Destabilisation of a Carbocation by α-Oxygen Substitution: the Hydrolysis of Orthocarbonates

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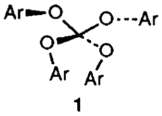
Tetraphenyl orthocarbonate is hydrolysed by general acids 10^1-fold slower than triphenyl orthoformate, whilst tetrakis(*p*-methoxyphenyl) orthocarbonate is hydrolysed 10^1-fold faster than tetraphenyl orthocarbonate, with a Brønsted α-value closer to triphenyl orthoformate than tetraphenyl orthocarbonate, indicating that cation stability, not an early transition state, is the cause of the lower rate of the orthocarbonate.

Substitution of an oxygen atom for a hydrogen at a carbocationic centre generally stabilises it, and this increase in stability is reflected in higher rates of hydrolysis or solvolysis of the appropriate derivatives: it is well known that orthoesters are much more labile to acid than acetals.[1] Oxygen, though, like fluorine, withdraws electrons inductively even though it releases them conjugatively, and in principle at some level of carbocation stability the sense of the net effect of both elements will change. The phenomenon is well recognised in the case of fluorine: α-fluorine substitution stabilises simple carbocations, but destabilises those which already have some stabilisation.[2]

In their 1974 review, Cordes and Bull[1] were able to deduce that the H_3O^+-catalysed hydrolysis of triethyl orthoformate was about an order of magnitude faster than that of tetraethyl orthocarbonate. These authors, however, took the carbocation-stabilising effect of α-oxygen substitution as axiomatic, and attributed the slower hydrolysis of the orthocarbonate to an earlier transition state. Moreover, their conclusions were, with the exception of one ^{1}H NMR study showing that dimethyl carbonate was stable under conditions under which tetramethyl orthocarbonate was hydrolysed,[3] founded upon dilatometric data which could not address the question of whether the hydrolysis of the dialkyl carbonate or alkyl formate was kinetically significant.[4]

We now present more extensive spectrophotometric data on the hydrolyses of tetraphenyl orthocarbonate, triphenyl orthoformate and tetrakis(*p*-methoxyphenyl) orthocarbonate. This method of following the reaction allows us to confirm that diphenyl carbonate is stable under the conditions used for hydrolysis of tetraphenyl orthocarbonate, and explicitly to take into account the previously found[5] comparable reactivity of phenyl formate and triphenyl orthoformate.†

The data demonstrate that *p*-methoxy substitution in tetraphenyl orthocarbonate, which would be expected to stabilise the trioxocarbonium ion, results in a faster rate and, as measured by Brønsted α value, a transition state closer in structure to that for the hydrolysis of triphenyl orthoformate than tetraphenyl orthocarbonate. The simple explanation for the lower reactivity of orthocarbonates, that the trioxocarbonium ion is less stable than the dioxocarbonium ion, appears to be the correct one.



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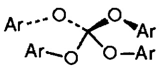

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In Fig. 1 are displayed Brønsted plots for the hydrolysis of tetraphenyl orthocarbonate, tetrakis(*p*-methoxyphenyl) orthocarbonate and triphenyl orthoformate by various carboxylic acids in 40% (v/v) aqueous acetonitrile at 70.0 °C, with an ionic strength of 1.0 mol dm^{-3} maintained with potassium chloride. At this concentration of acetonitrile, water structure is still maintained.[6] The Brønsted α-values are $0.93_2 \pm 0.04_6$,

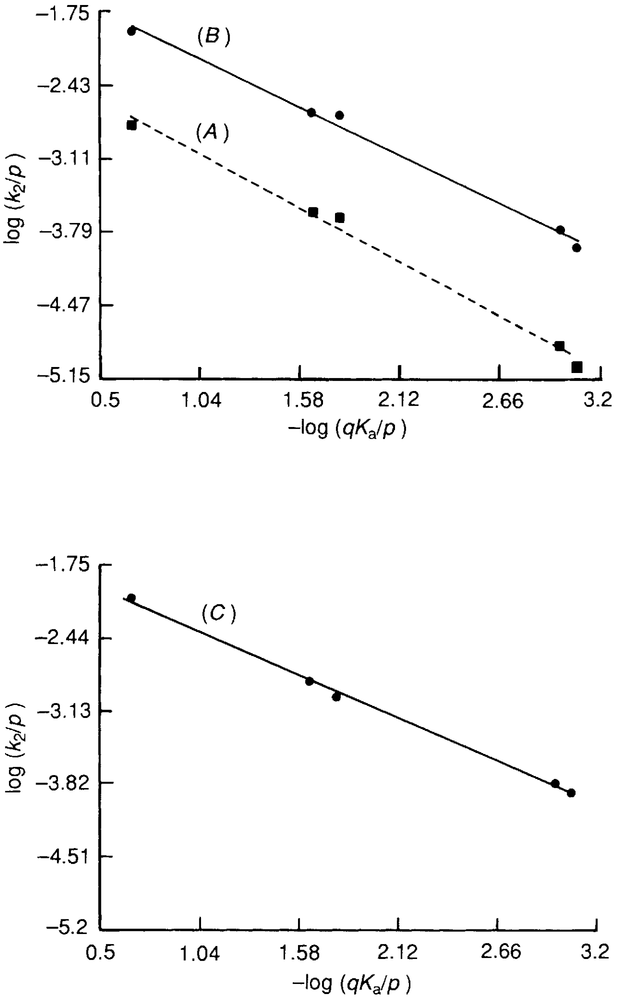

Fig. 1 Brønsted plots for the hydrolysis of (*A*) tetraphenyl orthocarbonate, (*B*) triphenyl orthoformate and (*C*) tetrakis(*p*-methoxyphenyl) orthocarbonate in 40% (v/v) aqueous acetonitrile at 70 °C, ionic strength maintained at 1.0 mol dm^{-3} with potassium chloride. The units of k_2 are mol^{-1} dm^3 s^{-1}, and of K_a, mol dm^{-3}. The catalysing acids are, in order of increasing pK_a, trichloroacetic acid, difluoroacetic acid, dichloroacetic acid, fluoroacetic acid and malonic acid (acting as a neutral acid). The pK_a values are the measured pH of 1:1 buffers in the medium used for kinetic studies, not thermodynamic pK values. p is the number of dissociable protons of the catalysing acid and q is the number of equivalent sites to which a proton can be attached.

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† First-order rate constants for tetraaryl orthocarbonates were calculated from the nonlinear least-squares program KALEIDAGRAPH, run on a Macintosh SE 30 PC. The $A_\infty - A_0$ values at 278 nm derived from this program corresponded to the liberation of two moles of phenol per mole of orthocarbonate.

The time courses of optical density at the same wavelength during the hydrolysis of triphenyl orthoformate were fitted to: $A = A_0 + c\,(\Delta\varepsilon_1\,[1 - \exp\,(-\,k_1t)] + \Delta\varepsilon_2\,\{1 - \exp\,(-k_1t) - [k_1/(k_2 - k_1)]\,[\exp\,(-k_1t) - \exp\,(-k_2t)]\})$ where c (initial concentration), $\Delta\varepsilon_1$ (absorption coefficient change between orthoformate and formate + phenol), and $\Delta\varepsilon_2$ (absorption coefficient change between formate and formic acid + phenol) were estimated independently.

$0.75_6 \pm 0.02_4$ and $0.82_9 \pm 0.03_9$, respectively. Solvent deuterium kinetic isotope effects (k_{H_2O}/k_{D_2O}) on catalysis by dichloroacetic acid are 1.8_3, 1.5_9 and 2.1_8, indicating that true general acid catalysis is being observed in all three reactions.

Since the pK_a values of phenol and *p*-methoxyphenol differ by only 0.27 units, the change of leaving group can account for only a maximum factor of *ca.* 1.8‡ of the rate difference between tetraphenyl orthocarbonate and tetrakis(*p*-methoxyphenyl) orthocarbonate, most of which must therefore arise from *p*-methoxy substitution in the cation fragment. Although the system is cross-conjugated, release of π-electron density from the methoxy groups into the benzene rings will make the p-type lone pairs of the oxygen atoms attached to the central carbon atom more able to support a positive charge.

The direction of change of Brønsted α with stabilisation of the cationic fragment is the same as that observed by Capon and Nimmo for hydrolysis of ArCH(OMe)OAr′.[7]

Aryl orthocarbonates have two preferred conformations, with S_4 (**1**) and the D_{2d} (**2**) symmetry.[8] Examination of models reveals that in neither of these conformations is approach to the oxygen lone pairs sterically hindered. In the S_4 conformation, moreover, each C–O bond is antiperiplanar to an sp^3 lone pair of electrons on each of the remaining three oxygen atoms. It is therefore clear that neither a steric nor any transition state ‘stereoelectronic’ effect is responsible for the lower reactivity of the orthocarbonate.

Ground-state stabilisation by accumulated n–σ* interactions,[9] rather than destabilisation of the carbocationic transition state, could be invoked as a cause of the faster rate of hydrolysis of phenyl orthoformate compared with phenyl orthocarbonate, but this explanation encounters three difficulties. The first is that the structural basis of the supposed epiphenomenon, the progressive shortening of the carbon–halogen bond of halogenomethanes, has now been attributed to the effect of electronegativity on hybridisation of the central carbon atom.[10] The second is that the order-of-magnitude effect of remote *p*-methoxy substitution in the orthocarbonate is difficult to reconcile with a ground-state effect. Thirdly, an economy of hypothesis results from the supposition that the same pattern of behaviour of oxygen and fluorine has the same physical origins.

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‡ This increase would be observed with a β_{lg} value of +1.0, quite unprecedented in class *n* reactions involving an oxygen leaving group, such as this one; observed effects vary from *ca.* 0, for the acid catalysed hydrolysis of acetals, to *ca.* −0.5.[1]