91. p-(2-*Chloroethylthio*)*phenyldichloroarsine*.

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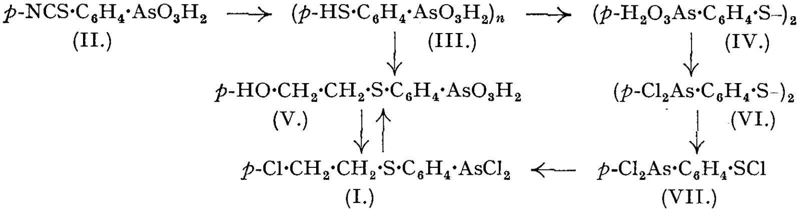
The substance named in the title has been synthesised from *p*-arsanilic acid by two methods. It possesses relatively mild vesicant properties.

In the course of a series of investigations on potential new chemical warfare agents, it was considered of interest to prepare p-(2-*chloroethylthio*)*phenyldichloroarsine* (I), which combines in its molecule structural features of the known vesicants phenyldichloroarsine and 2 : 2′-dichlorodiethyl sulphide. The substance proved to be a weaker vesicant than either of these compounds.



$$\begin{tikzcd}
\underset{\text{(II.)}}{p\text{-}NCS{\cdot}C_6H_4{\cdot}AsO_3H_2} \arrow[r] & (p\text{-}HS{\cdot}C_6H_4{\cdot}AsO_3H_2)_n \arrow[r] \arrow[d, "\text{(III.)}"] & (p\text{-}H_2O_3As{\cdot}C_6H_4{\cdot}S\text{-})_2 \arrow[d, "\text{(IV.)}"] \\
& \underset{\text{(V.)}}{p\text{-}HO{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}C_6H_4{\cdot}AsO_3H_2} \arrow[d, shift right] & (p\text{-}Cl_2As{\cdot}C_6H_4{\cdot}S\text{-})_2 \arrow[d, "\text{(VI.)}"] \\
& \underset{\text{(I.)}}{p\text{-}Cl{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}C_6H_4{\cdot}AsCl_2} \arrow[u, shift right] & \underset{\text{(VII.)}}{p\text{-}Cl_2As{\cdot}C_6H_4{\cdot}SCl} \arrow[l]
\end{tikzcd}$$

The preparation of *p*-thiocyanatophenylarsonic acid (II) from *p*-arsanilic acid, and its conversion into polymeric *p*-mercaptophenylarsonic acid (III) and thence into diphenyldisulphide *pp*′-diarsonic acid (IV) were carried out essentially by the methods described by Barber (*J.*, 1930, 2727). The mercapto-acid (III) reacted smoothly in alkaline solution with ethylene chlorohydrin, and the resulting *p*-(2-hydroxyethylthio)phenylarsonic acid (V) on treatment with concentrated hydrochloric acid and sulphur dioxide yielded the desired substance (I). An alternative method of synthesis involved the reduction of the disulphide acid (IV) to *diphenyldisulphide*-pp′-*bis*(*dichloroarsine*) (VI). Treatment of a chloroform solution of (VI) with chlorine gave a solution containing *p*-dichloroarsinophenylsulphenyl chloride (VII), which reacted with ethylene to yield (I). The identity of the product obtained by the second method was established by its conversion into the acid (V) by means of iodine and aqueous sodium hydrogen carbonate.

The work described in this paper was carried out in 1941. Simultaneously and independently, Morgan and Hamilton carried out a similar investigation, the results of which were transmitted to us after our work was complete. Subsequently, Morgan and Hamilton published their preparation of the acid (V) (*J. Amer. Chem. Soc.*, 1944, **66**, 874), but publication of our work was withheld for security reasons.

EXPERIMENTAL.

p-*Thiocyanatophenylarsonic Acid* (II).—The directions given by Barber (*loc. cit.*) were followed, with the exception that the addition of diazotised arsanilic acid to the cuprous thiocyanate was made in portions and the vigorous foaming which occurred was controlled by addition of a little capryl alcohol. The yield of recrystallised product was 50% (Barber claims 30%) (Found : neutralisation equiv., 129·5. Calc. for $C_7H_6O_3NSAs$: equiv., 129·5).

p-(2-*Hydroxyethylthio*)*phenylarsonic Acid* (V).—*p*-Thiocyanophenylarsonic acid (50 g.) was dissolved in 10% aqueous sodium hydroxide (500 c.c.) and the solution refluxed for 6 hours. The hot solution was acidified (Congo-red), and after several hours the crude *p*-mercaptophenylarsonic acid (III) (36·4 g.; 80%), an orange amorphous powder, was collected, washed with water, and dried at 60°.

The above crude mercapto-acid (30 g.) was dissolved in a solution of sodium hydroxide (16 g.) in water (400 c.c.), and ethylene chlorohydrin (9 c.c.) added. After standing at room temperature for 18 hours, the mixture was heated on the steam-bath for 2 hours. The hot solution was acidified (Congo-red), and on cooling the product (32·5 g.; 91%) crystallised. Recrystallisation from water gave nearly colourless leaflets (29·5 g.), m. p. 118° (Found : C, 34·1; H, 4·0; S, 11·2. Calc. for $C_8H_{11}O_4SAs$: C, 34·5; H, 4·0; S, 11·5%). The substance is dimorphous, and on crystallisation from dilute hydrochloric acid (5%) it usually separated in needles, m. p. 132—133°. From an aqueous solution needles or leaflets can be obtained by seeding with the appropriate form. The properties agree with those described by Morgan and Hamilton (*loc. cit.*).

Diphenyldisulphide-pp′-*diarsonic Acid* (IV).—Crude *p*-thiophenylarsonic acid (30 g.) was suspended in saturated aqueous sodium hydrogen carbonate (250 c.c.) and treated with the calculated volume (128 c.c.) of N-iodine. Excess of iodine is to be avoided, as oxidation proceeds further, though at a slower rate. When reaction was complete, the solution (filtered if necessary) was heated to boiling and just acidified to Congo-red. After cooling, the crystalline disulphide (27·5 g.; 92%) was collected, washed with water, dried and recrystallised from 50% aqueous acetic acid. It formed nearly colourless leaflets (24 g.), m. p. 220° (decomp.) (Found : C, 30·3; H, 2·7. Calc. for $C_{12}H_{12}O_6S_2As_2$: C, 30·9; H, 2·6%).

Diphenyldisulphide-pp′-*bis*(*dichloroarsine*) (VI).—Diphenyldisulphidediarsonic acid (10 g.) was dissolved in concentrated hydrochloric acid (50 c.c.) at room temperature. After a few minutes, crystallisation set in and the whole solution set to a thick paste. The colourless, crystalline material (11·25 g.) was collected on a sintered glass filter, washed with a little concentrated hydrochloric acid, and dried in a vacuum over sodium hydroxide. The substance is probably $(Cl_2OAs{\cdot}C_6H_4{\cdot}S{-})_2$; on treatment with hot water the original arsonic acid is produced. This oxychloride (10 g.) was suspended in concentrated hydrochloric acid (50 c.c.), chloroform (30 c.c.) and a trace of sodium iodide were added, and sulphur dioxide was passed into the mixture at room temperature, with occasional shaking, until the colour of iodine was discharged. The resulting pasty mixture was filtered, and the crystalline material was washed with a little cold chloroform and dissolved in boiling chloroform. The hot solution was dried ($CaCl_2$) and filtered; on cooling, colourless crystals of *diphenyldisulphide*-pp′-*bis*(*dichloroarsine*) (6 g.) separated. From the mother liquors and from the original chloroform washings a further quantity (1·9 g.) was obtained (total yield, 84%). The substance had m. p. 125·5—126·5° (Found : C, 28·8; H, 1·7; S, 13·0. $C_{12}H_8Cl_4S_2As_2$ requires C, 28·3; H, 1·6; S, 12·6%). When the reduction of the diarsonic acid was carried out without the intermediate isolation of the oxychloride, the yield was lower (65%).

p-(2-*Chloroethylthio*)*phenyldichloroarsine* (I).—(a) *By reduction of* p-(2-*chloroethylthio*)*phenylarsonic acid*. A solution of the arsonic acid (10 g.) in concentrated hydrochloric acid (50 c.c.) was heated on the steam-bath for 1 hour. A small amount of an oil separated from the hot solution, and on cooling a considerable oily layer separated. After addition of chloroform (20 c.c.) and a trace of sodium iodide, sulphur dioxide was passed in. The mixture became warm as reduction proceeded. When the colour of iodine had been discharged, the chloroform layer was collected and the aqueous layer extracted once with chloroform. The combined chloroform solutions were dried and evaporated, and the residual oil (10·6 g.; 96%) was distilled. p-(2-*Chloroethylthio*)*phenyldichloroarsine* was obtained as a colourless oil, b. p. 148—152°/0·05 mm. (7·75 g.; 68%) (Found : C, 30·8; H, 2·8; Cl, 32·2; S, 10·5. $C_8H_8Cl_3SAs$ requires C, 30·3; H, 2·5; Cl, 33·6; S, 10·1%). Titration of a chloroform solution with N/10-iodine in the presence of excess of aqueous sodium hydrogen carbonate required 98% of the calculated amount of iodine.

(b) *From diphenyldisulphide*-pp′-*bis*(*dichloroarsine*). The bis(dichloroarsine) (5 g.) was suspended in dry chloroform (50 c.c.), and a slow stream of dry chlorine was passed into the mixture at room temperature with occasional shaking. The solid gradually dissolved to give a bright yellow solution; when solution was complete, introduction of chlorine was stopped. The increase in weight of the solution was approximately 0·8 g. (theory, 0·71 g.). Excess of chlorine was removed by passing a stream of dry nitrogen through the liquid for 1½ hours. Ethylene was then passed in until the yellow colour of the solution was discharged and, very slowly, for a further hour. The chloroform was removed by distillation, leaving a brown oil (6 g.), from which a trace of crystalline material separated. The oil was taken up in chloroform, filtered, and distilled. The product (3·9 g.; 62%) had b. p. 144—152°/0·04 mm.; a redistilled sample, b. p. 152°/0·04 mm., gave poor analytical results (Found : C, 28·2; H, 2·5; Cl, 32·2%). That it consisted essentially of the required compound was, however, evident from its behaviour towards iodine; 0·1340 g. in chloroform and aqueous sodium hydrogen carbonate required 8·45 c.c. of 0·098N-iodine (calc., 8·6 c.c.), and after titration 4-(2-hydroxyethylthio)-

phenylarsonic acid was obtained from the aqueous layer by concentration and acidification. It had m. p. 118° undepressed in admixture with an authentic specimen.

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