# Hydrolysis of Alkylphenylphosphinanilides in Acidic Solution: the Influence of Cyclopropyl Groups

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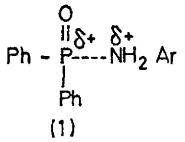
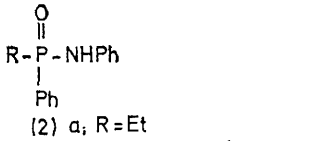
*Summary* The rate of hydrolysis of an alkylphenylphosphinanilide in acidic solution is greatly influenced by the nature of the alkyl group; in particular, cyclopropyl and 1-methylcyclopropyl give increased rates relative to isopropyl and t-butyl, respectively.

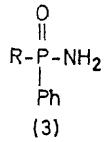
THE acid-catalysed hydrolysis of diphenylphosphinanilide is thought to have a dissociative (*A*1 or *A*1-like) mechanism.[1] In the rate-determining step, cleavage of the P–N bond in the *N*-protonated anilide is well advanced in the transition state (**1**), with consequent development of positive charge on the phosphinyl phosphorus atom. There is no reason to suppose that the hydrolysis of alkylphenylphosphinanilides will be fundamentally different. By synthesising the anilides (**2a**—**e**) and studying their hydrolysis, we therefore hoped to determine whether a cyclopropyl group is able to stabilise positive charge at an adjacent phosphinyl centre. The stabilisation of electron-deficient carbon centres by cyclopropyl groups is well documented.[2]



(1)



(2) a; R = Et
b; R = Cyclopropyl
c; R = Pr$^{i}$
d; R = 1-Methylcyclopropyl
e; R = But$^{t}$



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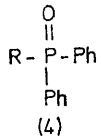

(4)

The phosphinanilides (**2a**—**d**)† were prepared from the appropriate alkylphenylphosphinic acids, which were themselves obtained by heating the alkyldiphenylphosphine oxides (**4a**—**d**) with powdered sodium hydroxide. t-Butylphenylphosphinanilide (**2e**) was prepared by oxidation of the product from the reaction of t-butylphenylchlorophosphine with aniline.

The anilides (**2a**—**d**) were completely hydrolysed by stirring with boiling 2M-hydrochloric acid for 90 min. The product in each case had i.r. and n.m.r. spectra identical to those of the corresponding phosphinic acid: if phosphinylium cations were intermediates in the hydrolyses, they did not rearrange to an appreciable extent. Reaction of (**2e**) was incomplete after 20 h, but on heating with 2:1 v/v 4M-hydrochloric acid–dioxan for 137 h, unrearranged phosphinic acid was again obtained.

The rates of hydrolysis of (**2a**—**e**) were examined by following the disappearance of absorption at 285 nm using dilute solutions (0·001—0·005M) in aqueous methanol containing 2·08M-hydrochloric acid. Linear first-order plots were obtained for (**2a**—**d**) and from these the pseudo-first-order rate constants ($k_\psi$) were deduced (see Table). Reaction of (**2e**) was too slow to be followed satisfactorily; the value of $k_\psi$ shown is an upper limit, and may far exceed the actual value.

TABLE. Hydrolysis of alkylphenylphosphinanilides (**2a**—**e**) in 1:1 v/v water–methanol containing 2·08M-HCl at 31·2°[a]

| Anilide | $10^5 k_\psi$/s$^{-1}$ | $\Delta H^{\ddagger}$/ kJ mol$^{-1}$ | $\Delta S^{\ddagger}$/ J K$^{-1}$ mol$^{-1}$ |
|---|---|---|---|
| (**2a**) | 690 | 56·6 | −100 |
| (**2b**) | 275 | 61·0 | −94 |
| (**2c**) | 11·0 | 68·1 | −97 |
| (**2d**) | 4·2 | 72·8 | −90 |
| (**2e**) | <0·004 | — | — |

[a] Values of $\Delta H^{\ddagger}$ (±5 kJ mol$^{-1}$) and $\Delta S^{\ddagger}$ (±17 J K$^{-1}$ mol$^{-1}$) determined from experiments at 31·2, 39·1, and 47·0°

A substantial rate enhancement is observed when isopropyl is replaced by cyclopropyl, (**2c**) → (**2b**), and t-butyl by 1-methylcyclopropyl, (**2e**) → (**2d**). Accepting that there is no increase in the equilibrium concentration of protonated anilide, it must be that the reactivity of the protonated species is enhanced, possibly as a result of the stabilisation of developing positive charge at the phosphinyl centre in a dissociative (*A*1) transition state. The large negative values of the entropy of activation for (**2a**—**d**) are similar to the value reported for $Ph_2P(O)NH{\cdot}C_6H_4NO_2$-*p* ($\Delta S^{\ddagger} = -92$ J K$^{-1}$ mol$^{-1}$), and are not necessarily inconsistent with an *A*1 mechanism.[1] However, it will be noted that the relative rate constants for (**2a**), (**2c**), and (**2e**) imply a mechanism which is very sensitive to steric hindrance; that (**2d**) hydrolyses much more slowly than (**2b**); and that both (**2b**) and (**2d**) are less reactive than (**2a**). These observations are more in accord with an associative (*A*2) mechanism, in which case the relatively high rates for the cyclopropyl compounds can be attributed to the size of their alkyl substituents allowing relatively unhindered nucleophilic attack.

In contrast to diphenylphosphinanilides, the corresponding amide [$Ph_2P(O)NH_2$] hydrolyses by an *A*2 mechanism.[3] We find that the rates of hydrolysis of the phosphinamides (**3**) (in aqueous HCl buffered with NaOAc, pH 1·85, 25·6°) vary with the nature of the alkyl group [values of $k_\psi$ for (**3a**—**e**) in the ratio 62:45:2·2:1·0:$< 1{\cdot}3 \times 10^{-3}$] in a way

† New compounds gave satisfactory spectra and elemental analyses.

which resembles the behaviour of the anilides (**2**). We conclude that the anilides (**2**) and the amides (**3**) hydrolyse by similar mechanisms, that these are apparently associative rather than dissociative, and that the question of the interaction of cyclopropyl groups with positive phosphinyl centres remains open.

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[1] P. Haake and D. A. Tyssee, *Tetrahedron Letters*, 1970, **3513**; see also G. Capozzi and P. Haake, *J. Amer. Chem. Soc.*, 1972, **94**, 3249.
[2] H. G. Richey, (ch. 25, p. 1201), and K. B. Wiberg, B. A. Hess, and A. J. Ashe, (ch. 26, p. 1295) in 'Carbonium Ions,' vol. III, eds. G. A. Olah and P. von R. Schleyer, Wiley-Interscience, 1972.
[3] P. Haake and T. Koizumi, *Tetrahedron Letters*, 1970, 4845.