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Cyclic Organophosphorus Compounds. Part X.[1] Synthesis of *N*-(2-Aminoethyl)phosphoramidic Acids, Cyclic Phosphorodiamidates, and Related Compounds

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Reaction between ethylenediamine and aryl phosphorodichloridates yields aryl hydrogen *N*-(2-aminoethyl)-phosphoramidates and not cyclic phosphorodiamidates as reported earlier. I.r. spectroscopy distinguishes between such acids and true cyclic phosphorodiamidates made from trimethylenediamine. 1,2-, 1,3-, and 1,4-Diamino-alkanes cyclise with phenyl phosphorodichloridothionate. *o*-Phenylenediamine behaves analogously to ethylene-diamine.

THE reaction of aryl phosphorodichloridates with trimethylenediamine takes a different course from that with ethylenediamine. The products in the former case are 2-aryloxy-2-oxoperhydro-1,3,2-diazaphosphorine (Ia—d), identified on the basis of the sharp i.r. absorption at 3300—3200 cm.$^{-1}$ typical of NH·P:O (Figure 1), together with the absence of strong but broad absorption over the 3500—2500 cm.$^{-1}$ range, and of strong bands at *ca.* 1650 and 1550 cm.$^{-1}$. The compounds are further characterised by their insolubility in water and solubility in organic solvents.

The products from ethylenediamine, however, are water-soluble and insoluble in organic solvents, and exhibit strong multi-band absorption at 3500—2500 cm.$^{-1}$ together with moderate absorption at *ca.* 1560 and 1670 cm.$^{-1}$ characteristic of ammonium salts of phosphoric acids. On this basis, phosphoramidate structures (IIa—c) in their zwitterionic form are assigned to these products rather than the cyclic structures [*e.g.* (IIIa)] proposed earlier.[2] Attempts to obtain such cyclic systems from aryl phosphorodichloridates under various conditions were unsuccessful. 1,4-Diaminobutane did not give characterisable products.

The correction thus necessary to Autenrieth and Bolli's conclusions prompted a re-examination of the reactions involving phenyl phosphorodichloridothionate.[2,3] The cyclic phosphorodiamidothionate structure (IIIb) assigned to the product from the dichloridothionate and ethylenediamine in water or in dichloroethane [4] is confirmed, as are the structures of the products [(Ie) and (IVa)] from similar reactions involving tri- and tetra-methylenediamines, on the basis of their i.r. spectra [see Figure 1 for compound (IVa)]; these lacked the features to be expected of the acyclic structures (II; $n = 2$—4, $X = S$, $Y = OH$, $R = OPh$). The comparatively high yield of 2-phenoxy-2-thioxoperhydro-1,3,2-diazaphosphepine is noteworthy in view of the low yields usually encountered in the formation of related 7-membered ring compounds.

Again, in contrast to an earlier report,[2] *o*-phenylenediamine and phenyl phosphorodichloridate give the phosphoramidate (Va) rather than the diazaphospholine (VIa), identified on the basis of the i.r. absorption at 3500—2500 cm.$^{-1}$ (Figure 2) and at *ca.* 1630 and 1530 cm.$^{-1}$. Such conclusions receive further confirmation

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[1] Part IX, R. S. Edmundson and E. W. Mitchell, *J. Chem. Soc.* (*C*), 1968, 3033.

[2] W. Autenrieth and E. Bolli, *Ber.*, 1925, **58***B*, 2144.

[3] W. Autenrieth and W. Meyer, *Ber.*, 1925, **58***B*, 848.

[4] H. Tolkmith and E. C. Britton, *J. Org. Chem.*, 1959, **24**, 705.

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by a comparison of these spectra with those (Figure 3) of the cyclic phosphonic diamide (VIb) obtained by cyclisation of the phosphonamidic acid (Vb) as its chloride (Vc).[5] No 2-phenoxy-1,3,2-diazaphospholine (VIa) could be isolated from high temperature reactions.

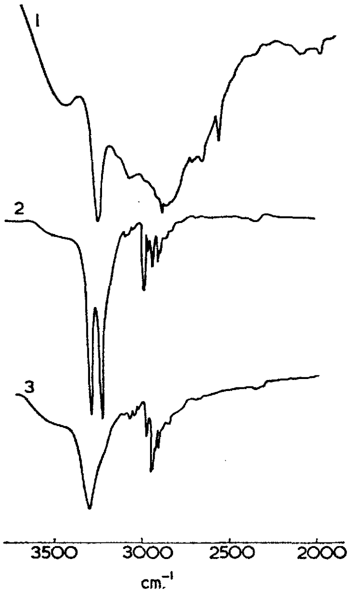


FIGURE 1 I.r. spectra of (1) phenyl hydrogen *N*-(2-aminoethyl)-phosphoramidate hemihydrate, (2) 2-oxo-2-phenoxyperhydro-1,3,2-diazaphosphorine, and (3) 2-phenoxy-2-thioxoperhydro-1,3,2-diazophosphepine

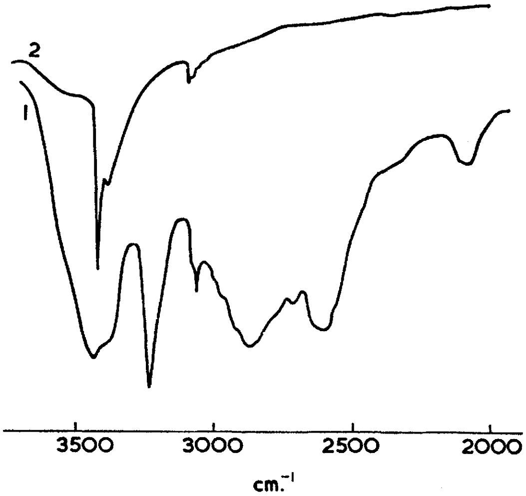


FIGURE 2 I.r. spectra of (1) phenyl hydrogen *N*-(2-aminophenyl)phosphoramidate sesquihydrate and (2) 2,3-dihydro-2-phenoxy-2-thioxo-1*H*-1,3,2-benzodiazaphosphole

The products from the recorded reactions of *o*-phenylenediamine with aryl phosphorodichloridothionates have been stated as being dependent upon the conditions.[3,6] Reaction in organic solvents was said to give the di(imidothionate) (VII) whereas fusion of the reactants was necessary for cyclisation to (VIc). Both procedures have now been shown to give the 2-phenoxy-2-thioxo-1,3,2-diazaphospholine (VIc), as demonstrated by i.r. (Figure 2) and molecular weight determinations.

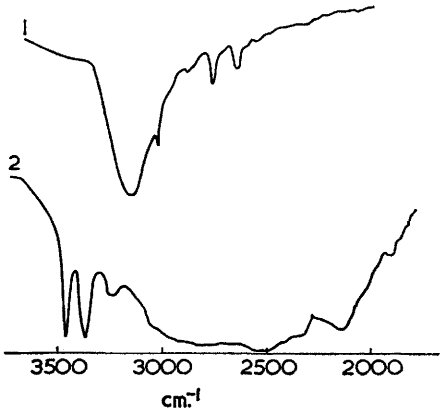
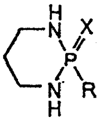


FIGURE 3. I.r. spectra of (1) 2,3-dihydro-2-oxo-2-phenyl-1*H*-1,3,2-benzodiazaphosphole and (2) *N*-(2-aminophenyl)-phenylphosphonamidic acid

Other methods tried for obtaining the diazaphospholidine (IIIa) were unsuccessful. Phenyl phosphorodiamidate gave no recognisable products other than



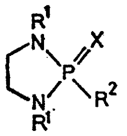
(I)

a; $X = O$, $R = OPh$
b; $X = O$, $R = m\text{-}MeC_6H_4\cdot O$
c; $X = O$, $R = p\text{-}Cl\text{-}m\text{-}MeC_6H_4\cdot O$
d; $X = O$, $R = o\text{-}ClC_6H_4\cdot O$
e; $X = S$, $R = OPh$

$NH_2\cdot[CH_2]_n\cdot NH\cdot P(:X)(Y)R$

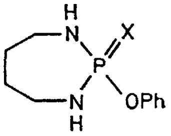
(II)

a; $n = 2$, $X = O$, $Y = OH$, $R = OPh$
b; $n = 2$, $X = O$, $Y = OH$, $R = m\text{-}MeC_6H_4\cdot O$
c; $n = 2$, $X = O$, $Y = OH$, $R = p\text{-}Cl\text{-}m\text{-}MeC_6H_4\cdot O$



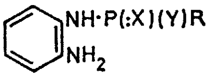
(III)

a; $R^1 = H$, $X = O$, $R^2 = OPh$
b; $R^1 = H$, $X = S$, $R^2 = OPh$
c; $R^1 = MeC_6H_4\cdot SO_2$, $X = O$, $R^2 = OPh$



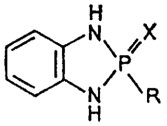
(IV)

a; $X = S$
b; $X = O$



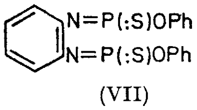
(V)

a; $X = O$, $R = OPh$, $Y = OH$
b; $X = O$, $R = Ph$, $Y = OH$
c; $X = O$, $R = Ph$, $Y = Cl$



(VI)

a; $X = O$, $R = OPh$
b; $X = O$, $R = Ph$
c; $X = S$, $R = OPh$



(VII)

$p\text{-}MeC_6H_4\cdot SO_2\cdot NH\cdot P(:O)(OH)(OR)$

(VIII)

$RO\cdot P(:O)(NH\cdot SO_2\cdot C_6H_4Me)_2 \xrightarrow{NaHCO_3} \xrightarrow{Br[CH_2]_2Br} (IIIc)$

(IX)

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[5] R. L. Dannley and F. L. Wagner, *J. Org. Chem.*, 1961, **26**, 3995.

[6] W. Autenrieth and O. Hildebrand, *Ber.*, 1898, **31**, 1111.

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ammonia when heated with ethylenediamine, nor did it react with dibromoethane under a variety of conditions.

2-Oxo-2-phenoxy-1,3-bis-*p*-tolylsulphonyl-1,3,2-diazaphospholidine (IIIc) was obtained in low yield by treatment of the sodium salt of ethylenediamine bistoluene-*p*-sulphonate with phenyl phosphorodichloridate. An alternative synthesis of this compound *via* the route shown did not prove feasible; addition of sodium toluene-*p*-sulphonamidate to phenyl phosphorodichloridate gave the phosphoramidate (VIII; R = Ph) rather than the diamidate (IX; R = Ph). The dipotassium salt of (IX; R = Et) did not react with dibromoethane.

EXPERIMENTAL

Reactions between Ethylenediamine and Aryl Phosphorodichloridates.—(a) *With phenyl phosphorodichloridate*. The phosphorodichloridate (21·1 g.) was added dropwise during 1 hr. to ethylenediamine hydrate (8·0 g.) and triethylamine (20 g.) in water (10 ml.) at 10—15°. After completion of the reaction, the mixture was diluted with water (10 ml.), stirred, and filtered. The solid was washed with a little cold water and gave *phenyl hydrogen* N-(2-*aminoethyl*)-*phosphoramidate* (5·0 g.), m.p. 195—196° (from aqueous dioxan) [Found (sample dried over P_2O_5 for 18 hr.): C, 43·6; H, 6·2; N, 12·5; P, 14·15. $C_8H_{13}N_2O_3P,0{\cdot}5H_2O$ requires C, 42·6; H, 6·35; N, 12·45; P, 13·8%]. A sample from another experiment had m.p. 219—221° (from aqueous acetone) (after drying *in vacuo* at 130°) (Found: C, 41·8; H, 6·5; N, 12·1; P, 13·2. $C_8H_{13}N_2O_3P,H_2O$ requires C, 41·0; H, 6·4; N, 11·95; P, 13·25%).

A sample of the hydrate sublimed at 200—220° (bath)/0·2 mm. gave a product, m.p. 200·5—201° (Found: N, 13·1; P, 14·3. $C_8H_{13}N_2O_3P$ requires N, 12·95; P, 14·35%).

(b) *With* m-*tolyl phosphorodichloridate*. The phosphorodichloridate (112·5 g.) was added dropwise to ethylenediamine hydrate (117 g.) in water (100 ml.) at 0—5°. After completion of reaction, the mixture was stirred for 45 min. The m-*tolyl hydrogen* N-(2-*aminoethyl*)*phosphoramidate* (12·3 g.) had m.p. 197—198° (from aqueous dioxan) (Found: C, 47·0; H, 7·0; N, 12·4; P, 13·3. $C_9H_{15}N_2O_3P$ requires C, 47·0; H, 7·0; N, 12·1; P, 13·45%).

(c) *With* p-*chloro*-m-*tolyl phosphorodichloridate*. Reaction between this and ethylenediamine in toluene at 10—15° yielded p-*chloro*-m-*tolyl hydrogen* N-(2-*aminoethyl*)*phosphoramidate* (87%), m.p. 216—216·5° (from methanol–acetone) (Found: C, 40·95; H, 5·5; Cl, 13·6; N, 10·6. $C_9H_{14}ClN_2O_3P$ requires C, 40·9; H, 5·3; Cl, 13·4; N, 10·6%).

2-*Aryloxy*-2-*oxoperhydro*-1,3,2-*diazaphosphorine*.—Dropwise addition of phenyl phosphorodichloridate (21·1 g.) to 1,3-diaminopropane (22·2 g.) dissolved in an equal volume of water at 0° gave 2-*oxo*-2-*phenoxyperhydro*-1,3,2-*diazaphosphorine* as an insoluble solid (4·5 g.), m.p. 144·5—146·5° (from ethanol), $\nu_{max.}$ 3285 and 3225 (NH), and 1230 (P=O) cm.$^{-1}$ (Found: C, 50·9; H, 6·4; N, 13·6; P, 14·8. $C_9H_{13}N_2O_2P$ requires C, 50·9; H, 6·1; N, 13·2; P, 14·6%).

When 1,3-diaminopropane (93 g.) was added dropwise to phenyl phosphorodichloridate (106 g.) in dichloroethane (500 ml.) at 10—15°, the same compound (35%), contaminated with amine hydrochloride, was precipitated.

Similarly prepared in dichloroethane were the following 2-*aryloxy*-2-*oxoperhydro*-1,3,2-*diazaphosphorine*, all recrystallised from dichloroethane: (Id) (88%), m.p. 169·5—170·5°, $\nu_{max.}$ 3270 (NH) and 1235 (P=O) cm.$^{-1}$ (Found: C, 43·9; H, 5·4; N, 11·3; P, 12·6. $C_9H_{12}ClN_2O_2P$ requires C, 43·8; H, 5·0; N, 11·4; P, 12·6%); (Ib) (68%), m.p. 139—141°, $\nu_{max.}$ 3295 and 3250 (NH), and 1235 (P=O) cm.$^{-1}$ (Found: C, 53·4; H, 7·4; N, 12·3; P, 13·35. $C_{10}H_{15}N_2O_2P$ requires C, 53·4; H, 6·7; N, 12·4; P, 13·7%); and (Ic) (74%), m.p. 164—166°, $\nu_{max.}$ 3290 and 3225 (NH), and 1233 (P=O) cm.$^{-1}$ (Found: C, 45·6; H, 5·5; N, 10·6; P, 11·9. $C_{10}H_{14}ClN_2O_2P$ requires C, 46·1; H, 5·4; N, 10·75: P, 11·9%).

2-*Phenoxy*-2-*thioxo*-1,3,2-*diazaphospholidine*.—(*a*) Phenyl phosphorodichloridothionate (11·1 g.) was added dropwise to ethylenediamine (monohydrate; 12·0 g.) in water (10 ml.) at room temperature. The resultant slurry was filtered, and the residue, washed well with ice-cold water, gave the cyclic diamidothionate (5·5 g., 52%), m.p. 90° (from ethanol) (lit.,[2] 189°) (Found: C, 44·6; H, 5·1. Calc. for $C_8H_{11}N_2OPS$: C, 44·9; H, 5·2%).

(*b*) Ethylenediamine (anhydrous; 7·5 g.) was added dropwise to phenyl phosphorodichloridothionate (11·1 g.) in dichloroethane (200 ml.) at room temperature, and the mixture was stirred for 1 hr. The filtered solution was evaporated to a semi-solid which gave the diamidothionate (8·3 g., 78%), m.p. 89—90° (from ethanol).

2-*Phenoxy*-2-*thioxoperhydro*-1,3,2-*diazaphosphorine*.—(*a*) Phenyl phosphorodichloridothionate (11·2 g.) was added dropwise to 1,3-diaminopropane (11·5 g.) in water (15 ml.) at room temperature. The insoluble yellow oily product was separated, washed with water, taken up in chloroform, and dried. The solvent was evaporated off and the residue was extracted with cyclohexane. Further extraction with ether and evaporation of the extract gave an oil which solidified on trituration with cyclohexane. The *diazaphosphorine* (6·3 g., 55%) had m.p. 51—52° (from propan-2-ol), $\nu_{max.}$ 3300br, 1593, and 1206 cm.$^{-1}$ (Found: C, 47·65; H, 5·8; P, 13·3. $C_9H_{13}N_2OPS$ requires C, 47·35; H, 5·75; P, 13·55%).

(*b*) 1,3-Diaminopropane (9·1 g.) and triethylamine (10·1 g.) were added dropwise to phenyl phosphorodichloridothionate (11·1 g.) in dichloromethane (150 ml.) at room temperature. The mixture was set aside for 48 hr., then washed with water and dried. Evaporation of the solvent gave the same diamidothionate (8·8 g., 77%).

Reactions with 1,4-*Diaminobutane*.—(*a*) Phenyl phosphorodichloridothionate (11·3 g.) was added in portions to triethylamine (10·1 g.) and 1,4-diaminobutane (4·4 g.) in dichloromethane (175 ml.) cooled in ice. The mixture was stirred at room temperature for 2 hr., filtered, and evaporated to an oil which was extracted with light petroleum (b.p. 60—80°; 2 × 100 ml.). Extraction of the residue with ether (3 × 100 ml.) and evaporation of the ether gave 2-*phenoxy*-2-*thioxoperhydro*-1,3,2-*diazaphosphepine* (5·2 g., 43%), m.p. 86—86·5° (from ether), $\nu_{max.}$ 3300 (NH), 1596, and 1214 cm.$^{-1}$ (Found: C, 50·15; H, 6·0; P, 12·85. $C_{10}H_{15}N_2OPS$ requires C, 49·5; H, 6·25; P, 12·75%).

(*b*) Phenyl phosphorodichloridate (4·3 g.) was added dropwise to a solution of triethylamine (4·1 g.) and the diaminobutane (1·8 g.) in dichloromethane (100 ml.) at room temperature. The reaction was only slightly exothermic and little precipitation occurred. After 24 hr. there was no further smell of the phosphorodichloridate. A trace of solid insoluble in all organic solvents tried was filtered off, and the filtrate was evaporated to give an intractable oil.

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*2-Oxo-2-phenoxy-*1,3-*bis*-p-*tolylsulphonyl*-1,3,2-*diazaphospholidine*.—Phenyl phosphorodichloridate (4·3 g.) was added in portions to the disodium salt of 1,2-bis-*p*-tolylsulphonylaminoethane (8·3 g.) suspended in benzene (50 ml.). When the exothermic reaction was over, the mixture was refluxed for 2 hr. and filtered hot. Evaporation of the filtrate gave the *diazaphospholidine* (1·6 g.), m.p. 202—204° (from benzene) (Found: C, 52·25; H, 4·5; N, 5·55; P, 6·05; S, 12·75. $C_{22}H_{23}N_2O_6S_2P$ requires C 52·2; H, 4·6; N, 5·55; P, 6·1; S, 12·6%).

Reaction of Sodium Toluene-p-*sulphonamidate with Phenyl Phosphorodichloridate*.—Sodium toluene-*p*-sulphonamidate (7·4 g.) was added in small portions to phenyl phosphorodichloridate (4·1 g.) in benzene at *ca*. 5° and the mixture was then stirred for 2 hr., and filtered. The filtrate was evaporated to give *phenyl hydrogen* N-p-*tolylsulphonylphosphoramidate* (2·4 g.), m.p. 185—186° (from ethanol–benzene), $\nu_{max.}$ 1175 (P=O) cm.$^{-1}$ (Found: N, 4·55; P, 9·7; S, 9·6. $C_{13}H_{14}NO_5PS$ requires N, 4·3; P, 9·45; S, 9·8%).

Ethyl NN′-*Bis*-p-*tolylsulphonylphosphorodiamidate*.—Ethyl phosphorodichloridate (16·3 g.) was added to sodium toluene-*p*-sulphonamidate (38·6 g.) stirred in boiling benzene (150 ml.) during 0·5 hr. The mixture was refluxed for 1 hr., cooled, and filtered. The solid was extracted with potassium hydrogen carbonate solution [leaving toluene-*p*-sulphonamide (20 g.)] and the extract was carefully acidified with 2N-hydrochloric acid to liberate *ethyl* NN′-*bis*-p-*tolylsulphonylphosphorodiamidate* (5·1 g.), m.p. 188° (from benzene–chloroform), $\nu_{max.}$ 3200 (NH) and 1237 (P=O) cm.$^{-1}$ (Found: N, 6·8; P, 7·45; S, 14·7. $C_{16}H_{25}N_2O_6PS_2$ requires N, 6·4; P, 7·1; S, 14·65%).

Reaction between Ethyl NN′-*Bis*-p-*tolylsulphonylphosphorodiamidate and* 1,2-*Dibromoethane*.—The diamidate (2·15 g.) was treated with potassium hydrogen carbonate (1·0 g.) and water and the solution was evaporated to dryness. The solid was dried azeotropically with benzene, then heated under reflux with a slight molar excess of 1,2-dibromoethane in toluene for 30 hr. and filtered hot. Acidification of the solid residue gave a quantitative recovery of the diamidate.

2,3-*Dihydro*-2-*oxo*-2-*phenyl*-1*H*-1,3,2-*benzodiazaphosphole*.—This, m.p. 269—271° (decomp.) (from chloroform) (lit.,[5] 277—278°), $\nu_{max.}$ 1256 (P=O) cm.$^{-1}$, was prepared by Dannley and Wagner's procedure.[5]

N-(2-*Aminophenyl*)*phenylphosphonamidic Acid*.— This, m.p. 216° (decomp.) (from water) (lit.,[5] 228°), $\nu_{max.}$ 1645, 1530, and 1140vbr (P=O) cm.$^{-1}$, was prepared by the literature method.[5]

Phenyl Hydrogen N-(2-*Aminophenyl*)*phosphoramidate*.—(i) A solution of *o*-phenylenediamine (16·2 g.) in dichloromethane (250 ml.) was added dropwise with stirring to phenyl phosphorodichloridate (10·3 g.) in the same solvent (50 ml.) at room temperature. The mixture was filtered; evaporation of the filtrate gave a gum which reacted exothermically with water to give the *phosphoramidate* (1·2 g.), m.p. 175—176° (decomp.) (from ethanol), $\nu_{max.}$ 1630, 1532, and 1220 (P=O) cm.$^{-1}$ (Found: C, 52·9; H, 5·8; N, 10·6; P, 11·7. $C_{12}H_{13}N_2O_3P,1{\cdot}5H_2O$ requires C, 52·9; H, 5·9; N, 10·3; P, 11·4%).

(ii) Use of triethylamine (2M) to remove hydrogen chloride in an otherwise identical experiment gave the phosphoramidate (31%), m.p. 174—176° (from ethanol).

(iii) A solution of *o*-phenylenediamine (5·4 g.) and phenyl phosphorodichloridate (10·6 g.) in bromobenzene (150 ml.) was refluxed with stirring for 3 hr. and filtered hot. The filtrate deposited the same phosphoramidate (0·3 g.), m.p. 160° [not depressed on admixture with a sample of the sesquihydrate which had been dried *in vacuo* (P_2O_5) at 100°] (Found: C, 53·75; H, 5·2; P, 11·7. $C_{12}H_{13}N_2O_3P$ requires C, 54·5; H, 5·0; P, 11·7%), $\nu_{max.}$ 1225 (P=O) cm.$^{-1}$; no peaks at 3450 and 3380 cm.$^{-1}$, as found for the hydrate.

2,3-*Dihydro*-2-*phenoxy*-2-*thioxo*-1*H*-1,3,2-*benzodiazaphosphole*.—(i) *o*-Phenylenediamine (2·0 g.) and phenyl phosphorodichloridothionate (2 g.) were heated together at 170—200° (bath) for 4 hr. Extraction of the blue solid with boiling ether gave the *cyclic phosphorodiamidothionate* (0·2 g., 8%), m.p. 176° (from benzene), *m/e* 262 (M^+), $\nu_{max.}$ 3410 (NH), 3075, 1592, 1495, 1389, 1280, 1202, 920, 902, 782, 748, and 698 cm.$^{-1}$ (Found: C, 55·3; H, 4·4; P, 11·45. $C_{12}H_{11}N_2OPS$ requires C, 55·0; H, 4·3; P, 11·8%).

(ii) A solution of *o*-phenylenediamine (5·4 g.) and triethylamine (10·1 g.) in 1,2-dichloroethane (75 ml.) was added rapidly to phenyl phosphorodichloridothionate (11·1 g.) in dichloroethane (100 ml.) and the mixture was refluxed for 4 hr. Evaporation to an oil, followed by trituration with water gave the cyclic phosphorodiamidothionate (7·5 g., 29%).

[9/861 *Received, May 22nd*, 1969]