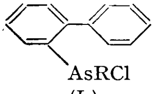
611. *The Interaction of Diazomethane and Diphenylchloroarsine.*

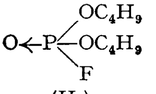
By Gerald H. Cookson and Frederick G. Mann.

The main product of the action of diazomethane on diphenylchloroarsine is methylenebisdiphenylarsine monoxide, of which a number of derivatives has been prepared.

In the early stages of our investigation of the synthesis of the 9 : 10-dihydroarsanthridine ring system, recorded in the previous paper, considerable difficulty was caused by the labile nature of a benzyl (or substituted benzyl) group directly joined to an arsenic atom. To avoid this difficulty, a promising alternative route appeared to be the preparation of a compound of type (I) (where R is an alkyl group), which, it was hoped, would react with diazomethane in such a manner that the chlorine atom would be replaced by the chloromethyl group; the chloromethyl arsine thus obtained might then be cyclised with loss of hydrogen chloride to give the corresponding 10-R-9 : 10-dihydroarsanthridine.

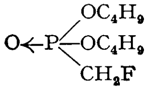


(I.)



$O\leftarrow P(OC_4H_9)_2F$

(II.)

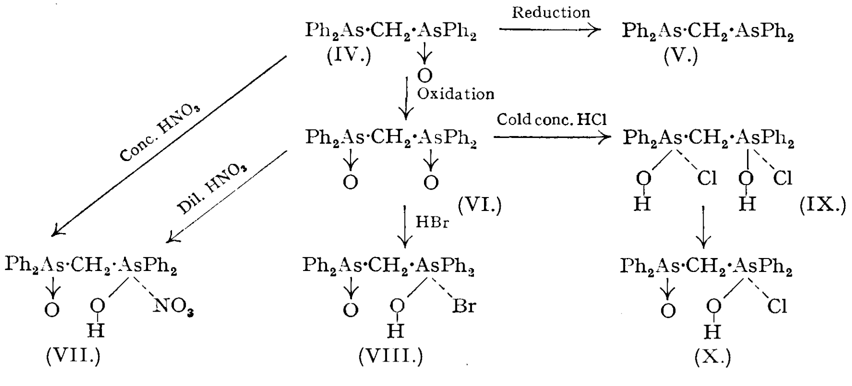


$O\leftarrow P(OC_4H_9)_2CH_2F$

(III.)

This desired reaction with diazomethane appeared probable because arsenic trichloride reacts with this reagent to give chloromethyldichloroarsine, $Cl{\cdot}CH_2{\cdot}AsCl_2$, and bis(chloromethyl)-chloroarsine, $(Cl{\cdot}CH_2)_2AsCl$, in low yield (Braz and Yakubovich, *J. Gen. Chem. Russia*, 1941, **11**, 41). Mercuric chloride reacts similarly with diazomethane to give chloromethylmercuric chloride, $Cl{\cdot}CH_2{\cdot}HgCl$, and bis(chloromethyl)mercury, $(Cl{\cdot}CH_2)_2Hg$ (Hallerman and Newman, *J. Amer. Chem. Soc.*, 1932, **54**, 2859). Furthermore, di-*sec.*-butyl fluorophosphonate (II) reacts with diazomethane to give the fluoromethyl derivative (III) (Saunders *et al.*, *J.*, 1948, 702).

For simplicity, initial experiments were performed using diphenylchloroarsine, Ph_2AsCl, instead of the much less accessible compounds of type (I). The interaction of diphenylchloroarsine and two molecular equivalents of diazomethane in ether at 0° was accompanied by a vigorous evolution of nitrogen, but the main product, irrespective of the order in which the reactants were mixed, was *methylenebis(diphenylarsine) monoxide* (IV). This compound,



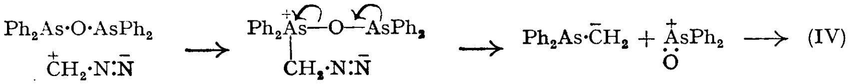
which formed beautiful needles, was also characterised by combination with picric, styphnic, and picrolonic acid, to give the crystalline *hydroxy-picrate*, *-styphnate*, and *-picrolonate*, respectively. Furthermore, the monoxide (IV), when treated in chloroform solution with hydrogen chloride and then with hydrogen sulphide, gave *methylenebis(diphenylarsine) monosulphide* (as IV).

Reduction of the mono-oxide (IV) with sulphur dioxide in the presence of dilute hydrochloric acid gave *methylenebisdiphenylarsine* (V). This crystalline arsine, both in the solid state and in pure ethereal solution, appeared to undergo no oxidation when exposed to air at room temperature. When dissolved in ether containing peroxides it was oxidised to methylenebisdiphenylarsine dioxide (VI), a deliquescent glass that could not be crystallised. This dioxide could be readily prepared by the oxidation of the monoxide (IV) in alcoholic solution with hydrogen peroxide. When an aqueous solution of the dioxide was treated with dilute nitric acid, or when the monoxide (IV) was dissolved in concentrated nitric acid which was then diluted with water, the crystalline *methylenebis(diphenylarsine) oxide hydroxy-nitrate* (VII) was obtained. The dioxide when treated with hydrobromic acid similarly gave the *oxide hydroxy-bromide* (VIII), but when treated with cold concentrated hydrochloric acid gave *methylenebis(diphenylarsine hydroxy-chloride)* (IX). This compound was unstable, however, and when placed in a vacuum or dissolved in hot water, readily lost one molecule of hydrogen chloride to form the *oxide hydroxy-chloride* (X). The behaviour of the dioxide (VI) is a striking example of the process of inductive deactivation, of which a variety of examples have been discussed by Mann and Watson (*J. Org. Chem.*, 1948, **13**, 502). It is clear that when one of the arsine oxide groups in the dioxide forms a salt as in (VII) or (VIII), the inductive effect of the strong positive pole on this arsenic atom considerably reduces the polar character and reactivity of the second arsine oxide group, which consequently does not normally form a hydroxy-salt with acids. In the presence of cold concentrated hydrochloric acid, however, this reduced activity is sufficiently strong to enable the bishydroxy-chloride (IX) to be formed, but the weak union of the second molecule of acid causes ready dissociation to the oxide hydroxy-chloride (X).

The other products isolated from the interaction of diazomethane and diphenylchloroarsine were diphenylarsonous acid (in small amount) and a deep-yellow syrup obtained by removal of the solvent under reduced pressure. The syrup appeared to contain a diazo-compound, since when treated with acids it rapidly evolved nitrogen and simultaneously lost its colour. After acid treatment however the only neutral compound isolated was diphenylarsine oxide, and the composition of the syrup was therefore not further investigated.

There is insufficient evidence on which to base any simple mechanism for the formation of the diarsine monoxide (IV). It is probable that this compound is a direct product of the main reaction and does not arise by the subsidiary oxidation of the diarsine (V), because the latter does not apparently undergo oxidation under the conditions employed. It is possible that a trace of water in the diazomethane solution hydrolysed the phenyldichloroarsine steadily into diphenylarsine oxide (XI), a process which might be rapid since both reactants were in solution, and that the oxide then combined with the diazomethane in its polar form to give the complex (XII). The latter might then break into the ions as shown, and these ions would then recombine to give the monoxide (IV):

(XI.)



$$\begin{matrix}\mathrm{Ph_2As{\cdot}O{\cdot}AsPh_2} \\ \mathrm{\overset{+}{C}H_2{\cdot}N{:}\bar{N}}\end{matrix} \longrightarrow \begin{matrix}\mathrm{Ph_2\overset{+}{As}{-}O{-}AsPh_2} \\ \mathrm{|} \\ \mathrm{CH_2{\cdot}N{:}\bar{N}}\end{matrix} \longrightarrow \mathrm{Ph_2As{\cdot}\bar{C}H_2} + \mathrm{\overset{+}{A}sPh_2 \atop \ddot{O}} \longrightarrow \mathrm{(IV)}$$

(XII.)

Although the reaction was carried out in apparently anhydrous conditions, the comparatively large volume of ether employed would make difficult the complete exclusion of the minute quantity of water (0·125 g. in a typical experiment) required to hydrolyse the dichloroarsine to the oxide (XI).

In view of these results, however, the investigation of the action of diazomethane on 2-*diphenylylethylchloroarsine* (I; R = Et) was discontinued.

EXPERIMENTAL.

An ethereal solution of diazomethane was prepared by the addition of nitrosomethylurea (19·2 g.) to a vigorously stirred mixture of 40% aqueous potassium hydroxide (58 c.c.) and dry peroxide-free ether (190 c.c.) at 0°. The ethereal layer was then separated and dried (KOH). A solution of pure diphenylchloroarsine (15 g.) in dry ether (200 c.c.) was added to the ethereal solution of diazomethane (2 mols.) during 30 minutes, while the mixture was kept vigorously stirred at 0°. Nitrogen was evolved and a white precipitate of the diarsine mono-oxide (IV) formed on the sides of the flask. The mixture was set aside at room temperature overnight, whereafter the effervescence had ceased although the solution was still yellow. The precipitate (2·6 g.) of (IV) was collected. The filtrate later deposited a small quantity of diphenylarsonous acid, m. p. 164—168° mixed or alone, and then a second crop (0·8 g.) of (IV.) Similar results were obtained when the diazomethane solution was added to that of the diphenylchloroarsine.

The ether was removed from the filtrate by evaporation in a nitrogen atmosphere under reduced pressure. The deep-yellow residual syrup when treated with even weak acids (*e.g.*, acetic acid) evolved nitrogen and became colourless. The only product isolated from this acid treatment was diphenylarsine oxide, $[Ph_2As]_2O$.

The *methylenebisdiphenylarsine monoxide* (IV) thus obtained (3·4 g., 25% calculated on chloroarsine used) was recrystallised from ethyl acetate or carbonate, and formed long white needles, m. p. 184—186°, very soluble in the lower alcohols, slightly so in benzene, and insoluble in light petroleum and water (Found: C, 61·8; H, 4·8. $C_{25}H_{22}OAs_2$ requires C, 61·5; H, 4·5%). An alcoholic solution when treated with picric acid gave the *hydroxy-picrate*, yellow needles which even after several recrystallisations from alcohol containing picric acid always softened at 140° and melted at 147° (Found: C, 51·8; H, 3·4;

N, 5·9. $C_{31}H_{25}O_8N_3As_2$ requires C, 51·9; H, 3·5; N, 5·9%). The *hydroxy-styphnate*, similarly prepared and recrystallised, formed pale yellow needles, m. p. 142—143° after softening at 134° (Found: C, 51·1; H, 3·3; N, 5·55. $C_{31}H_{25}O_9N_3As_2$ requires C, 50·8; H, 3·4; N, 5·7%). The *hydroxy-picrolonate* was precipitated as a pale yellow powder when hot alcoholic solutions of the mono-oxide and picrolonic acid were mixed; it had m. p. 152° after softening at 146° and was not recrystallised (Found: C, 56·3; H, 4·15; N, 7·6. $C_{35}H_{30}O_6N_4As_2$ requires C, 55·9; H, 4·0; N, 7·45%).

The *monosulphide* (as IV) was prepared by passing hydrogen chloride and then hydrogen sulphide through a hot chloroform solution of the mono-oxide. The oil remaining after removal of the solvent crystallised when stirred with *cyclo*hexane, and then separated from ethyl acetate as colourless crystals, m. p. 138—139° (Found: C, 59·2; H, 4·6. $C_{25}H_{22}SAs_2$ requires C, 59·5; H, 4·4%).

Sulphur dioxide was passed into a chloroform solution of the mono-oxide (IV) covered by a layer of dilute hydrochloric acid containing a trace of potassium iodide. When reduction was complete, the orange-coloured chloroform layer was separated and evaporated. The residue soon solidified and when recrystallised from alcohol gave beautiful long white needles of the *diarsine* (V), m. p. 96—97° (Found: C, 63·8; H, 5·0. $C_{25}H_{22}As_2$ requires C, 63·6; H, 4·7%).

A solution of the mono-oxide (0·6 g.) in alcohol (15 c.c.) was diluted with aqueous hydrogen peroxide (3·5 c.c., "20-vol.") and kept at 50° for 2½ hours. Evaporation in a vacuum gave methylenebis-(diphenylarsine oxide) (VI) as a deliquescent glass which was moderately soluble in water, but less so in alcohol. An attempt to prepare this dioxide by a Meyer reaction between diphenylchloroarsine (2 mols.) and methylene dibromide (1 mol.) was unsuccessful.

Methylenebis(diphenylarsine) oxide hydroxy-nitrate (VII) was precipitated when dilute nitric acid was added to an aqueous solution of the dioxide (VI), and when recrystallised from alcohol gave colourless needles, m. p. 176—178° (effer.) in a preheated bath (Found: C, 53·0; 52·9; H, 4·35, 4·2; N, 2·2. $C_{25}H_{23}O_5NAs_2$ requires C, 52·9; H, 4·1; N, 2·5%). This compound was even more readily prepared when a mixture of the mono-oxide (IV) and concentrated nitric acid was stirred at 20° until oxidation was complete, and the clear solution then diluted with water, precipitating the hydroxy-nitrate.

When an aqueous solution of the dioxide (VI) was treated with hydrobromic acid, the precipitated *oxide hydroxy-bromide* (VIII) (recrystallised from alcohol) formed colourless crystals, m. p. 149—151° (Found: C, 51·6, 50·9; H, 4·3, 4·1; Br, 13·7. $C_{25}H_{23}O_2BrAs_2$ requires C, 51·3; H, 3·9; Br, 13·7%).

When cold concentrated hydrochloric acid was added to an aqueous solution of the dioxide (VI), large colourless crystals of the *di(hydroxy-chloride)* (IX) containing 1·5 mols. of water separated from the solution; they had m. p. 127—130° with slight preliminary softening (Found: C, 49·5; H, 5·0. $C_{25}H_{24}O_2Cl_2As_2,1{\cdot}5H_2O$ requires C, 49·7; H, 4·5%). When this compound was recrystallised from a small quantity of hot water, it was converted into colourless crystals of the *oxide mono(hydroxy-chloride) hemihydrate* (X), m. p. 151—152° (Found: C, 54·3; H, 4·8. $C_{25}H_{23}O_2ClAs_2,0{\cdot}5H_2O$ requires C, 54·6; H, 4·4%). The same compound was obtained when the di(hydroxy-chloride) (IX) was placed in a vacuum over calcium chloride for a few hours.

A solution of chlorine in carbon tetrachloride was added to a chloroform solution of the mono-oxide (IV) until absorption of chlorine ceased. The solvent was removed under reduced pressure, and the residue immediately solidified when stirred with acetone. This material, when recrystallised from water, gave magnificent crystals of the compound (X), m. p. 151—152° (mixed and unmixed).

Preparation of 2-Diphenylylethylarsonous Acid.—Diphenylyl-2-arsonic acid. This compound was prepared by Aeschlimann *et al.* (*J.*, 1925, **127**, 66) who gave no experimental details. 2-Aminodiphenyl (102 g.) in water (500 c.c.) containing concentrated sulphuric acid (50 c.c.) was diazotised with a saturated solution of sodium nitrite (44 g.). This solution, kept at 0°, was added during 45 minutes to a mixture of sodium carbonate (150 g.), arsenious oxide (75·5 g.), and hydrated copper sulphate (3·3 g.) in water (750 c.c.), which was vigorously stirred and maintained at 60°. A heavy brown precipitate was filtered from the hot solution when the latter no longer gave a red dye with β-naphthol. White leaflets of the hydrated *disodium* salt of the arsonic acid crystallised as the solution cooled; a sample, recrystallised from alcohol, lost water of crystallisation at 95—110° but did not melt below 320° (Found: C, 35·65; H, 4·4. $C_{12}H_9O_3AsNa_2,4H_2O$ requires C, 35·55; H, 4·3%). The free acid (52 g.), obtained by acidification of an aqueous solution of the sodium salt, had m. p. 202—206° after crystallisation from alcohol. An attempted preparation of the acid by Scheller's method (Oneto and Wey, *J. Amer. Chem. Soc.*, 1941, **63**, 3068) was unsuccessful.

2-Diphenylyldichloroarsine was prepared in 88% yield by the reduction of the arsonic acid in hydrochloric acid with sulphur dioxide and a trace of potassium iodide at 60°. The dichloroarsine, which solidified on cooling, was very soluble in most organic liquids, but separated from light petroleum (b. p. 40—60°) as white needles, m. p. 47·5—48·5° (Found: C, 48·1; H, 3·2. Calc. for $C_{12}H_9Cl_2As$: C, 48·2; H, 3·0%). Aeschlimann *et al.* (*loc. cit.*) describe this compound as an oil. Treatment of the dichloroarsine with piperidine *N*-pentamethylenedithiocarbamate gave 2-*diphenylylarsinobis*-(N-*pentamethylenedithiourethane*) as crystals, m. p. 216°, after crystallisation from ethyl carbonate (Found: C, 52·4; H, 5·2; N, 5·2. $C_{24}H_{29}N_2S_4As$ requires C, 52·55; H, 5·3; N, 5·1%).

2-*Diphenylylethylarsonous acid.* The dichloroarsine (32 g.) was added to a warm solution of sodium hydroxide (17·1 g.) in water (40 c.c.), and the oily mixture cooled to 30° and vigorously stirred while ethyl bromide (8 c.c., 1 mol.) was slowly added down the reflux condenser. The mixture, which ultimately had formed a stiff smooth cream, was heated on the water-bath for 40 minutes, cooled, and, after the further addition of ethyl bromide (2 c.c.), again heated and cooled as before. Further addition of the bromide (2 c.c.) and 10% sodium hydroxide solution (20 c.c.) was then made, and the mixture heated under reflux for 1 hour, cooled, diluted with water (100 c.c.), and repeatedly extracted with ether. The united ethereal extracts contained only diphenyl (1·5 g.). The aqueous layer, after removal of dissolved ether, was neutralised to litmus with concentrated hydrochloric acid and, after filtration of the precipitated material (0·6 g.), was neutralised to Congo-red. The solution, when set aside overnight, deposited 2-*diphenylylethylarsonous acid hemihydrate*, which occurred in two crystalline modifications: (α) m. p. 160—161°, and (β) m. p. 151—152°. The first preparation gave large hexagonal plates of the α-form, but the mother-liquor, when set aside for 10 days while containing some of these crystals, suddenly deposited long crystals of the β-form, whereupon the plates of the α- changed to the β-form; the transformation took about 1 hour to spread through a crystal of 5-mm. width. It was possible to introduce a "seed" of the α-form on a glass fibre into the m. p. tube after the β-form had just melted, *i.e.*, at *ca.* 155°, whereupon the arsonous acid would resolidify and melt at 160—161°. The acid was recrystallised either from ethyl acetate or from water containing some methyl alcohol (Found, for material dried at 60°/0·5 mm. for 7 hours: C, 56·5; H, 5·5. $C_{14}H_{15}O_2As,0{\cdot}5H_2O$ requires C, 56·2; H, 5·4%). The S-p-*chlorobenzylthiuronium* salt, prepared in the usual way, crystallised from ethyl acetate as long needles containing 2·5 mols. of water of crystallisation, m. p. 84—85° (dependent on rate of heating) (Found: C, 49·2; H, 5·7; N, 5·4. $C_{22}H_{24}O_2N_2ClSAs,2{\cdot}5H_2O$ requires C, 49·3; H, 5·4; N, 5·2%).

When this arsonous acid (5·35 g.) was added to a mixture of concentrated hydrochloric acid (5 c.c.) and water (5 c.c.) at 15°, it immediately formed an oil which rapidly resolidified. Benzene (8 c.c.) and potassium iodide (0·1 g.) were added, and sulphur dioxide bubbled through the mixture for 30 minutes. The mixture was filtered, and the benzene solution washed with water, dried (Na_2SO_4), and distilled; 2-*diphenylylethylchloroarsine* had b. p. 136—137°/0·2 mm. (Found: C, 57·55; H, 4·8. $C_{14}H_{14}ClAs$ requires C, 57·45; H, 4·8%); yield, 3·75 g. (70%). The use of more dilute hydrochloric acid at 50°, or of chloroform instead of benzene at 0°, in the above reduction gave rise to an impure product.

This compound was characterised by conversion into 2-*diphenylylethylarsino*-N-*pentamethylenedithiourethane*, white crystals (from ethyl acetate), m. p. 124—125° (Found: C, 57·4; H, 5·5. $C_{20}H_{24}NS_2As$ requires C, 57·6; H, 5·8%).

Diazomethane reacted readily with the chloroarsine, but well-defined products could not be isolated.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE.

[*Received, July* 13*th*, 1949.]