11. *The Preparation and Properties of* 2-*Substituted* iso*Arsindolines. The Synthesis of* spiro-*Arsonium Salts.*

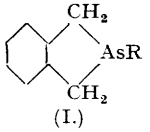
By Donald R. Lyon and Frederick G. Mann.

o-Xylylene dibromide in the presence of sodium and ether reacts with phenyl- and methyl-dichloroarsine to give 2-*phenyl*- and 2-*methyl*-iso*arsindoline* (I, R = Ph and R = Me). The latter combines with *o*-xylylene dibromide to give the quaternary *salt* (IV), which on heating undergoes cyclisation and loss of methyl bromide, furnishing As-spiro-*bis*iso*arsindolinium bromide* (V). *spiro*-Arsonium salts of this type have not previously been prepared.

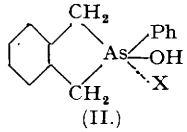
Arsenobenzene can be readily prepared by the action of sodium upon ethereal phenyldichloroarsine.

Preliminary tests indicate that 2-*phenyl*iso*arsindoline dihydroxide* may prove to be an effective drug against *Trypanosoma congolense* infection.

Although several types of organic compound containing an arsenic atom as part of a five-membered ring are known, the arsenic analogues of the *iso*indolines have not previously been described. We find that when an ethereal solution of equimolecular quantities of *o*-xylylene dibromide and phenyldichloroarsine is refluxed with metallic sodium in an atmosphere of nitrogen, no apparent reaction occurs; the addition of ethyl acetate, however, promotes the desired reaction, and, provided air be carefully excluded throughout, distillation of the final filtered solution ultimately furnishes 2-*phenyl*iso*arsindoline* (I, R = Ph) as a colourless liquid, b. p. **136—138°/0·3** mm., in 18% yield. Certain by-products are also formed. For instance, the arsine is initially contaminated with hydrocarbons formed by the direct action of the sodium on the dibromide (see preceding paper), and the undistilled residue contains arsenobenzene, formed by the direct action of the sodium on the dichloride. This novel method for preparing arsenobenzene is discussed later.



(I.)



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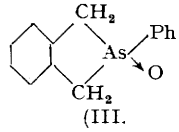
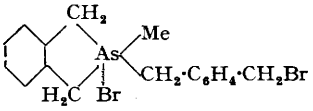


(III.)

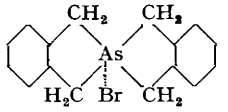
2-Phenyl*iso*arsindoline has the normal properties of a tertiary arsine. Oxidation with nitric acid readily gives the crystalline *hydroxy-nitrate* (II, X = NO_3), which in turn, treated with aqueous sodium hydroxide, furnishes the water-soluble *2-phenyliso**arsindoline dihydroxide* (II, X = OH); the latter can be dehydrated to the *oxide* (III), which, however, on exposure to damp air rapidly absorbs water, re-forming the dihydroxide. The latter also reacts with other acids; *e.g.*, with hydrobromic acid it gives the crystalline *hydroxy-bromide* (II, X = Br) and with picric acid the *hydroxy-picrate* (II, X = $C_6H_2O_7N_3$). In view of the therapeutic importance of the dihydroxide, we have investigated in some detail its production by other means from the arsine (I, R = Ph). This arsine unites with bromine to give the white, crystalline arsine dibromide, which is decomposed by alkalis to form the dihydroxide. The arsine is also oxidised by chloramine-T (sodio-toluene-*p*-sulphonchloroamide), furnishing *2-phenyliso**arsindoline hydroxy-toluene-*p*-sulphonamide* (II, X = $C_7H_7{\cdot}SO_2{\cdot}NH$), which is also readily decomposed by alkalis to furnish the dihydroxide. The arsine can also be directly converted into the dihydroxide by the action of hydrogen peroxide or aqueous potassium permanganate; the latter reagent apparently also gives other products and the yield of dihydroxide is low.

The arsine dihydroxide reacts with hydrogen sulphide to form the colourless *arsine sulphide* (as III). Methyl iodide unites directly with the arsine, giving the quaternary salt, *2-phenyl-2-methyliso**arsindolinium iodide*.

Initial attempts to prepare *2-methyliso**arsindoline* (I, R = Me) by the action of sodium on a boiling ethereal solution of equimolecular quantities of *o*-xylylene dibromide and methyldichloroarsine in the presence of ethyl acetate were unsuccessful, although interesting by-products were isolated. When, however, an excess of the dichloroarsine (1·5 mols.) was used, with prolonged boiling, 2-methyl*iso*arsindoline, b. p. 115°/17 mm., was obtained, but only in 4% yield. This arsine gives arsonium salts more readily than its phenyl analogue; *e.g.*, it unites vigorously with methyl iodide to give 2 : *2-dimethyliso**arsindolinium iodide*. Furthermore, it also unites with *o*-xylylene dibromide to give 2-o-(*bromomethyl*)*benzyl-2-methyliso**arsindolinium bromide* (IV). This salt when heated loses methyl bromide, giving the highly crystalline As-spiro-*bis*iso*arsindolinium bromide* (V), characterised also by conversion into the corresponding *iodide* and *picrate*. This synthesis of the bromide



(IV.)



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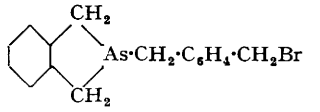

(VI.)

(V) is of great interest. It is the only known method for the preparation of spirocyclic arsonium salts in which the arsenic atom is linked solely to carbon atoms. Moreover, it is clear that, if the synthesis were repeated upon a derivative of *o*-xylylene dibromide having a suitable substituent in the benzene ring, the corresponding disubstituted analogue of the bromide (V) would possess molecular dissymmetry by virtue of the tetrahedral disposition of the four arsenic valencies, and thus be optically resolvable. The synthesis of such a salt will be investigated later.

If in the synthesis of the 2-methyl*iso*arsindoline (I, R = Me) only 1 equiv. of methyldichloroarsine is used, or if the refluxing is not sufficiently prolonged, distillation ultimately gives an unstable product which is almost certainly 2-*o*-(bromomethyl)benzyl*iso*arsindoline (VI); this crude product is readily soluble in hot alcohol, but the solution on boiling soon deposits the slightly soluble spiro-bromide (V). The latter compound can also be isolated from the undistilled residue in the distilling-flask. It would appear, therefore, that under the above conditions of preparation the initially formed 2-methyl*iso*arsindoline combines with unchanged dibromide, to give the arsonium bromide (IV). During the distillation, the latter loses methyl bromide, partly to give the *spiro*-bromide (V), which necessarily remains in the distilling flask, and partly to give the *iso*arsindoline (VI), which distils over. The identification of the crude unstable distillate as (VI) is confirmed by the facts that (*a*) the arsonium bromide (IV) is stable in boiling alcohol and therefore does not furnish the *spiro*-bromide (V) in these conditions, and (*b*) the *spiro*-bromide (V), being a salt, cannot be distilled, and its formation from the distillate must therefore occur during the boiling in alcohol.

In view of the isolation of arsenobenzene as a by-product in the preparation of 2-phenyl*iso*arsindoline, we have investigated its direct preparation. We find that sodium reacts spontaneously and vigorously with an ethereal solution of phenyldichloroarsine, furnishing arsenobenzene of high purity in 50% yield. (This reaction is in striking contrast to that given when *o*-xylylene dibromide also is present, in which case long heating and a catalyst are required to start the reaction.) *p*-Tolyldichloroarsine similarly furnishes arseno-*p*-toluene, $CH_3{\cdot}C_6H_4{\cdot}As{:}As{\cdot}C_6H_4{\cdot}CH_3$. The method of preparation is therefore clearly of considerable practical value.

The arsenobenzene was thus obtained as almost colourless crystals, stable in air, having m. p. 213—214° in a preheated apparatus, and a molecular weight of 917 in 0·44%, and 881 in 0·84%, boiling benzene solution, the theoretical molecular weight being 304.

Arsenobenzene has previously been prepared usually by reducing phenylarsonic acid with various reagents, although Blicke and Smith (*J. Amer. Chem. Soc.*, 1930, **52**, 2945) have prepared it by the three-days action of mercury on phenyldi-iodoarsine. The earliest recorded preparations clearly gave an impure product, described as yellow, and spontaneously inflammable in air. Even for apparently pure samples, wide ranges of m. p.'s and molecular weights have been recorded, as shown on p. 32 :

M. p.	*M.*	Solvent.	Reference.
196°	—	—	Michaelis and Schulte, *Ber.*, 1881, **14**, 912
212	399·8	Boiling C_6H_6	Michaelis and Schafer, *ibid.*, 1913, **46**, 1742
208	—	—	Binz, Bauer, and Hallstein, *ibid.*, 1920, **53**, 427
195	334	Boiling CS_2	Palmer and Scott, *J. Amer. Chem. Soc.*, 1928, **50**, 537
—	402	Boiling C_6H_6	,,
—	642·	Freezing $C_{10}H_8$	,,
212—213	895, 915	Boiling C_6H_6	Blicke and Smith, *ibid.*, 1930, **52**, 2949
210—212	867	Boiling C_6H_6	Blicke and Powers, *ibid.*, 1933, **55**, 315

The recorded molecular weights in benzene are widely discordant, although our results approximate closely to the most recent values of Blicke and his co-workers (above) and indicate marked association. This association is shown by other similar compounds; *e.g.*, Steinkopf, Schmidt, and Smie (*Ber.*, 1926, **59**, 1463) have shown that the molecular weight of arsenomethane in solution corresponds to $(MeAs:)_5$, and they consider the compound to be actually pentamethyl*cyclo*pentarsine. It is clearly of great interest to determine whether arsenobenzene has the simple structure, PhAs:AsPh, and if so, whether it has the *cis*- or the *trans*-configuration, or whether it has a more complex (associated) structure. Dr. Edna M. Davidson has kindly submitted samples of our highly crystalline arsenobenzene to crystallographic and *X*-ray analysis. The compound proves, however, to have twelve PhAs: groups in the unit cell, and this complexity in particular has at present prevented the elucidation of its structure.

The therapeutic properties of the above *iso*arsindolines have been investigated by the staff of Imperial Chemical Industries Limited, who find that the arsine dihydroxide (II, X = OH), and therefore necessarily the oxide also, have noteworthy properties.* Preliminary trials have shown that this compound possesses slight activity against *Trypanosoma rhodesiense* and *T. cruzi* in mice, but greater activity against *T. congolense*. In view of this encouraging result, we are now preparing various substituted derivatives of the dihydroxide, and also its antimony analogue, in order to test their activity against *Trypanosoma* infection.

Experimental.

The names of solvents used for recrystallisation are given in parenthesis immediately after the compounds concerned.

2-Phenylisoarsindoline (I, R = Ph).—*o*-Xylylene dibromide (52·8 g.), phenyldichloroarsine (44·6 g., 1 mol.), and fine sodium wire (40 g., 8·6 atoms) were added in turn to dry ether (500 c.c.) in a 1-l. round-bottomed flask to which was fitted a reflux water-condenser, a dropping-funnel, and an inlet tube through which a current of pure nitrogen was passed throughout the experiment. The mixture was now refluxed for 11 hours, 5 c.c. of ethyl acetate being added at the beginning, and two further additions of 2·5 c.c. after 3 and 7 hours' boiling, respectively. After the third addition, the sodium, which had hitherto appeared almost unchanged, rapidly disintegrated. The mixture was allowed to cool, the nitrogen replaced by a stream of carbon dioxide, and the latter employed to force the solution through a sintered-glass filter into a small Claisen flask without exposure to air, the apparatus described by Holliman and Mann (J., 1943, 549) being used. After distillation of the ether, the dark brown residue was distilled at low pressure, and the crude *iso*arsindoline (I, R = Ph) obtained, b. p. 136—142°/0·3 mm.; 9·5 g., 18·5% calculated on the dibromide used. Redistillation gave a fraction, b. p. 136—138°/0·3 mm., but analysis showed that this fraction, even when repeatedly distilled, was impure. It was therefore cooled in ice-water and cautiously treated with concentrated nitric acid. Vigorous oxidation occurred, and the dark red oil which formed crystallised ultimately when the mixture was diluted with water and stirred. This solid product, recrystallised from very dilute nitric acid, gave the *hydroxy-nitrate* (II, X = NO_3) as colourless crystals (10 g.), m. p. 149—150° (efferv.) (Found: C, 49·8; H, 4·4; N, 4·5. $C_{14}H_{14}O_4NAs$ requires C, 50·2; H, 4·2; N, 4·2%). When the powdered nitrate was treated with cold 10% aqueous sodium hydroxide solution in excess, the oily dihydroxide separated but rapidly dissolved on the addition of water. The solution was thoroughly extracted with chloroform; removal of the solvent from the extract gave an oil which readily solidified. After drying, crystallisation from ethyl carbonate furnished the *2-phenylisoarsindoline dihydroxide* (II, X = OH), colourless crystals, m. p. 78—79° (Found: C, 57·5; H, 5·6. $C_{14}H_{15}O_2As$ requires C, 57·9; H, 5·2%). The dihydroxide is freely soluble in water and in most organic solvents. Other methods of preparation are given below. The dihydroxide, when confined in a vacuum over phosphoric oxide, slowly gave the *oxide* (III), m. p. 130—131° (Found: C, 61·6; H, 5·1. $C_{14}H_{13}OAs$ requires C, 61·8; H, 4·8%), which on exposure to the air rapidly re-formed the dihydroxide.

A solution of the dihydroxide (II, X = OH, 8·5 g.) in chloroform (50 c.c.) was mixed with water (100 c.c.) and concentrated hydrochloric acid (15 c.c.), potassium iodide (0·1 g.) added, and sulphur dioxide passed through the chloroform layer for 30 minutes. This layer was then separated, dried (sodium sulphate), and distilled; after removal of the solvent, the pure *2-phenylisoarsindoline* (II), b. p. 136—138°/0·3 mm., was obtained (Found: C, 65·5; H, 5·1; *M*, cryoscopically in 0·52% ethylene dibromide solution, 246. $C_{14}H_{13}As$ requires C, 65·6; H, 5·1%; *M*, 256).

The following points concerning the above preparation of the arsine must be noted. (i) The yield of the arsine decreases if the refluxing is continued for more than 11 hours in spite of the inert atmosphere. Distillation of the ethereal solution should preferably be performed immediately the refluxing is complete. (ii) Increasing the amount of the initial addition of ethyl acetate did not apparently accelerate the onset of the reaction. A period of 7—8 hours' refluxing seemed to be necessary before the reaction became pronounced (as shown by the state of the sodium): it then proceeded rapidly. (iii) Much solid material separated from the ethereal solution as the reaction proceeded. In addition to unchanged sodium and sodium halide, this consisted of the amorphous material formed by the action of the sodium on the *o*-xylylene dibromide (see previous paper) and of arsenobenzene. The mixture was therefore rapidly but cautiously sieved to remove fragments of sodium, and then added in small quantities to much cold water. The brown, amorphous, insoluble material was washed with water until no longer sticky, collected, dried (10 g.), and then twice recrystallised from benzene, in which the amorphous component was freely soluble. Arsenobenzene (*ca.* 0·5 g.) was thus obtained in very pale yellow needles, m. p. 213—214° in preheated bath (Found: C, 47·6; H, 3·4. Calc. for $C_{12}H_{10}As_2$: C, 47·4; H, 3·3%). (iv) After distillation of the crude arsine (I, R = Ph), the black sticky residue in the Claisen flask was twice extracted with hot acetic acid to remove the viscous component. The solid, insoluble residue, after repeated recrystallisation from benzene, also furnished pure arsenobenzene (*ca.* 0·2 g.). (v) When benzene was used instead of ether in the original reaction, the mixture became black during the refluxing, and no volatile product other than benzene could subsequently be obtained.

* Patent protection pending.

The arsine dihydroxide (II, X = OH) was further characterised : (*a*) the addition of concentrated hydrobromic acid to its aqueous solution gave the *hydroxy-bromide* (II, X = Br), colourless needles from dilute hydrobromic acid, or from alcohol by ether precipitation : m. p. 132—133° (preliminary softening) (Found : C, 47·5; H, 3·9. $C_{14}H_{14}OBrAs$ requires C, 47·6; H, 4·0%); (*b*) mixing of aqueous solutions of picric acid and the dihydroxide, or of warm alcoholic solutions of picric acid and the hydroxy-nitrate, gave the *hydroxy-picrate* (II, X = $C_6H_2O_7N_3$), yellow needles from alcohol, m. p. 164—166° (decomp.) (Found : C, 48·2; H, 3·1; N, 8·4. $C_{20}H_{16}O_8N_3As$ requires C, 47·9; H, 3·2; N, 8·4%).

Other Methods for the Preparation of the Arsine Dihydroxide (II, X = OH).—(A) *Bromine.* A solution of bromine (0·8 g., 1 mol.) in chloroform (7 c.c.) was slowly added to an agitated solution of the arsine (1·3 g.) also in chloroform (10 c.c.). The bromine was rapidly absorbed, and the white solid arsine dibromide was precipitated. A 5% aqueous solution of sodium hydroxide was now added, and the mixture shaken until the dibromide disappeared. The chloroform was separated and evaporated, and the viscous arsine dihydroxide which remained ultimately crystallised.

(B) *Chloramine-*T. Solutions of the arsine (2·5 g.) and of hydrated chloramine-T (2·8 g., 1 mol.), each in alcohol (100 c.c.), were mixed and refluxed for 2 hours, sodium chloride rapidly separating. The solution was then filtered and evaporated, and the oily residue, when triturated with anhydrous ether, deposited 2-*phenyl*iso*arsindoline hydroxytoluene*-p-*sulphonamide* (II, X = $C_7H_7{\cdot}SO_2{\cdot}NH$), white crystals (ethyl carbonate), m. p. 122° (Found : C, 56·8; H, 5·2. $C_{21}H_{22}O_3NSAs$ requires C, 56·9; H, 5·0%). When this compound was decomposed by sodium hydroxide solution, chloroform readily extracted the liberated arsine dihydroxide. When cold alcoholic solutions of the sulphonamide and of picric acid were mixed, the above hydroxy-picrate was precipitated.

(C) *Hydrogen peroxide.* A solution of the arsine (1 g.) in acetone (20 c.c.) was diluted with " 20-volume " aqueous hydrogen peroxide (5 c.c.), and set aside overnight. Evaporation of the solvent then gave a residue of the arsine dihydroxide which readily solidified, particularly when seeded.

(D) *Potassium permanganate.* The arsine (1·5 g., 3 mols.) was added to a solution of potassium permanganate (0·6 g., 2 mols.) and anhydrous sodium carbonate (0·3 g.) in cold water (50 c.c.). Partial reduction of the permanganate occurred immediately on shaking, and gentle warming for a few minutes caused complete discharge of the permanganate colour. The presence of the arsine dihydroxide in the filtered solution was shown by adding nitric acid, which precipitated the above hydroxy-nitrate (II, X = NO_3; 0·8 g.). The low yield shows, however, that further oxidation had probably occurred.

Potassium persulphate and potassium dichromate in aqueous solution did not give a smooth conversion of the arsine into its dihydroxide. Furthermore, when air was bubbled through a solution of the arsine (1 g.) in alcohol (30 c.c.) for 8 hours at room temperature, subsequent evaporation of the solvent left a residue of almost unchanged arsine.

2-*Phenyl*iso*arsindoline Sulphide* (as III).—A solution of the arsine dihydroxide (2·5 g.) in chloroform (20 c.c.) was saturated with hydrogen sulphide, filtered, and the solvent evaporated. The white solid residual *sulphide* (2·5 g.) gave needles (alcohol), m. p. 108° (Found : C, 58·3; H, 4·7; S, 11·1. $C_{14}H_{13}SAs$ requires C, 58·3; H, 4·6; S, 11·1%).

2-*Phenyl*-2-*methyl*iso*arsindolinium Iodide.*—A solution of the arsine (I, R = Ph, 1 g.) in methyl iodide (8 g.) was refluxed for 15 minutes, a white solid rapidly separating. Excess of methyl iodide was evaporated off, and the residue recrystallised from alcohol, the *iodide* being obtained in magnificent, colourless needles, m. p. 189—191° (decomp.) (Found : C, 44·9; H, 4·0; I, 31·5. $C_{15}H_{16}IAs$ requires C, 45·2; H, 4·0; I, 31·9%). This iodide is freely soluble in cold water, and treatment of this solution with aqueous picric acid immediately gave the *picrate*, yellow crystals from alcohol, m. p. 122—123° (Found : C, 50·6; H, 3·8; N, 8·4. $C_{21}H_{18}O_7N_3As$ requires C, 50·5; H, 3·6; N, 8·4%).

2-*Methyl*iso*arsindoline* (I, R = Me).—*o*-Xylylene dibromide (52·8 g.), methyldichloroarsine (48·3 g., 1·5 mols.), fine sodium wire (40 g., 8·6 atoms), and ethyl acetate (5 c.c.) were added in this order to ether (800 c.c.) in the apparatus already described for (I, R = Ph), and the mixture refluxed for 24 hours. Three further acetate additions (5 c.c. each) were made after 9, 17, and 21 hours' refluxing respectively. No apparent reaction occurred, however, until *ca.* 18 hours' refluxing, whereupon the sodium steadily disintegrated. The solution was then filtered and distilled in carbon dioxide as already described, two colourless fractions being obtained : (i) b. p. 39°/17 mm., 4 g.; (ii) b. p. 115°/17 mm., 1·5 g. The latter was pure 2-*methyl*iso*arsindoline* (Found : C, 56·2; H, 5·7. $C_9H_{11}As$ requires C, 55·7; H, 5·7%); yield 3·9%.

2 : 2-*Dimethyl*iso*arsindolinium Iodide.*—A vigorous reaction occurred when the above arsine was refluxed with excess of methyl iodide, giving a white solid product. Recrystallisation of the latter from alcohol gave the crystalline *iodide*, m. p. 210—211° (slight darkening) (Found : C, 35·5; H, 4·4; I, 37·7. $C_{10}H_{14}IAs$ requires C, 35·7; H, 4·2; I, 37·8%). Mixing alcoholic solutions of this iodide and of picric acid precipitated the corresponding *picrate*, yellow needles from alcohol, m. p. 209° (Found : C, 43·8; H, 3·8; N, 9·8. $C_{16}H_{16}O_7N_3As$ requires C, 43·9; H, 3·7; N, 9·6%).

2-o-(*Bromomethyl*)*benzyl*-2-*methyl*iso*arsindolinium Bromide* (IV).—Powdered *o*-xylylene dibromide (0·81 g., 1 mol.) was added to 2-methyl*iso*arsindoline (0·60 g.) in a small flask having a ground glass stopper. The closed flask was gently warmed until the mixture formed a homogeneous liquid, which, when cooled and stirred, solidified. These operations were performed with a minimum exposure to the air, because of the highly hygroscopic properties of the resulting *bromide* (IV). The latter was then pulverised under and thoroughly washed with dry ether, and finally dried in a vacuum over phosphoric anhydride (Found : C, 44·5; H, 5·0; Br, 35·0. $C_{17}H_{19}Br_2As$ requires C, 44·5; H, 4·2; Br, 34·9%). Recrystallisation of this bromide was not attempted : it was freely soluble in cold alcohol.

As-spiro-*Bis*iso*arsindolinium Bromide* (V).—The above bromide (IV) was heated in a small flask at 14 mm. pressure. At 50—60° fusion to a viscous liquid, with slight effervescence began, and as the temperature was slowly raised to 200°, this liquid became more mobile and darker, and after *ca.* 15 minutes at 200° it slowly crystallised. The cold product, when stirred with a small quantity of alcohol, gave colourless crystals of the spirocyclic *bromide* (V), which were then recrystallised from dilute aqueous hydrobromic acid (Found : C, 53·2; H, 4·5; Br, 21·9. $C_{16}H_{16}BrAs$ requires C, 52·9; H, 4·4; Br, 22·0%) : recrystallisation from water causes slight hydrolysis (Found : C, 54·1; H, 5·35; Br, 21·05%). The bromide on heating decomposes at 235—239° with effervescence; its low solubility in cold alcohol and lack of hygroscopic properties differentiate it sharply from the parent bromide (IV).

When hot aqueous solutions of the bromide (V) and of picric acid were mixed and cooled, the spirocyclic *picrate* separated; yellow crystals from alcohol, m. p. 188—189° (Found : C, 51·7; H, 4·0; N, 8·3. $C_{22}H_{18}O_7N_3As$ requires C, 51·7; H, 3·6; N, 8·2%). When a similar solution of the bromide (V) was treated with excess of aqueous potassium iodide, the spirocyclic *iodide* was immediately precipitated. It was collected, dissolved in hot water, reprecipitated with potassium iodide, and finally recrystallised from hot water; colourless crystals of indefinite m. p. (decomp. starts *ca.* 200°) (Found : C, 46·8; H, 4·2; I, 30·65. $C_{16}H_{16}IAs$ requires C, 46·8; H, 3·9; I, 30·95%). It is markedly less soluble than the bromide in both cold and hot water.

A repetition of the above preparation of 2-methyl*iso*arsindoline was attempted, the only changes being that methyldichloroarsine (32·2 g., 1 mol.) was used, and the refluxing was limited to 10 hours. The solution, when filtered and distilled as before, gave the following colourless fractions : (*a*) b. p. 32—36°/15 mm., 1·5 g.; (*b*) b. p. 40—104°/15 mm., *ca.* 0·2 g.; (*c*) b. p. 115—120°/0·4 mm., 5 g. Fraction (*a*) also had b. p. 133—135°/760 mm., and was unchanged methyldichloroarsine. Fraction (*b*) gave no reaction with methyl iodide and therefore did not contain tertiary arsine. Fraction (*c*) slowly solidified, and when recrystallised from alcohol furnished *o*-xylylene dibromide, m. p. 93—95°. The alcoholic mother-liquor was boiled and concentrated, and when cooled it deposited colourless crystals of the *spiro*-bromide

(V), m. p. 235—239° (decomp.), almost insoluble in cold alcohol and only moderately soluble in hot alcohol. Their identity was confirmed by conversion into the *spiro*-picrate, m. p. 188—189°, and by mixed m. p. determinations. The b. p. of fraction (*c*) precludes the presence of free 2-methyl*iso*arsindoline; this fraction must therefore have consisted of the unchanged dibromide, and of the tertiary arsine (VI), which in the boiling alcohol furnishes the *spiro*-bromide (V).

The black, sticky residue from the above fractional distillation was washed with acetone, and the pale brown, insoluble product then extracted with boiling water. The filtered aqueous extract on cooling deposited a small quantity of the crystalline *spiro*-bromide (V), which was also characterised by conversion into the *spiro*-picrate, m. p. 188—190°, mixed and unmixed.

Arsenobenzene.—Fine sodium wire (5 g.) was added to a solution of phenyldichloroarsine (44·6 g., 1 mol.) in dry ether (200 c.c.) contained in a flask carrying a reflux water-condenser and an inlet tube through which dry nitrogen was passed throughout the experiment. A vigorous reaction ensued, the ether boiling and much white solid separating. When this reaction had subsided, more sodium wire (15 g.; total addition, 4·3 atoms) was added, and the mixture refluxed for 5 hours, by which time most of the sodium had disintegrated, and the solution had become pale orange. The cold mixture was now shaken and filtered, so that unchanged sodium remained in the flask, whereas the white solid was collected on the filter. Small fragments of sodium in the white solid were removed by hand, and the solid then washed with water and dried. The crude arsenobenzene (15 g., 49%) thus obtained was stable in air and almost colourless; it was recrystallised from benzene or (preferably) ethyl acetate, forming colourless crystals, m. p. 213—214° if determined in a preheated apparatus (Found: C, 47·1; H, 3·0%).

Arseno-p-*toluene.*—This was prepared precisely as the arsenobenzene, but from *p*-tolyldichloroarsine (23·7 g., 1 mol.) and sodium (10 g., 4·3 atoms) in ether (200 c.c.). The crude product (8 g., 48%), recrystallised from ethyl acetate, gave very pale yellow crystals of arseno-*p*-toluene, m. p. 185·5—186·5° in a preheated apparatus (Found: C, 50·65; H, 4·5. Calc. for $C_{14}H_{14}As_2$: C, 50·6; H, 4·3%). It is noteworthy that Michaelis (*Annalen*, 1902, **320**, 301) originally gave m. p. 184° for this compound, but later Michaelis and Schafer (*loc. cit.*) found that material crystallised from chloroform had m. p. 184° and that from benzene had m. p. 202°; Blicke and Smith (*loc. cit.*) found m. p. 218—219°. It is impossible to say whether the discrepancy in these m. p.'s was due to the method of determination, to impurities, or to the compound's being possibly a mixture of geometric isomers.

Dr. E. M. Davidson reports on a sample of arsenobenzene prepared by the above method and recrystallised from ethyl acetate: "The compound exists in very pale yellow monoclinic prismatic crystals elongated along the *b* axis, showing straight extinction and high birefringence with β along *b*, and the optic axial plane (010). The sign of birefringence is probably positive, although the nature of the crystals made optical determinations difficult. The unit cell dimensions were determined by single-crystal oscillation photographs: $a = 24{\cdot}13$, $b = 6{\cdot}16$, $c = 12{\cdot}14$ A., $\beta = 111°$; axial ratio = 3·92 : 1 : 1·97. Cell volume = 1687 A.^{3}. Space-group is $P2_1/a$. Density (measured), 1·778; density (calc.), 1·782. Number of PhAs groups in the unit cell = 12. From the *X*-ray data there is nothing to distinguish between six molecules, each of formula PhAs:AsPh, in the unit cell, and, for example, a cyclic structure of formula $(PhAs:)_6$ with two molecules in the unit cell. The positive sign of birefringence, if this can be confirmed, is in favour of the former."

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THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, October 26th*, 1944.]