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KINETICS OF HYDROLYSIS REACTIONS
IN WATER-GLYCEROL MIXTURES

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AUGUST 1968

By
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ABSTRACT

The second-order rate constants for the acid-catalyzed hydrolysis of 2,2-dimethyl-1,3-dioxolane (DMD), 2-isopropyl-2-methyl-1,3-dioxolane (IMD), and 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane (DHD) in aqueous glycerol mixtures ranging from 0-40 wt. % glycerol have been determined spectrophotometrically. Values of $w_g^-$, defined as the slopes of plots of $\log k_{obs}/H^+$ vs. $\log a_{H_2O}^-$, have been determined for IMD at 20°C, 25°C, 30°C, 35°C, 40°C, and 45°C. Values of $w_g^-$ for IMD and DHD have been determined at 25°C and 45°C. The $w_g^-$ values at 25°C for DMD, IMD, and DHD are -3.54, -1.81, and -2.78 respectively.

These values seem to be a rough measure of the hydration change between reactants and the transition state. $w_g^-$ Values are dependent upon the structure of the compound and on temperature. Methyl groups at the 2 position promote hydrophobic hydration in the ground state. This hydration is disrupted by the positive charge of the transition state. A group such as isopropyl insulates this hydration from the effect of the positive charge.

The temperature dependence of these values, $\delta_{T-w_g^-}(^\circ C^{-1})$, for DMD, IMD, and DHD are 0.124, 0.071, and 0.028 respectively. These values give an indication of how much hydrophobic hydration is involved with each compound.

The thermodynamic parameters of activation for these reactions in water and the various water-glycerol mixtures have been evaluated. The enthalpies and entropies of activation for DMD and IMD decrease with increasing glycerol content. The $\Delta H^\#$ and $\Delta S^\#$ for DHD are.
approximately independent of glycerol content. The $\Delta H^*$ for DMD ranges from 20.7 kcal/m in water to 17.6 kcal/m in 40% glycerol. The $\Delta H^*$ for IMD ranges from 20.0 kcal/m in water to 17.6 kcal/m in 40% glycerol. The $\Delta H^*$ for DHD is 19.3 kcal/m in water. The $\Delta S^*$ for DMD ranges from +7.1 e.u. in water to -2.4 e.u. in 40% glycerol. The $\Delta S^*$ for IMD ranges from +4.8 e.u. in water to -2.5 e.u. in 40% glycerol. The $\Delta S^*$ for DHD is -0.1 e.u. in water. The entropy of activation appears to be dependent upon the number of methyl groups that promote hydrophobic hydration in the ground state. When this hydration is disrupted in the transition state it is reflected in a more positive $\Delta S^*$.

The $\Delta H^*$ and $\Delta S^*$ for the hydrolysis of DHD in 50% (v/v) dioxane have also been evaluated. The $\Delta H^*$ is 18.2 kcal/m and the $\Delta S^*$ is -6.1 e.u.

The standard partial molar quantities for the transfer of DMD from water to water-glycerol solutions have been evaluated. The $\Delta \overline{H}^0$ and $\Delta \overline{S}^0$ generally increase with increasing glycerol content. This indicates that the lower energy requirements for the reaction in water-glycerol mixtures is primarily due to a ground state effect. The values of $\Delta \overline{H}^0$ and $\Delta \overline{S}^0$ for the transfer of DMD from water to 40% glycerol are 6.7 kcal/m and +21.1 e.u. respectively.

The results are discussed in terms of solvent-solute interactions and the differences in ground state and transition state hydration.
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I. INTRODUCTION

A. A-1 and A-2 Mechanisms

Hydrolysis reactions can be classified according to mechanism. Ingold\textsuperscript{1,2} classified acid catalyzed hydrolysis reactions under two main headings. The A-1 designation applies to a reaction which has a unimolecular rate determining step.

\[ S + H \xrightleftharpoons{k} \text{SH}^+ \]  
\[ \text{SH}^+ \xrightarrow{k'_1} \text{X}^+ \]  
\[ \text{X}^+ + H_2O \rightarrow \text{products} + H^+ \]

Equation 1 is an acid-base equilibrium, Equation 2 is rate determining and Equation 3 is a fast step.

The other general hydrolysis mechanism is the A-2 mechanism.

\[ S + H \xrightleftharpoons{k} \text{SH}^+ \]  
\[ \text{SH}^+ + H_2O \xrightarrow{k''} \text{products} + H^+ \]

Equation 4 is an equilibrium protonation, and Equation 5 is the slow step.

It is clear that the basis for the different classifications is the molecularity of the rate determining step.

B. Criteria for Classification of Reactions

1. Hammett-Zucker Hypothesis

Until recently the most widely used criteria for the classification of hydrolysis reactions was the Hammett-Zucker hypothesis.\textsuperscript{3} This
hypothesis makes use of the $H_0$ acid indicator scale which was originally defined by Hammett and Deyrup. The $H_0$ scale is based on the protonation of weak bases.

$$B + H^+ \rightleftharpoons BH^+$$

(6)

The $H_0$ scale is defined by Equation 7:

$$H_0 = -\log(C_{BH^+}/C_B) + \log K_{BH^+}$$

(7)

where $C_{BH^+}$ is the concentration of the protonated base, $C_B$ is the concentration of the base, and $K_{BH^+}$ is the ionization constant for the conjugate acid, $BH^+$. 

Equation 7 can be written:

$$H_0 = -\log h_0 = -\log a_{H^+} f_B / f_{BH^+}$$

(8)

where $a_{H^+}$ is the activity of the hydrogen ion, $f_B$ and $f_{BH^+}$ are the molar activity coefficients.

The first order rate constant, $k_1$, for an A-1 type reaction (Eq. 1-3) is given by Equation 9:

$$k_1 = \frac{k'}{K_{SH}} \frac{a_{H^+} f_S}{f_4}$$

(9)

where $k'$ is the rate coefficient for the rate determining step, $K_{SH^+}$ is the ionization constant for the dissociation of $SH^+$, and $f_S$ and $f_4$ are the activity coefficients for the substrate and the transition state respectively. Substituting for $a_{H^+}$ from Equation 8:

$$k_1 = \frac{k'}{K_{SH^+}} h_0 \frac{f_{BH^+} f_S}{f_B f_4}$$

(10)
Taking logarithms:

$$\log k_1 = -H_0 + \log \frac{f_{H^+}}{f_B} + \log f_S + \log \frac{f_{H^+aH_2O}}{f_\#} + \text{constant}$$  \hspace{1cm} (11)

A plot of $\log k_1$ versus $-H_0$ will be linear if the ratio of the activity coefficients remains constant with changing media.

The first order rate constant, $k_1$, for an A-2 type reaction (Eq. 4-5) is given by Equation 12.

$$k_1 = \frac{k''}{K_{SH^+}} C_{H^+} \frac{f_S f_{H^+aH_2O}}{f_\#}$$  \hspace{1cm} (12)

Taking logarithms:

$$\log k_1 = \log C_{H^+} + \log \frac{f_S f_{H^+aH_2O}}{f_\#} + \text{constant}$$  \hspace{1cm} (13)

A plot of $\log k_1$ versus log $C_{H^+}$ should be linear if the term $f_S f_{H^+aH_2O} / f_\#$ remains constant with changing media.

The Hamnett-Zucker hypothesis states that the reaction proceeds by the A-1 mechanism if plots of $\log k_1$ versus $-H_0$ are linear. If plots of $\log k_1$ versus log $C_{H^+}$ are linear the Hamnett-Zucker hypothesis states that the reaction has an A-2 mechanism.

2. w - Values

In 1961, J. F. Bumnett suggested a new empirical criterion of mechanism. He found that plots of $\log k_1 - H_0$ versus log $a_{H_2O}$ were approximately linear. The slopes were designated $w$, and Bumnett proposed that these $w$-values be used as an empirical criterion of
mechanism to replace the Hammett Zucker hypothesis. These \( w \)-values are associated with the involvement of water in the rate determining step. Bunnett proposed that when \( w \) was between 0 and -2.5 that water was not involved in the rate determining step and the reaction should be classified A-1. If the \( w \)-value was between +1.2 and +3.3 then water was acting as a nucleophile and the reaction should be classified as A-2. Both the Hamnett-Zucker hypothesis and Bunnett's \( w \)-value approach rely on the assumption that the activity coefficient term in Equation 11 will remain constant with changing media. This assumption can not be expected to be valid for some of the solutions to which it is applied. Both the Hamnett-Zucker hypothesis and Bunnett's approach require high acid concentration (e.g. 10.5 M \( \text{H}_2\text{SO}_4 \)). It is under these conditions of high acidity and high ionic strength that the solutions are not ideal and the activity coefficient ratios can not be expected to cancel.7

3. Entropy of Activation

Taft et al.8 noted that the entropies of activation for the hydration of olefins are small negative numbers (ca. -3 e.u.) while the entropies of activation for the dehydration of alcohols are large positive numbers (ca. +20 e.u.). It was pointed out that for the hydration of olefins the water molecule is not involved in the transition state and therefore does not lose translational or rotational motion. Therefore one expects and observes no large change in entropy.
The dehydration of alcohols involves the release of a water molecule and the gain of translational motion, therefore a large positive entropy of activation is to be expected.

Long et al.⁹ made the general statement that the entropy of activation should be positive for reactions that have an A-1 mechanism and that the entropy of activation for reactions that have an A-2 mechanism should be negative and fairly large.

C. Cosolvent as an Alternative Approach

In order to have a fuller understanding of the mechanism of hydrolysis reactions, it is important to consider the structure of the solvent and the changes in this structure which accompany the transformation from ground state to transition state. It would be desirable to have a detailed model of the ground state molecule with its solvation shell along with a detailed model of the activated complex and its solvation shell. It would then be possible to make a direct comparison between ground state and transition state and the role of the solvent could be determined. The transition state, with a lifetime on the order of a molecular vibration (ca. 10⁻¹⁴ sec.), precludes any direct measurement on it.

Information concerning the transition state can be obtained indirectly by determining the thermodynamic parameters of activation which are measures of the energy of the transition state minus the energy of the ground state. Since thermodynamic measurements can be made on the ground state molecule, the contribution from the transition state and the ground state can be separated.
Alter ing the structure of the solvent should reflect itself in both the thermodynamic parameters of activation and in the ground state measurements in proportion to the effect that a change in solvent has on each state. Addition of a cosolvent is a method of altering water structure.

As indicated by Bunnett, the hydration parameter, \( w \), should also give information concerning the role of water in hydrolysis reactions. Bunnett has suggested that the dependence of the rate of reaction on water activity is a measure of the degree of participation of water not only as a nucleophile, but also as a specific solvation agent.

Dividing Equation 12 by the hydrogen ion concentration and taking logarithms gives Equation 14.

\[
\log \left( \frac{k_{\text{obs}}}{C_{H^+}} \right) = w \log a_{H_2O} + \log \left( \frac{f_{S-H^+}}{f_{S-H}} \right) + C
\]  

(14)

This treatment will be somewhat analogous to that of Bunnett. If \( \log \left( \frac{k_{\text{obs}}}{C_{H^+}} \right) \) is plotted versus \( \log a_{H_2O} \) and the activity coefficient term does not change with changing media, then the slope of the line will be \( w \), the kinetic order of water.

The use of glycerol as a cosolvent provides a convenient method for varying the activity of water. Furthermore water-glycerol solutions allow for the use of low acid concentrations and thus low ionic strength. In relatively ideal solutions of low ionic strength, the assumption that the activity coefficient term does not vary with changing media is a reasonable one.
The choice of glycerol as a cosolvent is dictated by the fact that it forms relatively ideal solutions with water\(^{10}\) and activity data are available for water-glycerol mixtures.\(^{11}\)

The dioxolane system has been chosen as the substrate for kinetic investigation because the mechanism of ketal hydrolysis is well established and it is known to proceed via the A-1 reaction path.\(^{12-14}\) There is also a good deal of rate data for dioxolanes in the literature.\(^{15,16}\)

The mechanism for the acid catalyzed hydrolysis of a ketal is summarized for the specific case of 2,2-dimethyl-1,3-dioxolane in Equations 15-17.

\[
\begin{align*}
\text{CH}_2\text{O} & \text{CH}_3 + \text{H}_3\text{O}^+ \rightleftharpoons \text{CH}_2\text{O} + \text{CH}_3 \text{C} \text{H}_3 + \text{H}_2\text{O} \\
\text{CH}_2\text{O} & \text{CH}_3 + \text{H}_3\text{O}^+ \rightarrow \text{CH}_2\text{O} = \text{C} \text{CH}_3 \text{H} + \text{CH}_3 \text{COCH}_3 + \text{H}_2\text{O} \\
\text{CH}_2\text{O} & \text{CH}_3 + 2\text{H}_2\text{O} \rightarrow \text{CH}_2\text{OH} + \text{CH}_2\text{OH} + \text{CH}_3\text{COCH}_3 + \text{H}_3\text{O}^+ 
\end{align*}
\]
II. EXPERIMENTAL

A. Materials

1. The 2,2-dimethyl-1,3-dioxolane was prepared by the following modification of Leggetter and Brown's procedure.\textsuperscript{17} Acetone (135 ml.) was added to a stirred mixture of ethylene glycol (140 ml.), anhydrous magnesium sulfate (60 g.), and p-toluenesulfonic acid (1 g.). The mixture was kept in an ice bath during addition and then placed in a refrigerator for 16 hours. The mixture was filtered free of the magnesium sulfate and the crude distillate was then distilled over sodium to give 10 ml. (5\%) of material boiling at 91-92°C. Lit. B.P. 92-93°C.\textsuperscript{18} Other workers\textsuperscript{18} using a different method of synthesis also obtained low yields for this compound. Some of the 2,2-dimethyl-1,3-dioxolane was obtained from Aldrich Chemical Company. Some of the material obtained from Aldrich was found to contain an acid impurity. It was necessary to purify this material by distilling from Na/NaOH. Some of the previously determined rate constants had to be re-determined to insure that the acid impurity did not contribute to the rate of reaction.

2. The 2-isopropyl-2-methyl-1,3-dioxolane was prepared by the method described by Fife and Hagopian.\textsuperscript{19} B.P. 131-134°C. Lit. B.P. 128-132°C.\textsuperscript{18} Anal. Calcd. for C\textsubscript{7}H\textsubscript{14}O\textsubscript{2}: C, 64.58; H, 10.84. Found: C, 64.37; H, 10.80.

The nmr spectrum was taken neat with internal TMS and gave a doublet centered at $\delta$ 0.90 (CH\textsubscript{3}-CH-CH\textsubscript{3}), a singlet at $\delta$ 1.18 (CH\textsubscript{2}-C),...
a multiplet centered at δ 1.80 (CH₃-CH₂-), and a singlet at δ 3.68 (CH₂-O-). The infrared spectrum was taken neat and gave bands at 1179 cm⁻¹, 1149 cm⁻¹, and 1064 cm⁻¹ which are characteristic for dioxolanes.²⁰,²¹

The nuclear magnetic resonance spectra were recorded on a Varian Associates Model A-60 Analytical NMR spectrometer. The infrared spectra were recorded using a Beckman IR-5 spectrophotometer.

3. The 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane was obtained from Aldrich Chemical Company. The purity was determined by nmr. There were no noticeable impurities and it was used without further purification.

4. Reagent grade glycerol was distilled under aspirator pressure. This was essential since undistilled reagent grade glycerol retarded the rates of hydrolysis. The purity of the distilled glycerol was determined by measuring the refractive index at 25°C with a Bausch and Lomb Precision Refractometer.²² The water content was always less than 5% and was taken into account in the preparation of the aqueous glycerol mixtures.

5. The dioxane was purified using a modified version of Fieser's method.²³ The dioxane was passed through a column of acid alumina and then refluxed with sodium for 24 hours. The dioxane was then distilled from sodium.
B. Kinetic Measurements

The rates of hydrolysis of 2,2-dimethyl-1,3-dioxolane and 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane were followed by determining the concentration of acetone formed by using ultraviolet spectroscopy. The increase in acetone concentration was monitored at 265 nm. The rates of hydrolysis of 2-isopropyl-2-methyl-1,3-dioxolane were followed by determining the increase in concentration of isopropyl methyl ketone by monitoring its absorption at 278 nm.

A Beckman DU-2 or DU with thermostated cell compartments was used to follow the ketone absorption. The temperature could be controlled to ± 0.1°C.

The calculated amount of purified glycerol was weighed in a 50 ml. volumetric flask to the nearest 0.01 g. Perchloric acid was then added to the flask and distilled water was added until the liquid level was approximately 0.5 ml. from the mark. The flask was then placed in a thermostated water bath for 10-20 minutes. About 0.2 ml. of the dioxolane was added to the flask and enough water was added to the flask to bring the liquid level to the mark. The flask was shaken vigorously and a 3 ml. aliquot was placed in a 1.0 cm. silica cell and the cell was immediately placed in the cell compartment of the spectrophotometer. The cell was left in the compartment for about five minutes to allow the temperature of the cell to equilibrate. The absorbance values were then taken until the reaction was 60-80% complete.

The rates determined in 50% dioxane were done exactly the same way except 25 ml. of purified dioxane was pipetted into a 50 ml. flask.
and acid, substrate, and water was added to the mark. A typical set of data is given in Table I.

C. Calculation of Rate Constants

The data were treated in two ways. The rate constants were calculated by means of a computer program\textsuperscript{25} that uses the standard equation (Eq. 18) for calculating pseudo-first order rate constants.\textsuperscript{26}

\[
\frac{k_p}{2.303} = \frac{\log (D_\infty - D_t)}{(D_\infty - D_0)}
\]

Where \( k_p \) = pseudo-first order rate constant

\( t \) = time

\( t_0 \) = time equal to zero

\( D_\infty \) = optical density at \( t \) equal to infinity

\( D_t \) = optical density at time \( t \)

\( D_0 \) = optical density at time equal to zero

The computer program utilizes a variable infinity point method. To the experimentally determined infinity point the program adds or subtracts small increments until the least squares slope of \( \log (D_\infty - D_t) \) vs. \( t \) reaches a minimum root-mean-square deviation.

The rate constants that are reported in the tables were calculated using Swinbourne’s\textsuperscript{27} method (Eq. 19).

\[
D_t = D_\infty (1 - \exp k_p T) + D_{t+T} \exp (k_p T)
\]

Where \( D_1, D_2, \ldots, D_t \) are the optical densities measured at times \( t_1, t_2, \ldots, t_n \).
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<th>$D_t$(calc.)</th>
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infinity point 0.575

computer infinity point 0.558

\[ k_{\psi}/(H^+) = 0.174 \, \text{M}^{-1}\text{sec}^{-1} \]
Computer Method

\[ k_{\psi}/(H^+) = 0.171 \, \text{M}^{-1}\text{sec}^{-1} \]
Swinbourne's Method
$D_{t_1+T}, D_{t_2+T}, \ldots, D_{t_n+T}$ are the optical densities measured at time $t_1+T$, $t_2+T$, $\ldots$, $t_n+T$ where $T$ is a constant time interval on the order of $\frac{1}{2}$ half-life to two half-lives.

Plots of $D_t$ vs. $D_{t+T}$ give straight lines having slopes equal to exp $(k\psi T)$. The value of $k\psi$ will be given by Equation 20.

$$k\psi = \frac{2.303 \log (\text{slope})}{T}$$  \hspace{1cm} (20)

The data from Table I are graphed in this manner in Figure 1. The rates reported in the tables were actually calculated by the method of averages. The slope is given in Equation 21.

$$\text{slope} = \frac{n}{n/2} \sum_{n/2}^{n} D_t - \sum_{1}^{n/2} D_t$$  \hspace{1cm} (21)

$$= \frac{n}{n/2} \sum_{n/2}^{n} D_{t+T} - \sum_{1}^{n/2} D_{t+T}$$

Once $k\psi$ is determined, the second order rate constant $k_2$ is calculated by dividing $k\psi$ by the acid concentration. The acid concentration is constant since the reactions that were studied are acid-catalyzed. A sample calculation using the data in Table I follows:

$$\text{slope} = \frac{1062 \ - \ 659}{1631 \ - \ 1384} = \frac{403}{247} = 1.51$$  \hspace{1cm} (22)

$$k \text{ (40 min.)} = 2.303 \log 1.51$$  \hspace{1cm} (23)

$$k \text{ (40) } = 2.303 (0.179)$$  \hspace{1cm} (24)

$$k = \frac{2.303 (0.179)}{(40 \text{ min.}) (60 \text{sec/min})} = 0.000171 \text{ sec}^{-1}$$  \hspace{1cm} (25)

$$k_2 = \frac{k\psi}{[H^+]} = \frac{0.000171 \text{ sec}^{-1}}{0.001M} + 0.171 \text{ M}^{-1} \text{ sec}^{-1}$$  \hspace{1cm} (26)
Figure 1. Swinbourne plot of data from Table I.
D. Distribution Studies

A 0.04 mole sample of 2,2-dimethyl-1,3-dioxolane was weighed in a 100 ml. volumetric flask. Reagent iso-octane (Matheson, Coleman & Bell) was added to the mark. The resulting solution was 0.4 M in 2,2-dimethyl-1,3-dioxolane. Five ml. of this solution was placed in a Teflon screw-covered test tube and 7.0 ml. of water or water-glycerol solution was added. This was repeated using from 0-40% glycerol. The water and water-glycerol solutions were 0.001 N in NaOH to prevent any hydrolysis of the 2,2-dimethyl-1,3-dioxolane. The test tubes were then placed in a mechanical shaker with a thermostat control. The temperature could be regulated to ± 0.5°C. This experiment was conducted twice at 25°, 35°, and 45°C. After the samples were shaken for over 48 hours the test tubes were centrifuged and about one ml. of the organic phase was drawn off and placed in a stoppered 25 ml. erlenmeyer flask. These samples were then analyzed by gas chromatography. The instrument employed was a Perkin-Elmer F11 Gas Chromatograph (flame ionization). The column was a 200 ft. wall coated open tubular stainless steel column with an inside tube diameter of 0.01 in. The stationary phase was Ucon LB-550X. The carrier gas was nitrogen. The recorder used with this chromatograph was a Varian Aerograph Model 20. Typical instrument settings for analysis are given in Table II.

Each sample was injected from 3-4 times. The chromatograms were then Xeroxed on heavier paper. Each peak was then cut out and weighed on a Mettler balance. A sample of the 0.4 M 2,2-dimethyl-1,3-dioxolane in iso-octane was also injected and the ratio of the iso-octane peak to
TABLE II
TYPICAL INSTRUMENT SETTINGS FOR GAS CHROMATOGRAPHIC ANALYSIS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N_2 ) pressure</td>
<td>16 lbs/in²</td>
</tr>
<tr>
<td>Air pressure</td>
<td>20 lbs/in²</td>
</tr>
<tr>
<td>( H_2 ) pressure</td>
<td>30 lbs/in²</td>
</tr>
<tr>
<td>Oven temperature setting</td>
<td>60 (ca. 75°)</td>
</tr>
<tr>
<td>Injection temp. setting</td>
<td>5 (ca. 200°)</td>
</tr>
<tr>
<td>Recorder speed</td>
<td>80 in/hr</td>
</tr>
<tr>
<td>Sample size</td>
<td>0.8 µl</td>
</tr>
</tbody>
</table>

The 2,2-dimethyl-1,3-dioxolane peak was used as a standard to compare other ratios to. A sample calculation follows:

\[
W_i = \text{weight of iso-octane peak} \\
W_{DMD} = \text{wt. of 2,2-dimethyl-1,3-dioxolane peak}
\]

For 0.4 M sample: \( \frac{W_i}{W_{DMD}} = 3.05 \)

For sample extracted with \( H_2O \): \( \frac{W_i}{W_{DMD}} = 5.77 \)

Fraction of DMD left in iso-octane layer: \( \frac{3.05}{5.77} = 0.529 \)

Conc. of DMD in iso-octane layer: \( 0.400 \times 0.529 = 0.212 \text{ M} \)

Conc. of DMD in \( H_2O \) layer: \( (0.400 - 0.212)(5\text{ml}/7\text{ml}) = 0.134 \text{ M} \)

Equilibrium constant = \( K_D = 0.134/0.212 = 0.633 \)
III. RESULTS

A. Rate Constants

The second order rate coefficients for the hydrolysis of 2,2-dimethyl-1,3-dioxolane are listed in Table III. The first column gives the temperature at which the rate constants were determined. The temperature is known to ± 0.1°C. The second column gives the acid concentration. The third column gives the weight percent glycerol and the fourth column gives the second order rate constants with their average deviation. The values for the rate constants are the average of at least two separate determinations and are calculated by the Swinbourne method.

Table IV contains the rate constants for the hydrolysis of 2-isopropyl-2-methyl-1,3-dioxolane. Table V contains the rate constants for the hydrolysis of 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane. The rate constants for the hydrolysis of 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane in 50% dioxane are also included in Table V.

B. w -Values

Figure 2 is a plot of log \( k^+ / (H^+) \) vs. - log \( a_{H_2O} \) for 2,2-dimethyl-1,3-dioxolane at temperatures ranging from 20°C to 45°C. Plots for 2-isopropyl-2-methyl-1,3-dioxolane and 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane give similar straight lines. The activity of water at the various glycerol concentrations was calculated by using the empirical equation:

\[
a_{H_2O} = 1 - 0.018 m
\]

where \( m \) is the molality of glycerol in the water-glycerol mixtures.
TABLE III
RATE CONSTANTS FOR THE HYDROLYSIS OF 2,2-DIMETHYL-1,3-DIOXOLANE

<table>
<thead>
<tr>
<th>Temp. (°C)</th>
<th>Acid conc. (M)</th>
<th>% Glycerol (wt.)</th>
<th>k_2 (M^{-1}sec^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.0 ± 0.1</td>
<td>10^{-3}</td>
<td>0</td>
<td>0.0745 ± 0.0018^a</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>10</td>
<td>0.0890 ± 0.0038</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>20</td>
<td>0.0991 ± 0.0049</td>
</tr>
<tr>
<td></td>
<td>8.89x10^{-4}</td>
<td>30</td>
<td>0.121 ± 0.004</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>40</td>
<td>0.130 ± 0.0044</td>
</tr>
<tr>
<td>25.0 ± 0.1</td>
<td>b</td>
<td>0</td>
<td>0.151 ± 0.003</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>10</td>
<td>0.173 ± 0.002</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>20</td>
<td>0.179 ± 0.002</td>
</tr>
<tr>
<td></td>
<td>8.89x10^{-4}</td>
<td>30</td>
<td>0.212 ± 0.003</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>40</td>
<td>0.252 ± 0.008</td>
</tr>
<tr>
<td>30.0 ± 0.1</td>
<td>10^{-3}</td>
<td>0</td>
<td>0.265 ± 0.001</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>10</td>
<td>0.273 ± 0.003</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>20</td>
<td>0.310 ± 0.018</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>40</td>
<td>0.373 ± 0.005</td>
</tr>
<tr>
<td>35.0 ± 0.1</td>
<td>10^{-3}</td>
<td>0</td>
<td>0.457 ± 0.002</td>
</tr>
<tr>
<td></td>
<td>&quot;</td>
<td>10</td>
<td>0.460 ± 0.012</td>
</tr>
<tr>
<td></td>
<td>&quot;</td>
<td>20</td>
<td>0.529 ± 0.013</td>
</tr>
<tr>
<td></td>
<td>&quot;</td>
<td>30</td>
<td>0.584 ± 0.000</td>
</tr>
<tr>
<td></td>
<td>&quot;</td>
<td>40</td>
<td>0.632 ± 0.006</td>
</tr>
<tr>
<td>40.0 ± 0.1</td>
<td>10^{-3}</td>
<td>0</td>
<td>0.805 ± 0.003</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>10</td>
<td>0.839 ± 0.002</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>20</td>
<td>0.878 ± 0.010</td>
</tr>
<tr>
<td></td>
<td>8.89x10^{-4}</td>
<td>30</td>
<td>0.889 ± 0.013</td>
</tr>
<tr>
<td></td>
<td>10^{-3}</td>
<td>40</td>
<td>0.966 ± 0.011</td>
</tr>
<tr>
<td>45.0 ± 0.1</td>
<td>2.0x10^{-4}</td>
<td>0</td>
<td>1.39 ± 0.07</td>
</tr>
<tr>
<td></td>
<td>2.0x10^{-4}</td>
<td>10</td>
<td>1.40 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>&quot;</td>
<td>20</td>
<td>1.61 ± 0.04</td>
</tr>
<tr>
<td></td>
<td>&quot;</td>
<td>30</td>
<td>1.52 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>&quot;</td>
<td>40</td>
<td>1.61 ± 0.03</td>
</tr>
</tbody>
</table>

^aAverage deviation
b 8.89x10^{-4} to 7.12x10^{-3}
### TABLE IV

RATE CONSTANTS FOR THE HYDROLYSIS OF 2-ISOPROPYL-2-METHYL-1,3-DIOXOLANE

<table>
<thead>
<tr>
<th>Temp. (°C)</th>
<th>Acid conc. (M)</th>
<th>% Glycerol</th>
<th>$k_2 (M^{-1} \text{sec}^{-1})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>25.0 ± 0.1</td>
<td>$2 \times 10^{-3}$</td>
<td>0</td>
<td>$0.158 ± 0.000^a$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10</td>
<td>$0.178 ± 0.002$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>$0.186 ± 0.004$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>$0.198 ± 0.005$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40</td>
<td>$0.208 ± 0.003$</td>
</tr>
<tr>
<td>35.0 ± 0.1</td>
<td>$2 \times 10^{-3}$</td>
<td>0</td>
<td>$0.469 ± 0.001$</td>
</tr>
<tr>
<td>45.0 ± 0.1</td>
<td>$2 \times 10^{-4}$</td>
<td>0</td>
<td>$1.41 ± 0.07$</td>
</tr>
<tr>
<td></td>
<td>$2 \times 10^{-4}$</td>
<td>10</td>
<td>$1.41 ± 0.02$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>$1.51 ± 0.05$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>$1.47 ± 0.01$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40</td>
<td>$1.45 ± 0.09$</td>
</tr>
</tbody>
</table>

$^a$Average deviation
### TABLE V

RATE CONSTANTS FOR THE HYDROLYSIS OF
2,2-DIMETHYL-4-HYDROXYMETHYL-1,3-DIOXOLANE

<table>
<thead>
<tr>
<th>Temp. (°C)</th>
<th>Acid conc. (M)</th>
<th>Solvent</th>
<th>$k_2$ (M$^{-1}$sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.0</td>
<td>4.0x10$^{-3}$</td>
<td>H$_2$O</td>
<td>0.0225 ± 0.0023</td>
</tr>
<tr>
<td>25.0</td>
<td>3x10$^{-3}$</td>
<td>H$_2$O</td>
<td>0.0381 ± 0.0008</td>
</tr>
<tr>
<td>4.0x10$^{-3}$</td>
<td>10% Glycerol</td>
<td>0.0452 ± 0.0037</td>
<td></td>
</tr>
<tr>
<td>4.0x10$^{-3}$</td>
<td>20% Glycerol</td>
<td>0.0475 ± 0.0025</td>
<td></td>
</tr>
<tr>
<td>4.0x10$^{-3}$</td>
<td>30% Glycerol</td>
<td>0.0517 ± 0.0002</td>
<td></td>
</tr>
<tr>
<td>4.0x10$^{-3}$</td>
<td>40% Glycerol</td>
<td>0.0583 ± 0.0006</td>
<td></td>
</tr>
<tr>
<td>4.0x10$^{-2}$</td>
<td>50% Dioxane(v/v)</td>
<td>0.0136 ± 0.0002</td>
<td></td>
</tr>
<tr>
<td>35.0</td>
<td>3.0x10$^{-3}$</td>
<td>H$_2$O</td>
<td>0.113 ± 0.001</td>
</tr>
<tr>
<td>2.0x10$^{-2}$</td>
<td>50% Dioxane(v/v)</td>
<td>0.0341 ± 0.0002</td>
<td></td>
</tr>
<tr>
<td>40.0</td>
<td>2x10$^{-3}$</td>
<td>H$_2$O</td>
<td>0.192 ± 0.006</td>
</tr>
<tr>
<td>45.0</td>
<td>1.0x10$^{-3}$</td>
<td>H$_2$O</td>
<td>0.333 ± 0.004</td>
</tr>
<tr>
<td>1.0x10$^{-3}$</td>
<td>10% Glycerol</td>
<td>0.371 ± 0.011</td>
<td></td>
</tr>
<tr>
<td>1.0x10$^{-3}$</td>
<td>20% Glycerol</td>
<td>0.401 ± 0.016</td>
<td></td>
</tr>
<tr>
<td>1.0x10$^{-3}$</td>
<td>30% Glycerol</td>
<td>0.409 ± 0.010</td>
<td></td>
</tr>
<tr>
<td>1.0x10$^{-3}$</td>
<td>40% Glycerol</td>
<td>0.468 ± 0.004</td>
<td></td>
</tr>
<tr>
<td>1.0x10$^{-2}$</td>
<td>50% Dioxane(v/v)</td>
<td>0.100 ± 0.002</td>
<td></td>
</tr>
</tbody>
</table>
Figure 2. Effect of glycerol and temperature on the rates of hydrolysis for 2,2-dimethyl-1,3-dioxolane.
This equation was formulated by correlating data on the activity of water in water-glycerol solutions. The calculated activities of water are summarized in Table VI.

TABLE VI

ACTIVITIES OF WATER IN WATER-GLYCEROL SOLUTIONS

<table>
<thead>
<tr>
<th>Wt. % Glycerol</th>
<th>g/liter Glycerol</th>
<th>Molality Glycerol</th>
<th>Activity $H_2O$</th>
<th>Mole Fraction $H_2O$</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>102.2</td>
<td>1.025</td>
<td>0.978</td>
<td>0.978</td>
</tr>
<tr>
<td>20</td>
<td>209.4</td>
<td>2.71</td>
<td>0.951</td>
<td>0.951</td>
</tr>
<tr>
<td>30</td>
<td>321.8</td>
<td>4.65</td>
<td>0.916</td>
<td>0.915</td>
</tr>
<tr>
<td>40</td>
<td>439.8</td>
<td>7.24</td>
<td>0.870</td>
<td>0.867</td>
</tr>
</tbody>
</table>

The slopes of these plots ($w_g$-values) are summarized in Table VII for 2,2-dimethyl-1,3-dioxolane, 2-isopropyl-2-methyl-1,3-dioxolane, and 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane. The errors indicated are the 50% confidence limit. (See Appendix A.)

C. Activation Parameters

A detailed discussion of transition state theory is given by Eyring and by Frost and Pearson. A brief outline will be given here.
<table>
<thead>
<tr>
<th>Compound</th>
<th>Temperature (°C)</th>
<th>w_g</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,2-Dimethyl-</td>
<td>20</td>
<td>-3.94 ± 0.33</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>-3.54 ± 0.14</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>-2.71 ± 0.21</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>-2.54 ± 0.15</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>-1.22 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>-1.04 ± 0.21</td>
</tr>
<tr>
<td>2-Isopropyl-2-methyl-</td>
<td>25</td>
<td>-1.81 ± 0.17</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>-0.23 ± 0.22</td>
</tr>
<tr>
<td>2,2-Dimethyl-</td>
<td>25</td>
<td>-2.78 ± 0.29</td>
</tr>
<tr>
<td>4-hydroxymethyl-</td>
<td>45</td>
<td>-2.22 ± 0.19</td>
</tr>
</tbody>
</table>

TABLE VII

w_g - VALUES FOR 1,3-DIOXOLANES
Consider the reaction:

\[ A + B \rightleftharpoons AB^* \rightarrow \text{Products} \quad (28) \]

where A and B are the reactants and \( AB^* \) is the transition state or activated complex. Since transition state theory treats \( AB^* \) essentially as a normal molecule, an equilibrium constant can be defined for Equation 28.

\[ K^* = \frac{(AB^*)}{(A)(B)} \quad (29) \]

One of the vibrations of \( AB^* \) is equal to a translational degree of freedom along the reaction coordinate that proceeds to form the products. When this degree of freedom is treated as a classical vibration, the frequency \( \nu \) of that vibration at temperature T is defined as:

\[ h\nu - kT \quad (30) \]

where \( h \) is Planck's constant and \( k \) is Boltzmann's constant.

The rate of reaction will be equal to the concentration of the transition state times the frequency with which the transition state falls apart to give products.

\[ \text{rate} = \nu \frac{(AB^*)}{h} = \frac{kT(AB^*)}{h} \quad (31) \]

\[ \text{rate} = k_T(A)(B) \quad (32) \]

Since the rates are equal:

\[ k_T = \frac{kT}{h} \left( \frac{(AB^*)}{(A)(B)} \right) = \frac{kT}{h} K^* \quad (33) \]
The equilibrium constant $K^*$ can be related to a free energy of activation:

$$\Delta G^* = -RT \ln K^* = -RT \ln \frac{k_r h}{RT}$$  \hspace{1cm} (34)

The enthalpy of activation will then be defined as:

$$\Delta H^* = - R \frac{d(\ln K^*)}{d(1/T)} = - R \left[ \frac{d(\ln k_r)}{d(1/T)} + T \right]$$  \hspace{1cm} (35)

The entropy of activation will be defined as:

$$\Delta S^* = \frac{\Delta H^* - \Delta G^*}{T}$$  \hspace{1cm} (36)

Since the Arrhenius energy of activation is defined as:

$$E_{\text{act}} = -R \frac{d(\ln k_r)}{d(1/T)}$$  \hspace{1cm} (37)

Equation 35 becomes:

$$\Delta H^* = E_{\text{act}} - RT$$  \hspace{1cm} (38)

From Equation 37 it can be seen that a plot of the natural logarithm of the second order rate constant versus $1/T$ should give a straight line with a slope equal to $-E_{\text{act}}/R$. A typical plot for 2,2-dimethyl-1,3-dioxolane and 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane is given in Figure 3. Once $E_{\text{act}}$ is known $\Delta H^*$ can be evaluated. (Eq. 38) $\Delta G^*$ can be evaluated directly from the second order rate constant at a given temperature. (Eq. 34) Once $\Delta G^*$ and $\Delta H^*$ are known, $\Delta S^*$ can be evaluated. (Eq. 36)
Figure 3. Arrhenius plot for IMD ⊙, and DHD ☐.
<table>
<thead>
<tr>
<th>% Glycerol</th>
<th>DMD</th>
<th>IMD</th>
<th>DHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>21.3±0.2</td>
<td>20.6±0.4</td>
<td>19.9±0.4</td>
</tr>
<tr>
<td>10</td>
<td>20.1±0.3</td>
<td>19.5±0.1</td>
<td>19.8±0.8</td>
</tr>
<tr>
<td>20</td>
<td>20.3±0.3</td>
<td>19.7±0.1</td>
<td>20.1±0.6</td>
</tr>
<tr>
<td>30</td>
<td>18.5±0.3</td>
<td>18.9±0.2</td>
<td>19.5±0.3</td>
</tr>
<tr>
<td>40</td>
<td>18.1±0.3</td>
<td>18.2±0.6</td>
<td>19.6±0.1</td>
</tr>
<tr>
<td>ΔH*</td>
<td>0</td>
<td>20.7±0.2</td>
<td>20.0±0.4</td>
</tr>
<tr>
<td>10</td>
<td>19.5±0.3</td>
<td>18.9±0.1</td>
<td>19.3±0.8</td>
</tr>
<tr>
<td>20</td>
<td>19.7±0.3</td>
<td>19.7±0.4</td>
<td>19.5±0.6</td>
</tr>
<tr>
<td>30</td>
<td>17.9±0.3</td>
<td>18.3±0.1</td>
<td>18.9±0.3</td>
</tr>
<tr>
<td>40</td>
<td>17.6±0.3</td>
<td>17.6±0.6</td>
<td>19.0±0.1</td>
</tr>
<tr>
<td>ΔG*</td>
<td>0</td>
<td>18.6±0.1</td>
<td>18.5±0.1</td>
</tr>
<tr>
<td>10</td>
<td>18.5±0.1</td>
<td>18.5±0.1</td>
<td>19.3±0.1</td>
</tr>
<tr>
<td>20</td>
<td>18.5±0.1</td>
<td>18.4±0.1</td>
<td>19.2±0.1</td>
</tr>
<tr>
<td>30</td>
<td>18.4±0.1</td>
<td>18.4±0.1</td>
<td>19.2±0.1</td>
</tr>
<tr>
<td>40</td>
<td>18.3±0.1</td>
<td>18.4±0.1</td>
<td>19.1±0.1</td>
</tr>
<tr>
<td>ΔS*</td>
<td>0</td>
<td>7.1±0.7</td>
<td>4.8±1.3</td>
</tr>
<tr>
<td>10</td>
<td>3.5±1.0</td>
<td>1.4±0.5</td>
<td>-0.1±2.7</td>
</tr>
<tr>
<td>20</td>
<td>4.3±1.0</td>
<td>2.2±0.5</td>
<td>0.8±2.0</td>
</tr>
<tr>
<td>30</td>
<td>-1.6±1.0</td>
<td>-0.3±0.7</td>
<td>-1.1±1.0</td>
</tr>
<tr>
<td>40</td>
<td>-2.4±1.0</td>
<td>-2.5±2.0</td>
<td>-0.4±0.5</td>
</tr>
</tbody>
</table>
The values of $E_{\text{act}}$, $\Delta H^*$, $\Delta G^*$, and $\Delta S^*$ at various water-glycerol mixtures are given in Table VIII for 2,2-dimethyl-1,3-dioxolane (DMD), 2-isopropyl-2-methyl-1,3-dioxolane (IMD), and 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane (DHD). These values were obtained by means of a computer program that calculated a least squares slope for $E_{\text{act}}$. (See Appendix B.) The errors indicated are the 50% confidence limit. (See Appendix A.)

The values of $E_{\text{act}}$, $\Delta H^*$, $\Delta G^*$, and $\Delta S^*$ for 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane in 50% dioxane are given in Table IX.

**TABLE IX**

**ACTIVATION PARAMETERS FOR 2,2-DIMETHYL-4-HYDROXYMETHYL-1,3-DIOXOLANE IN 50% (v/v) DIOXANE**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_{\text{act}}$</td>
<td>18.8 ± 0.5 (kcal/m)</td>
</tr>
<tr>
<td>$\Delta H^*$</td>
<td>18.2 ± 0.5 (kcal/m)</td>
</tr>
<tr>
<td>$\Delta G^*$</td>
<td>20.0 ± 0.1 (kcal/m)</td>
</tr>
<tr>
<td>$\Delta S^*$</td>
<td>-6.1 ± 1.7 (e.u.)</td>
</tr>
</tbody>
</table>
D. Partial Molar Quantities of Transfer

The chemical potential or partial molar free energy of a system is given by: \( \mu = \mu^0 + RT \ln cy \) \( (39) \)

where \( \mu \) = chemical potential (G)

\( \mu^0 \) = chemical potential in the standard state (G^0)

R = gas constant

T = temperature (K^0)

c = molar concentration

y = molar activity coefficient

When 2,2-dimethyl-1,3-dioxolane is distributed between iso-octane and water or water-glycerol the chemical potential is the same for both phases. Thus for the case of water/iso-octane Equation 40 applies.

\[ \mu_1 = \mu_1^0 + RT \ln c_1y_1 = \mu_2 = \mu_2^0 + RT \ln c_2y_2 \] \( (40) \)

The subscripts 1 and 2 refer to the water layer and iso-octane layer respectively. Likewise when the system is water-glycerol/iso-octane Equation 41 applies.

\[ \mu_3 = \mu_3^0 + RT \ln c_3y_3 = \mu_4 = \mu_4^0 + RT \ln c_4y_4 \] \( (41) \)

The subscripts 3 and 4 refer to the water-glycerol layer and iso-octane layer respectively.
Subtracting Equation 40 from Equation 41 gives:

$$\mu_3 - \mu_1 = \mu_4 - \mu_2$$

(42)

or

$$\mu_3^0 - \mu_1^0 + RT \ln \frac{c_3y_3}{c_1y_1} = \mu_4^0 - \mu_2^0 + RT \ln \frac{c_4y_4}{c_2y_2}$$

(43)

The standard state for 2,2-dimethyl-1,3-dioxolane in iso-octane is the same for both the water/iso-octane case and the water-glycerol/iso-octane case i.e., a hypothetical one molar solution obeying the limiting law conditions which correspond to Henry's law, therefore:

$$\mu_2^0 = \mu_4^0$$

(44)

Since the solutions are reasonably dilute (ca. 0.2 M) Henry's law predicts that the activity coefficients will approach unity and thus cancel. Using this assumption and the condition stated in Equation 44, Equation 43 becomes:

$$\mu_3^0 - \mu_1^0 + RT \ln \frac{c_3}{c_1} = RT \ln \frac{c_4}{c_2}$$

(45)

If values are chosen so that $c_1 = c_3$ the difference in standard states, $\mu_3^0 - \mu_1^0$, may be evaluated and there will be no contribution due to energy of dilution term. Since the $RT \ln c_3/c_1$ term becomes zero, the difference in standard states, $\mu_3^0 - \mu_1^0$, is defined by Equation 46.

$$\mu_3^0 - \mu_1^0 = RT \ln \frac{c_4}{c_2}$$

(46)

The $K_D$ values that are listed in Table X were calculated by the method outlined in Section D in Chapter II. The values are the average
### Table X

**DISTRIBUTION CONSTANTS FOR 2,2-DIMETHYL-1,3-DIOXOLANE**

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>% Glycerol (wt.)</th>
<th>$K_D$ (C&lt;sub&gt;aqueous&lt;/sub&gt;/C&lt;sub&gt;iso-oct.&lt;/sub&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25.0</td>
<td>0</td>
<td>0.646 ± 0.013&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0.553 ± 0.003</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0.393 ± 0.000</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>0.374 ± 0.014&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>0.335 ± 0.037</td>
</tr>
<tr>
<td>35.0</td>
<td>0</td>
<td>0.504 ± 0.003</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0.495 ± 0.029</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0.402</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>0.437 ± 0.069</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>0.343</td>
</tr>
<tr>
<td>45.0</td>
<td>0</td>
<td>0.582 ± 0.021</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0.429 ± 0.027</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0.409 ± 0.033</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>0.518 ± 0.085</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>0.620</td>
</tr>
</tbody>
</table>

<sup>a</sup>$K_D$ when total concentration was 0.5 M is 0.673 ± 0.030.

<sup>b</sup>$K_D$ when total concentration was 0.2 M is 0.368 ± 0.000.
of two determinations. The errors indicated are the average deviations. The value is a single determination if no error is indicated. These values were obtained for solutions with a total 2,2-dimethyl-1,3-dioxolane concentration of 0.4 M.

The $K_D$ value for the water/iso-octane case is the ratio $c_1/c_2$. The $K_D$ value for the water-glycerol/iso-octane case is the ratio $c_3/c_4$. Since $K_D$ is independent of concentration for the range of concentrations studied, values can be chosen so that $c_1 = c_3$. (See Table X.) The corresponding values of $c_2$ and $c_4$ can then be used to define a new equilibrium constant. Equation 46 can be written:

$$
\mu_3^0 - \mu_1^0 = -RT \ln \frac{c_2}{c_4}
$$

(47)

The new equilibrium constant can then be defined as:

$$
K_{iso-octane} = \frac{c_2}{c_4}
$$

(48)

Equation 47 becomes:

$$
\mu_3^0 - \mu_1^0 = -RT \ln K_{iso-octane}
$$

(49)

This equilibrium constant is known as a function of temperature so the differences in standard partial molar enthalpies can be evaluated by using Equation 50.

$$
\ln \frac{K_{iso-octane}}{K_{iso-octane}} = -\frac{\Delta H^0}{R} (1/T' - 1/T)
$$

(50)
A plot of $\ln K_{iso-octane}$ versus $1/T$ should give a straight line with a slope equal to $-\Delta \bar{H}^0 / R$. (See Figure 4.)

The differences in the standard partial molar entropies can be determined from the relationship:

$$\Delta \bar{S}^0 = \frac{\Delta \bar{H}^0 - \Delta \bar{S}^0}{T}$$

(51)

The standard partial molar quantities are listed in Table XI. The errors indicated are the 50% confidence limit. (See Appendix A.) The values in Table XI represent the energy changes that take place when one mole of 2,2-dimethyl-1,3-dioxolane is transferred from a water solution to a water-glycerol solution.
Figure 4. Partial molar enthalpy plot for the transfer of 2,2-dimethyl-1,3-dioxolane from H2O to 40% glycerol.
TABLE XI
STANDARD PARTIAL MOLAR QUANTITIES
FOR 2,2-DIMETHYL-1,3-DIOXOLANE

<table>
<thead>
<tr>
<th>% Glycerol</th>
<th>$\Delta H^0$ (kcal/mol)</th>
<th>$\Delta G^0$ (e.u.)</th>
<th>$\Delta S^0$ (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>-1.3 ± 0.9</td>
<td>-4.8 ± 3.0</td>
<td>0.10 ± 0.03</td>
</tr>
<tr>
<td>20</td>
<td>1.4 ± 0.8</td>
<td>3.5 ± 2.7</td>
<td>0.30 ± 0.03</td>
</tr>
<tr>
<td>30</td>
<td>4.0 ± 1.3</td>
<td>12.2 ± 4.4</td>
<td>0.33 ± 0.03</td>
</tr>
<tr>
<td>40</td>
<td>6.7 ± 1.1</td>
<td>21.1 ± 3.7</td>
<td>0.39 ± 0.03</td>
</tr>
</tbody>
</table>
A. \( w \) - Values

The theory of \( w \)-values offers the extreme interpretation that \( w \) represents the change in the number of water molecules of hydration between the reactants and the transition state.\(^6\) For acid-catalyzed reactions the following equations apply.

\[
S(H_2O)_s + H(H_2O)^+ \rightleftharpoons SH(H_2O)^+_p + (s + n - p)H_2O \tag{52}
\]

\[
SH(H_2O)^+_p + (t - p)H_2O \rightleftharpoons T(H_2O)^+_t \rightarrow \text{products} \tag{53}
\]

Adding:

\[
S(H_2O)_s + H(H_2O)_n + (t - n - s)H_2O \rightleftharpoons T(H_2O)^+_t \rightarrow \text{products} \tag{54}
\]

\( S \) is the substrate and \( s \) is the number of water molecules that are hydrating \( S \); \( n \) is the number of water molecules that are hydrating the proton; \( SH^+ \) is the protonated substrate and \( p \) is the number of water molecules that are hydrating \( SH^+ \); and \( T^+ \) is the transition state and \( t \) is the number of water molecules that are hydrating \( T^+ \).

From Equation 54 it can be seen that the kinetic order of water, \( w \), is equal to the hydration of the transition state minus the hydration of the proton, minus the hydration of the neutral substrate.

There is some evidence that the proton exists as the tetra-hydrate \((H_2O)_4^+\).\(^{34}\) (See Figure 5.)
For Equation 54, \( n \) can be assigned a value of 4. Using similar reasoning the transition state hydration, \( t \), can be assigned a value of one. (See Figure 6.)

Let it be assumed that the substrate hydration, \( s \), will be weak in comparison to the hydration of both the proton and the transition state which are positively charged. Therefore \( s \) in Equation 54 can be assigned a value of zero. The predicted \( w_g \)-value will be \( (1-4-0) = -3 \). The values in Table VII show that this is in fairly
good agreement with the \( w_g \)-values for IMD at 25°C and for DHD at 25°C. This is clearly not the case for IMD at 25°C and 45°C and for IMD and DHD at temperatures other than 25°C. Figure 7 shows the temperature dependence of the \( w_g \)-values for 2,2-dimethyl-1,3-dioxolane. The fact that some of the evidence for the hydrated proton is based on mass spectrometry data would seem to indicate that this species is not particularly temperature dependent.\(^{34}\) By analogy it can be assumed that the hydrated positive charge of the transition state should also be relatively temperature independent. If both the hydration of the proton and the transition state hydration are temperature independent, then the temperature dependence of the \( w_g \)-values must be due to the substrate hydration. Therefore the assumption that the substrate hydration is unimportant in comparison to the hydration of the proton and the transition state seems to be incorrect.

The above approach appears to be an over-simplification. The hydration of the proton must be reconsidered. Knewstub and Tickner\(^{35}\) treated the aqueous proton in terms of a series of equilibria.

\[
\begin{align*}
H_3O^+ + 2H_2O & \rightleftharpoons H_5O_2^+ + H_2O & (55) \\
H_5O_2^+ + 2H_2O & \rightleftharpoons H_7O_3^+ + H_2O & (56) \\
H_7O_4^+ + 2H_2O & \rightleftharpoons H_9O_4^+ + H_2O & (57)
\end{align*}
\]

Even though \( H_9O_4^+ \) was calculated to be better than 90% of the mixture, it is not evident which species is involved in the equilibrium protonation of the substrate.
Figure 5. Effect of temperature on $v_g$-values for DMD.
For similar reactions the species involved in the protonation step should be the same and therefore \( n \) in Equation 54 should be constant. This is all that can be said about \( n \) since the exact species that is protonating the substrate is not known. The transition state will have two types of hydration. One type will be that due to the positive charge and the other will be similar to the hydration of a neutral molecule. Thus \( t \) in Equation 54 can be written:

\[
t = t_+ + t_n
\]  

(58)

where \( t_+ \) is the hydration of the positive charge and \( t_n \) is the hydration of that part of the transition state which remains structurally similar to the neutral molecule. The equation defining \( w_g \) will then be:

\[
w_g = t_+ + t_n - n - s
\]  

(59)

Since \( t_+ \) and \( n \) are the hydration numbers associated with the rather strong hydration of concentrated positive charges they should remain reasonably constant with changing temperature. Therefore the variation of \( w_g \) with temperature that is observed in Table VII and in Figure 7 is due in a formal sense to the \( t_n - s \) term.

Bunnett has given an operational definition of hydration.

Let water molecules of hydration be defined as all those bound with sufficient energy measurably to affect reaction rates or positions of equilibria. Obviously such a definition relates to the average degree of hydration of the species concerned.\(^6\)

Since it is the average hydration that is of concern it does not seem meaningful to interpret \( w_g \) in terms of the absolute number of
water molecules that are involved in hydration. However since it is reasonable to assume that $t_n - n$ is constant with changing temperature, the $w_g$-values can be taken as a crude measure of the change in hydration that accompanies the conversion of a ground state molecule to a transition state. The change of $w_g$ with temperature, $\delta T_{W_g}$, will give some measure as to how much hydration is being lost. The slope of the line in Figure 7 is $\delta T_{W_g}$ and equal to 0.124. This appears to be a measure of the amount of $(t_n - s)$ hydration that is being lost for DMD. The value of $\delta T_{W_g}$ for IMD is 0.071. This value is approximately one-half the value for DMD and thus it appears that IMD is losing less $(t_n - s)$ hydration as the temperature is raised. The value of $\delta T_{W_g}$ for DHD is 0.028. It can be seen that $w_g$ for DHD is relatively insensitive to temperature. Apparently the introduction of a polar group like -OH causes the $w_g$-value to remain relatively constant as the temperature is changed. This same effect has been observed for the hydrolysis of 2-phenyl-1,3-dioxolane ($\delta T_{W_g} = -0.029$)\(^{36}\) and for the deoxymercuration of 1-iodo-2-methoxymercuriethane ($\delta T_{W_g} = -0.004$) and 2-iodomercuriethanol ($\delta T_{W_g} = 0.027$).\(^{29,37}\)

B. Structure of Water

The dependence of $w_g$-values on structure and on temperature is most readily explained in terms of the substrate molecule and its interactions with surrounding water molecules. To understand the nature of neutral solute-water interactions it is necessary first to consider the structure of liquid water.\(^{38}\)
In 1957, Frank and Wen proposed the "flickering cluster" model for liquid water. The flickering cluster model proposes that the formation of one hydrogen bond facilitates the formation of other hydrogen bonds with neighboring water molecules. Since hydrogen bonding can take place in three dimensions, large clusters or "icebergs" can be present in liquid water. To account for the dielectric relaxation time of water, the clusters are said to be short lived or "flickering." They form when a negative energy fluctuation takes place and produces a "cold" region. They are disrupted when a positive energy fluctuation occurs.

Némethy and Scheraga accounted for the thermodynamic properties of liquid water by a detailed statistical - thermodynamical analysis of water. Their analysis predicts that seventy per cent of all the water molecules are involved in clusters. The Némethy and Scheraga theory predicts a two-state model for water. The two states are those water molecules which are incorporated in clusters and those which are monomeric or unbonded waters.

Wicke proposed a somewhat more complicated model for water. He suggests that instead of just two states for water there are three states. Not only are there tetrahedrally bonded networks of water structure but there are also smaller clusters. These smaller clusters can range from dimers to hexamers. They can be considered to be products of the network structures when the network structures break down.

The influence of a solute on the structure of water is an important consideration. In general the two theories are similar in
that they classify solutes as being either net structure forming or net structure breaking. Small charged ions such as Li$^+$ and F$^-$ are net structure makers while large singly-charged ions such as Cs$^+$ and Br$^-$ are net structure breakers. Although the water molecules immediately surrounding ions such as Cs$^+$ and Br$^-$ are more ordered, the water molecules at a greater distance from the ions are more disordered compared to liquid water. Thus the net effect is structure breaking.

Both Wicke's and Némethy and Scheraga's model predict increased structure in the region of a non-polar group such as CH$_3$- (hydrophobic hydration). They differ, however, in regard to the type of increased water structure. Némethy and Scheraga postulate that it is like ice, i.e., a tetrahedrally bonded network. Wicke maintains that it involves non-tetrahedral coordination of neighboring water molecules.

A convincing piece of evidence for increased water structure near compounds containing non-polar groups is the fact that certain alkyl amines form stable crystalline clathrate hydrates. The clathrate hydrate of trimethylamine, (CH$_3$)$_3$N·10H$_2$O, is particularly stable in that the clathrate melts at about 5°C. The clathrate of tert-butylamine, (CH$_3$)$_3$C NH$_2$·9$rac{3}{4}$H$_2$O, melts at -1°C and isopropylamine's clathrate, (CH$_3$)$_2$CHNH$_2$·8H$_2$O, is stable at -5°C. It seems that the non-polar alkyl portion of these amines interact with the surrounding water molecules to produce crystalline cages around the amines. According to Frank and Wen the non-polar alkyl groups do not transmit positive energy fluctuations readily and thus the water structure is stabilized because it is shielded from disruptive forces. The fact that these amines form crystalline hydrates does not prove that this type of
water structure is present in solution. However this fact coupled with partial molar heat capacities and entropy data strongly suggest that regions of increased water structure exist in the vicinity of non-polar groups.\textsuperscript{38}

For the considerations of the present work the exact nature of this increased water structure is unnecessary. Henceforth this type of water will be referred to as increased water structure or hydrophobic hydration.

The foregoing considerations are relevant in regard to the solvent/substituent effects on dioxolane hydrolysis. For IMD in aqueous solution there is increased water structure surrounding the methyl groups. When the IMD is transformed into a transition state the positive charge that is developing on the carbon and oxygen (Figure 6) acts as a positive energy fluctuation and the hydrophobic hydration is disrupted. As the temperature is raised $s$ becomes smaller because the hydrophobic hydration is melted and thus $w_g$ ($\approx t_n - s$) becomes more positive (Table VII). When IMD is in an aqueous solution there is increased water structure surrounding the methyl groups. When IMD is converted to a transition state the hydrophobic hydration about the 2-methyl group is disrupted by the positive charge of the transition state. The hydrophobic hydration about the methyl groups of the isopropyl group are shielded from the positive energy fluctuation. The reason for this is the fact that the positive charge of the IMD transition state is two carbon atoms away from the structured water interface while for IMD the hydrophobic hydration is only one carbon atom away. $(\delta T_w)_{\text{IMD}} \approx \frac{1}{2} (\delta T_w)_{\text{IMD}}$
It would be advantageous to have some model for the transition state. Hertz and Zeidler\textsuperscript{44} have shown that the relaxation rate for the nuclear spin of the proton in the water molecule is approximately proportional to the average time it takes for a water molecule to make one hindered rotation. Thus the longer it takes to make a hindered rotation the more structured the water. When studying non-polar solutes containing hydrogen it was necessary for them to use D\textsubscript{2}O. The relaxation rate was studied by means of the deuteron nuclear quadropole resonance signal. They studied a series of alkyl substituted ammonium salts. It was found that the relaxation time increases from (CH\textsubscript{3})\textsubscript{4}NX (X = Br, NO\textsubscript{3}) to (CH\textsubscript{3}CH\textsubscript{2})\textsubscript{4}NX to (CH\textsubscript{3}CH\textsubscript{2}CH\textsubscript{2})\textsubscript{4}NX in an approximate ratio of 1:2:4. This indicates that the longer carbon chains of the ethyl and propyl groups are acting as insulators so that the effect of the positive charge on the water structure is diminishing with increasing chain length. If the charged ammonium salts can be used as models for the dioxolane transition states then it can be seen why (\(\delta T_w\))\textsubscript{DMD} \(\approx \frac{1}{2}(\delta T_w)\)\textsubscript{DMD}. The (CH\textsubscript{3})\textsubscript{4}NX can be used as a model for the DMD transition state. Since the water interface is only one carbon removed from the positive charge there is only a slight amount of hydrophobic hydration. Since for (CH\textsubscript{3}CH\textsubscript{2})\textsubscript{4}NX the positive charge is two carbons away from the water interface it can be used as a model for the IMD transition state. Hertz and Zeidler's studies show that there is approximately twice as much increased water structure for (CH\textsubscript{3}CH\textsubscript{2})\textsubscript{4}NX as there is for (CH\textsubscript{3})\textsubscript{4}NX.

The \(\delta T_w\) for DHD (0.028) seems to indicate that very little hydration is being lost. The -OH group, although promoting increased
hydrogen bonding in the immediate vicinity, is probably acting as a net structure breaker much like Cs$^+$ and Br$^-$. 

C. Entropy of Activation, $\Delta S^*$

If water structure is being disrupted when the ground state molecule is transformed into a transition state it should be reflected in the entropy of activation. Since entropy is a measure of order-disorder, the entropy of activation should be sensitive to the change from the ordered water structure of the ground state to the disordered water of the transition state.

Many factors contribute to the entropy of activation of a reaction. Among these factors are structural effects which can be divided into polar, steric, and resonance effects. Mechanistic considerations and solvation changes will also influence the entropy of activation. If a class of compounds is chosen so that the reaction proceeds by the same mechanism, then the entropy contribution for that mechanism will be approximately the same for this series of compounds. If changes in structure are such that they do not alter the mechanism by introducing steric strain or resonance effects then these factors will be fairly constant for the series also. If these factors cancel out, the entropy of activation should then be an approximate measure of the changes in hydration between the ground state and the transition state.

The entropies of activation for the hydrolysis of a number of 1,3-dioxolanes are listed in Table XII. For the case of 1,3-dioxolane itself, $\Delta S^*$ is close to zero. This can be expected because one would
TABLE XII

ENTROPIES OF ACTIVATION FOR THE HYDROLYSIS OF 1,3-DIOXOLANES AT 25°C

<table>
<thead>
<tr>
<th>2-Substituent</th>
<th>$\Delta S^*$ (e.u.)</th>
<th>Solvent</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>H,H</td>
<td>1.4</td>
<td>H$_2$O</td>
<td>a</td>
</tr>
<tr>
<td>CH$_3$,H</td>
<td>5.6</td>
<td>H$_2$O</td>
<td>a</td>
</tr>
<tr>
<td>CH$_3$,CH$_3$</td>
<td>7.9</td>
<td>H$_2$O</td>
<td>a</td>
</tr>
<tr>
<td></td>
<td>7.1</td>
<td>H$_2$O</td>
<td>b</td>
</tr>
<tr>
<td></td>
<td>-3.3</td>
<td>50% dioxane</td>
<td>c</td>
</tr>
<tr>
<td>CH$_3$, CH$_3$CH$_2$</td>
<td>5.4</td>
<td>H$_2$O</td>
<td>a</td>
</tr>
<tr>
<td>CH$_3$, (CH$_3$)$_2$CH</td>
<td>4.8</td>
<td>H$_2$O</td>
<td>b</td>
</tr>
<tr>
<td>C$_6$H$_5$, H</td>
<td>-7.2</td>
<td>H$_2$O</td>
<td>d</td>
</tr>
<tr>
<td></td>
<td>-9.7</td>
<td>H$_2$O</td>
<td>e</td>
</tr>
<tr>
<td></td>
<td>-8.6</td>
<td>50% dioxane</td>
<td>c</td>
</tr>
<tr>
<td>C$_6$H$_5$, CH$_3$</td>
<td>-3.7</td>
<td>H$_2$O</td>
<td>e</td>
</tr>
<tr>
<td></td>
<td>-8.6</td>
<td>50% dioxane</td>
<td>c</td>
</tr>
<tr>
<td>C$_6$H$_5$, CH$_3$CH$_2$</td>
<td>-8.9</td>
<td>50% dioxane</td>
<td>c</td>
</tr>
<tr>
<td>C$_6$H$_5$, C$_6$H$_5$</td>
<td>-8.6</td>
<td>H$_2$O</td>
<td>e</td>
</tr>
</tbody>
</table>

aRef. 16.
bFrom Table VIII of this work.
cRef. 19 $\Delta S^*$ calculated at 30°C.
dRef. 36.
eRef. 45 $\Delta S^*$ calculated at 30°C from rate constants at two temperatures.
not predict very much hydrophobic hydration for this compound since there are no alkyl groups at the 2 position. It is convenient to chose this compound as a reference and compare the $\Delta S^*$ of other compounds to it. For the case of the 2-methyl compound the $\Delta S^*$ is +5.6 e.u. because the methyl group promotes water structure in the ground state and this water structure is disrupted in the transition state. The dimethyl case has a higher positive $\Delta S^*$ because it has two methyl groups to promote water structure and therefore more is lost in going to the transition state. For the 2-ethyl-2-methyl and 2-isopropyl-2-methyl compounds both groups are promoting water structure but only the water structure around the methyl group is being disrupted in the transition state. The water structure about the ethyl and isopropyl groups is too far removed from the reaction center to be affected. This agrees with the interpretation of $\delta_{T,Wg}$ for DMD and IMD. If 1,3-dioxolane is chosen as a standard and its $\Delta S^*$ subtracted from that of DMD and IMD one gets 5.7 e.u. and 3.4 e.u. respectively. The ratio of these numbers is 1.7. The ratio of $\delta_{T,Wg}$ for DMD and IMD is equal to 1.7. This would seem to indicate that the hydration parameter $w_g$ or more accurately $\delta_{T,Wg}$, is measuring the same effect as the entropy of activation.

The $\Delta S^*$ for some 2-phenyl substituted dioxolanes are also given in Table XII. If 2-phenyl-1,3-dioxolane is used as a standard it can be seen that when a methyl group is added the entropy of activation increases. The effect is approximately the same for both the phenyl substituted case and the hydrogen substituted case.
It is believed that the addition of a cosolvent such as dioxane breaks down water structure and therefore hydrophobic hydration will practically be non-existent. The entropies of activation for the hydrolysis of some 1,3-dioxolanes in 50% dioxane are also given in Table XII. For the case of DMD it can be seen that on going from water to 50% dioxane involves a loss of about 10 e.u. This can be interpreted to mean that the dioxane strips off the hydrophobic hydration in the ground state. Therefore no water is released in the transition state and therefore there is no positive contribution to entropy. A similar case exists for 2-methyl-2-phenyl-1,3-dioxolane. When the solvent is changed from water to 50% dioxane the $\Delta S^*$ changes about 5 e.u. Again it seems that the dioxane is removing the hydrophobic hydration in the ground state. This does not seem to be the case for 2-phenyl-1,3-dioxolane. The $\Delta S^*$ is approximately the same for water and 50% dioxane. All of the phenyl derivatives have about the same $\Delta S^*$ in 50% dioxane. It would seem that hydrophobic hydration is minimal for these compounds.

The $\Delta S^*$ for the hydrolysis of DHD in 50% dioxane is given in Table IX. The difference in $\Delta S^*$ for the reaction in water and 50% dioxane is 6 e.u. Comparing this to the difference for DMD it can be said that DHD does not lose as much hydration.

The $\Delta S^0$ for the protonation of alkyl amines presents more evidence for this type of hydrophobic hydration. Entropy data is presented in Table XIII. It can be seen from Table XIII that the trend is similar to that for the 1,3-dioxolanes. The trend shows that from $\text{NH}_3$ to
# TABLE XIII

**ENTROPY DATA FOR THE PROTONATION OF ALIPHATIC AMINES AT 25°C**

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\Delta S^0$ (e.u.)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{NH}_3$</td>
<td>0.6</td>
<td>a,b</td>
</tr>
<tr>
<td>$\text{CH}_3\text{NH}_2$</td>
<td>4.7</td>
<td>c</td>
</tr>
<tr>
<td>$(\text{CH}_3)_2\text{NH}$</td>
<td>9.5</td>
<td>c</td>
</tr>
<tr>
<td>$(\text{CH}_3)_3\text{N}$</td>
<td>15.2</td>
<td>c</td>
</tr>
<tr>
<td>$\text{CH}_3\text{CH}_2\text{NH}_2$</td>
<td>3.1</td>
<td>d</td>
</tr>
<tr>
<td>$\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_2$</td>
<td>1.7</td>
<td>d</td>
</tr>
<tr>
<td>$\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_2$</td>
<td>1.3</td>
<td>d</td>
</tr>
<tr>
<td>$\text{HOCH}_2\text{CH}_2\text{NH}_2$</td>
<td>2.8</td>
<td>e</td>
</tr>
</tbody>
</table>

---

ann

**Notes:**


(CH\textsubscript{3})\textsubscript{3}N there is an increase in \(\Delta S^0\) of about 15 e.u. or approximately 5 e.u. per methyl group.

The protonated amine with a positive charge on the nitrogen acts as a positive energy fluctuation and disrupts the hydrophobic hydration around the methyl groups. The more methyl groups there are the greater the disruption and the greater the contribution to a positive \(\Delta S^0\). If an ethyl, propyl, or butyl group replaces one of the hydrogens the effect decreases slightly because these longer groups are insulating the hydrophobic hydration from the positive charge. For the case of HOCH\textsubscript{2}CH\textsubscript{2}NH\textsubscript{2} the -OH is too far away from the positive charge and whatever the -OH does to the surrounding water structure it is not affected by the positive charge on the nitrogen.

Heat capacities of activation can also be used as evidence for the breakdown of hydrophobic hydration.\textsuperscript{46} It is believed that solvent reorganization during the activation process is very important.\textsuperscript{47} The difference between the ground and transition states with respect to the water-solute interactions and the water-water interactions that result from the presence of the solute are thought to be controlling factors for \(\Delta C^p\) and \(\Delta S^*\).

The heat capacity of activation has been determined for the hydrolysis of t-butyl chloride.\textsuperscript{48} t-Butyl chloride has three methyl groups to promote hydrophobic hydration. Energy is required to break down this hydration before the reaction can take place. The hydrolysis of t-butyl chloride has a heat capacity of activation of -83 cal/mole-degree. This is interpreted to mean that as the temperature is raised the hydration shell is melted and the reaction requires less energy to take place.
The fact that the $\Delta S^*$ for the hydrolysis of t-butyl chloride is $+10$ e.u. supports the idea of a disordered transition state relative to the initial state.$^{48}$

D. Partial Molar Quantities

The $\Delta H^*$ and $\Delta S^*$ for both DMD and IMD decrease with increasing glycerol (Table VIII). The $\Delta H^*$ and $\Delta S^*$ for DHD stays about the same with increasing glycerol. It appears that the addition of glycerol to the solution is somehow altering the energy requirements for DMD and IMD but is not affecting the hydrolysis of DHD.

Arnett$^{49}$ noticed that for the solvolysis of t-butyl chloride in water-ethanol mixtures$^{50}$ the $\Delta H^*$ also decreased until it reaches a minimum. He argued that it is not possible to say what is happening unless the effect of the solvent on the ground state is ascertained. Arnett and co-workers$^{49}$ have measured the partial molar enthalpies of solution ($\Delta H_2$) for t-butyl chloride in water-ethanol mixtures. At certain concentrations there is a maximum in the partial molar enthalpies of solution. This very nearly corresponds to the minimum observed for $\Delta H^*$. This was attributed to a change in water structure and to a change in the ground state solvation of t-butyl chloride.

The standard partial molar quantities for the transfer of DMD from water to water-glycerol solutions are summarized in Table XI. The standard partial molar free energies of transfer, $\Delta \overline{G^0}$, for DMD are shown in Figure 8 along with the free energies of activation.
Figure 8. Free energy contributions to the ground state and transition state of DMD in water-glycerol mixtures.
The standard partial molar free energy of transfer is the difference between the free energy of IMD in the standard state in a water-glycerol solution and the free energy of IMD in the standard state in water.

\[ \Delta \overline{G}^0 = G_{WG}^0 - G_W^0 \]  

(60)

The free energy of activation is equal to the free energy of the transition state minus the free energy of the initial state.

\[ \Delta G^* = G_{WG}^* - G_{WG}^0 \]  

(61)

The addition of Equations 60 and 61 will give Equation 62.

\[ \Delta G^* + \Delta \overline{G}^0 = G_{WG}^* - G_W^0 \]  

(62)

Equation 62 represents the difference between the transition state in water-glycerol solutions and the ground state in water. This treatment will also hold for enthalpy and entropy. If the transition state in water-glycerol solutions is the same as in water then \( G_{WG}^0 \) is varying but \( \Delta G^* + \Delta \overline{G}^0 \) should be constant. Figure 8 shows that \( \Delta G^* + \Delta \overline{G}^0 \) is very nearly constant. Thus from the standpoint of free energy the change in \( \Delta G^* \) with the addition of glycerol can be accounted for by a change in the free energy of the ground state.

Due to the compensation effect, changes in enthalpy and entropy often partially cancel each other and thus differences in free energy are rarely as great as they are for enthalpy and entropy. 49,51,52
Figure 9 shows the $\Delta \bar{H}^0$ and $\Delta H^*$ for DMD along with $\Delta H^* + \Delta \bar{H}^0$. As can be seen from the figure the sum $\Delta H^* + \Delta \bar{H}^0$, is not a constant. However as $\Delta H^*$ decreases with the addition of glycerol $\Delta \bar{H}^0$ increases. $\Delta \bar{H}^0$ is increasing at a faster rate than $\Delta H^*$ is decreasing. This is not surprising since the change in these values are a measure of solvation effects. The change in $\Delta H^*$ with changing solvent composition is a measure of the change in hydration between the ground state and the transition state and the effect will be somewhat limited to the hydration in the vicinity of the reaction center. The change in $\Delta \bar{H}^0$ with changing solvent composition will be a measure of the hydration change for the total molecule and thus can be expected to be larger.

Figure 10 shows $\Delta S^0$ and $\Delta S^*$ for DMD. This is analogous to the treatment for enthalpy. As $\Delta S^*$ decreases with the addition of glycerol, $\Delta S^0$ increases but at a faster rate.

Glycerol is causing the DMD to be destabilized relative to DMD in pure water. The total structure of water can be considered as a series of equilibria between waters with four, three, two, one, and no hydrogen bonds. Even though alcohols have a possibility of forming three hydrogen bonds, in fact they do not form more than two hydrogen bonds.\textsuperscript{55} The limit of two hydrogen bonds prohibits the alcohols from fitting into a rigid water structure. As glycerol is added to water, it can hydrogen bond with the free water molecules and with the lower aggregates but steric considerations rule out hydrogen bonding with the larger clusters. Thus the equilibrium will shift toward the non-bonded water molecules. The net result will be a breakdown of rigid
Figure 9. Enthalpy contributions to the ground state and transition state of DMD in water-glycerol mixtures.
Figure 10. Entropy contributions to the ground state and transition state of DMD in water-glycerol mixtures.
water structure and therefore a less structured solution. Therefore when DMD is transferred to a less structured solution the hydrophobic hydration is somewhat disrupted. The breaking up of this structured water around the DMD requires energy and thus $\Delta H^0$ increases as glycerol is added. The destruction of ordered water should make a positive contribution to entropy and thus $\Delta S^0$ becomes more positive with increasing glycerol.

In Figure 11 it can be seen that transferring DMD from water to 50% glycerol accounts for the decrease in the free energy of activation. The addition of glycerol destabilizes the ground state by 0.4 kcal/m and it only destabilizes the transition state by 0.1 kcal/m. The difference in transition states is within experimental error.

Figure 12 shows that there is an enthalpy difference of 6.7 kcal/m in the ground states between DMD in water and DMD in 40% glycerol. The enthalpy difference between transition states is 3.4 kcal/m. The difference between enthalpies of the transition state may or may not be real since the experimental error for $\Delta H^0$ is large. In any event the addition of glycerol destabilizes the ground state by about twice as much as it destabilizes the transition state.

Likewise Figure 13 shows that for 40% glycerol the system is 21.1 e.u. more random in the ground state than it is in water. The entropy difference for the transition states is 11.6 e.u. Again the effect on the ground state is twice that of the transition state.
Figure 11. Dissection of free energy contributions for IMD hydrolysis in water and 40% glycerol.
Figure 12. Dissection of enthalpy contributions for IMD hydrolysis in water and 40% glycerol.
Figure 13. Dissection of entropy contributions for IMD hydrolysis in water and 40% glycerol.
E. Isokinetic and Isoequilibrium Temperature

Figure 14 shows a plot of $\Delta H^*$ versus $\Delta S^*$ for the hydrolysis of DMD and IMD. The values for DHD would fall off of the line. The equation for the line in Figure 14 is:\(^5\!\!^5\)

$$\Delta H^* = \Delta H^*_O + \beta \Delta S^*$$ \hspace{1cm} (63)

$\Delta H^*_O$ is the intercept and equal to $\Delta H^*$ when $\Delta S^*$ is zero. The free energy of activation is given in Equation 64.

$$\Delta G^* = \Delta H^* - T \Delta S^*$$ \hspace{1cm} (64)

Substituting for $\Delta H^*$ in Equation 64 gives:

$$\Delta G^* = \Delta H^*_O - (T - \beta) \Delta S^*$$ \hspace{1cm} (65)

When $T = \beta$, $\Delta G^* = \Delta H^*_O$ and all the rates are equal. A similar relationship holds for $\Delta H^O$ and $\Delta S^O$. Figure 15 shows $\Delta H^O$ plotted versus $\Delta S^O$. The slope, $\beta$, for Figure 14 is called the isokinetic temperature and the slope for Figure 15 is called the isoequilibrium temperature. The slope for Figure 14 is $322^0K (49 \pm 3^0C)$ and the slope for Figure 15 is $311^0K (39 \pm 4^0C)$.

This can be interpreted to mean that at the isokinetic or isoequilibrium temperature the hydrophobic hydration is already melted off so that the addition of glycerol to the solution does not affect the rate or equilibrium. That both the isokinetic and isoequilibrium temperatures are within experimental error of each other indicates that the changes in enthalpies and entropies of activation are due to changes in the ground state.
Figure 14. Enthalpy-entropy relationship for the hydrolysis of IMD and IMD in water-glycerol mixtures. ○ IMD ● IMD □ 2-ethyl-2-methyl-1,3-dioxolane (Ref. 16).
Figure 15. Enthalpy-entropy relationship for the transfer of DMD from water to water-glycerol mixtures.
V. SUMMARY

It appears that the use of a cosolvent such as glycerol provides a twofold approach to the problem of hydration. \( \omega_g \)-Values \( \omega_g = \frac{d \log k_{obs}/(H^+)/d \log a_{H_2O}}{} \) seem to be a rough measure of the hydration change between reactants and the transition state. These \( \omega_g \)-values are dependent upon the structure of the compound and on temperature. Methyl groups at the 2 position promote hydrophobic hydration in the ground state. This hydration is disrupted by the positive charge of the transition state. A group such as isopropyl insulates this hydration from the effect of the positive charge. Values of \( \delta T^{\omega_g} \) give an indication of how much hydrophobic hydration is involved with each compound.

The addition of glycerol to the solution breaks up some of the ground state hydration and the energy requirements are less in water-glycerol solutions. The standard partial molar quantities for the transfer of 2,2-dimethyl-1,3-dioxolane from water to water-glycerol solutions provides evidence that the lower energy requirement is primarily a ground state effect.

The entropy of activation appears to be dependent upon the number of methyl groups that promote hydrophobic hydration in the ground state. When this hydration is disrupted in the transition state it is reflected in a more positive \( \Delta S^* \).

The isokinetic and isoequilibrium temperature also supports the idea that the ground state hydration is being disrupted with the addition of glycerol.
VI. APPENDICES

A. Appendix A

The errors for the activation parameters were calculated by determining the standard deviation of the slope for plots of 
\( \ln k_{\text{obs}}/(H^+) \) vs. \( 1/T \). The equation for the line will be:

\[
y = mx + b
\]  
(1)

where \( y = \ln k_{\text{obs}}/(H^+) \), \( x = 1/T \), \( m = \) slope \( , \) and \( b = \) intercept.

The standard deviation of the slope was calculated by means of Equations 2 and 3.\(^{56}\)

\[
S^2 = \frac{\sum y^2 - b \sum y - m \sum xy}{n - 2}
\]  
(2)

Where \( n = \) number of points.

\[
\text{standard deviation} = \sqrt{\frac{S^2}{\sum x^2 - (\sum x)^2/n}}
\]  
(3)

The 50% confidence limit was obtained by multiplying the standard deviation by the proper "Student's t value."\(^{57}\)

The errors in \( \Delta G^* \) are calculated by estimating a 5% error in the rate constant. The errors in \( \Delta S^* \) are calculated as outlined in Reference 12.

\[
Te_{S} = \sqrt{e_H^2 + e_G^2}
\]  
(4)

The errors for the partial molar quantities were calculated in the same way except a 10% error was assumed for the equilibrium constant.
B. Appendix B

The computer program listed on the following pages was written in Fortran IV and can be used on the IBM 7040 or the IBM 360 computer. The program was used to calculate the activation parameters. It was slightly modified to calculate the partial molar quantities.
C
C THIS PROGRAM WILL CALCULATE THE ENERGY OF ACTIVATION, ENTHALPY OF
ACTIVATION, THE FREE ENERGY OF ACTIVATION, AND THE ENTROPY OF
ACTIVATION. N IS THE NUMBER OF POINTS, T IS THE TEMPERATURE FOR
THE FREE ENERGY CALCULATION, AND Z IS THE RATE AT T.
C
1 DIMENSION TEMP (50), RATE (50), X (50), Y (50)
2 1 READ(5, 8) NMBR, CMPD, GLYC, RTES
4 8 FORMAT (I5, A5, F5.0, A5)
5  READ(5, 2) N, T, Z
7 2 FORMAT(I5, F5.0, F10.0)
10 WRITE(6, 25)
11 25 FORMAT (1H)
12 WRITE(6, 40) NMBR, CMPD, GLYC, RTES
13 40 FORMAT (6H NO = , I5, 12H COMPOUND = , A5, 12H GLYCEROL = , F5.3, 12H
1 RATE = , A5)
14 WRITE(6, 25)
15 3 READ(5, 4) (TEMP(J), J = 1, N)
22 4 FORMAT (1 of 8.0)
23 5 READ(5, 4) (RATE(J), J = 1, N)
30 360 SUMY = 0.0
31 SUMX = 0.0
32 SUMXY = 0.0
33 SUMYY = 0.0
34 SUMXX = 0.0
35 I = 1
36 DO 20 J = I, N
37 X(J) = TEMP(J)**(-1)
38 Y(J) = ALOG (RATE(J))
40 SUMX = SUMX + X(J)
DIF
42 SUMY = SUMY + Y(J)
43 SUMXX = SUMXX + X(J)*X(J)
44 SUMYY = SUMYY + Y(J)*Y(J)
45 20 SUMXY = SUMXY + X(J)*Y(J)
47 G = FLOAT (N-I + 1)
50 SLOPE = (G*SUMXY-SUMX*SUMY)/(G*SUMXX-SUMX*SUMX)
51 B= (SUMX*SUMXY - SUMY*SUMXX)/(SUMX*SUMX - G*SUMXX)
52 S = (SUMYY -(B*SUMY)- SLOPE*SUMXY)/(G - 2.)
53 R = 1.9872
54 DEV =(SQRT(ABS(S/(SUMXX-(SUMX*SUMX/G)))))*R
55 WRITE(6,26)
56 26 FORMAT(47HO TEMP RATE CALC DIF )
57 WRITE(6,25)
60 DO 27 J = I,N
61 CALC = EXP(SLOPE*X(J)+B)
62 DIF = RATE(J) - CALC
63 27 WRITE(6,28) TEMP(J), RATE(J), CALC, DIF
65 28 FORMAT (3H ,F7.2, F12.5, F14.5, F12.5)
66 WRITE(6,25)
67 FACT =-R*SLOPE
68 HACT = FACT - R*T
70 C = 6.6238*10.**(-27)
72 A = 1.3802*10.**(-16)
73 FACT =-R*T*(ALOG((C*Z)/(A*T)))
74 SACT =(HACT-FACT)/T
75 WRITE(6,30) EACT, DEV, HACT, FACT, SACT
76 30 FORMAT (8H EACT = ,F6.0, 14H STD DEV = ,F7.1, 8H HACT = ,F6.0/
78 FACT = ,F6.0/ 8H SACT = ,F6.21)
77 IF (NMBR) 33,1,1
100 33 STOP
101 END
VII. BIBLIOGRAPHY

29. L. L. Schaleger and N. Watamori, unpublished work.
32. Reference 10, Chapter 2.


