Hydrolysis of (*N*-Aryl)alkylphenylphosphinic Amides in Acidic Solution: Influence of Different *P*-Alkyl Groups, including Cyclopropyl, and of Substituents in the *N*-Aryl Group[1]

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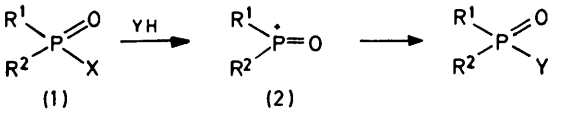
The (*N*-phenyl)alkylphenylphosphinic amides RPhP(O)NHPh (R = ethyl, cyclopropyl, isopropyl, 1-methylcyclopropyl, or t-butyl) give the corresponding alkylphenylphosphinic acids without rearrangement on hydrolysis in aqueous hydrochloric acid. The pseudo-first-order rate constants at 31.2 °C in 1 :1 v/v water–methanol 2.08M in hydrochloric acid ($10^5 k_\psi$ 690, 275, 11.0, 4.22, and <0.003 5 s^{-1}, respectively) show that replacement of an isopropyl group by cyclopropyl, and of a t-butyl group by 1-methylcyclopropyl, causes a substantial increase in rate. This is attributed to reduced steric inhibition of an associative (*A*2) hydrolysis mechanism rather than stabilisation of a dissociative (*A*1 or *A*1-like) transition state by the cyclopropyl groups. The hydrolysis reactions have large negative values of $\Delta S^{\ddagger}$. For the substituted amides RPhP(O)NH·C_6H_4·X-*p* (X = OMe, H, Br, or NO_2) reducing the nucleophilicity of the leaving group does not materially reduce the sensitivity of hydrolysis to steric hindrance nor, by implication, the associative nature of the mechanism.

EXHAUSTIVE studies have established beyond doubt the remarkable ability of the 'bent' C–C bonds in cyclopropane rings to stabilise adjacent electron-deficient carbon atoms by σ participation.[2] By contrast, the ability of cyclopropyl groups to interact with electron-deficient centres other than carbon has received little attention. In this paper we describe initial attempts to investigate the interaction between cyclopropyl substituents and electron-deficient phosphinyl centres such as would be present in the phosphinylium cation intermediate (2) of an $S_N1(P)$ reaction.

Whereas dissociative $S_N1(P)$ mechanisms may be comparatively common for derivatives of quinquevalent



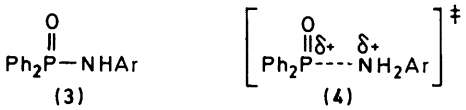
(1) (2)

phosphorus acids (1) in which one or both of the groups R^1 and R^2 is joined to phosphorus by an oxygen or a

[1] Preliminary communications, M. J. P. Harger, *J.C.S. Chem. Comm.*, 1973, 774; M. J. P. Harger, A. J. Macpherson, and D. Pickering, *Tetrahedron Letters*, 1975, 1797.

[2] H. G. Richey (ch. 25), and K. B. Wiberg, B. A. Hess, and A. J. Ashe (ch. 26) in 'Carbonium Ions,' vol. III, eds. G. A. Olah and P. von R. Schleyer, Wiley–Interscience, 1972. More recent work includes E. N. Peters and H. C. Brown, *J. Amer. Chem. Soc.*, 1973, **95**, 2397; G. A. Olah and P. W. Westerman, *ibid.*, p. 7530; C. F. Wilcox, L. M. Loew, and R. Hoffmann, *ibid.*, p. 8192.

nitrogen atom,[3] the same is not true when both R^1 and R^2 are alkyl or aryl groups. Thus phosphinic acids and their derivatives generally display a very strong preference for reaction by associative $S_N2(P)$ mechanisms.[4-7] Nevertheless, the results of a thorough kinetic investigation of the acid-catalysed hydrolysis of (*N*-aryl)diphenylphosphinic amides (3) led Haake and Tyssee [8] to conclude that in this case reaction does occur by a dissociative (*A*1 or *A*1-like) mechanism, in which rate-



(3) (4)

determining cleavage of the P–N bond in the *N*-protonated substrate is well advanced in the transition state (4), with consequent development of positive charge on the phosphorus atom.

In seeking information on the interactions between cyclopropyl groups and electron-deficient phosphinyl centres we therefore turned our attention to the hydrolysis of the (*N*-aryl)alkylphenylphosphinic amides (6) and (8) having cyclopropyl groups attached to phosphorus and, for comparison, (5), (7), and (9) having simple alkyl substituents.

(5)	R = Et	(10)
(6)	R = cyclopropyl	(11)
(7)	R = Pr^i	(12)
(8)	R = 1-methylcyclopropyl	(13)
(9)	R = Bu^t	(14)

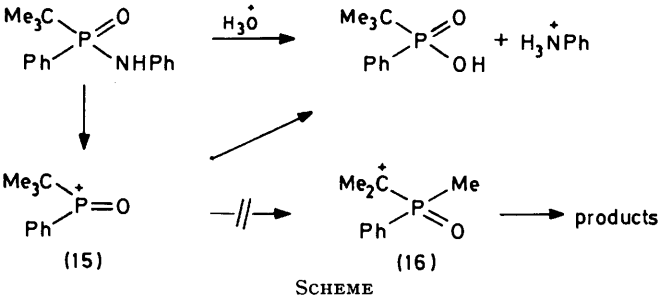
RESULTS AND DISCUSSION

The phosphinic acids (10)—(13) and the corresponding acid chlorides were prepared by methods previously described.[9] Reactions of the phosphinic chlorides with aniline, *p*-methoxyaniline, *p*-bromoaniline, and *p*-nitroaniline afforded the amides (5)—(8) (X = H, OMe, Br, or NO_2). Anticipating that steric hindrance would make the reaction of aniline with the acid chloride derived from (14) very slow, we chose instead to prepare the amide (9; X = H) by oxidation (H_2O_2) of the product of the reaction of chloro(phenyl)-t-butylphosphine with aniline. No attempt was made to obtain amides (9) with X ≠ H.

Products of Hydrolysis of (N-*Phenyl*)*alkylphenylphosphinic Amides* (5)—(9) (X = H).—Suspensions of the amides (0.2 mmol) in aqueous 2M-hydrochloric acid (5 ml) were stirred and boiled gently under reflux for 90 min. For each of (5)—(8) (X = H) the resulting clear solution was extracted with chloroform (5 ml and 3 × 2 ml) and the extract evaporated. The residual solid product had i.r. and n.m.r. spectra identical with those of the appropriate authentic alkylphenylphosphinic acid. A portion of the solution used for n.m.r. study was treated with an excess of diazomethane and examined by g.l.c. (3% OV 17; 210 °C). Only one important peak was observed, having the same retention time (2—3 min) as the appropriate methyl alkylphenylphosphinate obtained from the reaction of the corresponding phosphinic acid with diazomethane; other peaks were either entirely absent or in total amounted to not more than 1.5% of the principal peak. The t-butyl amide (9; X = H) was largely unchanged even after 20 h. However, when boiled with aqueous 4M-hydrochloric acid containing dioxan to increase its solubility, it was completely hydrolysed within 137 h; the product was identical (i.r. and n.m.r.) with authentic t-butylphenylphosphinic acid and was homogeneous (>99%) by g.l.c. (after treatment with diazomethane).

If a phosphinylium ion (15) were an intermediate in the hydrolysis of (*N*-phenyl)-t-butylphenylphosphinic amide it could, in principle, rearrange to a tertiary carbocation (16) by a 1,2-shift of a methyl group from carbon to phosphorus (Scheme). The resulting carbocation would, however, be destabilised by the adjacent electron-withdrawing phosphinyl group,[10] and this could account for the absence of products other than those of simple hydrolysis. Other workers have noted that the highly hindered di-t-butylphosphinic chloride also undergoes solvolysis without rearrangement by what is thought to be a dissociative $S_N1(P)$ mechanism.[5]

Even if rearrangement is not a characteristic of simple phosphinylium ions, it might still be possible for the cyclopropyl-substituted amides (6) and (8) (X = H) to



(15) (16)

SCHEME

give rearrangement products by dissociative hydrolysis if σ participation by the 'bent' cyclopropyl C–C bonds were to lead to delocalised ('non-classical') cationic intermediates. Again, however, the products were

[3] A. J. Kirby and S. G. Warren, 'The Organic Chemistry of Phosphorus,' Elsevier, 1967, ch. 10; W. S. Wadsworth and H. Horton, *J. Amer. Chem. Soc.*, 1970, **92**, 3785; W. S. Wadsworth, *J.C.S. Perkin II*, 1972, 1686; K. E. DeBruin and D. M. Johnson, *Phosphorus*, 1974, **4**, 13.

[4] P. Haake and P. S. Ossip, *J. Amer. Chem. Soc.*, 1971, **93**, 6919.

[5] P. Haake and P. S. Ossip, *J. Amer. Chem. Soc.*, 1971, **93**, 6924.

[6] R. J. Brooks and C. A. Bunton, *J. Org. Chem.*, 1975, **40**, 2059.

[7] B. Krawiecka, J. Michalski, and Z. Skrzypczyński, *J.C.S. Chem. Comm.*, 1974, 1022.

[8] P. Haake and D. A. Tyssee, *Tetrahedron Letters*, 1970, 3513; see also ref. 17.

[9] M. J. P. Harger, *J.C.S. Perkin I*, 1975, 514.

[10] D. Howells and S. Warren (*J.C.S. Perkin II*, 1973, 1472, 1645) have commented on the instability of α-phosphinyl carbocations.

solely those of straightforward hydrolysis, and of themselves gave no positive information concerning the interactions of cyclopropyl groups and electron-deficient phosphinyl centres. Indeed if one considers only the products of hydrolysis there is no need to postulate a mechanism which is dissociative (*A*1 or *A*1-like).

Rates of Hydrolysis of (N-*Phenyl*)*alkylphenylphosphinic Amides* (5)—(9) (X = H).—The rates of hydrolysis of the amides (5)—(8) (X = H) were determined spectrophotometrically at 31.2, 39.1, and 47.0 °C. A portion (2.7 ml) of a stock solution of hydrogen chloride in aqueous methanol was placed in a 10 mm silica cell housed in the sample compartment of a thermostatted (±0.1 °C) cell holder. An identical cell containing aqueous methanol (1 : 1 v/v) was placed in the reference compartment. A solution of the appropriate amide in methanol (0.3 ml) was added to the sample cell and the contents were mixed thoroughly to give a solution of the amide (0.001—0.005M initially) in 1 : 1 v/v water–methanol 2.08M in hydrochloric acid. The cell was tightly stoppered and the spectrum of the mixture was recorded at regular intervals; a minimum of 16 scans was obtained, extending over at least 4 half-lives. At 285 nm the anilides absorb quite strongly (ε 500—900) but their hydrolysis (or methanolysis) products are transparent. Plots of log A_{285} against time were strictly linear, and gave the values of the pseudo-first-order rate constants (k_ψ) shown in Table 1. For the fastest reactions, having half-lives of less than 2 min, the values of k_ψ shown are the average of two determinations. The discrepancy between duplicate determinations can be accommodated by an uncertainty of ±3% although the maximum possible error in k_ψ is estimated to be ±5%. Plots of log (k_ψ/T) *versus* $1/T$ were linear;[11] the values of the enthalpy ($\Delta H^\ddagger$) and entropy ($\Delta S^\ddagger$) of activation (Table 1) were deduced by the method of least squares.[12] The uncertainties in $\Delta H^\ddagger$ (±5 kJ mol^{-1}) and $\Delta S^\ddagger$ (±17 J K^{-1} mol^{-1}) correspond to an uncertainty of ±5% in k_ψ. Activation parameters were not determined for (*N*-phenyl)-t-butylphenylphosphinic amide (9; X = H) which was hydrolysed extremely slowly. At 31.2 °C the absorbance at 285 nm decreased by less than 5% during 17 days ($k_\psi < 3.5 \times 10^{-8}$ s^{-1}), and even at 47.0 °C reaction was only *ca.* 7% complete after 14.7 days (k_ψ *ca.* 5.9×10^{-8} s^{-1}).

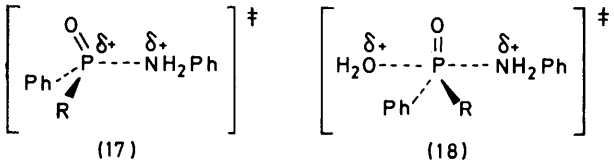
Perhaps the outstanding feature of the kinetic measurements is the substantial rate enhancement observed when isopropyl is replaced by cyclopropyl [(7) ⟶ (6); 20—25 fold increase], or t-butyl by 1-methylcyclopropyl [(9) ⟶ (8); >1 000 fold increase]. If we accept that a significant increase in the equilibrium concentration of the reactive protonated form of the amide is unlikely, it must be that the reactivity of the protonated species is enhanced. This is precisely what would be expected if the cyclopropyl group, and even more so 1-methylcyclopropyl, were able to stabilise the developing positive charge at the phosphinyl centre in a dissociative transition state (17). The large negative values of the entropy of activation for (5)—(8) (X = H) might be thought to indicate associative mechanisms, although a similar value of $\Delta S^\ddagger$ for (*N*-*p*-nitrophenyl)diphenylphosphinic amide was not thought incompatible with an *A*1 mechanism.[8] However the rate of hydrolysis decreases by a factor in excess of 10^5 along the series (5) ⟶ (7) ⟶ (9) as the *P*-alkyl group changes along the series Et ⟶ Pr^i ⟶ Bu^t. While steric inhibition of solvation of a dissociative transition state might well give rise to some decrease in rate with increased size of the *P*-alkyl group, the observed changes seem too extreme to be accounted for by such an effect. Rather, it seems probable that nucleophilic participation of water (or methanol) is important in the hydrolysis transition state, which might resemble (18) more closely than (17).† That being so, the relatively high reactivity of the cyclopropyl compounds (6) and (8) (X = H) should be ascribed primarily to the size of their alkyl groups allowing relatively unhindered nucleophilic attack at phosphorus.[13] The

TABLE 1

Hydrolysis of (*N*-phenyl)alkylphenylphosphinic amides (5)—(9) (X = H) in 1 : 1 v/v water–methanol 2.08M in hydrochloric acid [a]

Amide RPhP(O)NHPh	31.2 °C	39.1 °C	47.0 °C	$\Delta H^\ddagger$ / kJ mol^{-1}	$\Delta S^\ddagger$ / J K^{-1} mol^{-1}
	$10^5 k_\psi$/s^{-1}				
(5) R = Et	690	1 250	2 183	56.6	−100
(6) R = cyclopropyl	275	532	948	61.0	−94
(7) R = Pr^i	11.0	22.7	43.5	68.1	−97
(8) R = 1-methylcyclopropyl	4.22	8.60	18.3	72.8	−90
(9) R = Bu^t	<0.003 5		*ca.* 0.006		

[a] Estimated maximum possible errors are ±5% in k_ψ, ±5 kJ mol^{-1} in $\Delta H^\ddagger$, and ±17 J K^{-1} mol^{-1} in $\Delta S^\ddagger$.



(17) (18)

† An S_N2-like transition state (18) is shown for simplicity, but the present results would not distinguish between a direct-displacement associative mechanism and one involving a five-coordinate intermediate.

[11] A. J. Gordon and R. A. Ford, ' The Chemist's Companion,' Wiley, 1972, p. 136.

[12] H. W. Salzberg, J. I. Morrow, S. R. Cohen, and M. E. Green, ' Physical Chemistry—A Modern Laboratory Course,' Academic Press, 1969, p. 27.

[13] R. W. Taft (ch. 13) in ' Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, 1956, has pointed out that the steric effect of a ring is in general markedly less than for the corresponding open-chain substituent.

faster hydrolysis of (6) relative to (8), and the lower reactivity of both of these relative to (5), can then also be readily understood.

Haake and Koizumi [14] concluded that diphenylphosphinic amide, $Ph_2P(O)NH_2$, unlike its *N*-phenyl analogue, undergoes acid-catalysed hydrolysis by an associative (*A*2) mechanism. We recently had cause to determine the relative rates of hydrolysis of some primary alkylphenylphosphinic amides and found, as would be expected for a reaction which follows an *A*2 pathway, a high sensitivity to steric hindrance.[9] Thus, at 25.6 °C in aqueous hydrochloric acid buffered at pH 1.85 with sodium acetate, the values of k_ψ for $RPhP(O)NH_2$ with R = Et, cyclopropyl, Pr^i, 1-methylcyclopropyl, or Bu^t were in the ratios $62 : 45 : 2.2 : 1.0 : <1.3 \times 10^{-3}$. The variation in rate now observed for the (*N*-phenyl)alkylphenylphosphinic amides (5)—(9) (X = H) (k_ψ in the ratios $164 : 65 : 2.6 : 1.0 : <1 \times 10^{-3}$ at 31.2 °C) is similar, and encourages the view that these compounds also react by associative (*A*2) mechanisms rather than dissociative mechanisms such as that proposed for (*N*-phenyl)diphenylphosphinic amide. A fundamental change in mechanism would not, however, be expected to accompany replacement of a *P*-phenyl group in $Ph_2P(O)NHPh$ by an alkyl group since conjugation between a tetrahedral phosphoryl centre and an unsaturated substituent like phenyl is of relatively little importance.[15] Indeed, the influence of *P*-aryl substituents on the rate of the acid-catalysed hydrolysis of (*N*-phenyl)diphenylphosphinic amide shows clearly that the important interaction between the aryl group and the phosphorus atom is inductive rather than conjugative.[16,17] We therefore sought to clarify the apparent differences in the mechanisms of hydrolysis of (*N*-phenyl)alkylphenylphosphinic amides and their diphenyl counterparts by varying the nucleophilicity of the leaving group.

Influence of the N-*Aryl Group on the Hydrolysis of* (N-*Aryl*)*alkylphenylphosphine Amides*.—Pseudo-first-order rate constants for the hydrolysis of the *N*-arylphosphinic amides (5)—(8) (X = OMe, Br, or NO_2) are shown in Table 2. In general these values were obtained by the method described above for the *N*-phenyl compounds but by using measurements at 298 (ε *ca.* 1 500), 294 (ε *ca.* 800), and 320 nm (ε *ca.* 13 000), respectively for X = OMe, Br, and NO_2, and a smaller initial concentration (*ca.* 10^{-4}M) for X = NO_2. However, for the slow reactions of (7) and (8) (X = NO_2), reaction solutions were prepared on a larger scale and portions (4 ml) were sealed under nitrogen in glass ampoules and immersed in a thermostatted water bath at 31.2 ± 0.1 °C. An ampoule was removed from the bath and its contents transferred to a 10 mm silica cell which was flushed with nitrogen and tightly stoppered. The spectrum was recorded at intervals over 48 h, the cell being immersed in the water bath between scans. At the end of that period the contents of the cell were replaced by a fresh portion of the reaction mixture from a new ampoule. In this way a total of 32 spectra extending over a period of 164 h ($>4 \times t_{0.5}$) were recorded for (7; X = NO_2) and 45 spectra extending over 329 h ($>4 \times t_{0.5}$) for (8; X = NO_2). The spectra of all the *p*-nitroanilide hydrolysis mixtures showed well defined isosbestic points at 238, 283, and 393 nm [shifted to 386 nm for (8)].

For every amide the hydrolysis mixture was examined after not less than 10 half-lives at 31.2 °C (or in some cases a time at 60 °C corresponding to *ca.* 10 half-lives at 31.2 °C) to obtain the infinity spectrum. Except for the *p*-nitroanilides the infinity spectra showed the complete disappearance of absorption at the wavelengths used in deducing rate constants; only absorptions corresponding to the expected hydrolysis products, RPhP(O)OH and $H_3\overset{+}{N}\cdot C_6H_4X$, remained. Although the infinity spectra for the *p*-nitroanilides also showed only those absorptions expected of the products, the presence of *p*-nitroaniline (protonated) meant that there was no wavelength at which the absorbance of the mixture decreased to zero. At 320 nm, however, the extinction coefficient of the products was only a small fraction (4—6%) of that of the *p*-nitroanilides. Moreover at 418 nm the extinction coefficient of the products was the same as at 320 nm, whereas the extinction coefficient of the *p*-nitroanilides was negligible. Thus at any instant the difference between the measured absorbances of the mixture at 320 and at 418 nm provided a measure of the absorbance at 320 nm due to unchanged *p*-nitroanilide.

TABLE 2

Hydrolysis of (*N*-aryl)alkylphenylphosphinic amides (5)—(8) (X = OMe, H, Br, or NO_2) in 1 : 1 v/v water–methanol 2.08M in hydrochloric acid at 31.2 °C [a]

	X in amide = OMe		X in amide = H [b]		X in amide = Br		X in amide = NO_2	
Amide	$10^5 k_\psi/s^{-1}$	k_{rel}	$10^5 k_\psi/s^{-1}$	k_{rel}	$10^5 k_\psi/s^{-1}$	k_{rel}	$10^5 k_\psi/s^{-1}$	k_{rel}
(5) R = Et	1 540	100	634	100	402	100	32.8	100
(6) R = cyclopropyl	675	43.8	270	42.6	172	42.8	14.0	42.7
(7) R = Pr^i	28.2	1.83	10.9	1.72	6.64	1.65	0.503	1.53
(8) R = 1-methylcyclopropyl	9.87	0.64	3.97	0.63	2.89	0.72	0.256	0.78

[a] Values of k_ψ are averages of two determinations agreeing to within ±3%; the maximum possible error is estimated to be ±5%. [b] The values of k_ψ as shown here for (5)—(8) (X = H) differ from those obtained previously (Table 1). Although the variations are within the possible experimental error the new values are preferred for the present comparisons since they were obtained under exactly the same conditions as were the values of k_ψ for the other compounds in this Table.

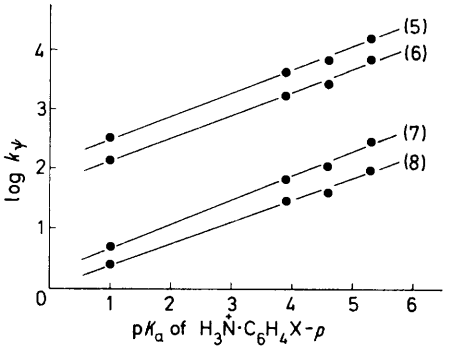
[14] P. Haake and T. Koizumi, *Tetrahedron Letters*, 1970, 4845; T. Koizumi and P. Haake, *J. Amer. Chem. Soc.*, 1973, **95**, 8073.

[15] A. J. Kirby and S. G. Warren, ' The Organic Chemistry of Phosphorus,' Elsevier, 1967, p. 275.

[16] G. Tomaschewski and G. Kühn, *J. prakt. Chem.*, 1968, **38**, 222.

[17] D. A. Tyssee, L. P. Bausher, and P. Haake, *J. Amer. Chem. Soc.*, 1973, **95**, 8066.

Substituents in the *N*-aryl group will influence the conversion of RPhP(O)NHAr into the hydrolysis transition state, whether it be (17) or (18), in two ways. First, they will have an effect on the basicity of the amide. It is not known whether *N*-arylphosphinic amides are protonated predominantly on nitrogen or on oxygen, but in either case electron-withdrawing substituents will reduce the amount of substrate present in its reactive *N*-protonated form. Secondly, they will influence the ease with which the P–N bond in the *N*-protonated amide breaks: electron-withdrawing substituents in the departing aniline will make it less nucleophilic and so facilitate P–N bond cleavage. For substituted (*N*-phenyl)diphenylphosphinic amides $Ph_2P(O)NH{\cdot}C_6H_4X$ it has been found that the rate of hydrolysis decreases as X changes in the series MeO ⟶ H ⟶ NO_2 (ratios of k_ψ are 2.84 : 1.00 : 0.046 in aqueous dioxan);[8] presumably a large decrease in the basicity of the amide is only partially compensated by an increasing lability of the P–N bond in the protonated form. The results in Table 2 now show that for the (*N*-aryl)alkylphenylphosphinic amides (5)—(8) the rate of hydrolysis is also increased by electron-donating substituents (X = OMe) and decreased by electron withdrawal (X = Br or NO_2). The magnitude of the variation in rate as X changes in the series MeO ⟶ H ⟶ Br ⟶ NO_2 is similar for each of the types of amide (5)—(8) (ratios of k_ψ are 2.43—2.59 : 1.00 : 0.61—0.73 : 0.046—0.064) and does not of itself suggest that changing the nature of the *P*-alkyl group causes any marked change in mechanism. Equally, there seems no reason to suppose that the mechanism by which the amides (5)—(8) react is fundamentally different from that for the hydrolysis of (*N*-aryl)diphenylphosphinic amides. Indeed, just as the values of log k_ψ for the hydrolysis of (*N*-aryl)diphenylphosphinic amides are linearly related to the pK_a values of the anilinium ions, with a slope of 0.4, so also is there a linear relationship (Figure) with a similar slope (0.38 ± 0.2) for each of the types of amide (5)—(8).[18]



It is also clear from the relative values (k_{rel}) of the rate constants in Table 2 that neither increasing (X = OMe) nor decreasing (X = Br or NO_2) the nucleophilicity of the leaving group has any substantial effect on the high sensitivity of the hydrolysis of (*N*-phenyl)alkylphenylphosphinic amides to steric hindrance. It therefore seems necessary to postulate that even the *p*-nitroanilides (X = NO_2), for which dissociative hydrolysis will be most favourable, react by way of an associative transition state.

Conclusions.—A complete description of the mechanism of hydrolysis of an *N*-arylphosphinic amide must be concerned both with the breaking of the P–N bond and with the making of the new P–O bond. Our results relate particularly to the latter process and show that any hindrance to bond making is strongly reflected in the reduced rate of hydrolysis. Although the results are not necessarily in conflict with suggestions that P–N bond breaking is well advanced in the transition state,[8] it seems unwise to describe the mechanism as *A*1-like or merged *A*1–*A*2 * since structural changes which discourage associative reaction and encourage dissociative reaction do not cause a shift to an *A*1 mechanism. For that reason our investigation does not reveal whether cyclopropyl groups are able to stabilize adjacent electron-deficient phosphinyl centres.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were recorded with Perkin-Elmer 237 and 257 instruments, u.v. spectra with a Unicam SP 800 spectrophotometer fitted with a cell holder through which water from a thermostatically controlled bath was circulated, and n.m.r. spectra with a Varian T-60 spectrometer (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'. Methanol used in rate measurements was AnalaR.

Alkylphenylphosphinic acids (10)—(13) and the corresponding alkylphenylphosphinic chlorides were prepared by methods previously described.[9]

Phenyl-t-butylphosphinic Acid (14).—Chloro(phenyl)-t-butylphosphine [9] (6.4 g) was added slowly to a stirred, ice-cold mixture of 28% hydrogen peroxide (4.5 ml), water (25 ml), and sodium hydroxide (5.5 g). The mixture was heated at 80 °C for 30 min, cooled, and acidified with concentrated hydrochloric acid. The resulting precipitate of crude phosphinic acid was collected and dissolved in 2M-sodium hydroxide, and the solution was washed with chloroform. The solid obtained on acidification of the aqueous portion was crystallised from petroleum (b.p. 60—80 °C)–chloroform (4 : 1) to give phenyl-t-butylphosphinic acid, m.p. 157—158° (lit.,[19] 156°), $\nu_{max.}$ (Nujol) *ca.* 2 600, 2 260, and 2 160 (all br, OH), 1 720 (OH def.), and 1 190 cm^{-1} (P=O), δ(CCl_4) 12.73 (1 H, s, OH), 8.1—7.3 (5 H, m, Ph), and 1.02 (9 H, d, J_{PH} 16 Hz).

(*N-Phenyl*)*ethylphenylphosphinic Amide* (5; X = H).—A solution of redistilled aniline (1.17 g, 12.6 mmol) in dry carbon tetrachloride (15 ml) was stirred at 0 °C in nitrogen while ethylphenylphosphinic chloride (1.08 g, 5.74 mmol) in carbon tetrachloride (5 ml) was added during 1 min.

* The idea of a merged *A*1–*A*2 mechanism was introduced in ref. 17 and reappeared in a communication by T. Koizumi, Y. Kobayashi, and E. Yoshii (*J.C.S. Chem. Comm.*, 1974, 678).

[18] D. D. Perrin ('Dissociation Constants of Organic Bases,' Butterworths, London, 1965) gives the following pK_a values: *p*-methoxyanilinium, 5.3; anilinium, 4.6; *p*-bromoanilinium, 3.9; *p*-nitroanilinium, 1.0.

[19] H. Hoffmann and P. Schellenbeck, *Chem. Ber.*, 1966, **99**, 1134.

Chloroform (5 ml) was added to facilitate stirring when a sticky solid separated, and stirring was continued for 2 h at room temperature. Volatile material was removed on a rotary evaporator and water (15 ml) and chloroform (40 ml) were added to the residue. The layers were separated, the aqueous portion was extracted with more chloroform (3 × 15 ml), and the combined organic extracts were washed with aqueous 5% potassium carbonate (20 ml) and dried (Na_2SO_4). The residue remaining after evaporation was crystallised from ethyl acetate to give fine needles of (N-*phenyl*)*ethylphenylphosphinic amide* (1.16 g, 4.72 mmol, 82%), m.p. 167—170°, $\nu_{max.}$ (Nujol) 3 165 (NH), 1 600 (NH def.), and 1 195 and 1 180 cm^{-1} (P=O), $\delta(CDCl_3)$ 8.23—7.33 (5 H, m, PPh), 7.33—6.73 (6 H, m, reduced to 5 H, m with D_2O, NPh and NH), 2.45—1.63 (2 H, m, CH_2), and 1.40—0.67 (3 H, m, Me) (Found: C, 68.2; H, 6.6; N, 5.6. $C_{14}H_{16}NOP$ requires C, 68.55; H, 6.6; N, 5.7%).

The following compounds were similarly obtained from the appropriate phosphinic chlorides: (N-*phenyl*)*cyclopropylphenylphosphinic amide* (6; X = H) (81%), m.p. 191—193° (from 1 : 1 ethyl acetate–chloroform), $\nu_{max.}$ (Nujol) 3 180, 1 600, and 1 185 cm^{-1}, $\delta(CDCl_3)$ 8.16—7.33 (5 H, m, PPh), 7.25—6.70 (5 H, m, NPh), 5.62br (1 H, d, J_{PH} 10 Hz, NH), and 1.60—0.63 (5 H, m, cyclopropyl) (Found: C, 69.75; H, 6.15; N, 5.85. $C_{15}H_{16}NOP$ requires C, 70.0; H, 6.3; N, 5.45%) (reaction time of 18 h and a larger volume of chloroform in the work-up to compensate for lower solubility); (N-*phenyl*)*isopropylphenylphosphinic amide* (7; X = H) (66%), m.p. 168—171° (from 4 : 1 ethyl acetate–chloroform), $\nu_{max.}$ (Nujol) 3 170, 1 600, 1 180, and 1 160 cm^{-1}, $\delta(CDCl_3)$ 8.13—7.33 (5 H, m, PPh), 7.23—6.67 (5 H, m, NPh), 5.93br (1 H, d, J_{PH} 11 Hz, exchanged with D_2O, NH), 2.63—1.85 (1 H, m, CH), 1.23 (3 H, dd, J_{PH} 17.5, J_{HH} 7 Hz, Me), and 1.07 (3 H, dd, J_{PH} 17.5, J_{HH} 7 Hz, Me) (Found: C, 69.6; H, 6.8; N, 5.4. $C_{15}H_{18}NOP$ requires C, 69.5; H, 7.0; N, 5.4%) (reaction time of 42 h); (N-*phenyl*)-1-*methylcyclopropyl*(*phenyl*)*phosphinic amide* (8; X = H) (70%), m.p. 207.5—209° (from 4 : 1 ethyl acetate–chloroform), $\nu_{max.}$ (Nujol) 3 190, 1 605, and 1 170 cm^{-1}, $\delta(CDCl_3)$ 8.07—7.30 (5 H, m, PPh), 7.20—6.70 (5 H, m, NPh), 5.30br (1 H, d, J_{PH} 10 Hz, NH), 1.57—1.03 (2 H, m, cyclopropyl), 1.22 (3 H, d, J_{PH} 13 Hz, Me), and 0.75—0.37 (2 H, m, cyclopropyl) (Found: C, 70.65; H, 6.7; N, 5.1. $C_{16}H_{18}NOP$ requires C, 70.8; H, 6.7; N, 5.2%) (reaction time of 20 h).

(N-*Phenyl*)*phenyl-t-butylphosphinic Amide* (9; X = H).—A solution of redistilled aniline (3.23 g, 35.0 mmol) in dry carbon tetrachloride (15 ml) was stirred in nitrogen while chloro(phenyl)-t-butylphosphine [9] (3.01 g, 15.0 mmol) in carbon tetrachloride (10 ml) was added over 5 min. The mixture was stirred at room temperature for 48 h, solid was removed by filtration, and the filtrate was added dropwise during 5 min to stirred, ice-cold, 30% hydrogen peroxide (40 ml). After addition of 1M-sodium hydroxide (8 ml), the mixture was shaken at room temperature for 1 h. The layers were separated, the aqueous portion was extracted with chloroform (2 × 20 ml), and the combined organic extracts were concentrated to an oil. Water (30 ml) was added and evaporated off under reduced pressure to remove unchanged aniline. Crystallisation of the residual solid from methanol (100 ml) afforded (N-*phenyl*)*phenyl-t-butylphosphinic amide* (1.81 g, 6.65 mmol, 44%), m.p. 263—264°, $\nu_{max.}$ (Nujol) 3 190 (NH), 1 605 (NH def.), and 1 160 cm^{-1} (P=O), $\delta(CDCl_3)$ 8.17—7.33 (5 H, m, PPh), 7.25—6.77 (5 H, m, NPh), 4.97br (1 H, d, J_{PH} *ca.* 10 Hz), and 1.23 (9 H, d, J_{PH} 16 Hz) (Found: C, 70.2; H, 7.3; N, 5.1. $C_{16}H_{20}NOP$ requires C, 70.3; H, 7.4; N, 5.1%).

(N-p-*Methoxyphenyl*)*ethylphenylphosphinic Amide* (5; X = OMe).—A solution of *p*-methoxyaniline (1.23 g, 10.0 mmol) in a mixture of carbon tetrachloride (20 ml) and chloroform (5 ml) was stirred under anhydrous conditions and ethylphenylphosphinic chloride (0.94 g, 5.0 mmol) in carbon tetrachloride (5 ml) was added dropwise. After a further 2 h at room temperature the solvent was removed on a rotary evaporator and the residue dissolved in chloroform. The resulting solution was washed with water (twice) and aqueous 5% sodium hydrogen carbonate, and evaporated. The solid so obtained was crystallised from acetone to give (N-p-*methoxyphenyl*)*ethylphenylphosphinic amide* (0.77 g, 2.8 mmol, 56%), m.p. 147—148° (Found: C, 65.6; H, 6.65; N, 4.9. $C_{15}H_{18}NO_2P$ requires C, 65.4; H, 6.6; N, 5.1%).

The following compounds were similarly prepared from the appropriate alkylphenylphosphinic chlorides and substituted anilines: (N-p-*methoxyphenyl*)*cyclopropylphenylphosphinic amide* (6; X = OMe) (59%), m.p. 157—159° (from acetone) (Found: C, 67.0; H, 6.3; N, 4.85. $C_{16}H_{18}NO_2P$ requires C, 66.9; H, 6.3; N, 4.9%); (N-p-*bromophenyl*)*ethylphenylphosphinic amide* (5; X = Br) (48%), m.p. 210—214° [from methanol then from acetone–chloroform (7 : 1)], homogeneous by t.l.c. [R_F 0.45 on silica with ether–methanol (20 : 1)] (Found: C, 51.9; H, 4.7; N, 4.2. $C_{14}H_{15}BrNOP$ requires C, 51.9; H, 4.7; N, 4.3%); N-p-*bromophenyl*)*cyclopropylphenylphosphinic amide* (6; X = Br) (71%), m.p. 172—175° (from acetone) (Found: C, 53.5; H, 4.4; N, 4.2. $C_{15}H_{15}BrNOP$ requires C, 53.6; H, 4.5; N, 4.2%).

(N-p-*Methoxyphenyl*)-1-*methylcyclopropyl*(*phenyl*)*phosphinic Amide* (8; X = OMe).—A solution of *p*-methoxyaniline (0.43 g, 3.5 mmol) in benzene (5 ml) and chloroform (5 ml) was stirred under anhydrous conditions and 1-methylcyclopropyl(phenyl)phosphinic chloride (0.358 g, 1.67 mmol) dissolved in benzene (5 ml) was added. The mixture was stirred at room temperature for 16 h and the product isolated as described for (5; X = OMe). Crystallisation from ethyl acetate and then from petroleum (b.p. 60—80 °C)–acetone (1 : 1) afforded (N-p-*methoxyphenyl*)-1-*methylcyclopropyl*(*phenyl*)*phosphinic amide* (0.203 g, 0.68 mmol, 40%), m.p. 145—147° (Found: C, 68.1; H, 6.7; N, 4.8. $C_{17}H_{20}NO_2P$ requires C, 67.8; H, 6.7; N, 4.65%). It seems likely that an improved yield would have resulted from heating the reaction mixture.

The following compounds were obtained by similar methods from the appropriate alkylphenylphosphinic chlorides and substituted anilines: (N-p-*methoxyphenyl*)-*isopropylphenylphosphinic amide* (7; X = OMe) (71%), m.p. 174—176° (from acetone) (Found: C, 66.4; H, 7.1; N, 4.9. $C_{16}H_{20}NO_2P$ requires C, 66.4; H, 7.0; N, 4.8%) (reaction period of 16 h at room temperature followed by 3 h at reflux temperature); (N-p-*bromophenyl*)-1-*methylcyclopropyl*(*phenyl*)*phosphinic amide* (8; X = Br) (58%), m.p. 210—212° [from chloroform–ethyl acetate (1 : 1)] (Found: C, 54.8; H, 5.0; N, 3.9. $C_{16}H_{17}BrNOP$ requires C, 54.9; H, 4.9; N, 4.0%) (an improved yield would probably have resulted from heating the mixture); (N-p-*bromophenyl*)-*isopropylphenylphosphinic amide* (7; X = Br) (63%), m.p. 183—185° (from acetone) (Found: C, 53.3; H, 5.1; N, 4.1. $C_{15}H_{17}BrNOP$ requires C, 53.3; H, 5.1; N, 4.1%) (reaction period of 20 h at room temperature followed by 3 h at reflux temperature).

(N-p-*Nitrophenyl*)*ethylphenylphosphinic Amide* (5; X = NO_2).—A mixture of ethylphenylphosphinic chloride (0.415 g, 2.2 mmol), *p*-nitroaniline (0.28 g, 2.0 mmol), and pyridine (0.32 g, 4.0 mmol) dissolved in dry benzene (8 ml) was boiled gently under reflux for 15 h. The mixture was allowed to cool and chloroform (20 ml) was added. The resulting solution was washed with 0.4M-hydrochloric acid (10 ml), aqueous 5% sodium hydrogen carbonate, and water, and concentrated to an oil. Trituration with ethyl acetate gave a pale yellow solid which on crystallisation from ethyl acetate (twice) afforded almost colourless (N-p-*nitrophenyl*)-*ethylphenylphosphinic amide* (0.223 g, 0.77 mmol, 35%), m.p. 166.5—168° (Found: C, 58.2; H, 5.1; N, 9.8. $C_{14}H_{15}N_2O_3P$ requires C, 57.95; H, 5.2; N, 9.7%). T.l.c. on silica [ether–methanol (10 : 1)] revealed a single spot, R_F 0.37; *p*-nitroaniline (R_F 0.67) was absent.

The following compounds were prepared by similar methods from the appropriate alkylphenylphosphinic chlorides and *p*-nitroaniline: (N-p-*nitrophenyl*)*cyclopropylphenylphosphinic amide* (6; X = NO_2) (46%), m.p. 163—164° [from ethyl acetate–chloroform (12 : 1) and then from acetone], homogeneous by t.l.c. (R_F 0.45) (Found: C, 59.8; H, 5.1; N, 9.2. $C_{15}H_{15}N_2O_3P$ requires C, 59.6; H, 5.0; N, 9.3%); (N-p-*nitrophenyl*)*isopropylphenylphosphinic amide* (7; X = NO_2) (48%), pale yellow, m.p. 215—217° (from acetone) (Found: C, 59.25; H, 5.7; N, 9.25. $C_{15}H_{17}N_2O_3P$ requires C, 59.2; H, 5.6; N, 9.2%) (60 h heating); (N-p-*nitrophenyl*)-1-*methylcyclopropyl*(*phenyl*)-*phosphinic amide* (8; X = NO_2) (37%), m.p. 198—202° (from ethyl acetate) (65 h heating), R_F 0.50, contaminated (t.l.c.) with a trace of *p*-nitroaniline, and purified by preparative t.l.c. followed by crystallisation from ethyl acetate; m.p. 201—203° (Found: C, 60.7; H, 5.5; N, 9.0. $C_{16}H_{17}N_2O_3P$ requires C, 60.75; H, 5.4; N, 8.9%) [the buff-coloured crystals turned yellow over several weeks, but remained homogeneous to t.l.c. analysis and gave an unchanged u.v. spectrum; similar but less marked behaviour was exhibited by (7; X = NO_2)].

I.r. Spectra of (N-*Aryl*)*alkylphenylphosphinic Amides* (X ≠ H).—All these amides, as Nujol mulls, displayed one or more broad absorption maxima in the regions 3 200—3 040 cm^{-1} (NH) and 1 195—1 160 cm^{-1} (P=O). The *p*-bromoanilides and *p*-nitroanilides, respectively, absorbed at 1 590br and 1 600 cm^{-1} (NH def.) but the *p*-methoxyanilides showed no strong absorption in the region 1 700—1 530 cm^{-1}. Other bands included *ca.* 1 240 and 1 030 cm^{-1} (ArOMe) for *p*-methoxyanilides and *ca.* 1 345 cm^{-1} (NO_2) for *p*-nitroanilides.

N.m.r. Spectra of (N-*Aryl*)*alkylphenylphosphinic Amides* (X ≠ H).—Those amides which were sufficiently soluble in $CDCl_3$ to be examined showed the expected resonances for PPh, P·NH, and *P*-alkyl. The N·C_6H_4X system appeared as four principal lines (AA′MM′) centred at δ *ca.* 7.5 (X = NO_2), 7.0 (X = Br), or 6.8 (X = OMe), and for the *p*-methoxyanilides, a singlet (3 H) at δ 3.65.

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