

*Cyclic Diarsines. Part II. 1:4-Disubstituted Diethylenediarsines.*

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[Reprint Order No. 5706.]

The synthesis and properties of various 1:4-disubstituted diethylenediarsines are described. These compounds contain a novel heterocyclic ring, which constitutes the arsenic analogue of piperazine.

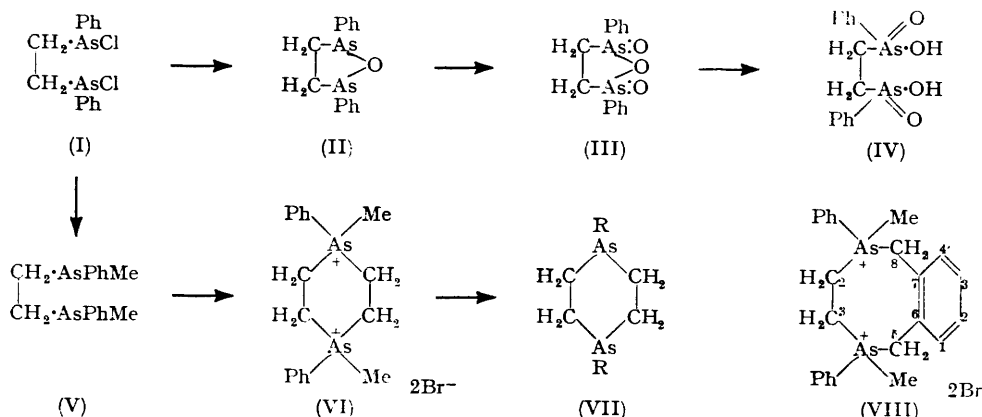
It has been shown by Mann and Baker (*J.*, 1952, 4142 \*) that *o*-phenylenebis(dimethylarsine) when heated with ethylene dibromide readily underwent cyclisation to 1:4-dimethylethylene-*o*-phenylenediarsine dimethobromide, and that 1:4-dimethylethylene-*o*-phenylenediarsine, obtained by thermal decomposition of this salt, again united with ethylene dibromide to give diethylene-*o*-phenylenediarsine dimethobromide. This type of cyclisation by double quaternisation with ethylene dibromide is clearly promoted by the tertiary arsine groups' being held rigidly in the most favourable position by the *o*-phenylene group. We have investigated a similar synthesis with the *o*-phenylene group replaced by a  $\cdot\text{CH}_2\cdot\text{CH}_2\cdot$  group, although the great disadvantage of the conformational mobility of the arsine groups around the connecting  $\cdot\text{CH}_2\cdot\text{CH}_2\cdot$  link was fully recognised.

Three synthetic routes have been investigated. An attempt to cyclise *s*-ethylenebis(phenylchloroarsine) (I) (Chatt and Mann, *J.*, 1939, 610) with ethylene dibromide in hot aqueous sodium hydroxide suspension, *i.e.*, by the Meyer reaction, proved abortive, because (I) readily and preferentially reacts with the alkali to form *s*-ethylenebis(phenylarsinous) anhydride, *i.e.*, 1:3-diphenyl-1:3-diarsa-2-oxacyclopentane (II), which has high stability in an alkaline medium. When treated with hydrogen peroxide, (II) gave *s*-ethylenebis(phenylarsinic) anhydride, *i.e.*, 1:3-diphenyl-1:3-diarsa-2-oxacyclopentane 1:3-dioxide (III), which with warm acids gave *s*-ethylenebis(phenylarsinic acid) (IV) (cf. Quick and Adams, *J. Amer. Chem. Soc.*, 1922, 44, 805; Chatt and Mann, *loc. cit.*); consequently hot dilute nitric acid converted the cyclic (II) directly into the acid (IV). The stability of the five-membered ring in the compounds (II) and (III) recalls the ready formation of *o*-phenylenediarsine oxydichloride (Kalb, *Annalen*, 1921, 423, 74) and the remarkably easy anhydride formation shown by compounds such as *o*-carboxyphenylmethylchloroarsine and -arsinous acid (Aeschlimann and McClelland, *J.*, 1924, 125, 2025). Other examples of similar stable five-membered rings occur in Parts III and IV (following papers).

In a second route, diethylphenylarsine was quaternised with an excess of ethylene dibromide, but this reaction yielded a mixture of 2-bromoethyldiethylphenylarsonium bromide,  $[\text{AsEt}_2\text{Ph}\cdot\text{C}_2\text{H}_4\text{Br}]\text{Br}$ , and *s*-ethylenebis(diethylphenylarsonium bromide),  $[\text{AsEt}_2\text{Ph}\cdot\text{C}_2\text{H}_4\cdot\text{AsEt}_2\text{Ph}]\text{Br}_2$ , both in impracticably low yields. It is highly probable that the latter product on thermal decomposition would yield ethylenebis(ethylphenylarsine), which might then undergo cyclisation with ethylene dibromide. The former compound when heated might give 2-bromoethylphenylarsine, which could then undergo a direct bimolecular cyclisation by quaternisation. Owing to the low yields, these reactions were not investigated.

\* This paper is regarded as Part I of this series.

The bischloroarsine (I) was therefore converted by the Grignard reaction into ethylenebis(methylphenylarsine) (V), which however, when heated with ethylene dibromide in various proportions and at various temperatures gave only hygroscopic amorphous products, produced apparently by extensive linear condensation. Mixtures in toluene and chlorobenzene when heated gave only methylphenylarsinic acid, the foul odour



indicating that the acid probably arose by the oxidation of methylphenylarsine: this rupture of the molecule is similar to that of *s*-ethylenebis(phenylarsinic acid) which when treated with hot hydrochloric acid and sulphur dioxide gives phenyldichloroarsine (Chatt and Mann, unpublished work).

When however an equimolecular mixture of the diarsine (V) and ethylene dibromide in methanol was heated to  $100^\circ$ , 1 : 4-dimethyl-1 : 4-diphenyldiethylenediarsonium dibromide (1 : 4-diphenyl-1 : 4-diarsacyclohexane dimethobromide) (VI) was formed, accompanied by a considerable quantity of polymeric material. The dibromide (VI), when heated under reduced pressure, readily gave the crystalline 1 : 4-diphenyldiethylenediarsonine (1 : 4-diphenyl-1 : 4-diarsacyclohexane) (VII; R = Ph). These compounds are the first examples of a novel heterocyclic system, the arsenic analogue of piperazine.

The tertiary arsine groups in (VII; R = Ph) have normal reactivity: for example, a solution of the arsine in cold methyl iodide forms a monomethiodide, and when boiled a dimethiodide; the arsine, treated with warm dilute nitric acid, is oxidised to the di(hydroxynitrate). Yet all attempts to condense the arsine with ethylene dibromide to form 1 : 4-diphenyltriethylenediarsonium dibromide gave only amorphous products; trimethylene dibromide and *o*-xylylene dibromide gave similar results. This recalls the properties of 1 : 2 : 2 : 4 : 5 : 5-hexamethylpiperazine (Mann and Senior, *J.*, 1954, 4476), which readily gives diquaternary salts with simple alkyl halides, but will not undergo diquaternisation with alkylene dibromides. The explanation may be the same for both compounds, namely, that they are "locked" in the *Z* form, and cannot thus assume the *C* form in which only could this cyclisation occur.

It is noteworthy that no indication of *cis-trans*-isomerism could be detected in the dibromide (VI) or in the corresponding di-iodide or ditoluene-*p*-sulphonate, although theoretically this isomerism could exist irrespective of the conformation of the ring system.

In order to give a possibly less rigid molecule, an attempt was made to replace the phenyl groups in the diarsine by methyl groups. Several examples are known (for references, see Mann, Millar, and Smith, *J.*, 1953, 1131) of phenyl groups, attached to cyclic arsenic atoms, being replaced by iodine by the action of hot hydriodic acid. This reagent, however, disrupted the ring in (VII; R = Ph), with the formation of *s*-ethylenebis(di-iodoarsine). Hot hydrobromic acid however gave the colourless crystalline 1 : 4-dibromodiethylenediarsonine (VII; R = Br), which with methylmagnesium bromide gave the liquid 1 : 4-dimethyldiethylenediarsonine (VII; R = Me).

Attempts to condense this diarsine with ethylene dibromide, by heating an equimole-

cular mixture alone at 125°, or in methanol at 100°, gave a hygroscopic amorphous product, apparently again formed by extensive linear condensation. This product moreover yielded no crystalline derivatives, and gave no decisive product on thermal decomposition. It is probable that the conditions necessary for the required cyclic condensation could be discovered, but the low over-all yield of (VII; R = Me) precluded further investigation.

A novel type of heterocyclic system was obtained by the condensation of *s*-ethylenebis(methylphenylarsine) (V) and *o*-xylylene dibromide, which yielded 1:4-diphenyl-1:4-diarsa-6:7-benzocyclooct-6-ene dimethobromide (VIII), together with much yellow resinous material. The salt (VIII) was deliquescent and was therefore converted by sodium iodide into the dimethiodide; thermal decomposition under reduced pressure of both these salts gave a yellow syrup which on attempted oxidation or quaternisation gave no solid derivatives.

#### EXPERIMENTAL

Unless otherwise stated, all compounds were colourless, and molecular weights were determined ebullioscopically in acetone.

*s*-Ethylenebis(phenylarsinous) Anhydride (II).—*s*-Ethylenebis(phenylchloroarsine) (I) (5.0 g.) and a solution of sodium hydroxide (4.0 g., 8 mols.) in water (10 c.c.) were boiled under reflux for 3 hr., and the oily product, which solidified on cooling, was recrystallised from methanol, affording the anhydride (II), m. p. 94° (Found: C, 48.2; H, 4.2%; *M*, 336. C<sub>14</sub>H<sub>14</sub>OAs<sub>2</sub> requires C, 48.3; H, 4.0%; *M*, 348). The addition of ethylene dibromide (1.1 c.c., 1 mol.) or of trimethylene dibromide (1.3 c.c., 1 mol.) to the above mixture gave the same result.

*s*-Ethylenebis(phenylarsinic) Anhydride (III).—Aqueous hydrogen peroxide (30%) was added dropwise to a solution of the anhydride (II) (1 g.) in acetone (15 c.c.), heat being evolved with deposition of the anhydride (III), which crystallised from ethanol as a monohydrate, m. p. 191° (effervescence) (Found: C, 42.5; H, 4.3. C<sub>14</sub>H<sub>14</sub>O<sub>3</sub>As<sub>2</sub>·H<sub>2</sub>O requires C, 42.2; H, 4.0%).

The anhydride (III) readily dissolved in warm dilute hydrochloric acid, which on cooling precipitated the crystalline arsenic acid (IV), m. p. 200° (effervescence) (Found: C, 42.2; H, 4.1. Calc. for C<sub>14</sub>H<sub>16</sub>O<sub>4</sub>As<sub>2</sub>: C, 42.2; H, 4.0%). Use of the anhydride (II) and warm dilute nitric acid in the experiment also gave (IV), m. p. and mixed m. p. 200° (effervescence).

Diethylphenylarsine and Ethylene Dibromide.—A mixture of the arsine (5.4 g.) and the dibromide (22.5 c.c., 10 mols.) was boiled under reflux in nitrogen for 6 hr., and cooled. The yellow oil which separated above the excess of dibromide was collected, and when set aside for several days became semicrystalline. These crystals were extracted with boiling acetone (10 c.c.). The insoluble residue consisted of the very hygroscopic *s*-ethylenebis(diethylphenylarsonium) dibromide, which was therefore precipitated in ethanolic solution as the dipicrate, yellow crystals, m. p. 166–167° (decomp.) (ca. 0.1 g.) (Found: C, 45.4; H, 4.2; N, 9.25. C<sub>34</sub>H<sub>38</sub>O<sub>14</sub>N<sub>6</sub>As<sub>2</sub> requires C, 45.2; H, 4.2; N, 9.3%).

The acetone filtrate slowly deposited 2-bromoethyldiethylphenylarsonium bromide (ca. 0.1 g.), m. p. 106° after further crystallisation from acetone (Found: C, 36.2; H, 4.5. C<sub>12</sub>H<sub>18</sub>Br<sub>2</sub>As requires C, 36.2; H, 4.8%).

The high proportion of ethylene dibromide in the above experiment was employed to increase the yield of the second product, which appeared the more promising for subsequent cyclisation. The use of ethylene dibromide (5 mols.) gave essentially the same result.

*s*-Ethylenebis(methylphenylarsine) (V).—A solution of the chloroarsine (I) (50 g.) in benzene (200 c.c.) was slowly added to a cooled stirred Grignard reagent prepared from methyl iodide (31 c.c., 4 mols.) and magnesium (12.0 g., 4 atoms) in ether (200 c.c.); the mixture was then stirred for 45 min. at 15° and boiled under reflux for 30 min., all operations being performed under nitrogen. After hydrolysis with ammonium chloride (100 g.) in water (400 c.c.) the organic layer was separated, dried, and distilled under nitrogen, giving the diarsine (V), b. p. 163–165°/0.2 mm. (33.2 g., 74%) (Found: C, 52.7; H, 5.4. C<sub>16</sub>H<sub>20</sub>As<sub>2</sub> requires C, 53.0; H, 5.5%).

For characterisation, the diarsine was dissolved in cold methyl iodide, from which the dimethiodide was deposited, and after crystallisation from water, decomposed at ca. 250° without melting (Found: C, 33.6; H, 4.2. C<sub>18</sub>H<sub>26</sub>I<sub>2</sub>As<sub>2</sub> requires C, 33.4; H, 4.0%). This salt furnished the dimethopicrate, yellow crystals, m. p. 217–218° (decomp.), from aqueous ethanol (Found: C, 42.4; H, 3.4; N, 10.1. C<sub>30</sub>H<sub>30</sub>O<sub>14</sub>N<sub>6</sub>As<sub>2</sub> requires C, 42.4; H, 3.5; N, 9.9%). The diarsine in acetone solution was readily converted by hydrogen peroxide into the dioxide,

which was precipitated as the *di(hydroxypicrate)*, yellow crystals, m. p. 171—172° (decomp.), from water (Found : C, 39.6; H, 3.2; N, 9.95.  $C_{28}H_{28}O_{16}N_6As_2$  requires C, 39.4; H, 3.05; N, 9.85%).

1 : 4-Dimethyl-1 : 4-diphenyldiethylenediarsonium Dibromide (VI).—A solution of the diarsine (V) (23.1 g.) and ethylene dibromide (5.32 c.c., 1 mol.) in methanol (35 c.c.) was heated in a tightly stoppered bottle at 100° for 6 hr. The cold solution was diluted with ethanol (100 c.c.), and after 1 hr. the deposited crystalline *dibromide* (VI) (4.1 g.) was collected and recrystallised from methanol; it sublimed at *ca.* 255° (some decomp.) (Found : C, 39.5; H, 4.7.  $C_{18}H_{24}Br_2As_2$  requires C, 39.3; H, 4.4%). The initial filtrate, when set aside for 1 day, deposited a second crop (3.4 g., 21% in all) of the dibromide. Evaporation of this filtrate then gave a sticky gum which could not be crystallised and from which well-defined derivatives could not be obtained.

The dibromide gave a *dimethopicrate*, yellow crystals, m. p. 244° (decomp.), from dimethylformamide (Found : C, 42.75; H, 3.2; N, 9.95.  $C_{30}H_{28}O_{14}N_6As_2$  requires C, 42.6; H, 3.3; N, 9.9%).

A solution of the diarsine (V) (10.2 g.) and ethylene dibromide (2.44 c.c., 1 mol.) in toluene (70 c.c.) was boiled under reflux in nitrogen for 8 hr., and then concentrated under reduced pressure to *ca.* 10 c.c. and diluted with ether (80 c.c.). The white solid which slowly separated furnished methylphenylarsinic acid, m. p. and mixed m. p. 175° after crystallisation from much acetone (Found : C, 42.3; H, 4.6%; M, ebullioscopic in ethanol, 208. Calc. for  $C_7H_9O_2As$  : C, 42.0; H, 4.5%; M, 200). Berthelm (*Ber.*, 1915, 48, 350) gives m. p. 179.5°. The solubility of the acid in various liquids and the pH of its aqueous solution agree with those recorded by Gibson and Johnson (*J.*, 1928, 92). Use of chlorobenzene instead of toluene in the above experiment gave the same result.

1 : 4-Diphenyldiethylenediarsine (VII; R = Ph).—The dibromide (VI) (44 g.) was gently heated at 0.5 mm. with a brush flame until decomposition was complete. The brown distillate and the charred residue were together extracted with boiling chloroform (75 c.c.), which was then boiled (charcoal), filtered, evaporated to *ca.* 40 c.c., and diluted with hot ethanol (40 c.c.). The solution on cooling deposited the *diarsine* (VII; R = Ph), m. p. 142—144° after crystallisation from acetone (Found : C, 53.6; H, 5.2%; M, 346.  $C_{16}H_{18}As_2$  requires C, 53.3; H, 5.0%; M, 360) : 8.4 g., 29%. The yield was not improved by carrying out the thermal decomposition in a Silicone bath at 300°.

A solution of this diarsine in an excess of cold methyl iodide deposited the *monomethiodide*, m. p. 211° (effervescence) after crystallisation from ethanol (Found : C, 40.3; H, 4.1.  $C_{17}H_{21}IAs_2$  requires C, 40.6; H, 4.2%). The above solution, when boiled under reflux for 4 hr., gave the *dimethiodide*, m. p. 221° (effervescence) after crystallisation from methanol (Found : C, 33.6; H, 3.8.  $C_{18}H_{24}I_2As_2$  requires C, 33.5; H, 3.7%). A mixture of the diarsine and methyl toluene-*p*-sulphonate (2 mols.) when heated at 150° for 1 hr. furnished the *di(metho-toluene-p-sulphonate)*, m. p. 266° (effervescence) after crystallisation from ethanol (Found : C, 52.9; H, 5.4.  $C_{32}H_{38}O_6S_2As_2$  requires C, 52.45; H, 5.2%); this salt, which has almost the same carbon and hydrogen content as the mono(methosulphonate), was identified by conversion into the above dimethiodide, m. p. and mixed m. p. 223° (effervescence).

Nitric acid, diluted with an equal volume of water, readily converted the diarsine into the *di(hydroxynitrate)*, m. p. 188° (effervescence) after crystallisation from water (Found : C, 37.5; H, 3.7; N, 5.15.  $C_{16}H_{20}O_8N_2As_2$  requires C, 37.1; H, 3.8; N, 5.4%).

The diarsine, when heated with equimolecular quantities of ethylene dibromide, alone at 125° or in methanol at 100°, of trimethylene dibromide in methanol at 100°, or of *o*-xylylene dibromide in boiling toluene, gave in each case apparently amorphous products which furnished no crystalline derivatives.

A mixture of the diarsine (VII; R = Ph) (1 g.) and hydriodic acid (20 c.c.) of constant b. p., when boiled under reflux for 2 hr., gave an oil which solidified on cooling and when recrystallised from chloroform afforded *s*-ethylenebis(*di-iodoarsine*), deep yellow crystals (0.4 g., 20%), m. p. 136° (Found : C, 4.2; H, 1.0.  $C_2H_4I_4As_2$  requires C, 3.5; H, 0.65%). Acetone solutions of this compound and of piperidine *N*-pentamethylenedithiocarbamate when mixed deposited *s*-ethylenebis[tetrakis-(*N*-pentamethylenethiocarbamoylthio)arsine], m. p. 198—199° (effervescence) after crystallisation from acetone (Found : C, 37.9; H, 5.0.  $C_{26}H_{44}N_4S_8As_2$  requires C, 38.1; H, 5.4%).

Repetition of the above experiment using, however, hydrobromic acid (20 c.c.) of constant b. p., and boiling for 3 hr., gave an oil which also solidified on cooling, and afforded 1 : 4-dibromodiethylenediarsine (VII; R = Br), m. p. 168—170° after crystallisation from acetone (Found : C, 13.35; H, 2.2.  $C_4H_8Br_2As_2$  requires C, 13.1; H, 2.2%). It similarly gave 1 : 4-

*di-(N-pentamethylenethiocarbamoylthio)diethylenediarsine* (VII;  $R = C_5H_{10}N \cdot CS_2$ ), m. p. 185—186° (effervescence) after crystallisation from chloroform (Found: N, 5.4.  $C_{16}H_{28}N_2S_4As_2$  requires N, 5.3%).

1: 4-Dimethyldiethylenediarsine (VII;  $R = Me$ ).—A solution of the dibromodiarsine (4.2 g.) in benzene (100 c.c.) was added under nitrogen to a Grignard reagent prepared from methyl iodide (2.9 c.c., 4 mols.) and magnesium (1.10 g., 4 atoms) in ether (50 c.c.), which was then boiled under reflux for 15 min. and hydrolysed with aqueous ammonium chloride. The organic layer, when dried and distilled under nitrogen, gave the *diarsine* (VII;  $R = Me$ ) (1.5 g., 56%), b. p. 113—114°/24 mm. (Found: C, 30.9; H, 6.0.  $C_6H_{14}As_2$  requires C, 30.5; H, 5.9%).

When a mixture of this diarsine and ethylene dibromide (1 mol.) was heated alone at 125° or in methanol at 100° for 3 hr., only an amorphous hygroscopic material [Found: C, 21.8; H, 5.1. Calc. for  $(C_8H_{18}Br_2As_2, H_2O)_n$ : C, 21.7; H, 4.6%] was formed. This product when heated at 0.5 mm. decomposed with much blackening; the residue was extracted with warm dilute nitric acid, which was evaporated to dryness in a desiccator, giving a colourless non-crystalline residue which furnished an amorphous picrate. Lack of material prevented further investigation of the diarsine.

A mixture of the diarsine (V) (4.23 g.) and powdered *o*-xylylene dibromide (3.08 g., 1 mol.) under nitrogen rapidly set to a hard mass, which was heated at 100° for 1 hr. The crude deliquescent dimethobromide (VIII) was extracted with ethanol, leaving a yellow resinous material. The extract, added to an excess of sodium iodide in ethanol, deposited 1:4-diphenyl-1:4-diarsa-6:7-benzocyclooct-6-ene dimethiodide diethanolate (as VII), m. p. 160—161° (effervescence), when recrystallised from ethanol (Found: C, 41.7; H, 4.55.  $C_{24}H_{28}I_2As_2, 2C_2H_6O$  requires C, 41.4; H, 4.9%).

We gratefully acknowledge a grant provided by the Department of Scientific and Industrial Research (E. R. H. J.).

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[Received, September 6th, 1954.]