Alkylphenylphosphinic Amides: Formation of Stable, Crystalline Hydrochlorides, and Hydrolysis in Acidic Solution

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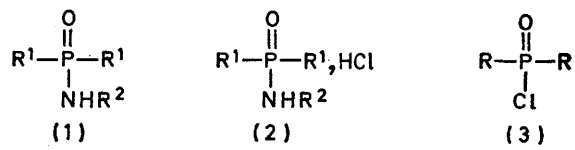
Alkylphenylphosphinic amides $RPhP(O)NH_2$, having R = cyclopropyl (8), 1-methylcyclopropyl (9), ethyl (15), isopropyl (16), and t-butyl (17), have been synthesised, and their reactions with anhydrous hydrogen chloride in benzene investigated. At room temperature amides (8) and (15) liberated ammonium chloride as expected, but (9), (16), and (17) formed stable, crystalline amide hydrochlorides $RPhP(O)NH_2,HCl$. The stability of these hydrochlorides is attributed to steric inhibition of nucleophilic attack at phosphorus by their relatively bulky alkyl groups. In accord with this explanation, the pseudo-first-order rate constants for hydrolysis of amides (9), (16), and (17) at pH 1·85 and 25·6° (10^5k_ψ = 2·48, 5·50, and <0·0032 s^{-1} respectively) are substantially smaller than those for (8) and (15) (10^5k_ψ = 111 and 153 s^{-1}).

ELLIS, SMITH, AND TRIPPETT [1] have shown that phosphinic amides (1) are converted into phosphinic chlorides (3) by the action of hydrogen chloride in an inert solvent. Although no intermediates were isolated in that investigation, the overall change can be pictured as



(1) (2) (3)

formation of an amide hydrochloride (2) which subsequently collapses to give the phosphinic chloride and amine hydrochloride ($R^2NH_3^+Cl^-$). In this paper we describe the isolation of some stable phosphinic amide hydrochlorides, and examine possible reasons for their stability.

RESULTS AND DISCUSSION

An interest in the influence of cyclopropyl groups on reactions occurring at an adjacent phosphorus centre led us to prepare the phosphinic acids (6) and (7) and derivatives of them, such as the amides (8) and (9). The acids were obtained by fusion of the known phosphine oxides (4) [2] and (5) [3] with sodium hydroxide,

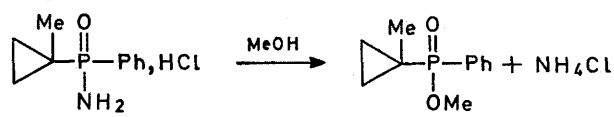
(4) X = Ph (5)
(6) X = OH (7)
(8) X = NH_2 (9)

following the general procedure of Horner and his co-workers.[4] The preferential, and seemingly exclusive, elimination of a phenyl group from the phosphine oxides is doubtless a consequence of the relative stability of the phenyl anion.

† Although the phosphinic amide (9) is itself soluble in water, the crystals which separate when the salt (0·25 mmol) is dissolved in water (0·6 ml) consist of the phosphinic acid (7) and the amide (9) in a ratio of *ca.* 9 : 1. Similar behaviour is observed when equally high concentrations of amide are hydrolysed in aqueous 1M-hydrochloric acid.

[1] K. Ellis, D. J. H. Smith, and S. Trippett, *J.C.S. Perkin I*, 1972, 1184.
[2] E. E. Schweizer, C. J. Berninger, and J. G. Thompson, *J. Org. Chem.*, 1968, **33**, 336.
[3] P. F. Cann, D. Howells, and S. Warren, *J.C.S. Perkin II*, 1972, 304.

When dry hydrogen chloride was passed into a dilute solution of 1-methylcyclopropyl(phenyl)phosphinic amide (9) in benzene at room temperature, a colourless solid separated almost immediately. It was obvious from the amount of material (0·425 g from 0·390 g of amide) that this solid could not simply be ammonium chloride, as had been anticipated, although its extreme insolubility in chloroform, benzene, and other aprotic solvents was suggestive of salt-like character. It did dissolve readily in chloroform containing methanol, and could be recovered in high yield by precipitation with ether. Although stable for many weeks at room temperature, the salt rapidly decomposed on dissolution in water, when the phosphinic acid (7) was formed (together with some unchanged amide †), or on addition of pyridine to a suspension of the salt in benzene, when pyridine hydrochloride and the parent amide (9) were obtained. Moreover, prolonged heating of a solution of the salt in methanol afforded the ester (11) and ammonium chloride. These observations, together with the results of elemental analysis, show the salt to be a phosphinic amide hydrochloride (10).

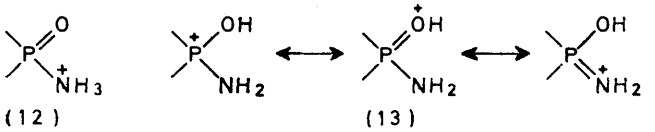


(10) (11)

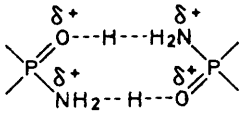
There has been considerable discussion as to whether phosphinic amides in solution are protonated predominantly at oxygen or at nitrogen, the evidence seeming to favour the latter in the cases so far examined.[5] Clearly it would be of interest to know the location of the proton in the crystalline hydrochloride (10), *i.e.* whether the salt is better represented by (12) or by (13). The i.r. spectrum of (10) in Nujol contains strong absorptions at 3220, 3160, 3060, and 1560 cm^{-1} of similar appearance to the N–H stretching and deformation bands [6,7] in the spectrum of the amide (9) at 3300, 3230, 3125, and 1570 cm^{-1}. Unlike the amide,

[4] L. Horner, H. Hoffmann, and H. G. Wippel, *Chem. Ber.*, 1958, **91**, 64.
[5] (*a*) P. Haake and T. Koizumi, *Tetrahedron Letters*, 1970, 4849; (*b*) T. Koizumi and P. Haake, *J. Amer. Chem. Soc.*, 1973, **95**, 8073; (*c*) K. E. DeBruin, A. G. Padilla, and D. M. Johnson, *Tetrahedron Letters*, 1971, 4279.
[6] D. E. C. Corbridge, in 'Topics in Phosphorus Chemistry,' eds. M. Grayson and E. J. Griffith, Interscience, New York, 1969, vol. 6, p. 235.
[7] R. A. Chittenden and L. C. Thomas, *Spectrochim. Acta*, 1966, **22**, 1449.

however, the salt also shows broad absorption in the region 2800—1800 cm^{-1} (maxima at *ca.* 2380, 2140, and 2070 cm^{-1}), comparable with the O–H stretching bands [6,8] in the spectrum of the phosphinic acid (7). Together with the disappearance of the very strong P=O absorption of the amide at 1170 and 1155 cm^{-1}, this might be thought to indicate *O*-protonation. However, the spectrum of the hydrochloride does contain weaker absorption at 1140 and 1120 cm^{-1} which might be due to P=O, and with the evidence presently available we do not feel able to make a confident choice between structures (12) and (13). Indeed, it might be that the extra proton is more or less equally shared between oxygen and nitrogen in a structure such as (14).



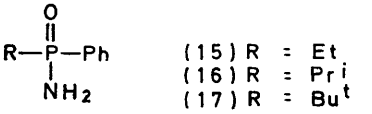
(12) (13)



(14)

A further point of interest is the remarkable stability of the phosphinic amide hydrochloride (10), especially in view of the known [5b,9] ease with which P–N bonds are cleaved in acidic media [*e.g.*, the second-order rate constant for the acid-catalysed hydrolysis of $Ph_2P(O)NH_2$ at 29·2° [5b] is *ca.* $3{\cdot}5 \times 10^4$ times greater than that for $PhCONH_2$ at 52·4° [10]]. While the ability of the cyclopropyl group to stabilise positive charge may be a contributing factor the contrasting behaviour of the amides (8) and (9) suggests that it is not of prime importance. Thus (8) reacts rapidly (<10 min) at room temperature with hydrogen chloride in benzene to give cyclopropyl(phenyl)phosphinic chloride and ammonium chloride, whereas the hydrochloride of amide (9) can be recovered in 95% yield after 15 h under similar conditions. An alternative explanation for the stability of the hydrochloride (10) is that the bulk of the 1-methylcyclopropyl group hinders its collapse by nucleophilic attack of chloride ion on phosphorus. To test this idea we have prepared the alkylphenylphosphinic amides (15)—(17) in which the size of the alkyl group varies widely. On treatment with hydrogen chloride in benzene, the isopropyl- and t-butyl-phosphinic amides both gave stable crystalline amide hydrochlorides whereas ammonium chloride was rapidly liberated in the case of the less hindered ethylphenylphosphinic amide (15).

With a view to gaining a more quantitative idea of the steric effects of the alkyl groups in alkylphenylphosphinic amides, we have examined briefly the acid-catalysed hydrolysis of the amides (8), (9), and (15)—(17). Because hydrolysis was accompanied by only slight



(15) R = Et
(16) R = Pr^i
(17) R = Bu^t

changes in absorption spectra, the disappearance of the phosphinic amides was followed by g.l.c. This necessitated the use of an internal standard. Benzamide satisfied two important requirements of the standard, namely adequate solubility in the aqueous reaction medium and a suitable g.l.c. retention time. As regards its stability, extrapolation from published data [10] suggested that hydrolysis of benzamide should be negligible ($t_{\frac{1}{2}} > 10$ years) under the mild reaction conditions, and this was confirmed by control experiments. Accordingly, dilute solutions (*ca.* 0·010M) of the phosphinic amides in an aqueous HCl–NaOAc buffer of pH 1·85 containing benzamide were maintained at 25·6°, and samples were periodically withdrawn, quenched with K_2CO_3 (to give pH *ca.* 9), and analysed by direct injection into the gas chromatograph. The concentration of unchanged phosphinic amide (t_R 3—4 min) in each sample was determined by comparison of its peak area with the area of the benzamide (t_R 1·2 min) peak. For the phosphinic amides (8), (9), (15), and (16), plots of log[phosphinic amide] *vs.* time gave satisfactory straight lines, from the slopes of which the values of the pseudo-first-order rate constants (k_ψ) were deduced (Table).

Hydrolysis of alkylphenylphosphinic amides at 25·6° and pH 1·85 in aqueous HCl buffered with NaOAc

	$RPhP(O)NH_2$	$10^5 k_\psi/s^{-1}$
(8)	R = Cyclopropyl	111
(9)	R = 1-Methylcyclopropyl	2·48
(15)	R = Et	153
(16)	R = Pr^i	5·50
(17)	R = Bu^t	<0·0032

The possible error in k_ψ is estimated to be ±10% for (8), (9), and (16), and ±15% for (15), the lack of precision resulting primarily from the poor shape of the g.l.c. peaks for low concentrations of phosphinic amide. Phenyl-t-butylphosphinic amide (17) was less than 20% hydrolysed after 82 days. Control experiments showed that neither ethylphenylphosphinic amide (and by implication the other phosphinic amides) nor benzamide suffered significant decomposition on g.l.c. analysis of these mildly basic aqueous solutions.*

Diphenylphosphinic amide has been shown to hydrolyse by an associative (*A*2) mechanism, in which nucleophilic attack of water on the protonated substrate is rate-determining.[5b,9c] Assuming that alkylphenylphosphinic amides react by similar mechanisms, their relative rates of hydrolysis should reflect the extent

* The low reactivity of $PhCONH_2$ and $Ph_2P(O)NH_2$ towards hydrolysis in alkaline media has previously been noted.[5b]

[8] J. T. Braunholtz, G. E. Hall, F. G. Mann, and N. Sheppard, *J. Chem. Soc.*, 1959, 868.

[9] (*a*) D. A. Tyssee, L. P. Bausher, and P. Haake, *J. Amer. Chem. Soc.*, 1973, **95**, 8066; (*b*) P. Haake and D. A. Tyssee, *Tetrahedron Letters*, 1970, 3513; (*c*) P. Haake and T. Koizumi, *ibid.*, p. 4845; (*d*) G. Tomaschewski and G. Kühn, *J. prakt. Chem.*, 1968, **38**, 222.

[10] I. Meloche and K. J. Laidler, *J. Amer. Chem. Soc.*, 1951, **73**, 1712.

to which the alkyl groups sterically inhibit nucleophilic attack at phosphorus in the protonated amides. Granted that the differing electronic effects of the alkyl groups may have some influence, both on the equilibrium concentration of protonated amide and on its reactivity towards water, there can be little doubt that the large variation in the value of k_ψ for hydrolysis (see Table) is primarily a consequence of the varying steric effect of the alkyl groups. The similar reactivity of the amides (15) and (8), having ethyl and cyclopropyl groups, and of (16) and (9), having isopropyl and 1-methylcyclopropyl groups, is noteworthy, and these results also emphasise the extremely labile nature of the (unhindered) P–N bond in acidic media. Of immediate concern is the marked difference in reactivity between those three amides [(9), (16), and (17)] which formed isolable hydrochlorides and the two less hindered amides [(8) and (15)] which did not. We conclude that the stability of the hydrochloride formed by an alkylphenylphosphinic amide is a function of the size of the alkyl group. Although the detailed structures of these salts have not been established, it is hoped that further work will shed light on this problem and, indeed, on the whole question of *O*- and *N*-protonation of phosphinic amides.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were recorded with Perkin-Elmer 237 and 257 instruments, and n.m.r. spectra with a Varian T-60 spectrometer and tetramethylsilane as internal standard. G.l.c. analyses were performed on a Pye 104 flame ionisation chromatograph fitted with a 1·5 m × 4 mm i.d. glass column packed with 3% silicone OV 17 on silanised 100—120 mesh diatomite C 'Q'. Petroleum refers to the fraction b.p. 60—80° unless otherwise indicated.

Cyclopropyldiphenylphosphine Oxide (4).—A solution of triphenylphosphine (78·6 g, 0·30 mol) and 1,3-dibromopropane (60·6 g, 0·30 mol) in xylene (170 ml) was stirred under nitrogen at 130° for 22 h. The precipitate was washed with benzene and crystallised from chloroform–ethyl acetate (1 : 1) to give 3-bromopropyltriphenylphosphonium bromide (120·4 g, 0·26 mol, 87%), m.p. 229—230° (lit.,[11] 229—230°) which was converted into cyclopropyltriphenylphosphonium bromide (75%) by cyclisation with sodium hydride in tetrahydrofuran–dimethylformamide following the procedure of Schweizer, Berninger, and Thompson.[2] The product (74·7 g, 0·195 mol) was then hydrolysed by heating (*ca.* 80°) with 20% sodium hydroxide (1·95 l) for 45 min. The cooled reaction mixture was extracted with chloroform (600 and 3 × 300 ml) and the extracts were dried (Na_2SO_4) and concentrated to *ca.* 100 ml. Addition of petroleum (500 ml) afforded cyclopropyldiphenylphosphine oxide (44·4 g, 0·183 mol, 94%), m.p. 131—132° (lit.,[2] 132—133°).

1-*Methylcyclopropyldiphenylphosphine Oxide* (5).—Cyclopropyldiphenylphosphine oxide (30·1 g, 0·124 mol) was methylated using n-butyl-lithium and methyl toluene-*p*-sulphonate in tetrahydrofuran, following the procedure of Cann, Howells, and Warren.[3] Crystallisation of the crude product from ether–petroleum (1 : 1; 300 ml) gave stout, pale yellow needles (14·1 g), the i.r. spectrum of which contained a weak absorption at 895 cm^{-1} attributable to unchanged cyclopropyldiphenylphosphine oxide. Chromatography on a short column of neutral alumina (elution with ether) gave almost colourless material which on recrystallisation from ether–petroleum (4 : 1; 150 ml) afforded colourless 1-methylcyclopropyldiphenylphosphine oxide (12·4 g, 0·0485 mol, 39%), m.p. 100—102° (lit.,[3] 95—96°), having negligible i.r. absorption at 895 cm^{-1}.

Ethyldiphenylphosphine Oxide.—The phosphonium salt obtained by boiling a solution of triphenylphosphine (26·2 g, 0·100 mol) and ethyl iodide (18·7 g, 0·120 mol) in toluene (100 ml) for 7 h was hydrolysed by stirring with 20% aqueous sodium hydroxide (1 l) on a steam-bath for 1 h. The cooled reaction mixture was extracted with chloroform (4 × 100 ml) and the combined extracts were concentrated to 50 ml. Addition of petroleum (200 ml) gave crystals of ethyldiphenylphosphine oxide (20·2 g, 0·088 mol, 88%), m.p. 117—119° (lit.,[4] 121°).

Isopropyldiphenylphosphine Oxide.—A sample, m.p. 141—145° (lit.,[12] 145—146°), was similarly prepared by hydrolysis of isopropyltriphenylphosphonium iodide.[13]

Cyclopropylphenylphosphinic Acid (6).—Following the general procedure of Horner, Hoffmann, and Wippel,[4] a mixture of cyclopropyldiphenylphosphine oxide (4·11 g, 17·0 mmol) and sodium hydroxide (1·36 g, 34·0 mmol) was ground to a fine powder and heated under nitrogen. The temperature of the oil-bath was raised slowly (over *ca.* 1 h) to 220° and maintained at 220—230° for 2 h, during which time a small amount (*ca.* 0·9 ml) of colourless liquid (benzene) distilled off. After cooling, the bulk of the material was dissolved in water (30 ml), chloroform (20 ml) was added, and the layers were separated. Unchanged phosphine oxide (0·36 g) was recovered from the chloroform layer. The aqueous portion was acidified with 12M-hydrochloric acid and extracted with chloroform (15 and 3 × 10 ml), and the extracts were concentrated to a colourless solid. Crystallisation from ethyl acetate (12 ml) afforded *cyclopropylphenylphosphinic acid* (2·45 g, 13·5 mmol, 79%; based on phosphine oxide consumed, 87%), m.p. 103—105°, $\nu_{max.}$ ($CHCl_3$) 3000—2000vbr (shallow maxima at *ca.* 2650, 2260, and 2150, OH), 1650 (OH def.), and 1165 and 1130 cm^{-1} (P=O), δ ($CDCl_3$) 12·68 (1H, s, OH), 8·2—7·3 (5H, m, Ph), and 1·3—0·5 (5H, m, cyclopropyl). The analytical sample had m.p. 105—106° (Found: C, 59·2; H, 6·1; P, 17·3. $C_9H_{11}O_2P$ requires C, 59·3; H, 6·1; P, 17·0%) after recrystallisation from ethyl acetate.

The following were prepared from the appropriate alkyldiphenylphosphine oxides in the same way.

1-*Methylcyclopropyl(phenyl)phosphinic acid* (7) (77%; based on phosphine oxide consumed, 90%), m.p. 121—122° (from ethyl acetate), $\nu_{max.}$ (Nujol) *ca.* 2650, 2260, and 2120 (all br and shallow, OH), 1725 (OH def.), and 1170, 1150, and 1135 cm^{-1} (P=O), δ ($CDCl_3$) 13·03 (1H, s, OH), 8·2—7·3 (5H, m, Ph), and 1·4—0·25 [7H, including δ 1·08 (3H, d, J_{PH} 13·5 Hz, methylcyclopropyl)] (Found: C, 61·2; H, 6·6; P, 15·5. $C_{10}H_{13}O_2P$ requires C, 61·2; H, 6·7; P, 15·8%).

Ethylphenylphosphinic acid (78%; based on phosphine oxide consumed, 89%), m.p. 79—80° (from ethyl acetate) (lit.,[4] 78—80°).

Isopropylphenylphosphinic acid (72%; based on phosphine oxide consumed, 86%), m.p. 83—84° (from petroleum–

[11] Neth. P. Appl. 6,411,861/1965 (*Chem. Abs.*, 1965, **63**, 16,366*a*).

[12] M. Epstein and S. A. Buckler, *Tetrahedron*, 1962, **18**, 1231.

[13] G. Wittig and D. Wittenberg, *Annalen*, 1957, **606**, 1.

benzene, 7 : 1) (lit.,[14] 88—89°). In this preparation a temperature of 280° was used. A sample of the product had m.p. 87—88° after further crystallisation.

Cyclopropylphenylphosphinic Chloride.—A solution of cyclopropylphenylphosphinic acid (2·37 g, 13·0 mmol) and thionyl chloride (3·1 g, 26·0 mmol) in benzene (18 ml) was stirred and boiled under reflux in an atmosphere of dry nitrogen for 2 h. Volatile material was removed on a rotary evaporator and benzene (10 ml) added to, and then evaporated from, the residue to remove last traces of thionyl chloride. Distillation (bulb–tube) gave *cyclopropylphenylphosphinic chloride* (2·42 g, 12·1 mmol, 93%), b.p. 95—100° (oven temp.) at 0·05 mmHg, $\nu_{max.}$ (liquid film) 1240 and 1225 cm^{-1} (P=O), δ (CCl_4) 8·2—7·3 (5H, m, Ph) and 1·75—0·6 (5H, m, cyclopropyl) (Found: C, 54·2; H, 4·8; Cl, 17·7. $C_9H_{10}ClOP$ requires C, 53·9; H, 5·0; Cl, 17·7%).

The following compounds were similarly obtained from the appropriate phosphinic acids.

1-*Methylcyclopropyl(phenyl)phosphinic chloride* (100%), b.p. 110° (oven temp.) at 0·3 mmHg, $\nu_{max.}$ (liquid film) 1260 and 1220 cm^{-1}, δ (CCl_4) 8·2—7·4 (5H, m, Ph), 1·6—1·1 (2H, m, cyclopropyl), 1·27 (3H, d, J_{PH} 15·5 Hz), and 0·9—0·5 (2H, m, cyclopropyl) (Found: C, 56·2; H, 5·8; Cl, 15·9. $C_{10}H_{12}ClOP$ requires C, 56·0; H, 5·6; Cl, 16·5%).

Ethylphenylphosphinic chloride (96%), b.p. 125—135° (oven temp.) at 0·3 mmHg (lit.,[15] 155—156° at 9 mmHg).

Isopropylphenylphosphinic chloride (96%), b.p. 120—130° (oven temp.) at 0·5 mmHg (lit.,[16] 116—121° at 3 mmHg).

Cyclopropylphenylphosphinic Amide (8).—A solution of cyclopropylphenylphosphinic chloride (1·68 g, 8·4 mmol) in ether (10 ml) was dripped into a stirred, ice-cold solution of ammonia (25 mmol) in anhydrous ethanol (5 ml). After 1 h at room temperature, the filtered reaction mixture was concentrated to an oil which was dissolved in chloroform (20 ml), washed with 5% sodium hydrogen carbonate solution (10 ml), dried (Na_2SO_4), and evaporated. The resulting solid was crystallised from benzene (12 ml) to give *cyclopropylphenylphosphinic amide* (1·17 g, 6·5 mmol, 78%), m.p. 118—119°, $\nu_{max.}$ (Nujol) 3330, 3240, and 3125 (NH_2), 1555 (NH_2 def.), and 1175 cm^{-1} (P=O), δ ($CDCl_3$) 8·3—7·2 (5H, m, Ph), 3·50br (2H, s, NH_2), and 1·2—0·5 (5H, m, cyclopropyl) (Found: C, 59·6; H, 6·55; N, 7·8. $C_9H_{12}NOP$ requires C, 59·65; H, 6·7; N, 7·7%).

The following compounds were prepared from the appropriate phosphinic chlorides by the same procedure.

1-*Methylcyclopropyl(phenyl)phosphinic amide* (9) (84%), m.p. 125—127° (from benzene), $\nu_{max.}$ (Nujol) 3300, 3230, 3125, 1570, 1170, and 1155 cm^{-1}, δ ($CDCl_3$) 8·2—7·2 (5H, m, Ph), 3·50br (2H, s, NH_2), 1·4—1·0 (2H, m, cyclopropyl), 1·10 (3H, d, J_{PH} 13 Hz, Me), and 0·6—0·3 (2H, m, cyclopropyl) (Found: C, 61·7; H, 7·2; N, 7·1. $C_{10}H_{14}NOP$ requires C, 61·5; H, 7·2; N, 7·2%), using a 2 h reaction time.

Ethylphenylphosphinic amide (15) (65%), m.p. 105—109° (from benzene), $\nu_{max.}$ (Nujol) 3290, 3225, 3115, 1585, and 1170 cm^{-1}, δ ($CDCl_3$) 8·2—7·3 (5H, m, Ph), 3·43br (2H, s, NH_2), 2·25—1·5 (2H, m, CH_2), and 1·35—0·7 (3H, m, Me) (Found: C, 57·0; H, 7·4; N, 8·5. $C_8H_{12}NOP$ requires C, 56·8; H, 7·15; N, 8·3%).

Isopropylphenylphosphinic amide (16) (52%), m.p. 129—131° (from benzene), $\nu_{max.}$ (Nujol) 3290, 3225, 3115, 1570, and 1175 cm^{-1}, δ ($CDCl_3$) 8·2—7·2 (5H, m, Ph), 3·37br (2H, s, NH_2), 2·4—1·7 (1H, m, CH), 1·10 (3H, dd, J_{PH} 17, J_{HH} 6·5 Hz, Me), and 1·02 (3H, dd, J_{PH} 17, J_{HH} 6·5 Hz, Me) (Found: C, 59·35; H, 7·4; N, 7·5. $C_9H_{14}NOP$ requires C, 59·0; H, 7·7; N, 7·65%) using an overnight reaction period.

Chloro(phenyl)-t-butylphosphine.[17]—An ethereal solution of the Grignard reagent obtained from t-butyl chloride (0·50 mol) and magnesium (0·50 g atom) was added over 1 h to a stirred solution of dichloro(phenyl)phosphine (44·8 g, 0·25 mol) in ether (60 ml) at −20°. After stirring at room temperature for 1 h, solid matter was removed by filtration and the filtrate concentrated to an oil which on distillation gave chloro(phenyl)-t-butylphosphine (40·5 g, 0·20 mol, 80%), b.p. 133—137° at 30 mmHg (lit.,[17] 81—82° at 0·8 mmHg). The n.m.r. spectrum (CCl_4) contained the expected[17] doublet at δ 0·99 (J_{PH} 14 Hz) but also a small doublet (integral ratio 17 : 1) at δ 1·21 (J_{PH} 19 Hz) due to an impurity. This material was used without further purification.

Phenyl-t-butylphosphinic Amide (17).—A solution of chloro(phenyl)-t-butylphosphine (3·01 g, 15·0 mmol) in ethanol-free chloroform (10 ml) was added over 10 min to a stirred solution of ammonia (1·5 g) in chloroform (45 ml) at −20°. The filtered reaction mixture was then dripped into ice-cold 30% hydrogen peroxide (50 ml) with vigorous stirring. After a further 30 min at room temperature the layers were separated, the aqueous portion extracted with chloroform (2 × 15 ml), and the combined chloroform extracts were washed with water and concentrated to an oil which was then purified. A solution of the oil in dry benzene (100 ml) was stirred at room temperature while dry hydrogen chloride was bubbled in for 30 min. The white solid (amide hydrochloride) which separated was collected and suspended in dry chloroform (50 ml), and pyridine (3 ml) in chloroform (5 ml) was added dropwise. Ether (150 ml) was then added, the remaining insoluble matter (pyridine hydrochloride) removed by filtration, and the filtrate concentrated to an oil which was dissolved in chloroform (30 ml) and washed with water and 5% potassium carbonate solution. Evaporation of the solvent and crystallisation of the residue from ether–petroleum (1 : 10; 22 ml) gave the phosphinic amide (0·83 g, 4·2 mmol, 28%), δ ($CDCl_3$) 8·2—7·3 (5H, m, Ph), 3·17br (2H, s, NH_2), and 1·10 (9H, d, J_{PH} 16 Hz, Bu^t). Because this material was not sharp-melting, it was chromatographed on neutral alumina. Elution with ether–methanol (25 : 1) gave a solid which was crystallised from petroleum and dried at 0·3 mmHg for 3 h. The resulting *phenyl-t-butylphosphinic amide* had m.p. 85—86°, $\nu_{max.}$ (Nujol) 3380, 3200, and 3120 (NH_2), 1580 (NH_2 def.), and 1160 cm^{-1} (P=O) (Found: C, 60·9; H, 8·3; N, 6·7. $C_{10}H_{16}NOP$ requires C, 60·9; H, 8·2; N, 7·1%). The n.m.r. spectrum was identical with that obtained previously.

Methyl 1-*Methylcyclopropyl(phenyl)phosphinate* (11).—A suspension of 1-methylcyclopropyl(phenyl)phosphinic acid (0·196 g, 1·00 mmol) in ether (5 ml) was stirred and cooled while an excess of diazomethane in ether was added. The oil remaining after evaporation of volatile material was

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distilled (bulb–tube) to give *methyl 1-methylcyclopropyl(phenyl)phosphinate* (0·159 g, 0·76 mmol, 76%), b.p. 100—105° (oven temp.) at 0·1 mmHg, $\nu_{max.}$ (liquid film) 1215 and 1180 cm^{-1} (P=O), δ (CCl_4) 8·0—7·4 (5H, m, Ph), 3·66 (3H, d, J_{PH} 10·5 Hz, OMe), and 1·4—0·3 [7H, including δ 1·11 (3H, d, J_{PH} 13 Hz, methylcyclopropyl)] (Found: C, 63·3; H, 7·25. $C_{11}H_{15}O_2P$ requires C, 62·85; H, 7·2%).

Reaction of 1-Methylcyclopropyl(phenyl)phosphinic Amide with Hydrogen Chloride.—The phosphinic amide (0·390 g, 2·00 mmol) was dissolved with warming in dry benzene (15 ml) and the solution allowed to cool almost to room temperature. Dry hydrogen chloride was bubbled slowly through the solution for 10 min to give crystals of *1-methylcyclopropyl(phenyl)phosphinic amide hydrochloride* (0·425 g, 1·84 mmol, 92%), m.p. 112—114° (some softening at *ca.* 100°), $\nu_{max.}$ (Nujol) 3220, 3160, 3060, 2800—1800 (vbr, with maxima at *ca.* 2380, 2140, and 2070), 1560, 1140, and 1120 cm^{-1}; δ ($CDCl_3$–MeOH; 6 : 1) 8·2—7·4 (5H, m, Ph) and 1·55—0·4 [7H, including δ 1·19 (3H, d, J_{PH} 14·5 Hz, methylcyclopropyl)] (Found: C, 51·6; H, 6·6; Cl, 15·8; N, 6·1. $C_{10}H_{15}ClNOP$ requires C, 51·8; H, 6·5; Cl, 15·3; N, 6·05%). Addition of ether to a $CHCl_3$–MeOH solution similar to that used for the n.m.r. spectrum reprecipitated the hydrochloride (74% recovery).

When hydrogen chloride was bubbled through a suspension of the amide hydrochloride (46·7 mg, 0·20 mmol) in benzene (2 ml) for 1 h and the mixture left at room temperature for a further 14 h, unchanged (m.p. and i.r. spectrum) phosphinic amide hydrochloride (95%) was recovered by filtration.

Reaction of Phenyl-t-butylphosphinic Amide with Hydrogen Chloride.—This reaction under the same conditions yielded *phenyl-t-butylphosphinic amide hydrochloride* (100%), m.p. 126—130°, $\nu_{max.}$ (Nujol) 3240, 3170, 3080, 2800—1800 (vbr, with maxima at *ca.* 2420, 2200, and 2040 cm^{-1}), 1570, 1140, and 1120 cm^{-1} (Found: C, 51·5; H, 7·3; Cl, 14·75; N, 6·1. $C_{10}H_{17}ClNOP$ requires C, 51·4; H, 7·3; Cl, 15·2; N, 6·0%).

Reaction of Cyclopropylphenylphosphinic Amide with Hydrogen Chloride.—Under the same conditions this reaction gave a precipitate having an i.r. spectrum essentially the same as that of authentic ammonium chloride. Evaporation of the supernatant liquid afforded (impure) cyclopropylphenylphosphinic chloride (91%), identified by comparison of its i.r. and n.m.r. spectra with those of the authentic material, and by hydrolysis (0·5M-NaOH) to cyclopropylphenylphosphinic acid, m.p. 106—107°.

Reaction of Ethylphenylphosphinic Amide with Hydrogen Chloride.—This similarly gave a precipitate of ammonium chloride (97%) and a product which on alkaline hydrolysis was converted into ethylphenylphosphinic acid, m.p. 80—81°.

Reaction of Isopropylphenylphosphinic Amide with Hydrogen Chloride.—The phosphinic amide (0·055 g, 0·30 mmol) was dissolved in warm, dry benzene (2·8 ml), the solution was cooled in an ice-bath, and dry hydrogen chloride immediately bubbled through. After 5 min crystals of *isopropylphenylphosphinic amide hydrochloride* (0·053 g, 0·24 mmol, 80%), m.p. 74—76°, $\nu_{max.}$ (Nujol) 3240, 3170, 3080, 2800—1800 (vbr, with maxima at *ca.* 2420, 2160, and 2080), 1570, and 1130 cm^{-1} (Found: C, 49·0; H, 6·9; N, 6·5. $C_9H_{15}ClNOP$ requires C, 49·2; H, 6·9; N, 6·4%) were collected by filtration. This compound was noticeably hygroscopic. In preliminary experiments using more dilute solutions at room temperature with a longer reaction time, the only solid which could be isolated was ammonium chloride.

Reactions of 1-Methylcyclopropyl(phenyl)phosphinic Amide Hydrochloride.—(a) *With water.* The salt (57·9 mg, 0·25 mmol) was dissolved in water (0·6 ml) and the clear solution kept at room temperature. Crystals began to form after 10 min. After 2 h the crystals (48·0 mg), m.p. 101—104°, were collected and found to have an i.r. spectrum similar, but not identical, to that of 1-methylcyclopropyl(phenyl)phosphinic acid. A portion of the product was treated with diazomethane and examined by g.l.c. (column temp. 210°); two peaks having the same retention times as methyl 1-methylcyclopropyl(phenyl)phosphinate and 1-methylcyclopropyl(phenyl)phosphinic amide (ratio *ca.* 9 : 1) were observed. From the bulk of the reaction product, the phosphinic acid (82%) and amide (10%) were isolated and characterised by comparison (m.p., i.r., and n.m.r.) with authentic specimens. Repeated experiments showed the behaviour described above to be reproducible. A similar mixture of phosphinic acid and amide, m.p. 101—104°, crystallised from solution when 1-methylcyclopropyl(phenyl)phosphinic amide (0·25 mmol) was hydrolysed in aqueous 1M-hydrochloric acid (0·6 ml).

(b) *With pyridine.* A suspension of the salt (58·0 mg, 0·25 mmol) in benzene (2 ml) was stirred at room temperature while a solution of pyridine (24 mg, 0·3 mmol) in benzene (1 ml) was added dropwise. Pyridine hydrochloride, identified by its i.r. spectrum, was removed by filtration. Concentration of the filtrate gave crude 1-methylcyclopropyl(phenyl)phosphinic amide (45·5 mg, 0·23 mmol, 93%), identified by comparison of its i.r. and n.m.r. spectra with those of the authentic material, which after washing with 5% aqueous potassium carbonate and crystallisation from benzene afforded the pure phosphinic amide, m.p. and mixed m.p. 125—126°.

(c) *With methanol.* A solution of the salt (69·5 mg, 0·30 mmol) in anhydrous methanol (1·5 ml) was heated in a stoppered tube at 65° for 142 h. Volatile material was removed by evaporation and the residue was extracted with ether, leaving ammonium chloride (81%). Distillation of the ether extract gave methyl 1-methylcyclopropyl(phenyl)phosphinate (29·0 mg, 0·14 mmol, 46%), b.p. 100—110° (oven temp.) at 0·1 mmHg, i.r. and n.m.r. spectra identical with those of the authentic material.

Rates of Hydrolysis of Phosphinic Amides.—Solutions of the phosphinic amides (*ca.* 0·010M) in aqueous HCl (0·212M) buffered at pH 1·85 with NaOAc (0·200M) and containing benzamide (0·008M) as internal g.l.c. standard were kept in a thermostatted bath at 25·6 ± 0·2°. Samples (0·3 ml) were withdrawn and quenched by addition to potassium carbonate (10 mg). Except in the case of amide (17), for which reaction was <20% complete after 82 days, 9—15 samples were taken over periods of 2—4·5 half-lives. The quenched samples were analysed by direct injection into the chromatograph (column temp. 232°). The stability of benzamide under the reaction conditions was confirmed by allowing a hydrolysis to proceed for 270 h, extracting with ether, and treating the extract with diazomethane; g.l.c. examination revealed the absence of methyl benzoate (0·1% hydrolysis of benzamide to benzoic acid would have led to a detectable peak).

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