114. *The Cyano-ethylation of Arsines, and the Preparation of Amidino-alkyl-arsines and Carboxy-alkyl-arsines.*

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It is shown that primary and secondary arsines, of the type $RAsH_2$ and R_2AsH respectively, readily unite with vinyl cyanide to form 2-cyanoethyl-arsines of type $AsR(CH_2\cdot CH_2\cdot CN)_2$ and $AsR_2\cdot CH_2\cdot CH_2\cdot CN$. 2-Cyanopropylene similarly gives 2-cyano-*n*-propyl-arsines. The cyano-ethyl-arsines can be readily converted into the corresponding amidino-arsines, the therapeutic action of which is now being investigated. The 2-cyano-alkyl-arsines can also be readily hydrolysed to the corresponding 2-carboxy-alkyl-arsines.

Other more general methods for the synthesis of ω-carboxy-alkyl-arsines are discussed.

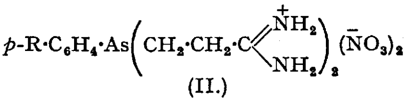
Many examples of the direct union of vinyl cyanide with ammonia and with primary and secondary amines have been recorded. The cyanide reacts with ammonia, either liquid or in aqueous solution, to give a mixture of 2-cyanoethylamine, bis-2-cyanoethylamine and tris-2-cyanoethylamine, the proportion of these amines depending on the conditions (Hoffmann and Jacobi, D.R.-P. 598,185; Whitmore *et al.*, *J. Amer. Chem. Soc.*, 1944, **66**, 725; Buc, Ford, and Wise, *ibid.*, 1945, **67**, 92; Wiedemann and Montgomery, *ibid.*, p. 1994). Primary amines similarly furnish the corresponding 2-cyanoethylamines, $NHR\cdot CH_2\cdot CH_2\cdot CN$, and the bis-2-cyano-ethylamines, $NR(CH_2\cdot CH_2\cdot CN)_2$, and secondary amines also give the 2-cyanoethylamines, $NR^1R^2\cdot CH_2\cdot CH_2\cdot CN$ (Hoffmann and Jacobi, *loc. cit.*; Roh and Wolff, D.R.-P. 641,597; Holcomb and Hamilton, *J. Amer. Chem. Soc.*, 1942, **64**, 1309; Whitmore *et al.*, *loc. cit.*); it is claimed that some of these reactions are reversible at high temperatures. Amides and imides unite similarly with vinyl cyanide (Wegler, D.R.-P. 734,725; 735,771; Galat, *J. Amer. Chem. Soc.*, 1945, **67**, 1414).

The union of vinyl cyanide with amines when sluggish has usually been promoted by the addition of basic catalysts such as sodium alkoxides, but acidic catalysts have occasionally been used. For example, Whitmore *et al.* (*loc. cit.*) have shown that neither carbazole nor tetrahydro-quinoline will react with pure vinyl cyanide, but that the addition of benzyltrimethylammonium hydroxide to the carbazole or of glacial acetic acid to the tetrahydroquinoline induces the production of the 2-cyanoethyl derivative in high yield.

We have consequently investigated the interaction of vinyl cyanide with primary and secondary arsines. We find that phenylarsine, $Ph\cdot AsH_2$, readily combines with vinyl cyanide to form the crystalline *phenylbis-2-cyanoethylarsine* (I, R = H). Gentle boiling, without the aid of catalysts, is sufficient to induce this combination, but addition of alkaline catalysts, such as a trace of aqueous potassium hydroxide or of sodium methoxide, makes the reaction exceedingly vigorous. This cyano-arsine, unlike the liquid aryldialkylarsines, does not apparently undergo oxidation even on long exposure to air. Otherwise it has the normal

$p\text{-R}\cdot C_6H_4\cdot As(CH_2\cdot CH_2\cdot CN)_2$

(I.)



$$p\text{-R}\cdot C_6H_4\cdot As\left(CH_2\cdot CH_2\cdot C\begin{matrix}\overset{+}{N}H_2\\ NH_2\end{matrix}\right)_2(\overset{-}{N}O_3)_2$$

(II.)

$p\text{-R}\cdot C_6H_4\cdot As(CH_2\cdot CH_2\cdot CO_2H)_2$

(III.)

properties of tertiary arsines; for example, with alkyl iodides it forms quaternary salts, and with potassium palladochloride it forms the crystalline non-ionic *dichlorodi(phenylbis-2-cyanoethylarsine)palladium*, $[Cl_2Pd\{Ph\cdot As(CH_2\cdot CH_2\cdot CN)_2\}_2]$.

This combination with vinyl cyanide appears to be general for primary arylarsines. Thus *p*-aminophenylarsine, $NH_2\cdot C_6H_4\cdot AsH_2$, similarly furnishes p-*aminophenylbis-2-cyanoethylarsine* (I, R = NH_2), which on acetylation gives the p-*acetamidophenyl* derivative (I, R = NHAc), and on treatment with aqueous potassium cyanate gives the p-*carbamido*-derivative (I, R = $NH\cdot CO\cdot NH_2$). The amino-group in (I, R = NH_2) has the normal properties of an aromatic amine: for example, the compound after diazotisation condenses with alkaline β-naphthol to form *2-hydroxynaphthalene-1-azo-*p*-phenylbis-2-cyanoethylarsine*, $HO\cdot C_{10}H_6\cdot N_2\cdot C_6H_4\cdot As(CH_2\cdot CH_2\cdot CN)_2$.

The secondary aryl-arsine, diphenylarsine, Ph_2AsH, also combines with vinyl cyanide to form *diphenyl-2-cyanoethylarsine*, $Ph_2As\cdot CH_2\cdot CH_2\cdot CN$. 2-Cyanopropylene combines similarly with diphenylarsine to form diphenyl-2-cyano-*n*-propylarsine, $Ph_2As\cdot CH_2\cdot CHMe\cdot CN$, but this cyanide, unlike all the previous cyanides, could not be obtained crystalline, and has been identified only as crystalline derivatives.

These cyanoethyl-arsines have several interesting synthetic applications which we are now investigating. Thus the dicyanide (I, R = H), when treated with a mixture of alcohol and chloroform saturated with hydrogen chloride gives the crystalline but very deliquescent bis(imino-ether) hydrochloride, $Ph\cdot As[CH_2\cdot CH_2\cdot C(OEt){:}NH,HCl]_2$; this on subsequent treatment with ammonia forms the corresponding diamidine, which with nitric acid forms the highly crystalline, water-soluble *phenylbis-2-amidinoethylarsine dinitrate* (II, R = H). Other crystalline salts of this diamidine, such as the *dipicrate*, *disalicylate*, and *di-3 : 5-dinitrobenzoate*, have been isolated.

The *p*-acetamidophenyl *dinitrate* (II, R = NHAc), and the *p*-chlorophenyl *dinitrate* (II, R = Cl) have also been obtained crystalline, but the *p*-aminophenyl and the *p*-ureidophenyl compounds have been isolated solely as the *tripicrate* and *dipicrate* respectively. Diphenyl-2-cyanoethylarsine also furnished the crystalline *diphenyl-2-amidinoethylarsine nitrate*, $Ph_2As[CH_2\cdot CH_2\cdot C({:}\overset{+}{N}H_2)NH_2]\overset{-}{N}O_3$.

The therapeutic activity of these arsine-amidines, which is now being examined, may prove of interest. It is known that diamidines and also certain 3-covalent arsenic derivatives have a beneficial effect on patients suffering from various forms of trypanosomiasis: whether the presence of both such groups in one molecule will stimulate, or completely suppress, such action has still to be determined. Arsenical amidines have been previously recorded only by Linsker and Bogert (*J. Amer. Chem. Soc.*, 1943, **65**, 932; 1944, **66**, 191) who prepared compounds such as *p*-$(HO)_2As\cdot C_6H_4\cdot C({:}\overset{+}{N}H_2)\cdot NH_2,\overset{-}{Cl}$ and $CN\cdot C_6H_4\cdot As{:}As\cdot C_6H_4\cdot C({:}\overset{+}{N}H_2)\cdot NH_2,\overset{-}{Cl}$, in all of which, however, the amidino-group was linked directly to the benzene ring.

Our dicyano-compounds also undergo ready alkaline hydrolysis. Thus *phenylbis-2-carboxyethylarsine* (III, R = H); the corresponding p-*chlorophenyl* compound (III, R = Cl), *diphenyl-2-carboxyethylarsine*, $Ph_2As\cdot CH_2\cdot CH_2\cdot CO_2H$, and *diphenyl-2-carboxy-*n*-propylarsine*, $Ph_2As\cdot CH_2\cdot CHMe\cdot CO_2H$, have been similarly prepared.

The acyl chlorides and esters of these acids, particularly of the dicarboxylic acids, offer a wide field of synthetic application. We are, for example, attempting to convert the acid (III, R = H) into its dicarboxylic chloride and then to cyclise this with aluminium chloride to the tricyclic diketo-arsine which would be analogous in general structure to the julolidine of von Braun, Heider, and Wyczatkowska (*Ber.*, 1918, **51**, 1215).

It is clear that the vinyl cyanide addition reaction can furnish ultimately only those alkylarsines which carry a 2-cyano- or 2-carboxy-group. We have consequently sought other reactions by which these groups can be introduced in any desired position in the alkyl radical. This can be readily achieved for the carboxylic acids, but not for the corresponding cyanides. For example, a mixture of phenyldichloroarsine (IV) and 1-bromo-3-cyanopropane, when refluxed with aqueous sodium hydroxide, yields ultimately *phenyl-3-carboxy-*n*-propylarsonic acid* (V), which when reduced with sulphur dioxide and hydrochloric acid gives *phenyl-3-carboxy-*n*-propylchloroarsine* (VI). This compound, when subjected to the original reaction, similarly furnishes *phenylbis-3-carboxy-*n*-propylarsine oxide* (VII), which is readily reduced to the tertiary

$$\begin{tikzcd}
\underset{\text{(IV.)}}{Ph\cdot AsCl_2} \arrow[r] & \underset{\text{(V.)}}{Ph\cdot AsO(OH)\cdot[CH_2]_3\cdot CO_2H} \arrow[r] & \underset{\text{(VI.)}}{Ph\cdot AsCl\cdot[CH_2]_3\cdot CO_2H} \arrow[r] & Ph\cdot AsO([CH_2]_3\cdot CO_2H)_2 \arrow[d, "\text{(VII.)}"] \\
 & & & \text{(VIII.)}\ Ph\cdot As([CH_2]_3\cdot CO_2H)_2
\end{tikzcd}$$

arsine (VIII). Similar reactions are given by 1-bromo-5-cyano-*n*-pentane. All attempts to convert the crystalline dicarboxy-arsine (VIII) into its esters or amide failed, however, and the corresponding dicyanide could not be prepared.

As an alternative attempt to prepare such cyano-arsines, phenyldimethylarsine was combined with 1-bromo-3-cyanopropane to form *phenyldimethyl-3-cyano-n-propylarsonium bromide*, $(AsPhMe_2\cdot[CH_2]_3\cdot CN)Br$. It was hoped that this compound on heating would dissociate to give methyl bromide and phenylmethyl-3-cyano-*n*-propylarsine, and the process could then be repeated with a second addition of the bromo-cyanide to give ultimately phenylbis-3-cyano-*n*-propylarsine. The above arsonium salt on heating, however, dissociated mainly into its two original components and the required tertiary cyano-arsine could not be obtained.

It is known that certain compounds containing ω-benzyloxyalkyl groups can be converted into the corresponding ω-hydroxyalkyl compounds even by the action of cold aqueous hydrobromic acid (Bennett, *J.*, 1925, **127**, 1279; Bennett and Hock, *J.*, 1927, 477). This indicated a method by which ω-hydroxyalkylarsines might be obtained and then converted through the chloro- into the ω-cyano-alkylarsines. Consequently, a mixture of phenyldichloroarsine and 2-benzyloxyethyl chloride $Ph\cdot CH_2\cdot O\cdot[CH_2]_2\cdot Cl$ was boiled in aqueous sodium hydroxide solution, and the crystalline *phenyl-2-benzyloxyethylarsonic* acid, $Ph\cdot AsO(OH)\cdot[CH_2]_2\cdot O\cdot CH_2Ph$ thus obtained. All attempts to convert this by reduction into the chloroarsine, $PhAsCl\cdot[CH_2]_2\cdot O\cdot CH_2Ph$, failed. As an alternative approach, phenyldichloroarsine was treated with 3-benzyloxypropylmagnesium chloride, and phenylbis-3-benzyloxypropylarsine, $PhAs([CH_2]_3\cdot O\cdot CH_2Ph)_2$, obtained as an oil which could not be crystallised or distilled, and was identified as its *methiodide* and other crystalline derivatives. The benzyloxy-groups in this arsine proved to be firmly attached to the alkyl groups: the arsine was unaffected by boiling concentrated hydrochloric acid, and, although boiling hydrobromic acid appeared to give the desired action, the benzyl bromide thus formed apparently gave quaternary arsonium salts, and only intractable mixtures resulted. Furthermore, the arsine when heated with anhydrous pyridine hydrochloride gave only tarry products, although Prey (*Ber.*, 1941, **74**, 1219) has repeatedly used this reagent successfully for converting methoxyl into hydroxyl groups.

EXPERIMENTAL.

Unless otherwise stated, all the following compounds were colourless.

Preparation of Arsines.—(1) Phenylarsine, $PhAsH_2$, was prepared by the method of Palmer and Adams (*J. Amer. Chem. Soc.*, 1922, **44**, 1362).

(2) p-*Aminophenylarsine*, $NH_2\cdot C_6H_4\cdot AsH_2$. The preparation of this arsine has been briefly described (D.R.-P. 251,571) but without analytical data or statement of yield. Blicke and Oneto (*J. Amer. Chem. Soc.*, 1934, **56**, 686, footnote) state that their modifications of the preparation of this arsine will be described later, but these have not apparently yet been published.

Arsanilic acid (60 g.) and zinc dust (200 g.) were placed in a 2-l. flask fitted with the reflux condenser down which a stream of nitrogen was passed throughout the experiment. A solution of mercuric chloride (8 g.) in warm water (100 c.c.) was added with shaking, and then concentrated hydrochloric acid (600 c.c.) added dropwise during 12 hours, the mixture being periodically shaken. Crystalline plates of the hydrochloride or zincichloride of the arsine separated. The mixture was set aside, with occasional shaking, for 3 days. Excess of 20% aqueous sodium hydroxide was then added, and the liberated liquid arsine extracted with ether. The extract was separated, dried, and distilled (all these operations being carried out in an inert atmosphere), and the arsine was thus obtained as a colourless liquid, b. p. 84—92°/0·3 mm.; yield, 36 g. (77%). A drop of the arsine, exposed to the air in alcoholic solution, deposited yellow crystals of 4 : 4′-diaminoarsenobenzene, which, after recrystallisation from aqueous pyridine, had m. p. 224—226° (decomp., bath preheated to 215°) (Found: C, 43·4; H, 3·2; N, 8·7. Calc. for $C_{12}H_{12}N_2As_2$: C, 43·1; H, 3·6; N, 8·4). D.R.-P. 206,057 gives m. p. 139—141°: Ehrlich and Bertheim (*Ber.*, 1911, **44**, 1262) give m. p. 260°.

(3) p-*Chlorophenylarsine*, $Cl\cdot C_6H_4\cdot AsH_2$. This was prepared essentially by the method employed for the previous arsine, but using methyl alcohol as a solvent during the reduction and omitting the final basification. It readily crystallised after distillation, b. p. 92°/14 mm.; yield, 38%. Palmer and Adams (*J. Amer. Chem. Soc.*, 1922, **44**, 1369) prepared the arsine by a similar reduction followed by steam distillation, and obtained a yield varying between 29 and 47%.

An ethereal solution of the arsine on exposure to air deposited crystals of *p*-chlorophenylarsonic acid, which were purified by dissolution in aqueous ammonia and reprecipitation with hydrochloric acid; m. p. 383—385° (decomp.) with previous loss of water (Found: C, 30·7; H, 2·4. Calc. for $C_6H_6O_3ClAs$: C, 30·4; H, 2·5%). Palmer and Adams (*loc. cit.*) give m. p. 348° (decomp.).

(4) *Diphenylarsine*, Ph_2AsH. Diphenylarsonic acid (100 g.) and zinc dust (160 g.), amalgamated by the addition of mercuric chloride (4 g.) in water (70 c.c.), were covered with ether (400 c.c.) under a nitrogen atmosphere, and concentrated hydrochloric acid (400 c.c.) was added dropwise down a reflux condenser to the shaken mixture. After 3 days the ethereal layer was forced by CO_2 pressure through a tube into a closed funnel, where it was dried, and thence into a large Claisen flask (also filled with CO_2), where it was distilled; b. p. 161—162°/20 mm., yield, 72 g. (82%). The large flask is necessary because of persistent foaming during distillation. Dehn and Wilcox (*Amer. Chem. J.*, 1906, **35**, 45), who record this arsine without preparative details or yield, give b. p. 174°/25 mm., 155°/37 mm., the latter being clearly in error.

Preparation of Dicyanides.—(1) *Phenylbis-2-cyanoethylarsine* (I, R = H). (i) A mixture of phenylarsine (13 g.) and vinyl cyanide (17 c.c., 3 mols.) was refluxed in a nitrogen atmosphere for 5 hours. The excess of vinyl cyanide was then distilled at atmospheric pressure, and the residue under reduced pressure; the *arsine* was thus isolated as a viscous liquid, b. p. 200—210°/0·1 mm. [18 g. (77%)], which ultimately solidified, and then, when recrystallised from ethanol–*cyclo*hexane, afforded needles, m. p. 59—60° (Found: C, 55·7; H, 4·9; N, 10·6; *M*, cryscopic in 0·636% ethylene dibromide solution, 261. $C_{12}H_{13}N_2As$ requires C, 55·4; H, 5·0; N, 10·8%; *M*, 260).

(ii) Crystallisation of the arsine may initially require several days: when once it occurs, however, larger preparations not involving distillation of the arsine may be carried out. For example, vinyl cyanide (80 c.c.) was added slowly to phenylarsine (42 g.) maintained at 70°, and the mixture then refluxed for 4 hours. The excess of vinyl cyanide was distilled, and the residue taken up in acetone. Cautious aqueous dilution of the acetone solution, with scratching and seeding, caused the deposition of the pure crystalline arsine; 56 g. (79%).

When the arsine was warmed with methyl iodide, a syrup resulted which could not be crystallised. When the syrup was treated with sodium picrate, both in aqueous alcohol, the *methopicrate* of the arsine was deposited as an oil which slowly crystallised, and then separated from benzene–acetone as yellow needles, m. p. 115—118·5° (Found: N, 14·0. $C_{19}H_{18}O_7N_5As$ requires N, 13·9%).

When the arsine (0·32 g.) in acetone (0·5 c.c.) was added to an agitated solution of ammonium palladochloride (0·17 g., 0·5 mol.) in aqueous alcohol (6 c.c.), *dichlorodi*(*phenylbis-2-cyanoethylarsine*)-*palladium* separated as an oil which later solidified, and then crystallised from aqueous acetone in fine brownish-yellow crystals, m. p. 189—195° (decomp.) (Found: C, 41·5; H, 3·6; N, 7·8. $C_{24}H_{26}N_4Cl_2As_2Pd$ requires C, 41·25; H, 3·7; N, 8·0%).

The *mercurichloride* was prepared by mixing alcoholic solutions of the arsine and mercuric chloride. The gum which was precipitated later crystallised, and separated from aqueous acetone in fine needles, m. p. 139—141° (Found: C, 27·25; H, 2·6; N, 5·3. $C_{12}H_{13}N_2As,HgCl_2$ requires C, 27·1; H, 2·4; N, 5·3%).

(2) p-*Aminophenylbis-2-cyanoethylarsine* (I, R = NH_2). Vinyl cyanide (35 c.c., 2·5 mols.) was added dropwise during 1 hour to *p*-aminophenylarsine (35·7 g.) maintained at 55° in a nitrogen atmosphere and occasionally shaken. The mixture was then heated at 100° for 4 hours, and the excess of vinyl cyanide then distilled. The residual *arsine* when cooled and scratched solidified (55·6 g., 96%), and when recrystallised from ethyl alcohol–ethyl acetate and then from alcohol afforded needles, m. p. 77·5—78·5° (Found: C, 52·6; H, 5·0; N, 15·2. $C_{12}H_{14}N_3As$ requires C, 52·35; H, 5·1; N, 15·3%).

When a solution of this arsine in acetic acid–acetic anhydride was refluxed for 30 minutes and then poured into water, the p-*acetamidophenyl* derivative (I, R = NHAc) was deposited as an oil which rapidly solidified; crystallisation from aqueous acetone or acetone–*cyclo*hexane afforded crystals, m. p. 117—118·5° (Found: C, 53·3; H, 5·2; N, 13·2. $C_{14}H_{16}ON_3As$ requires C, 53·0; H, 5·05; N, 13·2%).

When chloroacetyl chloride (1 c.c., 1·8 mols.) was added dropwise to an agitated suspension of the arsine (I, R = NH_2) (2 g.) in water (6 c.c.) containing sodium carbonate (0·8 g., 1 mol.), the p-*chloroacetamidophenyl* derivative (I, R = $NH\cdot CO\cdot CH_2Cl$) separated. After 1 hour, this was collected (2·3 g., 90% of the theoretical) and recrystallised first from ethyl acetate–*cyclo*hexane and then from alcohol; m. p. 96° (Found: C, 47·7; H, 4·2; N, 12·0. $C_{14}H_{15}ON_3ClAs$ requires C, 47·8; H, 4·3; N, 11·9%).

When solutions of the arsine (I, R = NH_2) (5 g.) in N-hydrochloric acid (18·2 c.c., 1 mol. acid) and of sodium cyanate (1·2 g., 1 mol.) in water (15 c.c.) were mixed, the p-*carbamidophenyl* derivative (I, R = $NH\cdot CO\cdot NH_2$) was immediately precipitated as an oil which slowly solidified [5·8 g. (100%)]. Recrystallisation from aqueous alcohol and then from alcohol alone gave needles, m. p. 142—147° (Found: C, 49·4; H, 5·1; N, 17·7. $C_{13}H_{15}ON_4As$ requires C, 49·1; H, 4·7; N, 17·6%).

When a solution of the arsine (I, R = NH_2) in hydrochloric acid was diazotised and then added to an alkaline solution of β-naphthol, the deep red 2-*hydroxynaphthalene*-1-*azo*-p-*phenylbis*-2-*cyanoethylarsine* was immediately precipitated, but required crystallisation from aqueous pyridine, aqueous acetic acid, and alcohol in turn for purification; m. p. 86—90° after heating at 65°/0·1 mm. (Found: C, 61·9; H, 4·0; N, 12·7. $C_{22}H_{19}ON_4As$ requires C, 61·7; H, 4·4; N, 12·6%).

(3) p-*Chlorophenylbis-2-cyanoethylarsine* (I, R = Cl). *p*-Chlorophenylarsine (14·6 g.) and vinyl cyanide (5 c.c.) were heated slowly to 90°, more cyanide (10 c.c.) then slowly added, and the whole finally refluxed for 2 hours. The cold product was poured into water. The *arsine* separated and rapidly crystallised; 21 g. (92%). Recrystallisation from aqueous alcohol gave needles, m. p. 71—72° (Found: C, 48·8; H, 4·1; N, 9·3. $C_{12}H_{12}N_2ClAs$ requires C, 48·9; H, 4·1; N, 9·5%).

This arsine was characterised by conversion into *dichlorodi*-(p-*chlorophenylbis-2-cyanoethylarsine*)-*palladium*, yellow needles from aqueous acetone, m. p. 160—163° (decomp.) (Found: C, 37·6; H, 3·1; N, 6·9. $C_{24}H_{24}N_4Cl_4As_2Pd$ requires C, 37·5; H, 3·1; N, 7·3%).

Diphenyl-2-cyanoethylarsine.—When diphenylarsine and vinyl cyanide (1·25 mols.) were refluxed for 1·5 hours in a nitrogen atmosphere, and the excess of vinyl cyanide then removed, the residue consisted of the liquid cyano-arsine contaminated with crystalline tetraphenyldiarsine, $Ph_2As\cdot AsPh_2$. A small portion of the crude residue was heated at 0·6 mm.; the distillate of cyano-arsine then solidified on cooling. The main bulk of crude product, dissolved in alcohol, was therefore filtered to remove the diarsine, and then, when mixed with water and seeded, gave the solid *diphenyl-2-cyanoethylarsine* (83%), which was crystallised further from *cyclo*hexane and then from aqueous alcohol, the product being collected in a chilled filter; needles, m. p. 37—39° (Found: C, 63·5; H, 4·6; N, 5·0. $C_{15}H_{14}NAs$ requires C, 63·65; H, 4·95; N, 4·95%).

The crystals of tetraphenyldiarsine were stable whilst under alcohol, but on exposure to air fused with much heat generation (cf. Borgstrom and Dewar, *J. Amer. Chem. Soc.*, 1922, **44**, 2917). For identification, their alcoholic suspension was treated with alcoholic iodine until conversion into diphenyliodoarsine was complete, and the latter then treated in turn with piperidine *N*-pentamethylenedithiocarbamate. The precipitated crystals of *N*-pentamethylene-*S*-diphenylarsinodithiourethane, when recrystallised from ethyl acetate, had m. p. 109·5—110°, unchanged by an authentic specimen prepared from diphenylchloroarsine. Blicke and Oakdale (*J. Amer. Chem. Soc.*, 1932, **54**, 2993) give m. p. 114—115°. The diarsine must have arisen in our experiments by slight atmospheric oxidation in spite of the precautions taken.

*Diphenyl-2-cyano-*n*-propylarsine*, $Ph_2As{\cdot}CH_2{\cdot}CHMe{\cdot}CN$.—A mixture of diphenylarsine (7·8 g.) and 2-cyanopropylene (3·6 c.c., 1·25 mols.) was refluxed for 4 hours in a nitrogen atmosphere. The cold viscous product was dissolved in alcohol and a small quantity of tetraphenyldiarsine removed by filtration. Aqueous dilution of the filtrate reprecipitated the oily cyano-compound, which could not be obtained solid, even when a small portion was distilled at 2 mm. (bath temperature 280—290°). The following derivatives were prepared :

(*a*) An alcoholic solution of the viscous distillate, shaken with aqueous potassium palladochloride, furnished *dichlorobis(diphenyl-2-cyano-*n*-propylarsine)palladium*, yellowish-brown crystals, m. p. 172—174° (decomp.) after crystallisation from aqueous acetone (Found : N, 3·5. $C_{32}H_{32}N_2Cl_2As_2Pd$ requires N, 3·6%).

(*b*) Another portion of the distillate was warmed with methyl iodide and then set aside for 1 day. The residual viscous syrup, dissolved in alcohol and treated with alcoholic sodium picrate, deposited *diphenylmethyl-2-cyano-*n*-propylarsonium picrate*, yellow needles from aqueous alcohol, m. p. 125—129° (Found : C, 51·6; H, 3·9; N, 10·3. $C_{23}H_{21}O_7N_4As$ requires C, 51·1; H, 3·9; N, 10·4%).

(*c*) The hydrolysis of the cyanide to the crystalline acid is described later.

Preparation of Amidino-compounds.—(1) *Phenylbis-2-amidinoethylarsine.* A solution of the dicyanide (I, R = H) (3·6 g.) in alcohol (4·5 c.c., 5·5 mols.) and chloroform (20 c.c.) was saturated with dry hydrogen chloride at 0°, and then set aside in a stoppered flask at room temperature for 4 days. Removal of the solvent at 18 mm. followed by very gentle warming gave a syrup which rapidly crystallised. This bis(iminoether) hydrochloride was highly deliquescent and was not purified. Saturated alcoholic ammonia (60 c.c.) was added with shaking, and the clear solution set aside for 5 days. The solvent was then evaporated at 18 mm. (with intermediate filtration of the precipitated ammonium chloride) ; the residual diamidine dihydrochloride formed a froth-like glass which was also very deliquescent. Consequently it was dissolved in water and treated with saturated sodium nitrate solution. The *diamidine dinitrate monohydrate* (II) separated as an oil which ultimately solidified, and was then recrystallised from alcohol–*cyclo*hexane ; needles, m. p. 156—157° (Found : C, 33·4; H, 4·8; N, 19·2. $C_{12}H_{19}N_4As,2HNO_3,H_2O$ requires C, 32·9; H, 5·25; N, 19·2%) ; 4·2 g. (69%).

The amidine nitrate was hydrolysed by boiling 15% aqueous potassium hydroxide solution, and the arsinedicarboxylic acid (III) isolated, m. p. 83—85°, unchanged by admixture with an authentic specimen (see later), showing that it was the hydrated arsine, $PhAsR_2,H_2O$, and not the anhydrous arsine oxide, $PhAsR_2O$, which might have been formed by oxidation of the tertrary arsine by nitric acid, and could not have been definitely distinguished by the analyses only.

The following salts of the diamidine were prepared by treating a concentrated aqueous solution of the crude dihydrochloride with the sodium salt of the appropriate acid. *Dipicrate*, orange-yellow crystals from aqueous acetone, m. p. 189—190° (decomp., bath preheated to 180°) (Found : N, 18·9. $C_{12}H_{19}N_4As,2C_6H_3O_7N_3$ requires N, 18·6%). *Disalicylate monohydrate*, crystals from water, m. p. 98·5—103·5° (Found : C, 53·45; H, 5·6; N, 9·2. $C_{12}H_{19}N_4As,2C_7H_6O_3,H_2O$ requires C, 53·1; H, 5·6; N, 9·5%). *Bis-3 : 5-dinitrobenzoate*, very pale yellow needles from water, m. p. 90—105° (unchanged by repeated recrystallisation) (Found : C, 43·5; H, 3·8; N, 15·6. $C_{12}H_{19}N_4As,2C_7H_4O_6N_2$ requires C, 43·4; H, 3·8; N, 15·6%).

(2) p-*Aminophenylbis-2-amidinoethylarsine* (as II, R = NH_2). Prepared precisely as the previous diamidine, except that the chloroform solution in the first stage formed two layers. The crude diamidine dihydrochloride again formed a very deliquescent sticky glass, and the only crystalline salt isolated was the *tripicrate*, yellow crystals from water, m. p. 138° (decomp.) after drying at 100°/0·1 mm. (Found : C, 36·05; H, 3·2; N, 19·4. $C_{12}H_{20}N_5As,3C_6H_3O_7N_3$ requires C, 36·15; H, 2·9; N, 19·7%).

(3) p-*Acetamidophenyl-diamidine* (as II, R = NHAc). (i) The crude diamidine dihydrochloride obtained in the previous experiment was boiled with acetic acid–acetic anhydride for 20 minutes, and then evaporated under reduced pressure. An aqueous solution of the residue when treated (*a*) with sodium nitrate solution gave the *diamidine dinitrate monohydrate*, m. p. 136° (efferv. with preliminary softening) after repeated crystallisation from alcohol–*cyclo*hexane (Found : C, 34·3; H, 5·5; N, 19·7. $C_{14}H_{22}ON_5As,2HNO_3,H_2O$ requires C, 33·9; H, 5·25; N, 19·8%) ; (*b*) with sodium 3 : 5-dinitrobenzoate gave the *diamidine bis-3 : 5-dinitrobenzoate dihydrate*, pale yellow microcrystalline powder from water, m. p. indefinite (115—155°) (Found : C, 41·4; H, 4·1; N, 15·8. $C_{14}H_{22}ON_5As,2C_7H_4O_6N_2,2H_2O$ requires C, 41·45; H, 4·2; N, 15·5%).

(ii) *p*-Acetamidophenylbis-2-cyanoethylarsine (I, R = NHAc) was converted into the diamidine dihydrochloride in the usual way and then precipitated as the dinitrate monohydrate (92% yield), identical with that formed in (i).

(4) p-*Carbamidophenyl-diamidine* (as II, R = $NH{\cdot}CO{\cdot}NH_2$). Prepared in the usual way from the dicyanide (I, R = $NH{\cdot}CO{\cdot}NH_2$), and finally precipitated as the *dipicrate monohydrate*, orange crystals from water, m. p. 118—120° (Found : C, 35·6; H, 3·5; N, 20·4. $C_{13}H_{21}ON_6As,2C_6H_3O_7N_3,H_2O$ requires C, 36·2; H, 3·5; N, 20·3%).

(5) p-*Chlorophenyl-diamidine* (as II, R = Cl). Prepared in the usual way. *Dinitrate monoalcoholate*, plates from alcohol, m. p. 103—105° (Found : C, 33·2; H, 5·2; N, 17·0. $C_{12}H_{18}N_4ClAs,2HNO_3,C_2H_6O$ requires C, 33·5; H, 5·2; N, 16·8%) ; *dipicrate monohydrate*, yellow crystals from aqueous alcohol, m. p. 202° (decomp.) (Found : C, 37·0; H, 3·1; N, 17·9. $C_{12}H_{18}N_4ClAs,2C_6H_3O_7N_3,H_2O$ requires C, 37·3; H, 3·4; N, 18·1%).

(6) *Diphenyl-2-amidinoethylarsine.* Prepared as before. *Nitrate hemihydrate*, needles from alcohol, m. p. 162—164° (decomp.) (Found : C, 48·3; H, 4·9; N, 11·5. $C_{15}H_{17}N_2As,HNO_3,\frac{1}{2}H_2O$ requires C, 48·35; H, 5·1; N, 11·3%) ; *picrate*, yellow needles from alcohol, m. p. 193—195° (decomp.) (Found : C, 48·0; H, 4·0; N, 13·15. $C_{15}H_{17}N_2As,C_6H_3O_7N_3$ requires C, 47·6; H, 3·8; N, 13·2%).

Preparation of Arsine-carboxylic Acids.—(1) *Phenylbis-2-carboxyethylarsine* (III, R = H). The dicyanide (I, R = H) (25 g.) was added to a solution of potassium hydroxide (22 g., 4 mols.) in 50% aqueous alcohol (120 c.c.), refluxed for 4 hours, and the alcohol then distilled off. The residual solution, when cooled, diluted, and acidified, deposited the above *acid* as an oil which slowly crystallised; needles from chloroform–*cyclo*hexane, m. p. 83—84·5° (Found: C, 48·6; H, 4·9. $C_{12}H_{15}O_4As$ requires C, 48·3; H, 5·0%); 24 g. (84%).

(2) p-*Chlorophenylbis-2-carboxyethylarsine* (III, R = Cl). This *acid*, similarly prepared from the dicyanide, formed needles from aqueous alcohol, m. p. 67—69° (Found: C, 43·6; H, 4·4. $C_{12}H_{14}O_4ClAs$ requires C, 43·3; H, 4·2%).

(3) *Diphenyl-2-carboxyethylarsine*, similarly prepared, formed crystals from aqueous alcohol, m. p. 104—106° (Found: C, 59·3; H, 5·1. $C_{15}H_{15}O_2As$ requires C, 59·6; H, 5·0%).

(4) *Diphenyl-2-carboxy-*n*-propylarsine*, similarly prepared from the crude syrupy cyanide, was precipitated on acidification initially as an oil which slowly crystallised; m. p. 82° after crystallisation from aqueous acetic acid and then from alcohol (Found: C, 60·5; H, 5·45. $C_{16}H_{17}O_2As$ requires C, 60·7; H, 5·4%).

3-*Cyanopropyl Derivatives*.—A mixture of phenyldichloroarsine (IV) (164 g.) and 1-bromo-3-cyanopropane (120 g., 1·1 mols.) was added slowly with stirring to 40% aqueous sodium hydroxide solution (444 c.c., 6 mols. NaOH) and then refluxed for 6 hours. The cold product was just acidified with hydrochloric acid (phenolphthalein), filtered to remove sodium halide and phenylarsine oxide, and then acidified to Congo-red. The precipitated *phenyl-*3*-carboxy-*n*-propylarsonic acid* (V) (177 g., 89%) was collected and recrystallised from water or alcohol; needles, m. p. 143—145·5° (Found: C, 44·2; H, 4·8. $C_{10}H_{13}O_4As$ requires C, 44·1; H, 4·8%).

Sulphur dioxide was passed into a solution of this arsonic acid (99 g.) in concentrated hydrochloric acid (150 c.c.) containing potassium iodide (0·1 g.) until no more solid separated. The crystalline *phenyl-*3*-carboxy-*n*-propylchloroarsine* (VI) (88 g., 88%) was collected and recrystallised from light petroleum (b. p. 100—120°); needles, m. p. 45° (Found: C, 44·1; H, 4·5; Cl, 12·9. $C_{10}H_{12}O_2ClAs$ requires C, 43·7; H, 4·4; Cl, 12·9%). The first preparation of this compound gave an oil which did not crystallise for many days; in subsequent preparations, therefore, the hydrochloric acid was seeded with the crystalline chloroarsine before reduction, which then proceeded as described above. This is important, because attempts to purify the oily chloroarsine by distillation under reduced pressure caused decomposition and loss of hydrogen chloride.

A mixture of the chloroarsine (VI) (159 g.) and 1-bromo-3-cyanopropane (94 g., 1·1 mols.) was slowly added to 40% sodium hydroxide solution (350 c.c., 6 mols. NaOH), and the preparation continued as described above. Acidification finally to Congo-red precipitated a pasty mass which was collected, and an oily impurity extracted with acetone, leaving the pure crystalline *phenylbis-*3*-carboxy-*n*-propylarsine oxide* (VII), m. p. 133—136°, unchanged by recrystallisation from benzene–methyl alcohol (Found: C, 49·5; H, 5·5. $C_{14}H_{19}O_5As$ requires C, 49·1; H, 5·7%); 124 g. (63%). A portion of the oxide, dissolved in cold concentrated hydrochloric acid, rapidly deposited deliquescent crystals of the tertiary *arsine dichloride*, m. p. 152° (Found: Cl, 17·9. $C_{14}H_{19}O_4Cl_2As$ requires Cl, 17·9%).

A suspension of the arsine oxide (VII) (60 g.) in chloroform (110 c.c.) mixed with concentrated hydrochloric acid (2 c.c.) and water (15 c.c.) was saturated with sulphur dioxide. The chloroform layer was separated and diluted with light petroleum (b. p. 80—100°), whereby *phenylbis-*3*-carboxy-*n*-propylarsine* (VIII) was precipitated, m. p. 71—74° (Found: C, 51·2; H, 6·1. $C_{14}H_{19}O_4As$ requires C, 51·5; H, 5·8%). A portion of the arsine was dissolved in aqueous ammonia and evaporated to dryness; an aqueous solution of the residue when treated with silver nitrate gave the white microcrystalline *disilver* salt (Found: C, 31·6; H, 3·3. $C_{14}H_{17}O_4AsAg_2$ requires C, 31·2; H, 3·2%).

When a mixture of the dichloroarsine (IV) (23·1 g.) and 1-bromo-5-cyanopentane, b. p. 132°/13 mm. (20 g.), was added to 40% sodium hydroxide (62 c.c.), and the experiment continued as above, *phenyl-*5*-carboxy-*n*-pentanearsonic acid* was obtained, colourless crystals from diethyl carbonate, m. p. 101·5—103° (Found: C, 48·2; H, 6·0. $C_{12}H_{17}O_4As$ requires C, 48·0; H, 5·7%).

Quaternary Arsonium Bromides.—A mixture of phenyldimethylarsine (51·9 g.) and 1-bromo-3-cyanopropane (42·2 g., 1 mol.) was heated at 120° for 4 hours in a nitrogen atmosphere. The cold solid product, recrystallised from alcohol, gave *phenyldimethyl-*3*-cyanopropylarsonium bromide*, m. p. 170° (Found: C, 43·6; H, 5·2; N, 4·2. $C_{12}H_{17}NBrAs$ requires C, 43·6; H, 5·2; N, 4·2%); 72 g. (77%). An aqueous solution of the bromide, treated with sodium picrate, gave the *arsonium picrate*, orange-yellow plates from aqueous alcohol, m. p. 119° (Found: N, 11·8. $C_{18}H_{19}O_7N_4As$ requires N, 11·7%).

The arsonium bromide (72 g.) was heated under reduced pressure and three arbitrary fractions collected: (*a*) b. p. rising to 139°/20 mm., 16 g.; (*b*) b. p. 139—150°/20 mm. 16 g.; (*c*) b. p. rising to 130°/0·2 mm., 16 g. Fraction (*a*) when set aside very slowly deposited the original crystalline bromide in small amount. Fraction (*b*) also deposited this bromide (5 g.), but also contained phenyldimethylarsine, since with methyl iodide it readily gave phenyltrimethylarsonium iodide, colourless crystals from alcohol–ether, m. p. 248° unaffected by admixture with an authentic specimen (Burrows and Turner, *J.*, 1920, **117**, 1378, give m. p. 250°), and this iodide in turn furnished the arsonium picrate, m. p. 144° (Steinkopf and Schwen, *Ber.*, 1921, **54**, 1448, give m. p. 145°). Fraction (*c*) on refractionation gave 3 fractions: (i) b. p. 60—71°/1·2 mm. (2·4 g.), which formed an almost solid mass of the original bromide; (ii) b. p. 70—72°/1·5 mm. (3·3 g.); (iii) b. p. 72°/1·5 mm.—120°/0·1 mm. (6·1 g.). Fractions (ii) and (iii) also contained much arsonium bromide, but remaind liquid. It was clear therefore that the arsonium bromide on heating was dissociating mainly to phenyldimethylarsine and 1-bromo-3-cyanopropane, and that these products were recombining in the distilled material.

A mixture of phenyldimethylarsine (9·7 g.) and 1-bromo-5-cyano-*n*-pentane (9·4 g., 1 mol.), when heated under a CO_2-atmosphere in a sealed tube at 100° for 60 hours, first separated into two layers and ultimately again became homogeneous. The cold viscous product when scratched formed a deliquescent crystalline mass of phenyldimethyl-5-cyano-*n*-pentylarsonium bromide, which was identified as the *picrate*, yellow needles from aqueous alcohol, m. p. 58—59° (Found: N, 10·9. $C_{20}H_{23}O_7N_4As$ requires N, 11·1%). When the anhydrous bromide was heated, however, only phenyldimethylarsine was detected in the distillate, and this bromide also was therefore dissociating into its original components.

Both the above arsonium bromides were converted to the corresponding arsonium hydroxides, but these when heated gave no products that could be readily identified.

Attempts to condense either of the above bromoalkyl cyanides with the arsenic halides or with phenyldichloroarsine by the action of sodium in ether gave none of the desired tertiary cyano-arsines.

Benzyloxy-derivatives.—A mixture of phenyldichloroarsine (143 g.) and 2-benzyloxyethyl chloride (120 g., 1·1 mols.) was run slowly with stirring into 40% aqueous sodium hydroxide solution (420 c.c., 6 mols. NaOH) and the whole refluxed for 7 hours. The cold product formed two layers, the lower containing much crystalline sodium salt of the required arsonic acid (see later). Water was added until this salt dissolved, the mixture was then twice extracted with ether, and the aqueous layer then treated with concentrated hydrochloric acid until cloudy, filtered to remove sodium chloride, and then just acidified with more acid. Crystalline *phenyl-2-benzyloxyethylarsonic acid* (168 g., 82%) separated, and was collected and recrystallised from dilute methyl alcohol, m. p. 109° (Found: C, 56·6; H, 5·2. $C_{15}H_{17}O_3As$ requires C, 56·25; H, 5·3%). A small portion of the sodium salt, removed for identification and recrystallised from acetone containing a trace of water, gave the *trihydrate*, plates, m. p. 77°, resolidifying and then remelting at 248° (decomp.) (Found: C, 45·9; H, 6·1. $C_{15}H_{16}O_3AsNa,3H_2O$ requires C, 45·5; H, 5·6%); drying at 120°/20 mm. gave the hygroscopic anhydrous *salt*, m. p. 249° (decomp.) (Found: C, 53·0; H, 4·8. $C_{15}H_{16}O_3AsNa$ requires, C, 52·6; H, 4·7%). The addition of concentrated hydrochloric acid to the arsonic acid or its sodium salt gave an oil which crystallised on scratching, and when recrystallised from benzene or ethyl carbonate gave the *arsonic acid hydrochloride*, $RR'As(OH)_2Cl$, plates, m. p. 94° (Found: C, 50·65; H, 5·1; Cl, 9·55. $C_{15}H_{18}O_3ClAs$ requires C, 50·5; H, 5·05; Cl, 10·0%). The prolonged action of sulphur dioxide on the arsonic acid in cold concentrated hydrochloric acid gave only the above unchanged arsonic acid hydrochloride; at 100° an oil was formed which could not be crystallised or distilled, and yielded no crystalline derivatives.

A Grignard reagent was prepared by the action of 3-benzyloxypropyl chloride (40 g., 2 mols.) in ether (120 c.c.) on specially activated magnesium (5·53 g.) under a nitrogen atmosphere, the reaction being initiated by the addition of ethyl bromide (0·2 c.c.) and bromine (1 drop) and local warming. The product was refluxed for 1 hour to complete the formation of the reagent, and then cooled in ice and stirred whilst a solution of phenyldichloroarsine (21·7 g., 0·9 mol.) in light petroleum (b. p. 40—60°, 100 c.c.) was slowly added. After a further 2 hours' refluxing, the white cloudy mixture was cooled and hydrolysed by the addition of ammonium chloride (25 g.) dissolved in water (150 c.c.). The upper layer was then separated and dried, and the organic solvents were removed. The residual oily colourless arsine (40 g.) could not be distilled. It was identified by the formation of the following derivatives: (i) An aqueous solution of the arsine, treated with aqueous ammonium chloropalladite, deposited an oil which ultimately solidified and when recrystallised from alcohol afforded golden-yellow plates of *dichlorobis(phenylbis-3-benzyloxypropylarsine)palladium*, m. p. 69° (Found: C, 57·9; H, 5·7. $C_{52}H_{62}O_4Cl_2As_2Pd$ requires C, 57·9; H, 5·75%). (ii) The arsine reacted with warm methyl iodide to form an oil which crystallised when stirred with ether; reprecipitation from acetone solution by the addition of ether gave *phenylmethylbis-3-benzyloxypropylarsonium iodide*, m. p. 67—69·5° (Found: C, 55·1; H, 6·1; I, 21·8. $C_{27}H_{34}O_2AsI$ requires C, 54·7; H, 5·7; I, 21·45%). (iii) The arsine combined with hot benzyl bromide to give a viscous oil, which, treated in alcoholic solution with chloroplatinic acid, gave *phenylbenzylbis-3-benzyloxypropylarsonium chloroplatinate*, pinkish-yellow crystals from alcohol–acetone, m. p. 119·5—121° (Found: C, 52·9; H, 5·15. $C_{66}H_{76}O_4Cl_6As_2Pt$ requires C, 52·9; H, 5·1%). The almost quantitative yield of the last two products indicated the purity of the tertiary arsine. No crystalline oxide or oxide-salts of the arsine could be isolated. The arsine was debenzylated by hydrobromic acid (constant b. p.) at 90°, or by 50% hydrogen bromide in acetic acid at room temperature, but only one equivalent of benzyl bromide could be isolated, the second apparently forming a quaternary salt with the arsine.

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