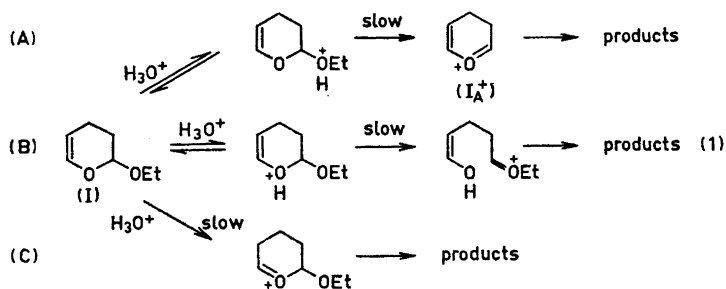# Determination of the Contributions of Concurrent Acetal and Vinyl Ether Hydrolyses on the Basis of the Different Solvent Isotope Effects in These Reactions

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The deuterium solvent isotope effect in the hydrolysis of 2-ethoxy-2,3-dihydropyran, $k_{D_3O^+}/k_{H_3O^+} = 1.26$, indicates that this reaction involves both a proton transfer mechanism of vinyl ether hydrolysis and an A-1 mechanism of acetal hydrolysis. The apparent activation entropy of the hydrolysis (+7.1 E.U.) is in agreement with this conclusion. The contributions of both of these reactions were calculated on the basis of rate coefficients in D_2O and in $D_2O - H_2O$ mixtures. The A-1 hydrolysis proceeds via a cyclic carbonium ion in spite of the fact that this ion is energetically unfavored owing to its planar structure; the contribution of the A-1 ring fission is negligible.

It was recently shown[1] that the hydrolysis of 2-alkoxytetrahydropyrans by the A-1 mechanism involves protonation of the exo-oxygen atom with a subsequent rate-determining heterolysis of the protonated substrate. The other possible route, A-1 ring fission, was not in accordance with the structural effects. The hemicyclic acetal, 2-ethoxy-2,3-dihydropyran (I), studied in the present work is kinetically interesting because route (A) in scheme (1) is

sterically unfavored owing to the planar structure of the intermediate $I_A{}^+$. Thus in this case route B is more probable than it is in the corresponding saturated compounds, the 2-alkoxytetrahydropyrans.[1] A third mechanism (route C), a rate-determining proton transfer to the double bond,[2] is also possible for the hydrolysis of 2-ethoxy-2,3-dihydropyran. The purpose of this investigation was to determine the contributions of these different mechanisms by kinetic methods.
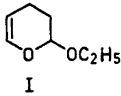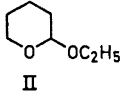
EXPERIMENTAL

Syntheses. 2-Ethoxy-2,3-dihydropyran was prepared from acrolein and ethyl vinyl ether by the method of Longley and Emerson.[3] The reaction product was distilled twice. Physical constants: b.p. $53-54°C/30-35$ torr, $n_D{}^{20}$ 1.4396, $d_4{}^{20}$ 0.9675, $(R)_D$ 34.88 (calc. 35.10). The purity of the product was checked by gas chromatography.

Kinetic measurements. The rate coefficients of the hydronium ion-catalyzed hydrolysis of 2-ethoxy-2,3-dihydropyran were determined in dilute hydrochloric acid solutions $(0.01-0.02$ M) at 25, 35, and 45°C. To determine the deuterium solvent isotope effect, some measurements were also made in deuterium oxide (0.016 M DCl) and in D_2O-H_2O mixtures $(0.01-0.04$ M $L_3O)^+$.

A 2 ml sample of the reaction mixture was run into a bottle to which 0.06 ml of concentrated ammonia had been introduced to neutralize the catalyst. The progress of the hydrolysis reaction was followed by measuring the height of the peak of the hydrolyzing compound and that of an internal standard with a Shandon Universal gas chromatograph. The standard substance was cyclopentanone (0.04 M).

Table 1. Kinetic data for the hydronium ion-catalyzed hydrolysis of 2-ethoxy-2,3-dihydropyran, 2-ethoxytetrahydropyran, and 2,3-dihydropyran.

Compound	t °C	k $M^{-1}s^{-1}$	E kcal/mole	$\log A$	$\Delta S^{\ddagger}$ E.U.	Ref.
I	25	0.0259 ± 0.0005	22.3 ± 0.6	14.8 ± 0.2	$+7.1 \pm 1.0$	This work
	35	0.0847 ± 0.0015				»
	45	$0.277 \ \pm 0.007$				»
II	25	0.121 (calc.)			$+16.0 \pm 2.9$	1
III	25	0.274 (calc.)			-14.0 ± 2.8	2
	25	$0.276 \ \pm 0.001$				This work

RESULTS AND DISCUSSION

The measured rate coefficients of the hydrolysis of 2-ethoxy-2,3-dihydropyran (I) in water at different temperatures are shown in Table 1. The rate coefficients of 2-ethoxy-2,3-dihydropyran are about one fifth of those of the corresponding "pure" acetal 2-ethoxytetrahydropyran and less than one tenth of the rate coefficients of the "pure" vinyl ether 2,3-dihydropyran. This difference is understandable in the reaction *via* route A owing to the steric strain in the planar structure of the transition state of this reaction. The inductive polar effect of the 2-ethoxy group on the proton transfer reaction of 2-ethoxy-2,3-dihydropyran can be roughly estimated from kinetic data for acyclic vinyl ethers.[2,4] The logarithms of the rate coefficients of vinyl ethers $CH_2=CHOR$ with different alkyl groups R vary linearly as the Taft σ^* values.[5] The slope of the plot is 2-3 units. The structural difference between 2-ethoxy-2,3-dihydropyran and 2,3-dihydropyran is nearly the same as that between methyl vinyl ether ($R=CH_3$) and ethoxymethyl vinyl ether ($R=C_2H_5OCH_2$). The σ^* values of these substituents differ by about half a unit and thus the rate coefficient of the proton transfer reaction of 2-ethoxy-2,3-dihydropyran can be estimated from the rate coefficient of 2,3-dihydropyran using Taft's equation. A value of $0.01-0.02$ $M^{-1}s^{-1}$ is obtained for the vinyl ether hydrolysis of 2-ethoxy-2,3-dihydropyran at 25°C. Thus the magnitude of the measured rate coefficient of 2-ethoxy-2,3-dihydropyran does not exclude either the A-1 hydrolysis or the proton transfer reaction.

The activation entropy in the hydrolysis of 2-ethoxy-2,3-dihydropyran is $+7.1\pm0.1$ E.U. (Table 1). This value is intermediate between the values of the corresponding acetal hydrolysis of 2-methoxytetrahydropyran ($+16.0$ E.U.) and the vinyl ether hydrolysis of 2,3-dihydropyran (-14.0 E.U.). The value points to a concurrent acetal and vinyl ether reaction in the hydrolysis of 2-ethoxy-2,3-dihydropyran.

The kinetic data for the hydrolysis of 2-ethoxy-2,3-dihydropyran (I), 2-methoxytetrahydropyran (IV), and 2,3-dihydropyran (III) in D_2O and in D_2O-H_2O mixtures at 25°C are collected in Table 2. In these experiments 2-methoxytetrahydropyran was chosen as a model compound undergoing acetal hydrolysis because its deuterium solvent isotope effect has previously been measured.[1] The data in Table 2 show that the gross solvent isotope effect, $k_{D_3O^+}/k_{H_3O^+}$, for the hydrolysis of 2-ethoxy-2,3-dihydropyran has a value of 1.26, which is intermediate between the values for acetal hydrolysis (2.94 for 2-methoxytetrahydropyran) and vinyl ether hydrolysis (0.453 for 2,3-dihydropyran). To estimate the contributions of these mechanisms, kinetic measurements were carried out also in D_2O-H_2O mixtures.

Let us denote by k' the rate coefficient of the reaction of 2-ethoxy-2,3-dihydropyran by the A-1 mechanism and by k'' that of the reaction by the proton transfer mechanism. Thus the measured rate coefficient can be expressed in the form
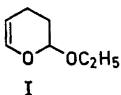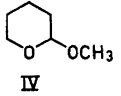
$$k_n = k_n{'} + k_n{''} \tag{2}$$

where the index n denotes the deuterium fraction of the solvent. When the rate coefficients in pure H_2O ($k_{0.0}$) and in pure D_2O ($k_{1.0}$) are set equal to the sum of the partial rate coefficients, we get the equations

$$k_{0.0} = k_{0.0}' + k_{0.0}''$$
$$k_{1.0} = k_{1.0}' + k_{1.0}'' \qquad (3)$$

We assume that the solvent isotope effect in the hydrolysis of 2-ethoxy-2,3-dihydropyran by the A-1 mechanism is of the same magnitude as that in the hydrolysis of 2-methoxytetrahydropyran and that the solvent isotope effect in the proton transfer mechanism is equal to that in the hydrolysis of 2,3-dihydropyran. This assumption should be valid fairly accurately because of the close structural similarity of the compounds in question. Thus

$$k_{1.0}'/k_{0.0}' = 2.94$$
$$k_{1.0}''/k_{0.0}'' = 0.453 \qquad (4)$$

Table 2. Rate coefficients of hydrolysis of 2-ethoxy-2,3-dihydropyran, 2-methoxytetra-hydropyran, and 2,3-dihydropyran in $D_2O - H_2O$ mixtures at 25°C.

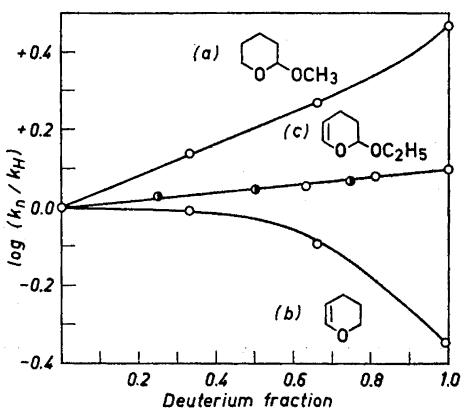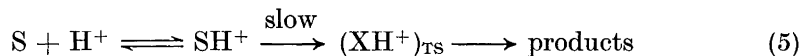| Compound	n_D	k (M⁻¹s⁻¹)	k_n/k_H	Ref.
I	0.000	0.0256 ± 0.0005	1.000	This work
	0.248	0.0274 ± 0.0003	1.070	»
	0.497	0.0284 ± 0.0007	1.109	»
	0.631	0.0290 ± 0.0013	1.133	»
	0.746	0.0299 ± 0.0005	1.168	»
	0.811	0.0308 ± 0.0004	1.203	»
	0.997	0.0322 ± 0.0004	1.258	»
IV	0.000	0.0941 ± 0.0023	1.000	1
	0.330	0.129 ± 0.002	1.371	This work
	0.661	0.175 ± 0.002	1.860	»
	0.997	0.277 ± 0.004	2.944	1
III	0.000	0.276 ± 0.0007	1.000	2 and this work
	0.330	0.271 ± 0.002	0.982	This work
	0.661	0.223 ± 0.001	0.808	»
	0.992	0.125 ± 0.0005	0.453	2

Fig. 1. Deuterium solvent isotope effects in $D_2O - H_2O$ mixtures for the hydrolysis of (*a*) 2-methoxytetrahydropyran, (*b*) 2,3-dihydropyran, and (*c*) 2-ethoxy-2,3-dihydropyran. The half filled circles in plot *c* describe both observed and calculated rate coefficients which are virtually equal in those cases.

On substituting the values $k_{0.0}=0.0256$ $M^{-1}s^{-1}$ and $k_{1.0}=0.0322$ $M^{-1}s^{-1}$ from Table 2 into eqns. (3) and (4) we get the rate coefficients $k_{0.0}'=0.0083$ $M^{-1}s^{-1}$ and $k_{0.0}''=0.017$ $M^{-1}s^{-1}$ for the acetal hydrolysis and vinyl ether hydrolysis, respectively, of 2-ethoxy-2,3-dihydropyran in water at 25°C. Using these partial rate coefficients, the overall rates of hydrolysis of 2-ethoxy-2,3-di-hydropyran in H_2O-D_2O mixtures at 25°C were calculated by substituting the experimental values of $k_n'/k_{0.0}'$ and $k_n''/k_{0.0}''$ from curves a and b in Fig. 1 into eqn. (2). Plot c in Fig. 1 shows that the calculated and measured rate coefficients for 2-ethoxy-2,3-dihydropyran are equal within the limits of experimental error and thus verify the calculated partial rate coefficients.
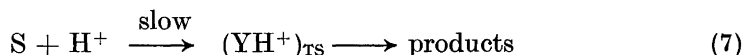
The relative contributions of routes A and B (scheme 1) in the A-1 hydrolysis of 2-ethoxy-2,3-dihydropyran must be determined by another method. In hydrolysis routes A and B lead to the same product. In alcoholysis (ethanolysis), however, route A leads to the original substrate but route B to the diacetal of glutaraldehyde. The product of the proton transfer reaction of 2-ethoxy-2,3-dihydropyran in ethanol is 2,6-diethoxytetrahydropyran. Thus we can measure the relative contributions of vinyl ether alcoholysis and the A-1 alcoholysis with a rate-determining ring fission by determining the ratios of the products of alcoholysis during the reaction. By gas chromatographic analysis it was found that the amount of the diacetal of glutaraldehyde was negligible (less than 5 %) compared to the amount of 2,6-diethoxytetrahydropyran. The analysis was carried out at the beginning of the alcoholysis reaction (less than 5 % of the total reaction) to avoid the effect of the slow alcoholysis of 2,6-diethoxytetrahydropyran to the diacetal of glutaraldehyde. Thus it can be concluded that the contribution of reaction (B) in the alcoholysis is negligible. If the solvent effect is similar in the proton transfer reaction and in the A-1 reaction of the same substrate, the same situation prevails also in the hydrolysis reaction. The rate coefficient of the A-1 reaction

$$S + H^+ \rightleftharpoons SH^+ \xrightarrow{slow} (XH^+)_{TS} \longrightarrow products \qquad (5)$$

is

$$k_{A1} = k_{A1}{}^\circ \frac{f_S f_{H^+}}{f_{XH^+}} \qquad (6)$$

where $k_{A1}{}^\circ$ is the standard rate coefficient and f's are the activity coefficients of the species in question referring to some chosen standard state. The rate coefficient of the vinyl ether hydrolysis

$$S + H^+ \xrightarrow{slow} (YH^+)_{TS} \longrightarrow products \qquad (7)$$

is

$$k_{PT} = \frac{f_S f_{H^+}}{f_{YH^+}} k_{PT}{}^\circ \qquad (8)$$

Thus the ratio of the rate coefficients of the A-1 reaction and the proton transfer reaction can be expressed by the equation

$$\frac{k_{A1}}{k_{PT}} = \frac{k_{A1}{}^\circ}{k_{PT}{}^\circ} \frac{f_{YH^+}}{f_{XH^+}} \qquad (9)$$

The first ratio on the right in this equation is constant and independent of the solvent. It can also be concluded that the ratio f_{YH^+}/f_{XH^+} is virtually independent of the solvent because both YH^+ and XH^+ are protonated forms of the same substrate. Thus we can conclude that the relative contributions of the A-1 reaction and the proton transfer reaction are nearly equal in the reactions of 2-ethoxy-2,3-dihydropyran in water and in ethanol and thus that the contribution of the reaction B is negligible also in the hydrolysis of 2-ethoxy-2,3-dihydropyran.

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