STERNUTATORS[1]

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INTRODUCTION

Among the chemical agents which have been most frequently employed because of their sternutatory properties are methyldichloroarsine, ethyldichloroarsine, diphenylcyanoarsine, diphenylchloroarsine, and diphenylaminechloroarsine.

I. METHYLDICHLOROARSINE, DICHLOROMETHYLARSINE, CH_3AsCl_2

Bayer (9) prepared methyldichloroarsine by warming cacodyl trichloride to 40–50°C. and by the action of hydrochloric acid on cacodylic acid. Uhling and Cook (143) prepared it by methylating a solution of sodium arsenite with dimethyl sulfate at 85°C., then reducing the disodium methyl arsenite to methylarsine oxide by means of sulfur dioxide, and finally converting the oxide to methyldichloroarsine by passing hydrogen chloride through the oil:

$$Na_3AsO_3 \xrightarrow{(CH_3)_2SO_4} Na_2CH_3AsO_3 \xrightarrow{SO_2} CH_3AsO \xrightarrow{HCl} CH_3AsCl_2$$

Auger (5) obtained methyldichloroarsine by adding methylarsinic acid to cooled phosphorus trichloride; also by the action of chlorine on methylarsine (4). Gibson and Johnson (53) obtained it by decomposing 10-methyl-5, 10-dihydrophenarsazine with dry hydrogen chloride at 110–130°C.:

$$NH(C_6H_4)_2AsCH_3 + 2HCl \rightarrow CH_3AsCl_2 + (C_6H_5)_2NH$$

By treating sodium dimethylarsenate with concentrated hydrochloric acid (density 1.19) (155, 156); by dissolving cacodylic acid in concentrated hydrochloric acid and saturating with hydrogen chloride (9, 151); by the hydrolysis of dimethyltrichloroarsine (151).

It was thought by Dehn and Wilcox (35) and by Palmer (101) that probably chlorine reacts with dimethylarsine with the formation of chloro-

[1] This is the fifth in a series of five articles on chemical warfare materials. For preceding articles see Chem. Rev. **14**, 251 (1934); **15**, 425 (1935); **16**, 195, 439 (1935).—*Editor.*

cacodyl hydrochloride which decomposes at the temperature of the reaction and forms cacodyl chloride; this could then react with chlorine with the formation of the pentavalent body, dimethylarsinetrichloride, $(CH_3)_2AsCl_3$, which decomposes at a temperature above 40–50°C. with the formation of methyldichloroarsine:

$$(CH_3)_2AsH \xrightarrow{Cl_2} (CH_3)_2AsCl \cdot HCl \xrightarrow{\text{decomposes}}$$

$$(CH_3)_2AsCl \xrightarrow{Cl_2} (CH_3)_2AsCl_3 \xrightarrow{\text{decomposes}} CH_3AsCl_2$$

Physical properties

Methyldichloroarsine is a colorless, heavy, mobile, strongly refractive liquid, boiling at 37°C. at 25 mm. (66), 55.5°C. at 50 mm. (53), 72.1°C. at 100 mm. (53), 89.1°C. at 200 mm. (53), 109.1°C. at 400 mm. (53), 123°C.

TABLE 1

Vapor pressure of methyldichloroarsine

log vapor pressure = 8.6944 − 2281.7/273 + t

TEMPERATURE	VAPOR PRESSURE OBSERVED	VAPOR PRESSURE CALCULATED	DIFFERENCE CALCULATED − OBSERVED
°C.	mm.	mm.	mm.
35	19.33	19.33	0.00
25	10.83	10.90	+0.07
15	5.94	5.91	−0.03
0	2.17	2.17	0.00
−15	0.67	0.71	+0.04
−16.8	0.56	0.61	+0.05
−17	0.53	0.60	+0.07

(35), 130–132°C. (155, 156), 131.8–132.4°C. at 12 mm. (63), 132°C. (151), 132.5°C. (53), 133°C. (5, 9, 66, 83, 95). It is somewhat soluble in water but more soluble in the usual organic solvents. $d_4^{20°}$, 1.8358 (vacuum) (53); $d_4^{20°}$, 1.8380 (83); $d_{4.0°}^{14.5°}$, 1.8471 (63). Its volatility at 20°C. amounts to 75 grams per cubic meter (3, 95). Its vapor tension at 25°C. is 10.83 mm. (83). The molecular heat of vaporization and Trouton's constant at 760 mm. are calculated as 7890 calories and 19.4 (53). Its index of refraction at 14.5°C. is as follows: $n_\alpha = 1.5624$, $n_D = 1.5677$, $n_\beta = 1.5814$, $n_\gamma = 1.5933$ (63). The molecular refraction values for the D line of sodium and the α, β, and γ hydrogen lines are, respectively, 28.50, 28.28, 29.06, and 29.35 (63).

Baxter, Bezzenberger, and Wilson (12) determined the vapor pressure of methyldichloroarsine by the "air current" or "transference" method. A known volume of air, as determined by the measured volume of water

run out of an aspirator, was saturated with the vapor of methyldichloroarsine by passing through a weighed receptacle maintained at constant temperature in a water thermostat. The loss in weight of the saturating tube furnished the weight of evaporated substance. From the latter quantity the volume of vapor was calculated on the assumption that the volume of a gram-molecule under standard conditions is 22.4 liters. The per cent of vapor by volume multiplied by the interior pressure, as determined by the barometric reading and an open-arm manometer attached to the aspirator, gives the vapor pressure. The control of the temperature in the thermostat was within 0.1°C.

A plot of the logarithm of the vapor pressure against the reciprocal of the absolute temperature gives a very nearly straight line, which, therefore, can be represented by an empirical equation of the form:

$$\log \text{vapor pressure} = A + B/273 + t$$

Vapor pressures calculated by means of these equations agree with the observed values within the experimental error. For a higher degree of accuracy the equations were not adequate, however, and can not be trusted for extrapolation over any considerable range.

Chemical properties

(*a*) *Reduction.* Upon reduction of methyldichloroarsine, methylarsine is formed (32, 101, 102).

(*b*) *Action with metals.* Magnesium does not act on methyldichloroarsine even when boiled in the presence of anhydrous ether, but when water is added the two react violently, giving essentially monomethylarsine, methylarsenide, $(CH_3As)_x$, being precipitated, and magnesium chloride left in solution. Zinc produces a similar decomposition (154).

(*c*) *Action with chlorine.* Upon passing chlorine into a carbon disulfide solution of methyldichloroarsine cooled to −10°C., methylarsenic tetrachloride, CH_3AsCl_4, forms as large crystals (9); it decomposes at 0°C. to methyl chloride and arsenic trichloride.

(*d*) *Action with hydrogen sulfide.* Upon passing hydrogen sulfide into methyldichloroarsine, methylarsenious sulfide, CH_3AsS, is formed (9); it smells of asafoetida, and forms in yellow crystals, m.p. 95°C.

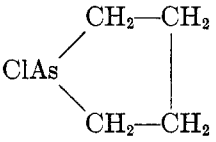
(*e*) *Action with potassium hydroxide.* Upon heating methyldichloroarsine with potassium hydroxide there is formed methylarseno oxide, CH_3AsO, yellow crystals, m.p. 95°C.; this compound smells of asafoetida (9).

(*f*) *Action with chloropicrin.* Methylarsenic acid, $CH_3AsO(OH)_2$, obtained by treating the sodium salt (from treating methyldichloroarsine with

sodium ethoxide) with chloropicrin, crystallizes from alcohol in colorless plates melting at 132–133°C. (150).

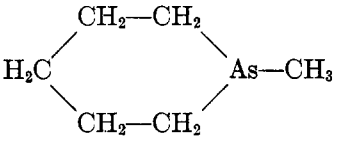
(*g*) *Action with isoamyl chloride.* When an ethereal solution of methyldichloroarsine is treated with a similar solution of isoamylmagnesium chloride (in an atmosphere of nitrogen) there is formed methyldiisoamyl arsine, $CH_3(C_5H_{11})_2As$, a liquid boiling at 95–96°C. at 11 mm. (129).

(*h*) *Action with* α,ϵ-dibromopentane. (1) Cyclotetramethylenearsine chloride,

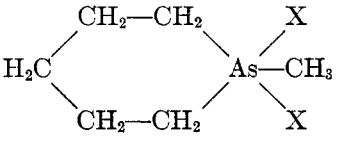


The Grignard reagent prepared from α,ϵ-dibromopentane in ether with magnesium is cooled and treated with methyldichloroarsine; the product, decomposed with hydrochloric acid and with chlorine, forms a clear liquid, boiling at 77°C. at 18 mm. (131).

(2) Methylcyclopentamethylene arsine, 1-methylarsepedine,



appears to be the first case of a heterocyclic compound with arsenic in the ring. Methyldichloroarsine added to the Grignard reagent prepared from α,ϵ-dichloropentane, magnesium, and methyl iodide in ether forms a colorless liquid, boiling at 160°C., and possessing the odor of mustard oil. It is insoluble in water and hydrochloric acid, but soluble in alcohol, ether, petroleum ether, benzene, and carbon tetrachloride. It is volatile with steam. It is not combustible, but when poured upon filter paper it causes the latter to inflame and clouds of arsenious oxide vapor are given off. In contact with air it is oxidized with formation of the oxide, which is colorless and possesses a more agreeable odor than the cycloarsine. It reduces ammoniacal silver nitrate and alkaline permanganate solutions. It combines additively with halogens (152) giving compounds of the type



It boils at 156°C. (153), 76°C. at 36 mm. (153), 65°C. at 20–22 mm. (153), 57–58°C. at 20 mm. (60). $d_4^{18°}$, 1.2180 (153).

Test

When a few drops of mercurous nitrate are brought in contact with methyldichloroarsine, a dark gray precipitate containing metallic mercury is formed (97).

Physiological properties

Methyldichloroarsine has a very irritating effect on the mucous membrane. Hyperemia, swelling, edema, ulceration, and necrosis take place on the skin of the dog, and similar changes, together with vesication, take place on human skin (64).

II. ETHYLDICHLOROARSINE, DICHLOROETHYLARSINE, $C_2H_5AsCl_2$

Preparation

Ethyldichloroarsine was first prepared by LaCoste in 1881 (73) and later by Steinkopf and Mieg (130) by treating mercury diethyl with arsenic trichloride. Dehn (33) found that when ethylarsine, in a sealed tube, was treated with any one of the following chlorides—mercury (ic), phosphorus (ous), tin (ous), arsenic (ous), or antimony (ous)—ethyldichloroarsine was obtained. It results when arsenic trichloride reacts with ethyl magnesium bromide at low temperature (6). McKenzie and Wood (84) prepared ethyldichloroarsine by first preparing ethyldiiodoarsine from ethyl iodide and a sodium hydroxide solution of arsenious oxide, through which sulfur dioxide was passed until the iodine color was removed. The ethyliodoarsine was then changed to the oxide with calcium chloride and anhydrous sodium carbonate, and the oxide converted to the chloride by passing in hydrogen chloride. Norris (99) prepared the chloroarsine by treating ethylarsenious oxide with hydrochloric acid. Arsenious oxide was combined with ethyl chloride at 100°C. with vigorous stirring to form ethylarsenious oxide; the oil was then chlorinated at 12 atmospheres and finally treated with sulfuric acid and sodium sulfite (26). It has also been prepared by the decomposition of 10-ethyl-5,10-dihydrophenarsazine with dry hydrogen chloride at 110–130°C. (53).

Physical properties

Ethyldichloroarsine is a clear, colorless liquid having a faint, fruity odor. It is slightly soluble in water and miscible in all proportions with alcohol, ether, and benzene (73). Its boiling point has been reported as 21.5°C. at 2.295 mm. (66), 74°C. at 74 mm. (53), 90°C. at 100 mm. (53), 109.6°C. at 200 mm. (53), 131.2°C. at 400 mm. (53), 145–150°C. (83, 130), 152.5–153.5°C. (63), 153°C. (66), 153–156°C. (137), 155.3°C. (53), 156°C. (3, 33, 57, 73, 123). Its vapor pressure at 20°C. is 0.022 mm. (137). $d_{4^\circ}^{20^\circ}$ (vacuum), 1.6595 (53); $d_{4.0^\circ}^{14.5^\circ}$, 1.7420 (63). Its volatility at 0°C. is 5.08 g. per

cubic meter (137). At 21.5°C. 22 g. saturates 1 cubic meter (3). Its molecular heat of vaporization and Trouton's constant at 760 mm. are calculated as 9180 calories and 21.4 (53). Its index of refraction at 14.5°C. has been reported as follows: $n_\alpha = 1.5537$, $n_D = 1.5588$, $n_\beta = 1.5713$, $n\gamma = 1.5820$ (63). The molecular refraction values for the D line of sodium and the α, β, and γ hydrogen lines are, respectively, 32.42, 32.18, 33.02, and 33.53 (63).

Chemical properties

(*a*) *Action with nitric acid.* Ethylarsinic acid, $C_2H_5AsO(OH)_2$, is obtained from ethyldichloroarsine by prolonged warming with dilute nitric acid (34, 73). It crystallizes in needles, m.p. 95–96°C. One hundred parts of water dissolve 70 parts of the acid at 27°C. and 112 parts at 40°C.; 100 parts of 96 per cent alcohol dissolve 70 parts of the acid at 25°C. (34).

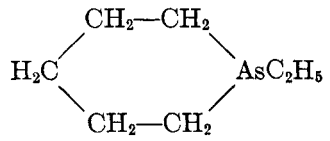
(*b*) *Action with sodium iodide.* Ethyliodoarsine, $C_2H_5AsI_2$, is prepared by the interaction of ethyldichloroarsine and sodium iodide in dry acetone solution; the product boils at 122.7°C. at 11 mm. (133). It is a reddish-yellow oil, boiling at 126°C. at 11 mm., and separates as a pale crystalline solid melting at −9°C. on cooling in solid carbon dioxide (20).

(*c*) *Action with hydrogen sulfide.* Ethylarsino sulfide, C_2H_5AsS, is prepared by the action of hydrogen sulfide on an alcoholic solution of ethyldichloroarsine. It is a yellow oil with an offensive odor. It is soluble in carbon disulfide and chloroform. $d_{4.0°}^{17.5°}$, 1.8218 (72).

(*d*) *Action with potassium carbonate.* Ethylarsine oxide, C_2H_5AsO, is obtained by treating ethyldichloroarsine with a benzene solution of potassium carbonate and fractionating *in vacuo*, all reactions taking place in carbon dioxide. It is colorless oil, boiling at 158°C. at 10 mm.; it is soluble in benzene, ether, and acetone (130).

(*e*) *Action with alkyl halides.* Ethyldipropylarsine, $C_2H_5[(C_3H_7)]_2As$, prepared by treating the Grignard solution obtained from propyl bromide and magnesium in ether with an ethereal solution of ethyldichloroarsine, is a highly refractive liquid boiling at 60–64°C. at 14 mm. (127). Ethyldiisobutylarsine, $C_2H_5[(CH_3)_2CH \cdot CH]_2As$, prepared by treating the Grignard solution obtained from isobutyl bromide and magnesium in ether with an ethereal solution of ethyldichloroarsine, is a strongly refractive liquid boiling at 86°C. at 16 mm. (127).

(*f*) *Action with* α,ϵ-*dibromopentane.* Cyclopentamethyleneethylarsine,



prepared by treating two molecules of the cooled Grignard solution of α,ϵ-dibromopentane in ether with one molecule of an ethereal solution of ethyldichloroarsine, has a not unpleasant, more ethereal than arsine-like odor when fresh, but develops the typical arsine odor in a day. It boils at 62–64°C. at 12.5 mm. (127).

(*g*) *Action with ethyl bromide.* Diethylarsinic acid, ethylcacodylic acid, $(C_2H_5)_2AsOOH$, is prepared by warming ethyl bromide for four to six hours with ethyldichloroarsine and sodium hydroxide. The large glistening plates have an acid reaction, are odorless, have a bitter taste, melt at 190°C. and are very deliquescent in air. The compound is easily soluble in water and alcohol, the solutions liberating carbon dioxide from alkali carbonates; it is unattacked by concentrated nitric acid or aqua regia (76, 77, 104).

(*h*) *Action with chloropicrin.* Ethylarsinic acid, $C_2H_5AsO(OH)_2$, is obtained by treating the sodium salt (prepared by reaction of sodium ethoxide on ethyldichloroarsine) with chloropicrin; it forms colorless needles, melting at 98–99°C. (150).

(*i*) *Action with ethyl-β-bromoethyl sulfide.* Ethyl(β-ethylsulfonylethyl) arsinic acid, $C_2H_5AsOOHC_2H_4SO_2C_2H_5$. The sodium salt of this acid is obtained by treating ethyldichloroarsine with sodium ethoxide, then adding slowly ethyl-β-bromoethyl sulfide; on acidifying with concentrated hydrochloric acid, the acid separates as colorless, short needles, m.p. 164–165°C., soluble in water, alcohol, almost insoluble in acetone (125).

Test

When mercurous nitrate solution is added to a solution of ethyldichloroarsine, a white precipitate which turns gray within a few seconds is formed (97).

Physiological properties

Ethyldichloroarsine is extremely irritating in its action upon the mucous membrane of the nose, eyes, and throat, and causes painful wounds on the skin. It is very dangerous for those working with it, since its vapor causes respiratory embarrassment, faintness and long-lasting paralysis, and anesthesia of the extremities (73).

III. DIPHENYLCYANOARSINE, CYANODIPHENYLARSINE, $(C_6H_5)_2AsCN$

Preparation

Sturniolo and Bellinzoni (138, 139) originally prepared diphenylcyanoarsine, and McKenzie and Wood (84) and others (96, 133) prepared it later by treating diphenylarsenious oxide, $[(C_6H_5)_2As]_2O$, or the ethoxy compound (resulting from the treatment of diphenylchloroarsine with sodium ethoxide) with dry hydrogen cyanide. Morgan and Vining (96) prepared

diphenylcyanoarsine by the following methods: (a) by stirring diphenylchloroarsine at 100°C. with 30 per cent hypochlorous acid forming diphenylcacodyl (tetraphenyldiarsine), $(C_6H_5)_2As—As(C_6H_5)_2$, which, when heated to 250°C. with mercuric or silver cyanide in a rotating autoclave, produces diphenylcyanoarsine; (b) by heating diphenylarsenious sulfide, $(C_6H_5)_2As—S—As(C_6H_5)_2$, with mercuric or silver cyanide for two hours at 160–200°C.; (c) by heating diphenylarsenious chloride, while vigorously stirred, with an excess of dry silver cyanide for three hours at 150–160°C.

Norris (99) prepared diphenylcyanoarsine by vigorously stirring diphenylchloroarsine with a saturated solution of sodium or potassium cyanide at 60°C.; Steinkopf and Schwen (134) prepared it by heating diphenylmethylarsine cyanobromide, $(C_6H_5)_2CH_3AsBrCN$, while Steinkopf, Donat, and Jaeger (127) obtained it by heating diphenylethylarsine cyanobromide, $(C_6H_5)_2C_2H_5AsBrCN$.

Physical properties

Diphenylcyanoarsine crystallizes in colorless, monoclinic plates, having the odor of garlic and bitter almonds. Its melting point has been reported as 28–30°C. (96), 30–34°C. (84), 31°C. (133, 145, 147), 31–32°C. (84), 31.5°C. (3, 95, 127, 133, 134, 137), 32–33°C. (63), 32–34°C. (138, 139), 35°C. (83, 138, 139). Its boiling point has been given as 185°C. (146), 191°C. at 10 mm. (66), 192°C. at 14 mm. (137), 192–194°C. at 12 mm. (66), 200–201°C. at 13.5 mm. (133), 204–205°C. at 12 mm. (63), 207–209°C. at 23 mm. (127), 213°C. at 21 mm. (84), 255°C. at 85 mm. (66), 257°C. at 103 mm. (66), over 300°C. (57, 144), 346°C. (3, 95). At 20°C., 0.1–0.15 mg. of it saturates 1 cubic meter of air (3). $d_4^{52°}$ 1.3160 (63). Its index of refraction at 52°C. is as follows: n_α = 1.6092, n_D = 1.6153, n_β = 1.6333 (63). The molecular refraction values at 52°C. for the D line of sodium and for the α and β hydrogen lines are, respectively, 67.65, 67.11, and 69.23 (63).

Chemical properties

(*a*) *Action with water.* Moist air, acting upon diphenylcyanoarsine, causes the liberation of hydrogen cyanide (138). By treating with water or by heating with water or by distilling in a current of steam or under reduced pressure (100 mm.) the compound is converted into diphenylarsenious oxide.

(*b*) *Action with oxidizing agents.* When heated with concentrated nitric acid on a water bath, or with hydrogen peroxide, or with bromine water, in the cold, diphenylcyanoarsine yields diphenylarsinic acid, $(C_6H_5)_2AsOOH$ (138).

(*c*) *Action with alkali.* Diphenylcyanoarsine is very sensitive to alka-

lies, being changed to the oxide easily by even the effect of the alkali of the glass vessel, the reaction occurring in the following stages (84):

$$2(C_6H_5)_2AsCN \xrightarrow{H_2O} 2(C_6H_5)_2As(CN)\begin{matrix}H\\ \diagup\\ \diagdown\\ OH\end{matrix} \xrightarrow{-HCN} 2(C_6H_5)_2AsOH \xrightarrow{-H_2O}$$

$$(C_6H_5)_2As—O—As(C_6H_5)_2$$

(*d*) *Action with chlorine.* On allowing chlorine to pass into a cooled benzene (or carbon tetrachloride) solution of the cyanoarsine, a solid soon separates; the passage of the halogen is continued until the liquid becomes green in tint. On removal, the solid fumes in air and melts at approximately 115°C.; it contains chlorine but no nitrogen. Upon boiling with water it dissolves, and on cooling, needles of diphenylarsinic acid separate. It seems likely that the compound in question is diphenylarsenic oxychloride, $(C_6H_5)_2AsCl_2—O—Cl_2As(C_6H_5)_2$, produced by the hydrolysis of the cyano group, thus (84):

$$(C_6H_5)_2AsCl_2 \cdot CN + H_2O \rightarrow (C_6H_5)_2AsCl_2 \cdot OH + HCN$$
$$2(C_6H_5)_2AsCl_2 \cdot OH \rightarrow H_2O + (C_6H_5)_2AsCl_2O(C_6H_5)_2AsCl_2$$

On allowing the filtrate resulting from the removal of the solid in the above to remain for several days at ordinary temperature, a crystalline product gradually deposits, which softens at 123°C. and melts at 127°C. This contains both chlorine and nitrogen and is apparently diphenylcyanoarsine dichloride, $(C_6H_5)_2As(CN)Cl_2$. Once isolated it appears to be fairly stable when dry; when boiled with water, it dissolves completely, and needles of diphenylarsinic acid separate on cooling, as represented by the equations (84):

$$(C_6H_5)_2As(CN)Cl_2 + 3H_2O \rightarrow HCN + 2HCl + (C_6H_5)_2As(OH)_3$$
$$(C_6H_5)_2As(OH)_3 \rightarrow H_2O + (C_6H_5)_2AsOOH$$

(*e*) *Action with methyl iodide.* Diphenyldimethylarsoniumtriiodide, $(C_6H_5)_2As(CH_3)_2I_3$, results when methyl iodide reacts at 100°C. with diphenylcyanoarsine. It crystallizes in violet needles, which melt at 69°C. and are insoluble in water or ether (133).

Job and Guinot (67) obtained French patent 521,469 on July 15, 1921 for the preparation of diphenylarsinecarboxylic acid, $(C_6H_5)_2AsCOOH$, by the hydrolysis of diphenylcyanoarsine. By treatment of diphenylarsinecyanide with hydrogen peroxide, or a substance yielding hydrogen peroxide, diphenylarsine formamide, $(C_6H_5)_2AsCONH_2$, is formed.

Treatment

Upon bubbling chlorine into solutions of diphenylcyanoarsine, the arsenic is oxidized to the pentavalent form. The resulting products are non-irritating when breathed by men, and give no reaction when titrated with iodine. It was found by Walton and Eldridge (146) that men gassed with diphenylcyanoarsine are markedly benefitted if given chlorine.

Physiological properties

Diphenylcyanoarsine irritates the mucous membrane, provoking sneezing (138). Hanzlik and Tarr (64) found the cyanoarsine to be a mild irritant, as is indicated by simple hyperemia without vesication, mild urticarial rash, moderate swelling and edema, and very little or no necrosis.

IV. DIPHENYLARSENIOUS CHLORIDE, DIPHENYLCHLOROARSINE, $(C_6H_5)_2AsCl$

Preparation

Diphenylchloroarsine was first prepared by LaCoste and Michaelis (74) in 1878 by the interaction of mercury diphenyl and arsenic trichloride; the procedure was later modified by Michaelis and coworkers (75, 89, 92). Michaelis has also prepared it by converting triphenylarsine into its dichloride and distilling under 13–14 mm. pressure (90). It has been made by heating triphenylarsine with arsenic trichloride as follows: (1) Pope and Turner (103) prepared it by slowly adding arsenic trichloride dropwise to the triphenylarsine at 350°C. and fractionating the product at 12–15 mm.; (2) Morgan and Vining (96) by heating the triphenylarsine with arsenic trichloride for three hours at 250–280°C. in a rotating autoclave under a pressure of 4.2 to 7 kg. per square centimeter and then fractionating in an atmosphere of carbon dioxide; (3) Oechslin (100) on July 10, 1920 obtained British patent 173,796 for the preparation of diphenylchloroarsine by heating triphenylarsine with arsenic trichloride at 250–350°C. at ordinary pressure. Upon heating phenylarsenious dichloride and triphenylarsine for four hours at 300°C. and distilling the resulting pasty mass under diminished pressure, Pope and Turner (103) were able to obtain nearly pure diphenylarsenious chloride. In view of the possible importance of these reactions, protection was secured by British patent 142,880 on June 11, 1918.

Norris (99) describes the preparation of diphenylchloroarsine as follows: aniline, dissolved in hydrochloric acid, is diazotized with sodium nitrite at 0–5°C., and the resulting benzenediazonium chloride converted into disodium phenylarsonate by condensation with sodium arsenite. This is first transformed into the free arsinic acid by neutralization with hydrochloric acid, and then reduced to phenyldihydroxyarsine (phenylarsenious

acid) by means of sodium sulfite. After dissolving in caustic soda, the dihydroxyarsine is condensed with benzenediazonium chloride to form the sodium salt of diphenylarsinic acid, which is then neutralized with hydrochloric acid, yielding the free arsinic acid. By dissolving in hydrochloric acid and introducing an excess of sulfur dioxide, the diphenylarsinic acid is reduced to diphenylarsenious chloride:

$$C_6H_5N_2Cl \xrightarrow{Na_3AsO_3} C_6H_5AsO_3Na_2 \xrightarrow{Na_2SO_3} C_6H_5As(OH)_2 \xrightarrow{C_6H_5N_2Cl}$$

$$(C_6H_5)_2AsOONa \xrightarrow{SO_2} (C_6H_5)_2AsCl$$

Contardi (29) devised an improvement in the method, which consisted in heating diphenylamine with arsenic trioxide instead of the trichloride. Fused diphenylamine was converted into the hydrochloride by heating with hydrochloric acid (density 1.18) with continuous agitation until the water was almost eliminated, and the residual white powder, dried at 50–60°C., was fused with arsenic trioxide, while being stirred continuously. The heating and stirring was continued for four hours after fusion, during which time the temperature gradually rose to 200°C., the reaction being complete when the evolution of water vapor ceased. Steinkopf, Schubart, and Schmidt (132) prepared the chloride by the reaction of chloroacetyl chloride, carbonyl chloride, phosphorus trichloride, or benzenesulfonyl chloride with diphenylarsine; Blicke, Patelski, and Powers (13) by the action of sulfur chloride, thionyl chloride, arsenic trichloride, phenylarsine oxychloride, or phosphorus trichloride on tetraphenyldiarsyl; Blicke and Powers (15) by the action of phenylchloroethoxyarsine, triphenylarsinedichloride, or triphenylarsine hydroxychloride on diphenylarsine and by the reaction of triphenylarsine dichloride, or triphenylarsine hydroxychloride, on tetraphenyldiarsyl.

Other methods of preparation of diphenylarsenious chloride are accomplished as follows: by gradually adding phenylmagnesium bromide to a large excess of arsenic trichloride in the presence of ether (87); by treating diphenylarsine oxide with an alcoholic solution of hydrochloric acid (90); by boiling benzene with arsenic trichloride (74); by the reduction of diphenylarsinic acid with sulfur dioxide (70); by the reaction between phenyldichloroarsine and diphenylarsine (14); by the Friedel-Crafts reaction using arsenic trichloride and phenyldichloroarsine (147); by heating phosphorus trichloride with triphenylarsine in a sealed tube to 160°C. (27); by the action of aromatic Grignard reagents on arsenic trioxide (16); by the reaction of diphenylarsine with phenyldichloroarsine (128); by the fractional distillation of (a) triphenylchlorodiarsine (128), (b) triphenylarsinedichloride (90), (c) monophenylarsenochloride (89); by the decomposition of diphenylarsenious sulfide with concentrated hydrochloric acid (90); by

the heating of phenylchloroarsine with mercury diphenyl (90); by the action of arsenic trichloride on an ethereal solution of triphenylbismuthine (28); by the reaction of arsenic trichloride on lead tetraethyl (59). Diphenylarsenious chloride is obtained as a by-product in the preparation of triphenylarsine (93, 115); also by the oxidation of (a) phenylhydrazine with pyroarsenic acid in the presence of copper at 75°C., (b) phenylhydrazine arsenate with arsenic acid in the presence of copper at 70°C. (157).

Physical properties

Diphenylchloroarsine is a pale yellow, oily liquid which decomposes upon heating, but in an atmosphere of carbon dioxide boils at the following temperatures: 333°C. (3, 57, 70, 74, 75, 79, 83, 90, 133, 144, 146), 285°C. at 320 mm. (66), 253°C. at 134 mm. (66), 245°C. at 102 mm. (66), 230°C. at 13–14 mm. (133), 224°C. at 55 mm. (66), 218°C. at 48 mm. (66), 214°C. at 42 mm. (66), 211°C. at 38 mm. (66), 205°C. at 30 mm. (66), 193–194°C. at 16 mm. (63), 193°C. at 20 mm. (66), 189°C. at 17 mm. (66), 185°C. at 15 mm. (103), 180°C. at 10 mm. (66), 179–181°C. at 11 mm. (66), 178.6°C. at 10 mm. (57), 172°C. at 7 mm. (65), 161–163°C. at 5 mm. (132). Its melting point has been given as follows: 34°C. (99), 37–38°C. (79), 37–41°C. (13), 37.5°C. (47), 38°C. (3, 83), 38–39°C. (132), 38.5–39.0°C. (43), 39–40°C. (96), 40–41°C. (63), 40–42°C. (15, 16), 41–42°C. (13), 42–43°C. (13), 43°C. (123), 44°C. (57, 146), 44–45°C. (144).

Diphenylchloroarsine exhibits dimorphism: the unstable modification, obtained by spontaneous crystallization of freshly redistilled material or by heating the stable form to 130°C. and cooling under "aseptic" conditions, forms silky needles melting at 18.2–18.4°C., while the stable modification forms rhombic, doubly refracting, biaxial crystals melting at 38.7–38.9°C. (56). The vapor pressure is 0.0001 at 0°C. and 0.0004 at 25°C. (144). The compound has a faint odor at ordinary temperatures; this becomes very irritating when heated. It is soluble in organic solvents, difficultly soluble in aqueous alkalies, and insoluble in water (133). $d_{4^\circ}^{18^\circ}$, 1.4820 (65); $d_{4^\circ}^{15^\circ}$, 1.42231 (74, 75, 133); $d_{4^\circ}^{42^\circ}$, 1.3870 (65); $d_{4^\circ}^{56^\circ}$, 1.3760 (63); $d_{4.0^\circ}^{52.5^\circ}$, 1.3680 (65); $d_{4.0^\circ}^{80\text{-}5^\circ}$, 1.3500 (65). Its index of refraction at 56°C. is: $n_\alpha = 1.6256$, $n_D = 1.6332$, $n_\beta = 1.6525$ (63). The molecular refraction values at 56°C. for the D line of sodium and the α and β hydrogen lines are, respectively, 68.66, 68.01, and 70.32 (63).

Henley and Sugden (65) calculate the parachor of diphenylchloroarsine by the formula:

$$[P] = M\gamma^{1/4}(D - d)$$

where M = molecular weight, γ = surface tension (dynes per centimeter) determined by the method of maximum bubble pressure, and D and d are

densities of liquid and vapor, respectively, which were determined by means of a U-shaped pyknometer.

Baxter, Bezzenberger, and Wilson (12) determined the vapor pressure of diphenylarsenious chloride by the "air current" or "transference" method (table 3).

TABLE 2

Parachor of diphenylchloroarsine

t	γ	D	$[P]$
°C.			
17.9	45.30	1.411	486.3
42.5	42.65	1.386	487.6
61.0	40.37	1.369	487.0
80.5	38.32	1.350	487.5
Mean value			487.1

TABLE 3

Vapor pressure of diphenylarsenious chloride

TEMPERATURE	VAPOR PRESSURE (OBSERVED)	VAPOR PRESSURE (CALCULATED)	DIFFERENCE (CALCULATED − OBSERVED)
°C.	*mm.*	*mm.*	*mm.*
75	0.0282	0.0278	−0.0004
65	0.0148	0.0146	−0.0002
55	0.0065	0.0074	+0.0009
45	0.0039	0.0036	−0.0003
25	0.0003	0.0008	+0.0005

Chemical properties

(*a*) *Action with water.* Diphenylchloroarsine is hydrolyzed slowly by water forming diphenylarsinic acid, $(C_6H_5)_2AsOOH$ (74, 75, 89, 90, 116).

(*b*) *Action with halogens.* With chlorine and bromine, diphenylchloroarsine combines additively, forming the corresponding diphenylarsine trihalides (75, 133). Diphenylchloroarsenic bromide, $(C_6H_5)_2AsClBr_2$, and the perbromide, $(C_6H_5)_2AsClBr_4$, result when dry bromine is added to cooled diphenylchloroarsine. The former, a yellow crystalline solid, m.p. 158°C. (70), fumes slightly in air and is soluble with partial decomposition in benzene or ether on prolonged boiling (114); the latter forms orange-red crystals, m.p. 150–151°C. (70). On exposure to moist air both bromides lose all the halogen present. When diphenylchloroarsine is treated with dry chlorine, diphenylarsenic chloride, $(C_6H_5)_2AsCl_3$, results. It crystallizes from dry benzene in colorless plates, m.p. 174°C.,

and is decomposed by water, forming hydrochloric acid and diphenylarsinic acid (74, 75, 89). Chlorine water oxidizes diphenylarsenious chloride to diphenylarsinic acid (90). The addition of chlorine to diphenylchloroarsine in neutral solution forms diphenylarsine trichloride (dichlorodiphenylarsonium chloride) $[(C_6H_5)_2AsCl_2]Cl$, m.p. 189°C., which on recrystallization from moist acetone is converted into dihydroxydiphenylarsonium chloride, $(C_6H_5)_2As(OH)_2Cl$ (70).

(*c*) *Action with metals.* Diphenylchloroarsine is attacked by zinc at 100°C. with the production of a small quantity of a crystalline compound which melts at 154°C. and which dissolves freely in benzene (75).

(*d*) *Action with acids.* On continued boiling with concentrated nitric acid, diphenylchloroarsine is oxidized to diphenylarsinic acid (70, 75, 133). On boiling with hydrochloric acid diphenylchloroarsine is decomposed with the liberation of arsenic trichloride (112). When the chloroarsine is heated with hypophosphorus acid at 100°C., diphenylcacodyl (tetraphenyldiarsine), $(C_6H_5)_2As—As(C_6H_5)_2$, is formed (96). When diphenylchloroarsine is treated with chlorosulfonic acid there are formed colorless prisms of the compound having the formula, $2[(C_6H_5)_2AsO(OH)]\cdot HCl$, m.p. 114°C., the substance, $(C_6H_5)_2AsO(OH)\cdot HCl$, m.p. 110–130°C., and benzenesulfonyl chloride, $C_6H_5SO_2Cl$ (132). When diphenylchloroarsine is treated with fluorosulfonic acid there is formed the compound $2[(C_6H_5)_2AsO(OH)]\cdot H_2SO_4$, m.p. 117°C. (132).

(*e*) *Action with a hydroxide.* Upon boiling an alcoholic solution of diphenylchloroarsine with alcoholic potassium hydroxide, diphenylarsenious oxide, $(C_6H_5)_2As—O—As(C_6H_5)_2$, m.p. 89–91°C. is formed (74, 75, 103); the melting point is also given as 92.5–93.5°C. (84).

(*f*) *Action with hydrogen peroxide.* The oxidation of diphenylchloroarsine is easily carried out with hydrogen peroxide at 40–50°C. and yields diphenylarsinic acid; probably $(C_6H_5)_2As(OH)_2Cl$ occurs as an intermediate product, $[(C_6H_5)_2As(OH)OAs(C_6H_5)_2(OH)_2]Cl$ being obtained when the oxidation is carried out in acetone with hydrogen peroxide (70).

(*g*) *Action with hydrogen and sodium sulfides.* Upon passing hydrogen sulfide into an alcoholic solution of diphenylchloroarsine, diphenylarsenious sulfide, $(C_6H_5)_2As—S—As(C_6H_5)_2$, separates as glistening white needles, m.p. 64°C. (72) or 67°C. It is readily soluble in benzene, carbon disulfide, chloroform, less soluble in alcohol, ether, and acetic acid, insoluble in alkalies and alkaline sulfides (90). When the chloroarsine is dissolved in benzene and shaken with a saturated solution of normal or acid sodium sulfide, diphenylarsenious sulfide is likewise formed (72, 84, 90, 96).

(*h*) *Action with thionyl chloride.* The interaction of diphenylchloroarsine and thionyl chloride on a water bath for ten minutes yields a definite crystalline, colorless addition compound of the composition, $(C_6H_5)_2AsCl—$

$SOCl_2$ (47). Under reduced pressure this compound melts at 188–192°C. and begins to decompose at 195°C.; the distillate has the odor of chlorobenzene.

(*i*) *Action with nitrosyl chloride.* A benzene solution of diphenylchloroarsine on treatment with a benzene solution of nitrosyl chloride yields a white, crystalline precipitate of diphenyldichloroarsine oxide, $[(C_6H_5)_2AsCl_2]_2O$, m.p. 117°C. (111).

(*j*) *Action with sodium iodide.* Diphenyliodoarsine, $(C_6H_5)_2AsI$, is prepared by adding diphenylchloroarsine to an acetone solution of sodium iodide; yellow, hexagonal crystals, melting at 40.5°C., separate (133). The compound is insoluble in water, sparingly soluble in cold alcohol, readily soluble in hot alcohol, ether, acetone, benzene, carbon disulfide, and carbon tetrachloride.

(*k*) *Action with silver cyanide.* When diphenylchloroarsine is heated with an excess of dry silver cyanide, diphenylarsenious cyanide, $(C_6H_5)_2AsCN$, is formed. It crystallizes in colorless, monoclinic plates which have the odor of garlic and bitter almonds (103, 138, 139).

(*l*) *Action with sodium thiocyanate.* Diphenylthiocyanoarsine, $(C_6H_5)_2AsCNS$, is formed by the reaction between acetone solutions of diphenylchloroarsine and sodium thiocyanate. It is a pale, brownish oil, boiling at 230–233°C. at 22–23 mm.; it is miscible with benzene and acetone in all proportions, but is decomposed by water (130).

(*m*) *Action with alkyl halides.* Diphenylchloroarsine when heated with methyl iodide in a sealed tube at 100°C. for three hours yields diphenyldimethylarsonium triiodide, $(C_6H_5)_2As(CH_3)_2I_3$. It crystallizes in violet needles, m.p. 69.5°C. It is insoluble in water and ether, but dissolves readily in hot alcohol, chloroform, ethyl acetate, and acetone (133).

Diphenylmethylarsine, $(C_6H_5)_2AsCH_3$, obtained when diphenylchloroarsine reacts with the ethereal solution of the Grignard reagent resulting from methyl bromide, boils at 156–157°C. at 11 mm. (134).

Diphenylethylarsine, $(C_6H_5)_2AsC_2H_5$, obtained when diphenylchloroarsine reacts with the ethereal solution of the Grignard reagent resulting from ethyl bromide, boils at 162–163°C. at 10 mm. (127).

Diphenylpropylarsine, $(C_6H_5)_2AsC_3H_7$, obtained when diphenylchloroarsine reacts with the ethereal solution of the Grignard reagent resulting from propyl bromide, boils at 177°C. at 10 mm. $d_{4^\circ}^{20^\circ}$, 1.1964. Its index of refraction at 20°C. is as follows: $n_F = 1.6220$, $n_D = 1.6054$, $n_C = 1.5986$ (69).

Diphenylbutylarsine, $(C_6H_5)_2AsC_4H_9$, is obtained when diphenylchloroarsine reacts with the ethereal solution of the Grignard reagent resulting from butyl bromide; its boiling point has been given as 183°C. at 10 mm., and 197°C. at 17 mm. (69).

Diphenylisobutylarsine, $(C_6H_5)_2AsCH_2CH(CH_3)_2$, is obtained when the chloroarsine reacts with the ethereal solution of the Grignard reagent resulting from isobutyl bromide. It boils at 185°C. at 10 mm.; $d_{4°}^{20°}$, 1.1819 (69).

Diphenylamylarsine, $(C_6H_5)_2AsC_5H_{11}$, is obtained when diphenylchloroarsine reacts with the ethereal solution of the Grignard reagent resulting from amyl bromide. Boiling point, 194°C. at 10 mm.; $d_{4°}^{20°}$, 1.1617; index of refraction at 20°C., $n_F = 1.5993$, $n_D = 1.5846$, $n_C = 1.5786$ (69).

Diphenyl-*dl*-amylarsine, $(C_6H_5)_2As(dl)C_5H_{11}$, is obtained when the chloroarsine reacts with the ethereal solution of the Grignard reagent resulting from *dl*-amyl bromide. Boiling point, 195°C. at 10 mm.; $d_{4°}^{20°}$, 1.1624 (69).

(*n*) *Action with zinc alkyls.* Diphenylmethylarsine, $(C_6H_5)_2AsCH_3$, prepared by the action of zinc methyl on diphenylchloroarsine (92), is a colorless, highly refractive oil, b.p. 306°C. or 163–170°C. at 15 mm., having a pungent, fruity odor. It is soluble in alcohol and benzene, and insoluble in water (20).

Diphenylethylarsine, $(C_6H_5)_2AsC_2H_5$, results when zinc ethyl reacts with the chloroarsine. It is a colorless liquid, b.p. 320°C., 162–163°C. at 10 mm. (74, 75, 92).

(*o*) *Action with sodium alcoholates.* The ethoxy compound, $(C_6H_5)_2AsOC_2H_5$, results when sodium ethoxide reacts with diphenylchloroarsine. It is a viscid oil, which partly solidifies when kept overnight (84).

Phenyldiphenylarsenite, $(C_6H_5)_2As—OC_6H_5$, is formed by treating a xylene solution of diphenylchloroarsine with sodium phenoxide. It is a colorless liquid, boiling at 230–231°C. at 15 mm.; $d_{4°}^{11°}$, 1.3113 (90).

Isoamyldiphenylarsenite, $(C_6H_5)_2As—OCH_2CH_2CH(CH_3)_2$, formed by treating a benzene solution of sodium isoamylate with diphenylchloroarsine in benzene, boils at 188–189°C. at 11 mm. It is pale green in color and has an odor resembling that of amyl alcohol (132).

Isoamyldiphenylthioarsenite, $(C_6H_5)_2As—SCH_2CH_2CH(CH_3)_2$, results on treatment of xylene solutions of diphenylchloroarsine with sodium isoamyl mercaptan. It is a greenish-yellow liquid, boiling at 215–220°C. at 11 mm. (132).

Allyldiphenylarsenite, $(C_6H_5)_2As—OC_3H_5$, is produced by treating a xylene solution of diphenylchloroarsine and sodium allylate. It is a pale green liquid, b.p. 180.5–181.5°C. at 11 mm. (132).

(*p*) *Action with phenylarsines.* When diphenylchloroarsine is mixed with phenylarsine in ether, hydrogen chloride is evolved and white needles of the triphenyldiarsine, $(C_6H_5)_2As—AsH(C_6H_5)$, separate. The reaction is carried out in an atmosphere of carbon dioxide (135).

Blicke and Powers (14), endeavoring to reproduce the work of Steinkopf

and Smie (135), were unable to obtain triphenyldiarsine, but obtained instead arsenobenzene and diphenylchloroarsine. Steinkopf and Smie merely analyzed their reaction product, which was not characterized by a melting point, and considered the arsenic analysis and the fact that a mixture of phenylarsinic and diphenylarsinic acids was obtained upon oxidation of their product with nitric acid sufficient proof for the claim that triphenyldiarsyl had been formed.

Tetraphenyldiarsine, phenylcacodyl, $(C_6H_5)_2As—As(C_6H_5)_2$, is obtained by the reaction of diphenylchloroarsine and diphenylarsine, dissolved in ether. It melts at 124–127°C. (14). It is also prepared when diphenylchloroarsine and phenylarsine are allowed to react in the ratio expressed in the following equation:

$$4(C_6H_5)_2AsCl + 2C_6H_5AsH_2 \rightarrow C_6H_5As{:}AsC_6H_5 + 2(C_6H_5)_2As—As(C_6H_5)_2 + 4HCl$$

Besides tetraphenyldiarsyl there is likewise produced arsenobenzene, m.p. 210–211°C. (14).

Pentaphenyltriarsine, $(C_6H_5)_2As—As(C_6H_5)—As(C_6H_5)_2$. When phenylarsine and diphenylchloroarsine react in absolute alcohol in an atmosphere of carbon dioxide at 70°C., gas evolution soon takes place and a thick, white, crystalline mass of the triarsine separates (135).

(*q*) *Action with chloramine-T.* Diphenylarsinic acid is obtained by the interaction of chloramine-T on diphenylchloroarsine (21). The acid crystallizes in fine needles, 2 to 3 cm. long, m.p. 178°C., and showing a tendency to sublime at 192–200°C. (74, 89). It crystallizes from alcohol in short prisms and is somewhat soluble in ether and benzene; it is unattacked by boiling nitric or chromic acids.

(*r*) *Action with chloropicrin.* By treating the sodium salt (obtained as the result of the reaction of sodium ethoxide on diphenylchloroarsine) with chloropicrin, diphenylarsinic acid is prepared, m.p. 173–174°C. (149).

(*s*) *Action with turpentine and olive oil.* When diphenylchloroarsine is treated with turpentine which has been exposed to the air for some time and to rancid olive oil, it is oxidized to diphenylarsinic acid, m.p. 172°C. (145).

Walton and Eldridge (146) found that when chlorine is bubbled through diphenylchloroarsine the arsenic is oxidized to the pentavalent form and the resulting product is non-irritating when breathed by man and gave no reaction when titrated with iodine. Men gassed with diphenylchloroarsine were markedly benefited if given chlorine.

Test

Fleury (40) devised an iodometric method whereby the amount of diphenylchloroarsine could be determined. Frahm and Boogaert (43) devised a method for the determination of diphenylchloroarsine, making use of the fact that diphenylchloroarsine can be saponified easily with sodium hydroxide solution and the resulting sodium chloride determined by the Volhard argentometric titration.

Physiological properties

Diphenylchloroarsine strongly attacks the skin and is poisonous (92). A concentration of 0.000015 g. to 0.000025 g. per liter produces irritation of the nose and throat, while a concentration of 0.0005 g. per liter produces an intolerable atmosphere in 30 seconds (126, 144). Yet it requires between 0.001 to 0.002 g. per liter to cause the death of dogs after an exposure of thirty minutes (144). The highest concentration endurable for one minute is 1 to 2 mg. per cubic meter of particles 10^{-4} to 10^{-5} (3). Hanzlik and Tarr (64) found diphenylchloroarsine produced simple hyperemia without vesication, mild urticarial rash, moderate swelling and edema, and very little or no necrosis.

After a quick death by asphyxiation with diphenylchloroarsine, Manier and Morelli (85) found that the adrenals of guinea pigs showed an increase in adrenaline. In the vesicant action of diphenylchloroarsine the adrenaline decreases as the symptoms become worse, but this effect is short.

Diphenylchloroarsine has a special affinity for fats. This explains the damage to the liver and the resulting, defective fat metabolism. The poison is fixed in the circulating food fat, and carried with it to the liver, where it produces hepatitis. The excessive concentration of arsenic in the adrenals suggests that it has an affinity for fats other than the glycerides of the higher fatty acids. This affinity for fats may be due in some instances to the fat-solvent power of the poison, in others to the formation of oleates (42).

When one ear of a mouse was painted with 6 per cent solution of diphenylchloroarsine in petroleum ether, Berger and Groll (17) found that respiration ceased within eight hours.

Uses

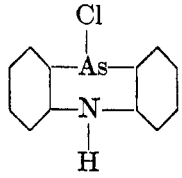
Tanner (140) found that pine piling treated with petroleum oil to which had been added diphenylchloroarsine showed pronounced resistance to marine borer attacks.

U. S. patent 1,565,237 was issued December 8, 1925 to Schmidt, Steindorff, Fluss, and Schaffrath (122) for treating seed grain for parasites; U. S. patent 1,652,291, December 13, 1927, to Tanner (142) for the use of an

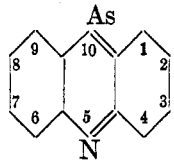
insecticide composed of diphenylchloroarsine; and U. S. patent 1,686,582, October 9, 1928, to Stoltzenberg (136) for the use of diphenylchloroarsine in destruction of cacti by action as vapor or spray or as injection of 5 per cent solutions in cresol or sulfuric acid.

V. DIPHENYLAMINECHLOROARSINE, PHENYLARSAZINE CHLORIDE, 10-CHLORO-5,10-DIHYDROPHENARSAZINE, $NH(C_6H_4)_2AsCl$

The reaction between arsenious halides and secondary aromatic amines was the subject of German patent 281,049 of F. Bayer and Company in 1913 (11). Wieland and Rheinheimer (148) made a comprehensive study of the derivatives of the compound obtained by condensing arsenious chloride and diphenylamine. To this compound Wieland and Rheinheimer gave the name phenarsazine chloride and ascribed to it the constitution



which is the same as that assigned to it by the patentees. Wieland and Rheinheimer prepared the compound phenarsazine, which undoubtedly has the structure



The product of the reaction between diphenylamine and arsenious chloride is the same as that derived from phenarsazine by the addition of hydrochloric acid. This compound has heretofore been variously known as diphenylaminearsenious chloride (29, 30) and 6-chlorophenarsazine (78, 79). In systematically describing this class of compounds, the name "phenarsazine" is retained for the parent substance and the atoms numbered as indicated. The products of the reaction between diphenylamine and arsenious chloride and its simple derivatives are regarded as substitution products of 5,10-dihydrophenarsazine.

Although the patent referred to was taken out in 1913 and issued in the German Empire in December 1914, the specification was not available elsewhere until September 1920. Burton and Gibson (22) had but a re-

stricted knowledge of this type of heterocyclic compound up to 1918, limited to that contained in a brief abstract of the patent, which referred only to the general reaction between arsenious chloride and diarylamines without mentioning any specific compound. Ball independently prepared the compound early in 1918 (unpublished report) by the action of arsenious chloride on diphenylamine and examined a number of its simpler derivatives. G. T. Morgan in 1918 (unpublished report) also studied the reaction and prepared certain analogues of 10-chloro-5,10-dihydrophenarsazine. The bulk of the investigations on this compound and its derivatives of recent years has been carried out by Gibson and his coworkers (22, 23, 24, 25, 46, 48).

Preparation

Diphenylaminechloroarsine is prepared: (a) when diphenylamine or methyldiphenylamine, arsenious chloride, and *o*-dichlorobenzene are boiled under a reflux for five hours (22, 144, 148); (b) when diphenylhydrazine is heated with arsenic trichloride (78); (c) when 2-bromo-6′-methylaminodiphenylarsinic acid, dry potassium carbonate, amyl alcohol, and a trace of powdered copper are boiled under a reflux for twelve hours (22, 148); (d) by condensation of phenyldichloroarsine with diphenylamine in *o*-dichlorobenzene solution (the presence of the solvent is not essential) (23, 58); (e) by condensation of β-chlorovinyldichloroarsine and diphenylamine with or without a solvent (23, 120); (f) by reducing diphenylamine-*o*-arsinic acid or phenarsazinic acid in hot alcohol–hydrochloric acid solution with sulfur dioxide, after adding a trace of iodine (46); (g) upon heating a perchloride of 10-methyl- or 10-phenyl-5,10-dihydrophenarsazine (123); (h) by treating fused diphenylamine with concentrated hydrochloric acid (density 1.08), heating and stirring until almost free from water, and then mixing with arsenious oxide and fusing for four hours (29); (i) by boiling aniline and arsenic trichloride for seventy-two hours, adding sodium hydroxide, and steam distilling; the crude oxy compound is then treated with hydrochloric acid and acetone (22); (j) upon boiling a mixture of 10,10′-oxy-5,10-dihydrophenarsazine, benzoyl chloride, and dry benzene under a reflux for six hours (22); (k) by condensation of (1) phenyl-*p*-tolylamine, (2) *p,p′*-ditolylamine, or (3) phenyl-α-naphthylamine with dichloroarsine and *o*-dichlorobenzene by boiling for sixteen hours (23); (*l*) by heating trianilinearsine hydrochloride (121).

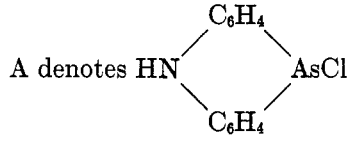
Physical properties

Diphenylaminechloroarsine crystallizes from carbon tetrachloride, ether, benzene, or xylene in yellow needles, melting at 186–187°C. (22), 187–190°C. (22), 189–190°C. (23), 190–191°C. (22), 191°C. (46), 191–192°C.

(22), 191–193°C. (105), 192–193°C. (78, 148), 192.5°C. (141), 193°C. (79, 148), 193–194°C. (126), 195°C. (3, 137, 144, 146). Fischer (39) found the chloroarsine to crystallize in three forms: the stable modification is orthorhombic and melts at 195°C.; of the metastable crystals, some are monoclinic and melt at 186°C. whereas others are triclinic melting at 182°C. The crystals sublime *in vacuo* (78, 148). The compound boils at 120–121°C. at 9–10 mm. (120), and at 410°C. with decomposition (3, 137, 144, 146). $d_{20°}^{20°}$, 1.6766 (120). Specific heat, 0.268 (126). It is soluble in concentrated sulfuric acid forming a dark red solution, but on addition of water the orange-yellow sulfate precipitates (58). Its heat of vaporization has been calculated as 54.8 calories per gram. Its vapor pressure is practically negligible at all temperatures, being only 5×10^{-16} mm. at 0°C. and 2×10^{-6} mm. at 100°C. (126). A saturated concentration at 20°C. contains 0.02 mg. per cubic meter (3). Its fumes are inflammable (126).

One of the most striking properties of phenylarsazine hydrochloride is its power of forming molecular compounds. When the phenarsazine is crystallized from the following solvents the crystals effloresce slowly in the air, but heating to 110°C. causes rapid dissociation, leaving the pure phenarsazine in each case:

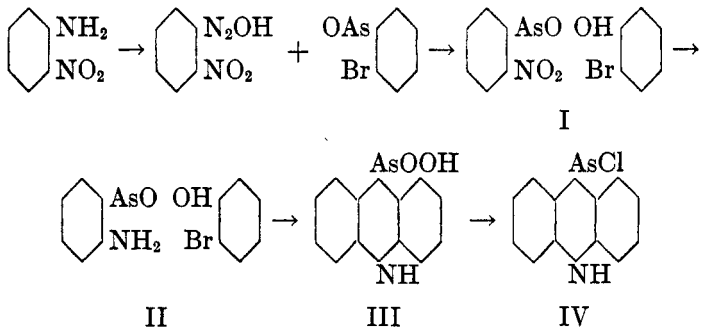
(a) acetic acid	$A \cdot C_2H_4O_2$
(b) *s*-tetrachloroethane	$2A \cdot C_2H_2Cl_4$
(c) chlorobenzene	$2A \cdot C_6H_5Cl$
(d) *o*-dichlorobenzene	$2A \cdot C_6H_4Cl_2$
(e) acetone	$2A \cdot C_3H_6O$
(f) carbon tetrachloride	$A \cdot CCl_4$



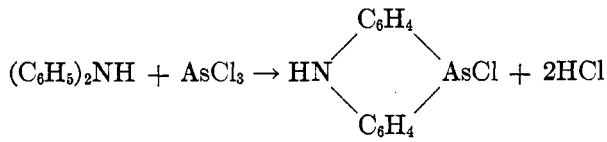
10-Chloro-5,10-dihydrophenarsazine is extremely soluble in arsenic trichloride, giving a dark green solution. A hot, concentrated solution on cooling deposits magnificent, scarlet scales of the compound $A \cdot AsCl_3$. This is sufficiently stable to permit filtration, but on exposure to air or washing with solvents yields the original chloro compound (22).

Constitution

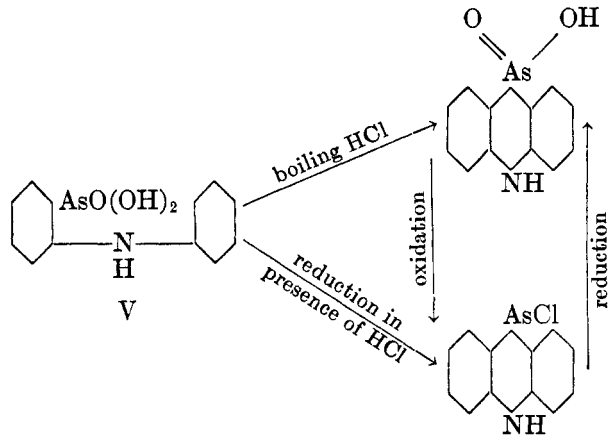
The constitution ascribed to 10-chloro-5,10-dihydrophenarsazine has been proved to be correct by the following synthesis, which may be represented diagrammatically:



Diazotized *o*-nitroaniline coupled with *o*-bromophenylarsenious oxide yields 2-bromo-6′-nitrodiphenylarsinic acid (I), reduction of which by ferrous hydroxide gives the corresponding amino derivative (II), which, when heated in amyl alcohol with potassium carbonate and a small quantity of copper powder, is readily converted into phenarsazinic acid (III); this substance, when reduced in hydrochloric acid–ethyl alcohol solution by sulfur dioxide, is converted into 10-chloro-5,10-dihydrophenarsazine (IV), identical with the substance prepared by the action of arsenious chloride on diphenylamine according to the equation:



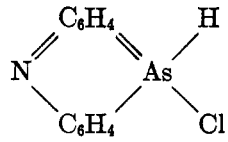
The presence of the :NH group is shown by the fact that the hydrogen may be replaced by acetyl or similar groups. A further verification of the structure is offered by the following series of reactions:



Diphenylamine-*o*-arsinic acid (V), prepared by the condensation of *o*-bromophenylarsinic acid and aniline, when reduced in alcohol–hydrochloric acid solution by sulfur dioxide in the presence of iodine, gives 10-chloro-5, 10-dihydrophenarsazine, or, if boiled with concentrated hydrochloric acid, yields the chloride of phenarsazinic acid, which may be reduced to the 10-chloro compound under suitable conditions (46).

Kappelmeier (70) has expressed the view that the constitution of 10-chloro-5,10-dihydrophenarsazine is more adequately expressed by formula I or II than by III (50). The first formal proof that the substance possesses formula III was given by Gibson and Burton (22), who also showed that the original method of preparation of these phenarsazine derivatives was strictly limited and could not be applied even to the nitro and carboxyl compounds (25, 46). As to the existence of the *N*-methyl derivatives which Wieland and Rheinheimer (148) claimed to have obtained in small quantity by the condensation of diphenylmethylamine with arsenic trichloride, Gibson and coworkers were only able to isolate from this reaction a small quantity of the phenarsazine (22, 49, 51); the desired synthesis was also unsuccessful as was also the methylation of the parent compound. Gibson, Johnson, and Vining (50) had already shown that the constitution of the phenarsazine may be represented by the formulas IV, V, VI, VII, or VIII, the compound being probably best represented by V or VI, which might be in equilibrium, although no definite proof could be advanced in favor of the transannular band formulas as against the *o*-quinoid formulas. Whereas all tervalent arsenic derivatives in this series are colored except the *N*-acetyl derivatives, the quinquevalent arsenic derivatives are colorless, unless a chromophoric group is present. Having adopted the transannular band for 10-chloro-5,10-dihydrophenarsazine, it seemed clear that the color of this substance must be associated with the presence of this band, since those derivatives are colorless. It was therefore necessary that two types of derivatives be assumed, those without the transannular band (the "true dihydrophenarsazines" according to Kappelmeier), and those with the transannular band, which are salts. The structure IV may be preserved by acetylation of the hydrogen atom of the :NH group, or this hydrogen atom may be bound to the nitrogen by its forming part of the chelate ring, provided a suitable group is present, as, e.g., the nitro group in the 4-position. If 10-chloro-5,10-dihydrophenarsazine does not contain the :NH group it must be capable of reacting in this form, since the *N*-acetyl derivatives are so readily formed by the residual reactions. From formulas V and VI and from formulas VII and VIII the former are to be preferred, since arsenic displays a remarkable tendency to pass into the "onium" condition; then the 10-chloro compound must have a formula which allows the free migration of the hydrogen atoms from N $\rightleftharpoons$ As. If

the nitrogen and arsenic are intimately connected, this wandering will be facilitated and this is an important reason for the adoption of the transannular band formula. On preparing 10-chloro-5,10-dihydrophenarsazines from substituted diphenylamines and arsenic trichloride the formation of an addition compound is often observed (changes of color and evolution of heat on simple mixing). It was now found that the following compounds condense: diphenylamine, *o*-, *m*-, and *p*-phenyltolylamines, 2,3'-, 2,4'-, and 4,4'-ditolylamines, α- and β-naphthylphenylamines, *m*- and *p*-phenylchlorobenzeneamines, 4,4'-, 3,4-, and 3,5-dichlorodiphenylamines, *p*-diphenylbenzidine, α- and β-dinaphthylamine, *p*-tolyl-α- and *p*-tolyl-β-naphthylamine, *m*- and *p*-phenylanilineamine, *N*,*N*'-di-*p*-tolylhydrazine, *m*- and *p*-dianilinebenzine, and *p*-diphenylhydroxylamine. No condensation was obtained with diphenylmethylamine, *o*-phenylanilineamine, *o*-, *m*-, and *p*-phenylnitrophenylamines, 4,4'- or 2,4-diaminodiphenylamine-, *p*-dinitrophenylamine, *o*-chlorodiphenylamine, 2,4- and 2,5-dichlorophenylphenylamine, 2,4-dichlorodiphenylamine, 2,4-dibromodiphenylamine, diphenylacetylamine, diphenylformylamine, diphenylbenzoylamine, *o*-diphenylaminebenzene, and dicyclohexylamine. The halodiphenylamines fall into two classes, those with at least one halogen atom in the *o*-position to the :NH group, which do not condense, and those which do not have the halogen atom in this position and which do condense with arsenic trichloride. Nitro derivatives as a rule do not condense, and the compounds which do not react all possess alkyl or phenylene substituting groups; the absence of a reaction is sometimes to be ascribed to steric hindrance. The red color of the solution obtained by Wieland and Rheinheimer by the reduction of 10-chloro-5,10-dihydrophenarsazine with zinc in acetic acid disappeared on further reduction and reappeared on addition of the starting product; it was therefore suggested that the completely reduced solution contains the compound IX, while the colored solution contains the quinhydrone substance (IV and IX). Razuvaev (105, 106, 107, 108), however, considers these colored compounds to be of the meriquinonoid type X. The existence of such a compound having an odd number of valence electrons in the molecule must, for the present, be considered doubtful. Neither is the formula IX in accordance with modern views on quinquevalent nitrogen, and it is suggested that the formula of the completely reduced substance should be represented by XI or XII, the absence of the color being due to the absence of the transannular band. Attempts to condense 10-chloro-5,10-dihydrophenarsazine with methylethylmalonate were unsuccessful, diphenylarsinic acid being obtained. The action of hydrogen chloride on 10-chloro-5,10-dihydrophenarsazine at high temperatures gives appreciable quantities of arsenic trichloride and diphenylarsine.



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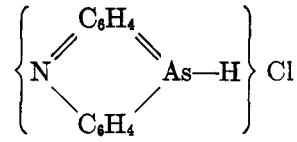

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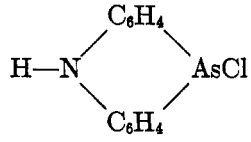

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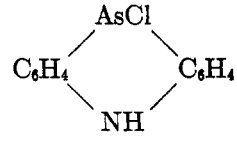

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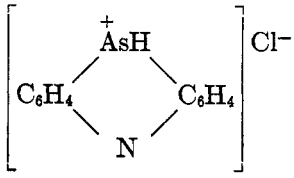

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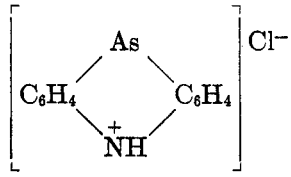

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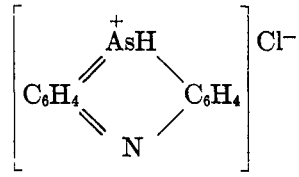

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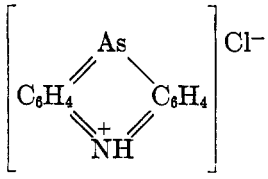

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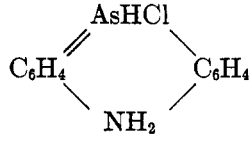

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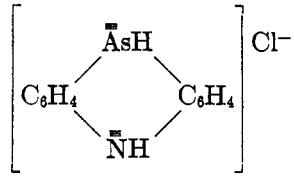

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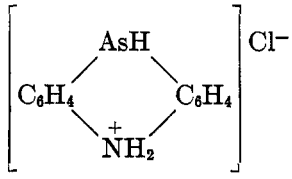
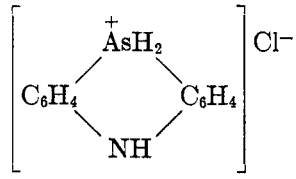


XI



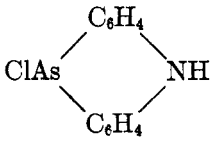
XII

Previous work in this series has shown that condensation between arsenious chloride and substituted diphenylamines ordinarily produces 5,10-dihydrophenarsazine derivatives, but Elson and Gibson (36) have shown that it does not take place: (i) when at least one nitro group is present, as in *o*-nitro, *m*-nitro, 4,4′-dinitro-, and 2,4-dinitrodiphenylamines; (ii) when an amino group occupies one ortho position as in *o*-aminodiphenylamine; (iii) when two amino groups are present, e.g., the cases of 2,4-diamino- and

4,4′-diaminodiphenylamines; (iv) when an alkyl or acyl group is substituted for the hydrogen in the :NH group, e.g., *N*-methyl, *N*-formyl, *N*-acetyl-, and *N*-benzoyldiphenylamines; (v) when the benzene nuclei are fully reduced, e.g., dicyclohexylamine; (vi) in the unique case of *N*,*N*′-diphenyl-*o*-phenylenediamine, the corresponding *m*-phenylene and *p*-phenylene compounds readily undergoing condensation.

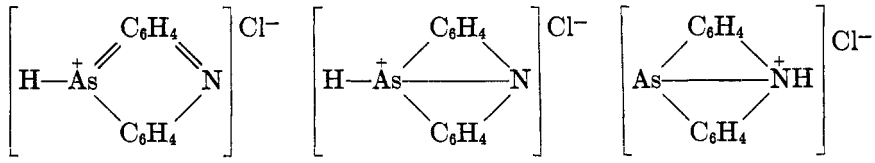
The last failure may be due to steric hindrance: cases (ii), (iii), and (v) may be explained by the stability of the addition compounds of arsenic trichloride and highly basic diphenylamine derivatives, for the initial formation of which, in the reaction, evidence has been brought forward (22, 55), and (iv) may be due to the hydrogen of the :NH group playing an essential part in the changes leading to the final condensation product. As regards case (i) it may be that the nitro group reduces the basicity of diphenylamine to such an extent that the initial compound formation mentioned above does not take place at all.

Kappelmeier previously showed (70) that the formulation of the reaction product of arsenic trichloride and diphenylamine as 10-chloro-5,10-dihydrophenarsazine,



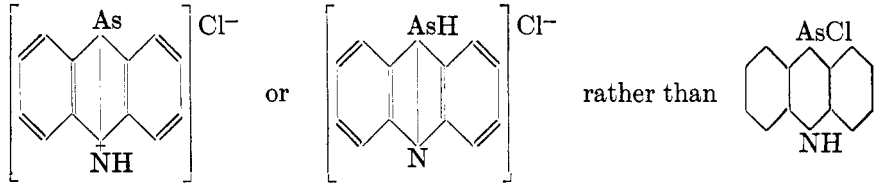
(formula I) is not in accordance with the salt-like properties and color of this substance; formula II, which gives an adequate account of these properties, was therefore preferred. Gibson and Johnson (55), however, prefer a formulation as a salt, but with a bridge between the arsenic and nitrogen atoms (III and IV), and it is now pointed out (71) that a decision on this point cannot be obtained from the synthesis, the sudden formation of a colored compound at the end of the reaction pointing to an intermolecular change. Kappelmeier does not agree with Gibson and Johnson either on the question whether the color is to be ascribed to a tervalent or to a quinquevalent arsenic atom; whereas Gibson and Johnson ascribe the color to the tervalent arsenic atom, Kappelmeier holds the opinion that tervalent as well as quinquevalent arsenic compounds may be colored or colorless, examples of both cases being known. The easy formation of a colorless *N*-acyl derivative, which, according to Gibson and Johnson, points to the existence or easy formation of an :NH group, is explained by Kappelmeier by primary addition to the nitrogen atom followed by splitting off of hydrogen chloride. The *o*-quinonoid formulation is preferred by Kappelmeier in view of the greater reactivity of the compound as compared with 10-

chloro-5,10-dihydrophenarsazine; moreover, in analogous compounds such as anthracene and acridine, the *o*-quinonoid formulation (7, 8) has been preferred in recent years to the bridged formula.



Gibson, Hiscocks, Johnson, and Jones (45) found the colors of 10-chloro-5,10-dihydrophenarsazine and of its methyl, nitro, and nitromethyl derivatives to be very intense. The parent substance and its methyl derivatives in the solid state have a brilliant yellow color, but the colors of the nitro derivatives depend on the position occupied by the nitro group. The previous knowledge of the visible color and known constitution of some of the latter compounds indicate that those possessing a deep crimson color have the nitro group in the 1- or 4- position, whereas those which are yellow have the nitro group in the 2- or 3-position in the phenarsazine nucleus. Although the exact relationships between chemical constitution and the absorption spectra of substances in solution are far from being understood, it is shown in the present discussion that in the series of closely related compounds the absorption spectra can be correlated with the position of the nitro group in the nucleus.

Evidence has been brought forward by Gibson and Johnson (50) to indicate that the constitution of 10-chloro-5,10-dihydrophenarsazine is more adequately represented either by

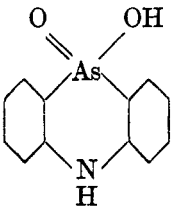


since apart from other properties, the *N*-substituted derivatives are colorless and they cannot possess a transannular band.

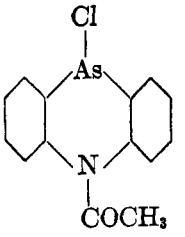
All the simple derivatives of 10-chloro-5,10-dihydrophenarsazine in which the arsenic atom is in the tervalent condition are yellow unless the hydrogen of the :NH group has been replaced by an acyl group, in which case the compounds are practically colorless (1, 123).

Wieland and Rheinheimer (148) suggested that the yellow color of 10-

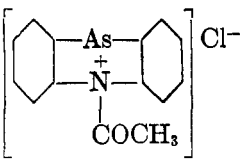
chloro-5,10-dihydrophenarsazine was due to an atomic intervention between the arsenic and nitrogen atoms which involves their possessing a quinonoid-like structure. Sufficient experimental evidence has now been proved to ascribe to this parent compound the constitution 1 or 2, which may be in equilibrium. Since visible color is absent in the case of phenarsazinic acid,



where a transannular N—As band is precluded, it would appear that the yellow color of 10-chloro-5,10-dihydrophenarsazine is due to the presence of the transannular structure indicated above. The colorless nature of 5-acetyl-10-chloro-5,10-dihydrophenarsazine,



is readily explained, since the presence of a transannular band as in



would necessitate the nitrogen atom carrying a positive charge although it has the negative acetyl group attached to it.

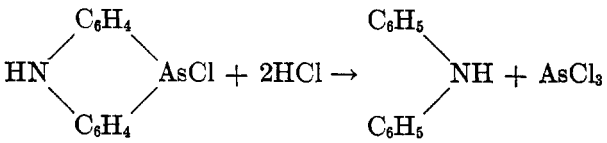
Gibson, Hiscocks, Johnson, and Jones (45) were of the opinion that it was reasonable to assume that any absorption in the visible and near ultraviolet spectrum of the parent substance may be associated with this transannular band. They found a strong absorption band in the near ultraviolet, the center of the band being at the frequency of 8.65×10^{14}, while marked absorption occurred in the extreme violet. A strong double

branched absorption band occurs further in the ultra-violet, with two maxima at frequencies of 10.0×10^{14} and 10.8×10^{14}.

A Hilger C-type quartz spectrograph and a Hilger sector photometer were used, with an iron–nickel arc as a source of radiation. A concentration of $M/10{,}000$ in optically pure ethyl alcohol gave the best results in the ultra-violet region for 1-cm. length of tube, but in certain cases it was necessary to supplement the results so obtained by using a concentration of $M/4000$ in order to follow the absorption band more fully.

Chemical properties

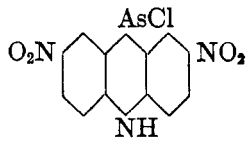
(*a*) *Action with acids.* When diphenylaminechloroarsine is heated with hydrochloric acid it is decomposed into diphenylamine and arsenic trichloride (55, 112, 123):



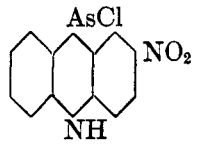
10,10′-Bis-5,10-dihydrophenarsazine, $[HN(C_6H_4)_2As]_2$, is prepared by treating a hot mixture of phenarsazine chloride in alcohol–acetone solution with hypophosphorous acid (density 1.136); on cooling the orange-yellow needles separate, m.p. 304–305°C. with decomposition. It is very sparingly soluble in the usual organic solvents. It is moderately stable under ordinary conditions, but when boiled with xylene or acetone it is rapidly oxidized, producing the colorless phenarsazinic acid (24).

Razuvaev, Godina, and Yemelyanova (111) found that the action of nitrous acid on 10-chloro-5,10-dihydrophenarsazine does not yield the expected nitroso derivative.

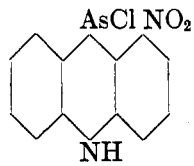
Wieland and Rheinheimer (148) found that when phenarsazine chloride was nitrated it led to the production of two mononitro compounds and a dinitro derivative. The chloride is dissolved in boiling acetic acid, the solution rapidly cooled to 18°C. and nitric acid (density 1.52) added dropwise, the temperature being maintained below 20°C. Each drop of acid produces a blue coloration, and when all has been added the temperature is raised to 25°C. when complete solution takes place; on subsequent cooling a deep-colored dinitro compound separates. The two mononitro derivatives are dissolved in cold acetone, the *p,p′*-dinitrophenarsazine chloride



remains undissolved. It forms pale yellow needles, melting above 300°C. Upon evaporating the acetone solution from the dinitro compound and extracting with benzene, the *p*-derivative,

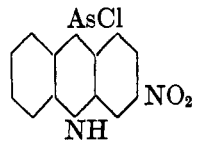


dark, greenish-yellow leaflets, remains practically insoluble; on heating it turns dark red at about 194–197°C. and melts at 276–278°C. with decomposition (46). The *o*-nitrophenarsazine chloride,

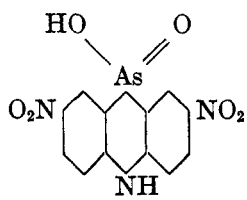


the benzene residue, is then dissolved in ether and finally crystallized from benzene and acetic acid as scarlet-red needles, m.p. 156°C. (148) or 165°C. (46).

Gibson and Johnson (54) prepared 10-chloro-3-nitro-5,10-dihydrophenarsazine,

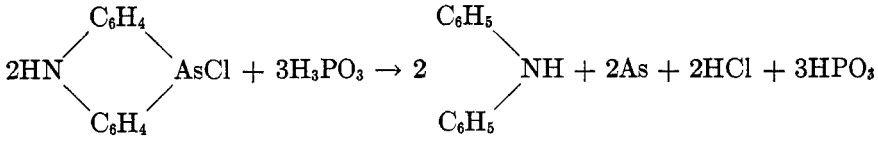


as orange-colored needles, decomposing at 268–271°C. Razuvaev and Koton (113) found that upon mild nitration of diphenylaminechloroarsine, diphenylenearsinic acid, $[(C_6H_4)_2As(OH)_2]NO_3$, is produced; a more energetic nitration results in the formation of *m*-dinitro acids. When phenarsazine chloride is added to warm concentrated nitric acid (density 1.4) and the solution raised to the boiling point 2,8-dinitrophenarsazinic acid is obtained.

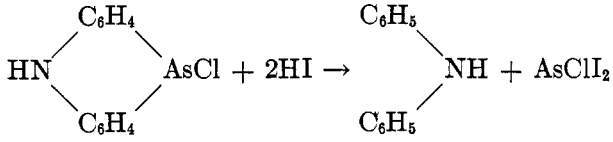


It crystallizes from nitrobenzene in pale yellow needles melting above 300°C. (148).

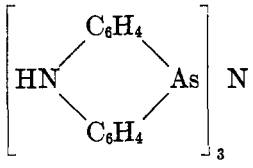
Upon heating diphenylaminechloroarsine to 120–180°C. with phosphorous acid, elementary arsenic is split off (109):



Upon treating 10-chloro-5,10-dihydrophenarsazine with hydriodic acid, the phenarsazine is decomposed (109):

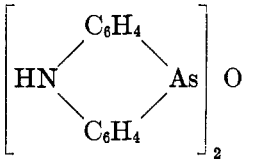


(*b*) *Action with alkali.* When ammonia is passed into a solution of phenarsazine chloride in dry boiling xylene, a colorless, chlorine-free body is obtained, which appears to be triphenarsazine amine,



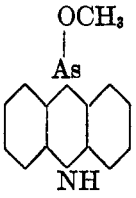
a sparingly soluble, white precipitate which melts with decomposition at 295–300°C. (148).

Phenarsazine oxide, 10,10′-oxy-5,10-dihydrophenarsazine,



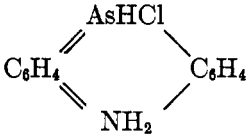
is produced by the action of alkali upon an acetone solution of phenarsazine chloride. It crystallizes from nitrobenzene or pyridine in colorless plates, which soon become yellow, m.p. 350°C. It is sparingly soluble in most solvents, and when boiled with alcohols yields ethers; with phenols, it yields phenyl ethers (148).

Phenarsazine methyl ether,



is prepared by treating a methyl alcohol suspension of phenarsazine chloride with sodium methylate. The ether crystallizes in long, colorless needles, melting at 194°C. to a yellow liquid (148). Upon boiling with alkali or water, it gives the oxide, which, when boiled with methyl alcohol, again gives the methyl ether.

(*c*) *Action with a metal.* 10-Chloro-5,10-dihydrophenarsazine is quantitatively reduced by the action of zinc dust and acetic acid in an inert atmosphere to 5,10-dihydrophenarsazine hydrochloride (110).

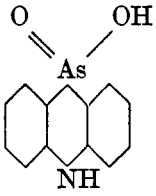


(*d*) *Effect of heat.* By heating dihydrophenarsazine chloride in tetrahydronaphthalene in the presence of oxygen or a trace of water, phenarsazinic acid is produced (124).

The hydrochloride of phenarsazinic acid is obtained by heating 10-chloro-5,10-dihydrophenarsazine for thirty minutes at 100–120°C. in an oil bath; it crystallizes from absolute alcohol, and melts at 207–208°C. (124).

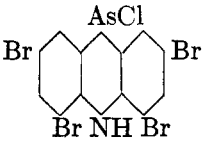
(*e*) *Action of hydrogen peroxide.* Phenarsazinic acid, prepared by suspending phenarsazinic chloride in acetic acid and adding a small excess of hydrogen peroxide and warming, is obtained as felt-like needles, m.p. above 300°C. (148).

(*f*) *Action of halogens.* Phenarsazinic acid,

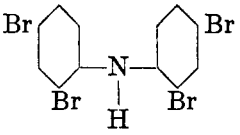


is prepared by treating phenarsazine chloride in water solution with iodine (114). On treating a hot glacial acetic acid solution of 10-chloro-5,10-

dihydrophenarsazine with bromine a colorless, well-defined crystalline substance is isolated from the cooled solution. It was expected that the fully brominated product would be 10-chloro-2,4,6,8-tetrabromo-5,10-dihydrophenarsazine (I), but the colorless product isolated was arsenic-free and analysis showed it to be tetrabromodiphenylamine (II), m.p. 186°C. (37).



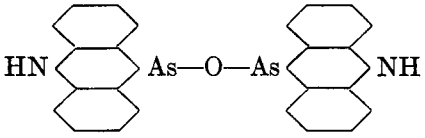
I



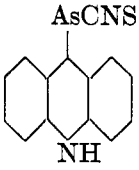
II

(*g*) *Action with silver cyanide.* 10-Cyano-5,10-dihydrophenarsazine

is obtained from the corresponding 10-chloro compound and silver cyanide in benzene solution. It melts with decomposition at 227–228°C. (62) or 223–224°C. (55). On hydrolysis, it forms the compound (62)



(*h*) *Action with potassium thiocyanate.* 10-Thiocyano-5,10-dihydrophenarsazine,

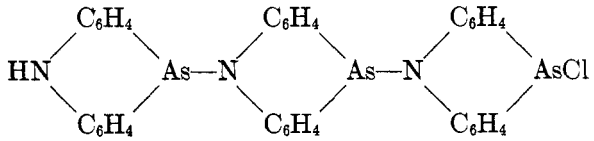


is obtained by treating 10-chloro-5,10-dihydrophenarsazine in acetone with a water solution of potassium thiocyanate on a water-bath; it crystallizes in yellow crystals from *o*-dichlorobenzene, and from carbon tetrachloride in red needles. Its melting point is given as 229–230°C. (124) or 238–240°C. (decomposition) (55). The yellow crystals with neutral solvents

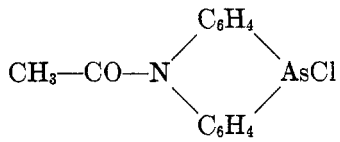
(xylene, toluene, chloroform, phenyl bromide, etc.) are transformed on boiling into a mixture of yellow needles and dark red plates, and on prolonged standing at room temperature into red plates, which, in turn, are converted back into the yellow form by recrystallization from solvents having an oxygen atom in their molecule. The mixture of the two forms causes no depression of the melting point (124).

(*i*) *Action with chloramine-T.* By treating a cold alcoholic solution of 10-chloro-5,10-dihydrophenarsazine with chloramine-T, phenarsazinic acid is prepared (21).

(*j*) *Action with pyridine.* On boiling phenarsazine chloride in dry pyridine for two hours, an orange-yellow, crystalline product is formed, triphenarsazine chloride, melting at 260–263°C. Its properties and analysis point to the following structure (148).

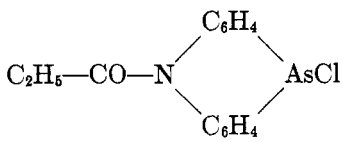


(*k*) *Action with acetyl chloride.* 10-Chloro-5-acetyl-5,10-dihydrophenarsazine,



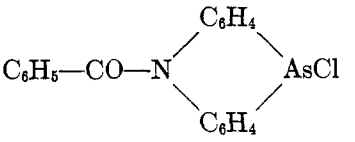
is prepared by boiling an excess of acetyl chloride, diluted with dry benzene, with 10-chloro-5,10-dihydrophenarsazine for four hours. The substance crystallizes on cooling and is obtained in small, colorless needles, m.p. 229–230°C. (21).

(*l*) *Action with propionic anhydride.* 10-Chloro-5-propionyl-5,10-dihydrophenarsazine,



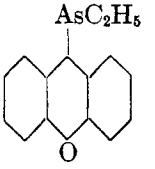
is prepared by boiling 10-chloro-5,10-dihydrophenarsazine with a large excess of propionic anhydride, and a small amount of pyridine, diluted with dry xylene, for ten hours. It crystallizes as colorless plates, melting at 135–136°C. (21).

(*m*) *Action with benzoyl chloride.* 10-Chloro-5-benzoyl-5,10-dihydrophenarsazine,



is prepared by boiling 10-chloro-5,10-dihydrophenarsazine in an excess of benzoyl chloride, diluted with dry xylene, for ten hours. After removal of excess xylene the dark colored viscous oil is allowed to stand for two days and the solid material filtered off; it is obtained as colorless crystals, m.p. 180–181°C. (21).

(*n*) *Action with ethyl bromide.* 10-Ethylphenoxarsine,



is obtained upon adding a warm benzene solution of phenarsazine chloride to the Grignard reagent prepared from ethyl bromide and magnesium; it boils at 194°C. at 20 mm. (2).

Aeschlimann (1) found that 10-chloro-5,10-dihydrophenarsazine reacts with two molecules of the respective Grignard reagents to give 10-methyl-, 10-ethyl-, and 10-phenyl-5,10-dihydrophenarsazine, hydrocarbons also being formed owing to the presence of the :NH group. When the reaction mixture is cooled during the addition of 10-chloro-5,10-dihydrophenarsazine, the formation of hydrocarbon does not take place and the heavy oil which separates from the ethereal solution should contain the :NH(MgI)R group. Treatment of this with methyl iodide, however, does not produce 5,10-dimethyl-5,10-dihydrophenarsazine, but 10,10-dimethyl-5,10-dihydrophenoxarsonium iodide, which is also the product when the methylation of 10-methyl-5,10-dihydrophenarsazine is attempted under various conditions. The latter compound, unlike 10-chloro-5,10-dihydrophenarsazine (148), which loses hydrogen chloride from the 5,10-position to produce phenarsazine when heated in a vacuum, loses methyl iodide under these conditions and re-forms 10-methyl-5,10-dihydrophenarsazine.

10-Methyl-, 10-ethyl-, 10-propyl-, 10-isopropyl-, 10-butyl-, 10-isobutyl-, 10-*sec*-butyl-, 10-amyl-, and 10-diethylmethyl-5,10-dihydrophenarsazines have been prepared by the action of the appropriate alkylmagnesium halide on 10-chloro-5,10-dihydrophenarsazine (1). These are all highly

crystalline compounds whose lack of color is explained by the theory of color of dihydrophenarsazines previously elaborated (50, 55). These compounds have a mildly irritating effect on the skin of the face and are readily decomposed by treatment at 110–130°C. with dry hydrogen chloride.

In table 4 are given the densities (reduced to vacuum standard) and the boiling points under various pressures of the above eight dichloroalkylarsines. From the slope of the boiling point–pressure curves (which are not quite accurately represented by an equation of the form $A - \log_e p = K/T$), the molecular heats of vaporization and Trouton's constant at 760 mm. are calculated to be: $MeAsCl_2$, 7890 calories, and 19.4; $C_2H_5AsCl_2$, 9180 calories, and 21.4; $C_3H_7AsCl_2$, 10,400 calories, and 23.1; iso-$C_3H_7AsCl_2$,

TABLE 4

Densities and boiling points of the dichloroalkylarsines

SUBSTANCE	$d_4^{20°}$ VACUUM	MELTING POINT	BOILING POINT AT					
			20 mm.	50 mm.	100 mm.	200 mm.	400 mm.	760 mm.
		°C.	°C.	°C.	°C.	°C.	°C.	°C.
$MeAsCl_2$	1.8358	−42.5		55.5	72.1	89.1	109.1	132.5
$EtAsCl_2$	1.6595			74.0	90.0	109.6	131.2	155.3
$PrAsCl_2$	1.5380	−28.2		88.8	107.5	126.9	151.2	175.3
iso-$PrAsCl_2$	1.4900		67.0	85.5	102.6	121.0	145.0	168.6
$BuAsCl_2$	1.4664		90.5	105.0	125.6	147.2	172.0	194.1
iso-$BuAsCl_2$	1.4465		77.8	95.8				
sec-$BuAsCl_2$	1.4128		85.0	99.4	113.7	132.1	156.7	181.3
$AmAsCl_2$	1.4035	−45.5	103.0	123.1	142.6	164.1	189.0	212.9

11,500 calories, and 26.0; $C_4H_9AsCl_2$, 12,200 calories, and 26.2; *sec*-$C_4H_9AsCl_2$, 10,700 calories, and 23.5; $C_5H_{11}AsCl_2$, 11,950 calories, and 24.6, respectively. The somewhat high values in some cases of Trouton's constant may indicate some association in the liquid state. If the densities of the *n*-alkyldichloroarsines are plotted against the number of carbon atoms, an anomaly is revealed in the case of the butyl compound.

The following 10-alkyl-5,10-dihydrophenarsazines have been prepared: 10-methyl-, m.p. 105°C. (1), 106–107°C. (53), 107–108°C. (123); 10-ethyl-, m.p. 71–72°C. (123), 75°C. (1, 126), 10-propyl-, m.p. 81–82°C. (114), 85.5–86.5°C. (53); 10-isopropyl-, m.p. 87–88°C. (53); 10-butyl-, m.p. 94–95°C. (53); 10-isobutyl-, m.p., 73–74°C. (53); 10-*sec*-butyl-, m.p. 85–86°C. (53); 10-amyl-, m.p. 90–92°C. (53); 10-isoamyl-, m.p. 76–78°C. (114); 10-diethylmethyl-, m.p. 110–111°C. (53); 10-phenyl-, m.p. 142°C. (1), 148–149°C. (114, 123); 10-α-naphthyl-, m.p. 154–155°C. (123).

In concentrated sulfuric acid, all the alkyl derivatives yield deep red

solutions; those of the ethyl, isopropyl, *sec*-butyl, and diethylmethyl compounds become green on addition of a little concentrated nitric acid; in all cases the color changes to brown or reddish-brown with excess concentrated nitric acid. They all possess a very pungent odor which, at the same time, is reminiscent of decaying fungus (53).

Patents

U. S. patent 1,696,539 was issued December 25, 1928 to D. B. Bradner for the purification of diphenylaminechloroarsine. The crude arsine is melted and poured into water and the mass agitated until it solidifies (19).

Bradner (18) received U. S. patent (reissue) 16,841, January 3, 1928, for the means of volatilizing diphenylaminechloroarsine and other irritating substances by passing a stream of hot products of combustion over the surface of the material to volatilize it.

Physiological action

The physiological action of the arsenical compounds consists of irritation of the nose, throat, eyes, and lungs, causing hyperemia and congestion. There is a feeling of suffocation, nausea, and vomiting. Following these initial symptoms, numbness of the limbs may occur, which may terminate in sharp pains of the legs and toes.

Following the acute symptoms there may be slight dizziness, headache, and effects on the nervous system consisting of sensory and motor disturbances. Anesthesia varying from mere numbness of the finger tips to a complete loss of sensation over a considerable part of one or more limbs is occasionally observed. In some instances paralysis may result. It is the opinion of observers that the motor or sensory nerve changes are functional in character, inasmuch as recovery from these conditions is rapid and uniform.

The respiratory tract may also be affected by the arsenical compounds; the mucous membrane of the nose, throat, and bronchi may be involved and there may be edema of the lungs. In this respect the physiological action of the arsenical compounds is similar to that of chlorine and phosgene, with the additional epithelium-destroying properties of "mustard." The edema produced by the arsenicals is not as severe as that resulting from phosgene poisoning. The destruction of the bronchial epithelium does not extend down the respiratory tract to the small divisions of the bronchial tree, as is the case in mustard poisoning. Irritation of the skin is not as severe as that following mustard gas poisoning, but the skin damage is more severe than that due to chlorine or phosgene. The acute inflammatory reaction of the eyes due to arsenical compounds is severe but rarely as permanent as that following gassing with mustard (57).

Winternitz (149) in experimental work with methyl-, ethyl-, and phenyldichloroarsines and their effect on animals, found that the principal toxic action was on the respiratory tract. Here these arsenicals caused a severe congestion of the larynx and trachea, with the production of a good deal of exudate. In addition the mucous membrane of the bronchi is congested, with the production of exudate which may occlude their lumen.

In the lungs the arsenical compounds produced congestion as well as edema. There were scattered areas of focal pneumonia which terminated in pus formation. Atelectasis as well as emphysema were found in the lung tissue. Congestion of the liver and spleen, as well as ulceration of the gastrointestinal tract, have been noted following gassing with arsenical compounds. The kidneys and liver show evidence of hemorrhagic changes as well as epithelial degeneration.

In addition, arsenical compounds gave evidence of skin-irritant properties which were not, however, as severe as the destruction of the skin caused by mustard. Animals subjected to the action of arsenical compounds show evidence of congestion of the eyes, which was not as severe as that caused by mustard.

Inhalation of these arsenical compounds was followed by sneezing, nausea, vomiting, pain in the chest and abdomen, and conjunctivitis. The full action of poisoning with arsenical compounds became intense within a short space of time, and disablement resulted even from the inhalation of a weak concentration of the poison. Upon swallowing arsenical compounds evidence of acute gastritis and enteritis was noted.

The pathological lesions resulting from gassing with arsenical compounds consist of the following: There may be intense involvement of the entire respiratory tract, beginning with the larynx and trachea and terminating in the fine bronchioles and air sacs. The inflammatory reaction consists of a more or less yellowish, fibrinopurulent exudate. The bronchioles show the presence of exudate and edema fluid which may occlude the lumen. The lungs are voluminous and heavier and firmer than normal with areas of edema, congestion, atelectasis, and emphysema. Scattered patches of focal pneumonia with or without pus formation may be seen. Scattered hemorrhages, both pulmonary and subpleural, are noted where the edema is considerable and the smaller bronchi are blocked.

In reviewing the post-mortem findings of the men who were gassed with arsenical compounds and who died immediately after gassing, it was found that bronchopneumonia and lobar pneumonia were the two principal causes of death.

Of the men who were gassed with arsenical compounds and who survived the gassing, but who gave evidence of residual disabilities and who died subsequently, the post-mortem findings showed that bronchopneumonia was the direct cause and chronic bronchitis the contributory cause of death.

Microscopically, the important changes following gassing with arsenical compounds are in the respiratory tract. The mucous membrane of the trachea was found to contain a fibrin network with large spaces full of edema fluid. The epithelial lining of the trachea was found to be lifted. In the early stages there was little polymorphonuclear infiltration, but this became more marked in a short time.

In the lungs the microscopic changes showed areas of congestion and edema interspersed with areas showing alveoli overdistended with air. The capillaries of the alveolar walls, particularly in the edematous areas, were tortuous and filled with red blood cells. The alveolar epithelium seemed to suffer very little and in most places was intact. In places much fibrin could be seen in the edematous alveoli. The bronchi showed a continuation of the findings in the tracheal mucous membrane, but the bronchioles usually presented an intact layer of epithelium.

Ulceration of the mucous membrane of the gastrointestinal tract was observed in some instances. Other organs, such as the liver, kidneys, and spleen, showed but little pathological changes. There was slight swelling and granulation of the parenchymal cells.

Animals that survive the acute effects of gassing with the arsenicals may show such complications as suppurative bronchitis, bronchopneumonia, or suppurative pleurisy.

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