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Vinyl Ether Hydrolysis. 9. Isotope Effects on Proton Transfer from the Hydronium Ion[1]

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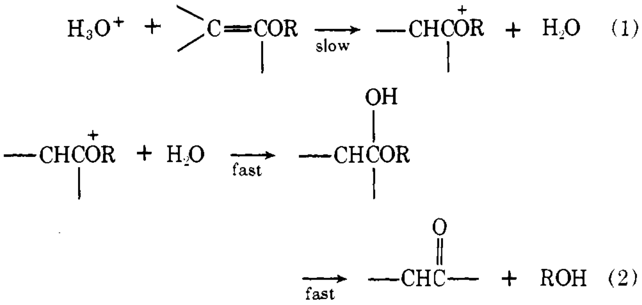
Abstract: Rates of vinyl ether hydrolysis catalyzed by the hydronium ion are reported for 14 substrates in H_2O solution and for 20 substrates in D_2O solution. These results, together with data already in the literature, provide kinetic isotope effects for rate-determining carbon protonation of 32 vinyl ethers. When fitted to expressions provided by Marcus rate theory, these data give an intrinsic barrier for this reaction of $\Delta G_0^{\ddagger} \simeq 5$ kcal/mol, a work term of $w^r \simeq 10$ kcal/mol, and a maximum isotope effect of $k_{H_3O^+}/k_{D_3O^+} \simeq 3.7$. These results suggest that the carbon protonation of certain enolate anions is an encounter plus desolvation-controlled reaction.

A number of systems are now known in which primary hydrogen isotope effects vary systematically with the free energy of reaction, showing a maximum near $\Delta G^\circ = 0$ and dropping off toward unity as ΔG° becomes strongly positive or strongly negative.[2] This behavior was predicted a number of years ago on the basis of considerations dealing with transition-state symmetry,[3] but that view has recently been disputed and the phenomenon has been attributed to proton tunneling.[4] A somewhat different approach is provided by Marcus rate theory,[5] which also predicts an isotope effect maximum near $\Delta G^\circ = 0$ but does not attempt to explain the phenomenon on a molecular level; the theory does, however, furnish an analytical expression relating k_H/k_D to ΔG°, which is a connection not easily made from the other two points of view.

In some systems, ΔG° is not available, and it is useful therefore to have another quantity to which k_H/k_D can be related. In this paper we show how Marcus theory also leads to a relationship between k_H/k_D and $\Delta G^{\ddagger}$, the free energy of activation, and we then use this relationship to correlate values of k_H/k_D for the hydronium ion catalyzed hydrolysis of vinyl ethers. This is a reaction whose first and rate-determining step is proton transfer from the hydronium ion to the substrate, eq 1; since the cationic intermediate thus formed reacts very rapidly with water to give a hemiacetal or hemiketal, which itself decomposes quickly to alcohol and aldehyde or ketone products (eq 2), equilibrium constants for the reaction step to which $k_h.k_D$ refers cannot be measured and ΔG° cannot be determined.



The reaction mechanism of eq 1 and 2 is based upon a variety of evidence,[6] chief among which is the occurrence of sizable kinetic isotope effects; the isotope effects reported here therefore serve to reinforce this mechanistic assignment.

Experimental Section[7]

Materials. Ethyl, phenyl, and α-naphthyl isopropenyl ethers were prepared by decarboxylation of β-ethoxy-, β-phenoxy-, and β-(α-naphthoxy)crotonic acids, respectively.[8] All other substrates (with the exception of methyl and ethyl vinyl ethers which were obtained commercially) were synthesized from the corresponding acetals or ketals by eliminating 1 equiv of alcohol; this was accomplished either in the liquid phase through the catalytic action of p-toluenesulfonic acid,[9] or in the vapor phase by passage through a hot gas chromatography column.[10] The propenyl ethers were also prepared by isomerizing the corresponding allyl ethers in Me_2SO solution with potassium *tert*-butoxide as the catalyst. *cis*- and *trans*-propenyl ethers were separated by gas chromatography and were distinguished by their vinyl hydrogen NMR coupling constants.

The physical properties of those of these vinyl ethers which had been prepared before were in good agreement with literature values; new compounds gave satisfactory carbon and hydrogen analyses. The identity of all substrates was further confirmed by their NMR spectra. Kinetic samples were purified usually by fractional distillation and occasionally by gas chromatography; in all cases, purity was monitored by gas chromatography. All other reagents were best available commercial grades.

Perchloric acid solutions were prepared by diluting 70% $HClO_4$, either with deionized H_2O purified further by distillation from alkaline potassium permanganate, or with D_2O (Bio-Rad) as received. Exact concentrations were determined by acidimetric titration.

Kinetics. Rates of vinyl ether hydrolysis were measured spectroscopically, for the most part by monitoring the decrease in vinyl ether absorption at 210–230 nm; in the case of styryl ethers, however, the increase in aromatic ketone absorption at ~260 nm was used instead. For the slower reactions, measurements were made with a Cary Model 11 spectrometer whose cell compartment was thermostated at 25.0 ± 0.05 °C; when half-lives became <20 s, a Durrum-Gibson stopped-flow apparatus, also operating at 25.0 °C was used.

Absorbance readings were taken over 4–5 half-lives, and the data so obtained were found to obey first-order kinetics exactly. Rate constants were evaluated graphically, either using end points determined after 10–12 half-lives, or by the Guggenheim[11] or Swinbourne[12] methods.

Results

First-order rate constants for the perchloric acid catalyzed hydrolysis of 14 vinyl ethers in H_2O are listed in Table S1,[13] and the corresponding data for D_2O solution appear in Table S2.[13] Table S2 also contains specific rates of hydrolysis in D_2O of six additional vinyl ethers whose rate constants in H_2O solution we have already published.[14]

For each substrate, duplicate and sometimes triplicate or quadruplicate kinetic runs were made at each of four or five acid concentrations in the range 0.001–0.05 M; the acid concentration was always varied by at least a factor of two and more often by factors of four or five. In all cases, strict proportionality between acid concentration and first-order rate constant was found. Second-order rate constants were therefore calculated simply by dividing first-order constants by acid concentration, and best values were obtained as simple averages of these quotients. The results for H_2O solution are summarized in Table I.

The 20 values of $k_{H_3O^+}/k_{D_3O^+}$ provided by these data, together with 12 others for vinyl ether hydrolysis in wholly aqueous solution at 25 °C available from the literature, are also listed in Table I. The presently determined isotope effects are probably accurate to ±5%; they were determined in D_2O solutions containing only 0.3–0.5 at. % H and are not corrected to 100% D_2O.

Rate constants for a few of the substrates used here have been measured before, and the agreement between present and previous results is good. Methyl *cis*-propenyl ether is reported[15] to have $k_{H_3O^+} = 0.245\ M^{-1}\ s^{-1}$ and a value of $k_{D_3O^+}$ which gives the isotope effect $k_{H_3O^+}/k_{D_3O^+} = 2.45$; these values are not significantly different from $k_{H_3O^+} = 0.255\ M^{-1}\ s^{-1}$ and $k_{H_3O^+}/k_{D_3O^+} = 2.62$ obtained here. Likewise, for the trans isomer $k_{H_3O^+}$ is reported[15] to be $0.0818\ M^{-1}\ s^{-1}$ and $k_{H_3O^+}/k_{D_3O^+} = 2.41$, which is consistent with the presently determined values $k_{H_3O^+} = 0.0720\ M^{-1}\ s^{-1}$ and $k_{H_3O^+}/k_{D_3O^+} = 2.48$. The rate of hydrolysis of methyl α-styryl ether has also been measured before[16] but at 30 °C rather than the 25 °C used here and in a solvent consisting of 95% water–5% dioxane. The rate constants reported are therefore understandably somewhat greater than those found here, e.g., $k_{H_3O^+} = 175$ vs. $54.3\ M^{-1}\ s^{-1}$, but they give an isotope effect, $k_{H_3O^+}/k_{D_3O^+} = 3.39 \pm 0.39$, in essential agreement with the present value, $k_{H_3O^+}/k_{D_3O^+} = 4.06 \pm 0.06$.

Table I. Isotope Effects on Hydrolysis of Vinyl Ethers Catalyzed by the Hydronium Ion in Aqueous Solution at 25 °C

Substrate	k_{H^+}, $M^{-1}\ s^{-1}$	k_H/k_D
Ethyl cyclooctenyl ether	623	4.2
Ethyl isopropenyl ether	579[a]	3.5
Ethyl cyclopentenyl ether	454[a]	3.1
Ethyl cycloheptenyl ether	436	3.4
Ethyl cyclononenyl ether	271	3.7
Ethyl α-styryl ether	118	4.1
Ethyl cyclohexenyl ether	80.0[a]	3.6
Methyl α-styryl ether	53.3	4.1
Methyl cyclohexenyl ether	42.3[a]	3.1
2,2-Dimethyl-4-methylene-1,3-dioxolane	18.0[b]	3.3[b]
2-Methoxy-2,3,4,5,6,7-hexahydrooxonin	8.1[c]	4.2[c]
2-Methyl-4-methylene-1,3-dioxolane	7.58[b]	3.0[b]
4-Methylene-1,3-dioxane	6.53[d]	2.6[d]
Phenyl isopropenyl ether	5.98[a]	3.0
4-Methylene-1,3-dioxolane	3.39[b]	2.6[b]
α-Naphthyl isopropenyl ether	2.59	3.1
Ethyl *p*-nitrostyryl ether	2.01	3.2
Ethyl vinyl ether	1.75[e]	2.9[e]
Methyl *cis*-β-methyl-β-styryl ether	1.67[f]	3.0[f]
2,3-Dihydrofuran	1.43[g]	3.1[g]
Isopropyl *cis*-propenyl ether	1.20	2.7
Methyl vinyl ether	0.760	2.8
Ethyl *cis*-propenyl ether	0.480	2.6
4-Methyl-1,3-dioxene	0.442[d]	2.4[d]
Isopropyl *trans*-propenyl ether	0.343	2.6
2,3-Dihydropyran	0.276[h]	2.2[h]
Methyl *cis*-propenyl ether	0.255	2.6
2-Chloroethyl vinyl ether	0.168[i]	2.5[i]
Ethyl *trans*-propenyl ether	0.160	2.4
Methyl *trans*-propenyl ether	0.0720	2.5
Methyl isobutenyl ether	0.0252[j]	1.7[j]
Phenyl vinyl ether	0.00328[a]	2.44

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Discussion

Marcus Theory. In Marcus rate theory the proton-transfer process is divided up into three discrete steps: (1) encounter of the reactants, (2) transfer of the proton, and (3) separation of the products (eq 3).

$$AH + B \xrightarrow[\text{encounter}]{w^r} AH \cdot B \xrightarrow[\text{proton transfer}]{\Delta G_R{}^\circ} A \cdot HB \xrightarrow[\text{separation}]{-w^p} A + HB \quad (3)$$

The energy required to bring the reactants together and form them into a reaction complex is called the work term w^r, with w^p as the corresponding quantity for the products, and the standard free energy of reaction within the reaction complex is $\Delta G_R{}^\circ$. The observed over-all free energy of activation, $\Delta G^\ddagger$, is then equal to w^r plus the barrier to proton transfer within the complex, $\Delta G_R{}^\ddagger$ (eq 4).

$$\Delta G^\ddagger = w^r + \Delta G_R{}^\ddagger \quad (4)$$

This barrier is also formulated by the theory as a simple quadratic function of $\Delta G_R{}^\circ$ and one other variable, $\Delta G_0{}^\ddagger$ (eq 5).

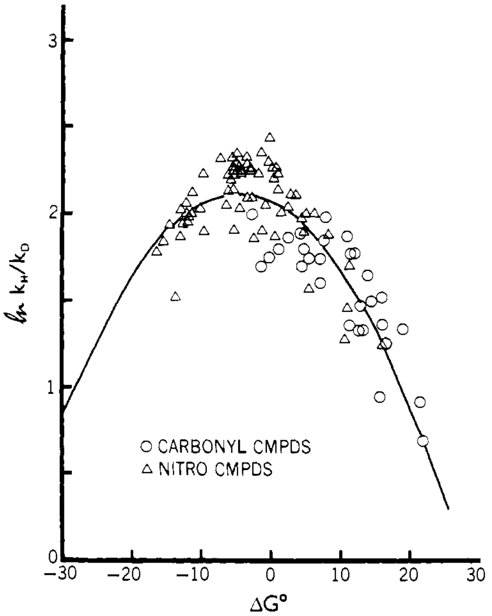


Figure 1. Correlation of k_H/k_D with ΔG° for the ionization of carbonyl and nitro compounds.

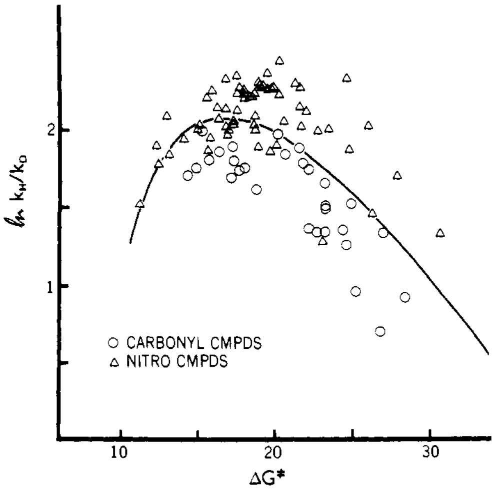


Figure 2. Correlation of k_H/k_D with $\Delta G^{\ddagger}$ for the ionization of carbonyl and nitro compounds.

$$\Delta G_R^{\ddagger} = (1 + \Delta G_R^\circ/4\Delta G_0^{\ddagger})^2\Delta G_0^{\ddagger} \qquad (5)$$

The latter is the value of $\Delta G_R^{\ddagger}$ when $\Delta G_R^\circ = 0$; as such, it is an "intrinsic" barrier, free of any nonkinetic, i.e., thermodynamic, component and is useful for classifying reactions as inherently fast or inherently slow.[5,17]

Substitution of eq 5 into eq 4 leads to the basic relation of Marcus theory, eq 6.

$$\Delta G^{\ddagger} = w^r + (1 + \Delta G_R^\circ/4\Delta G_0^{\ddagger})^2\Delta G_0^{\ddagger} \qquad (6)$$

Two such expressions, one for H transfer and one for D transfer, may be combined to give an equation relating hydrogen isotope effects to free energies of reaction. The result, eq 7, reduces to a particularly simple expression, eq 8, on two assumptions: (1) that $w_H^r = w_D^r$, (2) that $\Delta G_{R,H}^\circ = \Delta G_{R,D}^\circ = \Delta G_R^\circ$.

$$\begin{aligned}\Delta G_H^{\ddagger} - \Delta G_D^{\ddagger} = {} & w_H^r - w_D^r \\ & + (1 + \Delta G_{R,H}^\circ/4\Delta G_{0,H}^{\ddagger})^2\Delta G_{0,H}^{\ddagger} \\ & - (1 + \Delta G_{R,D}^\circ/4\Delta G_{0,D}^{\ddagger})^2\Delta G_{0,D}^{\ddagger} \qquad (7)\end{aligned}$$

$$\begin{aligned}\Delta G_H^{\ddagger} - \Delta G_D^{\ddagger} = {} & (\Delta G_{0,H}^{\ddagger} - \Delta G_{0,D}^{\ddagger}) \\ & \times [1 - (\Delta G_R^\circ/4)^2/\Delta G_{0,H}^{\ddagger}\Delta G_{0,D}^{\ddagger}] \qquad (8)\end{aligned}$$

This is equivalent to saying that there is no isotope effect on formation of the reaction complex nor on the free-energy change within this complex. These conditions will certainly not be generally met, but the isotope effects on the equilibria represented by w^r and ΔG_R° will usually be much smaller than the kinetic isotope effects which correspond to $(\Delta G_H^{\ddagger} - \Delta G_D^{\ddagger})$ and $(\Delta G_{0,H}^{\ddagger} - \Delta G_{0,D}^{\ddagger})$, and eq 8 would seem therefore to be a reasonable first approximation.

It is useful also to employ an intrinsic barrier which is the geometric mean of intrinsic barriers for H and D transfer: $\Delta G_0^{\ddagger} = (\Delta G_{0,H}^{\ddagger}\Delta G_{0,D}^{\ddagger})^{1/2}$. Substituting this into eq 8 and converting free-energy differences for H and D transfer into rate constant ratios then leads to eq 9.

$$\ln (k_H/k_D) = \ln (k_H/k_D)_{\max}[1 - (\Delta G_R^\circ/4\Delta G_0^{\ddagger})^2] \quad (9)$$

This expression requires $\ln (k_H/k_D)$ to have a parabolic dependence upon ΔG_R° and to pass through a maximum at $\Delta G_R^\circ = 0$. It predicts also that the sensitivity of k_H/k_D to changes in ΔG_R° will depend on the magnitude of $\Delta G_0^{\ddagger}$, i.e., that inherently slow reactions with large intrinsic barriers will show broad isotope effect maxima, whereas inherently fast reactions with small intrinsic barriers will give sharper isotope effect maxima.

This expression has been used to correlate isotope effects in a number of systems.[2a,18] A particularly well-documented example is shown in Figure 1 where data for some 100 carbonyl and nitro compound ionization reactions[19] are displayed. Least-squares analyses of these data gives $\Delta G_0^{\ddagger} = 8.1 \pm 0.4$ kcal/mol and $(k_H/k_D)_{\max} = 8.4 \pm 0.2$, which can be converted to an intrinsic barrier for the H transfer reaction of 7.5 ± 0.8 kcal/mol, in good agreement with the 8 kcal/mol obtained from a Brønsted plot for some of the same reactions.[17]

It should be noted that the isotope effect maximum of Figure 1 comes significantly below $\Delta G^\circ = 0$ at $\Delta G^\circ = -4.4 \pm 0.7$ kcal/mol. This is because the analysis was carried out using measured or overall free energies of reaction, ΔG°, rather than the unaccessible free energies of proton transfer within the reaction complex, ΔG_R°. Since $\Delta G^\circ = w^r + \Delta G_R^\circ - w^p$, ΔG° will equal ΔG_R°, and the maximum will come at $\Delta G^\circ = 0$ only when the work terms for formation of reaction complexes in the forward (w^r) and reverse (w^p) direction are equal: $w^r = w^p$.

As pointed out above, values of ΔG° sometimes cannot be obtained, and it is therefore useful to be able to correlate isotope effects with some other quantity. An expression which relates isotope effects to free energies of activation, eq 10,

$$\ln (k_H/k_D) = \ln (k_H/k_D)_{\max} \times \left[2\left(\frac{\Delta G^{\ddagger} - w^r}{\Delta G_0^{\ddagger}}\right)^{1/2} - \frac{\Delta G^{\ddagger} - w^r}{\Delta G_0^{\ddagger}}\right] \quad (10)$$

may be obtained by eliminating ΔG_R° between eq 6 and 9. In this expression, $\Delta G^{\ddagger}$ is approximately the geometric mean of $\Delta G_H^{\ddagger}$ and $\Delta G_D^{\ddagger}$, in keeping with the definition of $\Delta G_0^{\ddagger}$ as $(\Delta G_{0,H}^{\ddagger}\Delta G_{0,D}^{\ddagger})^{1/2}$, but w^r refers to either H or D transfer since eq 9 uses the assumption that $w_H^r = w_D^r$.

Figure 2 shows a correlation using eq 10; the data are the same 100 carbonyl and nitro compound ionization reactions used in the correlation based upon eq 9 shown in Figure 1. The scatter is now somewhat greater than before, perhaps because transition states are subject to extraneous interactions which affect $\Delta G^{\ddagger}$ but do not appear in ΔG°[20] and cancel out in the rate ratio k_H/k_D. Nevertheless, the analysis gives $\Delta G_{0,H}^{\ddagger} = 6.5 \pm 1.1$ kcal/mol and $(k_H/k_D)_{\max} = 8.4 \pm 0.2$, which are nicely consistent with the results obtained from the previous correlation using ΔG° based upon eq 9. The present correlation gives the additional information $w^r = 9.8 \pm 0.7$ kcal/mol.

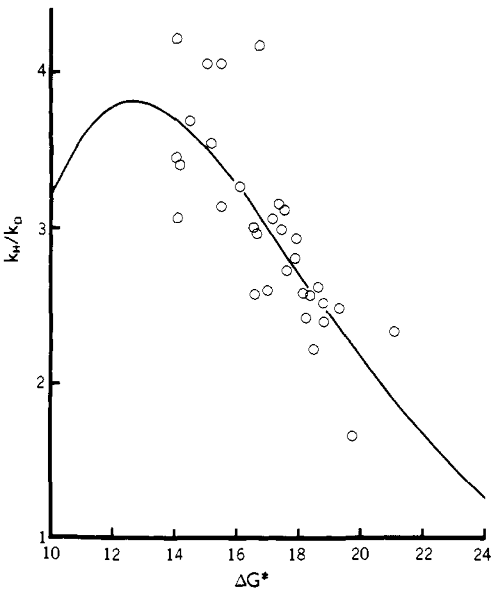


Figure 3. Correlation of $k_{H_3O^+}/k_{D_3O^+}$ with $\Delta G^{\ddagger}$ for the hydrolysis of vinyl ethers.

Vinyl Ether Hydrolysis Isotope Effect Correlations. Before eq 10 can be used to correlate the isotope effects on vinyl ether hydrolysis determined in the present work, allowance must be made for the fact that these isotope effects compare proton transfer from H_3O^+ and D_3O^+, and they therefore contain the secondary isotope effect produced by isotopic substitution in the nonreacting bonds of the hydronium ion. There is no reason to expect this secondary effect to pass through a maximum at $\Delta G_R° = 0$; it is believed instead to vary monotonically with the extent of proton transfer at the transition state, as measured by the Brønsted exponent α, in accordance with the relationship $(k_H/k_D)_{II} = l^{2\alpha}$ where l is the H–D fractionation factor of the hydronium ion.[21] An expression for α is available from Marcus theory (eq 11)

$$\alpha = d\Delta G^{\ddagger}/d\Delta G_R° = (1 + \Delta G_R°/4\Delta G_0^{\ddagger})/2$$
$$= [(\Delta G^{\ddagger} - w^r)/\Delta G_0^{\ddagger}]^{1/2}/2 \quad (11)$$

and the overall isotope effect $k_{H_3O^+}/k_{D_3O^+}$ may then be expressed as the product of primary and secondary effects as shown in eq 12.

$$\ln (k_{H_3O^+}/k_{D_3O^+}) = \ln (k_H/k_D)_I + \ln (k_H/k_D)_{II}$$
$$= \ln (k_H/k_D)_{I,max} \left[2 \left(\frac{\Delta G^{\ddagger} - w^r}{\Delta G_0^{\ddagger}} \right)^{1/2} - \frac{\Delta G^{\ddagger} - w^r}{\Delta G_0^{\ddagger}} \right]$$
$$+ (\ln l) \left(\frac{\Delta G^{\ddagger} - w^r}{\Delta G_0^{\ddagger}} \right)^{1/2} \quad (12)$$

Least-squares fitting of the data of Table I to this expression, using 0.69 as the value of l, leads to the correlation shown in Figure 3, for which $\Delta G_{0,H}^{\ddagger} = 4.9 \pm 3.9$ kcal/mol, $(k_H/k_D)_{I,max} = 5.4 \pm 0.9$, and $w^r = 8.4 \pm 5.0$ kcal/mol. Although the standard deviation in $k_{H_3O^+}/k_{D_3O^+}$ is only 13.5%, there are some marked deviations, notably in the vicinity of the isotope effect maximum. This is where proton tunneling should be most pronounced, and individual differences in the extent of tunneling may be contributing to the scatter. (In some nitro compound ionizations there is firm evidence for the tunnel effect,[22] and these data were therefore excluded from the correlations of Figures 1 and 2; information upon which a similar exclusion might be made in the case of vinyl ether hydrolysis is unfortunately lacking.) A somewhat different effect may be operating in the example which deviates most strongly from the correlation of Figure 3, the hydrolysis of 2-methoxy-2,3,4,5,6,7-hexahydrooxonin, for here there is evidence for a change in rate-determining step (although for catalysis by H_3O^+ the normal mechanism of eq 1 and 2 is believed to apply).[23] Nevertheless, exclusion of this point, as well as the two showing large deviations at the extreme right of Figure 3, does not affect the outcome materially: now $\Delta G_{0,H}^{\ddagger} = 4.3 \pm 3.0$ kcal/mol, $(k_H/k_D)_{I,max} = 5.2 \pm 0.5$, and $w^r = 9.7 \pm 3.2$ kcal/mol, and the standard deviation in $k_{H_3O^+}/k_{D_3O^+}$ is 10.2%, each of which is not significantly different from the corresponding result obtained using all of the data.

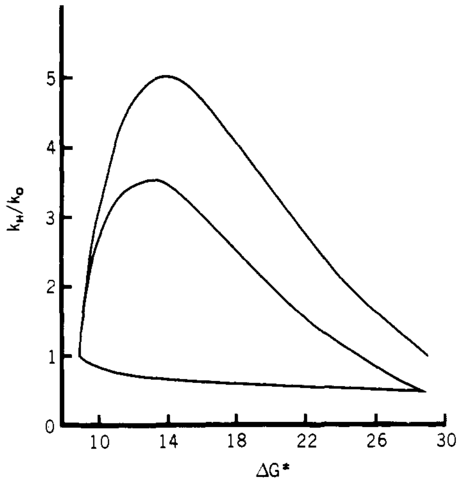


Figure 4. Solutions of eq 12 for $\Delta G_0^{\ddagger} = 5$ kcal/mol, $w^r = 9$ kcal/mol, and $(k_H/k_D)_{I,max} = 5$: upper line; primary isotope effect, lower line, secondary isotope effect, middle line, overall isotope effect.

The maximum primary isotope effect which these calculations produce, $(k_H/k_D)_{I,max} \simeq 5$ is low for O–H bond breaking, but it is consistent with the low vibrational frequencies of the aqueous hydronium ion and the isotope effects which may be calculated from them.[24] This maximum effect occurs at $\Delta G_H^{\ddagger} \simeq 14$ kcal/mol or $k_{H_3O^+} \simeq 200$ M^{-1} s^{-1}, where $\alpha = 0.5$. Because there is also a secondary isotope effect, and because the secondary effect is inverse and grows stronger as $\Delta G^{\ddagger}$ increases, the maximum in the observed isotope effect, $(k_{H_3O^+}/k_{D_3O^+})_{max} \simeq 3.7$ comes slightly earlier at $\Delta G_H^{\ddagger} \simeq 13$ kcal/mol and $k_{H_3O^+} = 2000$ M^{-1} s^{-1}, where $\alpha = 0.45$. Figure 4 shows how the primary, secondary, and overall isotope effects depend upon $\Delta G_H^{\ddagger}$ over the entire range of applicability of Marcus theory, $-4\Delta G_0^{\ddagger} \leq \Delta G_R° \leq \Delta G_0^{\ddagger}$, which in this case corresponds to $\Delta G^{\ddagger} = 9$-29 kcal/mol.

The values $\Delta G_{0,H}^{\ddagger} \simeq 5$ kcal/mol and $w^r \simeq 9$ kcal/mol obtained here are in good agreement with $\Delta G_0^{\ddagger}$ 4 kcal/mol and $w^r = 9$ kcal/mol obtained from a curved Brønsted relation for the hydrolysis of ethyl isopropenyl ether catalyzed by a group of carboxylic acids and monohydrogen phosphonate anions; they are also consistent with $\Delta G_0^{\ddagger} = 2$ kcal/mol and $w^r = 14$ kcal/mol obtained in the same way for the hydrolysis of ethyl cyclopentenyl ether.[1b] A further comparison may be made with values based upon a correlation of Brønsted exponents with free energies of activation. The relevant expression, eq 13

$$\Delta G^{\ddagger} = w^r + 4\Delta G_0^{\ddagger}\alpha^2 \quad (13)$$

may be obtained by combining eq 6 and 11, and least-squares analysis using the available data, which are listed in Table II, gives $\Delta G_0^{\ddagger} = 4.9 \pm 1.2$ kcal/mol and $w^r = 10.6 \pm 2.2$ kcal/mol; both of these values are in remarkably good agreement with the results obtained from the isotope effect analysis.

Isotope effects themselves should depend upon α, and an expression relating these two quantities appropriate to the present situation, eq 14

Table II. Brønsted Exponents for Vinyl Ether Hydrolysis Catalyzed by Carboxylic Acids in Wholly Aqueous Solution at 25 °C[a]

Substrate	α	$\Delta G_{RCO_2H}^{\ddagger}$,[b] kcal/mol
Ethyl cyclohexenyl ether	0.58	10.8
Phenyl isopropenyl ether	0.61	11.9
Ethyl cyclopentenyl ether	0.63	12.7
Ethyl isopropenyl ether	0.64	13.1
Methyl cyclohexenyl ether	0.66	13.9
Ethyl vinyl ether	0.70	15.7
Methyl *cis*-β-methyl-β-styryl ether	0.70	15.7
Phenyl vinyl ether	0.84	22.6

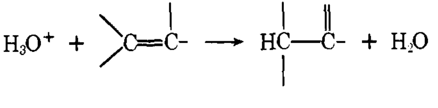
[a] Data from A. J. Kresge, H. L. Chen, Y. Chiang, E. Murrill, M. A. Payne, and D. S. Sagatys, *J. Am. Chem. Soc.*, **93,** 413 (1971), and A. J. Kresge and H. J. Chen, *ibid.*, **94,** 2818 (1972). [b] For a hypothetical carboxylic acid of pK_a = 4.00, which is the approximate midpoint of the pK_a range actually used.

$$\ln (k_{H_3O^+}/k_{D_3O^+}) = \ln (k_H/k_D)_{I,max}[4(\alpha - \alpha^2)] + 2\alpha \ln l \qquad (14)$$

may be obtained by combining eq 11 and 12. The eight values of α of Table II, together with corresponding isotope effects from Table I, when fitted to this expression, give $(k_H/k_D)_{I,max}$ = 6.2 (at α = 0.50) which leads to $(k_{H_3O^+}/k_{D_3O^+})_{max}$ = 4.4 (at α = 0.45). These values are somewhat greater than the results obtained before, from correlations of $k_{H_3O^+}/k_{D_3O^+}$ with $\Delta G^{\ddagger}$, but the difference is due at least in part to the fact that the isotope effects used in conjunction with eq 14 are hydronium ion rate ratios, whereas the α values refer to catalysis by considerably less reactive carboxylic acids. Since α will change with catalyst strength, decreasing with decreasing pK_a, values of α lower than those actually used would have been more appropriate. It is significant therefore that an arbitrary reduction of each α value by 0.1 leads to a significant reduction in $(k_H/k_D)_{I,max}$; the result is now 4.9, which corresponds to $(k_{H_3O^+}/k_{D_3O^+})_{max}$ = 3.5, and the latter, moreover, occurs at virtually the same value of α as before, α = 0.44. The results of this correlation of $k_{H_3O^+}k_{D_3O^+}$ with α thus provide strong support for the essential validity of the correlations using $k_{H_3O^+}/k_{D_3O^+}$ and $\Delta G^{\ddagger}$.

These correlations, taken as a whole, suggest that the intrinsic barrier in acid catalyzed vinyl ether hydrolysis is ~5 kcal/mol and the work term for forming a reaction complex from separated reactants in this process is ~10 kcal/mol. This is consistent with results for other proton transfers to carbon where work terms also tend to be large, and are generally greater than intrinsic barriers.[5b,17,18,25] This is presumably because carbon bases are poor hydrogen bond acceptors, and desolvation of the donor acid prior to proton transfer is therefore not compensated for by hydrogen bond formation between donor and acceptor within the reaction complex.

Comparison with Enolate Anion Protonation. In a preliminary account of this research,[26] isotope effects on the carbon protonation of enolate anions were used to supplement the data on vinyl ether hydrolysis by providing points on the high reactivity side of the isotope effect maximum. It was shown in that paper that isotope effects on a number of other reactions which involve rate-determining proton transfer to carbon do not correlate with isotope effects on vinyl ether hydrolysis, but, since enolate protonation bears a strong resemblance to vinyl ether hydrolysis (cf eq 1 and 15), it was thought that these two reactions might form a homogeneous set. It is of interest to examine this idea using the correlations for vinyl ether hydrolysis developed here.



$$H_3O^+ + \text{>C=C(O}^-\text{)-} \longrightarrow \text{HC-C(=O)-} + H_2O \qquad (15)$$

Table III. Isotope Effects for Carbon Protonation of Enolate Anions

Substrate anion derived from	$k_{H_3O^+}/k_{D_3O^+}$	$\Delta G_H^{\ddagger}$, kcal/mol	k_{H^+}, $M^{-1}\ s^{-1}$	Ref
β-Acetylcyclohexanone	1.7	8.9	1.8×10^6	*a*
Acetylacetone	1.4	8.3	5.6×10^6	*b*
3-Methylacetylacetone	1.0	8.4	4.7×10^6	*c*

[a] T. Riley and F. A. Long, *J. Am. Chem. Soc.*, **84,** 522 (1962). [b] F. A. Long and D. Watson, *J. Chem. Soc.*, 2019 (1958). [c] D. B. Dahlberg and F. A. Long, *J. Am. Chem. Soc.*, **95,** 3825 (1975).

Data for one additional enolate anion have recently become available; these together with information on the two original systems are listed in Table III. It is immediately apparent that the free energies of activation of all three reactions are quite similar, $\Delta G_H^{\ddagger}$ = 8.4–8.9 kcal/mol, and that these $\Delta G^{\ddagger}$s do not differ significantly from the work term obtained here for vinyl ether hydrolysis, w^r = 9 kcal/mol. This implies that no energy in addition to w^r needs to be put into the system to effect reaction, which in turn suggests that proton transfer is no longer rate determining; in other words, the proton-transfer part of the overall process has become so rapid that formation of the reaction complex, i.e., encounter of the reactants plus desolvation of the proton donor, is now the slow step. The rather small isotope effects observed may then be regarded as secondary effects on the encounter step. This is entirely reasonable since isotope effects of this magnitude have been found before in genuine encounter-controlled reactions such as the neutralization of H^+ by HO^-, for which k_H/k_D = 1.7,[27] the recombination of $(CH_3)_3N$ and H^+, where k_H/k_D = 1.3,[28] and the reaction of H^+ with the solvated electron, with k_H/k_D = 1.2.[29] The rate constants of these enolate anion protonation reactions are some four orders of magnitude below the encounter-controlled limit of $10^{10}\ M^{-1}\ s^{-1}$, but carbon protonation reactions in general seem to give limiting rate constants well below this value.[18,25,30]

It can be argued, on the other hand, that the reactants in enolate anion protonation by the hydronium ion are oppositely charged ions, and electrostatic attraction between them will serve to make w^r less than it is in the case of vinyl ether hydrolysis. If this lowering were sufficiently great, proton transfer might once again be rate determining, and that would make the isotope effects listed in Table III genuine examples of primary effects whose magnitude is lowered because the substrates are quite reactive and α is correspondingly small. It would seem, however, that this electrostatic effect cannot be very large. Estimates based on theoretical models put the increase in encounter rate of oppositely charged ions of moderate size over the rate for neutral molecules at no more than an order of magnitude,[31] and this is supported by the modest electrostatic effects observed in experimental studies of vinyl ether hydrolysis catalyzed by charged acis.[1b,32] It is quite likely, therefore, that the protonation of enolate anions by the aqueous hydronium ion is at least in part an encounter plus desolvation-controlled process.

Supplementary Material Available: Tables S1 and S2 of rates of hydrolysis in H_2O and D_2O solutions (10 pages). Ordering information is given on any current masthead page.

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Reactivity of Cyclic and Acyclic Olefinic Hydrocarbons in Acid-Catalyzed Hydration

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Abstract: The rates of hydration of ethylene, propene, 1-hexene, cyclohexene, 1-methylcyclohexene, 1-methylcyclopentene, and norbornene catalyzed by H_2SO_4 and D_2SO_4, and the hydration of cyclohexene catalyzed by $HClO_4$ and $DClO_4$, all at 25 °C, were measured. Ethylene is only a factor of 24 less reactive than *p*-nitrostyrene at $H_0 = -7.37$, but has a very steep slope of log k_{obsd} vs. H_0 of -1.54 so that ethylene rates extrapolated to low acidities appear quite small relative to other alkenes. All of the substrates are interpreted to react by rate-determining protonation on carbon to give the corresponding carbonium ions (the $A_{SE}2$ mechanism). Solvent isotope effects k_{H^+}/k_{D^+} range from 2.82 for propene to 1.06 for cyclohexene, and are only tenuously related to absolute reactivity. Norbornene is 770 times more reactive than cyclohexene, and at least part of this difference is attributed to the unsymmetrical π bond in this molecule endowing it with enhanced nucleophilicity on the exo face.

The steric course of electrophilic additions to cyclic alkenes[1] and the rates of solvolytic reactions of many cycloalkyl esters[2] have been the subject of intense chemical interest. However the effect of structure on the rates of the addition reactions has not been systematically studied; so a unified interpretation of the reactivity of cycloalkyl derivatives has not been possible.

We have recently been successful in the interpretation of the rates of acid-catalyzed hydration of acyclic alkenes in terms of structure effects, particularly σ^+ parameters.[3] It appeared highly desirable to extend this study to the corresponding reactivity of selected cyclic olefinic hydrocarbons. The study of hydration would also be useful for comparison with published studies of trifluoroacetic acid addition to alkenes[4] and stable cations generated from alkenes and other sources.[5]

Of particular interest is ethylene, the parent of the other alkenes. The kinetics of the reaction of ethylene with concentrated sulfuric acid to give ethyl hydrogen sulfate and diethyl sulfate (eq 1)

$$\mathrm{CH_2{=}CH_2 + H_2SO_4 \rightleftharpoons CH_3CH_2OSO_3H \rightleftharpoons (CH_3CH_2O)_2SO_2} \quad (1)$$

have received considerable attention because of their industrial importance. However, this reaction was studied[6] under conditions where high concentrations of the sulfates were present; so the results are not useful for understanding the mechanism of ethylene protonation in aqueous sulfuric acid. It was noted by Purlee and Taft[7] that ethylene reacts with 70% $HClO_4$ at 30 °C at an appreciable rate, but no rate constants were obtained. Apparently the only reported rate constants for the protonation of ethylene in aqueous acid were those of Baliga and Whalley in 0.3-0.63 M HNO_3 at 170-190 °C and 100-bar pressure.[8] In all these cases the conversion of ethylene to products at equilibrium was very high (>95%).[6-8]

It has been proposed in an excellent recent textbook[9] that isobutene "undoubtedly" hydrates via protonation on carbon to give the *tert*-butyl cation (eq 2)

$$\mathrm{Me_2C{=}CH_2 \xrightarrow{H^+} Me_3C^+ \xrightarrow{H_2O} Me_3COH} \quad (2)$$