

Protolytic Cleavage of Vinyl Ethers

General Acid Catalysis, Structural Effects and Deuterium Solvent Isotope Effects

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The kinetics of the acid-catalyzed cleavage of the following vinyl ethers have been studied in dilute hydrochloric acid solutions in water and in buffer mixtures of different composition: ethyl, 2-chloroethyl, isopropyl, butyl and isobutyl vinyl ethers, methyl isopropenyl ether, and 2,3-dihydropyran. Spectrophotometric and gas-chromatographic techniques were used. The reaction was found to exhibit general acid catalysis with a Brønsted α of approximately 0.5.

The plausible reaction mechanisms consistent with general acid catalysis are discussed and the other alternatives ruled out except a rate-determining proton transfer from the catalyst acid. The latter mechanism is also supported by the following lines of argumentation: a) The magnitude of α in comparison with those of related proton transfer reactions, when considered in terms of the relative stabilities of the protonated intermediates. b) The kinetic data for mixtures of light and heavy water. The rate constants gave an excellent fit to an equation that was derived for the rate-determining proton (or deuterium) transfer model and, moreover, an independent value was calculated for α from this equation which was in a substantial agreement with that derived from the measurements in buffer mixtures. The value of the gross isotope effect, k_D/k_H , which was 0.406 for the hydronium ion-catalyzed hydrolysis of 2-chloroethyl vinyl ether at 25°C, was also in accord with the values reported for other reactions proceeding through a rate-determining protonation of ethylenic linkage. c) The polar requirements for this proton transfer mechanism implied the hydrolysis rate to vary with the structure in a similar fashion as that of the corresponding acetals. In fact, a free energy correlation was found to exist between these two reactions which was fairly linear over several powers of ten of reactivity. This also excluded any possibility for a nucleophilic function of the conjugate base of the catalyst at the transition state of vinyl ether hydrolysis.

In a recent article¹ one of the authors discussed the similarity that existed between the hydration of olefins and the hydrolysis of vinyl ethers. Another feature of the latter reaction seemed to be the close resemblance of the structural rate effects to those involved in the hydrolysis of acetals. However,

at the time of finishing the manuscript relatively few and insufficient experimental data were available to allow more definite conclusions to be made. More recently, two kinetic studies of vinyl ether hydrolysis have been published.^{2,3}

Jones' and Wood's investigation² of a number of aliphatic vinyl ethers in a water-dioxane solvent (80 % in dioxane) at 25°C is an extension of Skrabals study⁴ of ethyl and isopropyl vinyl ethers. Unfortunately, none of the above authors did pay any attention to the possibility of general acid catalysis, although buffer mixtures were employed. Fife³ investigated extensively the hydrolysis of a cyclic vinyl ether, 2-ethoxy-1-cyclopentene-1-carboxylic acid, and its anion, whereupon he observed general acid catalysis. It is to be regretted that the acid-anion equilibrium had to enter as a perturbation yielding a rather complicated rate analysis. The vinyl ether studied was also structurally of a very particular type as it contained a carbonyl group directly attached to one of the carbon atoms of the ethylenic linkage. It was therefore questionable whether the results obtained would be directly applicable to the hydrolysis of vinyl ethers in general. Therefore a more detailed study of the hydrolytic cleavage of vinyl ethers seemed desirable.

EXPERIMENTAL

Materials. Ethyl vinyl ether was a technical product (Fluka, A. G.) which was repeatedly fractionated over metallic sodium. The following physical constants were recorded for the purified compound: b.p. 35.8–36.2°C/758 torr, n_D^{20} 1.3769, d_4^{20} 0.7500, $[R]_D$ 22.11 (calc. 21.91). The purity was also controlled by gas chromatography. The same analysis was also made on the other vinyl ethers employed, the purities being over 99 % in all cases.

2-Chloroethyl vinyl ether was prepared by the method described by Gretcher, Koch and Pittenger.⁵ The final purification of the product took place by careful fractional distillations in a Todd precision fractionation assembly. The physical constants of the 2-chloroethyl vinyl ether obtained were: b.p. 108.6–108.8°C/760 torr, n_D^{20} 1.4371, d_4^{20} 1.043, $[R]_D$ 26.77 (calc. 26.74).

Isopropyl vinyl ether was prepared by dropping freshly-synthesized α -chloroethyl isopropyl ether slowly into a mechanically stirred pyridine solution which was heated up to about 105°C. The crude vinyl ether, which was distilled off, was then carefully fractionated over metallic sodium. B.p. 55.0–55.6°C/750 torr, n_D^{20} 1.3839, d_4^{20} 0.7521, $[R]_D$ 26.77 (calc. 26.53).

Butyl vinyl ether and isobutyl vinyl ether were commercial products (Koch – Light Laboratories, Ltd.), which were further purified by fractional distillations. Butyl vinyl ether: b.p. 93.6–94.0°C/746 torr, n_D^{20} 1.4012, d_4^{20} 0.7797, $[R]_D$ 31.22 (calc. 31.19). Isobutyl vinyl ether: b.p. 82.2–82.6°C/746 torr, n_D^{20} 1.3962, d_4^{20} 0.7680, $[R]_D$ 31.35 (calc. 31.18).

Methyl isopropenyl ether was prepared from acetone dimethylketal.⁶ B.p. 35.2–35.6°C/752 torr, n_D^{20} 1.3824, d_4^{20} 0.7645, $[R]_D$ 21.97 (calc. 21.88).

2,3-Dihydropyran was from Eastman Kodak Co. The following physical constants were recorded for the repeatedly fractionated compound: b.p. 85.0–85.4°C/746 torr, n_D^{20} 1.4411, d_4^{20} 0.9256, $[R]_D$ 24.00 (calc. 24.37).

In mixing up the acid reaction solutions and the buffer mixtures for the kinetic measurements commercial reagent grade chemicals were used without further purification. Deuterium oxide was from Norsk Hydro-Elektrisk Kvaelstofaktieselskab, Norway. It was purified and analyzed by the methods described in connection with a study of 1,3-dioxolones.⁷

Kinetic methods. The rate measurements were made by spectrophotometry excepting those on 2,3-dihydropyran, the hydrolysis of which was followed by a gas-chromatographic method.

In the spectrophotometric method, the reaction solution (0.0002 to 0.02 M hydrochloric acid or a buffer mixture) was first thermostated to the required temperature, after which the vinyl ether was added. After being effectively mixed, a part of the solution was transferred into a thermostated cell housing attached to a Beckman DU Quartz Spectrophotometer. The progress of the reaction was then followed by optical density readings at 277 $m\mu$, where the carbonyl absorption shows a flat maximum. The initial concentration of vinyl ether varied from 0.02 to 0.04 M except in the cases of the less soluble butyl vinyl ethers, where approximately 0.004 M concentrations were employed. In addition to the initial and final readings, readings that corresponded to 15–80 % change were used to calculate the rate coefficients. First-order kinetics was obeyed in all cases. If the standard deviation of the calculated mean rate coefficient exceeded 1 %, the run was rejected. The temperature of the reaction solution, as measured from the inside of the thermostated cell, was kept constant within $\pm 0.05^\circ\text{C}$ during the experiments.

The hydrolysis rate of 2,3-dihydropyran was measured by gas chromatography. The thermostated reaction mixture consisted of hydrochloric acid (about 0.002 M), 2,3-dihydropyran (0.02 M) and 1,4-dioxane (0.01 to 0.015 M). The latter compound was used as an internal standard for the gas-chromatographic analysis of the samples taken from the reaction mixture. Before the analysis, the reaction was stopped in the samples that were withdrawn from the solution (10 ml) by adding an amount of concentrated aqueous ammonia (0.0025 ml) sufficient to neutralize the catalyst acid present. Although the reaction exhibits general acid catalysis, catalysis by ammonium ion and by water were in this case so slow that they did not interfere the analysis. The determination of the pyran remaining in the reaction mixture after different time intervals was made on a Shandon Universal Gas Chromatograph equipped with a DDP column. The standard error of the first-order rate coefficients derived from these measurements were 2 % or less.

The catalytic coefficients $k_{\text{H}_3\text{O}^+}$ measured at different temperatures for the hydronium ion-catalyzed hydrolysis of vinyl ethers are recorded in Table 1. Table 2 shows the results obtained for the corresponding reaction of 2-chloroethyl vinyl ether in mixtures of light and heavy water. Several of the values given are averages of duplicate measurements.

DISCUSSION

General acid catalysis. Under acidic conditions vinyl ethers are readily hydrolyzed to give an aldehyde and alcohol, *e.g.*

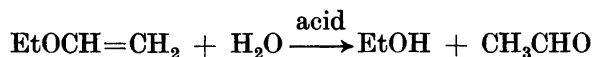


Table 1. Values of the catalytic coefficients for the hydronium ion-catalyzed cleavage of vinyl ethers in water solution at different temperatures. Δ is the maximum value of the standard error.

Substrate	$k_{\text{H}_3\text{O}^+}, \text{M}^{-1} \text{s}^{-1}$			$\Delta, \%$
	25°C	35°C	45°C	
2-Chloroethyl vinyl ether	0.168	0.394	0.975	0.6
Ethyl » »	1.89	4.21	9.50	0.7
Isopropyl » »	4.43	9.64	19.05	1.0
Butyl » »	2.02	4.74	11.23	0.8
Isobutyl » »	2.29	5.17	12.33	1.0
Isopropenyl methyl ether	970 ^a	2047 ^a		1.3
2,3-Dihydropyran	0.267	0.650	1.26	2.1

^a Calculated by the method of least squares from the values in buffer mixtures.

Table 2. Deuterium solvent isotope effects on the lyonium ion-catalyzed cleavage of 2-chloroethyl vinyl ether in H_2O - D_2O mixtures at 25°C. $k_{L_2O^+}$ = catalytic coefficient for the lyonium ions (L = H, D); n = deuterium atom fraction of the reaction solution; Δ = standard error.

n	$k_{L_2O^+}, M^{-1} s^{-1}$	$\Delta, \%$
0.000	0.168	0.6
0.246	0.158	0.5
0.493	0.144	0.4
0.740	0.112	0.4
0.988	0.0690	0.6
1.000	0.0667 ^a	

^a Extrapolated from measurements at lower deuterium atom fractions by means of a cubic polynomial which was obtained by the method of least squares.

In order to establish the nature of the acid catalysis it was necessary to conduct kinetic measurements in suitable buffer mixtures, in addition to those in solutions of strong acids. In the case of general acid catalysis, the overall first-order rate coefficient k which is measured in a buffer solution containing one undissociated acid, in addition to the hydronium ion, should be given by

$$k = k_{H_3O^+}[H_3O^+] + k_{HA}[HA] \quad (1)$$

Here $k_{H_3O^+}$ and k_{HA} are the catalytic coefficients for the hydronium ion and the undissociated acid, respectively. Hence a plot of $k/[H_3O^+]$ against $[HA]/[H_3O^+]$ should give a straight line with a slope of k_{HA} , if the ionic strength is kept constant in these experiments. In the case of specific hydronium ion catalysis the slope becomes equal to zero.

Fig. 1 shows results of experiments conducted in the $H_2PO_4^- - HPO_4^{2-}$ buffer system of a constant ionic strength of 0.08. It can be seen that the kinetic values are accurately represented by eqn. (1). The slopes of the lines drawn give the values $0.160 M^{-1} s^{-1}$ and $0.275 M^{-1} s^{-1}$ for the catalytic coefficient of $H_2PO_4^-$ at 25°C and 35°C, respectively. It follows from the relative acid strengths of $H_2PO_4^-$, HPO_4^{2-} , and H_2O , and from the value of the Brønsted α (see below), that catalysis by HPO_4^{2-} and by H_2O does not

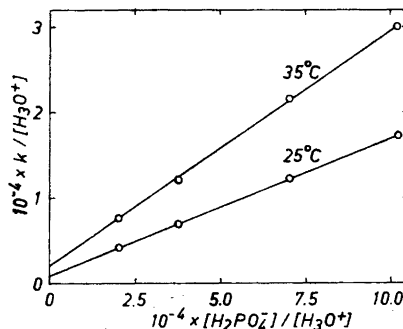


Fig. 1. Plot of $k/[H_3O^+]$ against $[H_2PO_4^-]/[H_3O^+]$ for the hydrolysis of methyl isopropenyl ether in $H_2PO_4^- - HPO_4^{2-}$ buffer solutions. Ionic strength is 0.08.

have any significant contribution to the overall rate in these buffer mixtures, the effective catalysts thus being H_3O^+ and H_2PO_4^- .

In moderately basic buffer solutions the hydronium ion-catalyzed reaction will become relatively unimportant and the catalysis is solely due to the undissociated acid component of the buffer and to the water itself acting as a general acid. This situation was found to prevail in the $\text{HCO}_3^- - \text{CO}_3^{2-}$ buffer system, in which the overall first-order rate coefficient obeyed the equation

$$k = k_0 + k_{\text{HCO}_3^-} [\text{HCO}_3^-]$$

Here k_0 is the first-order rate coefficient for the hydrolysis by water, and $k_{\text{HCO}_3^-}$ the catalytic coefficient for the bicarbonate ion. At 25°C and at the ionic strength of 0.08, the values of the rate coefficients were for methyl isopropenyl ether: $k_0 = 8.0 \times 10^{-5} \text{ s}^{-1}$, and $k_{\text{HCO}_3^-} = 0.84 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$. As the pH values of these buffer mixtures were around 10, the value of the first-order rate coefficient for the hydronium ion-catalyzed reaction was of the order of 10^{-7} s^{-1} and could be neglected.

Table 3 gives the catalytic coefficients of different acids for some vinyl ethers in water at 25°C. On the basis of the values obtained for methyl isopropenyl ether a Brønsted plot can be made which can be shown to be fairly linear over the whole range of acidity. The slope of this plot, the value of the Brønsted α , is 0.51 ± 0.02 . The catalytic coefficients for the acetic acid-catalyzed reactions of ethyl and isopropyl vinyl ethers, which have been calculated from the results of Skrabal⁴ along with those of the present investigation, are also in accord with a Brønsted α of the same magnitude. Skrabal measured his overall first-order rate coefficients in an acetate buffer in which the concentrations of H_3O^+ and CH_3COOH were $1.85 \times 10^{-4} \text{ M}$ and $9.09 \times 10^{-2} \text{ M}$, respectively. As he ascribed the rate solely to catalysis by the hydronium ion, he calculated values for the hydronium ion-catalyzed reaction, *viz.* $3.25 \text{ M}^{-1} \text{ s}^{-1}$ for ethyl vinyl ether and $8.67 \text{ M}^{-1} \text{ s}^{-1}$ for isopropyl vinyl ether at 25°C, which are almost twice those measured in the present study. The hydrolysis of ethyl vinyl ether had been preliminarily studied in the same laboratory⁸ in acetate buffers of different composition but, unfortu-

Table 3. Catalytic coefficients k_{HA} of different acids for the protolytic cleavage of vinyl ethers in water solution at 25°C.

Substrate	Catalyst	$k_{\text{HA}}, \text{M}^{-1} \text{ s}^{-1}$
Methyl isopropenyl ether	H_3O^+	970
»	H_2PO_4^-	0.160
»	HCO_3^-	0.00084
»	H_2O	0.00000144
Ethyl vinyl ether	H_3O^+	1.89
»	CH_3COOH	0.0028 ^a
Isopropyl vinyl ether	H_3O^+	4.43
»	CH_3COOH	0.0086 ^a

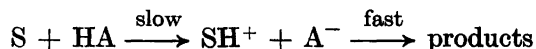
^a Calculated from the data of Skrabal⁴ using the values determined in the present study for the hydronium ion-catalyzed reaction.

nately, the concentration of sodium acetate was kept the same in these buffers and only that of acetic acid was varied. Conforming values were obtained for the apparent rate coefficient, because the concentrations of H_3O^+ and CH_3COOH were altered in the same proportion.

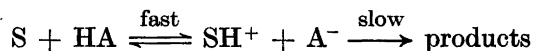
General acid catalysis was also overlooked in a recent study of Jones and Wood² in 80 % dioxane-water, when measuring the rate coefficient for ethyl isopropyl ether in an acetate buffer and ascribing the rate coefficient solely to catalysis by the hydronium ion. When comparing the value obtained in this way with that of ethyl vinyl ether, which latter was determined with perchloric acid as the catalyst, they found this compound to hydrolyze almost 20 000 times faster. From Table 3 it is seen that methyl isopropenyl ether is hydrolyzed only 500 times faster than ethyl vinyl ether by the hydronium ion-catalyzed reaction. Although the above results cannot be directly compared with each other, it can be safely concluded that only a minor part of the value reported by Jones and Wood for their isopropenyl ether is due to catalysis by the hydronium ion.

The conclusions to be drawn concerning the hydrolytic cleavage of vinyl ethers is simplified by the fact that only two commonly occurring reaction mechanisms are consistent with general acid catalysis:

A) Rate-determining proton transfer from the catalyst acid to the substrate:



B) Fast pre-equilibrium protonation of the substrate followed by a rate-determining bimolecular step between the substrate conjugate acid and the conjugate base of the catalyst acid:



In the latter mechanism, the rate-determining step consists either of removal of a proton different from the one that was added in the pre-equilibrium step or, alternatively, of a nucleophilic attack by A^- . In the case of this type of mechanism, the latter alternative is the only conceivable for vinyl ethers, because the conjugate acid of vinyl ether does not possess any proton that could be removed relatively easily excepting that primarily added.

The interpretation of the Brønsted α values is obviously different for the both types of reaction mechanism. In the case of the mechanism *B*, the rate coefficients measured for the different catalyst acids would reflect, in addition to the acidity of HA, the nucleophilic reactivity of the conjugate base of the catalyst toward carbon. Therefore characteristic deviations from the Brønsted catalysis law, not observed here, were probable. On the other hand, in the case of a rate-determining proton transfer reaction, the catalytic coefficient is determined by the ability of HA to donate a proton, and the interpretation of α is simple as it is a measure for the extent to which the proton is transferred from the catalyst to the substrate at the transition state. Thus the value of α gives an idea of the degree to which the transition state resembles the product of the rate-determining stage, *i.e.* the conjugate acid of the substrate molecule. In the present case it can be inferred from the magnitude of

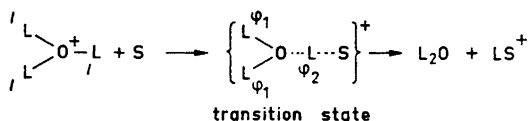
α that the proton is approximately half-transferred at the transition state, if it is the proton transfer step that governs the overall rate of the process.

Deuterium solvent isotope effects. To study in more detail the nature of the rate-determining step of the protolytic cleavage of vinyl ethers, measurements were made in light and heavy water and in their mixtures on the lyonium ion-catalyzed reaction of a vinyl ether. The results of these measurements were given in Table 2 of the experimental part.

The equilibrium theory of deuterium solvent isotope effects in H_2O - D_2O mixtures, as discussed in a generalized form by Salomaa, Schaleger and Long⁹ and by Kresge,¹⁰ leads to eqn. (2) for the relative rate coefficients of a proton (or deuteron) transfer from the catalyst lyonium ion L_3O^+ ($L = H, D$) to a substrate with no exchangeable hydrogens.

$$\frac{k_n}{k_H} = \frac{(1 - n + n \varphi_1)^2 (1 - n + n \varphi_2)}{(1 - n + n l)^3} \quad (2)$$

In this equation, k_H and k_n are the overall catalytic coefficients measured for the lyonium ions in water and in a solvent of deuterium atom fraction n , respectively, l is the isotopic fractionation factor for the lyonium ions, L_3O^+ , and φ_1 and φ_2 are the two fractionation factors referring to the two different types of hydrogens in the transition state of the reaction:



The magnitudes of the fractionation factors at the transition state will depend on the extent to which it resembles the initial state or the reaction products. To take an extreme situation in which the transition state is the same as the initial state, it can be easily seen that for this model $\varphi_1 = \varphi_2 = l$. In another extreme case in which the proton transfer is already completed at the transition state, the value of φ_1 becomes equal to unity because the L_2O -portion of the transition state is here similar to the solvent water itself, whose fractionation factor is unity by definition. Thus the value of φ_1 will change from l to unity when a proton (or deuteron) is moved from the catalyst to the substrate molecule and its magnitude in a particular situation, like that in the actual transition state of the reaction, reflects the extent of the transfer in the situation in question. By the principle of the linear free energy correlations the value of φ_1 should change with this extent according to an exponential law, whereupon $\varphi_1 = l^{1-\alpha}$ in which α is a measure of the proton transfer at the transition state, having a value between zero and unity. When this value is substituted for φ_1 in eqn. (2), the value of φ_2 can be then computed from the known value of k_n/k_H at $n = 1$, *i.e.*, from the value of k_D/k_H . In this way eqn. (2) can be transformed into

$$\frac{k_n}{k_H} = \frac{(1 - n + n l^{1-\alpha})^2 (1 - n + n l^{1+2\alpha} k_D/k_H)}{(1 - n + n l)^3} \quad (3)$$

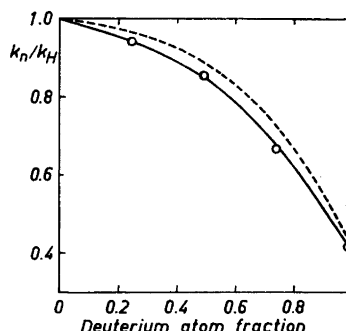
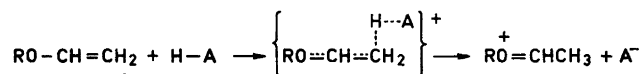


Fig. 2. Observed and calculated values for the deuterium solvent isotope effects on the lyonium ion-catalyzed hydrolysis of 2-chloroethyl vinyl ether in $\text{H}_2\text{O}-\text{D}_2\text{O}$ mixtures at 25°C . Solid line, calculated from eqn. (3) with $\alpha = 0.52$. Dashed line, calculated from eqn. (3) with $\alpha = 0.70$.

As the value of l can be considered to be known, eqn. (3) includes α as the only adjustable parameter. An equation that can be easily converted into the same form as eqn. (3) has been derived by Gold¹¹ in another way by applying the Brønsted catalysis law to the isotopically different catalytic species present, *viz.* H_3O^+ , H_2DO^+ , HD_2O^+ , and D_3O^+ .

The sensitivity of eqn. (3) to changes in α depends markedly on the value of k_D/k_H . Fortunately, the gross isotope effect is in the present case of such a magnitude ($k_D/k_H = 0.406$) that a reasonably good distinction can be made between the different possible values of α . The results of such calculations are shown in Fig. 2. The best fit to the experimental values is obtained with α equal to 0.52, shown by the solid curve in the figure, whereas smaller or bigger values of this quantity are in poorer agreement with the data. An example is shown by the dashed curve drawn in the figure with a value of 0.70 of α . From the standard errors of the rate coefficients of Table 2 and from the calculations based on eqn. (3) one obtains for α and its standard error a value of 0.52 ± 0.04 . In the calculations the value of 0.67 was used for l ,⁹ which substantially agrees with the values obtained from NMR measurements.^{12,13}

The above treatment indicates that, at the transition state of vinyl ether hydrolysis, the catalysing proton is roughly half-transferred from the catalyst to the substrate. This result confirms the conclusions drawn above from the measurements in buffer mixtures, giving additional evidence for a rate-determining proton transfer step:



It is of interest to note that the mesomeric oxonium-carbonium ion generated has the same structure as that formed in the rate-determining stage of the A-1 hydrolysis of acetals,¹ which in part explains the high reactivity of vinyl ethers in their hydrolysis reaction. Another significant part of their reactivity is to be derived from the relatively high free energy level of the initial state of hydrolysis.¹⁴

In terms of the Hammond hypothesis¹⁵ the above mechanism would imply that the more stable the oxonium-carbonium ion intermediate the closer the transition state would lie on the side of the initial reactants. Thus

the relatively small value of α can be rationalized by the strong resonance stabilization of the intermediate in question.* A direct comparison can be made to a similar reaction, which also involves a rate-determining protonation of the ethylenic linkage, *viz.* to the acid-catalyzed hydration of isobutene.¹⁶ As the intermediate in this case lacks resonance stabilization of the type present in the case of vinyl ethers, its relative energy level must be considerably higher than that of the intermediate derived from vinyl ethers. This also implies that in the case of isobutene the transition state must lie closer to the intermediate than in the reaction of vinyl ethers. In fact, from the values reported by Gold and Kessick¹⁶ for k_D/k_H (0.69) and for the spectroscopically measured fractionation factor φ_2 of eqn. (2) (0.256 ± 0.033), one can calculate a value of 0.74 ± 0.14 for α .

The actual magnitude of the gross deuterium isotope effect of vinyl ether hydrolysis, k_D/k_H , is also in general conformity with that expected for a rate-determining proton transfer from hydronium ion to ethylenic double bond. A number of similar reactions have been investigated for the gross isotope effect,^{3,17-19} whereupon k_D/k_H values have been obtained which are smaller than unity. Bunton and Shiner²⁰ have estimated from calculations based on different transition state models that, for a product-like transition state of this type of proton transfer, k_D/k_H is 0.9 to 1.6, for a transition state similar to the initial state, k_D/k_H is about unity, and that the maximum isotope effect with $k_D/k_H = 0.28$ will occur in the case of an intermediate type of the transition state.

Structural effects. The kinetic data relating to the hydronium ion-catalyzed hydrolysis of vinyl ethers of different structure are collected in Table 4. The rate coefficients recorded for 25°C are those calculated from the parameters of the Arrhenius equation, themselves obtained by the method of least squares from the plot of $\log k$ against $1/T$. The Arrhenius equation was satisfactorily obeyed in every case.

The activation parameters have magnitudes that may be well interpreted in terms of a rate-determining proton transfer from the hydronium ion.^{18,21} More conclusive evidence, in addition to that given in the preceding sections, comes from a further inspection of the structural effects in terms of possible free energy correlations.

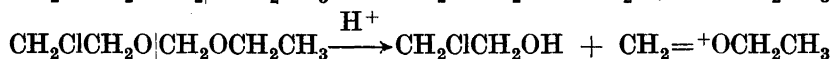
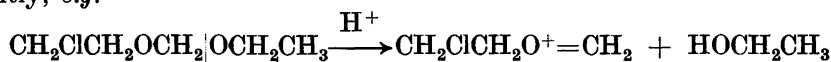
The method may be based on the fact that the product of the rate-determining stage of the postulated mechanism of vinyl ether hydrolysis has a structure similar to that of the intermediate generated in the rate-determining step of the A-1 hydrolysis of acetals. Thus the structural variations in the substrate molecules are expected to alter the rates of these two reactions in the same way.¹ In a more quantitative fashion, one could use the Taft σ^* — ρ^* correlations, but in the present case these correlations would be necessarily limited to a few representatives of the compounds listed in Table 4. A better method here is to consider more directly the effects of similar structural variations on the hydrolysis rates of vinyl ethers and acetals.

* To avoid confusion in the use of the word "stability", frequently found in the literature, it is to be emphasized that here this term is used in its thermodynamic sense. It is quite a different thing that the intermediate is very "unstable" in the kinetic sense as it decomposes readily into the reaction products.

Table 4. Energies and entropies of activation and rate coefficients at 25° for the hydronium ion-catalyzed cleavage of vinyl ethers in water solution.

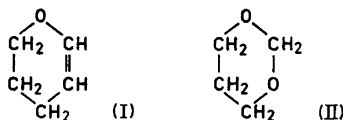
Substrate	<i>E</i> , kcal/mole	ΔS^* , e.u.	$k_{\text{H}_3\text{O}^+}$, M ⁻¹ s ⁻¹
2-Chloroethyl vinyl ether	16.6	- 8.5	0.165
Ethyl » »	15.2	- 8.2	1.87
Isopropyl » »	14.0	-10.7	4.45
Butyl » »	16.2	- 4.9	2.00
Isobutyl » »	15.9	- 5.7	2.25
Isopropenyl methyl ether	13.6	- 1.1	970
2,3-Dihydropyran	14.7	-14.0	0.274

Let ethyl vinyl ether be the reference compound for the hydrolysis of vinyl ethers, and k_{rel} the relative rate coefficient of another vinyl ether, say 2-chloroethyl vinyl ether, as compared with this reference compound. If formals are chosen as the representatives of acetals, the corresponding structural change is from diethyl formal to 2-chloroethyl ethyl formal. However, the hydrolysis of formals involves two distinct reactions occurring concurrently, *e.g.*



and therefore the structural effect we are dealing with cannot be calculated from the overall hydrolysis rates. To make a direct comparison with vinyl ethers it is necessary to consider the ratio of the rates of the individual fission reactions, *e.g.* that of the cleavages $\text{CH}_3\text{CH}_2\text{OCH}_2\text{OR}$ and $\text{CH}_2\text{ClCH}_2\text{OCH}_2\text{OR}$, which ratio represents a structural change similar to that from ethyl vinyl ether to 2-chloroethyl vinyl ether. Such individual fission rates have been determined for a number of asymmetric acetals of formaldehyde²³ and they can be used as such to describe the effect of structural variations corresponding to those of the alkyl vinyl ethers of Table 4. Thus, *e.g.*, k_{rel} for a 2-chloroethyl group is 0.0107 in the hydrolysis of formals.

A relative value for an α -methyl group in acetal hydrolysis is obtained simply from the known values of acetaldehyde acetals as compared with those of formals.^{24,25} 2,3-Dihydropyran (I) can be thought to be derived from the reference vinyl ether, ethyl vinyl ether, by a ring closure with an additional



ring carbon atom. In a similar fashion, the acetals of formaldehyde being the reference compounds for acetal hydrolysis, 1,3-dioxane (II) can be derived from dimethyl formal by exactly the same structural changes. The value of the rate coefficient of (II) in water solution at 25°C has been measured by

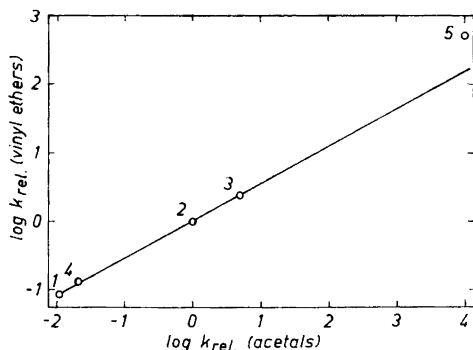


Fig. 3. Comparison of the structural rate effects of the hydronium ion-catalyzed hydrolysis of vinyl ethers with those of the hydrolysis of formaldehyde acetals in water solution at 25°C. 1. 2-Chloroethyl vinyl ether. 2. Ethyl vinyl ether. 3. Isopropyl vinyl ether. 4. 2,3-Dihydropyran. 5. Isopropenyl methyl ether.

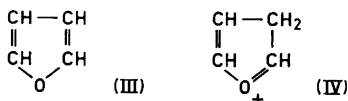
Pihlaja,²⁶ $5.14 \times 10^{-7} \text{ M}^{-1} \text{ s}^{-1}$, which gives $k_{\text{rel.}} = 2.06 \times 10^{-2}$ for this compound.

Fig. 3 shows the plot of the values of $\log k_{\text{rel.}}$ for the hydrolysis of vinyl ethers against those calculated for the hydrolysis of acetals of formaldehyde by the above method. It is seen that the plot is fairly linear over several units of $\log k$ indicating that the free energies of activation of the two reactions are linearly correlated. The only exception is the hydrolysis rate of isopropenyl methyl ether, which is somewhat faster than could be expected from the results for the other vinyl ethers. This is not surprising, because the enhanced reactivities of the both reactions brought about by an α -methyl substitution is expected to alter slightly the relative susceptibilities to structural changes. It is interesting to note that a compound of a rather different structural type, 2,3-dihydropyran, gives an excellent fit to the other data. Of the vinyl ethers of Table 3, butyl vinyl ether and isobutyl vinyl ether cannot be shown in the figure, because the individual fission rates have not been determined for the respective acetals of formaldehyde.

There is a large pattern of independent experimental evidence indicating the hydrolysis of acetals to proceed by the *A*-1 mechanism with no nucleophilic participation of the solvent water in the transition state²⁷ and therefore the reaction is not sterically hindered by the substituent groups. The latter must also be true of the hydrolytic cleavage of vinyl ethers since otherwise characteristic deviations from the above free energy relationship should be observed. Hence the structural rate effects support the conclusions drawn in the preceding sections.

The slope of the line in Fig. 3 is 0.54, which indicates that the hydrolysis of acetals is about twice more susceptible to similar structural variations than that of vinyl ethers. As the influence of the changes in structure is, at least in their most significant part, in their effect on the resonance stabilization of the oxonium-carbonium intermediate, it can be inferred from the above result, and from the Brønsted α of vinyl ether hydrolysis, that the transition state of acetal hydrolysis must lie very close to the intermediate oxonium-carbonium ion. This conclusion is consistent with that drawn recently for a similar reaction, the hydrolysis of acylals,²⁸ from the acid strength of the transition state as compared with those of the initial and final states.

The mechanism suggested above for the acid-catalyzed hydrolysis of vinyl ethers has a close relation to the low reactivity of furan and its derivatives in their hydrolysis reaction. Furan (III) itself, although a vinyl ether, has a



partial aromatic character, which partly accounts for its relative stability. Another reason is that the intermediate ion (IV) which would be generated from a proton transfer from the catalyst, unlike other vinyl ethers, lacks the resonance stabilization as the number of π electrons within the ring is four. The latter follows from the "4n + 2 rule" of the molecular orbital theory for cyclic systems.²⁹ The relative high energy level of (IV) thus also raises the barrier from the initial state to the transition state rendering the normal type of vinyl ether hydrolysis exceptionally difficult.

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