Fragmentation–Rearrangement of 2-Acyloxyalkylphosphonates—a Novel Route to Alkyl Metaphosphate Extrusion

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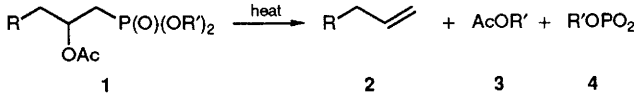
Thermolysis of dialkyl 2-acyloxyalkylphosphonates, resulting in the fragmentation to an alkene, ester and alkyl metaphosphate, represents the first example of a reaction in which alkyl group migration has to occur before the metaphosphate species can be extruded from the system.

Monomeric metaphosphates attract unceasing attention because of their role as critical intermediates in many organophosphorus reactions.[1] Since the early pyrolysis experiment by Clapp and Westheimer,[2] in which the formation of a neutral metaphosphate ester was demonstrated, numerous organic systems capable of generating metaphosphate derivatives have been reported, most notably the 2,3-oxaphosphabicyclo[2.2.2]octene system, extensively studied by Quin and coworkers.[3] We have shown that neutral metaphosphate species can be easily ejected from such simple precursors as 2-arylethylphosphorochloridates,[4] or mixed anhydrides of carboxylic and amidophosphoric acids.[5] The former reaction involves the anchimeric assistance of the 2-aryl group and the departure of the Cl^- ion; in the latter a four-centre transition state is involved, with the NR_2 group migrating from the phosphoryl to the carbonyl centre.

We have now discovered that dialkyl esters of 2-acyloxyalkylphosphonic acids **1**, when heated in polar, aprotic solvents, undergo smooth fragmentation to an alkene **2**, a new ester **3**, and alkyl metaphosphate **4** (Scheme 1). Formation of products **2**–**4** appears to involve migration of a phosphonate ester group R′ to the acyl group Ac, together with the cleavage of the P–C and C–OAc bonds. Alkenes **2** and esters **3** were unambiguously identified by ^1H NMR spectroscopy, mass spectrometry and gas chromatography, and by comparison with authentic samples. Metaphosphates **4** were identified in the aqueous phase as monoalkyl phosphates $R'OPO_3H_2$, by comparing their NMR (^1H, ^{31}P) spectra with those of authentic compounds. The reaction is first order with respect to **1**; the effect of the structure of the phosphonate substrate on the fragmentation rate is given in Table 1. The position and the electron-donating ability of the aromatic group in R (**1a**, **b** and **c**) have only a minor effect on the rate, indicating that no anchimeric assistance is involved in the cleavage of the C–OAc bond. Greater reactivity of the dimethyl phosphonate **1d** relative to **1a** is in agreement with the known[6] susceptibility of the methyl group in phosphate esters to nucleophilic displacement relative to other alkyl groups. As expected, phosphonodiamidate **1g** containing much less electrophilic ethyl groups in the $P(O)X_2$ function, failed to react under given conditions.



1 2 3 4

Scheme 1

Table 1 Structural effects on fragmentation of phosphonic derivatives R–$CH_2CH(OAc)CH_2$–$P(O)X_2$ **1** in sulfolane, 195 °C

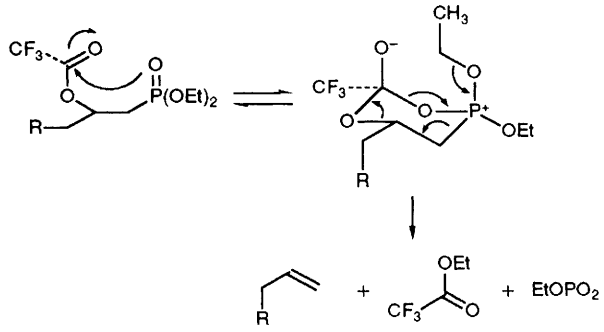
1[a]	X	R	Ac	k_{obs}[b]/10^{-4} s^{-1}	k_{rel}
a	OEt	Ph	$C(O)CF_3$	3.4	1.0
b	OEt	*p*-$MeOC_6H_4$	$C(O)CF_3$	4.7	1.4
c	OEt	CH_2Ph	$C(O)CF_3$	4.0	1.2
d	OMe	Ph	$C(O)CF_3$	10.0	2.9
e	OEt	Ph	$C(O)CH_3$	≤0.7[c]	≤0.2[c]
f	OEt	Ph	SO_2CH_3	200[d]	59[d]
g	NEt_2	Ph	$C(O)CF_3$	*e*	*e*

[a] Preparation of compounds **1** will be described in a full paper. All substrates gave NMR (^1H, ^{13}C, ^{31}P) and mass spectra in agreement with the expected structure. [b] Calculated by following the disappearance of **1** by GC; r = 0.991–0.998. [c] Upper limit; some other decomposition reactions contributed to the disappearance of the substrate. [d] Approximate. [e] No reaction observed.

The greatest effect on the reaction rate is exerted by the electrophilicity of the acyl centre in group Ac; the relative reactivities of the methanesulfonate (**1f**), trifluoroacetate (**1a**) and acetate (**1e**) are ~60 : 1 : <0.2.

The reaction is subject to solvent effects; the rate of the reaction of **1a** in diglyme is only about half of that in sulfolane, while no reaction was observed in refluxing 1,1,2,2-tetrachloroethane. The ionisation of the O–R′ bond in the phosphonate ester is not a prerequisite for the fragmentation; when **1a** was heated in sulfolane containing NaI (nucleophilic deethylation by I^-), the rate of the reaction was not significantly increased ($k_{rel} \approx 2$). The reaction is characterised by a large, negative entropy of activation: for **1a** (sulfolane, temperature range 178–213 °C) $\Delta S^{\ddagger} = -103$ J mol^{-1} K^{-1}. This value can be compared with that of $\Delta S^{\ddagger} = -50$ to -60 J mol^{-1} K^{-1} reported for the pyrolytic elimination of sulfoxides,[7] and is indicative of the more rigid arrangements of atoms in the transition than in the ground state of the molecule.

On the basis of the observed structure–reactivity relationship, medium effects, and the activation entropy, we conclude that the reaction involves donor–acceptor interaction between the phosphoryl oxygen and the electrophilic centre of the 2-acyloxy group, followed by the POR′ group dealkylation, accompanied by the cleavage of the P–C and the C–O bonds.



Scheme 2

Although at this stage the exact sequence of the individual steps and the contribution of their specific rate constants to the value of k_{obs} is not known, a two-step mechanism, compatible with the experimental results, is presented in Scheme 2 using **1a** as a model substrate. In terms of its relation to all previous fragmentations of neutral substrates leading to the extrusion of a metaphosphate ester, our reaction differs in that the alkyl group of the phosphonic ester function has to be additionally transferred intramolecularly to another nucleophilic centre in order to accomodate the bonding requirements of a metaphosphate species.

Financial support from the University of Pretoria and the Foundation for Research Development is gratefully acknowledged.

Received, 27th April 1992; Com. 2/02168D

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