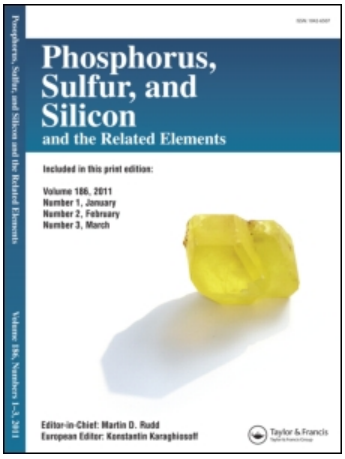

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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To cite this Article Cremlyn, Richard and Akhtar, Naseem(1979) 'SOME HETEROCYCLIC PHOSPHOROCHLORIDATES AND THE FORMATION OF OTHER HETEROCYCLIC ORGANOPHOSPHORUS COMPOUNDS', Phosphorus, Sulfur, and Silicon and the Related Elements, 7: 3, 247 — 255
To link to this Article: DOI: 10.1080/03086647908077476
URL: http://dx.doi.org/10.1080/03086647908077476

Phosphorus and Sulfur, 1979, Vol. 7. pp. 247–256
0308-664X/79/0703–0247$4.50/0

SOME HETEROCYCLIC PHOSPHOROCHLORIDATES AND THE FORMATION OF OTHER HETEROCYCLIC ORGANOPHOSPHORUS COMPOUNDS

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(*Received January 19, 1979; in final form March 5, 1979*)

Pyrrolidine, morpholine, and β-hydroxyethylmorpholine have been phosphorylated with phosphorus oxychloride, phenylphosphorodichloridate, *p*-chlorophenylphosphorodichloridate and thiophosphoryl chloride. The resultant phosphorodichloridates have been condensed with a wied range of nucleophilic reagents, e.g. amines, hydrazines, phenols and isobutanol. Piperazine with phosphorus oxychloride (2 mols) gave the N(1) N(4)-diphosphorotetrachloridate, which was characterized as the tetracyclohexylamidate. β-Hydroxyethylpiperazine was similarly phosphorylated to the N,O-diphosphorotetrachloridate which was characterized as the tetraphenylhydrazidate.

Condensation of pyrrolidine (2 mols) with phosphorus oxychloride (1 mol) afforded N,N′-dipyrrolidinophosphorochloridate which was reacted with phenylhydrazide and sodium azide. The phosphoroazide with triphenylphosphine afforded the corresponding triphenylphosphinimine. N-Phenyl N′-pyrrolidinophosphorochloridate with aqueous pyridine gave the corresponding pyrophosphoramide and the stability of the pyrophosphoramide towards hydrolysis was examined. 1,2-Cyclohexanediol was phosphorylated with phenylphosphorodichloridate and thiophosphorylchloride. *Trans*-4-*t*-Butylcyclohexyl N,N′-diphenylhydrazinophosphorothioate by reaction with formaldehyde gave a tetra-azaphosphorine P-sulfide. *Trans*-4-*t*-Butylcyclohexyl N-phenyl N′-phenylphosphorodiamidic hydrazide reacted with 1,4-dibromobut-2-ene to give a 1,2-diazahex-4-ene.

INTRODUCTION

In a search for new pesticides and as an extension to previous studies[1–4] on the synthesis and reactivity of alicyclic phosphorochloridates, we have now examined the phosphorylation of some heterocyclic compounds. Heterocyclic phosphorus compounds have also been obtained by phosphorylation of 1,2-cyclohexanediol; by reaction of *trans*-4-*t*-butylcyclohexyl N,N′-diphenylhydrazinophosphorothioate with formaldehyde; and from *trans*-4-*t*-butylcyclohexyl N-phenyl N′-phenylphosphorodiamidic hydrazide with 1,4-dibromobut-2-ene.

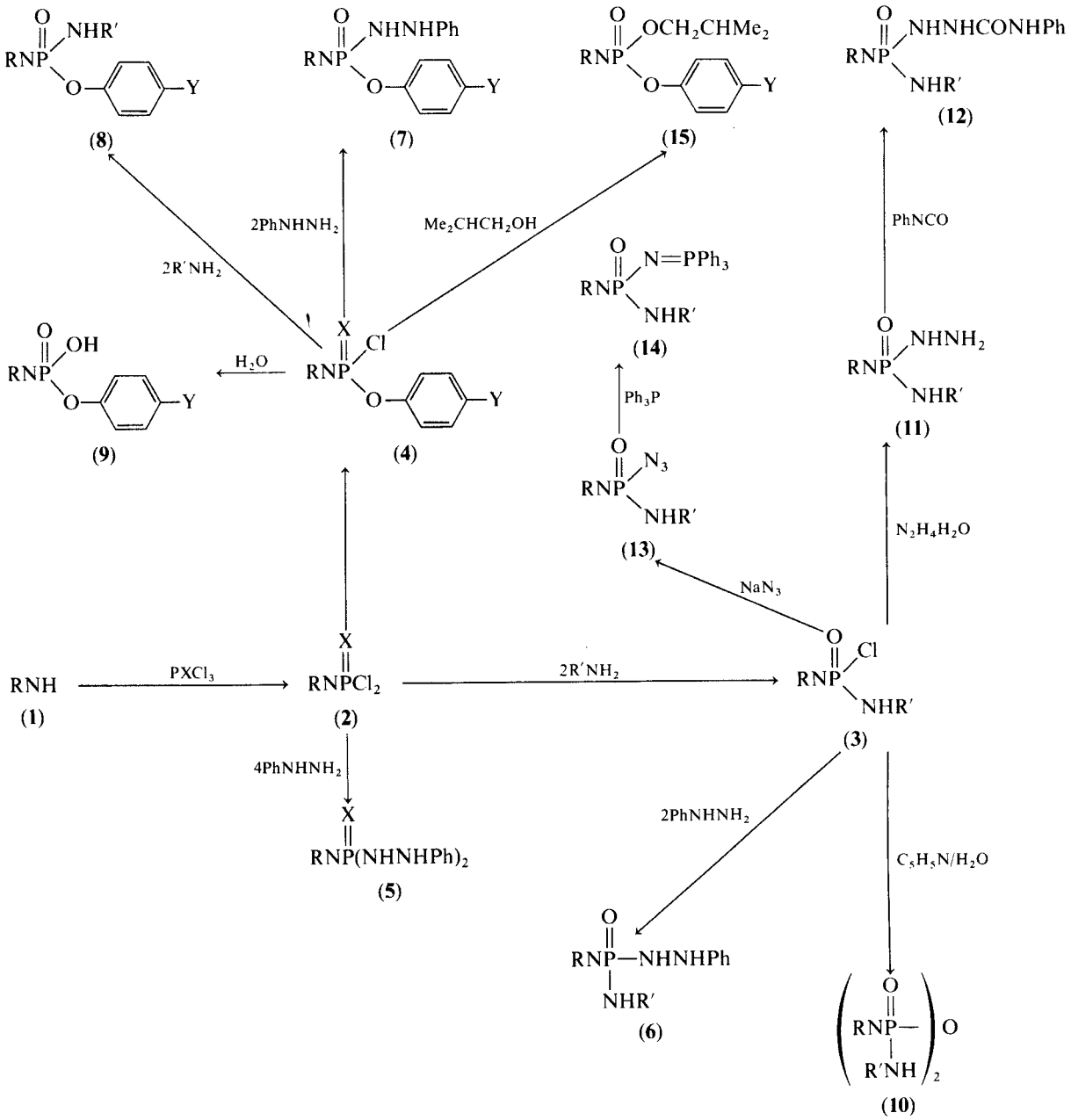
These heterocyclic organophosphorus compounds are of special interest as potential pesticides since many modern pesticides incorporate a heterocyclic nucleus.[5,6]

DISCUSSION

Heterocyclic Phosphorochloridates and Derivatives

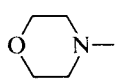
Treatment of pyrrolidine, morpholine, and β-hydroxyethylmorpholine (**1**) with equimolar quantities of phosphorylating agents (e.g. phosphorus oxychloride, phenylphosphorodichloridate, *p*-chlorophenylphosphorodichloridate, or thiophosphoryl chloride) and a tertiary base afforded the corresponding phosphorochloridates (**2**) in 60–90% yields (Scheme 1). Phosphorylation using the N-heterocyclic compound (2 mol) generally resulted in poor yields of the phosphorodichloridates, probably as a result of appreciable amounts of the disubstituted phosphorochloridate being formed (cf. Ref. 7). The phosphoramidic dichloridates (**2**) were stable at room temperature, although the O-phosphorodichloridates (**2c**, **23**) such as the compounds derived from β-hydroxyethylmorpholine (**1c**) and β-hydroxyethylpiperazine (**22**) (Scheme 2) fumed in air and darkened on standing. The greater reactivity of the O-phosphorodichloridates is a reflection of the enhanced electrophilic nature of the phosphorus atom when attached to oxygen than when it is adjacent to nitrogen.

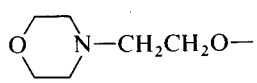
Condensation of the phosphorodichloridates (**2**) with an amine afforded the amidic chlorides (**3**). The O-phenyl and O-*p*-chlorophenyl derivatives (**4**) were generally obtained by phosphorylation of the heterocyclic compound with phenyl or *p*-chlorophenyl-phosphorodichloridate.



X = O or S

(a) R = 

(b) R = 

(c) R = 

SCHEME I

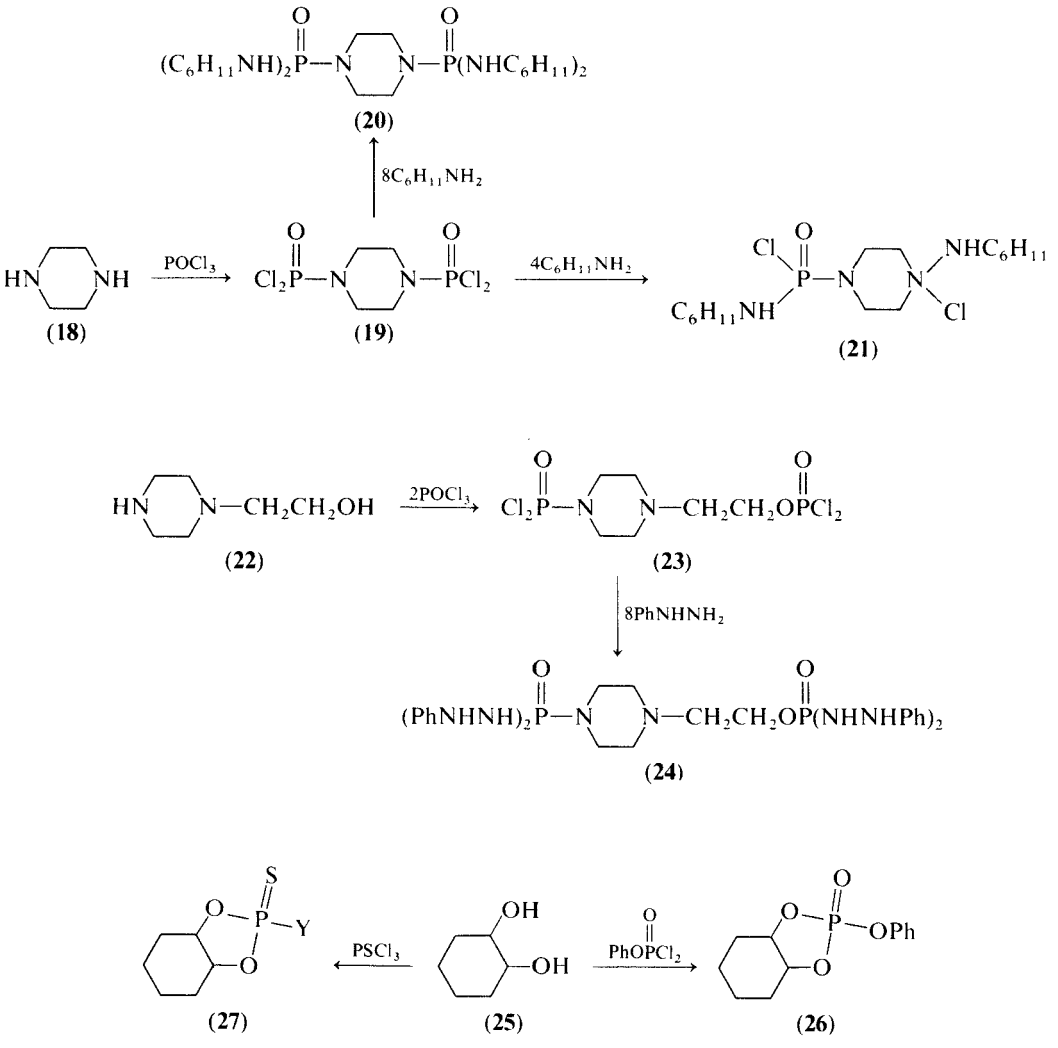
The liquid phosphorodichloridates were characterised by reaction with phenylhydrazine which afforded solid diphenylhydrazides (**5**); the phosphorochloridates (**3**, **4**) with phenylhydrazine afforded the corresponding monophenylhydrazides (**6**, **7**).

The O-arylphosphorochloridate (**4**) with amines likewise gave the phosphoramidates (**8**), and hydrolysis afforded the amidic phosphates (**9**), characterised as the cyclohexylammonium or barium salts.

N-Phenyl N′-pyrrolidinophosphorochloridate (**3a**; X = O, R′ = Ph) by partial hydrolysis afforded a low yield (27%) of the corresponding pyrophosphoramide (**10a**; R′ = Ph) (cf. Ref. 8); the low yield may be attributed to rapid decomposition of the intermediate phosphoramidic acid in the basic media. The phosphoramidic chloride (**3a**; R′ = Ph) with hydrazine hydrate gave the corresponding hydrazide (**11a**; R′ = Ph) as an oil; this was characterised by reaction with phenylisocyanate to give the solid N-phenylcarbamoyl derivative (**12**; R′ = Ph).

With sodium azide, the amidic chloride (**3**) afforded the azide (**13**) which with triphenylphosphine gave the triphenylphosphinimine (**14**).

Phosphoramidic chlorides containing an amidic hydrogen atom are susceptible to alkaline hydrolysis which probably involves a metaphosphate type intermediate[9] and the low yield (36%) of the amidic

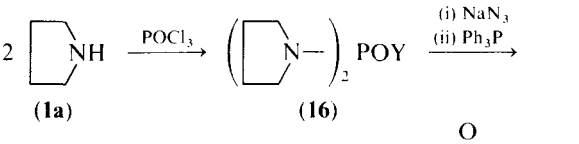


SCHEME 2

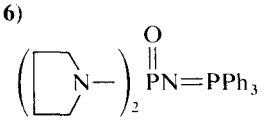
azide (**13a**; R′ = Ph) is probably a consequence of base-catalysed decomposition of the amidic chloride (**3a**; R′ = Ph). This suggestion is supported by the observation that N,N′-dipyrrolidinophosphorochloridate (**16**; Y = Cl) without any amidic protons affords an appreciably higher yield (64%) of the azide (**16**; Y = N_3).

O-Phenyl- and O-*p*-chlorophenyl-N-pyrrolidinophosphorochloridate (**4a**; X = O, Y = H or Cl) with isobutanol gave the corresponding O′-isobutyl derivatives (**15a**; Y = H or Cl).

Pyrrolidine (**1a**) (2 mol) reacted with phosphorus oxychloride (1 mol) and triethylamine to give dipyrrolidinophosphorochloridate (**16**; Y = Cl) which with phenylhydrazine gave the phenylhydrazide (**16**; Y = NHNHPh):



(**1a**) (**16**)



(**17**)

The chloridate (**16**; Y = Cl) with sodium azide afforded the azide (**16**; Y = N_3) which with triphenylphosphine gave the triphenylphosphinimine (**17**) (cf. Ref. 10).

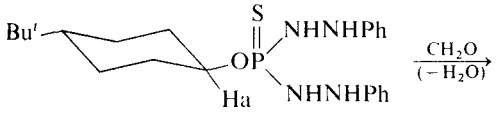
Piperazine (**18**) with phosphorus oxychloride and triethylamine, gave the N (**1**) N (**4**)-diphosphorotetrachloridate (**19**) (Scheme 2). Condensation with cyclohexylamine gave the tetracyclohexylamidate (**20**); and with less cyclohexylamine the dicyclohexylamidic chloride (**21**) was obtained.

β-Hydroxyethylpiperazine (**22**) with phosphorus oxychloride gave the N,O-diphosphorotetrachloridate (**23**), characterised as the tetraphenylhydrazide (**24**).

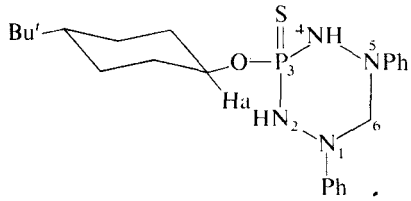
1,2-Cyclohexanediol (**25**) has been reacted with phenylphosphorodichloridate to give the phenyl phosphate (**26**). The diol (**25**) with thiophosphoryl chloride gave the chloridothioate (**27**; X = Cl), which was characterised as the morpholidate (**27**; Y = morpholino).

Formation of Other Heterocyclic Organophosphorus Compounds

Hydrazides are known[11] to condense with diketones to form heterocyclic products, but bis(*trans*-4*t*-butylcyclohexyl) phosphorohydrazide did not cyclise on treatment with acetylacetone or trifluoroacetylacetone in boiling methanol. The failure may be a reflection of the low nucleophilicity of the nitrogen atom adjacent to the phosphoryl group. On the other hand, *trans*-4-*t*-butylcyclohexyl N,N′-diphenylhydrazinophosphorothioate (**28**) condensed with formaldehyde to give the tetraazaphosphorine P-sulphide (**29**):



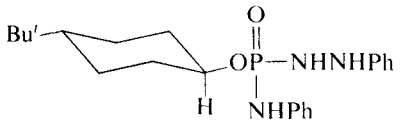
(**28**)



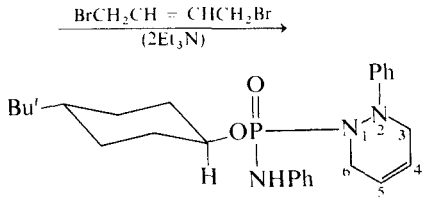
(**29**)

Several similar tetra-azaphosphorines have been recently reported by Majoral *et al.*,[12] and the synthesis of P—N—N heterocyclic compounds has been reviewed.[13]

The reactivity of the hydrazino hydrogen atoms in *trans*-4-*t*-butylcyclohexyl N-phenyl N′-phenylphosphorodiamidic hydrazide (**30**) are shown by the cyclisation occurring on treatment of this hydrazide with 1,4-dibromobut-2-ene to give the 1,2-diazacyclohex-4-ene (**31**):



(**30**)



(**31**)

The presence of the anilino group attached to the phosphorus atom appears to assist the cyclisation, possibly by releasing electrons to the phosphorus, because the analogous phosphorohydrazide to (**30**) in which is the anilino group was replaced by a phenoxy group did not undergo cyclisation under similar conditions.

The characteristic i.r. absorptions for the NH, P = O, P—O—C alip, P—O—C arom, and P—O—P bonds were in good agreement with reported values.[4,14,15] The P = S absorption band appeared in the region 745–855 cm^{-1}, this range is rather higher than reported[16] for a series of tetrathiophosphates, but in reasonable agreement with previous observations.[4] The mass spectra gave the molecular ions, the chloridates showed ions corresponding to M-Cl and the base peaks were generally the parent amines.

EXPERIMENTAL

I.r. spectra were determined as liquid films or Nujol mulls using a Perkin Elmer 257 spectrometer. N.m.r. spectra were measured with a Varian HA 100 spectrometer with tetramethylsilane as internal standard. Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. T.l.c. was carried out on silica gel G plates developed with iodine vapour. Mass spectra were determined with an AEI MS 9 spectrometer at 70 eV. ^{31}P n.m.r. spectra were obtained with a Bruker FX90 spectrometer operating at 36.43 MHz, using broad band decoupling and 86% H_3PO_4 as external reference. Chemical shifts are expressed in p.p.m; downfield shifts from the reference are defined as positive. Microanalyses were carried out by Butterworth Microanalytical Consultancy Ltd., Teddington, England.

N-Pyrrolidinophosphorodichloridate (**2a**; X = O)

A solution of pyrrolidine (**1a**) (7.1g; 0.1 mol) and triethylamine (10.1g, 0.1 mol) in ether (150 ml) was added dropwise over ½h to a stirred solution of phosphorus oxychloride (15.35g; 0.1 mol) in ether (50 ml) at −10°. After 5h at room temperature, triethylamine hydrochloride was filtered off and the filtrate evaporated *in vacuo*. The residual oil was distilled under reduced pressure to give the dichloridate (**2a**) as a pale yellow oil (17g, 90%), b.p. 63–65°/0.2 mm. n_D^{20} 1.4910 (lit.[14] 127–128°/16 mm.). (Found: C, 25.3; H, 4.3; N, 7.2. Calc. for $C_4H_8Cl_2NOP$: C, 25.5; H, 4.3; N, 7.45%). ν_{max} 1270 (P = O) cm^{-1}.

N-Morpholinophosphorodichloridothioate (**2b**; X = S)

A solution of morpholine (**1b**) (8.7g; 0.1 mol) and pyridine (7.9g; 0.1 mol) in petroleum ether (40–60°) (100 ml) was added dropwise to a stirred solution of thiophosphoryl chloride (16.9g; 0.1 mol) in petroleum ether (100 ml) at 0°. The mixture was stirred at 0° for 2h and at room temperature for 24h. Pyridine hydrochloride was filtered off and the filtrate evaporated *in vacuo*. Distillation of the residual oil under reduced pressure gave the dichloridothioate as a yellow oil (19g, 86%), b.p. 100–102°/1.5 mm. (lit.[17] 107–110°/2 mm). ν_{max} 745 (P = S) cm^{-1}.

N,N′-Dipyrrolidinophosphorochloridate (**16**; Y = Cl)

Pyrrolidine (**1a**) (7.73g; 0.11 mol) and triethylamine (11.0g; 0.11 mol) in ether (150 ml) was added dropwise to a stirred solution of phosphorus oxychloride (8.36g; 0.055 mol) in ether (50 ml) at 0°. After 20h at room temperature, triethylamine hydrochloride was filtered off and the filtrate evaporated. Recrystallisation of the residue from petroleum ether (40–60°) afforded the *phosphorochloridate* (9.3g; 77%), m.p. 32–35°. (Found: C, 43.1; H, 7.4; N, 12.5. $C_8H_{16}ClN_2OP$ requires C, 43.15; H, 7.2; N, 12.6%). ν_{max}1275 (P = O) cm^{-1}.

N-Morpholinophenylphosphorochloridate (**4b**; X = O, Y = H)

Method (a) Morpholine (17.42g; 0.2 mol) in petroleum ether (40–60°) (150 ml) was added dropwise to a stirred solution of phenylphosphorochloridate (21.1g; 0.1 mol) in petroleum ether (100 ml) at −5°. Stirring was continued for 2h <0° and for 4h at room temperature. Morpholine hydrochloride was filtered off and the filtrate washed with H_2O (3 × 100 ml), saturated $NaHSO_3$ (100 ml), and dried ($MgSO_4$). Evaporation *in vacuo* gave the *phenylphosphorochloridate* as a clear oil (6.9g; 26%), n_D^{25} 1.5322 T.l.c. (EtOAc-petroleum ether (60–80°) 1:1) showed a single spot R_f 0.60.

Method (b) A similar experiment using equimolar amounts of morphine, triethylamine, and phenylphosphorodichloridate in ether gave the identical *phosphorochloridate* (70%). ν_{max} 1590, 1490 (arom C = C), 1240 (P = O), 970, 940 (P—O—C) cm^{-1}. Ms. showed the molecular ion (M^+, 261), other major ions were at 226, 168, 150, 94, 93, 87, 86.

O-Phenyl N-Pyrrolidinophosphorochloridate (**4a**; X = O, Y = H)

Prepared by method (b) above as a liquid (77%), b.p. 143–144°/0.5 mm. n_D^{20} 1.5296. (Found: C, 48.7; H, 5.2; N, 5.6. $C_{10}H_{13}ClNO_2P$ requires: C, 48.9; H, 5.3; N, 5.7%). ν_{max}1595, 1495 (arom C = C), 1295, 1200 (P = O), 945 (P—O—C) cm^{-1}. Ms. showed the molecular ion (M^+, 245), major fragment ions were at 210, 175, 152, 94, 77, 70.

O-p-Chlorophenyl N-Pyrrolidinophosphorochloridate (**4a**; X = O, Y = Cl)

Was obtained by method (b) (75%), b.p. 168–170°/0.4 mm. ν_{max} 1590, 1485 (arom C = C), 1300, 1290, 1200 (P = O), 945, 930 (P—O—C) cm^{-1}.

N-Morpholino O-Phenylphosphorochloridothioate (**4b**; X = S, Y = H)

A solution of phenol (6.84g; 0.073 mol) and pyridine (5.74g; 0.073 mol) in ether (150 ml) was added dropwise to a solution of morpholinophosphorodichloridothioate (**2b**; X = S) (16.0g, 0.073 mol) in ether (100 ml) at room temperature. The mixture was boiled under reflux for 20h, cooled and pyridine hydrochloride filtered off. The filtrate was washed with H_2O (3 × 100 ml), dried ($MgSO_4$) and avaporated under reduced pressure. The residual oil by distillation under reduced pressure gave the *phosphorochloridothioate* (13.4g; 66%), b.p. 108°/0.3 mm. (The oil solidified on cooling (0°) to give a solid, m.p. 15–17°). T.l.c. ($Pr^iOH—C_6H_5CH_3—EtOAc—H_2O$ 5:1:2.5:1.25) showed one spot, R_F 0.83. (Found: C, 43.5; H, 4.7; N, 5.0. $C_{10}H_{13}ClNO_2PS$ requires: C, 43.2; H, 4.7; N, 5.0%). ν_{max}1585, 1485 (arom C = C), 960 (P—O—C), 845 (P = S) cm^{-1}. Ms. showed the molecular ion (M^+, 277), other major ions were at 242, (M—Cl), 191, 184, 149, 95, 94, 87, 86 (morpholine).

N-Phenyl N¹-Pyrrolidinophosphoramidic chloride (**3a**; R^1 = Ph)

Was obtained by reaction of aniline (2 mol) with N-pyrrolidinophosphorodichloridate (2a) (1 mol) in ether overnight as an oil (48%), b.p. 88–90°/0.4 mm. (Found: C, 48.9; H, 5.9; N. 11.5. $C_{10}H_{14}ClN_2OP$ requires: C, 49.1; H, 5.7; N, 11.45%). ν_{max} (liquid film) 3150 (NH), 1605, 1500 (arom C = C), 1225 (P = O) cm^{-1}.

N-(β-Dichlorophosphoroethyl) piperazino N¹-phosphorodichloridate (**23**)

N-β-Hydroxyethylpiperazine (**22**) (13.0g; 0.1 mol) and triethylamine (20.2g; 0.2 mol) in ether (150 ml) was added dropwise to a stirred solution of phosphorus oxychloride (30.6g; 0.2 mol) in ether (200 ml) at −20°. After 3h at 0° and 0.5h at room temperature, triethylamine hydrochloride (27.5g) was filtered off. The filtrate, by evaporation *in vacuo* gave the crude diphosphorodichloridate as a brown oil (10.24g, 28%). ν_{max} 1300–1270 (br P = O), 970 (P—O—C) cm^{-1}.

Piperazine-1,4-Diphosphorotetrachloridate (**19**)

Was similarly prepared from piperazine (**18**) (60%), m.p. 145–151° (lit.[18] 175°). (Found: C, 15.0; H, 2.5; N, 8.75. Calc. for $C_4H_8Cl_4N_2O_2P_2$: C, 15.2; H, 2.7; N, 8.9%).

β-Morpholinoethylphosphorodichloridate (**2c**; X = O)

β-Hydroxyethylmorpholine (**1c**) (6.55g; 0.05 mol) and triethylamine (5.05g; 0.05 mol) in ether (75 ml) was gradually added to a stirred solution of phosphorus oxychloride (7.65g; 0.05 mol) in ether (50 ml) at −10°. After 3h at 10°, triethylamine hydrochloride (6.8g) was filtered off and filtrate evaporated *in vacuo* to give the crude phosphorodichloridate (6.1g, 49%) which darkened and fumed in moist air. ν_{max} 1305–1270 br (P = O), 1035, 1010 (P—O—C) cm^{-1}.

Piperazino-N,N¹-Dicyclohexylphosphoramidic Dichloride (**21**)

Cyclohexylamine (0.71g; 0.0072 mol) was added dropwise to a stirred solution of piperazino-N,N¹-diphosphorodichloridate (0.57g; 0.0018 mol) in acetonitrile (45 ml) at 0°. After 1h at room temperature and 4° overnight, the precipitate was collected and washed with H_2O (200 ml). Recrystallisation from $CHCl_3$—Et_2O (2:1) gave the *diphosphoramidic dichloride* (0.7g, 88%), m.p. 206–210°. (Found: C, 42.9; H, 7.25; N, 12.3. $C_{16}H_{32}Cl_2N_4O_2P_2$ requires: C, 43.15; H, 7.2; N, 12.6%). ν_{max} 3200 (NH), 1245, 1235 (P = O) cm^{-1}. T.l.c. (Pr^iOH—$C_6H_5CH_3$—EtOAc—H_2O 5:1:2.5:1.25) showed a single spot, R_F 0.86.

Preparation of N-Substituted Phosphoramidates

The amine (2 mol) was added dropwise to a stirred solution of the appropriate phosphorochloridate (1 mol) in acetonitrile at room temperature. After stirring for 6h, the amine hydrochloride was filtered off and the filtrate was evaporated under reduced pressure. The residue was dissolved in ether, washed with H_2O, dried ($MgSO_4$), and the ether removed. The resultant product was crystallised from a suitable solvent to give the phosphoramidate.

N-Cyclohexyl O-Phenyl N¹-Pyrrolidinophosphoramidate (**8a**; Y = H, R^1 = C_6H_{11})

Reaction of O-phenyl N-pyrrolidinophosphorochloridate (4a; X = O, Y = H) (1 mol) with cyclohexylamine (2 mol) in acetonitrile for 6h at room temperature gave the *N-cyclohexylphosphoramidate* (81% from petroleum ether 60–80°) m.p. 70–71°. (Found: C, 62.5; H, 8.1; N, 9.0. $C_{16}H_{25}N_2O_2P$ requires: C, 62.3; H, 8.1; N, 9.1%). ν_{max} 3200 (NH), 1595, 1495 (arom C = C), 1230, 1200 (P = O), 920 (P—O—C) cm^{-1}.

N-Cyclohexyl O-p-Chlorophenyl N¹-Pyrrolidinophosphoramidate (**8a**; Y = Cl, R^1 = C_6H_{11})

Was obtained from petroleum ether (60–80°) as needles (70%), m.p. 74–76°. (Found: C, 56.5; H, 6.9; N, 8.4. $C_{16}H_{24}ClN_2O_2P$ requires: C, 56.1; H, 7.0; N, 8.2%). ν_{max} 3180 (NH), 1590, 1490 (arom C = C), 1225, 1205 (P = O), 940 (P—O—C) cm^{-1}.

N-Phenyl O-Phenyl N¹-Pyrrolidinophosphoramidate (**8a**; Y = H, R^1 = Ph)

Reaction with aniline was carried out in toluene and was completed by boiling under reflux for 1h. Recrystallisation from dichloromethane-petroleum ether (60–80°)-ethanol gave the *N-phenylphosphoramidate* as cream needles (61%), m.p. 122–123°. (Found: C, 63.7; H, 6.4; N, 9.3. $C_{16}H_{19}N_2O_2P$ requires: C, 63.6; H, 6.3; N, 9.3%). ν_{max} 3195, 3170 (NH), 1605, 1590, 1490 (arom C = C), 1210 (P = O), 920 (P—O—C) cm^{-1}.

N-Phenyl O-p-Chlorophenyl N¹-Pyrrolidinophosphoramidate (**8a**; Y = Cl, R^1 = H)

Was obtained (49%), m.p. 120–122°, from petroleum ether (60–80°). (Found: C, 56.8, H, 5.7; N, 8.1. $C_{16}H_{18}ClN_2O_2P$ requires: C, 57.1, H, 5.4; N, 8.3%). ν_{max} 3160, 3085 (NH), 1610, 1595, 1505, 1490 (arom C = C), 1220 (P = O), 930 (P—O—C) cm^{-1}.

1,4-Piperazinophosphoro N-Tetracyclohexylamidate (**20**)

Piperazine-1,4-diphosphorotetrachloridate (1 mol) was reacted with cyclohexylamine (8 mol) in acetonitrile at room temperature overnight. Removal of cyclohexylamine hydrochloride and crystallisation (benzene), gave the *tetracyclohexylamidate* (70%), m.p. 233–237°. (Found: C, 59.1; H, 9.8; N, 14.6. $C_{28}H_{56}N_6O_2P_2$ requires: C, 58.95; H, 9.8; N, 14.7%). T.l.c. (EtOAc-petroleum ether 60–80° 1:1) showed one spot, R_F 0.35. With Pr^iOH-$C_6H_5CH_3$-EtOAc—H_2O (5:1:2.5:1.25), one spot R_F 0.84. ^{31}P n.m.r. ($CDCl_3$) + 15.2.

The liquid phosphorodichloridates were characterised by preparation of the corresponding diphenylhydrazide derivatives. The phosphorodichloridate (0.01 mol) in acetonitrile (10 ml) was added to a solution of phenylhydrazine (0.04 mol) in acetonitrile (50 ml) at 0°. After 12h at 4° the precipitate was filtered off, washed with H_2O (200 ml) and stirred in dilute HCl (100 ml of 1%) for 1h. The solid diphenylhydrazide was purified by recrystallisation. The following compounds were obtained by this procedure:

Morpholinophosphoro N,N¹-Diphenylhydrazinothioate (**5b**; X = S) from ethanol (70%) m.p. 142–144°. (Found: C, 52.6; H, 5.8; N, 19.0. $C_{16}H_{22}N_5OPS$ requires: C, 52.9; H, 6.1; N, 19.3%). ^{31}P n.m.r. ($CDCl_3$) + 71.0.

β-Morpholinoethyl phosphoro-N,N¹-Diphenylhydrazide (**5c**; X = O) was obtained (52%) by chromatography (silica gel) m.p. 190–192°. (Found: C, 55.6; H, 7.0; N, 17.8. $C_{18}H_{26}N_5O_3P$ requires: C, 55.25; H, 6.7; N, 17.9%). N.m.r. ($CDCl_3$—$(CD_3)_2$ SO). δ: 0.94 t (2H, NCH_2), 2.55 t (2H, CH_2OP), 3.23 t (4H, CH_2NCH_2), 3.67 t (4H, CH_2OCH_2), 5.83 br (2H, 2 × P—N*H*), 6.27 br (2H, 2 × ArN*H*), 6.67–7.20 (10ArH). The signals at δ 5.83 and 6.27 were removed by D_2O treatment.

1-(N,N¹-Diphenylhydrazinophosphoro) piperazino-4-phosphoro-N,N¹-Diphenylhydrazide (**24**) from ethanol (45%), m.p. 179–182°. (Found: C, 55.7, H, 6.3, N, 21.7. $C_{30}H_{40}N_{10}O_3P_2$ requires: C, 55.4; H, 6.15; N, 21.5%). ^{31}P n.m.r. ($CDCl_3$) + 14.7. N.m.r. ($CDCl_3$—$(CD_3)_2SO$) δ: 0.95 (2H, NCH_2), 2.19 t (8 piperazine H), 2.60 t (2H, CH_2OP), 5.18 br (4H, 4 × P—NH, 6.13 br (4H, 4 ArNH), 6.60–7.26 (20ArH). The signals at δ 5.18 and 6.13 were removed after D_2O treatment.

Pyrrolidinophosphoro-N,N¹-Diphenylhydrazide (**5a**; X = O) (70% from ethanol), m.p. 183–185°. (Found: C, 57.8; H, 6.4; N, 21.4. $C_{16}H_{22}N_5OP$ requires: C, 58.0; H, 6.65; N, 21.15%).

Phosphorochloridates were also converted into the monophenylhydrazide derivatives by reaction with phenylhydrazine (2 mol) in acetonitrile for 6h at room temperature. The following were obtained by this method:

N-Morpholino-O-Phenylphosphoro N¹-Phenylhydrazide (**7b**; Y = H) (65% from ethanol), m.p. 138–140°. (Found: C, 57.6; H, 5.7; N, 12.9. $C_{16}H_{20}N_3O_3P$ requires: C, 57.7; H, 6.0; N, 12.6%). T.l.c. (Pr^iOH—$C_6H_5CH_3$—EtAc—H_2O 5:1:2.5:1.25) showed one spot, R_F 0.85. In EtOAc-petroleum ether 60–80° (1:1), one spot, R_F 0.54. ^{31}P n.m.r. ($CDCl_3$) + 6.0.

N,N¹-Dipyrrolidinophosphoro N¹¹-Phenylhydrazide (**16**; Y = NHNHPh) (72% from ethanol), m.p. 173–177°. (Found: C, 56.9; H, 7.75; N, 19.4. $C_{14}H_{23}N_4OP$ requires: C, 57.1; H, 7.8; N, 19.1%). T.l.c. (Pr^iOH—$C_6H_5CH_3$—EtAc—H_2O 5:1:2.5:1.25) showed one spot, R_F 0.75.

N-Phenyl N¹-Pyrrolidino phosphoro N¹¹-Phenylhydrazide (**6a**; R^1 = Ph) (56% from ethanol), m.p. 170–172°. (Found: C, 59.1; H, 6.5; N, 17.5. $C_{16}H_{21}N_4OP$ requires: C, 58.9; H, 6.6; N, 17.7%). T.l.c. (Pr^iOH—$C_6H_5CH_3$—EtOAc—H_2O 5:1:2.5:1.25) showed one spot, R_F 0.83.

O-Phenyl N-Pyrrolidinophosphoro N¹-Phenylhydrazide (**7a**; Y = H) (60% from toluene-petroleum ether), m.p. 111–112°. (Found: C, 60.6; H, 6.2; N, 13.4. $C_{16}H_{20}N_3O_2P$ requires: C, 60.6; H, 6.3; N, 13.25%).

O-p-Chlorophenyl N-Pyrrolidino N¹-Phenylhydrazide (**7a**; Y = Cl) (50% from methylene chloride-petroleum ether), m.p. 81–82°. (Found: C, 54.8; H, 5.5; N, 12.2. $C_{16}H_{19}ClN_3O_2P$ requires: C, 54.6; H, 5.4; N, 11.95%).

O-Phenyl N-Morpholino N¹-Piperidinophosphoraminothioate (**8b**; R^1 = *piperidino*, Y = H). This was obtained after two recrystallisations from petroleum ether (60–80°) as plates (31%), m.p. 56–59°. (Found: C, 55.65; H, 7.0; N, 9.1. $C_{15}H_{23}N_2O_2PS$ requires: C, 55.2; H, 7.1; N, 8.7%). T.l.c. (EtOAc-petroleum ether 60–80° 1:1) gave a single spot, R_F 0.71. Ms. showed the molecular ion (M^+, 32.6); and other major ions at 242 (M-piperidino), 233, 156, 149, 93, 86 (morpholine), 85, 84 (piperdine), 77. ^{31}P n.m.r. ($CDCl_3$) + 74.0.

Cyclohexylammonium O-Phenyl N-Morpholinophosphate (**9b**; Y = H)

O-Phenyl N-morpholinophosphorochloridate (**4b**; X = O, Y = H) (2g) was boiled under reflux with H_2O (50 ml) for 12h. Treatment with cyclohexylamine (2g), filtration and recrystallisation from acetone gave the *cyclohexylammonium* phosphate (46%), m.p. 295–299°. (Found: C, 56.0; H, 8.0; N. 8.2. $C_{16}H_{27}N_2O_4P$ requires: C, 56.1; H, 7.9; N, 8.2%). ν_{max} 2700, 2610, 2560 ($\overset{+}{N}H_3$), 1600, 1580, 1490 (arom C = C), 1170 (P = O), 935 (P—O—C), cm^{-1}. T.l.c. (Pr^iOH—$C_6H_5CH_3$—EtOAc—H_2O 5:1:2.5:1.25) showed a single spot, R_F 0.81.

O-p-Chlorophenyl N-Pyrrolinophosphoric Acid (**9a**; *Y = Cl*)

The acid was characterised as the barium salt (51%), m.p. 224–228°. (Found: C, 36.7; H, 4.2; N, 4.35. $C_{20}H_{24}Cl_2N_2O_6P_2Ba$ requires: C, 36.4; H, 3.6; N, 4.3%). ν_{max} 1225 (P = O), 925 (P—O—C) cm^{-1}.

P^1,P^2-Di N-Phenyl P^1,P^2-Di N^1-Pyrrolidinopyrophosphoramide (**10a**; R^1 = Ph)

N-Phenyl N¹-pyrrolinophosphorochloridate (**3a**; R^1 = Ph) (0.01 mol) was dissolved in pyridine (10 ml) and 1N-aqueous pyridine (5 ml) added with stirring. After 6h at room temperature, the solution was poured into ice-water (1l). The solid was collected, washed with water and recrystallised from acetonitrile-benzene (1:1) to give the *pyrophosphoramide* (27%), m.p. 163–167°. T.l.c. (Pr^iOH—$C_6H_5CH_3$—EtOAc—H_2O 5:1:2.5:1.25) showed a single spot, R_F 0.84. (Found: C, 55.1; H, 6.7; N, 12.85. $C_{20}H_{28}N_4O_3P_2$ requires: C, 55.3; H, 6.45; N, 12.9%). ν_{max} 3150, 3120 (NH), 1605, 1500 (arom C = C), 1235 (P = O), 930 (P—O—P) cm^{-1}. ^{31}P n.m.r. ($CDCl_3$) −2.3, −2.7.

Stability of P^1, P^2-Di N-Phenyl P^1,P^2-Di N^1-Pyrrolidinopyrophosphoramide (**10a**; R^1 = Ph)

(i) *With water* The pyrophosphoramide (0.5g) was boiled under reflux with H_2O (25 ml) for 30h. Cooling gave the unchanged pyrophosphoramide (0.45g), m.p. 164–168°.

(ii) *With ethanol* The pyrophosphoramide (0.5g) was boiled with ethanol (25 ml) for 24h, subsequent evaporation gave the unchanged pyrophosphoramide (0.45g), m.p. 163–165°.

(iii) *With aqueous dioxan* The pyrophosphoramide (**1g**) was boiled with 20% aqueous dioxan (40 ml) for 15h. The solvent was evaporated *in vacuo* and the residue dissolved in petroleum ether (60–80°) (30 ml). Treatment with aniline (1 ml) gave *N-phenyl N¹-pyrrolidino anilinium phosphate* (55% from acetonitrile-ether 1:2), m.p. 127–131°. (Found: C, 60.1; H, 6.7; N, 13.5. $C_{16}H_{22}N_3O_2P$ requires: C, 60.2; H, 6.9; N, 13.2%). ν_{max} 2640–2580, 1560–1530 ($\overset{+}{N}H_3$), 1605, 1500 (arom C = C), 1235 (P = O) cm^{-1}.

N-Pyrrolidino N¹-Phenylphosphoramidic Hydrazide (**11a**; R^1 = Ph)

N-Pyrrolidino N¹-phenylphosphoramidic chloride (**3a**; R′ = Ph) (2.45g; 0.01 mol) was added dropwise to hydrazine hydrate (2.5g; 0.05 mol) in acetonitrile (50 ml) at −10°. The mixture was stirred for 5h at 4°. Evaporation of the solvent *in vacuo* gave an oil which was extracted with ether (100 ml).

The extract was washed with H_2O (3 × 20 ml) dried ($MgSO_4$) and evaporated to give the *phosphoramidic hydrazide* as an oil (40%). (Found: C, 50.5; H, 7.3; N, 23.0. $C_{10}H_{17}N_4OP$ requires: C, 50.0; H, 7.1; N, 23.3%).

The oil was characterised by boiling with phenylisocyanate (1 mol equiv.) in petroleum ether (60–80°) for 3h to give the *N-phenylcarbamoyl derivative* (**12a**; R^1 = Ph) (69%), m.p. 195–198°. (Found: C, 56.6; H, 5.8; N, 19.65. $C_{17}H_{22}N_5O_2P$ requires: C, 56.8; H, 6.1; N, 19.5%).

N,N¹-Dipyrrolidinophosphoroazide (**16**; Y = N_3)

N,N¹-Dipyrrolidinophosphorochloridate (2.2g) dissolved in acetone (30 ml) was added to a solution of sodium azide (1.3g) in water (10 ml) at 40–50°. After 10h at room temperature, the mixture was concentrated and extracted with ether (150 ml). The extract was washed with H_2O (3 × 100 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give the *azide* as a pale yellow oil (1.48g, 64%). (Found: C, 42.0; H, 7.4; N, 29.95. $C_8H_{16}N_5OP$ requires: C, 41.9; H, 7.0; N, 30.6%). ν_{max} 2140 (N_3), 1260 (P = O) cm^{-1}.

N-Pyrrolidino N¹-Phenylphosphoramidic Azide (**13a**; R^1 = Ph)

Was similarly obtained from the amidic chloride (3a; R^1 = Ph) as an oil (36%). (Found: C, 48.1; H, 5.9; N, 27.6. $C_{10}H_{14}N_5OP$ requires: C, 47.8; H, 5.6; N, 27.9%). ν_{max}(liquid film) 3220–3160 (NH), 2140 (N_3), 1605, 1500 (arom C = C), 1235, 1220 (P = O) cm^{-1}.

N,N¹-Dipyrrolidinophosphorotriphenylphosphinimine (**17**)

N,N¹-Dipyrrolidinophosphoroazide (0.3g) was boiled under reflux with triphenylphosphine (0.34g) in benzene (30 ml) for 8 h. The solvent was evaporated *in vacuo* and the residue recrystallised from petroleum ether (60–80°)-tetrahydrofuran (2:1) to give the *triphenylphosphinimine* (0.28g, 46%) m.p. 125–129°. (Found: C, 67.2; H, 6.7; N, 9.0. $C_{26}H_{31}N_3OP_2$ requires: C, 67.4; H, 6.7; N, 9.1%). ν_{max} 3060 (arom C—H), 1205 (P = O) cm^{-1}. ^{31}P n.m.r. ($CDCl_3$) + 7.8 (N = PPh_3), +6.2 (P = O). T.l.c. (Pr^iOH—$C_6H_5CH_3$—EtOAc—H_2O 5:1:2.5:1.25) showed a single spot, R_F 0.64.

N-Pyrrolidino N¹-Phenylphosphoramidic Triphenylphosphinimine (**14a**; R^1 = Ph)

Was similarly prepared (50% from benzene), m.p. 163–160°. (Found: C, 69.4; H, 6.1; N, 9.0. $C_{28}H_{29}N_3OP_2$ requires: C, 69.3; H, 6.0; N, 8.7%). ν_{max} 3165 (NH), 1605, 1500 (arom C = C), 1220 (P = O) cm^{-1}.

O-Isobutyl O¹-Phenyl N-Pyrrolidinophosphoramidate (**15a**; Y = H)

O-Phenyl N-pyrrolidinophosphorochloridate (**4a**; X = O, Y = H) (4.9g, 0.02 mol) was boiled under reflux with triethylamine (2.02g, 0.02 mol) and isobutanol (1.48g; 0.02 mol) in toluene (75 ml) for 20h. The mixture was cooled and triethylamine hydrochloride was filtered off, and the filtrate evaporated under reduced pressure. The residue was dissolved in petroleum ether (60–80°, 150 ml), washed with H_2O (3 × 100 ml) and dried ($MgSO_4$). Evaporation and vacuum distillation gave the *phosphoramidate* as a liquid (3.8g, 67%) b.p. 139–141°/1.5 mm. (Found: C, 59.8; H, 7.9; N, 4.6. $C_{14}H_{22}NO_3P$ requires: C, 59.6; H, 7.8; N, 4.95). ν_{max} (liquid film) 1595, 1490 (arom C = C), 1280 (P = O), 1025 (P—O—C alip), 930 (P—O—C arom) cm^{-1}. Ms. showed the molecular ion (M^+, 283) and major fragment ions at 266, 208, 152, 134, 93, 77, 70 (pyrrolidine) 57, 41.

O-Isobutyl O¹-p-chlorophenyl N-Pyrrolidinophosphoramidate (**15a**; Y = Cl)

Was similarly prepared from the chloridate (**4a**; X = O, Y = Cl) (78%), b.p. 164–165°/1.5 mm. (Found: C, 52.7; H, 6.4; N, 4.2. $C_{14}H_{21}ClNO_3P$ requires: C, 52.9; H, 6.6; N, 4.4%). ν_{max} (liquid film) 3100, 3060 (arom C—H), 1595, 1485 (arom C = C), 1275 (P = O), 1040 (P—O—C alip), 920 (P—O—C arom) cm^{-1}. Ms. showed the molecular ion (M^+, 317) and other ions at 260, 241, 152, 128, 71, 70 (pyrrolidine), 57, 41.

1¹,2¹-Cyclohexylene 2-Phenoxy 2-Oxo-1,3,2-Dioxaphospholane (**26**)

A solution of 1,2-cyclohexanediol (**25**) (5.8g, 0.05 mol) and triethylamine (10.1g, 0.1 mol) in toluene (150 ml) was added to a stirred solution of phenylphosphorodichloridate (10.55g, 0.05 mol) in toluene (75 ml) at room temperature. The mixture was boiled under reflux for 6h, cooled and triethylamine hydrochloride filtered off. The filtrate was washed with H_2O (3 × 100 ml), $NaHSO_3$ (2 × 50 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give the *phenylphosphate* (**26**) as a pale yellow oil (6g, 45%). (Found: C, 56.4; H, 6.1; P, 12.0. $C_{12}H_{15}O_4P$ requires: C, 56.7; H, 5.9; P, 12.2%). T.l.c. (EtOAc-petroleum ether 60–80° 1:1) gave a single spot, R_F 0.59. ν_{max} (liquid film) 1280, 1240 (P = O), 1000, 925 (P—O—C) cm^{-1}. Ms. showed the molecular ion (M^+, 254), other ions were at 176, 174, 156, 140, 115, 99, 94, 83, 80.

1¹,2¹-Cyclohexylene 2¹-Chloro 2¹-thiono 1,3,2-Dioxaphospholane (**27**; Y = Cl)

1,2-Cyclohexanediol (**25**) (5.8g; 0.05 mol) and pyridine (7.9g, 0.1 mol) in benzene (75 ml) was added gradually to thiophosphoryl chloride (8.5g, 0.05 mol) in benzene (25 ml) at room temperature. The reaction mixture was boiled under reflux for 8h, cooled and pyridine hydrochloride filtered off. The filtrate was evaporated under reduced pressure to give the phosphorochloridothioate as a light brown oil (5.8g, 55%). Attempts to solidify the material by trituration from solvents failed. (Cf. lit.[19] m.p. 54–56°.) ν_{max} (liquid film) 990, 960, (P—O—C), 840 (P = S) cm^{-1}.

The phosphorochloridothioate (27; Y = Cl) was characterised by condensation with morpholine (2 mol) in ether, to give the N-*morpholino* derivative (27; Y = morpholino) (61% from ethanol), m.p. 122–124°. (Found: C, 45.4; H, 6.7; N, 5.3. $C_{10}H_{18}NO_3PS$ requires: C, 45.6; H, 6.8; N, 5.3%). ν_{max} 1020, 1010 d (P—O—C), 855 (P = S) cm^{-1}.

1,5-Diphenyl 3-(trans-4t-Butylcyclohexyloxy) perhydro-1,2,4,5,3-tetra-azaphosphorine P-Sulfide (**29**)

Aqueous formaldehyde (0.138g of 30%) was added to a stirred solution of *trans*-4-t-butylcyclohexyl N,N¹-diphenylhydrazinophosphorothioate[4] (**28**) (0.6g) in chloroform (20 ml). After stirring for 12h at room temperature, the mixture was left overnight, the solvent was evaporated under reduced pressure and

the residue crystallised from ethanol to give the *tetra-azaphosphorine P-sulphide* (**29**). (0.4g, 64%), m.p. 127–131°. (Found: C, 62.5; H, 7.6; N, 12.9. $C_{23}H_{33}N_4OPS$ requires: C, 62.2; H, 7.4; N, 12.6%). ν_{max} 3270 (NH), 1600, 1500 (arom C = C), P—O—C), 855 (P = S) cm^{-1}. N.m.r. ($CDCl_3$) δ: 0.84 s (9H, C $(CH_3)_3$), 1.00–2.22 (9H, cyclohexyl H), 4.27 m (1H, Ha), 4.55 br (2H, N—CH_2—N), 5.24 br (2H, 2NH), 7.20–7.58 (10ArH). The signal at δ 5.24 is removed by D_2O treatment. T.l.c. (xylene-MeOH 4:1) showed a single spot, R_F 0.38.

1-(trans-4-t-Butylcyclohexyl N-Phenylphosphoro)-2-Phenyl, 1,2-Diazahex-4-ene (**31**)

1,4-Dibromobut-2-ene (0.66g, 0.0025 mol) in benzene (30 ml) was gradually added to *trans*-4-t-butycyclohexyl N-phenyl N^1-phenylphosphoramidic hydrazide[4] (**30**). (1g, 0.0025 mol) in warm benzene (30 ml).

After addition, triethylamine (0.255g, 0.0025 mol) was added and the mixture boiled under reflux for 2h and further triethylamine (0.255g) added. After boiling for a further 10h, the mixture was cooled, washed with H_2O (3 × 50 ml), dried ($MgSO_4$), and evaporated. Recrystallisation of the residue from benzene-petroleum ether (60–80°) gave the *1,2-diazahex-4-ene* (**31**) (0.31g, 27%), m.p. 113–116°. T.l.c. (EtOAc-petroleum ether (60–80°) 1:1) showed a single spot, R_F 0.44. In Pr^iOH—$C_6H_5CH_3$—EtOAc—H_2O (5:1:2.5:1.25), a single spot R_F 0.74. (Found: C, 68.95; H, 8.3; N, 9.0. $C_{26}H_{36}N_3O_2P$ requires: C, 68.9; H, 7.95; N, 9.3%). ν_{max} 3170 (NH), 1220 (P = O) 1020, 1000 (P—O—C) cm^{-1}.

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