

and 30 μ l of a 10 % solution of phosgene in ether added. Mixing was performed by vibrating the vial. After 2 h at room temperature excess phosgene and the solvent were removed by suction through a syringe needle. The pressure in the vial was restored with nitrogen and 20 μ l of dimethylsulfoxide added. After 15 min at room temperature 1.5 μ l of triethylamine was added. The reaction mixture was vibrated and the formation of aldehyde (II) was followed by GLC. After about 20 min, 2 μ l of D(-)-propane-1,2-diol was injected into the vial, immediately followed by 20 μ l of a 10 % solution of *p*-toluenesulfonic acid in dimethylsulfoxide. The formation of acetal (IV) was followed by GLC. The reaction was complete after about 3 h, and 40 μ l of heptane was then added. The heptane solution was used to obtain GLC retention data and to identify the compounds by their mass spectra.

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Solvent Effects in the Hydrolysis of Orthoesters and Their Value as Criteria of Reaction Mechanism

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In recent papers¹⁻³ we concluded that the hydrolysis of an alkyl orthoformate is either an *A*-1 reaction or a rate-determining proton transfer reaction depending on the structure of the ester. The structural effects, the lack of general acid catalysis and the magnitude of solvent deuterium isotope effect, k_{D_2O}/k_{H_2O} about three, suggest that the hydrolysis of isopropyl and ethyl orthoformates proceeds by way of a protonation pre-equilibrium. In the hydrolysis of 2-methoxyethyl and 2-chloroethyl orthoformates general acid catalysis was detected and the solvent deuterium isotope effect is close to two. These results were best interpreted in terms of a rate-determining proton transfer reaction. This kind of mechanistic change is likely as the free energy of activation of the proton transfer step increases with the electronegativity of the alkyl groups attached to the oxygen atoms. Although the *A*-S_E2 mechanism is evident in the hydrolysis of these esters, the *A*-2 mechanism cannot be excluded on the basis of the above-mentioned kinetic data, as solvent deuterium isotope effects are almost equal for these mechanisms and, in addition, general acid catalysis should be detected in both of the reactions. It is noteworthy that Kresge and Preto⁴ ruled out the *A*-2 mechanism of hydrolysis of ortho-carbonates on the basis of the absence of nucleophilic catalysis.

This paper presents kinetic data for the hydrolysis of various orthoformates in water-dioxane mixtures and the mechanistic conclusions that can be drawn on the basis of the results, particularly in cases where a decision is to be made between an *A*-S_E2 and an *A*-2 mechanism.

Experimental. Ethyl, methyl, 2-methoxyethyl, and 2-chloroethyl orthoformates were the preparations used in the previous studies.⁵ The dioxane used as the solvent in the kinetic measurements was purified by the standard method.⁶

The performance of the kinetic experiments has been described previously.¹ The progress of the hydrolysis was followed spectrophotometrically by measuring the absorbance of the formed ester at 220 nm. The reactions took place in dioxane-water mixtures at 25°C. The concentration of the catalyst perchloric acid varied between 0.0001 and 0.02 M and the concentration of orthoester was about 0.02 M.

As there were reasons to suspect that in dioxane-water solvents, even at relatively low concentrations of perchloric acid, the first-order rate coefficients of the hydronium ion-catalyzed reaction were not strictly proportional to the perchloric acid concentration, the hydrolysis of a model compound, acetaldehyde diethyl acetal, in 0.1, 0.05, 0.01, and 0.001 M perchloric acid solutions was studied. The second-order rate coefficients, *i.e.*, the directly calculated first-order rate coefficients divided by the perchloric acid concentrations, were not constant, but increased with perchloric acid concentration. This is illustrated in Fig. 1, where the logarithms of the rate

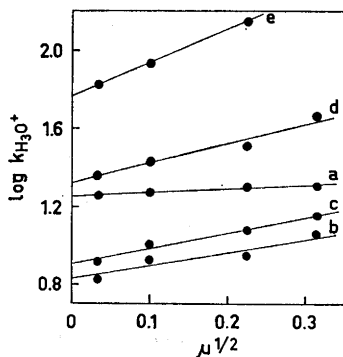


Fig. 1. Variation of the second-order rate coefficients of the hydrolysis of acetaldehyde diethyl acetal with the square root of ionic strength in dioxane-water mixtures. 25°C. Mole fraction of dioxane in the solvent: a, 0.2; b, 0.4; c, 0.6; d, 0.8; and e, 0.9.

coefficients are plotted against the square roots of the ionic strengths of the reaction solutions. The plots are linear for all the employed dioxane-water mixtures within the limits of experimental error and allow an extrapolation to infinite dilution. When the catalyst acid concentration is less than 0.001 M, the corrections to infinite dilution are, how-

ever, so small that they can be neglected. The hydrolysis of 2-chloroethyl orthoformate was studied in 0.0008–0.02 M perchloric acid solutions and therefore corrections were applied.

The second-order rate coefficients for the hydrolysis of ethyl, methyl, 2-methoxyethyl, and 2-chloroethyl orthoformates are collected in Table 1. The logarithms of

Table 1. Kinetic data for the hydrolysis of orthoformates $\text{CH}(\text{OR})_3$ in dioxane-water at 25°C. Perchloric acid as catalyst.

R	Mole fraction of dioxane	$10^4[\text{HClO}_4]$ M	$k_{\text{H}_3\text{O}^+}$ $\text{M}^{-1} \text{s}^{-1}$
CH_3CH_2	0	1.02	720
	0.275	1.06	262
	0.503	4.27	218
CH_3	0	1.02	202
	0.0861	5.09	179
	0.166	5.31	116
	0.275	10.6	60.4
	0.493	9.09	55.3
$\text{CH}_3\text{OCH}_2\text{CH}_2$	0	8.25	99.2
	0.0861	10.2	29.1
	0.166	5.09	27.8
	0.275	5.31	25.3
	0.493	10.6	21.6
ClCH_2CH_2	0	9.09	27.1
	0.0861	8.25	86.5
	0.166	51.0	3.35
	0.275	16.5	1.78
	0.440	106	0.70
	0.275	106	0.30
	0.440	85.1	0.24
	0.707	163	0.77

these rate coefficients are plotted against the mole fraction of dioxane in Fig. 2. The solvent effects are almost equal in the hydrolysis of ethyl, methyl, and 2-chloroethyl orthoformates; the rate coefficient is a minimum when the mole fraction of dioxane is about 0.4 and the rates in this solvent are from one fourth to one tenth of the rates in water.

As mentioned above, the A-2 mechanism cannot be excluded as the mechanism of hydrolysis of 2-chloroethyl orthoformate on the basis of previous kinetic data. The observed solvent effects illustrated in Fig. 2 (plot c) suggest, however, that the

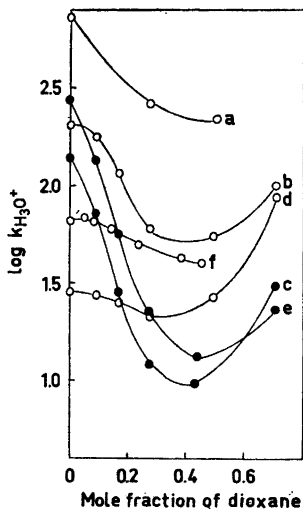


Fig. 2. The logarithms of the rate coefficients of hydrolysis versus the mole fractions of dioxane in dioxane-water mixtures. a, ethyl orthoformate; b, methyl orthoformate; c, 2-chloroethyl orthoformate ($\log k+1.5$); d, 2-methoxyethyl orthoformate; e, 2-methyl-4-methylene-1,3-dioxolane ($\log k+1.5$); and f, methyl acetate ($\log k+3$).

hydrolysis of this ester proceeds by a rate-determining proton transfer stage. This assumption is well founded as the solvent effects in the hydrolysis of 2-chloroethyl orthoformate are identical with those in the $A-S_E2$ hydrolysis of 2-methyl-4-methylene-1,3-dioxolane (plot e in Fig. 2). In contrast, solvent effects are markedly different in $A-2$ reactions, as shown by plot f in Fig. 2 for the $A-2$ hydrolysis of methyl acetate.⁷

The solvent effects in the hydrolysis of 2-methoxyethyl orthoformate are exceptional (plot d in Fig. 2). In contrast to the hydrolysis of the other orthoesters, only a slight retardation of the rate is observed when the proportion of dioxane increases to 50 mole %. We have previously concluded on the basis of other kinetic data that the hydrolysis of this ester proceeds by the $A-S_E2$ mechanism in water, but by the $A-1$ mechanism in 65 wt. % dioxane-water. Thus the observed exceptional differences in solvent effects must be due to this mechanistic change. Although the

solvent effect has features typical of $A-2$ reactions, there are no reasons to suspect that the hydrolysis of this ester proceeds by a rate-determining attack by water as this was not the case in the hydrolysis of the structurally closely similar ester, 2-chloroethyl orthoformate.

It is of interest to draw inferences about the reason for the change from the $A-S_E2$ mechanism to the $A-1$ mechanism in the hydrolysis of 2-methoxyethyl orthoformate when the polarity of the solvent decreases. As the solvation of the initial state is identical in both mechanisms, the reason for the mechanistic change must lie in differences in the solvation of the transition states. When the structures or the transition states of the proton transfer steps and the transition states in the subsequent heterolysis of the protonated substrate are considered, we conclude that the latter transition state resembles more closely the intermediate dialkoxymethyl cation as it lies close to this ion on the reaction coordinate. It is thus reasonable to assume that the more polar solvent, water, greatly stabilizes the latter ion-like transition state and consequently the transition state of the proton transfer reaction will lie on a higher energy level, and this reaction will be rate determining. In solvents of lower polarity, e.g. dioxane, the stabilization of an ion-like transition state is expected to be weak and thus the $A-1$ mechanism is favored.

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