Thermodynamic Characterization of the Initial and Transition States for the Hydrolyses of Vinyl Ethers and Acetals

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The standard free energy changes have been measured for the following two processes in aqueous solution: 1) decomposition of acetaldehyde diethyl acetal into ethyl vinyl ether and ethanol; 2) hydrolytic cleavage of acetaldehyde diethyl acetal to form acetaldehyde and two molecules of ethanol. Gas-chromatographic and distribution techniques were used as the experimental methods. The change of the standard free energy was also calculated for the former reaction in the gas phase and the result compared with the approximate value estimated by the group increment method of Franklin, whereupon satisfactory agreement was found.

The kinetic implications of the thermodynamic values were discussed and the free energy profiles were constructed for vinyl ether and acetal hydrolysis. It was shown that a significant part of the reactivity of vinyl ethers in their hydrolysis reaction is to be ascribed to the comparatively high free energy level of their initial state in water solution. The relative free energy of the transient intermediate of the both reactions, *viz.* that of the mesomeric alkoxy-methyl cation, was also estimated by different methods, the results being consistent within 1 kcal per mole.

It was shown in the preceding paper [1] that the hydronium ion-catalyzed hydrolysis of vinyl ethers, *e.g.*,

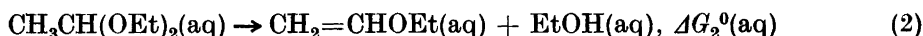$$EtOCH=CH_2 \xrightarrow{H_3O^+} EtOH + CH_3CHO$$
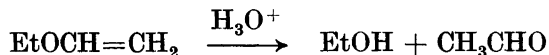
proceeds in aqueous solution through a rate-determining proton transfer from the hydronium ion to yield a transient oxonium-carbonium ion intermediate: $EtOC^+HCH_3 \longleftrightarrow EtO^+=CHCH_3$. It was also pointed out that, irrespective of the differences in the reaction mechanisms involved, the intermediate possesses the same structure as that generated in the *A*-1 hydrolysis of the corresponding acetal, *e.g.*,

$$(EtO)_2CHCH_3 \xrightleftharpoons{H_3O^+} SH^+ \xrightarrow{slow} EtO^+=CHCH_3 + EtOH$$
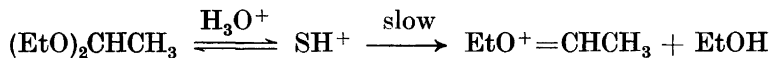
As an additional feature it may be noted that both reactions take place at comparable rates. In fact, in the case given as an example, the rate coefficients at 25°C happen to be almost the same, *viz.* 1.87 M^{-1} s^{-1} for ethyl vinyl ether [1] and 1.26 M^{-1} s^{-1} for acetaldehyde diethyl acetal,[2] respectively. It is to be emphasized, however, that the rate coefficients measure merely the free energy differences between the initial and transition states. Therefore, in a detailed thermodynamic discussion of structural or other rate factors the changes in the initial states should be accounted for as well as those in the respective transition states.

In order to obtain direct thermodynamic information of the stabilities of the initial and transition states relative to those of the final states, on the basis of which the reaction profiles could be constructed for vinyl ether and acetal hydrolysis, we have measured the standard free energy changes for the processes:

$$CH_3CH(OEt)_2(aq) \rightarrow CH_3CHO(aq) + 2\ EtOH(aq),\ \Delta G_1^0(aq) \tag{1}$$

$$CH_3CH(OEt)_2(aq) \rightarrow CH_2=CHOEt(aq) + EtOH(aq),\ \Delta G_2^0(aq) \tag{2}$$

The determination of the former free energy change could be made in a straightforward manner by analyzing the compositions of the equilibrium mixtures after hydrolysis of dilute acetal solutions in water. The latter could not be measured in the same way because of the very low equilibrium concentrations of vinyl ether under these circumstances. This free energy change was therefore determined by measuring the corresponding free energy change for a liquid phase reaction, from which, making use of the separately determined free energies of transfer of the reacting species into aqueous solution, ΔG_2^0 (aq) could be readily calculated.

EXPERIMENTAL

Materials. The ethyl vinyl ether that was used in the equilibrium measurements was freshly purified. The methods of purification and analysis were those of the preceding study.[1] Acetaldehyde diethyl acetal was synthesized from paraldehyde and ethyl alcohol by the standard textbook method and was subsequently further purified by careful fractional distillations over metallic sodium. Gas-chromatographic analyses that were made on the freshly purified acetal showed that the total amount of impurities (ethyl alcohol, acetaldehyde and ethyl vinyl ether) was less than 0.04 %. These impurities did not have any influence on the results of the equilibrium measurements, which involved the determination of the final equilibrium concentrations between the same species. The following physical constants were recorded for the purified acetal: b.p. 103.0°C/760 torr, n_D^{20} 1.3810, d_4^{20} 0.8261.

Equilibrium of acetal hydrolysis in dilute aqueous solution. The equilibrium of the reaction (1) was measured by hydrolyzing different initial concentrations of acetal in water with 0.05 M hydrochloric acid as the catalyst, and by analyzing the concentrations of acetaldehyde and acetal at the equilibrium. The determination of acetaldehyde took place by the iodometric method described earlier.[3] The very minute quantities of diethyl acetal present at the equilibria could be analyzed fairly accurately by gas chromatography using standard acetal solutions of known concentration. The measurements were made on a Shandon Universal Gas Chromatograph with an attached DDP column. In the experiments the initial acetal concentrations were below 0.3 M. Consistent equilibrium constants could be derived from measurements with different initial concentrations indicating that in the low concentration range employed the activity coefficients of the

species involved were kept constant. Because the reaction rates became extremely slow in the immediate vicinity of the equilibrium state, relatively long hydrolysis times had to be used before the final acetal concentration could be accurately determined. Under the conditions specified, no change in this concentration could be detected after a period of 3 to 4 days.

Equilibrium between acetal and vinyl ether in the liquid phase. The most practical way to determine the equilibrium constant for the reaction (2) was to measure first the corresponding equilibrium (2′) in the liquid phase with acetal itself as the solvent, and then to determine separately the free energies of transfer of the species involved from these conditions into dilute solution in water. The

$$CH_3CH(OEt)_2 \text{ (l)} \rightleftharpoons CH_2=CHOEt \text{ (acetal)} + EtOH \text{ (acetal)} \tag{2′}$$
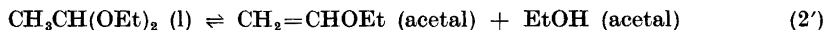
equilibrium (2′) was measured in the following way. Samples of acetal were sealed with p-toluenesulfonic acid as the catalyst (0.05 M) into glass bulbs, which were kept in a thermostat until the attainment of the equilibrium, after which the contents were analyzed for the ethanol and ethyl vinyl ether present by gas chromatography using standard solutions of known ethanol or ethyl vinyl ether content. In a number of additional measurements, ethanol was also primarily added to the acetal to give an initial concentration of 0.6 to 1.7 M. The equilibrium constants derived from these different measurements agreed with each other showing that the activity coefficients of the reactants did not change under the conditions of these measurements. Four days was found to be an adequate equilibration time within the accuracy of the analysis.

Distribution equilibria. The solubilities of liquid diethyl acetal and ethyl vinyl ether in water, needed for the thermodynamic calculations, were measured by analyzing the aqueous phase for the compound in question after saturation. This analysis was made by hydrolyzing samples withdrawn from the aqueous phase in approximately 0.05 M hydrochloric acid and by determining the aldehyde liberated.[3] In these distribution experiments and in those described below, the aqueous phase was made slightly alkaline by small additions of sodium hydroxide (about 0.001 M) in order to prevent any hydrolytic decomposition of the vinyl ether or acetal during equilibration between the two phases.

When determining the equilibrium distribution of ethanol between acetal and water equal volumes of the latter were used. Known amount of ethanol was added and, after the equilibrium was established, the organic phase was analyzed for ethanol by the method described above in connection with the equilibrium of the reaction (2′). From the result of this analysis, and from the amount of ethanol initially taken, the concentration of ethanol in the aqueous phase was then calculated allowing a small correction which was due to the solubility of acetal in water. Several parallel determinations were made. The concentration of ethanol in the aqueous phase varied from 0.1 to 0.6 M, in which concentration range constant values for the distribution ratio were obtained.

The procedure used to measure the distribution ratio of ethyl vinyl ether between acetal and water was the same excepting that, owing to the relatively high distribution coefficient in favor of acetal, the most accurate results could be obtained if the aqueous phase was analyzed for ethyl vinyl ether. This took place by a titrimetric determination of the aldehyde formed from the acid-catalyzed hydrolysis of ethyl vinyl ether. Although the aqueous solutions to be analyzed contained dissolved acetal, which would be also hydrolyzed to give acetaldehyde under acidic conditions, the determination of ethyl vinyl ether could be easily done when use was made of the fact that this compound exhibits general acid catalysis, whereas acetals do not. Thus, in a slightly alkaline buffer solution ethyl vinyl ether is hydrolyzed to acetaldehyde by the undissociated acid present, under which conditions diethyl acetal remains intact. In the actual determinations the hydrolysis was made in a phosphate buffer (Na_2HPO_4 0.5 M, KH_2PO_4 0.125 M) the pH of which was approximately 7.3. From the data of the preceding paper[1] it was estimated that the half-life for the $H_2PO_4^-$-catalyzed hydrolysis of ethyl vinyl ether in this buffer solution was approximately 5 h at 25°C. Accordingly, conforming values were obtained for the distribution coefficient of ethyl vinyl ether between acetal and water when the aldehyde analysis was made after a standing period of about 50 h in the phosphate buffer.

RESULTS AND DISCUSSION

Thermodynamic calculations. The results of the different equilibrium determinations are collected in Table 1 along with the respective standard errors of the measurements. The table also contains the values of the standard free energy changes for the reactions and transfer processes involved, as calculated for the standard states given in each connection.

The value of the standard free energy change for the reaction (1), -3.47 kcal, shows that in dilute solution in water acetal is almost completely hydrolyzed. If the initial concentration of acetal is smaller than 0.1 M, as is the case in most kinetic experiments, it can be calculated that less than 0.01 % of the acetal is remaining unhydrolyzed at the equilibrium. Although the acetal-aldehyde equilibrium has been investigated in a number of previous studies (see, *e.g.*, Refs. 4 and 5), the experimental conditions used in these investigations differ significantly from those prevailing in dilute solutions in water. A comparison of our result with those obtained earlier is therefore meaningless without an additional determination of the free energies of transfer of the reacting species from aqueous solution to the conditions in question.

The standard free energy change for the reaction (2), $\Delta G_2^0(aq)$, can be easily calculated from the values of Table 1. It is seen that

$$\Delta G_2^0(aq) = \Delta G_{2'}^0 + \Sigma \Delta \mu \text{ (transfer)}$$

in which $\Delta G_{2'}^0$ is the standard free energy change for the reaction (2'), and the summation on the right is computed as follows:

$$\Sigma \Delta\mu \text{ (transfer)} = (\mu_{v.e.}(aq) - \mu_{v.e.} \text{ (acetal)})$$
$$+ (\mu_{EtOH}(aq) - \mu_{EtOH}(acetal)) - (\mu_{acetal}(aq) - \mu_{acetal}(l))$$

Here the subscript "v.e." refers to vinyl ether. In this way the value $+ 3.27 \pm 0.045$ kcal is obtained for $\Delta G_2^0(aq)$.

From the standard free energy value determined above for the decomposition of acetal into vinyl ether and ethanol in aqueous solution some additional thermodynamic values may be derived. Consider the reaction (2'') in the liquid state and define the

$$CH_3CH(OEt)_2(l) \rightarrow CH_2=CHOEt \text{ (l)} + EtOH \text{ (l)}, \Delta G_{2''}^0 \text{ (l)} \qquad (2'')$$
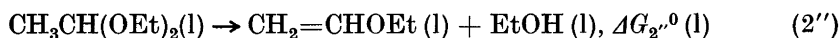
pure liquids as the respective standard states. To calculate the free energy change for this process from $\Delta G_2^0(aq)$ the changes in the chemical potentials of the species involved are needed, when transferred from dilute solution in water to the pure liquids. The values for acetal and vinyl ether can be taken from Table 1, whereas that for ethanol is easily calculated from the known value of the vapor pressure of pure ethanol and from the partial vapor pressures of ethanol over dilute aqueous solutions.[6] In this way, a value of $+ 1.42 \pm 0.02$ kcal is obtained for the transfer of one mole of ethanol from dilute solution in water to its pure liquid state at 25°C. Using this value and those of Table 1 it is found that $\Delta G_{2''}^0$ (l) $= + 3.86 \pm 0.05$ kcal/mole.

The standard free energy change for the gas phase reaction

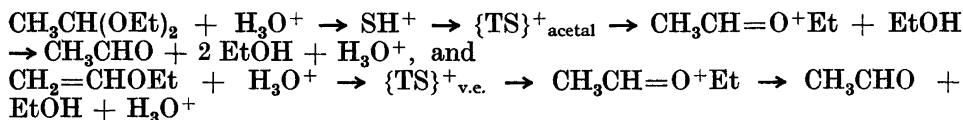$$CH_3CH(OEt)_2(g) \rightarrow CH_2=CHOEt(g) + EtOH(g), \Delta G_2^0(g)$$

Table 1. Experimental values for the reaction and distribution equilibria with the corresponding standard free energy changes in the system $CH_3CH(OEt)_2 - CH_2{=}CHOEt - EtOH - H_2O$ at 25°C. The choice of the standard states for each particular case is denoted as follows: A, hypothetical ideal dilute solution containing one mole of solute per liter of solution. B, pure liquid (mole fraction = 1).

Equilibrium	Standard states chosen			Equilibrium constant	$\Delta G°$ or $\Delta\mu$ kcal/mole
	Acetal	Vinyl ether	Ethanol		
$CH_3CH(OEt)_2(aq) = CH_3CHO(aq) + 2EtOH(aq)$	A	A	A	$349 \pm 15\ mole^2\,l^{-2}$	-3.47 ± 0.02
$CH_3CH(OEt)_2(l) = CH_2{=}CHOEt(acetal) + EtOH(acetal)$	B	A	A	$0.0115 \pm 0.007\ mole^3l^{-2}$	$+2.65 \pm 0.03$
$CH_2{=}CHOEt(l) = CH_2{=}CHOEt(aq)$	—	$B(l),\ A(aq)$	—	$0.0904 \pm 0.007\ mole\ l^{-1}$	$+1.42 \pm 0.01$
$CH_3CH(OEt)_2(l) = CH_3CH(OEt)_2(aq)$	$B(l),\ A(aq)$	—	—	$0.368 \pm 0.002\ mole\ l^{-1}$	$+0.592 \pm 0.003$
$CH_2{=}CHOEt(aq) = CH_2{=}CHOEt(acetal)$	—	$A(aq),\ A(acetal)$	—	16.9 ± 0.8	-1.67 ± 0.03
$EtOH(aq) = EtOH(acetal)$	—	—	$A(aq),\ A(acetal)$	0.46 ± 0.01	$+0.46 \pm 0.01$

in which unit fugasities (in atmospheric units) are chosen as the standard states, can be calculated from $\Delta G_{2''}{}^0$ (1) and from the vapor pressures of the compounds in question at 25°C. The vapor pressures of acetal and vinyl ether can be estimated from their normal boiling points [1,2] by the Trouton rule; the error involved in this estimation can be assumed to be largely cancelled out when calculating the free energy difference in question, because the compounds are on the different sides of the equation. For the vapor pressure of ethanol its wellknown value can be used.[6] The value obtained for $\Delta G_2{}^0(g)$, $+ 4.0 \pm 0.1$ kcal, is practically the same as that derived above for the reaction in the liquid phase. If the standard free energies of formation of the compounds involved are calculated by the group increment method of Franklin,[7] a value of $+ 2.0$ kcal can be estimated for $\Delta G_2{}^0(g)$. Because the limits of error of this approximate method can be considered to be several kilocalories in the case of nonhydrocarbons, the agreement between the experimental and estimated values is satisfactory.

Application to kinetics. The hydronium ion-catalyzed decomposition reactions of acetaldehyde diethyl acetal and ethyl vinyl ether in water can be represented by the following schemes:

$CH_3CH(OEt)_2 + H_3O^+ \rightarrow SH^+ \rightarrow \{TS\}^+_{acetal} \rightarrow CH_3CH=O^+Et + EtOH \rightarrow CH_3CHO + 2\ EtOH + H_3O^+$, and
$CH_2=CHOEt + H_3O^+ \rightarrow \{TS\}^+_{v.e.} \rightarrow CH_3CH=O^+Et \rightarrow CH_3CHO + EtOH + H_3O^+$

in which the respective transition states have been denoted by "TS". If we add one mole of ethanol to the initial, final and each intermediate state of the latter reaction, this does not change the free energy relationships of this reaction since it adds the same free energy to each phase. Table 2 gives the relative free energy values obtained in this way for the initial states of vinyl ether and acetal hydrolysis from the standard free energy changes given in the preceding section. The final state has been taken to represent the zero level of free energy on the relative scale of Table 2. The relative free energy values for the respective transition states, which are also shown in the table, have been calculated from the known values of the hydrolysis rate coefficients.[1,2] These give for the free energies of activation 17.32 kcal/mole for acetaldehyde diethyl acetal and 17.08 kcal/mole for ethyl vinyl ether, respectively, with an estimated accuracy of 0.006 kcal/mole.

Table 2. Relative values of the standard free energies for the hydronium ion-catalyzed hydrolysis of acetaldehyde diethyl acetal and ethyl vinyl ether in water solution at 25°C.

State	$G^0(aq)$, kcal/mole
Acetal hydrolysis (initial state)	$+ 3.47 \pm 0.02$
» » (transition state)	$+ 20.79 \pm 0.03$
Vinyl ether hydrolysis (initial state)	$+ 6.74 \pm 0.05$
» » » (transition state)	$+ 23.82 \pm 0.05$
Intermediate state	$+ 16.7 \pm 1$
Final state	0

At the present, there are no direct means of determining the thermo-dynamic stability of the transient oxonium-carbonium intermediate involved in the both reactions. However, some rough estimates can be made as described below.

It was noted in the preceding study [1] that the hydrolysis of vinyl ethers was less susceptible to structural variations than the hydrolysis of acetals, the plot of the respective log k values having a slope of 0.54. If these structural rate effects can be derived mainly from changes in the various stabilizing factors influencing on the transient intermediates, it is reasonable to assume that the susceptibility is the less the higher is the free energy difference between the transition state and the intermediate. As a first approximation, the relative susceptibilities as measured by changes in the values of log k should be inversely proportional to the respective barrier heights between the intermediates and the transition states. In this way it can be estimated that the relative barrier heights from the intermediate to the transition states of the hydrolysis of vinyl ethers and acetals are approximately in the ratio 1:0.54, which leads to a value of $+$ 17.2 kcal for the relative free energy of the intermediate state on the scale of Table 2.

According to Deno [8] the stability of t-butyl cation relative to that of 2-methylpropene is -15.5, as expressed in pK units, and the corresponding values for other alkyl cations should vary from this value in the same way as log (k/k_0), in which k_0 denotes the hydrolysis rate coefficient of t-butyl chloride and k that of the alkyl chloride that generates the carbonium ion in question. Of course, it is assumed that the hydrolysis takes place by the S_N-1 mechanism. The value of k_0 in water at 25°C is about 0.035 s^{-1}, as obtained by a short extrapolation from its value in a solvent containing 5 % of acetone.[9] To estimate the stability of the intermediate of vinyl ether hydrolysis relative to that of vinyl ether, a value is needed for the hydrolysis rate coefficient of the α-chloroether that generates the same intermediate, $viz.$ $CH_3CH(OEt)Cl$. In a recent article [10] one of the authors estimated the value 3000 s^{-1} for the hydrolysis rate coefficient of methyl chloromethyl ether in water at 25°C. Using the same method of calculation it can be shown that the hydrolysis rate coefficient of α-chloroethyl ethyl ether cannot differ grossly from a value of approximately 10^7 s^{-1}. In this way it can be calculated that the intermediate in question is less stable than ethyl vinyl ether by 7 pK units, which corresponds to a free energy difference of 9.5 kcal/mole. This, when put on the relative scale of Table 2, gives for the free energy value of the intermediate state $+$ 16.2 kcal/mole, which substantially agrees with that estimated above by another line of argumentation. In this connection it must be also emphasized that, although the intermediates of the two reactions have structures which are formally similar, their thermodynamic stabilities are not necessarily exactly the same because they are generated in different ways and, owing to their short lifetimes, the reorientation of their environments may lag behind their further reactions.

On the basis of the directly measured thermodynamic and kinetic values and that estimated above for the intermediate state, relative free energy profiles can be drawn for the hydrolytic decompositions of vinyl ether and acetal. Such profiles are shown in Fig. 1. Although the part of the profile
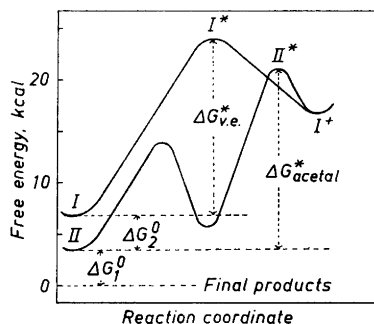
Fig. 1. Free energy profiles for the hydro-lytic decomposition of vinyl ether and acetal in water solution at 25°C. I and II are the initial states of vinyl ether and acetal, and I* and II* their respective transition states; I$^+$ is the reaction inter-mediate.

that relates to the pre-equilibrium protonation of acetal is not pertinent in this connection, it has been also drawn in the figure using approximate values. Because the pK values are around -4 for the conjugate acids of aliphatic ethers,[11] the free energy level of the protonated acetal will be higher than that of acetal by approximately 5.5 kcal/mole. In the figure, a value of 10^5 M^{-1} s^{-1} has been used as the rate coefficient for the proton transfer from the hydronium ion to acetal, because similar proton transfers take place at roughly this rate.[12]

Several points of interest become evident from Fig. 1. First, it is seen that vinyl ether when dissolved in water is thermodynamically in a much more favorable situation for the hydrolysis reaction to occur than acetal, because its initial energy level is higher by 3.3 kcal/mole. Thus a significant part or the reactivity of vinyl ethers in their hydrolysis can be ascribed to the rela-tively low stability of the initial state. Second, the free energy of the transition state of acetal hydrolysis differs from that of the transient oxonium-carbonium ion only by about 4 kcal. This indicates that the structure of the transition state of acetal hydrolysis must be very close to that of the transient inter-mediate. The same conclusion was drawn from studies on a related reaction, the hydrolysis of acylals.[13] Third, the smallness of this free energy difference also shows that the energy well of the intermediate is not deep, because of which the intermediate must further decompose at a rate with a free energy of activation less than this difference. This means that the rate coefficient for the decomposition of $CH_3CH{=}O^+Et$ into the reaction products is at least of the magnitude of about 10^{10} s^{-1}.

Considering the reverse reactions, the formation of acetal or vinyl ether from ethanol and acetaldehyde, it can be noted that both the kinetic and thermodynamic factors favor the formation of acetal in preference to vinyl ether. Of course, it is recognized that the conditions in synthesis largely differ from those of Fig. 1 as the acetal or vinyl ether formed will separate into another liquid phase. However, the same relative thermodynamic stabilities still hold as was shown in the first section of the present discussion. It is there-fore easily understood that practically no vinyl ether is obtained as the side product of acetal synthesis.

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