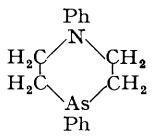
581. *The Preparation and Properties of Hexahydro-1 : 4-diphenyl-1 : 4-azaphosphine.*

By Frederick G. Mann and Ian T. Millar.

Phenylphosphinebis(magnesium bromide) reacts with di-(2-bromoethyl)-aniline to form the azaphosphine named in the title. The properties of the azaphosphine have been studied in detail, because it forms a eutropic series with 1 : 4-diphenylpiperazine and hexahydro-1 : 4-diphenyl-1 : 4-azarsine. Although many of the properties of the azaphosphine are similar to those of the azarsine, others are not intermediate between those of the piperazine and those of the azarsine.

It has been shown by Beeby and Mann (*J.*, 1951, 886) that phenylarsinebis(magnesium bromide), $Ph{\cdot}As(MgBr)_2$, reacts with di-(2-bromoethyl)aniline to form hexahydro-1 : 4-diphenyl-1 : 4-azarsine (I), and we have now investigated the analogous reaction with phenylphosphinebis(magnesium bromide), $Ph{\cdot}P(MgBr)_2$. This reagent was first prepared by Job and Dusollier (*Compt. rend.*, 1927, **184**, 54) and later by Lecoq (*Bull. Soc. chim. Belge*, 1933, **42**, 199), utilising the interaction of phenylphosphine, $Ph{\cdot}PH_2$, and ethylmagnesium bromide. We find that the preparation of this reagent, like that of its arsenic analogue (Beeby, Cookson, and Mann, *J.*, 1950, 1920), is greatly improved by the use of phenylmagnesium bromide : this advantage would of course be nullified in those (comparatively rare) cases in which the traces of diphenyl, which accompany the phenylmagnesium bromide, interfere with the ready isolation of the product obtained subsequently by the use of the phenylphosphinebis(magnesium bromide).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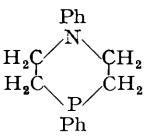
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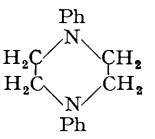
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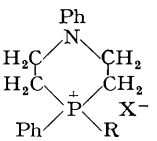
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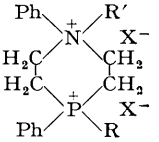

(V)

The compound $Ph{\cdot}P(MgBr)_2$ reacts with di-(2-bromoethyl)aniline to form hexahydro-1 : 4-diphenyl-1 : 4-azaphosphine (II), a colourless crystalline compound of m. p. 89—90°, which undergoes no appreciable oxidation on exposure to dry air at room temperature. It acts as a weak base, forming a dihydrochloride but an unstable monohydriodide and a monopicrate; the tertiary phosphine group permits the ready formation of co-ordination compounds, such as dibromobis(hexahydro-1 : 4-diphenyl-1 : 4-azaphosphine)palladium, $(C_{16}H_{18}NP)_2PdBr_2$.

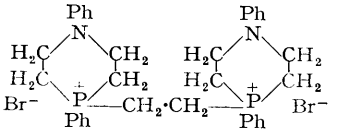
It is of great interest to compare the properties of our new azaphosphine (II) with those of the azarsine (I) and of 1 : 4-diphenylpiperazine (III), since the three compounds form a eutropic series. The piperazine (III) also forms a dihydrochloride but when heated with methyl iodide even at 100° forms only a monomethiodide (Dunlop and Jones, *J.*, 1909, **95**, 419); our own attempts to form diquaternary salts of the piperazine have at present failed. Beeby and Mann (*loc. cit.*) have shown that the azarsine (I) gives only monoquaternary salts, in which quaternisation occurs on the tertiary arsine group; the tertiary amine group in these salts is, however, not entirely inactivated, since it will give salts with strong acids such as hydrobromic acid.

Our investigation shows clearly, however, that in certain respects the azaphosphine (II) does not lie intermediate in properties between the azarsine (I) and the diamine (III). It combines with methyl bromide to form a monomethobromide (IV; R = Me, X = Br) and with methanolic methyl bromide at 100° to form a monomethobromide monohydrobromide (V; R = Me, R′ = H, X = Br); similarly, an excess of ethyl bromide even at 100° yields only a monoethobromide (IV; R = Et, X = Br), and again the reaction if carried out in ethanol gives the monoethobromide monohydrobromide (V; R = Et, R′ = H, X = Br). There is strong evidence, cited below, that when monoquaternisation

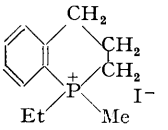
occurs in this way, it is the tertiary phosphine, and not the amine group, which has undergone reaction. In this respect the azaphosphine (II) resembles the azarsine (I).

When, however, the azaphosphine (II) is treated with cold methyl iodide, a vigorous reaction occurs with the formation of the crystalline monomethiodide (IV; R = Me, X = I), but when either the azaphosphine or its monomethiodide is boiled with methyl iodide under reflux, the dimethiodide (V; R = R′ = Me, X = I) is formed; this salt is unstable and when gently heated reverts to the monomethiodide. Similarly the azaphosphine when heated with an excess of methyl toluene-*p*-sulphonate gives a very deliquescent product which is evidently the dimethotoluene-*p*-sulphonate, since when treated with sodium picrate it gives the crystalline dimethopicrate (V; R = R′ = Me, X = $C_6H_2O_7N_3$). It appears therefore that, of the three compounds (I), (II), and (III), only the azaphosphine (II) will form diquaternary salts.

In view of this property of the azaphosphine, and the fact that ethylene dibromide will readily form a cyclic diquaternary salt with a suitable ditertiary arsine or with 1 : 4-dimethylpiperazine (Glauert and Mann, *J.*, 1950, 682; Mann and Mukherjee, *J.*, 1949, 2298), we have attempted to combine the azaphosphine with the dibromide in this way. In spite of the use of a variety of conditions, however, we have isolated only *s*-ethylenebis(hexahydro-1 : 4-diphenyl-1 : 4-azaphosphonium) dibromide (VI), a compound in which the tertiary nitrogen atoms have become markedly inert, for no further quaternisation with methyl iodide could be obtained. The formation of (VI) is, of course, precisely similar to the behaviour of the azarsine (I) under similar conditions.



(VI)



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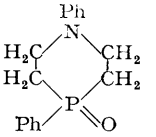
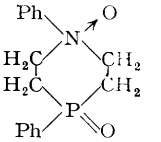


(VIII)



(IX)

The monoquaternary salts of the azaphosphine (II) are therefore closely similar to those of the arsine (I), for which very strong chemical and spectroscopic evidence was adduced to show that quaternisation occurred on the arsine group. Dr. N. Sheppard has investigated the monomethiodide of the azaphosphine and reports: " It was required to attempt to decide whether the monomethiodide of the azaphosphine had the structure (IV; R = Me, X = I) or whether the methyl group had united with the tertiary amine group to form a quaternary ammonium salt. Chemical evidence indicated that this compound had the former structure, and it was hence decided to compare its spectrum in the region of P–C stretching vibration frequencies with that of an authentic quaternary phosphonium salt having similar groups attached to the phosphorus atom: for this purpose, 1-ethyl-1 : 2 : 3 : 4-tetrahydro-1-methylphosphinolinium iodide (VII) (Beeby and Mann, *J.*, 1951, 411) was chosen. The spectra of both compounds were therefore obtained from 700 to 550 cm.$^{-1}$, a Hilger D209 infra-red spectrometer with a potassium bromide prism being used and the crystalline compounds incorporated as Nujol mulls.

" It is known from infra-red and Raman spectroscopic studies that P–C stretching modes of vibration have frequencies in the range 775—625 cm.$^{-1}$ [*e.g.*, trimethylphosphine, 708 and 653 cm.$^{-1}$ (Rosenbaum, Rubin, and Sandberg, *J. Chem. Phys.*, 1940, **8**, 366); trimethylphosphine oxide, 750 and 671 cm.$^{-1}$ (Daasch and Smith, *ibid.*, 1951, **19**, 22)]. The higher frequencies of this type are liable to be badly overlaid by absorption bands due to CH_2 groups and to the aromatic rings present in both the compounds under investigation, but it was considered that there was a reasonable chance that the lower frequency P–C vibration might give comparable absorption bands in the region of 700—600 cm.$^{-1}$ for the two substances, if they were of closely related structure.

" The spectrum of (VII) in the region of 700—550 cm.$^{-1}$ consisted of a single band of medium strength at 640 cm.$^{-1}$, whereas that of the methiodide (IV; R = Me, X = I) consisted of two bands at 640 (medium) and 690 cm.$^{-1}$ (strong). The strong 690-cm.$^{-1}$ absorption band is very probably a frequency originating in the monosubstituted benzene rings of the methiodide (Sheppard, *J. Inst. Petroleum*, 1951, **37**, 95), and it seems reasonable

to assign tentatively the 640-cm.$^{-1}$ band, common to both spectra, as being the corresponding P–C stretching frequencies of the two molecules. Although it would be necessary to investigate the spectra of a much wider range of quaternary phosphorus derivatives before such an assignment could be taken as entirely reliable, it appears probable that the new methiodide is therefore a quaternary phosphonium salt, *i.e.*, that it has the structure (IV; R = Me, X = I)."

The oxidation of the phosphine (II) also gives evidence for the greater reactivity of the phosphine compared with the amine group. When an acetone solution of the phosphine was treated either with a 3% solution of hydrogen peroxide at room temperature for 24 hours, or with a 30% solution at 70—80° for 8 hours, the colourless crystalline monoxide, m. p. 143—144°, was obtained. The evidence that this compound is the phosphine oxide (VIII), and not the amine oxide, is as follows: (*a*) It can also be obtained by the oxidation of the azaphosphine with ethanolic chloramine-T, a reagent which is known to convert tertiary phosphines readily into their oxides but is apparently without action on tertiary amines (Mann and Pope, *J.*, 1922, **121**, 1052; Chaplin and Mann, *J.*, 1937, 527). (*b*) Dr. R. N. Haszeldine, who has investigated the infra-red absorption spectrum of the oxide, finds that it shows a moderately strong band at 7·87 μ, which can be assigned to the P:O linkage. Here again the behaviour of the azaphosphine (II) is analogous to that of the azarsine (I).

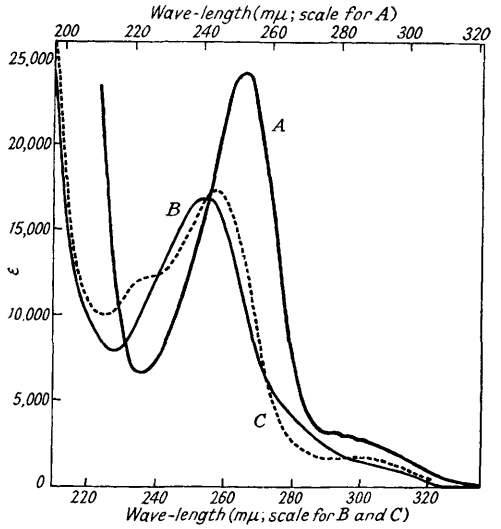
When, however, a solution of the azaphosphine in acetic acid was similarly treated with 30% hydrogen peroxide at 70—80° for 7 hours, stable colourless crystals were ultimately obtained, the composition of which, after they had been recrystallised from ethanol and then dried at 50°/0·5 mm., indicated that the compound was the monohydrate of the dioxide (IX) combined with one molecular equivalent of hydrogen peroxide, *i.e.*, the compound had the composition $C_{16}H_{18}O_2NP,H_2O_2,H_2O$. It is noteworthy that Bennett and Glynn (*J.*, 1950, 211) showed that 1 : 4-diphenylpiperazine (III) when similarly oxidised formed a dihydrated dioxide which also crystallised with 1 mol. of hydrogen peroxide, *i.e.*, it had the composition $C_{16}H_{18}O_2N_2,H_2O_2,2H_2O$. They concluded that the hydrogen peroxide unit formed a hydrogen-bonded bridge between the two oxygen atoms of the dioxide, which, they considered, must therefore have the *cis*-configuration. Our compound, like that of Bennett and Glynn, gave an immediate blue colour when treated in aqueous solution with potassium iodide–starch.

It has been shown by Beeby and Mann (*loc. cit.*) that, when the azarsine (I) is boiled with hydriodic acid, the phenyl group attached to the arsenic atom is replaced by an iodine atom, the heterocyclic ring remaining unaffected; this reaction is shown by several types of heterocyclic tertiary arsines having an aryl group linked to the arsenic atom (Lyon, Mann, and Cookson, *J.*, 1947, 662; Beeby, Cookson, and Mann, *J.*, 1950, 1917; Beeby, Mann, and Turner, *J.*, 1950, 1923). No such fission of the phenyl group occurs in the azaphosphine (II), which, even when heated for 9 hours under reflux with hydriodic acid, gave only the hydriodide of the unchanged phosphine.

The azaphosphine (II) readily combines with iodine in benzene to give a tri-iodide, which forms chocolate-brown crystals, m. p. 255—257°, and can be recrystallised unchanged from ethanol or benzene. This compound is insoluble in boiling water and even in boiling sodium hydrogen carbonate solution; its aqueous ethanolic solution contains no ionic iodine. It is immediately converted by sodium hydroxide into the azaphosphine oxide (VIII), and by cold sulphurous acid into the lemon-yellow crystalline hydriodide of the azaphosphine oxide; this salt is hydrolysed by cold aqueous sodium hydrogen carbonate to the oxide (VIII), which in turn when treated with hydriodic acid regenerates the yellow hydriodide. The precise structure of this hydriodide remains uncertain; the hydriodic acid may have neutralised the tertiary amine group of the phosphine oxide, or (more probably) have united with the P:O bond of the latter to give (IV; R = OH, X = I). It is clear from these reactions, however, that two of the iodine atoms of the original tri-iodide must be linked to the phosphorus atom; the position and mode of linkage of the third iodine atom also remain uncertain.

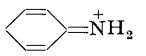
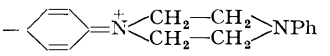
The ultra-violet absorption spectra of the piperazine (III) and of the azaphosphine and azarsine are shown in the Figure. Apart from the strong principal band due to the phenyl

groups which all the spectra show, it is of interest to note that the piperazine (III) shows two small secondary bands at 278—280 ($\varepsilon_{max.}$ 3000) and 282—284 mμ ($\varepsilon_{max.}$ 2990); the azaphosphine shows a slight inflexion at 310 mμ ($\varepsilon_{max.}$ 1000), whereas the azarsine shows a marked secondary band at 295—302 mμ ($\varepsilon_{max.}$ 1750). Aniline has a secondary band at 280 mμ ($\varepsilon_{max.}$ 1430) (Doub and Vandenbelt, *J. Amer. Chem. Soc.*, 1947, **69**, 2714), which has been attributed to polar forms such as (X) and analogous canonical forms. It is possible that the secondary bands in 1 : 4-diphenylpiperazine are due to similar polar forms such as (XI) (where charge separation can occur at one or both of the nitrogen atoms), and that the broader inflexions at greater wave-length shown by the azaphosphine and (more strongly) by the azarsine arise from a similar cause. This point could probably be determined if stable salts of the piperazine with two equivalents of acid, or if



Absorption spectra of:
A, 1 : 4-*Diphenylpiperazine* (mμ *scale at top of Figure*).
B, *Hexahydro*-1 : 4-*diphenyl*-1 : 4-*azaphosphine* (mμ *scale at base of Figure*).
C, *Hexahydro*-1 : 4-*diphenyl*-1 : 4-*azarsine* (mμ *scale at base of Figure*).

suitable diquaternary salts of the piperazine or the azarsine were available, since in such derivatives charge separation of the type shown in (XI) would not be possible. We find

(X)   (XI)

that 1 : 4-diphenylpiperazine dihydrochloride is too strongly dissociated in dilute solution to give reliable results, and diquaternary salts of the piperazine and the azarsine are at present unknown. In the case of the azaphosphine, the above inflexion is already so slight that investigation of its diquaternary salts for this purpose would probably prove fruitless.

Tests carried out in the Smith, Kline, and French Laboratories, Philadelphia, U.S.A., under the direction of Dr. Glenn E. Ullyot, show that the azaphosphine (II), when administered orally to rats in doses of 50, 100, and 150 mg./kg., failed to afford protection against histamine-induced bronchospasm.

We are now investigating the application of phenylphosphinebis(magnesium bromide) for the synthesis of other types of heterocyclic derivatives of phosphorus.

Experimental

The azaphosphine and all its derivatives, unless otherwise stated, were colourless.

Phenylphosphine.—Reduction of phenyldichlorophosphine to phenylphosphine in 25% yield by lithium aluminium hydride has been described by Horvat and Furst (*J. Amer. Chem. Soc.*, 1952, **74**, 562). We find Michaelis and Kohler's original method (*Ber.*, 1877, **10**, 807), in which the dichlorophosphine is treated with ethanol, to be more satisfactory. This method apparently entails three distinct reactions. First, the dichlorophosphine is hydrolysed to phenylphosphonous acid: $Ph{\cdot}PCl_2 + EtOH = Ph{\cdot}P(OH)_2 + 2EtCl$. Secondly, the acid

when heated to *ca.* 250° undergoes thermal decomposition, forming phenylphosphonic acid and phenylphosphine: $3Ph{\cdot}P(OH)_2 = 2Ph{\cdot}PO_3H_2 + Ph{\cdot}PH_2$. Thirdly, the phosphonic acid on stronger heating decomposes to phosphoric acid and benzene: $Ph{\cdot}PO_3H_2 = HPO_3 + C_6H_6$. The second reaction is, however, strongly exothermic; consequently if suitable quantities are employed, it proceeds, when once started, spontaneously but quietly; the use of larger quantities, however, may lead to an uncontrollable reaction, whereas smaller quantities require external heating for distillation at this stage, with a considerable fall in yield. We find the following modification of Michaelis and Kohler's method probably represents optimum conditions.

Phenyldichlorophosphine (250 c.c.) was run dropwise into ethanol (600 c.c.); ethyl chloride was freely evolved, and external cooling was applied when necessary to the mixture. A stream of nitrogen was then led through the flask, and the excess of ethanol was removed under reduced pressure. The residual solution (which partly crystallised if allowed to cool) was transferred to a smaller distilling flask fitted with an inlet tube for nitrogen, and having a wide outlet tube, which was connected through an efficient condenser to a receiver; the latter in turn had an outlet tube, so that uncondensed vapour could be passed through permanganate–acetone solution. The whole preparation was performed in a vigorous draught. A slow stream of nitrogen was then led through the apparatus, and the solution was gently heated over a gauze; as soon as the vigorous reaction started, the flame was withdrawn. The phenylphosphine distilled rapidly, with only slight foaming; if necessary, the upper part of the flask was occasionally cooled to moderate the distillation. (When this reaction subsided, the flask was again heated and a second fraction, consisting mainly of benzene with very little phosphine and a high-boiling component, was collected; it was found advisable, however, to ignore this fraction, because the low phosphine content did not justify its laborious refractionation.) The first fraction was washed with water, dried ($CaCl_2$), and fractionally distilled in nitrogen. The early runnings of ethanol and benzene were followed by the phenylphosphine, b. p. 157—159° (yield: 36 g., 54%). A very small residue remained in the distillation flask.

The phosphine, which is rapidly oxidised in air, was sealed in weighed ampoules. In the following preparation and use of the Grignard reagent, the quantities of reagents were adjusted to that of the phosphine to be used, so that exposure of the latter to the air was reduced to a minimum. The phosphine when in benzene solution is much less readily oxidised than when pure.

Hexahydro-1 : 4-*diphenyl*-1 : 4-*azaphosphine* (II).—A Grignard reagent was prepared from bromobenzene (13·7 g., 2·3 mols.), magnesium (2·22 g., 2·4 atoms), and ether (90 c.c.) in a flask fitted with a stirrer, reflux condenser, dropping funnel, and an inlet tube through which nitrogen was passed throughout the experiment, the ethereal solution being finally boiled under reflux for 30 minutes to ensure completion of the preparation. The solution was then cooled and vigorously stirred, whilst a solution of phenylphosphine (4·2 g., 1 mol.) in benzene (40 c.c.) was run in during 15 minutes. The mixture was then boiled under reflux with stirring for 2·5 hours, benzene (30 c.c.) being later added to replace the ether carried out in the nitrogen stream. The solution of phenylphosphinebis(magnesium bromide) was cooled to 30° and di-2′-bromoethylaniline (9·4 g., 0·8 mol.) in benzene (30 c.c.) added with vigorous stirring during 30 minutes, the complete mixture being then boiled as before for 2 hours. It was finally cooled in ice-water and hydrolysed with aqueous ammonium chloride solution. The organic layer was separated, the aqueous layer (which tended to become semi-solid) was repeatedly extracted with benzene, and the united organic solutions, without filtration or drying, were concentrated under reduced pressure in nitrogen. The residue, which solidified considerably on cooling, was recrystallised from ethanol and afforded the *azaphosphine* (II), m. p. 89—90° (Found: C, 75·0; H, 7·1; N, 5·3%; *M*, ebullioscopic in 0·679% ethanol solution, 241. $C_{16}H_{18}NP$ requires C, 75·3; H, 7·1; N, 5·5%; *M*, 255); the yield was 4·3 g. (55%). The azaphosphine is slightly hygroscopic, and was dried at 60°/0·5 mm. for 4 hours before analysis.

The azaphosphine when dissolved in a minimum of cold concentrated hydrochloric acid rapidly deposited a heavily hydrated crystalline *dihydrochloride* which when dried in a vacuum over phosphoric anhydride gave the anhydrous salt, m. p. 165—166° (Found: C, 59·0; H, 6·5; N, 4·5. $C_{16}H_{18}NP,2HCl$ requires C, 58·5; H, 6·3; N, 4·3%). The azaphosphine also gave a crystalline *monohydriodide*, m. p. 190—191°, which became brown on exposure to light (Found: C, 49·9; H, 5·3; N, 3·5. $C_{16}H_{18}NP,HI$ requires C, 50·1; H, 5·0; N, 3·65%), and a *monopicrate*, which separated as orange crystals, m. p. 131—132° (preliminary softening), when hot ethanolic solutions of the phosphine and of an excess of picric acid were mixed and cooled (Found: C, 54·2; H, 4·5; N, 11·4. $C_{16}H_{18}NP,C_6H_3O_7N_3$ requires C, 54·5; H, 4·4; N, 11·6%).

Dibromobis(*hexahydro*-1 : 4-*diphenyl*-1 : 4-*azaphosphine*)*palladium*. When mixed ethanolic

solutions of the phosphine and of potassium palladobromide were boiled, this *compound* was precipitated and, when collected, washed with ethanol, and recrystallised from ethanolic benzene (1 : 1), gave orange-yellow crystals, m. p. 184—185° (Found: C, 49·4; H, 4·9; N, 3·3. $C_{32}H_{36}N_2Br_2P_2Pd$ requires C, 49·45; H, 4·7; N, 3·6%).

Quaternary salts. A solution of the azaphosphine in an excess of cold methyl bromide, when set aside in a sealed tube for 24 hours, deposited the crystalline *monomethobromide* (IV; R = Me, X = Br), which had m. p. 152° after being collected, washed with light petroleum (b. p. 60—80°), and dried (Found: C, 58·1; H, 6·2; N, 3·9. $C_{17}H_{21}NBrP$ requires C, 58·3; H, 6·1; N, 4·0%). No satisfactory solvent for recrystallisation could be found.

The *monomethobromide hydrobromide* separated when a solution of the azaphosphine (0·2 g.) in methyl bromide (2 c.c.) and methanol (2 c.c.) was heated in nitrogen in a sealed tube at 100° for 6 hours and then cooled. The salt, after recrystallisation from methanol, had m. p. 279—283° (decomp.) (Found: C, 47·5; H, 5·5; N, 3.3. $C_{17}H_{21}NBrP,HBr$ requires C, 47·35; H, 5·15; N, 3·25%).

Both these salts, when treated in aqueous solution with sodium picrate, deposited the *monomethopicrate* (IV; R = Me, X = $C_6H_2O_7N_3$), which crystallised from water in orange-red crystals, m. p. 118° (Found: C, 55·35; H, 5·1; N, 11·1. $C_{23}H_{23}O_7N_4P$ requires C, 55·4; H, 4·65; N, 11·2%).

A solution of the azaphosphine in an excess of cold ethyl bromide, when either set aside at room temperature for 3 days or heated in a sealed tube at 100° for 6 hours, deposited crystals of the *monoethobromide* (IV; R = Et, X = Br), m. p. 175—176° (Found: C, 59·2; H, 6·6; N, 4·1. $C_{18}H_{23}NBrP$ requires C, 59·3; H, 6·4; N, 3·85%). This salt also could not be recrystallised.

The *monoethobromide hydrobromide* was prepared (*a*) by heating the azaphosphine in ethanolic ethyl bromide at 100° for 6 hours or (*b*) by the addition of hydrobromic acid to a cold concentrated aqueous solution of the monoethobromide. It was recrystallised from methanol or hydrobromic acid, and had m. p. 278—284° (decomp.) (Found: C, 48·6; H, 5·4; N, 3·3; Br, 36·7. $C_{18}H_{23}NBrP,HBr$ requires C, 48·55; H, 5·4; N, 3·15. Br, 35·9%). When this salt in aqueous solution was treated with aqueous sodium hydroxide (1 mol.), the monoethobromide, m. p. 174° (alone and mixed), was recovered.

The azaphosphine dissolved in methyl iodide with considerable evolution of heat: the residue, when recrystallised from acetone–light petroleum (b. p. 60—80°) gave the *monomethiodide* (IV; R = Me, X = I), m. p. 155—156° (Found: C, 51·1; H, 5·1; N, 3·7. $C_{17}H_{21}NIP$ requires C, 51·4; H, 5·3; N, 3·5%). A methanolic solution treated with sodium picrate gave the above monomethopicrate, m. p. 118° (alone and mixed).

The azaphosphine or its monomethiodide, when boiled under reflux with methyl iodide, readily deposited the *dimethiodide* (V; R = R′ = Me, X = I), m. p. 118° after recrystallisation from methanolic acetone (Found: C, 39·6; H, 4·7; N, 2·7. $C_{18}H_{24}NI_2P$ requires C, 40·1; H, 4·5; N, 2·6%). This salt was highly hygroscopic, but drying in a vacuum even at very moderate temperatures caused loss of methyl iodide.

When aqueous solutions of this salt and of sodium picrate were mixed, the *dimethopicrate* was precipitated, and when collected, washed with water, and recrystallised from dioxan formed yellow crystals, m. p. 172—174° (Found: C, 48·7; H, 3·85; N, 13·1. $C_{30}H_{28}O_{14}N_7P$ requires C, 48·6; H, 3·8; N, 13·2%).

A mixture of the azaphosphine and an excess of methyl toluene-*p*-sulphonate was heated at 100° for 6 hours in a sealed tube, and the cold syrupy product, when thoroughly washed with ether, left a residue of the crystalline dimethotoluene-*p*-sulphonate. This was highly deliquescent and could not be recrystallised; it was therefore characterised by conversion into the above dimethopicrate, m. p. 172—174° (alone and mixed).

s-*Ethylenebis*(*hexahydro*-1 : 4-*diphenyl*-1 : 4-*azaphosphonium*) *Dibromide* (VI).—A mixture of the azaphosphine (0·51 g.) and pure dry ethylene dibromide (0·38 g., 1 mol.) was heated under nitrogen in a sealed tube at 130—135° for 7 hours. Unchanged ethylene dibromide was then removed at 100°/14 mm., and the greyish-brown residue, m. p. 240—245°, extracted with boiling ethanol (15 c.c.) to remove coloured impurities. The almost white residue was then thrice recrystallised from more ethanol, and the *dibromide* (VI) obtained as the crystalline *monoethanolate*, m. p. 273—274° (Found: C, 57·85; H, 6·0; N, 4·0. $C_{34}H_{40}N_2Br_2P_2,C_2H_6O$ requires C, 58·05; H, 6·2; N, 3·8%).

Other experiments in which the azaphosphine was heated with ethylene dibromide (1·1 mols.) at 150—160° for 6 hours, and with the dibromide (1·5 mols.) at 135—145° for 6 hours, gave the same product.

The dibromide (VI) was recovered unchanged after it had been boiled under reflux with an excess of methyl iodide for 30 minutes. When treated in aqueous solution with aqueous sodium picrate, the dibromide (VI) deposited the *dipicrate*, mustard-yellow crystals, m. p. 190—191°, from ethanol (Found : C, 55·3; H, 4·7; N, 11·2. $C_{46}H_{44}O_{14}N_8P_2$ requires C, 55·5; H, 4·5; N, 11·25%).

When the azaphosphine was heated with trimethylene dibromide (1 mol.) in a sealed tube for 6 hours at 140—145°, or at 170—175°, the product was a pale amber glass which could not be crystallised and did not yield a homogeneous picrate.

The structures of the azaphosphine derivatives described above show clearly however that, when the phosphine group in (II) has undergone salt formation, either by direct union with acids or by quaternisation, the tertiary amine group becomes partly deactivated, and although it can still form reasonably stable salts with strong acids such as hydrochloric and hydrobromic acid, it cannot do so with weak acids such as hydriodic and picric acids. Many similar examples of partial deactivation have been given by Mann and Watson (*J. Org. Chem.*, 1948, **13**, 502).

The Azaphosphine Monoxide (VIII).—(*a*) A solution of the azaphosphine (0·2 g.) in acetone (10 c.c.) became warm when diluted with 3% aqueous hydrogen peroxide (15 c.c.); it was next set aside for 24 hours and then evaporated to small bulk, and on cooling deposited the crystalline *monoxide*, m. p. 145—147° after recrystallisation from water (Found : C, 70·5; H, 6·45; N, 5·4. $C_{16}H_{18}ONP$ requires C, 70·8; H, 6·7; N, 5·2%).

When the acetone solution of the azaphosphine was diluted with an equal volume of 30% hydrogen peroxide and heated at 70—80° for 8 hours, the above monoxide, m. p. 143—144° (alone and mixed), was again obtained.

(*b*) A solution of the azaphosphine (0·255 g.) and chloramine-T (0·28 g., 1 mol.) in ethanol (35 c.c.) was boiled under reflux for 1 hour, and then concentrated by distillation. Addition of dilute potassium hydroxide to the cold solution precipitated a gum which when recrystallised from water gave the monoxide, m. p. 145° (alone and mixed).

The monoxide was unaffected by exposure to air. Its aqueous solution when treated with picric acid deposited the yellow *hydroxypicrate*, m. p. 165—167° (preliminary darkening) after recrystallisation from water (Found : C, 52·7; H, 4·2; N, 11·0. $C_{22}H_{21}O_8N_4P$ requires C, 52·8; H, 4·2; N, 11·2%). A solution of the monoxide in concentrated hydrochloric acid, when evaporated in a vacuum at room temperature, deposited crystals of the *hydroxychloride-hydrochloride*, m. p. 225° after drying in a vacuum over phosphoric anhydride for 5 days (Found : C, 54·8; H, 6·1; N, 4·1. $C_{16}H_{18}ONP,2HCl$ requires C, 55·8; H, 5·9; N, 4·1%). The low carbon value is due to the fact that the salt was too hygroscopic to allow recrystallisation, and drying in a vacuum even at 40° caused partial loss of hydrogen chloride.

The Azaphosphine Dioxide (IX).—A solution of the azaphosphine in acetic acid was diluted with an equal volume of 30% hydrogen peroxide, heated at 70—80° for 7 hours, and then evaporated, first at 70° and later at room temperature in a vacuum. The residual syrup, when recrystallised from ethanol, gave the *monohydrated dioxide–hydrogen peroxide* addition compound, m. p. 149° (vigorous effervescence with formation of a yellow liquid) after heating at 50°/0·5 mm. for 6 hours over phosphoric anhydride (Found : C, 56·7; H, 6·1; N, 4·5. $C_{16}H_{18}O_2NP,H_2O_2,H_2O$ requires C, 56·6; H, 6·55; N, 4·1%). An aqueous solution of the compound is neutral, and gives no precipitate with sodium hydroxide but an immediate blue colour with potassium iodide–starch.

Action of Hydriodic Acid on the Azaphosphine.—A mixture of the azaphosphine (0·2 g.) and pure hydriodic acid of constant b. p. (25 c.c.) was boiled under reflux in nitrogen for 9 hours, and then concentrated under reduced pressure, the crystalline azaphosphine hydriodide, identical in properties with that previously described, separating.

The Azaphosphine Tri-iodide.—(*a*) Hot benzene solutions of the azaphosphine and of iodine, when mixed and cooled, deposited chocolate brown crystals of the *tri-iodide*, m. p. 255—257° (decomp.) after recrystallisation from ethanol (Found : C, 30·5; H, 2·9; N, 2·2. $C_{16}H_{18}NI_3P$ requires C, 30·2; H, 2·9; N, 2·2%).

(*b*) When solutions of the azaphosphine and of iodine, each in hydriodic acid, were mixed and set aside, the tri-iodide slowly separated.

When aqueous sodium hydroxide was added to a hot aqueous suspension of the tri-iodide, a clear solution was at once obtained, and on cooling deposited the crystalline monoxide, m. p. 143—144° (alone and mixed).

When an aqueous solution of sulphur dioxide was added to a cold aqueous suspension of the tri-iodide, the latter was rapidly converted into the lemon-yellow crystalline *azaphosphine oxide hydriodide*, which, when collected, washed with sulphurous acid, and dried in vacuum at

room temperature, had m. p. 257—260° (preliminary softening) (Found: C, 47·8; H, 4·8; N, 3·4. $C_{16}H_{18}ONP,HI$ requires C, 48·1; H, 4·8; N, 3·5%). This salt was precipitated when hydriodic acid was added to a cold saturated solution of the azaphosphine monoxide. It is soluble in cold water, and its aqueous solution when either boiled for a few minutes, or treated with cold aqueous sodium hydrogen carbonate, deposited the monoxide, m. p. 144—145° (alone and mixed).

Since Beeby and Mann (*loc. cit.*) obtained the monomethiodide of the azarsine (I) by boiling with methyl iodide, it was clearly desirable to determine whether a dimethiodide would be formed under the more vigorous conditions employed to prepare the azaphosphine dimethiodide. A solution of the azarsine in an excess of methyl iodide was therefore heated under nitrogen in a sealed tube at 100° for 8 hours. The product, however, yielded only the former monomethiodide, m. p. 181° (alone and mixed) (Found: N, 3·2. Calc. for $C_{17}H_{21}NIAs$: N, 3·2%).

1 : 4-*Diphenylpiperazine Dihydrochloride*.—This salt, which was briefly described without adequate characterisation by Hofmann (*Proc. Roy. Soc.*, 1858, **9**, 277), is readily prepared by passing hydrogen chloride into a warm ethereal solution of the piperazine (III); the precipitated dihydrochloride, when recrystallised from ethanol containing a small proportion of concentrated hydrochloric acid, forms colourless crystals, m. p. 222—223° (Found: N, 9·2. Calc. for $C_{16}H_{18}N_2,2HCl$: N, 9·0%). Contrary to Hofmann's statement, the dry salt is stable, but when boiled with water gives the free base.

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