Evidence for Elimination–Addition Mechanisms in the Reactions of *N*-t-Butyl-*P*-alkylphosphonamidic Chlorides with t-Butylamine and Isopropylamine [1]

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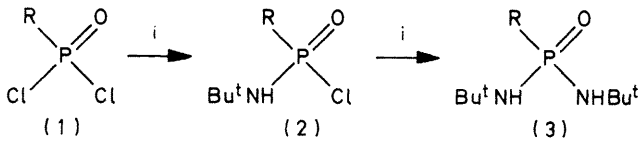
The phosphonamidic chlorides $RP(O)(Cl)NHBu^t$ (2; R = Me, Et, or Pr^i) can be prepared directly from the corresponding phosphonic dichlorides $RP(O)Cl_2$ and t-butylamine. t-Butylphosphonic dichloride reacts with t-butylamine only at high temperatures and then gives the diamide $Bu^tP(O)(NHBu^t)_2$ as the only detectable product. The phosphonamidic chloride (2; R = Bu^t) can, however, be prepared indirectly by oxidation (SO_2Cl_2) of $Bu^tP(Cl)NHBu^t$ obtained from Bu^tPCl_2 and t-butylamine. The phosphonamidic chlorides react with t-butylamine and isopropylamine in dichloromethane at rates that are unusually insensitive to steric effects in both the substrate and the amine; the slowest reaction [(2; R = Bu^t) + Bu^tNH_2] is only 30 times slower than the fastest [(2; R = Me) + Pr^iNH_2]. This is attributed to the reactions proceeding by elimination–addition mechanisms rather than by nucleophilic attack at phosphorus. In competitive experiments with t-butylamine and isopropylamine a rather small preference (1.4—4.0) for formation of the product derived from the less hindered amine is consistent with the (partial) involvement of a reactive monomeric metaphosphonimidate intermediate.

Nucleophilic substitution at a phosphoryl (P=O) centre usually occurs by an associative mechanism with a five co-ordinate transition state or intermediate.[2] For a phosphonic chloride RP(O)(Cl)Y (R = alkyl or aryl) the influence of the group Y (Cl, OR, NR_2 *etc.*) on the rate of attack at phosphorus is determined by its electronic nature [I effect and $p\pi(Y) \longrightarrow d\pi(P)$ back-donating ability] and its bulk,[3] with the steric effect generally being of major importance.[4,5] On each count reaction would be expected to be faster with Y = Cl than with Y = $NHBu^t$. We therefore expected no difficulty in stopping the reaction of t-butylphosphonic dichloride (1; R = Bu^t) with t-butylamine (2 equiv.) at the end of the first stage of the sequence shown in Scheme 1. In the event we found that reaction did not occur at a useful rate at room temperature, and when it did take place, at higher temperatures (>100 °C), none of the required phosphonamidic chloride (2; R = Bu^t) could be detected; only the diamide (3; R = Bu^t) was obtained together with unchanged starting material (1). Thus it seems that the second stage in Scheme 1 (R = Bu^t) must be the faster, and by implication must be occurring by a non-associative mechanism.

Although phosphonamidic chlorides derived from secondary amines are well documented,[6] there have been few reports of those derived from primary amines or ammonia.* Indeed the only examples contained in an extensive list of phosphonic acid derivatives are $Cl_3CP(O)(Cl)NHR$ (R = Ph or cyclohexyl) and $PhP(O)(Cl)NHAr$ (various Ar).[6] We therefore pursued the preparation of the phosphonamidic chlorides (2) (various alkyl groups R) with a view to gaining general information on their stability as well as particular information on the mechanism by which they react with t-butylamine.

Results and Discussion

Unlike the t-butyl compound, other alkylphosphonic dichlorides (1) (R = Me, Et, or Pr^i) reacted quite readily with t-butylamine. Half-lives at 23 °C, using a large excess of the amine as a 1.33M-solution in dichloromethane, were *ca.* 100 min (R = Pr^i), <4.1 min (R = Et), and <0.3 min (R = Me).† By contrast t-butylphosphonic dichloride had a half-life of *ca.* 290 days at 20 °C, and even then gave products (unidentified) that were seemingly not the result of nucleophilic attack by the amine. These large differences in rate are reasonable for an associative mechanism with a high sensitivity to steric hindrance, and can be compared with the relative rates of hydrolysis for (1): 6.2×10^{-5} (R = Bu^t); 1.0 (R = Pr^i); 26 (R = Et); 128 (R = Me).[5]



Scheme 1. *Reagent:* i, $2Bu^tNH_2(-Bu^tNH_3Cl)$

From a preparative standpoint the behaviour of the less hindered phosphonic dichlorides was also in sharp contrast to that of the t-butyl compound; with 2 equiv. of t-butylamine in ether at room temperature or below, the phosphonamidic chlorides (2) could be obtained without difficulty. The isolated yields were *ca.* 95% when R = Me or Et but only 44% (after purification) with R = Pr^i, when the crude product contained small amounts of diamide (3) and unchanged (1), suggesting some competition from the second stage of Scheme 1. The elusive t-butyl compound was eventually obtained in 70% yield from the reaction of the phosphonous dichloride Bu^tPCl_2 with t-butylamine [7] [much faster than the reaction of the phosphonic dichloride (1; R = Bu^t)] and oxidation of the resulting $Bu^tP(Cl)NHBu^t$ with sulphuryl chloride. All the phosphonamidic chlorides (2) proved to be stable crystalline compounds and were obtained analytically pure. Their mass spectra did not show molecular ions although the most abundant fragment ions still contained chlorine and corresponded to (M^+ − Me). Subsequent loss of HCl (pronounced metastable peaks) gave ions of reasonable abundance (6—30%) except for (2; R = Bu^t), when HCl was lost only after C_4H_8, had been eliminated from (M^+ − Me).

With an excess of t-butylamine the phosphonic dichlorides

* Phosphonamidic chlorides are distinguished from the better known phosphoramidic chlorides by the presence of a C–P bond.

† We were able to obtain only very approximate rate data when R = Me or Et (see Experimental section) and can do no more than put upper limits on the values of $t_{0.5}$.

Table 1. Reactions of RP(O)(Cl)NHBu^t with amines in CH_2Cl_2 at 23.0 °C under first-order conditions [a]

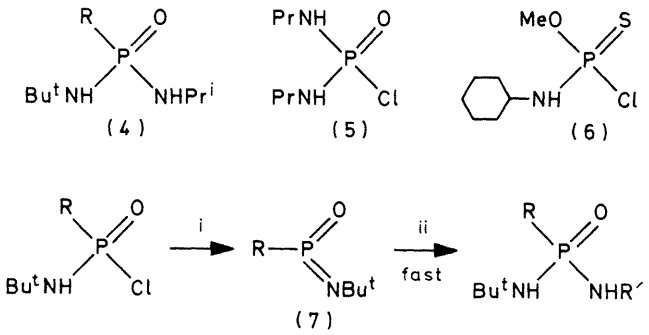
Amine	$10^3 k_\psi/s^{-1}$			
	R = Me	R = Et	R = Pr^i	R = Bu^t
Bu^{t}NH$_2$	2.2	1.1	0.34	0.23
Pr^{i}NH$_2$	~6.5	2.5	0.55	0.37

[a] [Amine] = 1.33M.

(1) gave the diamides (3), this occurring at room temperature except for compound (1; R = Bu^t) when a temperature of 140 °C was employed.*

Reactions of N-*t*-*Butyl*-P-*alkylphosphonamidic Chlorides.*— The phosphonamidic chlorides (2) reacted readily with an excess of t-butylamine in dichloromethane ($t_{0.5} \leqslant 50$ min at 23 °C) to give the expected diamides (3) (Scheme 1, stage 2). The reactions were followed by g.l.c. (3% OV 17). With R = Me or Et the substrate (in the presence of Bu^{t}NH$_2$ and Bu^{t}NH$_3$Cl) was not eluted from the column and only the appearance of the product could be monitored. The greater stability (or lower reactivity) of the more hindered substrates having R = Pr^i or Bu^t did allow their disappearance to be followed, but even here there was probably some loss on the column and the appearance of product was considered more reliable. Good first-order plots were obtained using a large excess of the amine (20 mol per mol substrate) as a 1.33M-solution in dichloromethane at 23.0 °C, and from these the values of the pseudo first-order rate constants k_ψ shown in Table 1 were deduced.† Comparing these results with those above for the phosphonic dichlorides (1) it can be seen that when R = Me ($t_{0.5}$ 5.2 min) or Et ($t_{0.5}$ 10.4 min) it is the phosphonamidic chlorides that react less quickly with t-butylamine. Having been unable to obtain precise data for the phosphonic dichlorides [all that is known is that they are more reactive by factors of at least 2.6 (R = Et) and 17 (R = Me)] we cannot say whether the differences in reactivity are sufficiently large to be compatible with associative mechanisms for the phosphonamidic chlorides. When R = Pr^i ($t_{0.5}$ 34 min) it is the phosphonamidic chloride (2) that reacts more quickly, but the three-fold rate difference is not so large as to make its preparation from (1) impractical.‡ The outstanding result is for R = Bu^t ($t_{0.5}$ 50 min). This shows that the phosphonamidic chloride (2) is at least 5 000 times more reactive than the phosphonic dichloride (1), and thus explains our original observation; any attempt to prepare (2) from (1) will inevitably be doomed to failure.

The reactivity of the phosphonamidic chlorides (2) relative to each other is also highly significant. As shown in Table 1, only a ten-fold decrease in rate occurs as the size of the group R increases from Me to Bu^t. Such a low sensitivity to steric hindrance is in dramatic contrast to the usual situation and must surely be a consequence of a non-associative mechanism. A very different picture emerged when aniline was used in place of t-butylamine. The methyl- and ethyl-phosphonamidic chlorides had half-lives of 3 and 22 h respectively at 23 °C while the isopropyl compound was only *ca.* 10% consumed after 18 days and the t-butyl compound showed no perceptible change. Here steric effects in the substrate clearly do have a profound effect on reactivity and an associative mechanism does seem possible. Moreover, these reactions with aniline are much slower than those with t-butylamine, the differences being *ca.* 35 (R = Me), 125 (R = Et), $>10^3$ (R = Pr^i), and $>10^4$ (R = Bu^t). The higher reactivity of t-butylamine could in principle be because it is a more powerful nucleophile, or because it is a stronger base.



Scheme 2. *Reagents:* i, R′NH$_2$ (− R′NH$_3$Cl); ii, R′NH$_2$

To see how the enhanced nucleophilicity of a less sterically crowded amine would affect the rates of reaction, the phosphonamidic chlorides (2) were treated with isopropylamine in place of t-butylamine. Rates were measured in the same way as for t-butylamine, and under the same conditions, and the products were isolated and characterised as the unsymmetrical diamides (4). The rate constants (Table 1) show that, as with t-butylamine, there is a rather small dependence on the size of the *P*-alkyl group. Of more immediate concern is the fact that they show the extent to which isopropylamine is more reactive than t-butylamine. Steric effects in an amine are known to reduce its nucleophilicity towards carbon centres, although the magnitude of this reduction varies considerably with the nature of the substrate.[9] The limited available data suggest that the same is true for (associative) attack at phosphoryl centres,[10–12] *e.g.* s-butylamine is 60 times more reactive than t-butylamine towards (Pr^{i}O)$_2$P(O)Cl[10] but only *ca.* 4.5 times more reactive towards the relatively unhindered MeP(O)(OEt)Cl.[11] For the phosphonamidic chlorides (2) the reactivity of isopropylamine exceeds that of t-butylamine by a factor of only 1.6—3. This difference would be remarkably small for an associative mechanism, bearing in mind that the bulk of the NHBu^t groups in the substrates would be likely to make them particularly sensitive to steric effects in the nucleophile. It therefore seems unlikely that isopropylamine and t-butylamine are acting primarily as nucleophiles in the rate-limiting step, in which case their high reactivity relative to aniline (pK_a 4.6) must be ascribed to their greater basicity (pK_a 10.6 and 10.45 respectively).[13]

It is now recognised that some phosphoric acid derivatives in which the phosphorus atom is attached to one or more NH groups [*e.g.* (5) [14] and (6) [15]] can undergo alkaline hydrolysis by an elimination–addition (EA) mechanism, with hydroxide acting initially as a base rather than a nucleophile.[2,3] A similar mechanism (Scheme 2) seems likely for our reactions of phosphonamidic chlorides with isopropylamine and t-butylamine, albeit amines are comparatively weak bases and the reaction medium (CH_2Cl_2) is non-hydroxylic. The postu-

* Quast *et al.* (ref. 8) converted the phosphonic dichloride (1; R = Bu^t) into the diamide (3) by heating it with excess of t-butylamine in acetonitrile at 150 °C for 24 h.

† For R = Pr^i or Bu^t the disappearance of reactant gave equally good first-order plots but values of k_ψ up to 25% larger, probably because of some loss of material on the g.l.c. column. The first few % of reaction appeared to be somewhat slower than the rest, perhaps because the Bu^{t}NH$_3$Cl by-product exerts a small catalytic effect.

‡ Our preparation of compound (2; R = Pr^i) was assisted by the use of a solvent (ether) in which it has limited solubility. By coming out of solution its concentration is reduced, and with it the unwanted further conversion of (2) into the diamide (3).

(8) (9)

lated intermediate metaphosphonimidate (7) contains three co-ordinate phosphorus in the +5 oxidation state. It is therefore related to the highly electrophilic monomeric metaphosphates (8) and (9) [16] and would be expected to react very rapidly with amines and other nucleophiles. It might also be expected to discriminate rather poorly between different nucleophiles. We therefore examined the reactions of the phosphonamidic chlorides (2) with mixtures of isopropylamine and t-butylamine. Using a 20-fold excess of an equimolar mixture of the amines in dichloromethane at 0 °C the product ratios (4) : (3) were as shown in Table 2. Of the two methods of analysis, g.l.c. is thought to be quantitatively the more reliable (see Experimental section). The rather small discrimination in favour of isopropylamine is in marked contrast to the strong discrimination shown by substrates that cannot react by an EA mechanism; even with one as reactive and sterically undemanding as $Ph_2P(O)Cl$ the selectivity for isopropylamine is in the order of 100 : 1. That the phosphonamidic chlorides should give rather more of the product (4) derived from the less hindered amine is not inconsistent with a monomeric metaphosphonimidate intermediate (7); high reactivity need not entirely destroy the ability to select on steric grounds. However, the increasing selectivity as the size of the R group in (2) decreases does require comment. It may be that there is some contribution from an associative reaction of isopropylamine (but not t-butylamine) with the less hindered phosphonamidic chlorides (R = Me, Et), and this would also explain why for these compounds the reaction with isopropylamine is 2—3 times faster than that with t-butylamine, whereas for (2; R = Pr^i or Bu^t) the difference is only 1.6 (Table 1).

Experimental

M.p.s were determined using sealed capillary tubes in a heated block. I.r. spectra were recorded with Perkin-Elmer 237 and 257 instruments, and ^1H n.m.r. spectra with a Varian EM 390 spectrometer, tetramethylsilane as internal standard. ^{31}P N.m.r. spectra were recorded at 24.3 MHz with a JEOL JNM-FX60 spectrometer; positive chemical shifts are downfield from external 85% H_3PO_4. Mass spectra were obtained with a V.G. Micromass 16B instrument. G.l.c. analyses were performed on a Pye 104 flame-ionisation chromatograph fitted with a 1.5 m × 4 mm internal diameter glass column packed with the stated stationary phase coated on silanised 100—120 mesh diatomite C 'Q'; peak areas were measured with a Columbia Scientific Industries Supergrator 1. Dichloromethane was distilled from calcium hydride. Amines were dried over, and distilled from, potassium hydroxide. Light petroleum refers to the fraction with b.p. 60—80 °C. Ether refers to diethyl ether.

The following were prepared by published procedures: t-butylphosphonous dichloride,[17] b.p. 140 °C at 740 mmHg, solidified when cool; methylphosphonic dichloride,[18] b.p. 97 °C at 80 mmHg [initially contaminated with *ca.* 10% MeP(O)(OMe)Cl; purified by being melted and allowed to cool slowly to room temperature when the phosphonic dichloride formed large crystals which were separated from liquid material]; ethylphosphonic dichloride,[19] b.p. 102—103 °C at 68 mmHg; isopropylphosphonic dichloride,[19,20] b.p. 112—114 °C at 75 mmHg; t-butylphosphonic dichloride,[20] purified by sublimation at 70—80 °C and 15 mmHg.

Table 2. Products from competitive reactions of $RP(O)(Cl)NHBu^t$ with equimolar mixtures of Pr^iNH_2 and Bu^tNH_2 in CH_2Cl_2 at 0 °C

	(4) : (3)			
	R = Me	R = Et	R = Pr^i	R = Bu^t
By g.l.c.	3.95	2.36	1.45	1.39
By ^{31}P n.m.r.	3.65	2.49	1.43	1.37

P-*Methyl*-N-*t-butylphosphonamidic Chloride* (2; R = Me).—A solution of methylphosphonic dichloride (1.09 g, 8.2 mmol) in ether (10 ml) was stirred and cooled in ice while t-butylamine (1.24 g, 17.0 mmol) in ether (6 ml) was added during 20 min. After a further 20 min at room temperature the mixture was diluted with an equal volume of dichloromethane (to dissolve the product) and filtered to remove Bu^tNH_3Cl. Evaporation of the solvent afforded the product (2; R = Me) (1.31 g, 94%) as a powder, $\nu_{max.}$ (Nujol) 3 180 (NH) and 1 205 cm^{-1} (P=O); $\delta(CDCl_3)$ 3.8br (1 H, s), 1.92 (3 H, d, J_{PH} 16 Hz), and 1.38 (9 H, s), which was dissolved in dichloromethane (20 ml), washed quickly with ice–water, dried (Na_2SO_4), and the solvent removed to give the pure compound. Crystallisation from benzene–light petroleum (1 : 1) gave the pure *phosphonamidic chloride* (2; R = Me) (1.08 g, 6.4 mmol, 78%), m.p. 121—123 °C, *m/z* 156 and 154 (M^+ − Me, 100%), 134 (M^+ − Cl, 9), and 118 (M^+ − Me − HCl, 36), *m** 91 (Found: C, 35.1; H, 7.7; Cl, 21.2; N, 8.2. $C_5H_{13}ClNOP$ requires C, 35.4; H, 7.7; Cl, 20.9; N, 8.3%); same i.r. and ^1H n.m.r. spectra as the crude material. (A sample which sublimed at 80 °C and 0.2 mmHg had m.p. 135—136 °C and the same i.r. spectrum but did not analyse correctly.)

P-*Ethyl*-N-*t-butylphosphonamidic Chloride* (2; R = Et).—t-Butylamine (1.84 g, 25.1 mmol) was added dropwise during 15 min to an ice-cold solution of ethylphosphonic dichloride (1.80 g, 12.2 mmol) in ether (20 ml) and stirring was continued for a further 45 min at room temperature. The mixture was diluted with dichloromethane (12 ml) and filtered to remove Bu^tNH_3Cl. Volatile matter was evaporated off and the residue was dissolved in dichloromethane (30 ml), washed quickly with ice–water, and dried (Na_2SO_4). After evaporation of the solvent, crystallisation from ether–light petroleum (1 : 3) gave the *phosphonamidic chloride* (2; R = Et) (2.14 g, 11.7 mmol, 95%), m.p. 95.5—97 °C; *m/z* 170 and 168 (M^+ − Me, 100%), 148 (M^+ − Cl, 7), and 132 (M^+ − Me − HCl, 28), *m** 104; $\nu_{max.}$ (Nujol) 3 170 (NH) and 1 205 cm^{-1} (P=O); $\delta(CDCl_3)$ 3.4br (1 H, s), 2.07 (2 H, dq, J_{PH} 15, J_{HH} 7.5 Hz), 1.38 (9 H, s), and 1.25 (3 H, dt, J_{PH} 23, J_{HH} 7.5 Hz) (Found: C, 39.0; H, 8.2; Cl, 19.6; N, 7.5. $C_6H_{15}ClNOP$ requires C, 39.2; H, 8.2; Cl, 19.3; N, 7.6%).

P-*Isopropyl*-N-*t-butylphosphonamidic Chloride* (2; R = Pr^i).—t-Butylamine (3.50 g, 48.0 mmol) was added during 2 min to a solution of isopropylphosphonic dichloride (3.87 g, 24.0 mmol) in ether (30 ml) which was stirred and cooled in ice. Solid began to precipitate immediately. The mixture was stirred at room temperature for 4 h, diluted with ether (10 ml), and filtered. The solid (Bu^tNH_3Cl + product) was extracted with ether–dichloromethane (2 : 1) and the extract combined with the filtrate. G.l.c. (3% OV 17 at 140 °C) showed a little $Pr^iP(O)Cl_2$ (R_t 1.0 min) and $Pr^iP(O)(NHBu^t)_2$ (R_t 5.2 min) in addition to the major component (R_t 3.2 min). The volatile

material was evaporated off and the residue was dissolved in hot ether (30 ml), a small amount of insoluble material being filtered off. The solution was concentrated to *ca.* 7 ml and diluted with an equal volume of light petroleum to give crystals of the *phosphonamidic chloride* (2; R = Pr^i) (2.08 g, 10.5 mmol, 44%), pure by g.l.c., m.p. 142—143 °C after recrystallisation from benzene–light petroleum (1 : 1); *m/z* 184 and 182 (M^+ − Me, 100%), 162 (M^+ − Cl, 5), and 146 (M^+ − Me − HCl, 6, *m** 117; $\nu_{max.}$ (Nujol) 3 180 (NH) and 1 210 cm^{-1} (P=O); δ($CDCl_3$) 2.85br (1 H, s), 2.15 (1 H, d × septet, J_{PH} 14, J_{HH} 7 Hz), 1.38 (9 H, s), and 1.26 (6 H, dd, J_{PH} 21, J_{HH} 7 Hz) (Found: C, 42.6; H, 8.5; Cl, 18.0; N, 7.1. $C_7H_{17}ClNOP$ requires C, 42.5; H, 8.7; Cl, 17.9; N, 7.1%).

N,P-*Di-t-butylphosphonamidic Chloride* (2; R = Bu^t).—A solution of t-butylphosphonous dichloride (5.02 g, 31.6 mmol) in dichloromethane (20 ml) was stirred under nitrogen and cooled in ice while t-butylamine (4.75 g, 65 mmol) in dichloromethane (10 ml) was added dropwise during 20 min. After a further 20 min at room temperature, g.l.c. (3% OV 17 at 105 °C) showed very little Bu^tPCl_2 (R_t 2.4 min) and a single major product (R_t 4.8 min) (no peak of $R_t > 4.8$ min), δ(CH_2Cl_2) 1.23 (9 H, d, J_{PH} 1 Hz) and 1.10 (9 H, d, J_{PH} 13 Hz) (in addition to Bu^tNH_3Cl which was filtered off).

The volatile material was evaporated off and the residue [$Bu^tP(Cl)NHBu^t$],[7] dissolved in dichloromethane (30 ml), was oxidised by dropwise addition of sulphuryl chloride (4.70 g, 35 mmol) in dichloromethane (10 ml) at 0 °C during 10 min. The mixture was stirred at room temperature for 50 min, when it showed δ(CH_2Cl_2) 1.66 (9 H, d, J_{PH} 27 Hz) and 1.55 (9 H, s) (presumed to be a complex of the product and $SOCl_2$). Volatile material [including some $Bu^tP(O)Cl_2$] was removed by pumping briefly at 1 mmHg and the residue was dissolved in dichloromethane (20 ml). This solution was shaken well with ice–water (exothermic; gas evolved) (to break down the presumed complex), dried (Na_2SO_4), and concentrated. The crude product [containing some $Bu^tP(O)Cl_2$] was purified by crystallisation from light petroleum. After being dried over KOH and P_2O_5 at 4 mmHg for 12 h, pure (by g.l.c.) *phosphonamidic chloride* (2; R = Bu^t) (4.65 g, 22.0 mmol, 70%) was obtained; m.p. 151—152 °C (after recrystallisation from ether–light petroleum); *m/z* 198 and 196 (M^+ − Me, 100%), 176 (M^+ − Cl, 4), 142 and 140 (M^+ − Me − C_4H_8, 48), and 104 (14), *m** 102 and 100; $\nu_{max.}$ (Nujol) 3 200 (NH) and 1 200 cm^{-1} (P=O); δ($CDCl_3$) 2.5br (1 H), 1.39 (9 H, s), and 1.25 (9 H, d, J_{PH} 19 Hz) (Found: C, 45.5; H, 9.0; Cl, 17.0; N, 6.6. $C_8H_{19}ClNOP$ requires C, 45.4; H, 9.05; Cl, 16.75; N, 6.6%). This compound could also be purified by sublimation at 110 °C and 4 mmHg.

Phosphonic Diamides (3) *and* (4).—(*a*) A solution of the phosphonic dichloride (4 mmol) in dichloromethane (6 ml) was stirred and cooled in ice while t-butylamine (20 mmol) (diluted with CH_2Cl_2 when R = Me) was slowly added. After 18 h at room temperature the mixture was filtered to remove Bu^tNH_3Cl. The volatile material was evaporated from the filtrate and the residue, dissolved in dichloromethane (8 ml), was washed with water (2 ml) made just strongly acidic with HCl. The crude product was purified by crystallisation. The following compounds were thus obtained: N,N′-*di-t-butyl*-P-*methylphosphonic diamide* (3; R = Me), m.p. 93—95 °C (from light petroleum), δ_P (CH_2Cl_2) 21.6 (Found: C, 52.15; H, 11.1; N, 13.5. $C_9H_{23}N_2OP$ requires C, 52.4; H, 11.2; N, 13.6%); N,N′*di-t-butyl*-P-*ethylphosphonic diamide* (3; R = Et), m.p. 127—128 °C (from light petroleum), δ_P ($CDCl_3$) 27.8 (Found: C, 54.5; H, 11.3; N, 12.7. $C_{10}H_{25}N_2OP$ requires C, 54.5; H, 11.4; N, 12.7%); N,N′-*di-t-butyl*-P-*isopropylphosphonic diamide* (3; R = Pr^i), m.p. 158—159 °C [from benzene–light petroleum (1 : 1)], δ_P (CH_2Cl_2) 29.9 (Found: C, 56.8; H, 11.4; N, 12.0. $C_{11}H_{27}N_2OP$ requires C, 56.4; H, 11.6; N, 12.0%).

(*b*) t-Butylphosphonic dichloride (5.5 g, 31.4 mmol) in acetonitrile (21 ml) was heated with t-butylamine (15 g) in a sealed tube at 140 °C for 16 h. Work-up as in (*a*) gave *N,N′, P*-tri-t-butylphosphonic diamide (3; R = Bu^t), m.p. 176—177 °C (from light petroleum) (lit.,[8] 181—182 °C), δ_P (CH_2Cl_2) 32.3. (Reaction was probably incomplete under the conditions used here, *cf.* ref. 8).

(*c*) Isopropylamine (4.0 mmol) was added to a solution of the *N*-t-butylphosphonamidic chloride (2) (0.75 mmol) in dichloromethane (1.2 ml). The mixture was left at room temperature overnight and then worked up as in (*a*), except that the initial filtration was omitted as Pr^iNH_3Cl remained in solution. The following compounds were prepared in this way: N-*isopropyl*-N′-*t-butyl*-P-*methylphosphonic diamide* (4; R = Me), distilled at 105—110 °C (oven temp.) at 0.1 mmHg to give an oil which solidified, m.p. 45—46 °C, δ_P (CH_2Cl_2) 23.4 (Found: C, 49.8; H, 10.8; N, 14.5. $C_8H_{21}N_2OP$ requires C, 50.0; H, 11.0; N, 14.6%); N-*isopropyl*-N′-*t-butyl*-P-*ethylphosphonic diamide* (4; R = Et), distilled at 105—110 °C (oven temp.) at 0.1 mmHg to give an oil which solidified, m.p. 55.5—56.5 °C, δ_P (CH_2Cl_2) 28.2 (Found: C, 52.3; H, 11.1; N, 13.5. $C_9H_{23}N_2OP$ requires C, 52.4; H, 11.2; N, 13.6%); N,P-*di-isopropyl*-N′-*t-butylphosphonic diamide* (4, R = Pr^i), crystallised from light petroleum, m.p. 161—162 °C, δ_P (CH_2Cl_2) 31.2 (Found: C, 54.6; H, 11.2; N, 12.6. $C_{10}H_{25}N_2OP$ requires C, 54.5; H, 11.4; N, 12.7%); N-*isopropyl*-N′,P-*di-t-butylphosphonic diamide* (4; R = Bu^t), crystallised from benzene–light petroleum (1 : 4), m.p. 173.5—175 °C, δ_P (CH_2Cl_2) 33.3 (Found: C, 56.6; H, 11.5; N, 11.9. $C_{11}H_{27}N_2OP$ requires C, 56.4; H, 11.6; N, 12.0%).

The identities of the phosphonic diamides (3) and (4) were confirmed spectroscopically. Their ^1H n.m.r. spectra (in $CDCl_3$) consisted of signals from the following structural units as appropriate: NBu^t, δ 1.31 (9 or 18 H, s); NPr^i, δ 3.5 (1 H, m), and 1.17 (6 H, d, J_{HH} 6 Hz, sometimes showing slight non-equivalence of the diastereotopic Me groups); PMe, δ 1.43 (3 H, d, J_{PH} 15 Hz); PEt, δ 1.63 (2 H, dq, J_{PH} 15, J_{HH} 7.5 Hz) and 1.08 (3 H, dt, J_{PH} 18, J_{HH} 7.5 Hz); PPr^i, δ 1.12 (6 H, dd, J_{PH} 16, J_{HH} 7 Hz) (CH signal obscured); PBu^t, δ 1.09 (9 H, d, J_{PH} 15 Hz); NH, δ *ca.* 2 (2 H, br). The i.r. spectra (as Nujol mulls) included absorptions at 3 300—3 200 (NH) and 1 175—1 160 cm^{-1} (P=O). The mass spectra contained low-abundance molecular ions and prominent fragments corresponding to M^+ − Me, $RP(O)NH_2^+$, and *m/z* 58 (100% except when R = Bu^t); in addition compounds (3) gave M^+ − 71 and *m/z* 135 (100% when R = Bu^t), and (4) gave *m/z* 121; (4; R = Bu^t) also gave *m/z* 177.

Rate Measurements.—(*a*) N-*t-Butyl*-P-*alkylphosphonamidic chlorides* (2) *with t-butylamine or isopropylamine.* A solution of the amine (0.50 mmol) in dichloromethane containing naphthalene (0.8—1.2 mg) as g.l.c. standard was placed in a stoppered tube suspended in an oil bath maintained at 23.0 °C. The phosphonamidic chloride (0.025 mmol) was added as a concentrated solution in dichloromethane to give a reaction mixture in which [amine] = 1.33M. Samples were withdrawn at regular intervals (5—20 min) and injected directly on to the g.l.c. column (3% OV 17 at 140—150 °C). For each reaction *ca.* 11 samples were analysed over a period of 4 × $t_{0.5}$, together with an infinity sample obtained by prolonged reaction and/or use of a higher temperature (55 °C). The minimum possible time between g.l.c. analyses was 5 min. For the relatively fast reaction of compound (2; R = Me) with t-butylamine insufficient data were obtained from a single experiment sampled at t = 0, 5, 10 min *etc.*, and additional

data were obtained by repeating the experiment and sampling at t = 2.5, 7.5, 12.5 min *etc.* A similar procedure was adopted for the reaction of (2; R = Et) with isopropylamine. For the even faster reaction of (2; R = Me) with isopropylamine the required data was obtained from three separate experiments. For each sample, the peak area A of the diamide product (3) or (4) was determined (relative to the area of the naphthalene standard) and a plot of log $(A_\infty - A)$ *vs.* time was constructed. These plots were linear (except that the first few % of reaction was sometimes anomalously slow, see Discussion section) and gave the values of the pseudo first-order rate constant k_ψ shown in Table 1. For (2; R = Bu^t or Pr^i) it was also possible to follow the disappearance of the substrate by g.l.c. (see Discussion section).

(*b*) N-*t-Butyl*-P-*alkylphosphonamidic chlorides* (2) *with aniline*. The solvent was dichloromethane with [$PhNH_2$] = 1.33M and T = 23.0 °C. For compounds (2; R = Pr^i) and (2; R = Bu^t) the method was as in (*a*) with g.l.c. now being used to monitor the consumption of the substrate (the product being rather involatile). After 18 days there had been no significant reaction of (2; R = Bu^t) and *ca.* 10% consumption of (2; R = Pr^i). For (2; R = Me) and (2; R = Et) the substrate (partly) decomposed on g.l.c., and the reactions were therefore carried out on a larger scale and monitored by ^1H n.m.r. spectroscopy. This gave $t_{0.5}$ values of *ca.* 3 and 22 h (ignoring the anomalously slow first 10% of reaction).

(*c*) P-*Alkylphosphonic dichlorides* (1) *with t-butylamine*. The solvent was dichloromethane with [Bu^tNH_2] = 1.33M. For compound (1; R = Bu^t) samples of the reaction mixture (containing naphthalene as g.l.c. standard) were sealed in glass ampoules and maintained at 20 ± 2 °C; the reaction was monitored by g.l.c. (3% OV 17 at 143 °C). A small amount of the phosphonic dichloride was rapidly consumed, apparently by reaction with traces of water, but its concentration then decreased by only 14% during 64 days ($t_{0.5}$ 291 days). Neither the phosphonamidic chloride (2; R = Bu^t) nor the phosphonic diamide (3; R = Bu^t) were detected, suggesting that even this very slow disappearance of substrate was not caused by direct reaction with t-butylamine. ^1H and ^{31}P N.m.r. spectroscopy confirmed the presence of unchanged phosphonic dichloride and the absence of any single substantial product.

For the dichloride (1; R = Pr^i), 12 samples taken during a period of 7 h at 23.0 °C were analysed by g.l.c. (3% OV 17 at 145 °C). The growth and subsequent decline of the phosphonamidic chloride (2; R = Pr^i) (maximum at t *ca.* 60 min) and the growth of the phosphonic diamide (3; R = Pr^i) were monitored (relative to naphthalene, included as g.l.c. standard). Calibration of the detector with authentic samples of compounds (2) and (3) showed that the molar response for the phosphonamidic chloride was only 0.6 times that for the diamide, so that the amount of (2) that had been formed at any instant was taken to be the [actual area of the peak for (2)] + 0.6 [area of the peak for (3)]. The value of k_ψ for the conversion of (1) into (2) was found to be *ca.* 1.2×10^{-4} s^{-1}.

For compounds (1; R = Me) and (1; R = Et), the combination of high rates and g.l.c. instability of substrates and phosphonamidic chlorides (2) made it impossible to follow the reactions. Rough values of $t_{0.5}$ at 23 °C were obtained by very rapidly cooling the reaction mixtures after 0.25 min (R = Me) or 3 min (R = Et), quenching with 4M-aqueous HCl, and measuring by ^1H n.m.r. spectroscopy (naphthalene included as standard for integration) the yields of the phosphonamidic chlorides (*ca.* 50% for R = Me; 40% for R = Et). These values may have been considerably lower than the true yields (because of loss of product after quenching) and the values of $t_{0.5}$ (0.25 min for R = Me, 4.1 min for R = Et) should be regarded as approximate upper limits.

Competitive Reactions of t-Butylamine and Isopropylamine with N-*t-Butyl*-P-*alkylphosphonamidic Chlorides* (2).—The phosphonamidic chloride (2) (0.16 mmol) was added at 0 °C to dichloromethane containing equimolar amounts of t-butylamine and isopropylamine (1.6 mmol each) and having [total amine] = 1.3M. After 48 h at 0 °C the mixture was concentrated and examined by ^{31}P n.m.r. spectroscopy. In each case the spectrum contained two peaks, corresponding to the phosphonic diamides (3) and (4). The molar ratios (4) : (3) are shown in Table 2 but were not exactly reproducible. The products were also analysed by g.l.c. on 3% OV 225 at 154 °C when R = Me, Et, or Pr^i [(3) eluted before (4)] and on 3% OV 17 at 140 °C when R = Bu^t [(4) eluted before (3); not resolved on OV 225]. For each reaction mixture the peak areas were corrected to compensate for the unequal response of the detector towards the two products. The required correction factors were obtained using authentic mixtures of the diamides of known composition. Because the diamides gave non-linear signals (halving the sample size reduced the peak area by a factor >2, presumably because of irreversible interactions with the column packing) it was necessary to determine the correction factors with authentic mixtures in which the (4) : (3) ratio was very close to that in the reaction mixture, *and* to inject equal amounts of the authentic and reaction mixtures. The results are shown in Table 2.

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