At high concentrations the exponential decay on the − to + cycle results from having only reactions 1, 4, 5, and 7 participating in the ecl process. On the + to − cycle, when the radical anion diffuses away from the electrode surface it can encounter $P\cdot^+$, A, B, or C. Because B and C are not electroactive, they will have simple exponential distributions from the electrode into the solution. The concentrations of both $P\cdot^+$ and A will be zero at the electrode surface and go through a maximum at some distance from the electrode surface. The concentration of $P\cdot^+$ near the electrode surface will be greater than that of A because of moderate cation stability. But at distances further out into solution, the relative concentration of A will increase. As $P\cdot^-$ diffuses away from the electrode it will first encounter mostly $P\cdot^+$ giving reaction 5, but with increasing amounts of A, giving reaction 6. This could easily cause an increase in luminescence intensity with time. However, Q, the product of reaction 6, will start to accumulate in solution and will be available to quench the reaction, resulting in the abrupt decrease in intensity as shown in Figure 3.

At higher excitation frequencies the concentration distance profiles of all species will be compressed. There will be less time for reactions 2 and 3 to occur and the probability of $P\cdot^-$ encountering $P\cdot^+$ as it diffuses away from the electrode surface will be increased.

Acknowledgments. This work was supported in part through funds provided by the U. S. Atomic Energy Commission under Contract No. AT (30-1)-905. T. C. W. thanks the National Institutes of Health and the Proctor and Gamble Company for fellowship support. We thank L. N. Klatt for helpful discussions.

Medium Effects on the Activation Parameters for A-1 Dioxolane Hydrolysis in Water–Glycerol Mixtures[1]

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Abstract: Kinetic data for the A-1 hydrolysis of 2,2-dimethyl-1,3-dioxolane (**1**), 2-isopropyl-2-methyl-1,3-dioxolane (**2**), and 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane (**3**) in 0, 10, 20, 30, and 40 wt % aqueous glycerol at temperatures from 20 to 45° have been collected. The partial molar free energy and enthalpy of transfer of **1** from water to 40% glycerol have been measured, permitting the medium effects on the activation parameters to be dissected into ground- and transition-state contributions. It is found that both contributions are important. The directions of these changes are discussed in terms of the effects of glycerol, cations, and the nonpolar residues of organic solutes upon the structure of liquid water. The significance of these results with respect to the entropy criterion of mechanism is discussed. The partial molar enthalpy of transfer of **3** from water to 40% glycerol has been determined and the medium effect upon its enthalpy of activation dissected.

Kinetic solvent effects upon organic reactions taking place in aqueous media are not well understood. This is largely because the properties of liquid water, and the often dramatic changes in those properties which occur upon the addition of solutes, defy rigorous theoretical description. Although the Hughes–Ingold theory of solvent effects[3] is often able to predict the direction and approximate magnitude of medium effects on free energies of activation, $\delta_M\Delta G^*$, it has proven totally inadequate in dealing with enthalpies and entropies of activation, which parameters are not only more sensitive to solvent changes but are correspondingly more informative. The failure of electrostatic theory has been shown to be due in part to neglect of neutral solute–water interactions which can be more important energetically than ion–water interactions.[4–6]

To learn more about the part played by the aqueous solvent in the activation process, we have initiated a study of kinetic solvent effects on simple acid-catalyzed reactions in water–glycerol mixtures. Unlike the monohydric alcohols, which behave as "soluble hydrocarbons" in dilute solution in water,[7] glycerol forms relatively ideal aqueous mixtures.[8] The available evidence[9] indicates that the structure of liquid water is gradually disrupted with the addition of increasing amounts of glycerol. Glycerol is also a good ionizing solvent, the dielectric constants at 25° of pure and 50 wt % glycerol being 40 and 64, respectively.[10]

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[1] (a) Taken from the Ph.D. Thesis of C. N. R., 1968. Portions of this material have appeared elsewhere: L. L. Schaleger, C. N. Richards, and N. Watamori, Abstracts, 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., 1967, p O 176; *Chem. Commun.*, 381 (1966). (b) Work supported in part by the National Science Foundation (Grant No. GP-7392) and by the Petroleum Research Fund, administered by the American Chemical Society (Grant No. 351-G). Grateful acknowledgment is made to that foundation and to the donors of that fund.

[2] NDEA Title IV Predoctoral Fellow in Chemistry, 1966–1968.

[3] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter 7.

[4] E. M. Arnett, W. G. Bentrude, J. J. Burke, and P. M. Duggleby, *J. Amer. Chem. Soc.*, **87**, 1541 (1965).

[5] E. M. Arnett in "Physico-Chemical Processes in Mixed Aqueous Solvents," F. Franks, Ed., American Elsevier, New York, N. Y., 1967, pp 105 ff, and references cited therein.

[6] R. E. Robertson, *Progr. Phys. Org. Chem.*, 4, 213 (1967).

[7] F. Franks and D. J. G. Ives, *Quart. Rev., Chem. Soc.*, **20**, 1 (1966).

[8] R. H. Stokes and R. A. Robinson, *J. Phys. Chem.*, **70**, 2126 (1966); R. A. Robinson and R. A. Stokes, "Electrolyte Solutions," 2nd ed, Butterworths, London, 1959, pp 241–245.

[9] L. L. Schaleger and N. Watamori, *J. Phys. Chem.*, 73, 2011 (1969).

[10] H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd ed, Reinhold, New York, N. Y., 1958, p 161.

Table I. w Values for Dioxolane Hydrolysis[a]

Temp, °C	Compound DMD (**1**)	 IMD (**2**)	 DHD (**3**)
20.0 ± 0.1	−3.94 ± 0.33[b]		
25.0	−3.54 ± 0.14[c]	−1.81 ± 0.71[d]	−2.78 ± 0.29[e]
30.0	−2.71 ± 0.21		
35.0	−2.54 ± 0.15		
40.0	−1.22 ± 0.08		
45.0	−1.04 ± 0.21	−0.23 ± 0.22	−2.22 ± 0.19

[a] w is the least-squares gradient of a plot of log (k_{obsd}/c_{H^+}) *vs.* log a_{H_2O}. [b] Probable error. [c] At 25° in water, $k_2 = 0.151\ M^{-1}\ sec^{-1}$. [d] At 25° in water, $k_2 = 0.158\ M^{-1}\ sec^{-1}$. [e] At 25° in water, $k_2 = 0.0381\ M^{-1}\ sec^{-1}$.

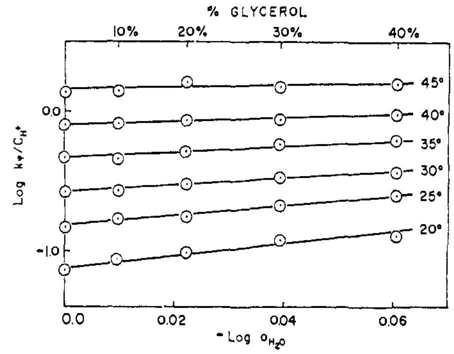


Figure 1. Variation of k_{obsd}/c_{H^+} for DMD hydrolysis with glycerol content of the medium at various temperatures.

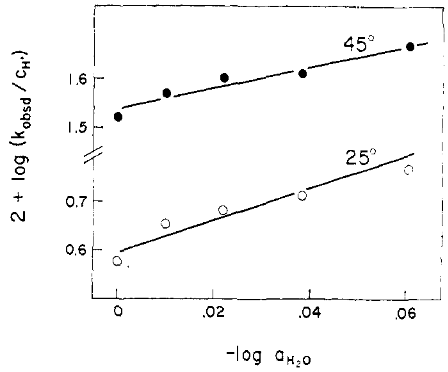


Figure 3. Variation of k_{obsd}/c_{H^+} for DHD hydrolysis with glycerol content of the medium at 25 and 45°.

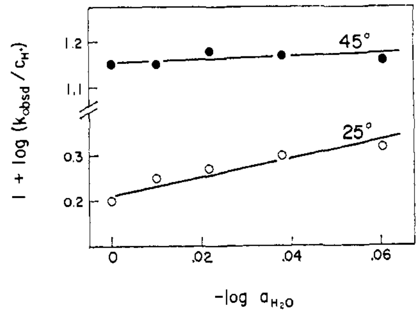
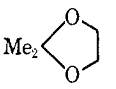


Figure 2. Variation of k_{obsd}/c_{H^+} for IMD hydrolysis with glycerol content of the medium at 25 and 45°.

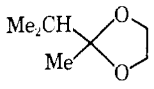
Therefore, ion-pair intermediates, the existence of which can have important kinetic consequences,[11] are not expected to be sufficiently long-lived to be detectable at the concentrations and ionic strengths employed in this study.

Solvent and temperature effects on the hydrogen-ion-catalyzed kinetics of the deoxymercuration of $CH_3OCH_2CH_2HgI$ and $HOCH_2CH_2HgI$ in water-glycerol mixtures have recently been reported.[9] It was found that the medium effect on the ratio of rate constants, δ_M log k_1/k_2, was mirrored by that on the ratio of substrate solubilities, δ_M log S_1/S_2, implying that the former arises as a result of changes in the nature of solvent-ground state rather than solvent-transition state interactions. Significantly, ΔH^* and ΔS^* were medium invariant for both substrates.

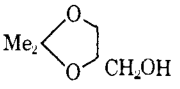
We now report solvent and temperature effects on the hydrolysis kinetics of 2,2-dimethyl-1,3-dioxolane (**1**, DMD), 2-isopropyl-2-methyl-1,3-dioxolane (**2**, IMD), and 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane (**3**, DHD). Some of the thermodynamic properties of transfer of **1** and **3** from water to 40% glycerol have also been determined.



1(DMD)



2(IMD)



3(DHD)

Results

Log-log plots of the second-order rate constants k_2 for the hydrolysis of **1–3** (obtained by dividing the pseudo-first-order rate constant by the stoichiometric hydrogen ion concentration) *vs.* the activity of water in solvents containing 0–40 wt % glycerol are shown in Figures 1–3. These are formally analogous to Bunnett plots[12] of log (k_{obsd}/h_0) *vs.* log a_{H_2O} for reaction kinetics in moderately concentrated aqueous mineral acid media. In keeping with earlier usage, a solvation parameter w has been defined as d log (k_{obsd}/c_{H^+})/d log a_{H_2O}; w values for **1–3** are reported in Table I. It is interesting that Bunnett's w values for acetal hydrolysis in 1–4 M aqueous perchloric acid,[12] which vary from about −1 to −4, are on the same order as the values reported in Table I.

The effect of glycerol on ΔH^* and ΔS^* for the hydrolysis of **1–3** is shown in Table II. These parameters and associated errors were evaluated by least-squares regression analysis, as reported previously.[9]

The distribution of DMD between an isooctane layer and a water or water-glycerol layer at 25° was followed by vapor phase chromatography to analyze the initial (c_{org}^0) and equilibrium (c_{org}) concentrations of DMD in the organic phase. The distribution constant K_D, defined as the molar concentration ratio of

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(11) H. Weiner and R. A. Sneen, *J. Amer. Chem. Soc.*, **87**, 287, 292 (1965).

(12) J. F. Bunnett, *ibid.*, **82**, 499 (1960); **83**, 4956 (1961).

Table II. Activation Parameters for Hydrolysis of Dioxolanes in Water–Glycerol Mixtures at 25°

Wt % glycerol	DMD	IMD	DHD
	ΔH^*, kcal mol^{-1} [a]		
0	20.7 ± 0.2[b]	20.0 ± 0.4	19.3 ± 0.4
10	19.5 ± 0.3	18.9 ± 0.1	19.3 ± 0.8
20	19.7 ± 0.3	19.7 ± 0.4	19.5 ± 0.6
30	17.9 ± 0.3	18.3 ± 0.1	18.9 ± 0.3
40	17.6 ± 0.3	17.6 ± 0.6	19.0 ± 0.1
	ΔS^*, cal mol^{-1} deg^{-1} [a]		
0	7.1 ± 0.7[b]	4.8 ± 1.3	-0.1 ± 1.3
10	3.5 ± 1.0	1.4 ± 0.5	-0.1 ± 2.7
20	4.3 ± 1.0	2.2 ± 0.5	$+0.8 \pm 2.0$
30	-1.6 ± 1.0	-0.3 ± 0.7	-1.1 ± 1.0
40	-2.4 ± 1.0	-2.5 ± 2.0	-0.4 ± 0.5

[a] Error limits are probable errors (see ref 9). [b] Kankaanpera reports $\Delta H^* = 21.0$ kcal mol^{-1} and $\Delta S^* = +7.9$ cal mol^{-1} deg^{-1} for DMD: A. Kankaanpera, *Ann. Univ. Turku, Ser. A1*, **95**, 1 (1966).

DMD in the aqueous phase (c_{aq}) to DMD in the organic phase (c_{org}) was found not to change when $c_{org}{}^0$ was varied from 0.2 to 0.5 *M*. The data of Table III indicate that DMD is rather less soluble in aqueous glycerol than in water. The data can be fitted to the equation

$$\log K_D = 6.24 \log a_{H_2O} - 0.191$$

Table III. Constants for Distribution of DMD between Isooctane and Water or Water–Glycerol Mixtures at 25°

Wt % glycerol	K_D (exptl)[a]	K_D (calcd)
0	0.660 ± 0.022[b]	0.664
10	0.533 ± 0.003	0.555
20	0.393 ± 0.000	0.471
30	0.371 ± 0.009	0.373
40	0.298	0.270

[a] Defined as c_{aq}/c_{org}. [b] Average deviation from the mean of two or more experiments.

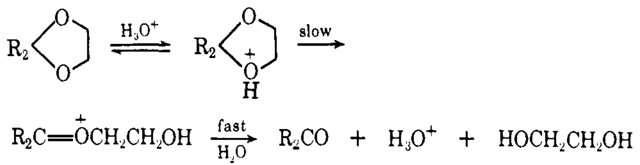
Agreement between values calculated from this expression and experiment is shown in Table III. The free energy of transfer from water to 40% glycerol, $\Delta\bar{G}_{t(0\rightarrow40)}$, for DMD is 515 cal mol^{-1}.

The heat of solution of DMD at 25° was determined by calorimetry to be -2.89 ± 0.03 kcal mol^{-1} in H_2O and -0.84 ± 0.02 kcal mol^{-1} in 40% glycerol. The heat of transfer, $\Delta\bar{H}_{t(0\rightarrow40)}$, is 2.05 ± 0.04 kcal mol^{-1}, and the entropy of transfer is therefore +5.1 cal mol^{-1} deg^{-1} on the molar scale.

The heats of solution of DHD at 25° are -3.35 ± 0.05 and -1.25 ± 0.06 kcal mol^{-1} in H_2O and 40% glycerol, respectively, giving a value of 2.10 ± 0.08 kcal mol^{-1} for $\Delta\bar{H}_{t(0\rightarrow40)}$.

Discussion

The hydrolysis of simple ketals takes place by way of the A-1 reaction mechanism[13]



$$R_2C{=}\overset{+}{O}CH_2CH_2OH \xrightarrow[H_2O]{fast} R_2CO + H_3O^+ + HOCH_2CH_2OH$$

One troublesome feature of water–alcohol solvent systems is the possibility of the alcohol becoming mechanistically involved.[13] In the present study, glycerol could conceivably compete for the intermediate carbonium ion leading to ketal interconversion; diminution of the water content might concomitantly cause the attack of water on the carbonium ion to become rate determining. This possibility seems unlikely since the media employed were highly aqueous, containing not more than 12 mol % glycerol. The linearity of rate *vs.* composition of ΔH^* *vs.* ΔS^* plots (see below) would seem to rule against any such cosolvent-induced change of mechanism in these solvents.[13b]

Despite structural similarities among **1**, **2**, and **3**, their activation parameters for hydrolysis show significant differences. Although *w* values are negative for all three compounds at every temperature of measurement, those for DMD hydrolysis are much more sensitive to temperature than those for IMD hydrolysis, whereas those for the hydrolysis of DHD are virtually independent of temperature.

The positive response of *w* to temperature is reflected by a downward trend in ΔH^* and ΔS^* with increasing glycerol content. Figure 4 shows that the well-known phenomenon of compensation[14] between ΔH^* and

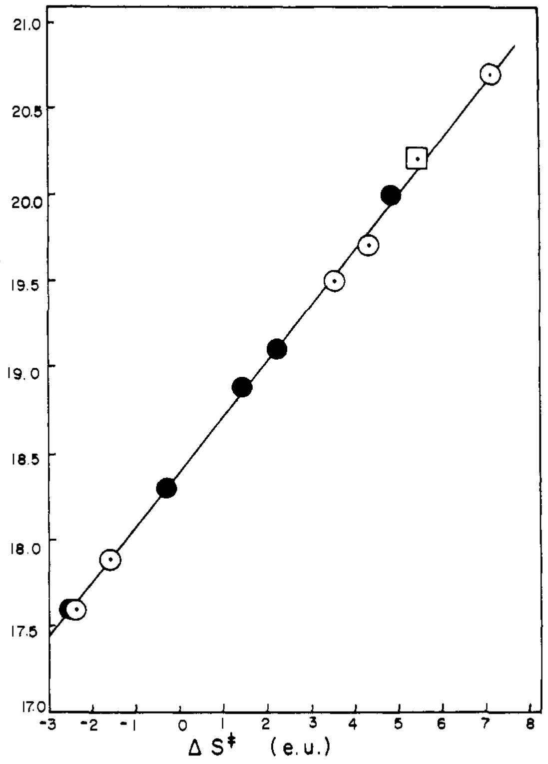


Figure 4. Correlation of ΔH^* and ΔS^* for hydrolysis of DMD (●) and IMD (○) in 0–40 wt % glycerol and for hydrolysis of 2-ethyl-2-methyl-1,3-dioxolane (□) in water.

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(13) (a) E. H. Cordes, *Progr. Phys. Org. Chem.*, 4, 1 (1967); (b) A. M. Wenthe and E. H. Cordes, *J. Amer. Chem. Soc.*, 87, 3173 (1965), have shown that carbonium ion formation remains largely rate determining in the hydrolysis of $Me_2C(OMe)_2$ in the rather less aqueous solvent, equimolar CD_3OD–D_2O.

(14) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963, Chapter 9.

ΔS^* is operative for DMD and IMD but not for DHD. The value of the slope, β, is 322°. The unusual feature of Figure 4 is that a double correlation exists, the lines for DMD and IMD being coincident. In fact, the corresponding point[15] for hydrolysis of a third compound, 2-ethyl-2-methyl-1,3-dioxolane (**4**), also falls on the line. The existence of such a multiple correlation strongly suggests[16] that a single interaction mechanism,[17] presumably solvational in character, dominates the cooperative changes in ΔH^* and ΔS^* that occur as a result of medium effects and, within this series, *as a result of substituent effects.* If other interaction mechanisms such as internal steric, inductive, or hyperconjugative effects were important here, dispersion into discrete lines would result.[14,18]

A second interaction mechanism is apparently operative in the hydrolysis of DHD, since its activation parameters are not correlated by the line in Figure 4. To test whether the exceptional behavior of DHD is due to some special function of the hydroxymethyl group (such as intramolecular nucleophilic assistance), the Taft $\rho^*\sigma^*$ plot shown in Figure 5 for reactions of various 4-substituted 2,2-dimethyl-1,3-dioxolanes in water was constructed. The data for this plot are given in Table IV. A good straight line is obtained with $\rho^* = -1.1$, about as expected for an A-1 mechanism. The point for DHD (**3**) falls on the line showing that, steric effects being equal, the influence of the hydroxymethyl group is purely inductive.[19] However, the fact that DMD reacts faster and 2,2,4,4,-tetramethyl-1,3-dioxolane reacts slower than predicted (see Figure 5) deomonstrates the existence of a rate-retarding steric interaction as previously pointed out.[16,20]

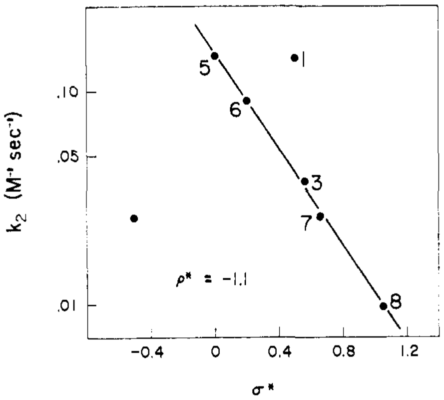

Figure 5 Taft plot of log k_2 *vs.* σ^* for hydrolysis of 4-substituted 2,2-dimethyl-1,3-dioxolanes in H_2O at 25°. The compounds are identified in Table IV. The unidentified point showing a large negative deviation from the line is for the reaction of 2,2,4,4-tetramethyl-1,3-dioxolane.

Table IV. Substituent Effects on Rates of Hydrolysis of 4-Substituted 2,2-Dimethyl-1,3-dioxolanes in H_2O at 25°

4 substituent	$10k_2$, M^{-1} sec^{-1}	σ^*
Dimethyl	0.25	−0.49
Methyl (**5**)	1.46[a]	0
CH_2CH_2OH (**6**)	0.87[b]	0.20[c]
Hydrogen (**1**)	1.51[d]	0.49
CH_2OH (**3**)	0.38[d]	0.56
CH_2OMe (**7**)	0.60[a]	0.65
CH_2Cl (**8**)	0.098[a]	1.05

[a] Reference 15. [b] L. L. Schaleger and K. Inn, unpublished work. [c] Obtained by dividing σ^* for CH_2OH by 2.8. Other σ^* values are from R. W. Taft in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, p 619. [d] This work.

These medium effects can in principle be resolved into their ground-state and transition-state components if independent thermodynamic data for the ground state are obtained.[4] The following equation applies to the present case

$$\Delta P^*(\text{aq glycerol}) - \Delta P^*(H_2O) = \Delta\bar{P}_t^{\,TS} - \Delta\bar{P}_t^{\,S} - \Delta\bar{P}_t^{\,HClO_4} \quad (1)$$

where ΔP^* is an activation parameter and the $\Delta\bar{P}$'s are partial molar quantities of transfer of transition state, substrate, and $HClO_4$ from water to aqueous glycerol.

The free energy transfer of $HClO_4$ from water to 40% glycerol, $\Delta\bar{G}_{t(0\rightarrow 40)}{}^{HClO_4}$, is not available. However, the corresponding number for HCl may be estimated from Harned and Nestler's emf measurements[21] in 50% glycerol by assuming proportionality between $\Delta\bar{G}_t$ and log a_{H_2O}. At 25°, $\Delta\bar{G}_{t(0\rightarrow 50)}{}^{HCl}$ and $\Delta\bar{G}_{t(0\rightarrow 40)}{}^{HCl}$ thus are +815 and +525 cal mol^{-1}, respectively, on the molar scale. Although the possibility of a large anion effect cannot be dismissed, +500 cal mol^{-1} is probably a reasonable estimate of $\Delta\bar{G}_{t(0\rightarrow 40)}{}^{HClO_4}$. The corresponding enthalpy of transfer of perchloric acid has recently been determined[22] to be 100 ± 30 cal mol^{-1}. The combination of these activation and transfer quantities according to eq 1 permits the partial quantities of transfer of the transition states for DMD and DHD to be estimated. These numbers are given in Table V.

Table V. Thermodynamic Quantities of Transfer from Water to 40% Glycerol at 25°

Species	$\Delta\bar{G}_t$, kcal mol^{-1}	$\Delta\bar{H}_t$, kcal mol^{-1}	$\Delta\bar{S}_t$, cal mol^{-1} deg^{-1}
$HClO_4$	(0.5)[a]	0.10 ± 0.03[b]	(−1)
DMD	0.5 ± 0.1	2.05 ± 0.04	5.1 ± 0.3
$(DMD)_{TS}$[c]	0.7 ± 0.3	−1.0 ± 0.4	−5.7
DHD		2.10 ± 0.08	
$(DHD)_{TS}$[c]		1.9 ± 0.5	

[a] Estimated value; see text. [b] Reference 22. [c] These refer to the transition states in DMD and DHD hydrolysis.

Table V shows that added glycerol destabilizes both hydronium ion and the cationic transition state for DMD hydrolysis to approximately the same extent. The transition states in the acid-catalyzed deoxy-

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(15) A. Kankaanpera, *Ann. Univ. Turku, Ser. A1*, **95**, 1 (1966).

(16) Reference 14, pp 342–347.

(17) Reference 14, p 141.

(18) C. D. Ritchie and W. F. Sager, *Progr. Phys. Org. Chem.*, **2**, 323 (1964).

(19) The same approach has been used previously to show that DHD as well as 2,2-dimethyl-1,3-dioxolane-4-carboxylic acid react *via* the normal A-1 mechanism: T. C. Bruice and D. Piszkiewicz, *J. Amer. Chem. Soc.*, **89**, 3568 (1967).

(20) P. Salomaa and A. Kankaanpera, *Acta Chem. Scand.*, **16**, 1532 (1962).

(21) H. S. Harned and F. H. M. Nestler, *J. Amer. Chem. Soc.*, **68**, 655 (1946).

(22) Private communication from Professor J. H. Stern.

mercuration of both $CH_3OCH_2CH_2HgI$ and $HOCH_2CH_2HgI$ were found to be similarly destabilized (400 cal mol^{-1}).[9] However, unlike the polar mercurials, both of which were found to be solubilized by added glycerol, DMD is considerably more soluble in water.

Because of the compensation phenomenon, changes in ΔH are small compared to those in ΔG or ΔS. Table V shows that the 3.1 kcal mol^{-1} decrement in ΔH^* for DMD hydrolysis is the result of the additive contributions of $\Delta\bar{H}_t^{DMD}$ (2.05 kcal mol^{-1}) and $-\Delta H_t^{TS}$ (1.0 kcal mol^{-1}). Similarly, the lowering of ΔS^* by 9.5 cal mol^{-1} deg^{-1} is due to the approximately equal contribution of $\Delta\bar{S}_t^{DMD}$ and $-\Delta\bar{H}_t^{TS}$. Electrostatic considerations appear relatively unimportant. Apparently added glycerol causes a strengthening of solvent–transition state interactions and a weakening of solvent–ground state interactions. By implication a similar situation may be presumed to hold in the hydrolysis of IMD and 2-ethyl-2-methyl-1,3-dioxolane.

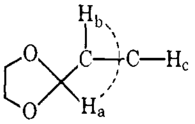
The hydrolysis of DHD, however, presents a somewhat different picture. The virtual absence of medium effects on ΔH^* and ΔS^* is seen from Table V to be due to a fortuitous cancellation of ground- and transition-state contributions. The dissimilar behavior of DHD is the result of a positive change in the partial molar enthalpy of the transition state. This may be related to the alleged rate-retarding steric effect of a substituent in the 4 position (see above). A comparative analysis of the kinetic medium effects on DHD and, say, 2,2-dimethyl-4-ethyl-1,3-dioxolane might be enlightening in this regard.

The results clearly direct attention to the importance of specific solute–solvent interactions; any explanation must take into account the peculiar nature of liquid water. Although a definitive theory of the structure of liquid water has yet to be formulated, several more or less elaborate models have been advanced.[23] We shall find it convenient to adopt a qualitative two-state model,[9, 24] wherein a bulky ice-like form is taken to be in dynamic equilibrium with a dense form of higher energy. The bulky form will be considered to be nearly saturated and the dense form relatively unsaturated with respect to capacity for additional hydrogen bond formation.

According to this model, glycerol behaves as a structure breaker because it is predisposed to mix with, and thereby stabilize, the dense, unsaturated form of water. Nonpolar residues of organic solutes, on the other hand, are considered to be structure promoters,[25, 26] a hydrocarbon–"iceberg" interface being more favorable than one between a nonpolar surface and the dense, dipolar form of water. Such hydrophobic hydration, or promotion of water structure by nonpolar groups, was originally proposed[27] to account for the fact that the dissolution of gaseous hydrocarbons in water is an exothermic process.

The medium effect on DMD hydrolysis can be viewed accordingly: (i) DMD behaves as a structure maker in H_2O but not in 40% glycerol ($\Delta\bar{H}_t$ and $\Delta\bar{S}_t$ both positive) and (ii) the transition state is an apparent structure breaker in H_2O compared to aqueous glycerol ($\Delta\bar{H}_t$ and $\Delta\bar{S}_t$ both negative). Charges in general are thought to disrupt water structure.[26] This effect of charge should be of reduced importance in the mixed solvent and hence the transfer of transition state from water to the mixed medium is exothermic. In this view, the activation process for DMD hydrolysis in pure water involves a reorganization of nearest neighbor solvent molecules from an associated ice-like state to one in which charge–dipole and dipole–dipole attractive forces predominate.

It is now possible to account for the considerable effect which nonpolar substituents are known to exert on the entropy of activation for A-1 hydrolysis in water. The ground-state factor should be influenced both by the amount of hydrophobic surface exposed and the distance from that surface to the site of protonation. The effectiveness of charge in disrupting hydrophobic hydration should diminish rapidly with distance. In discussing the effects of substituents upon thermodynamic parameters for protonation of amines in water, Everett and coworkers[28] have assumed that the ionic charge destroys the hydrophobicity of nonacidic hydrogen atoms whose van der Waals envelopes lie within a radius of 3.5 Å from the center of charge. Examination of models shows that in dioxolanes protons of types a and b, but not of type c, would have their hydrophobicity neutralized by O-protonation.



The effect of substituents upon the transition-state solvation factor must also be considered. It is proposed that in the absence of steric shielding, $\Delta\bar{S}_t^{TS}$ for cationic transition states will be relatively immune to substituent effects. This has not been demonstrated, however. Steric shielding would have the effect of equalizing $\Delta\bar{S}_t^{GS}$ and $\Delta\bar{S}_t^{TS}$ if only solvational effects are involved.

We would like to propose, then, that the variations in ΔS^* that occur with 2-alkyl substitution in A-1 dioxolane hydrolysis[13, 15, 29] are governed mainly by the ground-state solvation factor. We might therefore expect a proportionality between ΔS^* and the number of protons of types a and b. The available data are presented in Table VI and Figure 6. It is seen that the correlation is satisfactory. Furthermore, the intercept of the plot, -1.5 eu, corresponding to what ΔS^* would be in the absence of hydrophobic hydration, agrees with the values of ΔS^* for hydrolysis of DMD, IMD, and DHD in 40% glycerol, a solvent in which hydrophobic interactions are not expected to play a major role.

Whatever the detailed interpretation, several general conclusions may be drawn from the present study. First, no general theory of solvent effects in aqueous media which ignores ground-state interactions is likely

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[23] For a recent authoritative review, see D. Eisenberg and W. Kauzmann, "The Structure and Properties of Liquid Water," Oxford University Press, New York, N. Y., 1969.

[24] H. S. Frank, *Fed. Proc. Fed. Amer. Soc. Exp. Biol., Suppl. 15*, **24** (2), 1 (1965).

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[27] H. S. Frank and M. W. Evans, *J. Chem. Phys.*, **13**, 507 (1945).

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[29] L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 1 (1963).

Table VI. Entropies of Activation (eu) for Hydrolysis of 2-R_1-2-R_2-1,3-Dioxolanes in H_2O at 25°

Compound R_1, R_2	n^a	ΔS^*	Ref
CH_3, CH_3 (**1**)	6	7.1	This work
CH_3, CH_3 (**1**)	6	7.9	15
CH_3CH_2, CH_3 (**4**)	5	5.4	15
$(CH_3)_2CH$, CH_3 (**2**)	4	4.8	This work
CH_3, H (**9**)	4	5.6	15
H, H (**10**)	2	1.4	15

[a] n is the number of protons of types a and b.

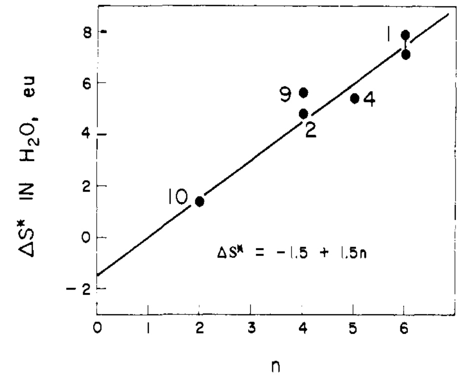

Figure 6. Variation of ΔS^* in H_2O for the compounds of Table VI with the number (n) of type a and b protons.

to be successful. Second, the suggestion that differences in entropies of activation for dioxolane hydrolysis owe more to solute–solvent interactions of a highly specific nature than to any gross internal feature of the reaction raises serious doubts as to the validity of drawing subtle mechanistic inferences from entropic considerations. It does appear, however, that much of this specificity may be washed out in less aqueous media. For example, we have found that the entropies of activation for the A-1 hydrolysis of seven substrates of various types which vary from −7 to +8 cal mol^{-1} deg^{-1} in H_2O are reduced to a common value of −1.6 ± 1.2 cal mol^{-1} deg^{-1} in 40% glycerol.[30] Whether ΔS^* will serve to distinguish among A-1, simple A-2, and A-SE2 mechanisms in such a mixed solvent in which the water structure factor is of reduced importance remains to be established.

Experimental Section

Materials. DMD purchased from the Aldrich Chemical Co. was redistilled from Na-NaOH prior to use. Alternatively it was prepared from acetone and ethylene glycol by the method of Legetter and Brown.[31] DHD was used as received from the Aldrich Chemical Co.

The 2-isopropyl-2-methyl-1,3-dioxolane was prepared by the method of Fife and Hagopian,[32] bp 131–134° (lit.[33] 123–132°).

Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.37; H, 10.80.

The preparation of glycerol and perchloric acid solutions has been described.[9]

Kinetics. The buildup of acetone (or methyl isopropyl ketone) was monitored at 265 (or 278) nm in a thermostated cell compartment of a Beckman DU-2 ultraviolet spectrophotometer.[9] Temperature could be controlled to within ±0.1° and was checked frequently.

Swinbourne's method[34] was used in the calculation of pseudo-first-order rate constants, k_{obsd}. Second-order rate constants were obtained by dividing k_{obsd} by the stoichiometric concentration of $HClO_4$. The latter never exceeded 2×10^{-3} M. Activation parameters and w values were computed by standard linear least-squares techniques.[9] The activities of aqueous glycerol solutions have been given by Scatchard, *et al.*[35] All reactions were shown to proceed to completion in 40% glycerol.

Distribution Measurements. A 0.40 M solution (5 ml) of DMD in reagent grade isooctane was placed in a Teflon screw-covered test tube with 7 ml of water or water–glycerol mixture. The aqueous phase was 10^{-3} M in NaOH to prevent hydrolysis. The tubes were placed in a mechanical shaker bath at 25.0 ± 0.5°. After shaking for 48 hr, the test tubes were centrifuged and 1 ml of the organic phase was withdrawn and analyzed by glc. The instrument employed was a Perkin-Elmer F11 flame ionization chromatograph fitted with a 200 ft × 0.01 in. open tubular column coated with Ucon-LB550X. Three or four samples of 0.8 μl were injected for each run; parallel analysis of the 0.40 M stock solution of DMD in isooctane provided a reference standard. Isooctane/DMD peak area ratios for the equilibrated sample, r_e, and the stock solution, r_0, were determined by cutting out the peaks from Xerox copies of the recorder trace and weighing. K_D was obtained from the expression $(5r_e/7r_0)(1 - r_0/r_e)$. The constancy of K_D was not affected by varying the initial concentration of DMD from 0.20 to 0.50 M.

The adiabatic solution calorimeter had been described.[4] Three or more 100-μl portions of thermally equilibrated liquid ketal from a calibrated Hamilton gas-tight syringe were injected into 220 ml of solvent contained in the calorimeter and held at 25 ± 1°.

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