid (5 c.c.), and the solution then diluted with water (30 c.c.) (Found : As, 26·0%).

2 : 3-Diaminophenylarsinic acid has been obtained (D.R.-P. 256343) by reduction of 2-nitro-3-aminophenylarsinic acid. That required for this investigation was, however, prepared as follows: 2-Nitro-3-carbethoxyaminophenylarsinic acid (5 g.) (Newbery, Phillips, and Stickings, this vol., p. 3053) was dissolved without cooling in a solution of sodium hydroxide (5 g.) in water (25 c.c.), and glucose (4 g.) was added immediately. A reaction occurred during which no ammonia was liberated. When this had subsided, the liquid was boiled for 5 minutes, acidified strongly to Congo-red, treated with charcoal, and filtered. On neutralisation to Congo-red with 10*N*-sodium hydroxide and cooling, the diamino-acid separated (yield, 1·5 g. or 45%). Purified by Christiansen's method (*loc. cit.*), it consisted of colourless plates, m. p. 198° (decomp.), sparingly soluble in water. The calcium, barium, and magnesium salts are relatively soluble and the acid gives a rich red colour with acidified dichromate solution. It differs considerably from the isomeric 3 : 4-diaminophenylarsinic acid, which gives a characteristic insoluble calcium salt (plates), decomposes at 158°, and gives a purple colour with acidified dichromate solution. This acid, moreover, is considerably more basic than 2 : 3-diaminophenylarsinic acid. The orientations of the latter acid, which is undoubtedly an *o*-phenylenediamine derivative, and of 2-nitro-3-carbethoxyaminophenylarsinic acid would therefore appear to be firmly established. *Benziminazole*-4(7)-*arsinic acid*, obtained from 2 : 3-diaminophenylarsinic acid and formic acid as described under benziminazole-5(6)-arsinic acid, forms colourless prisms, m. p. 277° (decomp.), from boiling water, in which it is sparingly soluble (Found: As, 30·9; N, 11·5%). It is markedly amphoteric, but appears to be somewhat less basic than the 5(6)-arsinic acid. The calcium salt is amorphous, and soluble in cold but insoluble in boiling water; the magnesium salt forms clusters of colourless prisms. 4 : 4′-*Arsenobenziminazole* is an amorphous yellow solid (Found in substance dried at 100°: As, 38·8; N, 14·5%), insoluble in water, alkalis and organic solvents, but soluble in dilute hydrochloric acid to give a hydrochloride, which is precipitated by excess of the mineral acid.

2-*Methylbenziminazole*-4(7)-*arsinic acid*, obtained in 50% yield from 2 : 3-diaminophenylarsinic acid and acetic anhydride in the presence of boiling 4*N*-hydrochloric acid, forms anhydrous needles, m. p. 280—282°, from boiling water (Found: As, 28·9; N, 10·7%). It is readily soluble in alkalis and dilute mineral acids. Its magnesium and calcium salts are amorphous.

2 : 2′-*Dimethyl*-4 : 4′-*arsenobenziminazole* is a yellow, amorphous solid, resembling its lower homologue in all its properties. It can

readily be dried in a vacuum, differing from 2 : 2′-dimethyl-5 : 5′-arsenobenziminazole (p. 3137) in this respect (Found: As, 36·0; N, 13·3. $C_{16}H_{14}N_4As_2$ requires As, 36·4; N, 13·6%).

2-α-*Hydroxyethylbenziminazole*-4(7)-*arsinic acid* was obtained in poor yield from 2 : 3-diaminophenylarsinic acid, *l*-lactic acid, and 4*N*-hydrochloric acid. It forms colourless needles from boiling water, is amphoteric, and gives an amorphous magnesium salt (Found: As, 26·0; N, 9·5%).

Condensation of Dibasic Acids with 2 : 3- *and* 3 : 4-*Diaminophenylarsinic Acids*.—(1) *Oxalic acid.* (a) 3 : 4-Diaminophenylarsinic acid (2 g.), 4*N*-hydrochloric acid (14 c.c.), and crystalline oxalic acid (1·2 g.) were boiled under reflux for 40 minutes. On cooling, 2 : 3-*dihydroxyquinoxaline*-6(7)-*arsinic acid* separated (yield, 1·5 g. or 60%). Crystallised many times from boiling water, in which it was very sparingly soluble, it formed colourless hexagonal plates, not molten at 300° (Found: As, 25·0; N, 9·2. $C_8H_7O_5N_2As,H_2O$ requires As, 24·8; N, 9·2%). It is insoluble in dilute mineral acids, but readily soluble in alkalis, giving with sodium hydroxide mono- and di-sodium salts. It also forms very sparingly soluble calcium, barium, and magnesium salts.

(b) 2 : 3-Diaminophenylarsinic acid, treated similarly, gave a 75% yield of 2 : 3-*dihydroxyquinoxaline*-5(8)-*arsinic acid*, which crystallised in prisms not molten at 300°. Like its isomeride, it is very sparingly soluble in boiling water and gives very sparingly soluble calcium, barium, and magnesium salts (Found: As, 24·9; N, 9·2. $C_8H_7O_5N_2As,H_2O$ requires As, 24·7; N, 9·2%). The arseno-derivative has properties identical with those of the compound derived from the isomeric 6(7)-arsinic acid.

(2) *Malonic acid.* (a) 3 : 4-Diaminophenylarsinic acid (2 g.), malonic acid (1 g.), and 4*N*-hydrochloric acid (14 c.c.), boiled under reflux for 1 hour, gave a trace only of red, amorphous material on cooling. The filtrate contained about 1 g. of unchanged diamino-acid. The red material was purified by solution in glacial acetic acid and reprecipitation by ether. It was insoluble in water, dilute mineral acids, and most organic solvents, but readily soluble in alkalis, giving neutral solutions (Found: As, 24·8%).

(b) 3 : 4-Diaminophenylarsinic acid, treated in methyl alcohol with ethyl malonate as described by Lewis and Bent (*loc. cit.*), gave the same material, which was purified similarly and dried at 90°. It appears to be malon-*o*-phenyleneamide-4-arsinic acid and, unlike the quinoxalinearsinic acids, gives soluble calcium, barium, and magnesium salts (Found: As, 24·8; N, 9·2. Calc. for $C_9H_9O_5N_2As$: As, 25·0; N, 9·3%).

(3) *Succinic acid.* 3 : 4-Diaminophenylarsinic acid (2 g.), 4*N*-

hydrochloric acid (14 c.c.), and succinic acid (2 g.) gave, on refluxing for 1 hour and cooling, a 60% return of unchanged 3 : 4-diaminophenylarsinic acid. No cyclic arsinic acid could be detected.

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