Kinetic Study on the Alkaline Hydrolysis of Some Tetracoordinate P^V Esters of 2,4-Dinitrophenol

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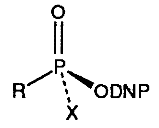
The alkaline hydrolysis of 2,4-dinitrophenyl esters of benzylphosphinic, benzylphosphonic and benzylphosphonamidic acid does not proceed through a carbanion-promoted dissociative mechanism, a possible alternative pathway to the usual $S_N2(P)$ process; this is a further indication of the clear preference for associative displacement at phosphorus.

We have recently reported[1] that the alkaline hydrolysis of aryl phosphinates possessing ionizable α-hydrogen atoms follows an associative, $S_N2(P)$ mechanism, although, in principle, these substrates could react through carbanion-promoted dissociative mechanisms. Our previous work[1a] provided evidence that 4-nitrophenyl (methylsulfonyl)methylphenylphosphinate hydrolyses *via* an associative bimolecular process despite its strict analogies with 4-nitrophenyl *N*-phenyl-*P*-phenylphosphonamidate which undergoes hydrolysis through an E1cB mechanism.[2] These two substrates, differing only in the nature of the potential internal nucleophilic centre, carbon and nitrogen respectively, have very similar acidity and possess the same leaving group (*p*-nitrophenoxide ion). Since it is now generally thought that E1cB-like mechanisms require substrates with a good nucleofuge and labile α-proton as well as 'stable' intermediates, the different behaviour of these esters is attributed to the different stability of the putative intermediates.[1a] In order to direct the reaction toward a dissociative carbanion-promoted pathway it seemed to us appropriate to increase the nucleofuge ability as well as the intermediate stability.

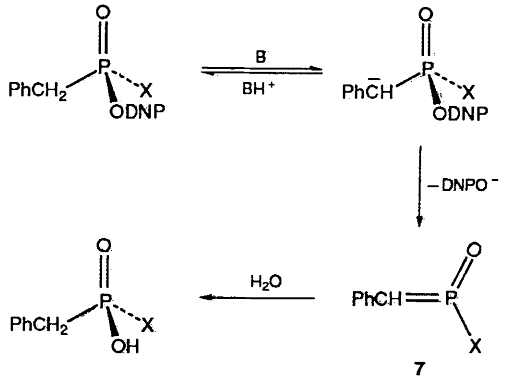
On this basis we have undertaken the present study on the alkaline hydrolysis of the 2,4-dinitrophenyl phosphinate **1**, phosphonate **2** and phosphonamidate **3** and, for comparison, of the corresponding esters **4**, **5** and **6**, which are devoid of α-protons.



	R	X
1	$PhCH_2$	Ph
2	$PhCH_2$	EtO
3	$PhCH_2$	Et_2N
4	Ph	Ph
5	Ph	EtO
6	Ph	Et_2N

DNP = 2,4-dinitrophenyl

In esters **1**–**3** the presence of a very good leaving group (2,4-dinitrophenoxide ion) is a prerequisite for the intervention of a dissociative mechanism and the presence of a ligand (X) able to donate a lone pair (in esters **2** and **3**) could favour the dissociative pathway, depicted in Scheme 1, by virtue of an extra driving force, the ligand lone pair cooperating with the internal nucleophile in the unimolecular expulsion of the leaving group. The feasibility of this step (most likely the rate-determining one) is supported by recent NMR and X-ray crystallographic studies on benzyl phosphorinanes[3] which claim that carbanions arising from these phosphonyl derivatives upon deprotonation of the benzylic group strongly interact with the highly polarized P=O group.



Scheme 1

Moreover, the electron donating ligand could also stabilize, through some π-bonding, the putative intermediate (**7**, Scheme 1) thus further favouring the E1cB path. It is however necessary to point out that bonding and electronic structure of phosphorus compounds are the object of a widespread debate and that, sometimes, conflicting results arise from theoretical studies.[4]

Results and Discussion

The reactions were carried out at 25 °C in 20% aq. dioxane, $pK_w = 14.62$,[5] ionic strength 0.1 mol dm^{-3} (KCl), and were followed spectrophotometrically by monitoring the release of 2,4-dinitrophenoxide ion at 400 nm. UV spectra showed that the stoichiometric amounts of acid and phenol were liberated.

The pseudo-first-order rate constants for the hydrolysis of esters **1**–**6** were proportional to hydroxide ion concentration according to the rate law (1):

$$k_{obs} = k_{OH}[OH^-] \qquad (1)$$

Values of the second-order rate constants k_{OH} together with the employed pH range are reported in Table 1. The useful pH range in which eqn. (1) holds has a lower limit due to the uncatalysed hydrolysis of the esters: the intervention of this spontaneous reaction causes deviation from linearity (upward curvature) in the plots (not shown) of log k_{obs} *versus* pH.

From these data it appears that replacement of benzyl (entry 1–3) by phenyl group (entry 4–6) does not cause any significant change in reactivity. The ratios of the second-order rate con-

Table 1 Second-order rate constants for the hydrolysis of the esters **1**–**6** in 20% dioxane at 25 °C and μ = 0.1 mol dm^{-3}

Ester	pH range	k_{OH}/dm^3 mol^{-1} s^{-1}
1	8.25–10.50	(8.50 ± 0.52) × 10^3
2	12.32–13.62	6.65 ± 0.12
3	13.09–13.62	(1.85 ± 0.02) × 10^{-2}
4	9.20–10.50	(2.96 ± 0.23) × 10^3
5	12.32–13.32	23.54 ± 0.82
6	13.09–13.62	(2.47 ± 0.17) × 10^{-2}

stants for the three pairs of esters **1**:**4**, **2**:**5** and **3**:**6** are similar, to within a factor of 10 (2.8, 0.3 and 0.7 respectively). An analogous small effect has been previously reported for the alkaline hydrolysis of methyl dibenzylphosphinate and diphenylphosphinate.[6]

In the case of aryl phenylmethanesulfonates ($C_6H_5CH_2SO_2OAr$), which undergo hydrolysis through a carbanion-promoted dissociative mechanism, it was found[7] that the hydroxide rate constant for hydrolysis of 4-nitrophenyl phenylmethanesulfonate in water is some three orders of magnitude greater than that for corresponding benzenesulfonate ester which cannot react *via* dissociative mechanisms. Data available for the 2,4-dinitrophenyl esters of the same acids point to an even larger difference in reactivity, although the rate constant for the hydrolysis of 2,4-dinitrophenyl benzenesulfonate has been determined in a somewhat different medium (20% aq. dioxane).[8]

The present results indicate that all the esters employed in this work react through the same mechanism, which must be the associative one. This implies that the presence of both a very good leaving group and a π-donor group bound to phosphorus is not enough to divert the reaction flux toward carbanion-promoted dissociative pathways, supporting our previous conclusions[1] about the predominance of associative processes in the alkaline hydrolysis of this type of phosphorus derivatives. It now appears clear that, in these systems, carbanions are not efficient internal nucleophiles in sharp contrast with their role played in sulfonyl (as well as acyl)[9] transfer processes.

From the pK_a values of sulfuric and phosphoric acids (-3 and 2.1, respectively)[10] and from those of 4-nitrophenyl benzylaminosulfonate (8.19 ± 0.02 in water at 25 °C)[11] and 4-nitrophenyl *N*-phenyl-*P*-phenylphosphonamidate (12.37 in 50% aq. ethanol)[2] it appears that these phosphoryl derivatives possess pK_a values 4–5 units higher than those of the analogous sulfonyl compounds, independent of the nature of the acidic site. Since it is reasonable to suppose that such difference holds also between esters **1**–**3** and phenylmethanesulfonates (the pK_a of the 4-nitrophenyl derivative is 21.7)[7] a considerably lower acidity of the α-protons of these P^V esters may be the cause of the observed different mechanistic behaviour: for substrates having exceedingly high pK_a the dissociative mechanism will not be efficient because there is only a little conjugate base in solution.

Moreover, the difference in the stability of putative intermediates involved in the two processes [$C_6H_5CH{=}SO_2$ and $C_6H_5CH{=}P(O)X$] should be taken into account.

Further inspection of Table 1 reveals that the presence of substituents with lone pairs of p-electrons markedly reduces the rate of hydrolysis (ester **3** reacts five orders of magnitude slower than ester **1**) and that the observed reactivity order, phosphinates > phosphonates > phosphonamidates, is opposite to the order of the substituent electron releasing power. This effect is consistent with an associative mechanism: as previously stated[12] the π-donor substituent increases the electron density at phosphorus, thus inhibiting the nucleophilic attack of the negatively charged hydroxide ion.

Experimental

Esters were prepared from the corresponding acid chloride as described below; the reactions of chlorides with the appropriate nucleophile (2,4-dinitrophenol, ethanol or diethylamine) were carried out in anhydrous dichloromethane at room temp. and were followed by TLC. The reaction mixtures were then washed sequentially with diluted hydrochloric acid, water and finally with phosphate buffer solution at pH *ca.* 7; the organic phases were dried (Na_2SO_4) affording, after removal of the solvent, the crude products. Materials were routinely checked for purity by TLC. Structures were confirmed by ^1H NMR spectroscopy using a Varian Gemini 200 spectrometer (200 MHz) with tetramethylsilane as internal standard and deuterioacetone as solvent.

Kinetics were carried out as previously described[1] employing a Kontron Uvikon 941 spectrophotometer.

2,4-*Dinitrophenyl Benzylphenylphosphinate* (**1**).—Phenylphosphinic acid (Aldrich) was benzylated as described in the literature.[13] Treatment of the anhydrous sodium salt of benzylphenylphosphinic acid with phosphorus pentachloride afforded the corresponding acid chloride which was bulb-to-bulb distilled (at 4 × 10^{-4} mBar and oven temperature ≅ 200 °C). The acid chloride was finally treated with equimolar 2,4-dinitrophenol and triethylamine to give **1** which had m.p. 149–150 °C (from propan-2-ol) (Found: C, 57.6; H, 4.0; N, 7.0. $C_{19}H_{15}N_2O_6P$ requires C, 57.3; H, 3.8; N, 7.0%).

2,4-*Dinitrophenyl ethyl benzylphosphonate* (**2**). Diethyl benzylphosphonate (Aldrich) was hydrolysed to give the monoester.[14] The desired product **2** was obtained from the sodium salt of the monoester following the procedure above described and had m.p. 50–51 °C (from benzene–light petroleum, b.p. 60–90 °C) (Found: C, 48.9; H, 4.1; N, 7.5. $C_{15}H_{15}N_2O_7P$ requires C, 49.2; H, 4.1; N, 7.6%).

2,4-*Dinitrophenyl* N,N-*diethyl*-P-*benzylphosphonamidate* (**3**). Benzylphosphonyl dichloride, prepared as reported in the literature,[15] was treated first with two equivalents of diethylamine and subsequently with equimolar 2,4-dinitrophenol and triethylamine to afford the required ester **3** which had m.p. 100–101 °C (from propan-2-ol) (Found: C, 51.7; H, 5.3; N, 10.6. $C_{17}H_{20}N_3O_6P$ requires C, 51.9; H, 5.1; N, 10.7%).

2,4-*Dinitrophenyl ethyl phenylphosphonate* (**5**). Phenylphosphonic dichloride (Aldrich) was treated with equimolar 2,4-dinitrophenol and triethylamine and successively with equimolar ethanol and triethylamine to give the diester. This had m.p. 109–110 °C (from carbon tetrachloride) (Found: C, 47.3; H, 3.6; N, 7.8. $C_{14}H_{13}N_2O_7P$ requires C, 47.6; H, 3.7; N, 7.9%).

2,4-*Dinitrophenyl* N,N-*diethyl*-P-*phenylphosphonamidate* (**6**). Phenylphosphonic dichloride (Aldrich) was treated with two equivalents of diethylamine and successively with equimolar 2,4-dinitrophenol and triethylamine. Usual work-up of the reaction gave an oil which did not crystallise although TLC and NMR analyses showed no impurities. Further confirmation of the purity of **6** was obtained from the observation that the alkaline hydrolysis of this compound gives a nearly stoichiometric amount of products as judged from the UV absorbance at 400 nm and the known extinction coefficient of 2,4-dinitrophenolate.

2,4-*Dinitrophenyl diphenylphosphinate* (**4**) was prepared as reported in the literature.[16]

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