Concerted Catalysis in the Enolisation of Aldehydes

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At high buffer concentrations the enolisation of aldehydes is markedly catalysed simultaneously by acidic and basic species; the magnitude of the 'third-order term' can be related directly to the importance of the individual acid and base catalysed terms.

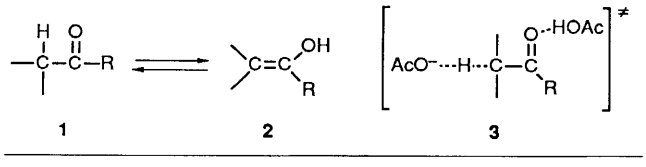
Compared with keto–enol tautomerism of ketones, tautomerism of aldehydes (**1** ⇌ **2**, R = H) has been less extensively studied. Recently, however, simple enols **2** have been synthesised from lithium enolates,[1,2] using silyl derivatives[3] or reactive enol acetates as precursors[4] or by photolysis,[5] and the rates of conversion to the keto form directly measured.[6] We have carried out the first study of the reverse reaction (enolisation of aldehydes, **1**, R = H) at high concentrations of acetic acid-acetate buffers which shows the existence of an important third-order term for the catalysis of this reaction.

It has previously been demonstrated that for the two ketones acetone and cyclohexanone there is upward curvature in plots of the observed rates of enolisation against buffer concentration.[7–9] These curved plots can be analysed in terms of eqn. (1) which relates the observed rate of enolisation (k_{obs}) to the rate constants for the individual water catalysed (k_0), general acid (k_A) and general base catalysed (k_B) (by acetic acid and acetate ion respectively) pathways and to the third order term, k_{AB} where both species appear in the rate term. The latter becomes important only when high concentrations of both acetate ion and acetic acid are present and accounts for the upward curvature of the k_{obs} against [buffer] plots.

$$k_{obs} = k_0 + k_A[HOAc] + k_B[AcO^-] + k_{AB}[HOAc]\,[AcO^-] \quad (1)$$

We have now found that the simple aldehydes ethanal, propanal, 3-chloropropanal and 2-methylpropanal all show a measurable third order term (k_{AB}). Table 1 summarises the results,† together with the rate constants for acid (k_A) and base (k_B) catalysed enolisation. Since the k_{AB} term is most accurately measured at high buffer concentration, total buffer concentrations up to 2.0 mol dm^{-3} in water were used (ionic strength being maintained constant at 2.0 using KNO_3). Of particular interest is the observation that the same k_{AB} value is obtained with [AcO$^-$]:[HOAc] ratios of 0.25, 1.0 and 3.0, which would rule out artefacts such as solvent effects giving rise to the observed curvature. The values in Table 1 have been corrected for the appreciable hydrate content of the aldehydes, measured independently using NMR techniques in 2.0 mol dm^{-3} KNO_3. The hydrate equilibrium (which is established rapidly relative to the rate of enolisation) was shown not to vary significantly with buffer concentration once ionic strength is kept constant.

The k_{AB} term for ethanal is an order of magnitude greater than that for the ketone, acetone (see Table 1). A distinct trend in the magnitude of k_{AB} as structure is varied now becomes apparent, the reduction in the basicity of the carbonyl group [ketone **1** (R = Me) to aldehyde **1** (R = H) or introduction of electron-withdrawing groups] causes an increase in the third-order term. It is apparent from Table 1 that k_{AB} is in fact largest when both k_A and k_B are significant. This is shown in terms of the direct relationship between log [$k_A.k_B$] and log k_{AB} shown in Fig. 1.



1 **2** **3**

This simple relationship for aldehydes is also apparent for ketones. We have measured k_A, k_B and k_{AB} for four further ketones under the same conditions (see Table 1) and the data for five of the ketones show a linear log–log relationship between $k_A.k_B$ and k_{AB} (Fig. 1). The two correlations do not coincide however, the aldehyde line having approximately double the slope (1.03 *vs.* 0.58). Interestingly the aldehyde butanal and the ketone pentan-3-one show significant negative deviations from the respective lines (k_{AB} being apparently less than predicted); both are acyclic and have extended alkyl chains.

It has been argued[8,9] that the third-order term for acetone enolisation represents concerted catalysis **3**, while it is now accepted that the k_A and the k_B terms are stepwise non-concerted reactions in which there is C–H proton removal in the rate determining step from the protonated ketone or the

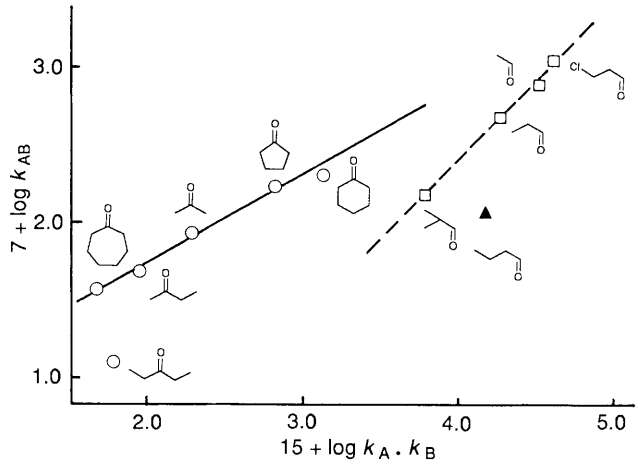


Fig. 1 Plot of the log of the third-order term for the catalysis of enolisation of ketones (solid line) and aldehydes (broken line) by acetic acid–acetate against the log of the product of the rate constants for the stepwise pathways for catalysis. The value of k_{AB} for butanal (△) is less than 3.3 mol^2 dm^{-6} s^{-1}.

Table 1 Rate constants for acetic acid–acetate catalysis of enolisation of aldehydes and ketones[a]

Aldehyde or ketone	$10^7 k_A$/ mol dm^{-3} s^{-1}	$10^7 k_B$/ mol dm^{-3} s^{-1}	$10^7 k_{AB}$/ mol^2 dm^{-6} s^{-1}
Ethanal	4.7	60	21
Propanal	4.3	36	12.6
3-Chloropropanal	3.3	115	30
2-Methylpropanal	3.0	17	4.2
Butanal	5.0	23	<3.3
Acetone	7.7	2.2	2.15
Butan-2-one	0.45	1.7	1.23
Pentan-3-one	0.46	1.15	0.32
Cyclopentanone	0.82	6.7	4.5
Cyclohexanone	2.4	4.7	5.2
Cycloheptanone	0.80	0.52	0.96

[a] Measured in H_2O at 25 °C; μ = 2.0 (KNO_3).

† The rates of enolisation were measured in H_2O at 25 °C using the iodine trap method; the zero order disappearance of I_2/I_3^- at the isosbestic point of 351 nm was followed. The aldehydes were distilled under N_2 directly before use. The reaction solutions (in a Cary 210 spectrophotometer) were deoxygenated; otherwise (with ethanal and proanal) rapid initial liberation of I_2/I_3^- was noted when the aldehyde was added.

ketone respectively.[10] The k_{AB} term for ethanal shows a solvent deuterium isotope effect (k_{H_2O}/k_{D_2O} = 1.8) which is similar in magnitude to that already reported[8] for acetone (2.0).

Why is the concerted mechanism more important for aldehydes? Aldehydes are significantly less basic than ketones (the pK_a of ethanal has been estimated at −8.1,[11] or −10.2,[12] acetone at −5[13]) while the enol content is higher (pK_T = 6.29 for ethanal,[5] 8.33 for acetone[14]); the C–H acidity is also significantly higher (pK_a = 16.5 for ethanal[14] and 19.1 for acetone[15]). It has been predicted from an analysis of More O'Ferrall Jencks diagrams that the concerted pathway will be most significant when the enol form is relatively stable.[6] Our results are consistent with this.

The data in Table 1 (and Fig. 1) provide for the first time a basis on which a prediction can be made on whether a given structural change is likely to increase or decrease the third-order term for enolisation of aldehydes and ketones. However, the concerted pathway remains elusive in aqueous solution and will only be observed if one or other of the alternative stepwise pathways is not dominant (as is the case for the formation of many stabilized enols such as those of 1,3-diketones).

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