Ortho Ester Hydrolysis: Rate-determining Addition of Water to a Carboxonium Ion Intermediate

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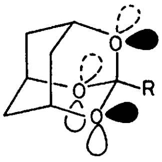
Summary Hydrolysis of 2,4,10-trioxa-adamantane (I) and 3-methyl-2,4,10-trioxa-adamantane (II) suggests that the rate-determining step is the addition of water to a carboxonium ion intermediate.

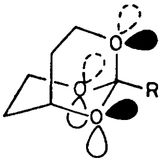
OUR continuing interest in stereoelectronic effects and their influence on the rates of hydrolysis of ortho esters[1] has led us to investigate the 2,4,10-trioxa-adamantanes, a class of rigid ortho esters whose lone pair orientations seemed well suited to effect stereoelectronic control of the kind proposed by Deslongchamps.[2] We have measured the rates of hydrolysis of the ortho esters (I) and (II) of this type, at several acid concentrations and at two temperatures; the rate constants and activation parameters are shown in the Table.



(I) R = H
(II) R = Me

$RC(OEt)_3$

(III) R = H
(IV) R = Me



(V) R = H

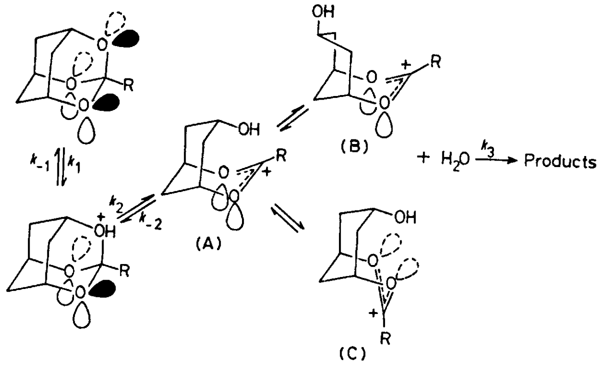
TABLE. Hydrolysis of 2,4,10-trioxa-adamantanes (I) and (II) in water–dioxan (40:60) at 25·2 °C; [HCl]: 0·05—2 M.[a]

Ortho esters	k_{H^+}/dm^3 mol^{-1} s^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal K^{-1} mol^{-1}
(I)	$3{\cdot}3 \times 10^{-2}$	$12{\cdot}0 \pm {\cdot}4$	-25 ± 3
(II)	$6{\cdot}2 \times 10^{-4}$	$16{\cdot}8 \pm {\cdot}5$	-17 ± 2

[a] Reactions were monitored spectroscopically by following the appearance of the band of the diol-ester at 225 nm.

These results contrast sharply with those reported for the corresponding acyclic ortho esters, ethyl orthoformate (III) and ethyl orthoacetate (IV).[3] Three points, in particular, are noteworthy. (i) The activation entropies of (I) and (II) are large and negative whereas those of (III) and (IV) are positive ($\Delta S^{\ddagger}$ + 8 and + 7 cal K^{-1} mol^{-1} respectively). (ii) Substitution of a hydrogen by methyl causes a decrease in rate by a factor of 50 for the cyclic compounds [compare (I) and (II)] whereas the same substitution has reverse effects on the acyclic ortho esters (III) and (IV). (iii) The rates of hydrolysis of the cyclic compounds are very much less than those of the acyclic ortho esters: k_{I}/k_{III} = *ca.* 8×10^{-6} (R = H); k_{II}/k_{IV} = *ca.* 3×10^{-9} (R = Me).

Such contrasting behaviour by these two groups of compounds strongly suggests that the rate-determining step for each is not the same and that the slow step for the cyclic compounds therefore no longer involves an *A*1 or S_E2 mechanism.[4] Indeed, the large negative entropy of activation of the trioxa-adamantanes implies a bimolecular reaction[5] involving either direct substitution, *i.e.* an *A*2 mechanism, or rate-determining attack by water on a preformed carboxonium ion (A, B, or C, Scheme). The lowering of the reaction rate caused by methyl substitution at the 3 position (k_{II}/k_{I} = *ca.* 0·021) is consistent with either of the latter mechanisms.



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However if hydrolysis of the trioxa-adamantanes were to involve an *A*2 mechanism, then 2,8,9-trioxabicyclo[3.3.1]-nonane (V), whose structure and lone pair orientation in the ground state are very similar to those of the trioxa-adamantanes, should undergo hydrolysis by the same mechanism and at a rate very similar to (I). It does not; (V) reacts very much faster than (I) (k_{V}/k_{I} = *ca.* 4×10^4) and at a rate comparable to the acyclic compounds (k_{V}/k_{III} = *ca.* 0·3).[6]

Thus we think that the attack of water on the carboxonium ion is the rate-determining step of the reaction; to the best of our knowledge this has not previously been reported.

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