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Enolization of Aldehydes and Ketones: Structural Effects on Concerted Acid−Base Catalysis

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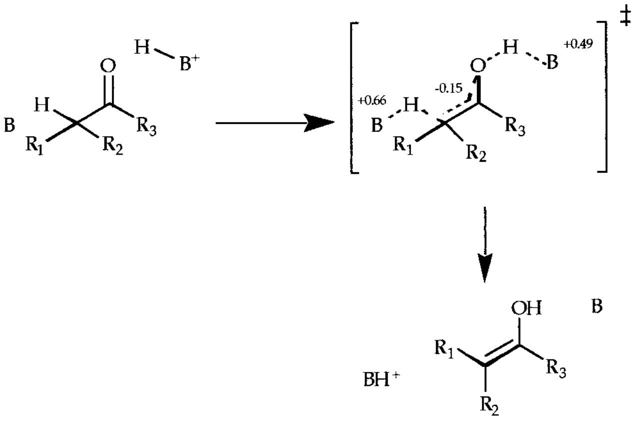
Abstract: The third-order term (k_{AB}) for the concerted acid−base catalyzed enolization of a selection of simple aldehydes and ketones has been measured in a series of substituted acetic acids at 25 °C at constant ionic strength 2.0 ($NaNO_3$). While there is no direct correlation of the magnitude of the third-order term with either the rate constants for acid (k_A) or base (k_B) catalysis, a simple log−log relationship exists between the product of the consecutive rate constants ($k_A \cdot k_B$) and the concerted (third order) rate constants (k_{AB}). This implies that the concerted pathway is important only when *both* the general acid and the general base terms are significant; this will be useful in designing other systems which might show such concerted catalysis. In the case of aldehydes, a slope of 0.97 was found for this plot, which compares to the result for 4-substituted cyclohexanones (0.51) and other ketones (0.59), as measured in acetic acid buffers. The resultant Brønsted β_{AB} value of 0.20 found for propanal **(2)** is consistent with the overall observation that concerted catalysis is largely independent of the buffering species, and that process is overall base catalyzed. The solvent isotope effect on the concerted acid−base catalyzed enolization rate term, $k_{AB}(H_2O)/k_{AB}(D_2O) = 1.33$, indicates that the transition state for proton transfer to the carbonyl is more advanced than in the case of ketones. In general we have found that carbonyl compounds with large measured (or estimated) enol contents show significant third-order terms.

Introduction

The most reliable method for evaluation of tautomeric equlibrium constants, K_E ([enol]/[ketone]), is by direct measurement of forward (k_E) and reverse (k_K) rate constants, measured under the same conditions. Rate measurements for the enolization of ketones (k_E) are easily determined, for example, by halogen scavenging.[1] However, it is only within the past decade that reliable data for the ketonization rate constants (k_K) have been obtained. Photochemical generation of enols has allowed the accurate determination of equilibrium constants for many monocarbonyl compounds.[2]

$$K_E = k_E/k_K \tag{1}$$

Scheme 1



Tautomerization can occur by both acid and base catalyzed mechanisms, which have been well established.[3,4] As an alternative to these well-accepted consecutive acid−base catalyzed pathways, the possibility of a concerted mechanism involving both catalytic species is plausable.[5] This is represented in Scheme 1, where the partial charges on the transition state were calculated from Brønsted values given by Hegarty and Jencks.[5f] To date, data are available only for a few aldehydes and ketones for this possible pathway so that there is little evidence on how the magnitude of k_{AB} varies with structure.[6] There are limitations, however, on the number of ketones which are sufficiently water soluble to permit direct measurement of enolization rates in the absence of cosolvents. Moreover, unsymmetrically substitued ketones can in most cases enolize on either side of

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the carbonyl group, which could make the interpretation more difficult. We have therefore studied both aldehydes and 4-substituted cyclohexanones, despite the experimental difficulties involved. Taken together, the chosen acyclic and cyclic ketones, together with the aldehydes, give a reasonable structural variation. Moreover, it has recently been predicted on theoretical grounds[7] that aldehydes would show marked concerted catalysis, and the results which we now report have confirmed this.

In general, contributions from each of the catalyzed pathways may be described by eq 2. This may also be expressed more simply, in eq 3, in terms of the observed rate constant, k_{obs}, as measured in the presence of a catalytic buffer, AH, which exhibits general acid, general base, and concerted catalysis, denoted by k_A, k_B, and k_{AB}, respectively. The buffer independent rate constant, which of course includes terms for hydronium, hydroxide, and water catalysis, is denoted by k_o.

$$\mathrm{d[KH]}/\mathrm{d}t = [\mathrm{KH}]\{\sum_i k_{\mathrm{BH}_i^+}[\mathrm{BH}_i^+] + \sum_i k_{\mathrm{B}_i}[\mathrm{B}_i] + \sum_i k_{\mathrm{B}_i,\mathrm{BH}_i^+}[\mathrm{B}_i][\mathrm{BH}_i^+]\}(2) \quad (2)$$

$$k_{\mathrm{obs}} = k_o + k_A[\mathrm{AH}] + k_B[\mathrm{A}^-] + k_{AB}[\mathrm{AH}][\mathrm{A}^-] \quad (3)$$

Results

We have extended our study to include a series of substituted cyclohexanones. Available keto−enol equilibrium constants are listed in Table 1, along with second- and third-order buffer-catalyzed rate constants, measured in acetic acid in aqueous solution. Of particular interest is the observation that the same k_{AB} term is obtained at 25%, 50%, and 80% of the buffer ionized, which would rule out artifacts such as salt or solvent effects giving rise to the curvature of the observed rate vs concentration plots (see Figure 1). Specific salt effects can cause upward or downward deviations in plots of rate against buffer concentration if the buffer salt and the salt used to maintain ionic strength constant have different effects on the ratios of activity coefficient for the reactants and transition state. Thus $\mathrm{NO^-}_3$ seems to be a good model for $\mathrm{CH_3CO_2}^-$ in this instance. At the highest buffer concentrations up to 10% acetic acid was present, which might have induced a medium effect ("solvent sorting"), but the observation that the same k_{AB} term is obtained at high and low pH indicates that this is not important.

There were limitations on the number of ketones that could be studied under the present conditions; the substrates were required to be sufficiently water soluble to permit direct measurement of the enolization rates in the absence of cosolvent. For example, 4-chlorocyclohexanone was synthesized but was not included in the study for this reason. Moreover unsymmetrically substituted ketones can in most cases enolize on either side of the carbonyl group, making interpretation more difficult. This study also encompasses a number of aromatic ketones and aldehydes, despite the experimental difficulties involved in the measurement of the latter compounds. For all the compounds examined the second-order rate constant for the base-catalyzed reaction was greater than that catalyzed by acid, see Table 1.

Manipulation of the structure can have different effects on the magnitude of the pK_a of the carbonyl, enol, or the protonated carbonyl species and subsequently on the value of the different rate constants. Increasing the alkyl chain length causes an increase in the pK_a^K of the keto tautomer and hence the base catalyzed rate constant, k_B, of enolization decreases. This is probably due to the electron donating inductive effect of the methyl group making the forming carbanion less stable.[4c] Similarly other electron donating substituents are expected to have the same effect. The reduction in the size of the base-catalyzed rate constant could also be explained in terms of increasing steric hindrance to the approaching base.

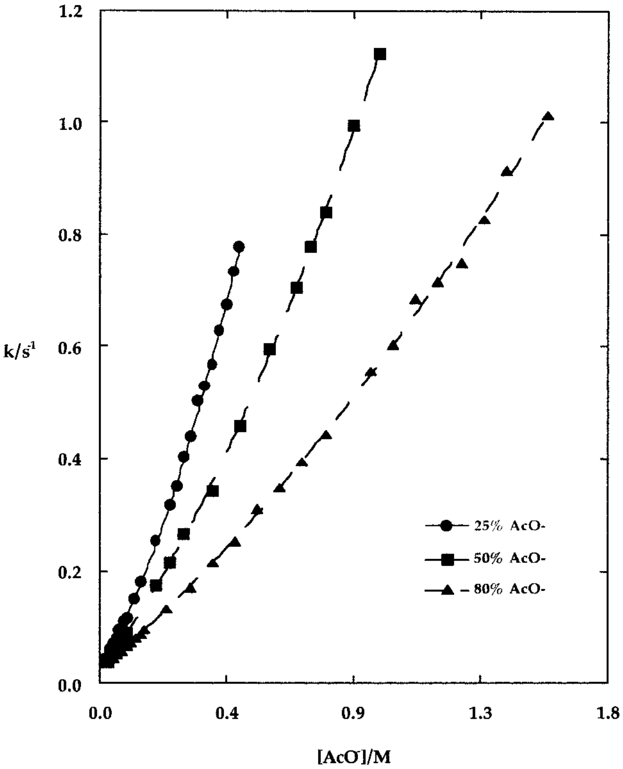

Figure 1. First-order rate constants for the enolization of cyclohexanone (**17**) plotted against the acetate anion concentrations.

A preliminary examination was carried out on the ketone 3-hydroxy-3-methyl-2-butanone **(11)** as a model for the aromatic carbonyls. This compound was chosen on steric grounds as it is expected to interfere with concerted catalysis much as an aromatic ring would. The compound however fits the logarithmic relationship between the consecutive and concerted rate constants, with a slope of 0.59, see Figure 2**.** The rate constant for the base-catalyzed reaction is quite substantial even compared to that for acetone **(8)**. The value for the acid-catalyzed rate constant is smaller than that for the unsubstitued butanone **(9)**; this is probably a consequence of the electron-withdrawing hydroxy substituent, which would be expected to cause a decrease in pK_a^K. Although the rate constant for the base-catalyzed mechanism is dominant, a value of 7.5×10^{-8} M^{-2} s^{-1} was calculated for the concerted pathway. Thus, it appeared likely that even though the substituents were bulky they did not interfere in this case significantly with the concerted route.

Discussion

It is useful to explain the observation of concerted catalysis in terms of a three-dimensional free energy diagram, as seen in the More O'Ferrall−Jencks diagram in Figure 3.[7a] The structures of the product (top right-hand corner) and the intermediates in the consecutive acid- and base-catalyzed reactions are given with the associated energies relative to the reactant in (kcal/mol). The concerted reaction is independent of either of the intermediates shown, and is represented by the diagonal line

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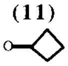
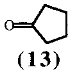
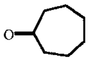
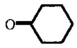
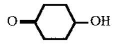
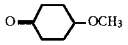
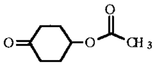
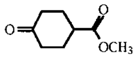
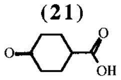
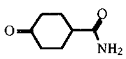
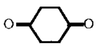
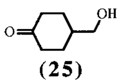
Table 1. Second- and Third-Order Rate Constants for Acetic Acid Buffer Catalysis in the Enolization of Aldehydes and Ketones in Aqueous Solution at 25 °C and Ionic Strength 2.0 M

Aldehyde or Ketone	pK_E	pK_a^K	$pK_a^{(OH+)}$	AcOH $10^7k_A{}^a$	 $10^7k_B{}^a$	 $10^7k_{AB}{}^b$
CH_3CHO **(1)**	6.23^c	16.73^c	--	4.7	60	21
CH_3CH_2CHO **(2)**	--	--	--	4.3	36	12.6
$ClCH_2CH_2CHO$ **(3)**	--	--	--	3.3	115	30
$(CH_3)_2CHCHO$ **(4)**	3.86^d	15.49^d	--	3.0	17	4.2
$CH_3(CH_2)_2CHO$ **(5)**	--	--	--	5.0	23	<3.3
$PhCH_2CHO$ **(6)**	$2.89^{e,f}$	--	--	42.8	130	0.0
$PhCH_2CH_2CHO$ **(7)**	--	--	--	5.37	45.1	22.3
CH_3COCH_3 **(8)**	8.33^g	19.27^g	-2.85^h -3.06^j	0.76^i 0.80	2.15^i 2.08	2.15^i 2.10
$CH_3COCH_2CH_3$ **(9)**	7.49^g	--	-3.48^j	0.457	1.7	1.24
$CH_3CH_2COCH_2CH_3$ **(10)**	7.43^g	--	-3.88^j	0.455	1.15	<0.83
$CH_3COC(OH)(CH_3)_2$ **(11)**	--	--	--	0.18	3.33	0.75
 **(12)**	--	--	--	<0.17	2.07	<0.83
 **(13)**	7.94^g	--	--	0.818	6.72	4.50
 **(14)**	8.00^g	--	--	0.80	0.52	0.945
$PhCOCH_3$ **(15)**	7.96^k	18.31	-4.36^h -3.87^j	0.67	7.88	0.0
$^-SO_3C_6H_4COCH_3$ **(16)**	--	--	--	2.0	23.3	0.0
 **(17)**	6.39^g	--	--	2.33^i 2.38	4.28^i 4.60	4.67^i 4.97
 **(18)**	--	--	--	1.93	22.3	8.53
 **(19)**	--	--	--	2.33	20.6	5.97
 **(20)**	--	--	--	4.85	27	14.2
 **(21)**	--	--	--	2.53	25.1	14.8
 **(22)**	--	--	--	10.7	20.3	0.0
 **(23)**	--	--	--	2.15	27.3	12.1
 **(24)**	--	--	--	22.8	315	121
 **(25)**	--	--	--	2.32	24.4	7.42

[a] Units M^{-1} s^{-1}. [b] Units M^{-2} s^{-1}. [c] Reference 2d. [d] Reference 2i. [e] Reference 2j. [f] Total (*E* and *Z*) enol content. [g] Reference 2e. [h] Reference 9a. [i] Reference 5f. [j] Reference 9c. [k] Reference 2c.

for a hypothetical situation with a Brønsted $\beta_{AB} = 0$. Experimentally, the reaction shows a net base catalysis with a Brønsted $\beta_{AB} = +0.15$.[5f] This is also represented as the transition state to the right of the diaganol, indicating that proton donation to the base is running slightly ahead of protonation of the carbonyl group.[5f] The concerted reaction, while entropically unfavorable,

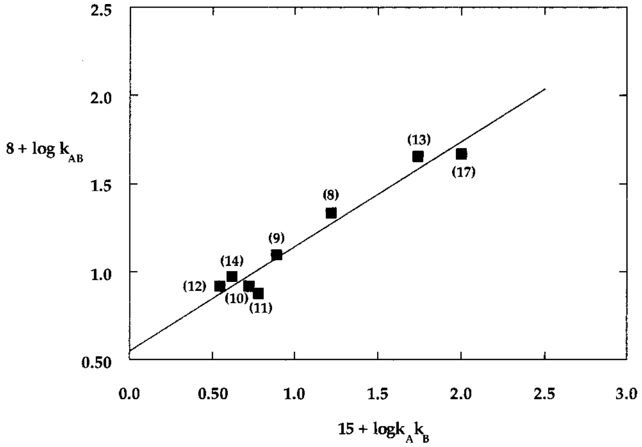


Figure 2. Correlation showing the log−log relationship between $k_A \cdot k_B$ and k_{AB}, for a selection of nonaromatic ketones.

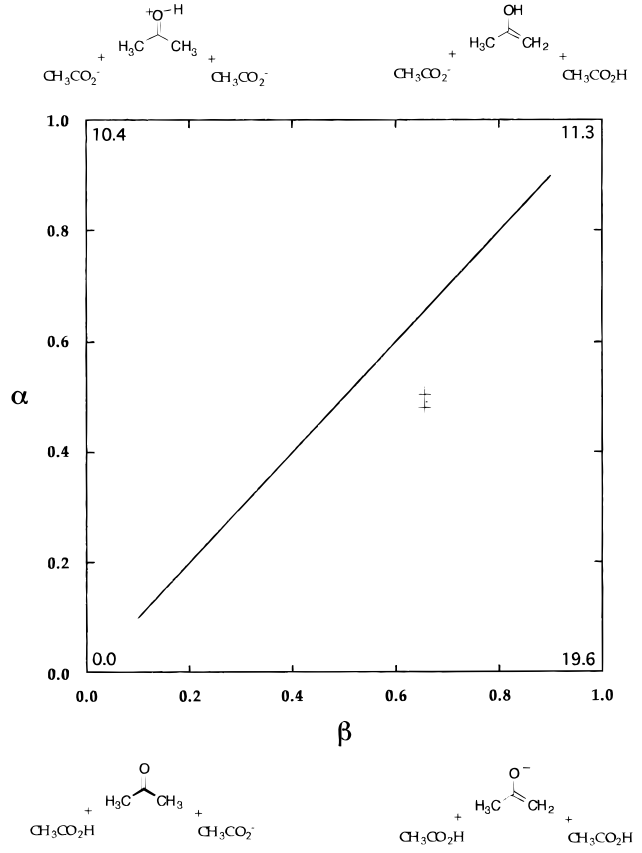


Figure 3. More O'Ferrall-Jencks diagram for the enolization of acetone (*8*) catalyzed by acetic acid, energies in kcal/mol.

avoids the high-energy intermediates associated with the consecutive reactions. This is only true for weak acid−base pairs, and agrees with the observation of concerted catalysis only for acids of pK_a = 2.8. Finally, the solvent isotope effect $k_{AB}(H_2O)/k_{AB}(D_2O) = 2.0$ is also quite different from that expected for a stepwise reaction.

By this analysis it is anticipated that stable enols are also more likely to use the concerted route because in these cases the product corners will be lower, increasing the energetic advantage by avoiding the consecutive pathway intermediates. This agrees with the findings of this study. In general those enols which have, or are expected to have, a large K_E value also show a large concerted rate constant. A trend in the magnitude of the k_{AB} term has emerged: on reducing the basicity of the carbonyl group, i.e., in going from a ketone to an aldehyde or by the introduction of an electron withdrawing group, an increase in the third-order term is observed. It is apparent that when the acid catalyzed and base catalyzed terms are both large that is when the k_{AB} term is most significant.

Although accurate thermodynamic data are now generally available for many ketones, especially the pK_E values, it is only in recent years that reasonable methods have been developed for the evaluation of p$K_a^{(OH^+)}$ values of protonated ketones, although several experimental problems still remain regarding aldehydes.[9,10] We have looked for various relationships between k_{AB} and structural or other thermodynamic or reactivity data and have found that there is a simple relationship between log k_{AB} and log k_A + log k_B. This implies that k_{AB} is largest only when k_A and k_B are both significant; while a larger variation is found in k_B than in k_A (43-fold and 5-fold, respectively), the correlation between k_{AB} and either k_B or k_A alone shows scatter. In this respect the availability of data for the cyclic ketones is particularly useful since the acyclic ketones have k_A values which are all quite similar. Consistent with analysis, cyclobutanone **(12)** and 3-pentanone **(10)** do not show a measurable third-order term within the limits of experimental error, while the kinetic data for cyclobutanone **(12)** could be correlated by using k_B alone.

The aromatic ketones acetophenone **(15)** and 4-acetylbenzenesulfonic **(16)** acid (sodium salt) were also studied**.** Substantial rate constants were observed for both of the consecutively catalyzed mechanisms for each of the aromatic ketones, but no concerted catalysis was observed.

Aldehydes. Compared to the study of keto−enol tautomerism of ketones, the tautomerization of aldehydes has been much less extensively studied, probably because the enolization processes are often complicated by oxidation and hydration. Arguments based on free energy relationships (Figure 3) predict that aldehydes should show a marked concerted catalysis. In these cases the product corners of the free energy diagrams will be much lower and there will be a greater energetic advantage to avoiding the intermediates along the consecutive routes. Consistent with this, the k_{AB} term for acetaldehyde **(1)** was found to be an order of magnitude greater than that for acetone **(8)**. Replacing the electron donating methyl group next to the carbonyl by a hydrogen, as is the case in going from acetone **(8)** to acetaldehyde **(1)**, causes a decrease in pK_a of the keto tautomer which in turn shows as an increase in the overall base-catalyzed rate constant. As in the case of the ketones, the simple logarithmic relationship between $k_A \cdot k_B$ and k_{AB} was obeyed (Figure 4), but with an increased slope (0.97).

Aldehydes are expected to be less basic than their ketone counterparts, for example, benzaldehyde (pK_a = −4.48)[9c] is less basic than acetophenone **(15)** (pK_a = −3.87).[9c] Conversely, the pK_a values for aldehydes for C-deprotonation are generally lower than their ketone counterparts, and since they are more acidic, the values for the base-catalyzed rate constants are quite substantial for the aldehydes. Although aldehydes are generally less basic than ketones, the acid-catalyzed rate constant for the enolization reaction, k_A, does not vary significantly. This

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(8) (a) Arnett, E. M.; Joris, L.; Mitchell, E.; Murty, T. S. S. R.; Gorrie, T. M.; Scheleyer, P. v. R. *J. Am. Chem. Soc.* **1970**, *92*, 2365. (b) Arnett, E. M.; Mitchell, E. J.; Murty, T. S. S. *J. Am. Chem. Soc.* **1974**, *96*, 3875.

(9) (a) Levi, A.; Modena, G.; Scorrano, G. *J. Am. Chem. Soc.* **1974**, *96*, 6585. (b) Bagno, A.; Lucchini, V.; Scorrano, G. *Bull. Soc. Chim. Fr.* **1987**, 563. (c) Bagno, A.; Lucchini, V.; Scorrano, G. *J. Phys. Chem.* **1991**, *95*, 345.

(10) (a) Cox, R. A.; Yates, K. *J. Am. Chem. Soc.* **1978**, *100*, 3861. (b) Lucchini, V.; Modena, G.; Scorrano, G.; Cox, R. A.; Yates, K. *J. Am. Chem. Soc.* **1982**, *104*, 1958. (c) Bagno, A.; Scorrano, G.; More O'Ferrall, R. A. *Rev. Chem. Intermed.* **1987**, *7*, 313.

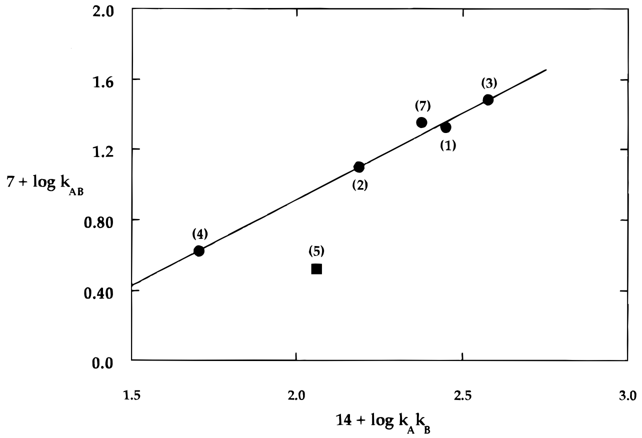

Figure 4. Correlation showing the log−log relationship between k_A·k_B and k_{AB} for a selection of aldehydes (compound **5** was excluded).

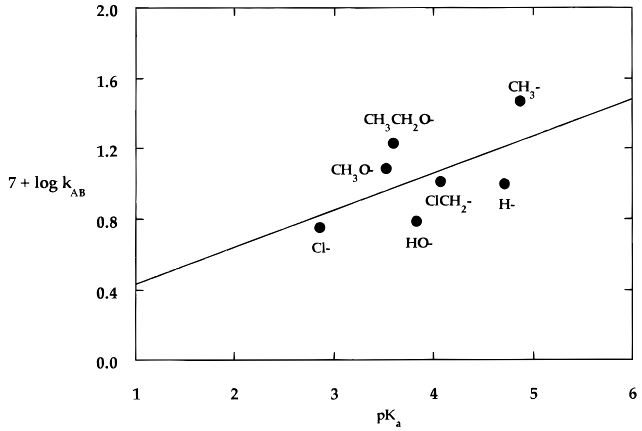

Figure 5. Brønsted plot of the third-order rate constants for the enolization of propanal **2** catalyzed by a selection of substituted acetic acids.

suggests that the increased rate of C-deprotonation of the protonated species compensates for the drop in carbonyl basicity.

Brønsted Exponent. The third-order rate constant, k_{AB}, for the enolization of propanal **(2)** was determined for a variety of substituted acetic acids: cloroacetic acid, 5.63×10^{-7} M^{-2} s^{-1}; methoxyacetic acid, 1.22×10^{-6} M^{-2} s^{-1}; ethoxyacetic acid, 1.70×10^{-6} M^{-2} s^{-1}; glycolic acid, 6.12×10^{-7} M^{-2} s^{-1}; chloroacetic acid, 1.03×10^{-6} M^{-2} s^{-1}; acetic acid, 9.97×10^{-7} M^{-2} s^{-1}; and propanoic acid, 2.93×10^{-6} M^{-2} s^{-1}. The resultant Brønsted plot (Figure 5) gives a β_{AB} value of 0.2. This compares with the value obtained for the enolization of the ketone acetone **(8)**, 0.15, reported by Hegarty and Jencks.[5f] This is consistent with the overall observation that concerted catalysis is largely independent of the buffering species, and that process is overall, net base catalyzed. The solvent isotope effect on the concerted acid−base catalyzed enolization rate term, $k_{AB}(H_2O)/k_{AB}(D_2O) = 1.33$, is smaller than that observed for acetone **(8)**,[5f] which indicates that at the transition state, proton transfer to the carbonyl is more advanced in this case.

Aromatic Aldehydes. There was no measurable acid−base catalyzed term in the case of the aldehyde, 2-phenylethanal **(6)**. However, a significant contribution to the overall rate was made by the concerted rate constant in the case of the longer chain 3-phenylpropanal **(7)**. It may be inferred from this result that even though larger concerted catalyzed terms are expected for aldehydes than ketones, the concerted route may not always be viable (probably for steric reasons). When the values obtained for 3-phenylpropanal **(7)** were compared to those for the analogous aliphatic aldehyde, the acid−base catalyzed rate constant for the aromatic aldehyde was somewhat larger than that for propanal **(2)**.

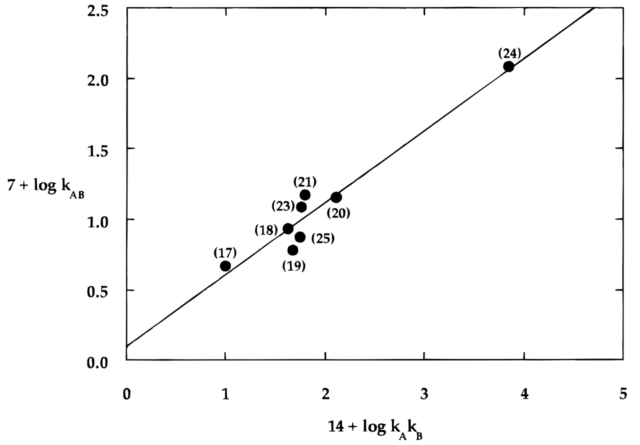

Figure 6. Correlation showing the log−log relationship between k_A·k_B and k_{AB} for a selection of 4-substituted cyclohexanones.

Cyclohexanones. In the series of cyclohexanones studied it is expected that the substituents, even though in the γ-position, will destabilize the keto tautomer, resulting in larger K_E values, as a result of polar effects. The substituted cyclohexanones, with the exception of 4-carboxycyclohexanone **(22)**, all exhibit a greater value for the third-order term than those previously reported for other aliphatic ketones, the enol content of which is on average one or two orders of magnitude less than that expected for the substituted cyclohexanones. These compounds also conform to the log−log relationship (Figure 6) that was found in the case of aldehydes and ketones, with a slope of 0.51. The k_A value for the 4-substituted cyclohexanones is close to that for cyclohexanone **(17)**, which indicates that there is a partial cancellation of effects in the acid-catalyzed reaction in contrast to that for the base-catalyzed reaction. The magnitude of the rate constant for the base-catalyzed enolization reaction is, however, much greater than that reported for any of the unsubstituted cycloalkanones.

Conclusion

The third-order term for the concerted acid−base catalyzed enolization is readily observable in the case of simple aldehydes and ketones. Third-order terms are observed for weak acid base pairs (p$K_a \geqslant 2.8$), where both the general acid and general base terms are significant. This is reflected quantitatively in a simple log−log relationship that exists between the product of the consecutive rate constants (k_A·k_B), and the concerted rate constant (k_{AB}). This is more significant in the case of aliphatic aldehydes, with a dependence of approximately 1.0, which compares to the value obtained for cyclic and acyclic ketones, which have a dependence of approximately 0.5, and finally in the case of aromatic ketones, no third-order term is observed. These results would tend to imply that steric effects may be important, although at this point the exact structure of the transition state is not clear. There also appears to be a relationship between the third-order term and the enol content of the carbonyl compound when comparing *structurally similar* compounds.

Experimental Section

Kinetics. All rate constant were measured in aqueous solution at 25 °C. Acetic acid buffers were prepared by partial neutralization of the acid with aqueous potassium hydroxide, and ionic strengths were maintained at 2.0 M by the addition of the appropriate quantity of potassium nitrate. The rates of enolization of the aldehydes and ketones were measured using the iodine trap method which depends on a rapid and irreversible trapping of the enol form by I_2/I_3^-. The concentration of I_2/I_3^- was measured at an isosbestic point (351 nm)[11] where $\epsilon = (2.6 \pm 0.1) \times 10^4$ by using the equilibrium constant for triiodide formation appropriate to $\mu = 2.0$ (630 M^{-1}).[5f] The carbonyl compounds were used in a 10^2-10^3)-fold excess. Under these conditions reversal of iodination is negligible[12] and iodine, unlike bromine or chlorine at low pH, does not induce oxidation of the aldehyde.[2c,13] The zero-order rate of iodine uptake was measured in deoxygenated solutions and was reproducible under these conditions. The individual rate constants were obtained from buffer dilution curves, typically covering 12 buffer dilutions over the range 0.01 to 2.0 M total buffer concentration. However, due to the dominance of the base-catalyzed and the third-order terms in the ionization of aldehydes, the k_A values were not obtained with the same precision and are accurate only to ±20%. Plots of absorbance against time were linear in each case from 10 s after mixing to at least 90% iodine consumption. Independent experiments showed that the observed rate was independent of the initial iodine concentration and was proportional to the ketone or aldehyde concentrations. The observed rate constants (see eq 4) were obtained with eq 5, where dA/dt is the rate of change of absorbance at 351 nm, where iodide was maintained in a constant large excess.

$$d[I_2]/dt = k_{obs}[\text{ketone}] \qquad (4)$$

$$k_{obs} = 1/[\text{ketone}]\epsilon_{I_3^-}\{1 + (1/K_{I_3^-}[I^-])\}\, dA/dt \qquad (5)$$

The concentration of free aldehyde in solution was obtained by correcting for the hydrate, measuring aldehyde/hydrate ratios in 2.0 M aqueous KNO_3 as follows: acetaldehyde **(1)**, 45% hydrate; propanal **(2)**, 41.5% (H_2O), 44.7% (D_2O); 3-chloropropanal **(3)**, 80%; 2-methylpropanal **(4)**, 33.3%; and butanal **(5)**, 31.5%. These values were obtained by integration of the α and β protons of the aldehyde and the hydrate at 270 MHz, when present. Although it is known that the hydrate concentration decreases as the ionic strength increases,[14a] the hydrate concentration was shown not to vary once ionic strength was kept constant. The percentage hydrate obtained where they could be compared with literature values at 25 °C in water ($m = 0$) compare quite closely: acetaldehyde **(1)** 51.5%[14b,c] and 2-methylpropanal **(4)**, 30%.[14d,e] It is surprising that we could not obtain a reproducible value for 3-chloropropanal **(3)** so the values for the rate constants in Table 1 were calculated by assuming 0% hydrated. Electron-withdrawing substituents are known to increase the percentage of hydrate at equilibrium, and Luz and Samuel[14f] have shown that the pK^h ($= -\log$[hydrate]/[ketone or aldehyde]) is related to the Taft σ^* values (eq 6), where Δ is the number of aldehydic hydrogens. This predicts that the percentage of hydration of 3-chloropropanal **(3)** should be 75%. Although the percentage hydration of acetone **(8)** (0.2%)[14g] and cyclopentanone **(13)** (0.2%)[7b] reported in water at 25 °C is small, a value of 7.4% has been reported for cyclohexanone.[7b] No correction was made to take account of the small amount of hydrate in the case of ketones. This approximation does not appreciably change the correlations observed, since concentration appears in both coordinates.

$$pK^h = 1.70\Sigma\sigma^* + 2.03\Delta - 2.81 \qquad (6)$$

All the aldehydes were distilled under nitrogen and used fresh. As has been noted, acetaldehyde **(1)** in particular causes experimental difficulties if not pure, due to the formation of oligomers, such as a cyclic trimer.[2c] It was found that when the rate of iodine uptake was measured in air there was an initial rapid generation of iodine when the aldehyde was added. This was most marked with acetaldehyde **(1)**, but decreased with increasing chain length. This initial increase in absorption could be eliminated by following the rates of reaction in sealed cuvettes using solutions which had been flushed with oxygen free nitrogen. There was a residual initial small increase in the case of acetaldehyde, but the experimental pseudo-zero-order rate constant was not affected by this.

In acetic acid buffer solutions the observed first-order rate constants can be written as in eq 3. Since K_a is the acidity constant for the ionizaton of the acid, this can be rewritten as eq 7, or eq 8 where r is the buffer ratio $[AH]/[A^-] = [H^+]/K_a$. This is a quadratic curve and k_{AB} was obtained by using a least-squares computer program, using the values of k_A and k_B from the initial linear portion of the buffer dilution plots, where the contribution of the k_{AB} term is negligible.

$$k_{obs} = k_o + k_A[H^+][A^-]/K_a + k_B[A^-] + k_{AB}[H^+][A^-]^2/K_a \qquad (7)$$

$$k_{obs} = k_o + \{k_A.r + k_B\}[A^-] + k_{AB}.r[A^-]^2 \qquad (8)$$

Buffer ratios of 25% ($r = 3$), 50% ($r = 1$), and 80% base ($r = 0.25$) were used in each case. Similar results were obtained by using plots of $(k_{obs} - k_o)/[AcO^-]$ against $[AcO^-]$, which gave rk_{AB} as slope and $(k_A r + k_B)$ as intercept; such plots were useful in determining the relative significance of each term. In the case of the aldehydes, the k_A term is in all cases a relatively small contributor (typically 10%) to the reaction flux and the error in this term is correspondingly larger (±20%).

Commercially available substrates were freshly distilled immediately prior to use. All other substrates were prepared by suitable modifications of existing literature procedures.[15] Melting points were determined on a Gallenkamp melting point block or on a Büchi 530 melting point apparatus and are uncorrected. Elemental analyses of compounds were performed by the Microanalytical Laboratory, University College Dublin. ^1H NMR spectra were recorded at 60 MHz on a JEOL JNM-

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PMX spectrometer—tetramethylsilane was the internal reference used. Deuterated chloroform, deuterated methanol, deuterated DMSO, and deuterated water were the solvents used. The IR spectra were recorded on a Perkin-Elmer 1710 Fourier Transform spectrometer or on a Mattson Instruments Galaxy Series FTIR 3000 spectrometer. Spectroscopic measurements in the ultraviolet and visible regions were obtained using a Cary 210 spectrometer, equipped with moveable thermostated cell compartment, the temperature of which was controlled by using a Techne TE8D Temp-ette water bath and pump and a Techne RB12 Refrigerated Bath. pH measurements were made with a Radiometer pH meter 26 and a Metrohm combined pH glass electrode, which was standardized using E. I. L. buffers to ±0.02 pH units.

Reagents and solvents were purified, where stated, using standard techniques. Inorganic materials used in kinetic measurements were AnalaR grade, where possible. Potassium nitrate was recrystallized from water and its crystals finely ground and dried for 12 h under vacuum at 100 °C. The composition of the potassium hydroxide pellets was determined by titration with a standard solution of hydrochloric acid, which had been prepared by dilution of Rhône Poulenc Volucon ampules. Water used for kinetic measurements was initially purified by doubly distilling it by using an Exelo Water Still and then degassed with a Millipore Filtration Apparatus. Organic solvents used during kinetic work were HPLC grade where possible.

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