Stereoelectronic Control of Acetal Cleavage. Separation of the π-Donor and σ-Acceptor Properties of Oxygen†

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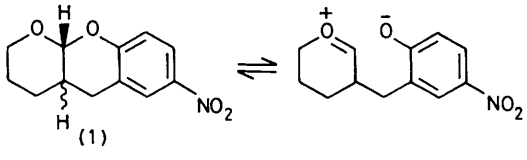
Summary The lone pair electrons of the oxygen atom in ring A assist the fragmentation of the acetal (**2ca**), but not that of the isomer (**2ta**), with a *trans* ring-junction.

THE first evidence[1] that acetal cleavage is subject to stereoelectronic control[2] involved the hydrolysis of the tricyclic system (**1**). Compound (**1c**), with the ring-junction *cis*, which has a lone pair on the donor oxygen *antiperiplanar* to the *p*-nitrophenolate leaving group, is significantly more reactive than the isomer (**1t**) with a *trans*-ring-junction, which has not. Interpretation of the data is complicated, however, because the loss of the endocyclic leaving group is

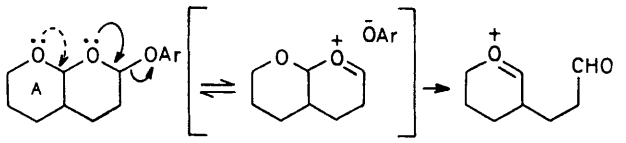


(1)

readily reversible. As a result, the spontaneous hydrolyses of (**1c**) and (**1t**) have different rate-determining steps,[1] and are thus not directly comparable; while the acid-catalysed reactions give not a single product but a mixture of (**1c**), (**1t**), and open-chain compound.[1]

† No reprints available.

We report our results with a new system (**2**, Ar = *p*-nitrophenyl‡) which avoids these complications and allows us to monitor the cleavage of a conformationally locked acetal by following the release of an exocyclic leaving group.

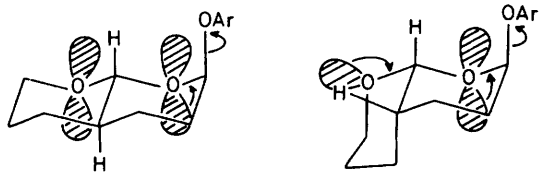


(2) (3) (4)

Loss of *p*-nitrophenolate from (**2**) would generate the oxo-carbonium ion (**3**), an acetal with a much better leaving group (aldehyde oxygen). As long as one of the lone pairs on the oxygen atom of ring A is in a position to participate, therefore, the loss of *p*-nitrophenolate is expected to trigger a concerted fragmentation, to form (**4**) directly. If acetal cleavage is subject to stereoelectronic control, such participation should be possible in the isomer (**2ca**) with the ring-junction *cis*, but not in (**2ta**), in which the conformation at the centre concerned is locked by the *trans*-ring-junction. In compound (**2ta**), therefore, the oxygen atom of ring A should be unable to exercise its π-donor function, and should act simply as a σ-acceptor, destabilising the oxocarbonium ion (**3t**), and thus slowing the departure of the *p*-nitrophenolate leaving group.

Our results are consistent with this expectation (Table). The spontaneous hydrolysis of (**2ta**) is 1380 times slower than that of 2-(*p*-nitrophenoxy)tetrahydropyran (**5**), while the isomer (**2ca**) is hydrolysed < 7 times more slowly than (**5**). These differences are entirely accounted for by differences in the enthalpies of activation. The effect of the *trans*-fused A-ring of (**2ta**) is to increase $\Delta H^{\ddagger}$ by 10 kcal (42 kJ) mol^{-1}, compared with (**5**). For (**2ca**) the increase is only 2·8 kcal (12 kJ) mol^{-1}, so that the enthalpy barrier associated with stereoelectronic control in this system is 7·2 kcal (30 kJ) mol^{-1}. It is probably no more than coincidental that this figure is the same, within experimental error, as our estimate for this barrier in the hydrolysis of (**1t**).

(5)



(2ta) (2ca)

TABLE. Relative rates of hydrolysis[a]

	k_{rel}[b]	$\Delta H^{\ddagger}$ /(kcal mol^{-1})	$\Delta S^{\ddagger}$ /(cal K^{-1} mol^{-1})
(**5**)	1·0	24·1	+ 2·2
(**2ta**)	7·2 × 10^{-4}	34·1	+20·3
(**2ca**)	0·15	26·9	+ 7·9

[a] Data refer to the spontaneous (pH-independent) release of ArO$^-$ (*p*-nitrophenolate) in aqueous solutions of pH 9·75, at 39 °C and ionic strength 1·0 M. [b] Based on a figure of 3·22 × 10^{-4} s^{-1} for the hydrolysis of (**5**), measured at 39·2 °C and ionic strength 0·1 M by T. H. Fife and L. H. Brod, *J. Amer. Chem. Soc.*, 1970, **92**, 1681.

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‡ The reaction of 4a,6,7,8a-tetrahydro-4*H*,5*H*-pyrano[2,3-*b*]pyran[3] (0·5 g) with an excess of *p*-nitrophenol (2·5 g) in toluene (30 ml) containing acetic acid (0·5 ml) for 60 h at 70 °C gave, after alkaline extraction, a mixture of (**2ca**) (m.p. 84—85 °C) and (**2ta**) (m.p. 165—7 °C), which were separated by column chromatography. Only small amounts of the diastereoisomer (**2te**), and no (**2ce**) were present (n.m.r. spectrum).

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[2] A. J. Kirby and S. Chandrasekhar, *J.C.S. Chem. Comm.*, 1978, 171; P. Deslongchamps, *Tetrahedron*, 1976, **31**, 2463.
[3] Y. Bahurel, M. Lissac-Cahn, G. Descotes, J. Delman, and J. Duplan, *Bull. Soc. chim. France*, 1970, 4006.