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Simple Enols. 2.[1] Kinetics and Mechanism of the Ketonization of Vinyl Alcohol

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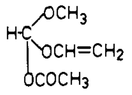
Abstract: The kinetics of the conversion of vinyl alcohol into acetaldehyde in aqueous solution at 15 °C were found to depend on pH according to the equation $k_0 = k_{H_2O} + (k_{H^+} \times 10^{-pH}) + (k_{HO^-} \times K_w)/10^{-pH}$ where $k_{H_2O} = 1.38 \times 10^{-2}$ s^{-1}, $k_{H^+} = 20.2$ M^{-1} s^{-1}, and $k_{HO^-} = 1.50 \times 10^7$ M^{-1} s^{-1}. Under the same conditions, k_{H^+} for the hydrolysis of ethyl vinyl ether is 1.19 M^{-1} s^{-1}. The solvent deuterium isotope effect, k_{H^+}/k_{D^+}, for the ketonization of vinyl alcohol is 4.75 and for the hydrolysis of ethyl vinyl ether is 2.98; the entropies of activation for the two reactions are -13.3 (esd = 1.7) and -11.0 (esd = 1.8) cal deg^{-1} mol^{-1} at 25 °C. General-base catalysis ($\beta = 0.77$) was observed for the ketonization of vinyl alcohol with eight carboxylate ions, and general-acid catalysis ($\alpha = 0.45$) was observed with five carboxylic acids stronger than and including formic acid. The variation of k_{H^+} with solvent composition in H_2O-Me_2SO mixtures was much less for the ketonization of vinyl alcohol than for the hydrolysis of ethyl vinyl ether, and as a result of this, k_{H^+} for the former reaction is 325 times greater than for the latter in 92.5 mol % Me_2SO; the isotope effects, k_{H^+}/k_{D^+}, for the two reactions in 85.9 mol % Me_2SO are 5.33 and 2.05. It is concluded that these experimental results are best explained by a mechanism for the acid-catalyzed ketonization of vinyl alcohol in which protonation of the double bond by the acid catalyst is concerted with removal of the enolic proton by water acting as a general base and by a mechanism for the base- and water-catalyzed reactions that involves a rate-limiting C-protonation of the enolate anion. The pK_{enol} for acetaldehyde at 25 °C was estimated to be 6.66 or 6.44 from the value of k_{H^+} for the ketonization of vinyl alcohol determined in this investigation and previously reported values of k_{H^+} for the enolization of acetaldehyde.

Introduction

The kinetics of the enolization of aldehydes and ketones have been extensively studied.[2-5] Three methods have been most widely used: (i) trapping the enol with halogen and measuring the disappearance of the latter, (ii) measuring exchange of the α-hydrogen with a deuterium or tritium label, (iii) measuring racemization of a carbonyl compound with an asymmetric α-carbon. The reverse reaction, the ketonization of enols, has been relatively little studied owing to the difficulty of obtaining simple enols. However, if this could be overcome it would have the advantage that the reaction would now be studied in the thermodynamically favorable sense, and it should be possible to use a direct method rather than the indirect ones needed to study enolization. We have recently shown that vinyl alcohol, the enol of acetaldehyde, may be generated in solution from several precursors,[1] and we now report an investigation of the kinetics of its ketonization when generated in this way. The corresponding enolization reaction appears to have been studied twice before,[6,7] but this is the first kinetic investigation of the ketonization of vinyl alcohol or of any simple enol.

Experimental Section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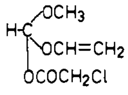
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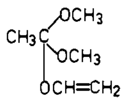
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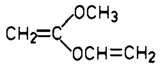
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The kinetics of the ketonization of vinyl alcohol were studied by following the disappearance of the C═C—O chromophore at 210 nm in a similar way to that described by Kresge and Chiang[8] in their investigation of the hydrolysis of vinyl ethers. In order to make sure that the ketonization reaction was being studied and not an earlier step in the sequence for its generation, several different precursors described in part 1[1] were used, viz., methoxy(vinyloxy)methyl acetate (**1**), methoxy(vinyloxy)methyl chloroacetate (**2**), dimethyl vinyl orthoacetate (**3**), and ketene methyl vinyl acetal (**4**). These gave identical first-order rate constants under identical conditions at pH <5, consistent with the ketonization of vinyl alcohol. At pH >5, non-first-order behavior was found with precursors **1** and **2**, indicating that a step other than ketonization of vinyl alcohol was starting to become rate limiting. Therefore kinetics were studied at these pH by using a stock solution of vinyl alcohol in acetone-water (99:1, v/v) at -25 to -30 °C prepared from ketene methyl vinyl acetal (**4**) at -30 °C as described in part 1[1] after checking its ^{1}H NMR spectrum (Perkin Elmer RS 34). This stock solution was also used for runs at a selected number of pH <5 as an additional check that the reaction being studied with the other precursors was ketonization of vinyl alcohol. Again the rate constants obtained with different precursors under the same conditions were, within experimental error, identical with one another. In a typical run, 20 μL of a stock solution of precursor in dioxan (10^{-2}-10^{-3} M) at room temperature or of vinyl alcohol in acetone-water (99:1, v/v) at -25 to -30 °C was added to 2 mL of the reaction solution in the thermostated cell carriage of a Cary 16 spectrophotometer, which was operating on-line with a Digico Micro 16P minicomputer or an Apple II microcomputer. Between 40 and 80 absorbance values were collected at convenient time intervals via the A/D converter (10 or 12 bits), and first-order rate constants were calculated by a generalized least-squares method.[9,10] Reactions were normally followed to more than 90% completion. A check was kept on whether the reactions were really first order by comparing the first, second, and third half-lives. Rate constants for the pH-rate profile were measured in solutions (*I* = 1.00 M) whose pH had been adjusted with low concentrations of HCl, Tris (1.5×10^{-4} M), sodium acetate (1.0-2.0×10^{-4} M), triethylamine (4×10^{-4} M), and a mixture of potassium dihydrogen phosphate (4×10^{-4} M) and sodium hydroxide. A constant check was

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[1] Part 1: Capon, B.; Rycroft, D. S.; Watson, T. W.; Zucco, C. *J. Am. Chem. Soc.* **1981**, *103*, 1761-1765.

[2] See: Bell, R. P. "Acid Base Catalysis"; Oxford University Press: Oxford, 1941. Bell, R. P. "The Proton in Chemistry"; 1st ed., Methuen: London, 1959; 2nd ed., Chapman and Hall: London, 1973.

[3] See: Forsén, S.; Nilsson, M. In "The Chemistry of the Carbonyl Group"; Zabicky, J., Ed.; Interscience: London, 1970; Vol. 2, pp 157-240.

[4] See: Lamaty, G. In "Isotopes in Organic Chemistry"; Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1976; Vol. 2, pp 33-88.

[5] Toullec, J. *Adv. Phys. Org. Chem.* **1982**, *18*, 1-77.

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[7] Talvik, A.; Hiidmaa, S. *Org. React.* (*Tartu*) **1968**, *5*, 297-309.

[8] Kresge, A. J.; Chiang, Y. *J. Chem. Soc. B* **1967**, 53-57, 58-61.

[9] Deming, W. "Statistical Adjustment of Data"; Dover: New York, 1964.

[10] Wentworth, W. E. *J. Chem. Educ.* **1965**, *42*, 96-103, 162-167.

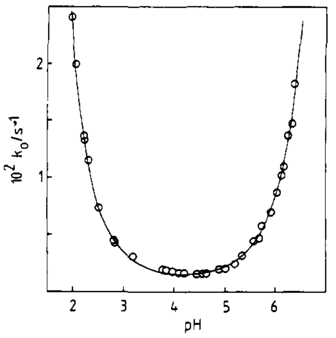

Figure 1. pH–rate profile for the ketonization of vinyl alcohol at 15 °C. The circles are the experimental points, and the line is drawn according to eq 1 with the parameters listed in Table I.

maintained to detect any drift in the pH of the solutions, and the pH of the reaction solutions of those precursors that generate acid (**1** and **2**) were checked after every run (Radiometer PHM 64 pH Meter). The pD–rate profile was obtained similarly, with pD being taken as meter reading + 0.4.[11]

General-acid–base catalysis was studied in buffer solutions by varying the concentrations of buffer while maintaining the ionic strength constant at 1.00 M with potassium chloride for a series of buffers with different buffer ratios. The values of k_{obsd} for reaction in cyanoacetate, chloroacetate, 2-chloropropionate, methoxyacetate, and formate buffers were corrected for small variations in pH by plotting $k_{obsd} - k_{H^+}a_{H^+} - k_{HO^-}a_{HO^-} - k_{H_2O}$ vs. ($[A^-] + a_{H^+}$) for each buffer ratio ($r = [HA]/[A^-]$) where $a_{H^+} = 10^{-pH}$, $a_{HO^-} = K_w/10^{-pH}$, and $[A^-]$ and $[HA]$ are the concentrations of basic and acidic forms of the buffer that were added. Plots of the slopes of these lines (k_{cat}) against r were themselves straight lines with slope k_{HA} and intercept k_{A^-} (see Table S4 and Table III).[12] With formate buffer, $k_{HCO_2^-}$ is 12 times greater than k_{HCO_2H}, and with acids weaker than this no general-acid catalysis was detected. Plots of k_{obsd} vs. $[A^-]$ at constant buffer ratio were straight lines with slopes that were within experimental error, independent of the buffer ratio. The average of these for each buffer was taken as the catalytic constant, k_{A^-} (Table III).

Reactions in mixtures of water and dimethyl sulfoxide (Me_2SO) were carried out with ketene methyl vinyl acetal (**4**) as precursor. NMR experiments showed that this compound was converted much more rapidly into vinyl alcohol under the reaction conditions than the latter was converted into acetaldehyde. Some experiments were also carried out with dimethyl vinyl orthoacetate (**3**), but this was found to be converted too slowly into vinyl alcohol when the concentration of Me_2SO was greater than 60%. The kinetic experiments were therefore carried out with **4** by following the appearance of acetaldehyde at 283 nm at 15 °C by using a method similar to that described by Kreevoy and Williams.[13] Under these conditions the hydration of acetaldehyde ($k_{H^+} = 930\ M^{-1}\ s^{-1}$ at 25 °C in water)[14] is much faster than the ketonization of vinyl alcohol, and we detected no interference from the former reaction. In 100% water, the rate of ketonization was measured by measuring the disappearance of the enol at 210 nm. At each solvent composition, a series of runs was carried out at different acid concentrations, and second-order constants (k_{H^+}) were obtained from the linear plots of k_{obsd} vs. $[H^+]$. A parallel series of experiments was carried out on the hydrolysis of ethyl vinyl ether at one acid concentration for each $Me_2SO–H_2O$ mixture, and second-order constants were calculated by dividing k_{obsd} by $[H^+]$. In a typical run, the solvent (0.4 mL) was placed in a 2-mm quartz cuvette, and when it was thermally equilibrated, 5–10 μL of **4** or ethyl vinyl ether were added and the first-order rate constant was calculated as described above from the absorbance at 283 nm at various time intervals.

The enthalpy and entropy of activation for the hydronium ion catalyzed ketonization of vinyl alcohol and hydrolysis of ethyl vinyl ether were measured in the temperature range 19.0–36.8 °C. A series of experiments was performed at each temperature at different concentrations of HCl. Second-order constants were obtained from the slopes of plots of k_{obsd} vs. 10^{-pH}, and E_a and A were evaluated from the equation $k_2 = Ae^{-E_a/RT}$ by a generalized least-squares method;[9,10] $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were obtained from E_a in the usual manner.[15]

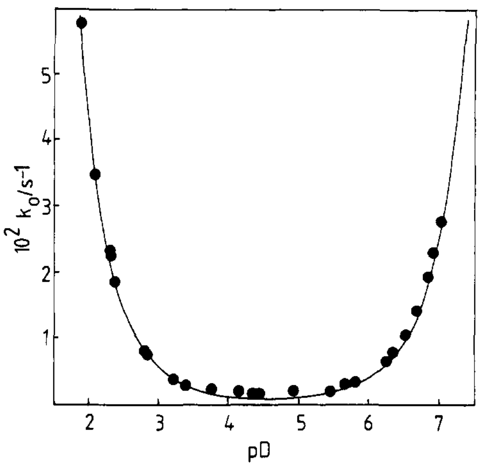

Figure 2. pD–rate profile for the ketonization of vinyl alcohol at 15 °C. The filled circles are the experimental points, and the line is drawn according to eq 2 with the parameters listed in Table I.

Table I. Rate Constants and Solvent Isotope Effects for the Ketonization of Vinyl Alcohol and the Hydrolysis of Ethyl Vinyl Ether at 15.0 °C ($I = 1.00$ M) (Esd in parentheses)

Ketonization of Vinyl Alcohol	
$k_{H^+} = 20.2\ (0.22)\ M^{-1}\ s^{-1}$	$k_{HO^-}/k_{DO^-} = 3.39\ (0.10)$
$k_{D^+} = 4.25\ (0.050)\ M^{-1}\ s^{-1}$	$k_{H_2O} = 1.38 \times 10^{-2}\ (1.4 \times 10^{-3})\ s^{-1}$
$k_{H^+}/k_{D^+} = 4.75\ (0.076)$	$k_{D_2O} = 1.18 \times 10^{-3}\ (4.1 \times 10^{-4})$
$k_{HO^-} = 1.50 \times 10^7\ (2.3 \times 10^5)\ M^{-1}\ s^{-1}$	$k_{H_2O}/k_{D_2O} = 11.7\ (4.2)$
$k_{DO^-} = 4.42 \times 10^6\ (1.2 \times 10^5)\ M^{-1}\ s^{-1}$	
Hydrolysis of Ethyl Vinyl Ether	
$k_{H^+} = 1.19\ (0.011)\ M^{-1}\ s^{-1}$	$k_{H^+}/k_{D^+} = 2.98\ (0.051)$
$k_{D^+} = 0.400\ (0.0058)\ M^{-1}\ s^{-1}$	

Results

The pH–rate profile for the ketonization of vinyl alcohol at 15 °C is given in Figure 1 and Table S1 and the pD–rate profile in Figure 2 and Table S2. These were determined in solutions of ionic strength 1.00 M, which either contained HCl (pH 1.95–3.78) or DCl (pD = 1.57–4.45) or to which low concentrations (ca. 10^{-4} M) of acids and bases, insufficient to cause appreciable general catalysis, had been added to adjust the pH. The results were fitted by a generalized least-squares method[9,10] to eq 1 and 2. K_w (H_2O)

$$k_0\ (H_2O) = k_{H_2O} + (k_{H^+} \times 10^{-pH}) + (k_{HO^-} \times K_w\ (H_2O))/10^{-pH} \quad (1)$$

$$k_0\ (D_2O) = k_{D_2O} + (k_{D^+} \times 10^{-pD}) + (k_{DO^-} \times K_w\ (D_2O))/10^{-pD} \quad (2)$$

was taken to be $4.4978 \times 10^{-15}\ M^2$ (antilog −14.347) and K_w (D_2O) to be $5.7677 \times 10^{-16}\ M^2$ (antilog −15.239),[16] and the best fits to eq 1 and 2 were obtained with the parameters given in Table I. It is seen from the standard deviations that k_{H^+}, k_{D^+}, k_{HO^-}, k_{DO^-} and the corresponding isotope effects are fairly accurately defined but that the values of k_{H_2O}, k_{D_2O}, and the corresponding isotope effect are only approximate. It does however appear that there is definitely a measurable water reaction as k_{H^+} and k_{HO^-} can only account for about 20% of the value of k_0 at the minimum of the pH–rate profile (pH 4.47). The hydrolysis of ethyl vinyl ether was also studied (Table S3), and the values of k_{H^+} and k_{D^+}

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(14) Bell, R. P.; Rand, M. H.; Wynne-Jones, K. M. A. *Trans. Faraday Soc.* **1956**, *52*, 1093–1102.

(15) Cf.: Bunnett, J. F. In "Investigation of Rates and Mechanisms of Reactions"; Friess, S. L., Lewis, E. S., Weissberger, A., Eds.; Interscience: New York, 1961; Part I, p 201.

(16) Covington, A. K.; Robinson, R. A.; Bates, R. G. *J. Phys. Chem.* **1966**, *70*, 3820–3824.

Table II. Enthalpies and Entropies of Activation for the Ketonization of Vinyl Alcohol and Hydrolysis of Ethyl Vinyl Ether (Esd in parentheses)

temp, °C	k_{H^+}, M^{-1} s^{-1}
Ketonization of Vinyl Alcohol	
33.7	82.09 (1.9)
31.0	68.45 (1.4)
28.0	55.85 (1.9)
25.0	45.91 (2.0)
22.5	39.03 (0.8)
19.0	30.59 (2.3)
E_a = 11.82 (0.52) kcal mol^{-1}	
A = 2.31 × 10^{10} M^{-1} s^{-1}	
$\Delta H^{\ddagger}_{298}$ = 11.23 (0.52) kcal mol^{-1}	
$\Delta S^{\ddagger}_{298}$ = −13.26 (1.74) cal deg^{-1} mol^{-1}	
Hydrolysis of Ethyl Vinyl Ether	
36.8	9.279 (2.19)
33.7	7.445 (2.56)
30.0	5.755 (2.44)
25.0	3.798 (2.04)
23.0	3.248 (1.74)
19.0	2.374 (2.41)
E_a = 13.97 (0.54) kcal mol^{-1}	
A = 6.62 × 10^{10} M^{-1} s^{-1}	
$\Delta H^{\ddagger}_{298}$ = 13.37 (0.54) kcal mol^{-1}	
$\Delta S^{\ddagger}_{298}$ = −11.02 (1.83) cal deg^{-1} mol^{-1}	

Table III. Catalytic Constants for the General-Acid- and General-Base-Catalyzed Ketonization of Vinyl Alcohol at 15.0 °C (I = 1.00 M)[a]

acid	pK_a (15 °C)	k_{A^-}, M^{-1} s^{-1}	k_{HA}, M^{-1} s^{-1}
cyanoacetic	2.452[f]	0.108	0.605
chloroacetic	2.845[b]	0.245	0.524
2-chloropropionic	2.879[c]	0.274	0.424
methoxyacetic	3.551[d]	0.896	0.219
formic	3.758[d]	1.98	0.163
3-chloropropionic	4.096[c]	2.15	
acetic	4.758[e]	6.78	
pivalic	5.026[c]	8.72	

[a] Plot of log (k_{A^-}/q) vs. (pK_a + log (p/q)) yielded a β value of 0.745 (0.041) when all eight points were used and 0.767 (0.017) when the points for formate and pivalate were omitted. Plot of log (k_{HA}/p) vs. (−pK_a + log (q/p)) yielded an α value of 0.451 (0.047). The values of p and q for the carboxyl acids were taken to be 1 and 2.[12] [b] Ives, D. J. G.; Pryor, J. H. *J. Chem. Soc.* 1955, 2104. [c] At 18 °C: Kortüm, G.; Vogel, W.; Andrussow "Dissociation Constants of Organic Acids in Aqueous Solution"; Butterworths: London, 1961. [d] Serjeant, E. P.; Dempsey, B. "Ionization Constants of Organic Acids in Aqueous Solution"; Pergamon Press, Oxford, 1979. [e] Kortüm, G.; Vogel, W.; Andrussow "Dissociation Constants of Organic Acids in Aqueous Solution", Butterworths: London, 1961. [f] Feates, F. S.; Ives, D. J. G. *J. Chem. Soc.* 1956, 2798.

are also given in Table I. The value of the isotope effect (k_{H^+}/k_{D^+} = 2.98 at 15 °C) is in reasonable agreement with those previously reported: 2.95 at 26.5 °C,[8] 2.47 at 25 °C,[17] and 3.2 at 25 °C.[18] The variation of k_{H^+} with temperature for both the ketonization of vinyl alcohol and the hydrolysis of ethyl vinyl ether was determined, and the values of ΔH^* and ΔS^* are given in Table II. The value of ΔS^* for the hydrolysis of ethyl vinyl ether (−11.02 cal deg^{-1} mol^{-1}) is in good agreement with those reported previously: −11.1 and −8.2 cal deg^{-1} mol^{-1}.[8,17]

General-acid–base catalysis of the ketonization of vinyl alcohol was studied in buffers of eight carboxylic acids and their salts. With the weaker acids, 3-chloropropionic, acetic, and pivalic, only general-base catalysis by their conjugate bases could be detected. A plot of log (k_{A^-}/q) vs. (pK_a + log (p/q)) for all eight bases yielded a straight line with slope β = 0.745 (0.041) (Figure 3).[19]

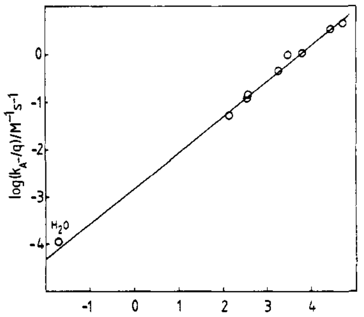


Figure 3. Brønsted plot for the general-base-catalyzed ketonization of vinyl alcohol. The circles are the experimental points, and the line is that obtained from the least-squares calculation for all the points except that for H_2O.

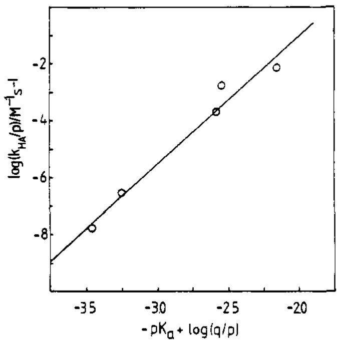
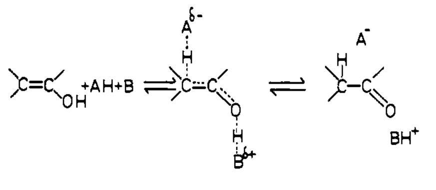


Figure 4. Brønsted plot for the general-acid-catalyzed ketonization of vinyl alcohol. The circles are the experimental points, and the line is that obtained from the least-squares calculation.

The point for formate fell above the line, and that for pivalate fell below it. When these two points were omitted from the plot, β = 0.767 (0.017). The point for water (q = 2, p = 3) lies close to the line, but that for hydroxide ion (q = 3, p = 2) lies well below it (log ($k_{\text{obsd}}/k_{\text{calcd}}$) = −2.58). The plot of log (k_{HA}/p) vs. (−pK_a + log (q/p)) for the five acids for which general-acid catalysis was detected yielded a line with slope α = 0.45 (0.047) (Figure 4). The point for $k_{H_3O^+}$ fell below this line with log ($k_{\text{obsd}}/k_{\text{calcd}}$) = 0.81.

Discussion

Hydronium Ion Catalyzed Reaction. The ketonization of enols and the enolization of carbonyl compounds involve two proton-transfer steps, and there has been extensive discussion as to whether the experimental results are best explained by a mechanism in which they are concerted (eq 3) or stepwise (eq 4), but up to now



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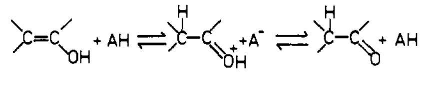

(4)

no clear picture has emerged.[2,5] Thus Jencks and co-workers[20] have demonstrated a third-order term for the enolization of cyclohexanone and acetone in carboxylic acid buffers and postulated a concerted mechanism. On the other hand, Bruice and Bruice

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(17) Salomaa, P.; Kankaanperä, A.; Lajunen, M. *Acta Chem. Scand.* **1966**, *20*, 1790–1801.

(18) Kreevoy, M. M.; Eliason, R. *J. Phys. Chem.* **1968**, *72*, 1313–1316.

(19) p is the number of dissociable protons that the acidic form of the catalyst has and q the number of equivalent points to which a proton can be attached to the basic form. For carboxylic acids, p = 1, q = 2; for H_3O^+–H_2O, p = 3, q = 2, and for H_2O–HO^-, p = 2, q = 3 (cf. ref 12, pp 198–199).

(20) Hand, E. S.; Jencks, W. P. *J. Am. Chem. Soc.* **1975**, *97*, 6221–6230. Hegarty, A. F.; Jencks, W. P. *Ibid.* **1975**, *97*, 7188–7189.

could not detect a third-order term in the enolization of oxaloacetic acid in carbonate, phosphate, and imidazole buffers.[21] It is of course possible that the importance of the third-order term is substrate dependent. Up to now it seems to have been generally thought that the hydronium ion catalyzed reaction of ketones and their enols follows a stepwise mechanism.[5] Thus Swain and co-workers[22] and Toullec and Dubois[23] concluded on the basis of isotope effects that the enolization of α-phenylisocaprophenone and of acetone follows a stepwise mechanism, and Lienhard and Wang came to a similar conclusion for the enolization of cyclohexanone.[24] The basis of Lienhard and Wang's conclusion was that the value of the hydronium ion catalyzed ketonization of the enol (3360 M^{-1} min^{-1} at 25 °C), estimated from the experimentally determined rate constant for enolization and a previously determined equilibrium constant,[25] was very similar to the rate constant for the hydronium ion catalyzed hydrolysis of 1-methoxycyclohexene (2810 min^{-1} at 25 °C). This was taken as evidence for "a mechanism of ketonization in which the bond between the enol oxygen and its hydrogen remains substantially intact during the protonation at carbon", i.e., a nonconcerted mechanism.

It is not clear if these conclusions can be extended to the enolization of aldehydes, but we are now able to apply Lienhard and Wang's test to the acetaldehyde–vinyl alcohol tautomerization using an experimentally determined rather than an estimated value of the rate constant for the hydronium ion catalyzed ketonization. At 25 °C, this has the value 45.9 M^{-1} s^{-1} compared to 3.80 for the hydronium ion catalyzed hydrolysis of ethyl vinyl ether (Table II). Since k_{H^+} for ethyl vinyl ether is 2.3 times greater than that for methyl vinyl ether at 25 °C,[26] the enolization of vinyl alcohol is 27.8 times faster than the hydrolysis of methyl vinyl ether. This ratio is an order of magnitude larger than the value that was estimated for 1-hydroxycyclohexene and 1-methoxycyclohexene[24] and suggests that the mechanism may be one in which the bond between enol oxygen and its hydrogen is partially broken in the transition state.

Tidwell and his co-workers have developed a linear free energy relationship to correlate the rate constants for the protonation of double bonds (eq 5).[27,28] With the σ_p^+ values for the HO and

$$\log k_2 = -10.5\sigma_p^+ - 8.92 \qquad (5)$$

MeO substituents of −0.91[29] and −0.78,[30] the calculated rate constant for protonation of vinyl alcohol is 23 times greater than that of methyl vinyl ether, in good agreement with the ratio calculated above. However it remains to be asked why the σ_p^+ constant for the hydroxyl group is more negative than for a methoxy group. The σ_p^+ constant for the hydroxyl group was not estimated in the normal way[30] from the rate of solvolysis of the corresponding cumyl chloride but from a statistical analysis of the rates of several aromatic electrophilic substitution reactions.[29] Therefore if in these reactions the phenolic protons were also partly transferred in the transition state, this would be reflected in the value of σ_p^+. This has in fact already been postulated for one of the reactions used to define the σ_p^+ constant by de la Mare,[31,32] who concluded that "H–O bond fission contributes to the rate-determining stage for the bromination of phenol".[32] If this is correct it implies that HO bond fission must also contribute to the "rate-determining stage" for the ketonization of vinyl alcohol.

Table IV. Rate Constants for the Hydronium Ion Catalyzed Ketonization of Vinyl Alcohol and Hydrolysis of Ethyl Vinyl Ether in Mixture of Dimethyl Sulfoxide and Water at 15.0 °C

Me_2SO, mol %	k_{H^+} for ketonization of vinyl alcohol,[a] M^{-1} s^{-1}	k_{H^+} for hydrolysis of ethyl vinyl ether,[a] M^{-1} s^{-1}	ratio
0.0	17.5	0.926	18.9
14.5		0.305	
27.6	10.9	0.0837	130
37.2	7.55	0.0351	215
50.4	4.11	0.0171	240
69.5	3.69	0.0172	215
75.5	4.39	0.0173	254
85.9	6.60	0.0223	296
92.5	10.06	0.0310	325
85.9[b]	1.24[c]	0.0109[d]	114

[a] Based on C_{H^+}. [b] D_2O. [c] k_{H^+}/k_{D^+} = 5.32 (Esd = 0.024). [d] k_{H^+}/k_{D^+} = 2.05 (Esd = 0.011).

One of the arguments used by de la Mare in drawing the above conclusion was based on the solvent isotope effect. Solvent isotope effects for the hydrolysis of enol ethers have been extensively studied, and Kresge and his co-workers have established a relationship between k_{H^+}/k_{D^+} and ΔG^* for the hydrolysis of vinyl ethers.[26] k_{H^+}/k_{D^+} for the ketonization of vinyl alcohol (4.75) is substantially greater than that for the hydrolysis of ethyl vinyl ether or for any of the vinyl ethers reported by Kresge and co-workers. From their correlation, the expected isotope effect for the hydrolysis of a vinyl ether with ΔG^* the same as we have observed for the ketonization of vinyl alcohol (15.34 kcal mol^{-1} at 25 °C) would be ca. 3.5. Therefore there is an isotope effect of ca. 1.36 in addition to that which would be expected if the ketonization of vinyl alcohol were similar to the hydrolysis of an enol ether. This of course could be explained if the ketonization proceeded by a concerted mechanism with partial transfer of the enolic proton to a water molecule in the transition state. However there is a possibility that this additional isotope effect could be explained if the mechanism were stepwise, since there would probably be a change on going to the transition state in the force constants of the vibrations associated with the enolic O–H bond and in the strength of the hydrogen bond made by this group to the solvent. Therefore if these effects caused a large secondary isotope effect of ca. 36%, the results could be explained by the stepwise mechanism.

The entropy of activation for the H_3O^+-catalyzed ketonization is −13.3 cal deg^{-1} mol^{-1} (1.7) compared to −11.0 (1.8) for the hydrolysis of ethyl vinyl ether (Table II). These are within experimental error, identical, and unfortunately do not provide any evidence that would enable us to distinguish between the two possible mechanisms, since if the mechanism were concerted the water molecule that removes the proton from the enolic hydroxyl would probably be hydrogen bonded to it in the initial state.

Kreevoy and Williams studied the effect of solvent composition on the hydrolysis of ethyl vinyl ether in Me_2SO–H_2O mixtures.[13] They found that k_{H^+} (ethyl vinyl ether) decreased by a factor of about 50 on going from 0 to 60–70 mol % Me_2SO and then increased slightly with increasing Me_2SO concentration. This dependence is very similar to that shown by the acidity of the medium as measured by protonation of *p*-nitroaniline. The rate constants of other acid-catalyzed reactions show a similar dependence on solvent composition when the mechanism is A-1 but a quite different dependence when the mechanism is A-2 with water acting as a nucleophile.[33] Here, k_{H^+} decreases much less with increasing concentration of Me_2SO.[33,34] It was therefore

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thought that if the mechanism of ketonization of vinyl alcohol were concerted with water acting as a general base to remove the proton, the variation of k_{H^+} (vinyl alcohol) with solvent composition would be different from that found with k_{H^+} (ethyl vinyl ether) and possibly closer to that found for an A-2 reaction. This is in fact what is found since at 15 °C the variation of k_{H^+} (ethyl vinyl ether) with $\mathrm{Me_2SO}$ concentration is similar to that reported by Kreevoy and Williams at 25 °C, but the variation of k_{H^+} (vinyl alcohol) is quite different (Table IV). The latter decreases by a factor of only 5 on going from 0 to 70 mol % $\mathrm{Me_2SO}$ and then increases with increasing $\mathrm{Me_2SO}$ concentration so that in 92.5 mol % $\mathrm{Me_2SO}$, $k_{\mathrm{H_3O}^+}$ (vinyl alcohol) is 0.57 times what it is in water compared to 0.033 for k_{H^+} (ethyl vinyl ether). This means that k_{H^+} (vinyl alcohol) is 325 times greater than k_{H^+} (ethyl vinyl ether) in 92.5 mol % $\mathrm{Me_2SO}$, and on the assumption that k_{H^+} (ethyl vinyl ether)/k_{H^+} (methyl vinyl ether) = 2.3,[26] it is 787 times greater than k_{H^+} (methyl vinyl ether). This large rate difference when "a (fixed) methyl group replaces the (mobile) proton" of vinyl alcohol suggests "that removal of the proton ... in the transition state is responsible for a large rate increase".[35]

The solvent isotope effect in $\mathrm{D_2O{-}Me_2SO}$ leads to a similar conclusion. Kreevoy and Williams showed that the solvent isotope effect on the hydrolysis of ethyl vinyl ether k_{H^+} (ethyl vinyl ether)/k_{d^+} (ethyl vinyl ether) at 25 °C decreases from 3.2 in water to 2.3 in water–$\mathrm{Me_2SO}$ mixtures with 82.8 mol % $\mathrm{Me_2SO}$.[13] We find a similar decrease at 15 °C from 2.98 in water to 2.05 in water–$\mathrm{Me_2SO}$ mixtures with 82.9 mol % $\mathrm{Me_2SO}$. For the ketonization of vinyl alcohol, however, the corresponding isotope effect *increases* from 4.75 to 5.33 with the same change in solvent. If we take the hydrolysis of ethyl vinyl ether as a model for the ketonization of vinyl alcohol by a nonconcerted mechanism, then the expected solvent isotope effect in 85.9 mol % $\mathrm{Me_2SO}$ would be 4.75 × 2.05/2.98 = 3.27. As the measured isotope effect is 5.33, there is an additional isotope effect above that predicted of 5.33/3.27 = 1.63. This seems to be too large to be a secondary isotope effect associated with the change in environment of the OH of the enol on going to the transition state for a nonconcerted reaction. A better explanation would be that the measured solvent isotope effect arises from two concerted proton transfers: from $\mathrm{H_3O^+}$ to the β-C of the enol and from the OH of the enol to a water molecule.

In summary, we have carried out a comparative study of the kinetics of the hydronium ion catalyzed ketonization of vinyl alcohol and hydrolysis of ethyl vinyl ether and found that they show substantial differences, which seem to be best explained by assuming that the ketonization of vinyl alcohol (and enolization of acetaldehyde) proceeds by a concerted mechanism (eq 3) with water acting as a general base. This process may be less unfavorable than it appears at first sight since the water molecule would be hydrogen bonded to the enol hydroxyl group in the initial state and hence there should be no unfavorable entropy loss on going to the transition state associated with loss of translational motion on bringing the vinyl alcohol and water together. The concerted mechanism also fulfills the criteria proposed by Jencks[36] for a concerted reaction as there is a large change in $\mathrm{p}K_\mathrm{a}$ in the course of the reaction since the estimated $\mathrm{p}K_\mathrm{a}$ of vinyl alcohol and the conjugated acid of acetaldehyde are 11.1[37] and −10.2[38] and the $\mathrm{p}K_\mathrm{a}$ of the catalyst, water, −1.73, lies between them.

Recently Toullec has argued in favor of the nonconcerted mechanism (eq 4) for the enolization of acetone (and ketonization of 2-propenol).[5] Unfortunately it has not yet been possible to carry out the kind of experiments with 2-propenol[39] that we have carried out with vinyl alcohol, but it is possible that the conjugate acid of acetone is much more stable than that of acetaldehyde and that the thermodynamic driving force for proton transfer to water in the transition state for ketonization of 2-propenol is much reduced. Our conclusion and those of Toullec are therefore not necessarily in conflict.

General-Acid Catalysis. The ketonization of vinyl alcohol is general-acid catalyzed with $\alpha = 0.45$. This lies intermediate between the values for protonation of ethyl vinyl ether (0.70)[40] and the enolate anion (0.23, see below) and is an indication that the mechanism of these reactions is, like that of the hydronium ion catalyzed reaction, concerted with water acting as a general base. The value of α for the hydrolysis of enol ethers does not vary very strongly with structure, and Kresge and his co-workers have shown that a variation of six powers of ten in reaction rate is accompanied by a variation in α of "little more than 0.2".[40] This suggests that the low value of α found for the ketonization of vinyl alcohol compared to that found for the hydrolysis of enol ethers arises from a difference in mechanism. If water were acting as a general base in the ketonization reaction, the species being protonated would be part way to the enolate anion for which $\alpha = 0.23$ for C-protonation. Therefore a lower α value than that found for the hydrolysis of enol ethers is reasonable.

This behavior contrasts with that found for the enolization[41] of acetone for which α based on catalysis by carboxylic acids is 0.66,[42] very close to the value for the hydrolysis of ethyl isopropenyl ether.[40] As indicated above, the additional methyl group may provide so much extra stabilization of the intermediate cation that would be formed on protonation of the enol that there is no need for proton transfer from the hydroxyl group.

The value of $k_{\mathrm{H_3O}^+}$ for the ketonization of vinyl alcohol falls below the Brønsted plot for catalysis by the carboxylic acids (log $(k_{\mathrm{obsd}}/k_{\mathrm{calcd}}) = -0.811$). This type of behavior has been reported frequently before and seems to be best explained as arising from differences in solvation of $\mathrm{H_3O^+}$ and the carboxylic acids.[43]

Base Catalysis. The ketonization of vinyl alcohol is general base catalyzed with $\beta = 0.77$. The generally accepted mechanism for this kind of reaction is that given in eq 6 and 7.[2–5] The

$$\mathrm{CH_2{=}CH{-}OH + A^- \rightleftharpoons CH_2{=}CH{-}O^- + AH} \qquad (6)$$

$$\mathrm{CH_2{=}CH{-}O^- + AH \xrightarrow{k_2} CH_3CHO + A^-} \qquad (7)$$

Brønsted β value of 0.77 for the overall reaction leads to an α value for the second step of 0.23. This is much lower than the α values for the hydrolysis of vinyl ethers[40] and implies that the transition state for C-protonation of the much more reactive enolate lies earlier on the reaction coordinate, which is reasonable.

On the assumption that this mechanism is correct, the rate constant for the carbon protonation of the enolate ion can be calculated from the equation $k_2 = k_{\mathrm{A}^-} \times K_\mathrm{a}$ (catalyst)/K_a (enol) if K_a (enol) is known. Guthrie and Cullimore's value of 11.1 for the $\mathrm{p}K_\mathrm{a}$ of vinyl alcohol,[37] k_2 for the acids listed in Table III falls in the range 1 to 5×10^7 $\mathrm{M^{-1}\ s^{-1}}$, well below the diffusion-controlled limit. The ratio of the rate constant for protonation of the enolate ion to that for protonation of the enol for those acids where general-acid and general-base catalysis have been studied fall in the range 2.19×10^7 to 7.94×10^7. These values are a little higher than those calculated recently for the protonation of the enol of acetone by acetic acid.[44]

A similar analysis for catalysis by $\mathrm{HO^-}$ leads to the quite reasonable rate constant for the C-protonation of the enolate ion by water of $1.5 \times 10^2\ \mathrm{s^{-1}}$. The deuterium isotope effect $k_{\mathrm{HO}^-}/k_{\mathrm{DO}^-} = 3.39$, but as the isotope effect on K_a (enol) is not known, it is

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(35) Cf. the similar argument used for the mechanism of breakdown of hemiacetals: Funderburk, L. H.; Aldwin, L.; Jencks, W. P. *J. Am. Chem. Soc.* **1978**, *100*, 5444–5459; see also ref 24.

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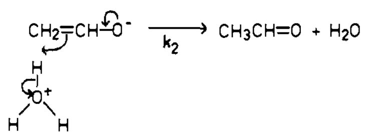
not possible to calculate the isotope effect on the rate of C-protonation of the enolate. The value of k_{HO^-} lies well below the Brønsted plot for the carboxylate ions (log $(k_{obsd}/k_{calcd}) = -2.58$). As for the anomalous value of $k_{H_3O^+}$, this seems to be best interpreted as being due to a solvation effect.[43,45]

Water-Catalyzed or Spontaneous Reaction. Vinyl alcohol undergoes a water-catalyzed or spontaneous ketonization with $k_{H_2O} = 1.38 \times 10^{-2}$ s^{-1} at 15 °C. The ratios k_{H_2O}/k_{H^+} and k_{H_2O}/k_{HO^-} are 6.8×10^{-4} and 9.2×10^{-10} compared to 3.1×10^{-7} and 3.3×10^{-11} M for the enolization of acetone.[46] The water-catalyzed reaction is therefore more significant in the acetaldehyde–vinyl alcohol equilibration than in the acetone–2-propenol equilibration mainly as a result of the H$^+$-catalyzed reaction being relatively more important for the latter. A possible mechanism for the water-catalyzed or spontaneous reaction is shown in eq 8 and 9.

$$CH_2{=}CH{-}OH + H_2O \underset{k_1}{\overset{k_1}{\rightleftharpoons}} CH_2{=}CH{-}O^- + H_3O^+ \qquad (8)$$



(9)

This is analogous to the mechanism proposed for general-base catalysis, and one argument in its favor is that the point for water catalysis fits on the **B**rønsted plot for catalysis by other bases. Also the high value of k_{H_2O}/k_{D_2O}, which is approximately 12, is also qualitatively consistent with this mechanism since it could arise from being a product of the equilibrium isotope effect for the first step and the kinetic isotope effect for the second. For this mechanism to be a valid one, two conditions must be obeyed: $k_1 > k_{H_2O}$ and $k_2 < 10^{10}$–10^{11} M^{-1} s^{-1}. If a value of 5×10^{10} M^{-1} s^{-1} is assumed for k_{-1} and a value of 11.1 for the pK_a of vinyl alcohol, k_1 is calculated to be 0.4 s^{-1}, i.e., about 30 times greater than k_{H_2O}, and $k_2 = k_{H_2O}/K_a = 10^9$ M^{-1} s^{-1}. The above conditions are therefore fulfilled, but not by a large margin, and in view of their obvious inaccuracies, there must be some doubt as to whether this is a valid mechanism for the ketonization of vinyl alcohol. Alternative mechanisms are a concerted mechanism and one in which the enol ionizes to enolate and hydronium ions, which then collapse faster to acetaldehyde than they diffuse apart, with the equilibrium of eq 7 not being established. However this would require the enolate ion to be protonated more rapidly on carbon than on oxygen, which is not very likely. Obviously with more reactive enols, e.g., 2-propenol, one of these mechanisms, especially the concerted mechanism, may be the preferred one.

Equilibrium Constant for the Acetaldehyde–Vinyl Alcohol Equilibrium. The value that we have obtained for k_{H^+} for the ketonization of vinyl alcohol, 45.9 M^{-1} s^{-1} at 25 °C, should enable us to determine the equilibrium constant K_{Enol} = [Enol]/[Aldehyde]. There are two values[6,7] for the reverse reaction, the enolization of acetaldehyde, available: 1×10^{-5} and 1.65×10^{-5} M^{-1} s^{-1}, which lead to values of K_{Enol} of 2.1×10^{-7} and 3.6×10^{-7} (pK_{Enol} = 6.66 and 6.44). Therefore, on this basis the equilibrium proportion of the enol appears to be much less than previously estimated by Guthrie (pK_{enol} = 5.3 or 4.7).[37,47] A similar conclusion has recently been reached concerning the proportion of enol in equilibrium with a number of ketones by the use of a different experimental approach.[48]

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Registry No. **1**, 72536-00-6; **2**, 72535-99-0; **3**, 77302-17-1; **4**, 77302-18-2; D$_2$, 7782-39-0; D$_2$O, 7789-20-0; H$_3$O$^+$, 13968-08-6; DO, 17693-79-7; vinyl alcohol, 557-75-5; ethyl vinyl ether, 109-92-2; vinyloxy anion, 35731-40-9; 2-propanol, 107-18-6; cyanoacetic acid, 372-09-8; chloroacetic acid, 79-11-8; 2-chloropropionic acid, 598-78-7; methoxyacetic acid, 625-45-6; formic acid, 64-18-6; cyanacetic acid anion, 23297-32-7; chloroacetic acid anion, 14526-03-5; 2-chloropropionic acid anion, 16336-84-8; methoxyacetic acid anion, 20758-58-1; formic acid anion, 71-47-6; 3-chloropropionic acid anion, 5102-76-1; acetic acid anion, 71-50-1; pivalic acid anion, 29650-96-2.

Supplementary Material Available: Tables of first-order rate constants for the ketonization of vinyl alcohol in water and D$_2$O, hydrolysis of ethyl vinyl ether in HCl and DCl, and general-acid–base catalysis of vinyl alcohol (7 pages). Ordering information is given on any current masthead page.

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