Tetrahedron Letters No.40, pp. 3513-3516, 1970. Pergamon Press. Printed in Great Britain.

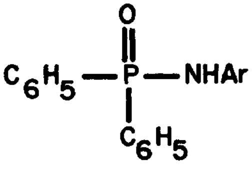
DISSOCIATIVE DISPLACEMENT AT PHOSPHORUS BY UNIMOLECULAR CLEAVAGE OF A P-N BOND. SOME COMMENTS ON ENTROPY OF ACTIVATION AS A CRITERION OF MECHANISM[1]

Paul Haake[2] and Donald A. Tyssee[3]

Department of Chemistry, University of California, Los Angeles 90024
and Hall-Atwater Laboratories of Chemistry, Wesleyan University
Middletown, Connecticut 06457

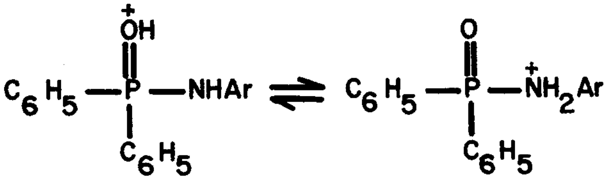
(Received in USA 16 July 1970; received in UK for publication 27 July 1970)

We have studied the acid-catalyzed hydrolysis of some phosphinanilides (1) and have found results of considerable interest which are relevant to the general problem of cleavage of P-N bonds.[4]



$C_6H_5-P(=O)(C_6H_5)-NHAr$

1



$C_6H_5-P(=\overset{+}{O}H)(C_6H_5)-NHAr \rightleftharpoons C_6H_5-P(=O)(C_6H_5)-\overset{+}{N}H_2Ar$

2 3

In 10% aqueous dioxane, the pseudo first-order rate constants (k_ψ) for acid-catalyzed hydrolysis of N-p-nitrophenyldiphenylphosphinamide (1: Ar=p-NO_2-C_6H_4) yield linear plots of log k_ψ vs. H_0;[5] There is clearly non-linear dependence of log k_ψ on log [acid] in both H_2SO_4 and $HClO_4$. This is evidence for an A_1 mechanism of hydrolysis. However, the slopes of log k_ψ vs. H_0 are 0.59 and 0.56 in H_2SO_4 and $HClO_4$ respectively. This extreme deviation from the unit slope expected of a Hammett base reacting by an A_1 mechanism caused us some doubt about the validity of the Hammett criterion applied to the hydrolysis of 1.[6]

Substituent effects indicate a different pathway for hydrolysis than observed for benzanilides.[7] Variation of Ar in 1(Ar=p-$CH_3OC_6H_4$, C_6H_5, and p-$NO_2C_6H_4$) (Table 1) indicates $\rho = -1.73$ compared to $\rho = +0.6$ in various substituted benzanilides.[7] Furthermore, the excellent correlation of log k_ψ for 1 with pK's of anilinium ions suggests protonation on nitrogen in the species undergoing hydrolysis and an A_1 mechanism, since this result indicates that the transition state appears to resemble N-protonated 1.[8]

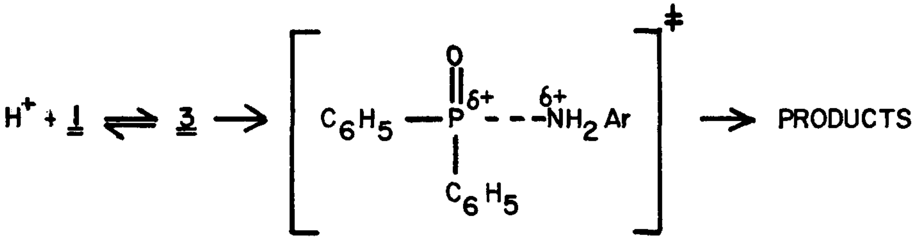
TABLE 1

Rate Constants for Hydrolysis of $(C_6H_5)_2P(O)NHAr$ (10^{-4}M.) in 10% Aqueous Dioxane, 0.49 M $HClO_4$, 25.2°

Ar%	$p\text{-}NO_2\text{-}C_6H_4$	C_6H_5	$p\text{-}CH_3O\text{-}C_6H_4$
$10^5k(sec^{-1})$	2.58	56.7	161.0

Rates of hydrolysis of 1($Ar = p\text{-}NO_2\text{-}C_6H_4$) at 25°, 35° and 45° gave E_a = 17.0 kcal/mole and $\Delta S^{\ddagger}$ = -22 eu. The value of $\Delta S^{\ddagger}$ falls in the range suggested[9] as characteristic of a bimolecular, rate-determining reaction of protonated substrate in conflict with the tentative conclusion from the Hammett criterion and substituent effects.

The solvent deuterium isotope effect in the hydrolysis of 1($Ar = p\text{-}NO_2\text{-}C_6H_4$) was evaluated in D_2O and H_2O with 0.49 M $HClO_4$. The reaction was 2.7 times faster in the deuterated medium. This is very close to what would be expected in an A_1 mechanism with the main isotope effect on the equilibrium involving protonation of substrate.[10] Therefore, there is strong evidence for an A_1 mechanism of hydrolysis, and together with the substituent effects and H_0 dependence, eq. 1 appears to be valid.



(1)

Although these anilides probably protonate predominantly on oxygen, it is apparently the N-protonated substrate (3) which undergoes P-N cleavage and hydrolysis.

On closer examination, we conclude that the $\Delta S^{\ddagger}$ value of -22 eu is not in conflict with this mechanism. It is known that the ΔS for protonation of 2,4-dinitroaniline is -21.5 e.u., and ΔS for protonation becomes increasingly negative with decreasing basicity of the aniline.[11] This is presumably due to the increased solvation requirements of a very acidic anilinium ion compared to H^+ + aniline. Therefore, ΔS (protonation) should depend on two factors: 1) the acidity of the protonated species; and 2) the number of acidic protons which have to be solvated in the protonated species. ΔS (protonation) may be about 0 for oxy bases of the kind involved in reactions considered by Schaleger and Long[9] because there is only one acidic proton in the conjugate acids. In **3**, there is two protons and they are undoubtedly very acidic, probably considerably more acidic than the protons of 2,4-dinitroanilinium ion. It appears reasonable to estimate that ΔS (protonation) for generation of **3** is about -20 e.u. We must then estimate ΔS (rate-determining step) in order to use entropy as a criterion of mechanism. In this reaction:

ΔS (protonation) estimated $\sim$ -20 eu;
$\Delta S^{\ddagger}$ (hydrolysis) observed = -22 eu;
therefore, ΔS (rate-determining step) estimated $\sim$ 0 eu

This estimated ΔS (rate-determining step) clearly supports an A_1 mechanism.[9]

We conclude that the postulates[9] regarding $\Delta S^{\ddagger}$ in acid-catalyzed reactions are likely to be correct for a substrate protonating on oxygen but are not generally valid unless one can predict ΔS for the equilibrium protonation of substrate. In any case, the $\Delta S^{\ddagger}$ criterion should be applied with some concern about ΔS for protonation.

These results indicate considerable lability of a P-N bond in a phosphorus amide when the N atom is positively charged. Of course, in this case, the leaving group is an aniline and the P-N bond will tend to cleave considerably more readily than when the leaving group is NH_3 or an aliphatic amine.

We have commented in an earlier publication on phosphinylium ions, $R_2\overset{+}{P}=O$, which were observed to be important fragments in the mass spectra of phosphinates.[12] The present data lends support to a role of these ions in the solution chemistry of phosphorus.[13]

REFERENCES

1. Research supported by grant AM-12743 from the U.S. Public Health Service and grant GP-13453 from the National Science Foundation.
2. To whom inquiries should be addressed at Wesleyan University.
3. Present address: Central Research Department, Monsanto Company, St. Louis, Missouri.

4. See, for example: T. C. Bruice and S. J. Benkovic, *Bio-Organic Mechanisms,* W. A. Benjamin, Inc., New York, 1966, Chap. 5; A. W. Garrison and C. E. Boozer, *J. Am. Chem. Soc.*, **90**, 3486 (1968).
5. Acidities to 6.86M H_2SO_4 and 4.38M $HClO_4$ were used. The 10% dioxane was necessary for solubility reasons.
6. We have observed such deviations from unit slope in the protonation of phosphine oxides; P. Haake, R. D. Cook and G. H. Hurst, *J. Am. Chem. Soc.*, **89**, 2650 (1967). Considering this precedent, the deviations from unit slope are not in real conflict with an A_1 mechanism.
7. G. Cauzzo, V. Mazzucato and A. Faffani, *Atti. Accad. Nazl. Lincei, Rend., Classe. Sci. Fix.*, *Mat. Nat.* **29**, 348 (1960), *C. A.*, **56**, 1279F (1962).
8. Although only three compounds were studied in this series, the p-nitro and p-methoxy compounds are the crucial ones for deciding substituent effects; the correlation with pK_a's of anilinium ions is, therefore, significant.
9. L. L. Schaleger and F. A. Long., *Adv. Phys. Org. Chem.*, **1**, 1 (1963).
10. E. Hogfeldt and J. Bigeleisen, *J. Am. Chem. Soc.*, **82**, 15 (1960); C. A. Bunton and V. J. Shiner, *ibid.*, **83**, 3214 (1961); O. Reitz, *Z. Phys. Chem.*, **A183**, 371 (1938); A. Lapidot and D. Samuel, *J. Chem. Soc.*, 1931 (1964).
11. A. I. Gebshtein, G. G. Sheglova and M. I. Temlein, *Zh. Neorg. Khim.*, **1**, 506 (1956).
12. P. Haake and P. S. Ossip, *Tetrahedron*, **24**, 565 (1968).
13. However, in phosphinyl halides, bimolecular reactions appear to be preferred: I. Dostrovsky and M. Halmann, *J. Chem. Soc.*, 1004 (1956); P. S. Ossip, Ph. D. Thesis, University of California, Los Angeles, 1968.