An Alternative Mechanism of Acetal Hydrolysis. General Acid Catalysis in the Hydrolysis of Some Unsymmetrical Acetals

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In a previous study[1] we showed that the hydrolysis of the 2,2,2-trichloroethyl acetal of acetone involves a rate-determining proton transfer to the oxygen atom and hence does not take place by the A-1 mechanism generally accepted for acetal hydrolysis.[2,3]
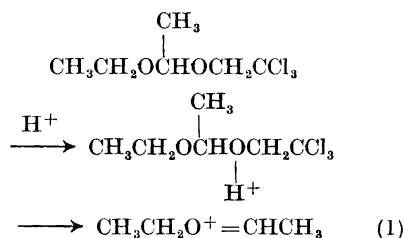
Although the above reaction is only a particular case of acetal hydrolysis, it is, however, justified to assume that the alternative mechanism is significant in the hydrolysis of many other acetals. This assumption is mainly based on the structural effects previously found in acetal hydrolysis. Salomaa[4] has shown that the hydrolysis reactions of unsymmetrical acetals of formaldehyde proceed mainly by protonation of the less basic oxygen atom and subsequent heterolysis of the protonated substrate. For instance, the contribution of the cleavage of the 2-chloroethoxy group in the hydrolysis of methyl 2-chloroethyl acetal of formaldehyde is more than 97 %. In this partial reaction structural effects are favorable for a rate-determining protonation; the low basicity of the oxygen atoms retards the proton transfer and simultaneously the electropositive alkyl group in the oxonium-carbonium ion formed facilitates the heterolysis of the protonated substrate. In spite of this fact a rate-determining protonation is unlikely in the hydrolysis of formaldehyde derivatives due to the relatively low stability of the intermediate ions formed in these reactions. Therefore, unsymmetrical acetals of acetaldehyde in which one of the alkyl groups contains highly negative substituents would be expected to be suitable model compounds. In the present paper we wish to report kinetic data on the hydrolytic cleavage of the ethyl trichloroethyl acetal of acetaldehyde.

Experimental. Ethyl trichloroethyl acetal of acetaldehyde was prepared by allowing ethyl vinyl ether to react with 2,2,2-trichloroethanol in the presence of p-toluenesulfonic acid as catalyst. After neutralization of the reaction mixture with sodium ethoxide, the product was purified by distillation. The following physical constants were recorded: b.p. 82°C/13 torr, n_D^{20} 1.4490, d_4^{20} 1.2387, $(R)_D$ 47.98 (calc. 48.10). NMR spectrum: 6 H at δ 1.30 (CH$_3$), 2 H at δ 3.62 (CH$_2$), 2 H at δ 4.03 (CH$_2$) and 1 H at δ 4.93 (CH).

The rate coefficients of the hydrolysis were measured by following the growth of the band due to the carbonyl group at a constant wavelength (276 nm) with a Unicam SP.800 spectrophotometer. The cell-housing was kept at a constant temperature (25°C) with water circulated from a Lauda electronically controlled thermostat. The temperature of the cell block was measured with a thermoelement. The acetal was added to a cell in which the acid solution had been thermostated. Owing to the low solubility of the studied compound in water, a 65/35 w/w dioxane-water mixture was used as solvent. The concentrations of the acetal in the reaction mixtures were about 0.02 M.

The kinetic data for the hydrolysis of the studied unsymmetrical acetal are collected in Table 1. The measured overall rate coefficient, $k_{H_3O^+} = 0.145$ M^{-1}s^{-1}, is the rate coefficient of the partial reaction (1) because

$$
\begin{array}{c}
CH_3 \\
| \\
CH_3CH_2O\overset{}{C}HOCH_2CCl_3
\end{array}
$$

$$
\xrightarrow{H^+} \begin{array}{c} CH_3 \\ | \\ CH_3CH_2O\overset{+}{C}HOCH_2CCl_3 \\ | \\ H \end{array}
$$

$$
\longrightarrow CH_3CH_2O^+ = CHCH_3 \qquad (1)
$$

the contribution of the other fission reaction, which leads to heterolysis of the protonated ethoxy group, is negligible as can be concluded on the basis of structural effects in acetal hydrolysis (see Ref. 4). The rate coefficient of hydrolysis of the studied unsymmetrical acetal is more than four powers of ten times as great as that of the corresponding symmetrical trichloroethyl acetal.[1] Because the proton transfer steps are almost identical in both reactions, the higher rate is mainly due to the greater stability of the ion formed in the heterolysis of the protonated substrate in the former reaction.

Table 1. Kinetic data for the hydrolysis of ethyl trichloroethyl acetal of acetaldehyde at 25°C in a 65/35 w/w dioxane-water mixture.

Catalyst Acid	Acid concn. M	$10^4 k$ s^{-1}	$k_{L_3O^+}$ M^{-1}s^{-1}
H_3O^+	0.212	308 ± 3	0.145
D_3O^+	0.203	603 ± 5	0.297
Cl_3CCOOH^a	0.0893	9.67 ± 0.09	
,,	0.0559	7.50 ± 0.05	
,,	0.0280	5.16 ± 0.02	

^{a} The molar ratios of acid to salt in the buffers were about 8:11. The ionic strengths were adjusted to 0.1 with sodium chloride.

The solvent deuterium isotope effect, $k_{D_3O^+}/k_{H_3O^+} = 2.05$, for the hydrolysis of the studied compound is markedly smaller than in the A-1 hydrolysis of acetals (2.7 − 3.1 at 25°C [4]). In the proton transfer reaction of trichloroethyl acetal of acetone, the solvent deuterium isotope effect is
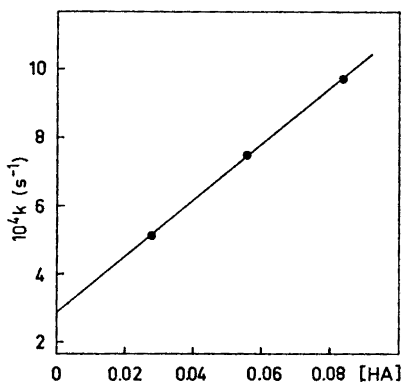

Fig. 1. Plot of the first-order rate coefficients of hydrolysis of ethyl trichloroethyl acetal of acetaldehyde in trichloroacetate buffers *versus* the concentration of trichloroacetic acid. Temperature 25°C. Solvent: 65 wt. % dioxane in water.

1.80.[1] Thus it seems probable that also the unsymmetrical acetal studied in this work hydrolyzes by the A-S_E2 mechanism. To get further evidence for this alternative mechanism, the hydrolysis was studied also in buffer solutions. The data collected in Table 1 show that the rate coefficients increase linearly with the concentration of the undissociated acid in trichloroacetate buffers of constant hydronium ion concentration (Fig. 1). Thus the studied reaction is subject to general acid catalysis in accordance with the A-S_E2 mechanism. The catalytic coefficient for trichloroacetic acid calculated by fitting eqn. (2) to the data by the method of least squares was $(8.06 \pm 0.18) \times 10^{-3}$M^{-1}s^{-1}.

$$k_{\text{tot.}} = k_{Cl_3CCOOH}[Cl_3CCOOH] + k_{H_3O^+}[H_3O^+] \qquad (2)$$

It is worth noting in this connection that the symmetrical trichloroethyl[1] and ethyl[2,3] acetals of acetaldehyde hydrolyze by the "normal" A-1 mechanism of acetal hydrolysis. Thus it is evident that the A-S_E2 mechanism is more common in the hydrolysis of unsymmetrical acetals than in the hydrolysis of symmetrical derivatives. The hydrolysis of a number of such compounds will be studied to obtain more information on the factors responsible for this change of mechanism.

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4. Salomaa, P. *Ann. Acad. Sci. Fennicae, Ser. A.* **II** (1961) No. 103.

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