

Comparison of Solvent Effects in *A*-1 and *A*-S_E2 Reactions

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Solvent effects have been studied by measuring the rates of hydrolysis of 2-methyl-1,3-dioxolane (*A*-1 mechanism) and 2-methyl-4-methylene-1,3-dioxolane (*A*-S_E2 mechanism) in water-dioxane and water-dimethyl sulfoxide mixtures. The kinetic data revealed that the solvent effects are almost identical in these reactions. This apparent similarity is discussed on the basis of the effects of solvent composition on the transition states of the reactions.

Although hydrolysis reactions in which proton transfer is a pre-equilibrium process (*A*-1) have been thoroughly studied in different solvents,¹ only limited information is available on the influence of solvent on hydrolysis reactions in which the proton transfer is rate determining (*A*-S_E2). Kreevoy and Williams² studied the *A*-S_E2 hydrolysis of ethyl vinyl ether in water-dimethyl sulfoxide mixtures and found that the rate coefficient varies with solvent composition in a way typical for *A*-1 reactions. They did not, however, suggest any reason for this similarity.

The purpose of this investigation was to collect further information on solvent effects in rate-determining proton transfer reactions and to compare these solvent effects with those in *A*-1 reactions. The model compounds chosen for the kinetic study were the structurally similar compounds, 2-methyl-1,3-dioxolane and 2-methyl-4-methylene-1,3-dioxolane, which hydrolyze by the *A*-1 and *A*-S_E2 mechanism, respectively. It was assumed that solvents have similar solvation effects on the substrates because of their structural similarity and it was therefore expected that information would be obtained on the effects of solvent composition on the transition states of the *A*-1 and *A*-S_E2 reactions.

EXPERIMENTAL

The dimethyl sulfoxide used as solvent in the kinetic experiments was purified thoroughly. The commercial product (E. Merck AG) was first distilled from calcium hydride at reduced pressure so that the boiling point did not exceed 50°C. Only the middle fraction was purified further. To remove water from the distillate, the latter was crystallized by freezing it three times during which the melting point rose to 18.45°C. By studying the effect of added water on the melting point of dimethyl sulfoxide, it

could be verified that the mol fraction of water in the purified product was less than 0.02. The water content remained unaltered during storage of the solvent in Teflon-stoppered glass flasks. Dioxane was purified by the standard method.³

2-Methyl-4-methylene-1,3-dioxolane was prepared by dehydrohalogenation of 2-methyl-4-chloromethyl-1,3-dioxolane.⁴ It boiled at 93–96°C/769 torr and had a refractive index n_D^{20} of 1.4232. 2-Methyl-1,3-dioxolane was the preparation used in previous studies.⁵ *m*-Nitroaniline was a commercial product from The British Drug Houses Ltd.

Water and dimethyl sulfoxide-water and dioxane-water mixtures were used as solvents in the kinetic experiments. The catalyst acid was perchloric acid; its concentration in the reaction mixtures did not exceed 0.15 M.

5 ml of acid solution was warmed to 25.0°C. 5–16 μ l of the hydrolyzing compound was added and the mixture was shaken vigorously. A part of the mixture was transferred with a thermostated pipet to the cell of a Unicam SP. 800 spectrophotometer, the cell housing of which was held at $25 \pm 0.1^\circ\text{C}$ and the formation of acetaldehyde was followed by measuring the absorbance at 275 nm at intervals. The rate coefficients were calculated from the measured absorbances. First-order kinetics was strictly obeyed in all cases.

The ratios of the protolytic forms of *m*-nitroaniline in water-dimethyl sulfoxide mixtures of varying acidity were measured by the spectrophotometric method.⁶ The concentration of *m*-nitroaniline was 5×10^{-4} M. The ratios were usually measured at six acid concentrations (0.001–0.05 M) in each solvent mixture. The perchloric acid was added to the solutions with an Agla microsyringe. The spectra of the neutral *m*-nitroaniline solution and the acid *m*-nitroaniline solutions in each solvent mixture were measured in the range 250–425 nm with a Beckman DK-2A Ratio Recording Spectrophotometer at $25 \pm 1^\circ\text{C}$. The equilibrium constants K_B^{25} in the various solvents were calculated by substituting the experimental data in eqn. (1), where A_B is the absorbance

$$K_B = \frac{A_B - A}{A - A_{BH^+}} \frac{1}{[H_3O^+]} \quad (1)$$

of *m*-nitroaniline in neutral solution, A its absorbance in acid solution, and A_{BH^+} the absorbance of protonated *m*-nitroaniline at the wavelength where the absorbance of the base was a maximum. The absorbance of the *m*-nitroanilium ion was taken to be equal to the absorbance of nitrobenzene under the same experimental conditions.

The addition of perchloric acid to solutions of *m*-nitroaniline in water produced a slight precipitate. Therefore the constants calculated by eqn. (1) from the experimental data for water solutions were plotted against the perchloric acid concentration for the evaluation of the dissociation constants at infinite dilution by extrapolation.

RESULTS AND DISCUSSION

Hydronium ion concentrations in DMSO-water and dioxane-water mixtures.

As the equilibrium and kinetic measurements were performed on solutions of varying perchloric acid concentration, we studied whether the hydronium ion concentrations are proportional to the perchloric acid concentrations under the experimental conditions. The hydronium ion concentrations were determined by measuring the rate coefficients of the *A*-1 hydrolysis of diethyl acetal in the solvents at 25°C. The second-order rate coefficients of these reactions are collected in Table 1.

The second-order rate coefficient is independent of the concentration of perchloric acid in DMSO-water mixtures when the concentration is less than 0.1 M. This is the case even when the mol fraction of dimethyl sulfoxide in the solvent is as high as 0.9. Kreevoy and Williams² studied the hydrolysis of ethyl vinyl ether in DMSO-water mixtures containing 69.8 and 92.5 mol % dimethyl sulfoxide using hydrochloric acid as the catalyst. They found the

Table 1. Second-order rate coefficients for the hydrolysis of diethyl acetal at 25.0°C in dimethyl sulfoxide-water and dioxane-water mixtures containing perchloric acid as catalyst.

Solvent mixture	Mol fraction of the organic component in the solvent	[HClO ₄] (M)	10 <i>k</i> (M ⁻¹ s ⁻¹)
DMSO-water	0.2	0.1	2.27
		0.05	2.28
		0.01	2.06
	0.4	0.1	0.497
		0.05	0.489
		0.01	0.496
	0.6	0.1	0.333
		0.05	0.340
		0.01	0.328
	0.8	0.1	0.295
		0.05	0.283
		0.01	0.268
	0.9	0.1	0.318
		0.05	0.312
		0.01	0.314
Dioxane-water	0.2	0.1	2.02
		0.05	2.00
		0.01	1.86
	0.4	0.001	1.81
		0.1	1.145
		0.05	0.886
	0.6	0.01	0.844
		0.001	0.660
		0.1	1.43
	0.8	0.05	1.20
		0.01	1.01
		0.001	0.823
	0.9	0.1	4.65
		0.05	3.26
		0.01	2.70
0.9	0.001	2.28	
	0.05	14.17	
	0.01	8.57	
		0.001	6.70

second-order rate coefficient to increase slightly with the total hydrochloric acid concentration in the first solvent mixture, but markedly in the second mixture.

The data in Table 1 reveal that in dioxane-water mixtures the hydronium ion concentration is directly proportional to the concentration of perchloric acid only in very dilute acid solutions (HClO₄ < 0.001 M). Thus the rates in solutions in which the acid concentration exceeded 10⁻³ M had to be extrapolated to infinite dilution to get comparable second-order rate coefficients. This procedure was applied also to the data for the hydrolysis of 2-methyl-1,3-dioxolane and 2-methyl-4-methylene-1,3-dioxolane. To avoid

Table 2. The acid-base equilibrium of *m*-nitroaniline in DMSO-water mixtures of varying perchloric acid concentration (< 0.09 M) at 25°C. λ_{\max} is the wavelength where the absorbance of *m*-nitroaniline is a maximum.

Mol fraction of DMSO	λ_{\max} (nm)	pK_{BH^+}
0.0004	357	2.455
0.0641	362	2.114
0.104	367	1.864
0.202	375	1.369
0.316	385	0.886
0.390	389	0.728
0.545	395	0.571
0.655	396	0.565
0.778	396	0.672
0.901	397	0.809

large corrections, relatively low perchloric acid concentrations (< 0.05 M) were used in the experiments.

Equilibrium constants. The results of the study of the protonation of *m*-nitroaniline in various DMSO-water mixtures at 25°C are collected in Table 2. The equilibrium constant is a minimum in the solvent containing about 60 mol % dimethyl sulfoxide. The pK_{BH^+} value of the protonated base is about 1.9 units smaller in this solvent than in water. Our data are in good agreement with Woldford's data^{1c} for the same equilibrium.

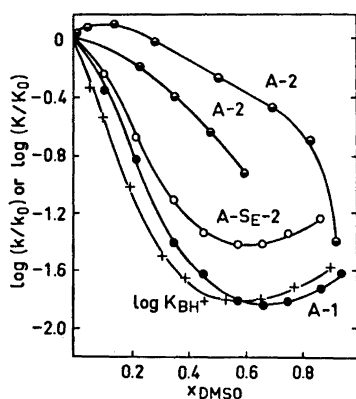


Fig. 1. Effect of solvent on the rates of acid-catalyzed reactions and on acid-base equilibria in dimethyl sulfoxide-water mixtures, 2-methyl-1,3-dioxolane (●), 2-methyl-4-methylene-1,3-dioxolane (○), ethyl acetate⁷ (⊖, upper plot), *t*-butyl acetate⁸ (⊖) and *m*-nitroanilinium ion (+). 25°C.

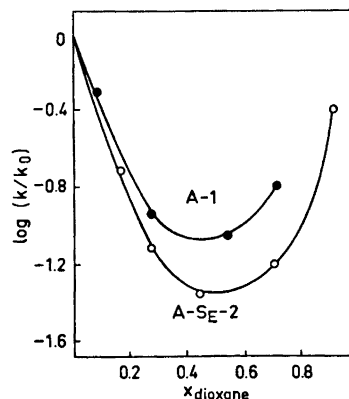


Fig. 2. The logarithms of the rate coefficients of the A-1 hydrolysis of 2-methyl-1,3-dioxolane (●) and the A-S_E2 hydrolysis of 2-methyl-4-methylene-1,3-dioxolane (○) in dioxane-water mixtures. 25°C.

Table 3. Second-order rate coefficients for the acid-catalyzed hydrolysis of 2-methyl-1,3-dioxolane (I) and 2-methyl-4-methylene-1,3-dioxolane (II) in dimethyl sulfoxide-water and dioxane-water mixtures at 25°C.

Compound	Mechanism	Solvent mixtures	Mol fraction of the organic component	10^3k (M ⁻¹ s ⁻¹)
I	A-1	DMSO-H ₂ O	0	13.5
			0.110	5.96
			0.220	2.02
			0.350	0.521
			0.453	0.329
			0.581	0.201
			0.662	0.186
			0.759	0.199
			0.873	0.241
			0.936	0.317
			II	A-S _E 2
0.110	3950			
0.223	1460			
0.355	538			
0.450	316			
0.579	261			
0.657	266			
0.750	299			
0.861	378			
0.926	429			
I	A-1	Dioxane-H ₂ O		
			0.0846	6.6
			0.275	1.5
			0.538	1.2
			0.713	2.2
			0.922	47
			0.922	47
II	A-S _E 2	Dioxane-H ₂ O	0	6830
			0.0846	3190
			0.166	1310
			0.275	520
			0.440	300
			0.707	430
			0.913	2800

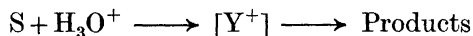
Rate coefficients. The second-order rate coefficients for the hydrolysis of 2-methyl-1,3-dioxolane and 2-methyl-4-methylene-1,3-dioxolane in DMSO-water and dioxane-water mixtures at 25°C are collected in Table 3. The logarithms of the relative rate coefficients are plotted against the mol fraction of DMSO in Fig. 1. The rates of the studied A-1 and A-S_E2 reactions pass through minima in solutions in which the mol fractions of dimethyl sulfoxide are about 0.6. The retardation of the A-S_E2 reaction is smaller than that of the A-1 reaction (by a factor of about 3 when the mol fraction of DMSO is 0.6). It is interesting to note in this context that, as revealed by the data for some A-2 reactions that are also plotted in Fig. 1,^{7,8} solvent effects are quite different in A-2 reactions. As shown previously, the differences in

solvent effects can be employed to distinguish between $A-S_E2$ and $A-2$ reactions,^{2,9} both of which show general acid catalysis.

The solvent effects are almost equal for the studied $A-1$ and $A-S_E2$ reactions in the dioxane-water mixtures (Fig. 2). The rate coefficients pass through minima when the protonation of dioxane is about 50 mol %. The retardation of the rate-determining proton transfer reaction with decreasing water content in dioxane-water mixtures is slightly greater than that of the $A-1$ reaction.

The measured pK_{BH^+} values of the *m*-nitroanilinium ion are also plotted in Fig. 1. The solvent effects are almost equal for the acid-base equilibrium and the hydronium ion-catalyzed reactions. Wolford^{1c} has previously found that the rate coefficients of the $A-1$ hydrolysis of diethyl acetal varies with solvent composition in the same manner as the pK_{BH^+} values of the *m*-nitroanilinium ion. Kreevoy and Williams² compared their rate coefficients for the $A-S_E2$ hydrolysis of ethyl vinyl ether in DMSO-water mixtures with the pK_{BH^+} values measured by Wolford.^{1c} Also in this case the solvent effects were similar.

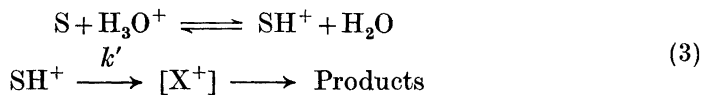
Comparison of solvent effects in acid-catalyzed reactions and in acid-base equilibria. To find a structural interpretation for the obvious similarity in the dependence of the rates of the $A-1$ and $A-S_E2$ reactions on solvent composition, the rate coefficients were expressed in terms of partial rate coefficients. The rate coefficient of the hydronium ion-catalyzed $A-S_E2$ hydrolysis



is given by eqn. (2)

$$k_{A-S_E2} = k_{A-S_E2}^\circ \frac{y_S y_{H_3O^+}}{y_{Y^+}} \quad (2)$$

where $k_{A-S_E2}^\circ$ is the standard rate coefficient. The molar activity coefficients y are defined to be unity in dilute solutions in water. The rate coefficient of the $A-1$ hydrolysis (eqn. 3) can be written



in the form

$$k_{A-1} = \frac{k'}{K_{SH^+}}$$

where

$$k' = k'^{\circ} \frac{y_{SH^+}}{y_{X^+}} \quad (4)$$

and

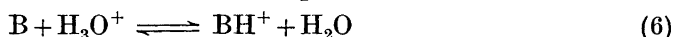
$$K_{SH^+} = K_{SH^+}^\circ \frac{y_{SH^+} f_{H_2O}}{y_S y_{H_3O^+}}$$

Thus

$$k_{A-1} = \frac{k'^{\circ}}{K_{SH^+}^\circ} \frac{y_S y_{H_3O^+}}{y_{X^+} f_{H_2O}} \quad (5)$$

The subscript H_2O in this equation may also be $(H_2O)_n$ or generally a solvent complex which donates the proton (see Ref. 2). The activity coefficients of water, f_{H_2O} , is referred to pure liquid water.

The equilibrium constant of the acid-base equilibrium



can be written in the form

$$K_{BH^+} = K_{BH^+}^\circ \frac{y_{BH^+} f_{H_2O}}{y_B y_{H_3O^+}} \quad (7)$$

The ratio of the rates of the $A-1$ and $A-S_{E2}$ reactions of the same substrate can be derived from eqns. (2) and (5):

$$\frac{k_{A-1}}{k_{A-S_{E2}}} = \text{constant} \times \frac{y_{Y^+}}{y_{X^+} f_{H_2O}} \quad (8)$$

As the ratio of the standard rate coefficients is constant, the ratio of the rates of $A-1$ and $A-S_{E2}$ hydrolyses depends on the activity coefficients on the transition states of the reactions and on the activity coefficients of water. Of course, this is only approximately true when the rate coefficients of hydrolysis of the studied 1,3-dioxolane derivatives are compared. As the compounds are closely related, however, it is reasonable to assume that the possible differences in the effects of solvents on the substrates can be neglected. Thus the ratios y_{X^+}/y_{Y^+} for the studied $A-1$ and $A-S_{E2}$ reactions in different solvents can be estimated by substituting the ratios of the measured rate coefficients and the activity coefficients of water in the solvents in eqn. (8). The rational activity coefficients of water in DMSO-water mixtures at 25°C have been calculated from vapor pressures measured at 70°C using the heats of mixing of water and dimethyl sulfoxide⁸⁻¹⁰ and the activity coefficients of water in dioxane-water mixtures from vapor pressures at 25°C.¹¹ The activity coefficients are listed in Table 4.

Let us first consider the kinetic data for the reactions in water-dimethyl sulfoxide mixtures. Values of the ratio y_{X^+}/y_{Y^+} , *i.e.* the ratio of the activity coefficients of the transition states of the $A-1$ and $A-S_{E2}$ reactions, in different solvent mixtures can be estimated from eqn. (8). The log k values were interpolated on the basis of the data in Fig. 1. The ratios of the activity coefficients shown in Table 4 reveal that the ratio increases by a factor of about six when going from pure water to the solvent in which the rate coefficients are at a minimum (60 mol % dimethyl sulfoxide). This difference in activity coefficients is so large that it cannot be due to experimental errors or to the approximations made.

As can be seen from the data in Table 4, the activity coefficient of water increases from 1 in pure water to about 4 in the dioxane-water mixture containing 90 mol % dioxane. From these values and the measured rate coefficients for the $A-1$ and $A-S_{E2}$ reactions, we can estimate that the activity coefficient of the $A-1$ transition state as compared to that of the $A-S_{E2}$ transition state decreases by a factor of about three on going from pure water to the dioxane-water mixture containing 50 mol % dioxane. Thus the effects of solvent composition on the ratio of the activity coefficients of the transition states are opposite in dioxane-water and DMSO-water mixtures.

Table 4. Logarithms of estimated ratios of the molar activity coefficients of the transition states in the A-1 hydrolysis of 2-methyl-1,3-dioxolane and the A-S_E2 hydrolysis of 2-methyl-4-methylene-1,3-dioxolane in dimethyl sulfoxide-water and dioxane-water mixtures. 25°C.

Solvent mixture	Mol fraction of the organic component	$\log f_{\text{H}_2\text{O}}$	$\log \frac{y_{\text{X}^{\ddagger}}}{y_{\text{Y}^{\ddagger}}}$
DMSO-H ₂ O	0.1	-0.03	0.12
	0.2	-0.07	0.23
	0.3	-0.15	0.37
	0.4	-0.23	0.53
	0.5	-0.31	0.66
	0.6	-0.37	0.78
	0.7	-0.43	0.89
	0.8	-0.49	0.97
	0.9	-0.55	1.03
Dioxane-H ₂ O	0.1	0.02	-0.05
	0.2	0.05	-0.15
	0.3	0.09	-0.28
	0.4	0.13	-0.37
	0.5	0.19	-0.47
	0.6	0.26	-0.59
	0.7	0.35	-0.74
	0.8	0.48	-0.98
	0.9	0.64	-1.38

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