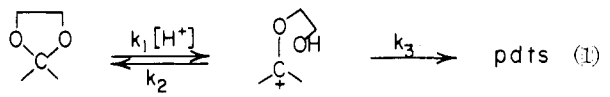
The Reversibility of the Ring-Opening Step in the Hydrolysis of Tropone Ethylene Ketal and Tropone Trimethylene Ketal

Robert A. McClelland,* Mahmood Ahmad, and George Mandrapilias

Contribution from Scarborough College and the Department of Chemistry, University of Toronto, West Hill, Ontario, M1C 1A4 Canada. *Received May 20, 1978*

Abstract: A kinetic analysis of the hydrolysis of the title ketals has provided rate constants associated with (a) the hydronium ion catalyzed (k_1) and noncatalyzed (k_4) ring opening to the intermediate oxocarbonium ion, (b) the reverse of these, the noncatalyzed (k_2) and the hydroxide ion catalyzed (k_5) ring closure, and (c) the reaction of the ion with water (k_3) and hydroxide (k_6) to give tropone. All six rate constants can be obtained because of the stability of the intermediate ion which allows its detection during the hydrolysis in acid solution, and allows its isolation as a BF_4^- salt, by treatment of the ketal with HBF_4 in ether. Although the values of k_2 are greater than the values of k_3, the differences are not great; thus the intramolecular reaction is not significantly favored. The effect of ring size on k_1 and k_2 is small, as it is on the equilibrium constants for ring opening. However, k_4 and k_5 are significantly greater for the ethylene ketal system. This is attributed to different transition states. That for the k_1, k_2 process resembles ketal with little C–O bond breaking in the direction of ring opening, while that for the k_4, k_5 process resembles the intermediate ion, with substantial C–O bond breaking in the ring-opening direction.

It is now generally accepted that the acid-catalyzed hydrolysis of acyclic acetals and ketals proceeds via an intermediate oxocarbonium ion whose formation is rate limiting.[1,2] Although this rate-limiting step is in principle reversible, under normal hydrolytic conditions the concentration of alcohol is so small compared to that of water that the reverse process is unimportant. In the case of cyclic acetals and ketals the sequence of steps in the hydrolysis is undoubtedly the same. Here, however, the step involving the formation of the oxocarbonium ion can conceivably be reversible even in aqueous solution, since the reverse process is intramolecular. This is summarized in a general sense in eq 1, recognizing that proton transfer in the



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first step may or may not be concerted with carbon–oxygen bond breaking or formation.[1]

In kinetic terms the question of reversibility revolves around the relative magnitudes of k_2 and k_3. In the case where $k_2 \ll k_3$ the formation of the ion is rate limiting (providing $k_3 \gg k_1[H^+]$ also), while with $k_2 \gg k_3$, the ring opening is reversible and the k_3 step is rate limiting. The classification $A2^+$ has been suggested for the latter, because of the involvement of a water molecule in the rate-limiting step.[3] Considerable indirect evidence exists consistent with such a behavior, as recently summarized.[3] Of particular importance is the fact that rate constants for hydrolysis of the cyclic compounds are in general considerably smaller than those of acyclic analogues (by factors ranging from "1.5 to 4.4 powers of ten[3]"). Defining in the normal way a second-order rate constant $k_{H^+}^{app}$ = rate/[S][H$^+$], this rate decrease is consistent with the $A2^+$ mechanism where $k_{H^+}^{app} = k_1k_3/(k_2 + k_3)$, or in other words, $k_{H^+}^{app} \ll k_1$. Further experimental support comes from the observation that $\Delta S^{\ddagger}$ values for the hydrolysis of the ring compounds are usually more negative than those of acyclic analogues, although it must be admitted that in most cases the actual values are not as negative as those of normal A2 processes. More concrete evidence for reversibility has been reported in the case of 2,3-*O*,*O*-benzylidenenorbornane-*exo*-2-*exo*-3-diols, where isomerization competes with hydrolysis.[4] It should also be noted that the behavior of certain cyclic acetals and ketals has also been interpreted in terms of a normal A2 hydrolysis mechanism, in which a water molecule reacts with the protonated cyclic acetal or ketal.[4,5]

In a study of oxocarbonium reactivity, we have observed that the intermediate ion derived from the diethyl ketal of tropone (I) is of sufficient stability to be observed during hydrolysis.[6] This presents the opportunity of following separately the formation and subsequent decay of this type of ion. In the case of a cyclic ketal this means that it is possible with an appropriate analysis to obtain the values of the various rate constants of eq 1, and thus directly investigate the question of the reversibility of the ring-opening step. In this paper such an analysis is reported for tropone ethylene ketal (II) and tropone trimethylene ketal (III).

Results

As will be described several different processes are observed for these two cyclic ketal systems. The rate constants referred to as k_{obsd} are the actual observed first-order rate constants for these processes at 25 °C, ionic strength = 0.1. The rate constants referred to in eq 2–6 as k_a, k_b . . . and k_{HA}, k_{A^-} describe the empirical dependency of k_{obsd} as a function of acidity and buffer concentration. These were obtained in the normal way; as an example values of k_{obsd} (extrapolated at each pH to zero buffer concentration) are plotted as a function of pH in Figure 1 for the processes associated with the ethylene ketal (II). The rate constants k_1 . . . k_6 of the Discussion section are based on our kinetic analysis. All values of k_a, etc. and k_1, etc. can be found in Table I.

In aqueous solutions with pH values greater than 6.5, the cyclic ketals undergo simple first-order spectral changes corresponding to the conversion of the ketal to tropone (for example, A → C, Figure 2), with a rate behavior

$$k_{obsd} = k_a[H^+] + k_b + k_{HA}[HA] \quad (2)$$

This rate dependency is identical with that observed by Fife and Anderson for I[7] and II.[8] Our value of k_a for II differs somewhat from that given by the above workers, but this can probably be attributed to a difference in ionic strength since the previous study employed $\mu = 0.6$.

In solutions with pH values less than 4, two separate first-order spectral changes can be observed, A → B → C, Figure 2. The first rapid change corresponds to conversion of the ketal to some intermediate, and follows

$$k_{obsd} = k_c[H^+] + k_{HA}[HA] \quad (3)$$

The second spectral change is slower and corresponds to con-

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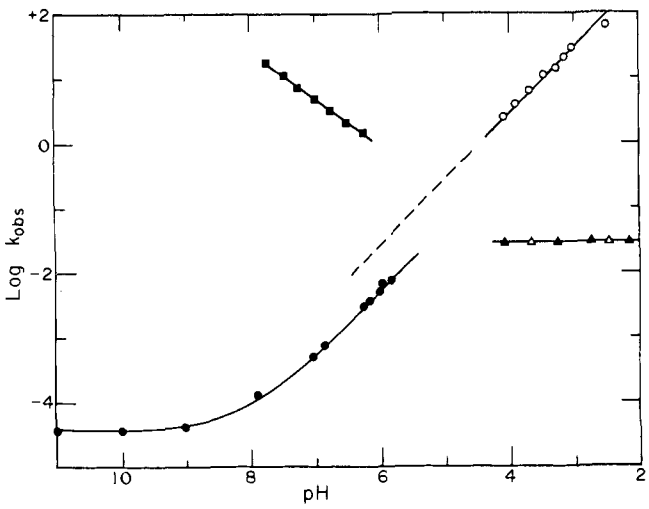


Figure 1. Observed rate constants in the tropone ethylene ketal system (extrapolated to zero buffer concentration) (25 °C, μ = 0.1). (●) Conversion of ketal to tropone (eq 2). (○) Conversion of ketal to intermediate oxotropylium ion (eq 3). (▲,△) Conversion of oxotropylium to tropone (eq 4); points represented by the symbol ▲ were obtained in experiments starting with ketal, while those represented by △ were obtained in experiments starting directly with ion. (■) Conversion of oxotropylium ion to tropone ethylene ketal (eq 5).

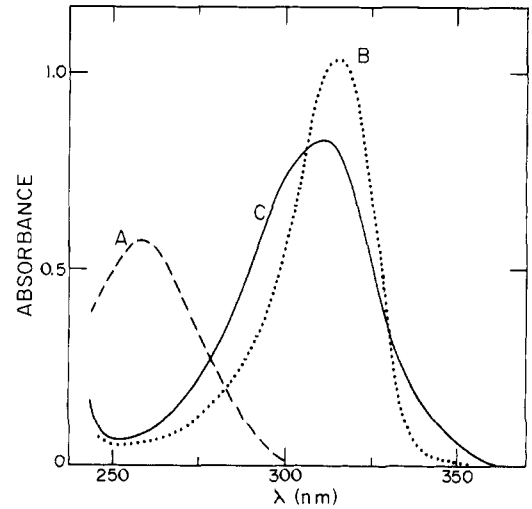


Figure 2. Ultraviolet spectra of ketal (A, - - - -), intermediate (pH < 4) (B, ...), and product (C, —) in the hydrolysis of tropone ethylene ketal. The spectrum C is identical with that of tropone. The spectrum B is also obtained on dissolving V in the same solutions and extrapolating to zero time.

Table I. Rate Constants[a] in the Hydrolysis of Tropone Ketals

	II	III	I[b]
$k_1 = k_c$	2.1×10^4	1.8×10^4	2.2×10^5
k_2	0.13	0.041	
$k_3 = k_d$	0.030	0.025	0.017
$k_{H^+}^{appc}$	3.9×10^3	6.8×10^3	
k_4	0.13	4.0×10^{-4}	8.6×10^{-3}
k_5	8.0×10^7	9.4×10^4	
k_6	2.3×10^4	2.6×10^4	1.0×10^4
pK_R	5.2	5.6	
k_a	4.9×10^3	7.1×10^3	
k_b	3.7×10^{-5}	8.6×10^{-5}	
k_c	8.0×10^7	1.2×10^5	
k_f		0.066	

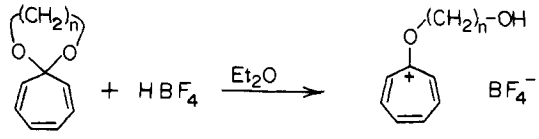
[a] Units are s^{-1} or $s^{-1}\ M^{-1}$, temp = 25 °C, μ = 0.1 (NaCl). [b] Reference 6. [c] $k_1k_3/(k_2 + k_3)$.

version of the intermediate to tropone. This follows

$$k_{obsd} = k_d + k_{A^-}[A^-] \quad (4)$$

We propose that the intermediate spectra correspond to the oxotropylium ions. A very similar spectrum is observed for ethoxytropylium borofluorate (IV) and also for the ketal I when dissolved in acid solution.[6] The rate constants for the conversion of IV to tropone take the same form as those of eq 4, with a very similar value for k_d (Table I).

We have also been successful in preparing the borofluorate salts of the oxotropylium ions derived from II and III, as outlined below. These salts exhibit spectra very similar to B in 70%



V, n = 2
VI, n = 3

H_2SO_4 (where they are stable) and also in water (where extrapolation to zero time is necessary). Moreover, in acid solutions with pH values less than 4 they are converted to tropone with a rate behavior identical quantitatively with that found for the second phase starting with the ketal (Figure 1).

Table II. Partitioning of Tropylium Ion VI to Ketal and Ketone

pH	$(\%\ ketal)_{obsd}$	$(\%\ ketal)_{calcd}$
6.50	59	63.0
6.90	63	64.2
8.45	72	75.7
11.0	73	78.3

In solutions with pH values greater than 6.5 V is converted to ketal, with first-order rate constants following

$$k_{obsd} = \frac{k_c K_w}{[H^+]} + k_{A^-}[A^-] \quad (5)$$

In these same solutions VI is converted to a mixture of ketal and tropone, the actual proportion being somewhat pH dependent (Table II). First-order rate constants for appearance of product obey

$$k_{obsd} = k_f + \frac{k_c K_w}{[H^+]} + k_{A^-}[A^-] \quad (6)$$

In solutions with pH values between 4.0 and 6.5 the system becomes complex. Experiments starting with the ketals reveal that no simple first-order process emerges in the hydrolysis to tropone. This is exemplified in Figure 3, where there is depicted the time dependency of the ketal concentration for three different pH values in this region. The experimental points in this figure are values of $(A - A_\infty)/(A_0 - A_\infty)$ where A refers to the absorbance at 255 nm, A_0 is the initial absorbance (approximately 0.5), and A_∞ is the final absorbance (approximately 0.05). (To be rigorous in equating the above to $[ketal]/[ketal]_0$ it is required that the extinction coefficient of the intermediate ion and the product be identical. They are not quite so, but are very similar and, moreover, small relative to ketal (Figure 1), so that the number arrived at must be reasonably precise.)

Discussion

For the purpose of the discussion specific rate constants will be defined as in eq 7. The pathways involving k_1, k_2, and k_3

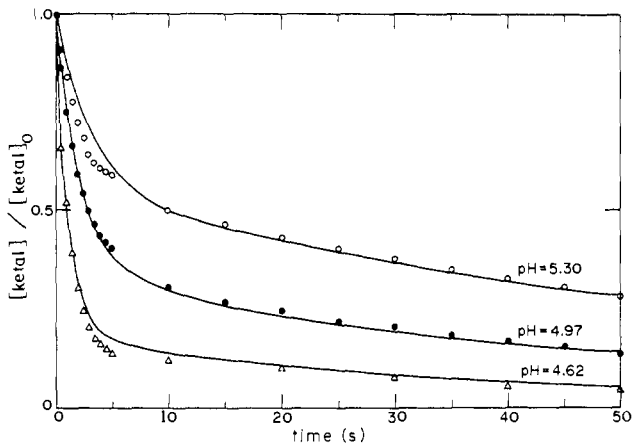
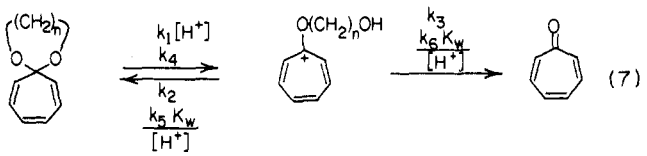


Figure 3. Tropone ethylene ketal concentration as a function of time at intermediate pH (25 °C, μ = 0.1). The points are experimental values of $(A - A_\infty)/(A_0 - A_\infty)$ while the curves are calculated (see text). The pH was maintained in these experiments using dilute acetate buffers.



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are the same as in eq 1, and refer to the processes usually associated with acetal and ketal hydrolysis. The additional pathways in k_4, k_5, and k_6 should be present for any acetal or ketal but are often not considered or detected. The structural features of the tropone ketal system are such that they assume particular importance here.[6,7] The ring-opening step is also catalyzed by general acids, while ring closure and conversion of the intermediate ion to tropone are general base catalyzed. It can also be noted that the rate constants k_3 and k_6 may be composite, depending on the relative rates of hemiketal formation and decomposition.[9]

Sufficient data are available for II and III to obtain for each all six rate constants of eq 7. The approach used in deriving these starts by recognizing that at pH < 4 what is being observed is the rapid and irreversible ring opening of the ketal to produce oxocarbonium ion, followed by the slower conversion of the latter to tropone. The ring opening becomes irreversible in these solutions regardless of the relative magnitudes of k_2 and k_3 or k_5 and k_6, simply because the equilibrium between ketal and ion is shifted to favor ion at these pH values. This will be seen in quantitative terms once the rate constants are derived. It is this aspect of the tropone ketal system, due obviously to the very great stability in the tropylium cation, that allows the following analysis to be carried out.

The rate constants obtained for the initial phase of pH < 4 (eq 3) refer then to acid-catalyzed ring opening and we can set $k_c = k_1$. Similarly the subsequent slower step represents the conversion of the intermediate ion to product and k_d of eq 4 must be k_3. The appearance of the terms in added buffers in these equations shows that the ring opening is also subject to general acid catalysis, while the conversion of the ion to product is subject to general base catalysis. This is not surprising; similar observations are made with the acyclic tropone ketal I.[6-8] Microscopic reversibility also demands that ring closure be general base catalyzed.

From this point the derivations differ somewhat for the ethylene and trimethylene ketals. For the former the key observation is that the addition of oxotropylium ion V to a solution with a pH value greater than about 6.5 results only in ketal, and it does so in a hydroxide-catalyzed process. Therefore we can set k_e of eq 5 to k_5. This observation also establishes that in the hydrolysis of the ketal in these solutions the ring opening is essentially reversible. That is, the intermediate ion has a large preference for returning to ketal rather than proceeding on to product. Defining an equilibrium constant $K_R = k_2/k_1$ (i) $= k_5K_w/k_4$ (ii), and assuming complete reversibility $k_a = k_3/K_R$ (iii) and $k_b = k_6K_w/K_R$ (iv). Since k_a and k_3 (= k_d) are known, (iii) provides K_R. This can then be used in (i), (ii), and (iv) to give respectively k_2, k_4, and k_6, since k_1 (= k_c), k_5 (= k_e), and k_b are also known.

For the n = 3 case one can start with the information that at pH > 6.5 the oxotropylium ion partitions to a mixture of ketal and ketone in pH-independent and hydroxide-catalyzed reactions (eq 6) The rate constant for the former corresponds to the sum of the rate constants for the pH-independent ring closure (k_2) and pH-independent hydrolysis of ion to tropone (k_3). Therefore $k_f = k_2 + k_3$, and knowing k_f and k_3 (= k_d) provides k_2. Similarly, the rate constant for the process in hydroxide is a sum, $k_e = k_5 + k_6$ (v). We can also derive an equation for the pH-independent rate constant for hydrolysis of ketal to tropone at high pH, $k_b = k_4k_6/(k_5 + k_6)$ (vi). This equation is based on a steady-state assumption in the intermediate ion, an assumption that is valid at high pH where no ion accumulates. We have a third relationship in the form $K_R = k_2/k_1 = k_5K_w/k_4$ (vii), where K_R is known since k_2 and k_1 are now available. This means that there are three equations (v, vi, and vii) in the unknown constants k_4, k_5, and k_6. There are two solutions of these equations, $k_4 = 4.0 \times 10^{-4}$, $k_5 = 9.4 \times 10^4$, and $k_6 = 2.6 \times 10^4$ or $k_4 = 1.1 \times 10^{-4}$, $k_5 = 2.6 \times 10^4$, and $k_6 = 9.4 \times 10^4$. The former must be the correct one for this system since the values of k_5 and k_6 are consistent with the products derived from the ion at high pH (Table II). If k_6 were to be greater than k_5, as in the second solution, ketone would have to be the major product.

These various kinetic interpretations are supported by several additional points.

(i) For k_6, it is only with the acyclic ketal I that a number is directly measured.[6] The derived numbers for II and III should be very similar to this, and this is the case.

(ii) For III, one kinetic observation was not used in the derivations, namely, k_a, the rate constant for H^+-catalyzed ketal hydrolysis above pH 6.5. Making the steady-state assumption in the intermediate ion this rate constant should equal $k_1k_3/(k_2 + k_3)$, the value for which is calculated to be 6.8×10^3 M^{-1} s^{-1}. This compares well with the observed value of 7.1×10^3 M^{-1} s^{-1}. (To be rigorous III should not show strict adherence to eq 2 since the changeover from one rate behavior to the other does not occur at the same place for each of the three steps. However, the maximum deviation of the calculated rates from the behavior expressed in eq 2 is 5%, and this is not outside experimental error.)

(iii) Partitioning of the ion VI can be expressed as

$$\frac{\text{ketal}}{\text{ketone}} = \frac{k_2 + k_5[OH^-]}{k_3 + k_6[OH^-]}$$

Table II compares observed and calculated results, and again reasonable agreement is seen. In these results the partitioning at lower pH mainly involves the k_2, k_3 pathways, while at higher pH this shifts to the k_5, k_6 pathways.

(iv) The values calculated for K_R show why clean first-order kinetics can only be observed above pH 6.5 or below pH 4.0. For the hydrolysis of the ketal in the intermediate region the kinetic system corresponds to

$$A \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} B \xrightarrow{k_3'} C$$

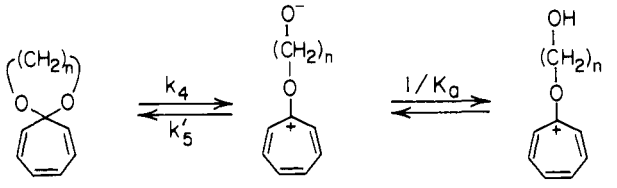
where no assumptions can be made, and the rigorous solutions of the differential equation must be employed.[10,11] Figure 2 compares calculated and observed curves for the disappearance of ketal II in the intermediate region, and shows reasonable

agreement. In the calculations, $k_1' = k_1[H^+] + k_4$, etc., and the effect of buffer (which was dilute) is ignored.

Acid-Catalyzed Ring Opening. This reaction is general acid catalyzed, and, although two mechanistic possibilities (concerted or stepwise) were originally proposed for this type of acetal hydrolysis, a number of studies[12-16] have now shown that the reaction is concerted. Making this assumption the k_1 process (or its reverse k_2) refers to one-step ring opening (or closing) with simultaneous proton gain (or loss). The k_3 process corresponds to water attack, with proton transfer to a second water molecule. (This also assumes that hemiketal formation from the ion is rate limiting[9].)

The ratio k_2/k_3 therefore measures the relative rates of reaction of the oxotropylium ion with the internal OH and a solvent water molecule. The values of these rate constants are fairly close in the two cases, with the intramolecular process somewhat favored. This means that the acid-catalyzed ring opening is "reversible" at least in the sense that $k_2 > k_3$. One can also look at the values of $k_{H^+}^{app} = k_1k_3/(k_2 + k_3)$, the only rate constant which is normally available for an acetal or ketal which gives a less stable oxocarbonium ion. The tropone system does not appear unusual; these $k_{H^+}^{app}$ values (Table I) are considerably smaller than the k_{H^+} value of the acyclic analogue I. The major contribution to this decrease, however, is seen in the rate constant k_1. The "reversibility", $(k_3/(k_2 + k_3))$, is also important but its contribution is less. In other words, the rings are more difficult to open (with hydronium ion), and this could well be the major factor contributing to the generally smaller values of k_{H^+} observed with acyclic acetals and ketals.

Noncatalyzed Ring Opening. A significant pH-independent reaction has been found in all cases where general acid catalysis is observed in acetal hydrolysis.[6,8,12,16] Although several mechanistic possibilities again exist, it is now generally concluded that this reaction simply represents the uncatalyzed decomposition of the ketal to give carbonium ion and alkoxide. For the cyclic ketals of this study, this implies the following two-step route for the k_4 process, and its reverse (k_5), with the first step rate limiting.



$$k_5 = k_5' K_a / K_w$$

One of the more interesting observations of this study is that the values of k_4 and k_5 differ in the two ring systems, both the ring opening and the ring closing being faster by a factor of ca. 10^3 for the five-atom ring as compared to the six-atom ring. The differences are particularly intriguing when it is seen that there is little effect of the ring size on the equilibrium constants for ring opening (the pK_R values) and on the rate constants k_1 and k_2 corresponding to H^+-catalyzed ring opening and its reverse.

Generally in comparing rings with five atoms and six atoms, it is concluded that the latter is favored because it is less strained, but this is compensated by the more favorable entropy of formation of the five-atom ring where there is restriction of movement of a fewer number of atoms.[18] Therefore the similarity in the ground-state energy differences (pK_R values) likely arises because of a cancellation of these two effects. This must also be true therefore for the k_1 process and its reverse k_2. This implies that the transition state for this reversible reaction resembles the ketal, and, for example, in the ring-opening direction little C-O cleavage has occurred at the transition state. This "early" transition state would be consistent with the nature of this system with its extremely stable oxocarbonium ion. Kinetic secondary deuterium isotope effects on the H^+-catalyzed hydrolysis of ortho esters and acetals show that the position of the transition state depends strongly on the stability of the intermediate ion, and suggest that when the ion is extremely stable, as it is here, this transition state is not very far advanced.[19]

In the case of the k_4, k_5 process, we propose a transition state with a considerable amount of bond breaking in the ring-opening direction. This shift to a "later" transition state can be explained by the fact that this reaction is now proceeding with no catalysis (in the ring-opening direction). This interpretation now accounts for the difference in the effect of ring size. In the ring-opening direction, a considerable amount of the strain of the five-atom ring would be relieved at this transition state. However, since the ring is not completely open, the more unfavorable entropy associated with opening the five-atom ring is not yet as important. In terms of the ring-closing direction, the reaction is more favorable in the case of the five-atom ring because of the entropy factor, and, since in this direction the transition state is early, ring strain has not yet achieved importance.

Experimental Section

Materials. Tropone,[20] tropone ethylene ketal,[21] and tropone trimethylene ketal[21] have been previously described. The tropylium salts V and VI were obtained as white, crystalline solids on addition of the ketal (0.01 mol) to a solution of HBF_4 (0.01 mol) in dry Et_2O (15 mL). The solids were filtered and washed with dry Et_2O, these operations being conducted under strictly anhydrous conditions. The identity and purity of the salts were verified by NMR spectroscopy: V (MeCN, TMS), δ 4.08 (2 H) t, 4.75 (2 H) t, 8.4–8.9 (6 H) m; VI (MeCN, TMS), δ 4.10 (2 H) t, 4.73 (2 H) t, 8.4–8.8 (6 H) m; a set of signals at ca. δ 2.25 could also be seen but was partially obscured by the MeCN signal; VI (67% H_2SO_4, external Me_4Si) δ 2.26 (2 H) q, 4.10 (2 H) t, 4.65 (2 H) t; this solvent obscures the signals at δ 8.4–8.9.

Kinetic Measurements. Kinetic investigations were carried out using a Unicam SP 1800 spectrometer with cell block thermostated at 25.0 ± 0.1 °C or a Durrum-Gibson stopped-flow spectrophotometer, also operating a 25.0 ± 0.1 °C. For kinetic runs carried out on the Unicam, substrate was dissolved in acetonitrile and 2 μL of this solution added to the appropriate aqueous solution, preequilibrated in the UV cell. Rate behavior analyzed in this way includes the hydrolysis of the ketals in neutral and basic solution (i.e., eq 2, λ 255 or 307 nm), the slow phase associated with the hydrolysis in acid solution (eq 4, λ 340 nm), and the conversion of the ion VI to ketal and tropone (eq 6, λ 255 nm). The fast phase associated with the ketal hydrolysis in acid (eq 3, λ 255 nm), as well as the two-phase plot associated with solutions of pH 4.5–5.5 (Figure 3), was observed on the Durrum-Gibson by placing the substrate in one syringe in 0.001 N NaOH and mixing this into the appropriate solution. The conversion of V to ketal in neutral solutions (eq 5, λ 255 nm) was also observed in the stopped-flow spectrophotometer, by placing the salt in 0.001 N HCl in one syringe and mixing with an appropriate buffer. Since the half-life of the ion even in 0.001 N HCl is 23 s, it was necessary to preequilibrate the 0.001 N HCl solution in an external water bath, add the substrate, and rapidly load and fire the stopped-flow apparatus. This could be accomplished in about 30 s, so that over half the substrate was hydrolyzed by the time the stopped-flow trace was obtained. This is not as serious a problem as might seem since the hydrolysis of the ion in 0.001 N HCl produces tropone, and this has very little UV absorbance at 255 nm. Except where indicated (Figure 3), plots of $\ln(A - A_\infty)$ or $\ln(A_\infty - A)$ vs. time were excellently linear, and observed rate constants were obtained as the least squares of slopes of these.

Products. Product analysis was carried out in general by comparison of UV spectra, as outlined in the main text. The data of Table II were obtained by calculating the mixture of A and C (Figure 2) necessary to generate the UV spectra observed after complete decomposition of the ion VI.

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(9) (a) An argument can be made that the formation of the hemiketal is essentially irreversible. That is, this species loses alcohol to give tropone more rapidly than it loses water to revert back to ion. The conversion to tropone either leaves behind an OH group which can hydrogen bond to solvent,[6] or, in neutral and basic solution, this conversion proceeds via ionization of OH.[11b,c] (b) M. Ahmad, R. G. Bergstrom, M. J. Cashen, A. J. Kresge, R. A. McClelland, and M. F. Powell, *J. Am. Chem. Soc.*, **99**, 4827 (1977). (c) J. L. Jensen and P. A. Lenz, *ibid.*, **100**, 1291 (1978).
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Acid-Catalyzed Hydrolysis of *N*-Vinylacetamides (Enamides). Substituent Effects of the Acetamido and Amino Groups and Linear Free Energy Correlations of Cyclohexene Reactivities

V. M. Csizmadia, K. M. Koshy, K. C. M. Lau, R. A. McClelland, V. J. Nowlan, and Thomas T. Tidwell*

Contribution from the Department of Chemistry, University of Toronto, Scarborough College, West Hill, Ontario, Canada M1C 1A4.

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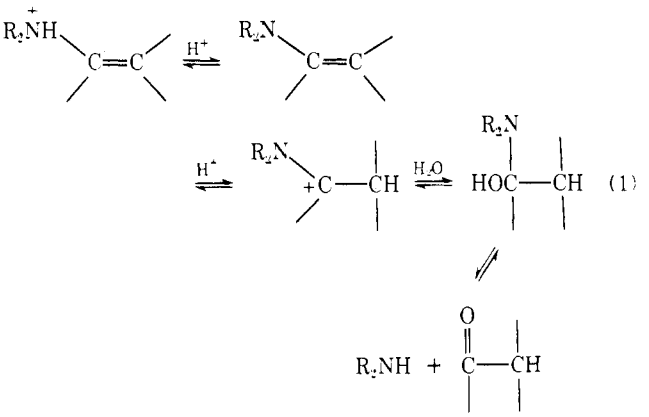
Abstract: The rates of acid-catalyzed hydration of *N*-vinylacetamide (**1**), *N*-(2-propenyl)acetamide (**2**), *N*-(1-phenylvinyl)-acetamide (**3**), and *N*-(1-cyclohexenyl)acetamide (**4**) have been measured. These compounds react through rate-limiting protonation on carbon (the $A_{SE}2$ mechanism) as evidenced by the observation of general acid catalysis for **2**, the solvent isotope effect $k_{H_3O^+}/k_{D_3O^+}$ for **1**, **3**, and **4**, and the correlation of the reactivity of **1**–**3** with the substituent effect-rate correlation established for this mechanism. A contrary mechanism previously proposed for 2-arylenamides is not substantiated. A new linear free energy correlation of the rates of hydration of 1-substituted cyclohexenes is established and also supports the $A_{SE}2$ mechanism for **4**. A σ_p^+ of −0.65 for the acetamido substituent is most compatible with these hydration results and data on various chemical processes available in the literature. Hydration rates of *p*-acetamidostyrene (**5**) and *p*-acetamido-α-methylstyrene (**6**) define a value of σ_p^+ for acetamido of −0.33 applicable to substituted styrenes. Literature data for the effect of amino substituents on the hydration of alkenes and styrenes are also analyzed and all of the data are satisfactorily accommodated by our previously proposed relationship $\log k_2 = -10.5\Sigma\sigma_p^+ - 8.92$. Over 110 compounds spanning 23 powers of ten in reactivity are included, with only modest curvature suggesting minimal saturation of the substituent effects.

The amide function is arguably the most important group for the linking of different organic subunits, so it is not surprising that the hydrolysis of amides has been a topic of continuing interest in a number of different laboratories.[1] Similarly the *N*-vinylamines (enamines) are of great practical use in organic synthesis,[2] and the mechanism of their hydrolysis has been studied in some detail.

In aqueous solution enamines have been found to react by the scheme shown in eq 1.[3] General-acid-catalyzed protonation on carbon is rate limiting near pH 10 but in more acidic solution protonation is very fast and decomposition of the intermediate immonium ion or carbinolamine becomes rate determining.[3b] The hydration of *p*-aminostyrene in aqueous acid at 80 °C has also been studied.[4] This compound is in equilibrium with the anilinium ion in acid, and below 5 M $HClO_4$ undergoes hydration by rate-determining protonation on carbon of the free amine, whereas in more acidic media protonation of the anilinium ion is rate limiting (eq 2).

We have been engaged in a study of substituent effects on electrophilic reactions of alkenes, especially acid-catalyzed hydrations.[5] This effort has been highly informative as to the



(1)

nature of both the interactions of the substituents and the mechanisms of electrophilic additions. Together with studies in other laboratories our efforts have established the $A_{SE}2$ mechanism of rate-limiting protonation on carbon (eq 3) for practically all acid-catalyzed alkene hydrations which have

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