

Alkaline Hydrolysis of Diethyl Esters of Alkanephosphonic Acids and Some Chloro-substituted Derivatives

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The rates of alkaline hydrolysis of diethyl esters of alkanephosphonic acids and some chloro-substituted derivatives have been measured at different temperatures. Activation energies and entropies are calculated. The strongly electronegative chloromethyl and dichloromethyl groups produce a small but significant decrease of the activation energy of the alkaline hydrolysis of the esters, in contrast to mesomeric substituents as alkoxy and dialkylamino which produce an increase of the activation energy.

It is well known that the rate of nucleophilic substitutions on phosphorus in phosphoryl compounds is strongly dependent on the leaving group as well as on the other two substituents linked to phosphorus.¹ Thus, when alkoxy groups or dialkylamino groups are substituted for alkyl groups, a great decrease of the rate of nucleophilic substitution is observed.¹⁻⁴ The rate decrease is always reflected in a rise of activation energy which, however, is compensated more or less by an increase of activation entropy. Typical examples are alkaline hydrolysis of fluorophosphates where alkoxy groups or dialkylamino groups are exchanged for alkyl groups.^{2,4} In these reactions the fluoride ion is the leaving group. The same effect is also observed for phosphate esters when a *p*-nitrophenoxy group or an alkoxy group is the leaving group.^{1,3}

The reason for the rise of activation energy has been attributed to an increase of π -bonding in the molecule caused by overlap of filled *p*-orbitals of the substituents with empty *d*-orbitals of phosphorus.^{1,2,4,5} The resulting reduction of positive charge on phosphorus as well as the corresponding strengthening of the bond between phosphorus and the leaving group, will both contribute to an increase of the activation energy. On the other hand, an increase of the number of electronegative substituents linked to phosphorus will result in a more effective delocalization of the electronic charge in the transition state and accordingly diminish the tendency of cooperative orientation of solvent molecules during the reaction.¹⁻⁴ The net effect should be an increase of the entropy of activation, which is also observed.

In the present work is studied the alkaline hydrolysis of diethyl esters of ethane- and methanephosphonic acids, monochloromethanephosphonic acid and dichloromethanephosphonic acid. Since the mesomeric substituents are kept unchanged in this series, and the chlorine atom is separated from phosphorus through a carbon atom, the electron distribution around phosphorus ought to be less affected than in compounds where the number of mesomeric substituents is varied.

EXPERIMENTAL

Diethyl ethanephosphonate was made by a Michaelis-Arbuzov reaction of triethyl phosphite and ethyl iodide, b.p._{0.5} 35°C, n_D^{20} 1.4163 (Refs. 6, 7, n_D^{20} 1.4165, 1.41637). Gas chromatographic purity > 98 %.

Diethyl methanephosphonate was made in the same way as the diethyl ethanephosphonate, but a five-fold excess of methyl iodide was used, b.p.₁₈ 67°C, n_D^{20} 1.4131 (Ref. 7, n_D^{16} 1.41207). Gas chromatographic purity > 99.9 %.

Diethyl monochloromethanephosphonate was made according to Kinnear and Perren⁸ by first isolating the dichloride, which in turn was treated with absolute ethyl alcohol to give the diester, b.p._{0.7} 60°C, n_D^{20} 1.4388 (Ref. 9, 1.4385). Gas chromatographic purity > 99 %.

Diethyl dichloromethanephosphonate was made according to Kinnear and Perren⁸ without isolating the dichloride, b.p._{0.7} 77°C, n_D^{20} 1.4539 (Ref. 9, 1.4357). Gas chromatographic purity > 99 %.

Diethyl trichloromethanephosphonate was synthesized according to Cadogan and Foster,¹⁰ b.p._{0.4} 72°C, n_D^{20} 1.4616. The compound was unstable on the gas chromatographic column.

Kinetic measurements were performed in water as well as in water-acetone mixtures. Usually, the concentrations of esters and sodium hydroxide were in the region of 0.05 M. The hydrolysis was found to obey second order kinetics.¹ The reaction was followed to approximately 70 % hydrolysis. Eight or nine separate determinations of the base concentration were performed after different time intervals. The average error of the calculated rate constant is estimated to ± 1 % for the alkyl substituted esters, and ± 2 %

Table 1. Data for the alkaline hydrolysis of phosphonate esters, $RPO(OC_2H_5)_2$.

R	$\nu_{P=O}$ cm ⁻¹	Solvent	Rate constants l M ⁻¹ sec ⁻¹ × 10 ⁴					Activation	Activation
			10°C	20°C	30°C	40°C	50°C	energy kcal/mole	entropy E.U.
C ₂ H ₅	1238	Water	—	—	0.407	0.872	1.72	14.0	—
		Water + 20 % acetone	—	—	0.310	0.642	—	14.0	34.8
CH ₃	1243	Water	—	—	3.20	6.57	12.75	13.4	—
		Water + 20 % acetone	—	—	2.40	4.80	—	13.1	33.7
ClCH ₂	1271	Water	—	25.1	49.8	97.3	—	12.3	—
		Water + 20 % acetone	—	19.2	37.5	71.5	—	12.0	31.9
Cl ₂ CH	1281	Water + 20 % acetone	61.2	128	258	—	—	12.3	27.0

Table 2. Alkaline hydrolysis of ethyl acetate and its chloro-substituted esters.^{11,12}

Compound	Solvent	Activation energy kcal/mole	Activation entropy E.U.
CH ₃ COOC ₂ H ₅ ¹¹	85 % EtOH	14.1	-21.1
CH ₂ ClCOOC ₂ H ₅ ¹²	91.8 % EtOH	12	-16
CHCl ₂ COOC ₂ H ₅ ¹²	91.8 % EtOH	12	-10

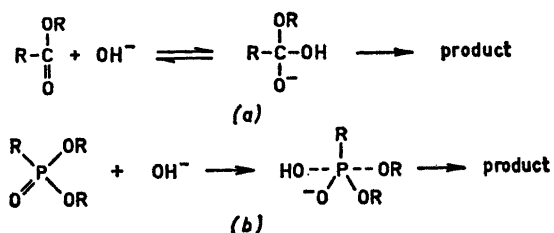
for the chloro containing esters. The reaction temperatures were kept constant within $\pm 0.01^\circ\text{C}$.

Diethyl trichloromethanephosphonate was found to hydrolyse so rapidly that it could not be studied by the present method. The compound also showed an abnormal decomposition, producing chloroform under the present reaction conditions.

RESULTS AND DISCUSSION

The rate constants for the alkaline hydrolysis of the various phosphonate esters, $\text{RPO}(\text{OEt})_2$, are recorded in Table 1. Using $\text{R} = \text{Me}$ as reference, the relative rate constants at 30°C are: Et: 0.13, Me: 1, ClCH_2 : 15.6, Cl_2CH : 108. For comparison, the relative rate constants for corresponding carboxylic acid esters, $\text{RC}(\text{O})\text{OEt}$, are from literature data^{11,12} estimated as: Et: 0.9 Me: 1, ClCH_2 : 258, Cl_2CH : ca. 5000, which shows that electronegative substituents exhibit a much greater influence on the rate of nucleophilic reaction in carbonyl compounds than in phosphoryl compounds.

Comparison of energies and entropies of activation for the alkaline hydrolysis, shows that corresponding phosphoryl and carbonyl esters have almost identical activation energies, but the activation entropies are 12–17 e.u. more positive for the esters of carboxylic acids (Tables 1 and 2). The reason for this difference is most likely the greater restriction laid upon the transition state of the alkaline hydrolysis of phosphonate esters. From isotopic exchange studies with ^{18}O -enriched water is known that esters of carboxylic acids freely exchange oxygen under alkaline conditions,¹³ which indicates that an intermediate with fully developed σ -bonds is formed (a). Under similar conditions, no oxygen exchange is observed in phosphate esters.¹⁴ This strongly points to a concerted mechanism for the hydrolysis of phosphate esters, with a bipyramidal sp^3d -hybridized transition state (b):



A transition state (b) which must satisfy the requirements for the synchronous movements of the incoming as well as the leaving group, will necessarily be much more restricted in its configuration than the intermediate (a) with all its degrees of freedom left undisturbed. The low entropy of the alkaline hydrolysis of phosphonate esters as compared with corresponding esters of carboxylic acids seems therefore reasonable.

The positive charge induced on phosphorus by the electronegative chlorine atom in α -position in the phosphonate esters will be counteracted to a certain degree by dative π -bonding by the ethoxy groups and by the phosphoryl oxygen.⁵ This effect is reflected in the rise of the frequency of the stretching vibration of the phosphoryl group on chlorination (Table 1). The introduction of the first chlorine atom has by far the strongest influence on the vibration of the phosphoryl bond. This corresponds with the change of activation energy upon chloro-substitution, the first chlorine atom producing a drop of 1 kcal; the next having almost no effect. The effect may be explained on the basis of a greater polarisability of the unchlorinated compound than of the chlorinated one: the introduction of the first strongly electronegative chlorine atom will diminish the susceptibility of phosphorus towards further polarisation from additional chlorine substituents.

The activation energy for the alkaline hydrolysis decreases only slightly upon chlorination of the phosphonate esters. This suggests that the increase in positive charge on phosphorus, induced by chlorine and which contributes to a decrease of activation energy, is nearly compensated by the charge neutralisation due to increased π back-bonding and by the bond strengthening of the leaving group. The fall in activation energy caused by chloro-substituted alkyl groups is opposite to the effect observed when alkoxy and amino groups are linked directly to phosphorus.²⁻⁴ Although these groups are strongly electronegative, their ability to participate in π -bonding with phosphorus dominates the electron distribution in the molecule and produces a rise in the activation energy.

The increase of activation entropy, on chlorination, for the alkaline hydrolysis of phosphonate esters is most reasonably due to a solvation effect^{1,4}: the chlorine substituents diminish the solvent constriction in the transition state due to their ability to spread the electronic charge. A similar, but even stronger increase of entropy is observed in the ionization of acetic acid and its chlorinated derivatives¹⁵ as well as in the alkaline hydrolysis of its esters (Table 2).

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