

## Rate-determining Proton Transfer to Weakly Basic Acetals, an Alternative Mechanism of Acetal Hydrolysis

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Several formaldehyde, acetaldehyde, and acetone acetals of 2,2,2-trichloroethanol, 2,2,2-trifluoroethanol, and phenol were prepared and their basicities were measured by the spectral shift method. It was found that the  $pK_a$  values of the conjugate acids of these acetals vary between  $-6.5$  and  $-9$ . The kinetics of the hydrolysis of the acetaldehyde and acetone derivatives in acid 65:35 (w/w) dioxane-water mixture was studied at different temperatures. The kinetic data showed that the acetaldehyde acetals hydrolyze by the *A-1* mechanism. The hydrolysis of 2,2-di-(2,2,2-trichloroethoxy)propane was exceptional; the weak basicity of the oxygen atoms, structural effects and the solvent deuterium isotope effect,  $k_{D_2O}/k_{H_2O} = 1.80$ , suggested a rate-determining proton transfer reaction. Estimated partial rate coefficients of hydrolysis were in accordance with this assumption. The same conclusion can be drawn on the basis of the detected general acid catalysis. Free energy profiles for the hydrolysis of the acetals were drawn on the basis of measured and estimated data.

In the normal hydrolysis of acetals, a protonation equilibrium precedes a rate-determining decomposition of the protonated substrate. In a previous work<sup>1</sup> it has been estimated that the transition state of the proton transfer reaction is on an energy level about 7 kcal/mole lower than that of the transition state of the rate-determining heterolysis. A low basicity of the acetal should, however, raise the barrier to proton transfer. Thus it would be expected that the proton transfer would be the rate-determining stage of the hydrolysis of an acetal of sufficiently low basicity. For this reason, the hydrolysis of acetals of 2,2,2-trichloroethanol, 2,2,2-trifluoroethanol, and phenol, which have strongly electronegative groups attached to the oxygen atoms, was studied.

In recent work, Fife<sup>2</sup> found an anomaly in acetal hydrolysis. He concluded from kinetic data that the hydrolysis of 2-*p*-substituted phenyl-1,3-dioxolanes is a general acid-catalyzed reaction because the "normal" mechanism of hydrolysis is retarded by steric factors. The basicity of the oxygen atoms

in these compounds must be so high that it cannot be reason for the anomaly. After our work was completed, Fife *et al.*<sup>3</sup> published kinetic data for aryl-substituted hemicyclic acetals which also provide evidence for an alternative mechanism of acetal hydrolysis.

### EXPERIMENTAL

*Syntheses.* Di-(2,2,2-trichloroethoxy)methane was the preparation synthesized by Salomaa and Linnantie.<sup>4</sup> The sample used for IR spectral measurements was purified by distillation.

Di-(2,2,2-trifluoroethoxy)methane was synthesized by the method of Shipp and Hill<sup>5</sup> from paraformaldehyde and trifluoroethanol using 94% sulfuric acid as solvent. The crude product was purified by distillation. The following physical constants were recorded: b.p. 30–32°C/25 torr,  $n_D^{20}$  1.3075,  $d_4^{20}$  1.3954,  $(R)_D$  29.06 (calc. 29.48). The purity was checked by gas chromatography.

Diphenoxymethane was prepared by a previously described method<sup>6</sup> from di-iodomethane, sodium, and phenol using xylene as solvent. After repeated distillations, a fraction boiling at 155–158°C/10 torr was collected. The product was found pure by gas chromatography. Physical constants:  $n_D^{20}$  1.5702,  $d_4^{20}$  1.1127,  $(R)_D$  58.99 (calc. 58.58).

1,1-Di-(2,2,2-trichloroethoxy)ethane was prepared from paraldehyde and trichloroethanol by removing liberated water as an azeotrope with hexane. The purified product had the physical constants: b.p. 120–121°C/4–5 torr,  $n_D^{20}$  1.4916,  $d_4^{20}$  1.4992,  $(R)_D$  62.82 (calc. 63.13).

1,1-Di-(2,2,2-trifluoroethoxy)ethane<sup>7</sup> was synthesized from trifluoroethanol and acetylene. The catalyst for this reaction was prepared by heating 1.5 g of mercuric oxide and 1.2 ml of boron trifluoride etherate with 1 g of trifluoroethanol. 59 g of trifluoroethanol was added and acetylene was passed into the mixture for 8 h. The temperature of the reaction mixture was kept under 50°C. After it had cooled to room temperature the mixture was neutralized with a solution of 0.6 g of sodium in 6 ml of ether and 6 g of trifluoroethanol. The product was purified by distillation. The purity was checked by gas chromatography. Physical constants: b.p. 114–115°/760 torr,  $n_D^{20}$  1.3162,  $d_4^{20}$  1.3209,  $(R)_D$  33.58 (calc. 34.12).

2,2-Di-(2,2,2-trichloroethoxy)propane was prepared by the method of Lorette and Howard.<sup>8</sup> 65 g of trichloroethanol, 5.2 g of 2,2-dimethoxypropane, 0.2 g of *p*-toluenesulfonic acid, and 75 ml of benzene were heated so that the azeotrope of benzene and methanol distilled through a column at 57–59°C. The reaction mixture was cooled and neutralized by rapidly adding sodium methoxide in methanol. On fractionation, the acetal distilled at 127–129°C/17.5–18.5 torr and crystallized in the receiving flask. This fraction was purified by crystallization from petroleum ether and finally from carbon tetrachloride. M.p. 64.0°C. To verify the structure and purity of the compound, its NMR spectrum was recorded with a Perkin-Elmer R-10 spectrometer. The integral showed that the prepared compound had four protons with a  $\delta$  value of 4.20 ppm ( $-\text{OCH}_2$  protons) and six protons with a  $\delta$  value of 1.50 ppm ( $\text{CH}_3$  protons). Peaks due to impurities were not recorded.

An attempt to prepare 2,2-di-(2,2,2-trifluoroethoxy)propane by the same method was unsuccessful because trifluoroethanol formed an azeotrope with benzene and this mixture boiled at a lower temperature than the azeotrope of methanol and benzene.

*IR experiments.* The basicities of the studied acetals were deduced from the O–D band of deuteromethanol dissolved in the acetals similarly as in a previous work.<sup>9</sup> The concentration of deuteromethanol in the acetal was about 0.5 M. In the case of 2,2-di-(2,2,2-trichloroethoxy)propane, which is a solid, the measurements were performed after adding the deuteromethanol to a saturated solution of the acetal in carbon tetrachloride. The  $\text{p}K_a$  values of the conjugate acids of the acetals were calculated from the equation

$$\text{p}K_a = 0.0789\Delta\nu - 10.91 \quad (1)$$

where  $\Delta\nu = \nu$  of the O—D band in carbon tetrachloride —  $\nu$  of the O—D band in the acetal. Eqn. (1) was derived previously from measured O—D band shifts of deuteromethanol in ethers.<sup>9</sup>

*Kinetic experiments.* In the kinetic experiments the liberation of the aldehyde or ketone was followed with a Beckmann DU Quartz Spectrophotometer. The temperature of the cell-housing was adjusted within  $\pm 0.05^\circ\text{C}$  to the desired level with water circulating from a thermostat.

Because of the low solubilities of the studied acetals in water a mixture containing 65 wt.% dioxane and 35 wt.% water was used as solvent in the kinetic experiments. Dioxane was purified by a standard method.<sup>10</sup> Perchloric acid was used as the catalyst.

The acid solution was brought to the desired temperature and acetal was added (about 0.1 M). The reaction mixture was transferred with a thermostated pipette to the cuvette of the spectrophotometer. The acid solution was used as the reference solution. The effect of the thermal expansion of the water-dioxane mixture was taken into account when the concentrations of acid in the reaction mixtures were calculated; densities reported by Tommila and Koivisto were used.<sup>11</sup>

The hydrolysis of the acetals of acetaldehyde was studied in solutions of moderately high acidity owing to their low rates of hydrolysis in dilute acid solutions. The rates of hydrolysis of the acetals of formaldehyde were so low that the spectrophotometric method could not be applied.

Table 1. O—D band shifts of deuteromethanol in acetals  $\text{R}_1\text{R}_2\text{C}(\text{OR}_3)_2$  and the  $\text{p}K_a$  values of the conjugate acids of the acetals.  $25^\circ\text{C}$ .

Compound $\text{R}_1$	$\text{R}_2$	$\text{R}_3$	Position of O—D band ( $\text{cm}^{-1}$ )	O—D band shift <sup>a</sup> ( $\text{cm}^{-1}$ )	$\text{p}K_a$
H	H	$\text{Cl}_3\text{CCH}_2$	$2651.1 \pm 0.3$	38.8	—7.9
H	H	$\text{F}_3\text{CCH}_2$	$2658.1 \pm 0.2$	31.8	—8.4
H	H	phenyl	$2631.7 \pm 0.2$	58.2	—6.5
H	$\text{CH}_3$	$\text{Cl}_3\text{CCH}_2$	$2649.0 \pm 0.3$	40.9	—7.7
$\text{CH}_3$	$\text{CH}_3$	$\text{Cl}_3\text{CCH}_2$	$2662.7 \pm 0.5$	27.2	—8.8

<sup>a</sup> O—D band position in carbon tetrachloride is  $2689.9 \text{ cm}^{-1}$ .

## RESULTS AND DISCUSSION

*Basicities.* The band shifts and the derived  $\text{p}K_a$  values of the studied acetals are collected in Table 1. The standard errors of the band positions are less than  $0.5 \text{ cm}^{-1}$ . The basicity of trifluoroethyl acetal of acetaldehyde could not be measured owing to the weakness of the O—D band. The  $\text{p}K_a$  values of the conjugate acids of the acetals of trichloroethanol and trifluoroethanol are of the order of  $-8 \text{ p}K$  units. Thus these acetals are about  $4 \text{ p}K$  units less basic than those previously studied.<sup>9</sup> The  $\text{p}K_a$  value of the conjugate acid of 2,2-di-(2,2,2-trichloroethoxy)propane seems to be too low because one would expect on the basis of polar effects of substituents that the basicity of this acetal is slightly higher than that of 1,1-di-(2,2,2-trichloroethoxy)ethane. A possible reason to this anomaly may be that the IR measurements were performed on solutions in carbon tetrachloride. The  $\text{p}K_a$  value of diphenoxymethane is  $-6.5$ .

The basicities of the different oxygen atoms in symmetric acetals can be estimated by subtracting  $0.3 \text{ p}K$  units from the measured basicities in Table 1 as discussed in a previous paper.<sup>9</sup>

*Kinetic experiments in moderately concentrated acid solutions.* The hydrolysis of the prepared acetaldehyde derivatives was studied in moderately concentrated acid solutions. To determine the effect of the acid concentration on the rate, the hydrolysis of 1,1-di-(2,2,2-trichloroethoxy) ethane was studied at different perchloric concentrations (0.5–3.0 M) at 45°C. The results are shown in Table 2 together with  $H_0$  values extrapolated from the values of

Table 2. Rate coefficients of hydrolysis of 1,1-di-(2,2,2-trichloroethoxy)ethane in moderately concentrated perchloric acid solutions at 45°C. Solvent: 65 wt.% dioxane and 35 wt.% water.

[HClO <sub>4</sub> ] (M)	log [HClO <sub>4</sub> ]	$H_0$	10 <sup>3</sup> $k$ (s <sup>-1</sup> )	log $k$
0.588	-0.231	+1.38	0.0877	-4.057
1.07	+0.029	+0.75	0.367	-3.435
1.69	+0.228	+0.06	1.74	-2.759
2.30	+0.362	-0.55	7.47	-2.127
2.92	+0.465	-1.07	25.5	-1.593

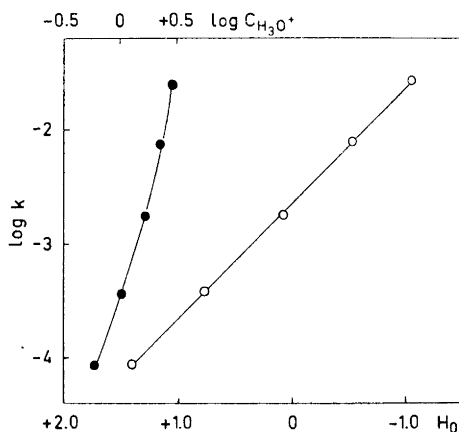


Fig. 1. The hydrolysis of 1,1-di-(2,2,2-trichloroethoxy)ethane in moderately concentrated perchloric acid solutions: log  $k$  versus  $H_0$  (open circles) and log  $k$  versus log  $c_{H_3O^+}$  (filled circles).

Paul and Long<sup>12</sup> for water-dioxane mixtures. The measured log  $k$  values are plotted against  $H_0$  and log  $c_{H_3O^+}$  in Fig. 1. The plot of log  $k$  against  $H_0$  is a straight line of unit slope. According to the hypothesis of Zucker and Hammett,<sup>13</sup> this means that the critical complex of the reaction contains no water molecule. The plot of log  $k$  versus log  $c_{H_3O^+}$  slopes upwards and thus the A-2 mechanism of hydrolysis can be disregarded.<sup>14</sup>

The rates of hydrolysis of the acetaldehyde acetals were studied in 2.30 M perchloric acid solutions (see, however, Table 2). On the basis of the dependence on  $H_0$  the first-order rate coefficients in 2.30 M solutions can be extrapolated to dilute perchloric acid concentrations by dividing by 42.9.

Table 3. Rate coefficients of hydrolysis of 1,1-di-(2,2,2-trichloroethoxy)ethane, 1,1-di-(2,2,2-trifluoroethoxy)ethane, and 2,2-di-(2,2,2-trichloroethoxy)propane in a 65 wt. % dioxane-water mixture at different temperatures and derived kinetic data.

Compound	$t^{\circ}\text{C}$	$10^6k$ ( $\text{M}^{-1}\text{s}^{-1}$ )	$\log A$	$E$ kcal/mole	$\Delta S^{\ddagger}$ E.U.	$10^6k^{25}\text{calc.}$ ( $\text{M}^{-1}\text{s}^{-1}$ )
$(\text{Cl}_3\text{CCH}_2\text{O})_2\text{CHCH}_3$	25	6.92	$11.4 \pm 0.4$	$22.6 \pm 0.6$	$-8.5 \pm 2.0$	6.87
	35	22.8				
	45	75.7				
$(\text{F}_3\text{CCH}_2\text{O})_2\text{CHCH}_3$	25	3.11	$12.3 \pm 0.3$	$24.3 \pm 0.5$	$-4.3 \pm 1.4$	3.11
	35	11.7				
	45	41.0				
$(\text{Cl}_3\text{CCH}_2\text{O})_2\text{C}(\text{CH}_3)_2$	25	5780	$11.6 \pm 0.3$	$18.9 \pm 0.4$	$-7.4 \pm 1.4$	5790
	35	16000				
	45	42900				

*Structural effects.* The rate coefficients of hydrolysis of the studied acetals at different temperatures are collected in Table 3. These rate coefficients are much smaller than those previously found for acyclic acetals.<sup>15</sup> For instance, ethyl acetals hydrolyze  $10^4$ – $10^5$  times faster than the corresponding trichloroethyl and trifluoroethyl acetals under the same conditions.

The effect of the aldehyde component on the rate coefficients of the hydrolysis of acetals is great. In previous studies of acetal hydrolysis it has been shown that the acetone derivatives hydrolyze 3000 times faster than the corresponding acetaldehyde derivatives<sup>15</sup> as the result of the inductive polar effect of the second methyl group attached to the reaction center. Because steric effects are negligible<sup>15</sup> in the hydrolysis of acyclic acetals it would be expected that the trichloroethyl acetal of acetone would also be hydrolyzed about 3000 times faster than the corresponding acetaldehyde derivative. The rate coefficients in Table 3 show, however, only a 800-fold increase in rate. A possible explanation of this small structural effect is that the compounds hydrolyze by different reaction mechanisms.

*Activation entropies.* The activation entropies of hydrolysis of the studied acetals given in Table 3 are all negative. These values are smaller than those previously found for acyclic acetals for which small positive activation entropies are typical.<sup>16</sup> As negative  $\Delta S^{\ddagger}$  values have been found for the cyclic acetals, 1,3-dioxolanes, without any change in reaction mechanism,<sup>17–19</sup> it can be concluded that the magnitudes of the activation entropies in Table 3 do not exclude the *A*-1 mechanism of acetal hydrolysis. Unfortunately, it is impossible to distinguish between *A*-1 mechanism of acetal hydrolysis and a rate-determining proton transfer reaction (*A*- $S_E2$  mechanism) on the basis of activation entropies. Small positive activation entropies have been obtained for the *A*- $S_E2$  hydrolysis of orthoesters<sup>20</sup> as for the *A*-1 hydrolysis of acetals. The *A*-2 mechanism can be disregarded in the hydrolysis of the studied acetals as the  $\Delta S^{\ddagger}$  values for *A*-2 reactions are much more negative than those in Table 3.<sup>21,16</sup>

*Free energy changes in acetal hydrolysis.* The free energy changes in the hydrolysis of diethyl acetal (*A*-1 mechanism) were determined by thermo-

dynamic and kinetic methods in a previous work<sup>1</sup> and the energy barrier of the proton transfer equilibrium was estimated. This free energy profile, which is typical of the *A-1* mechanism of acetal hydrolysis, is shown in Fig. 2.

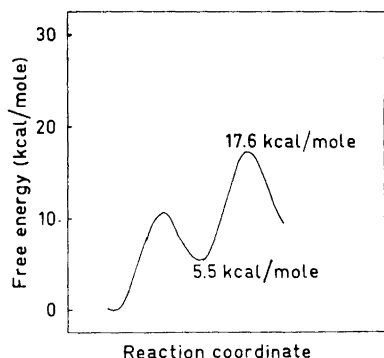


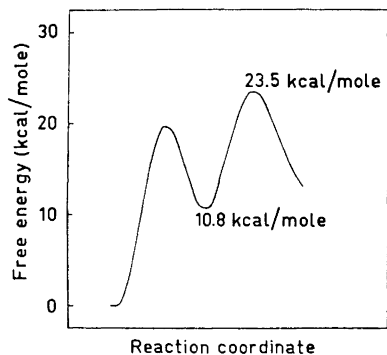
Fig. 2. Free energy profile for the hydrolysis of diethyl acetal (Salomaa, Kankaanperä<sup>1</sup>). The *A-1* mechanism of acetal hydrolysis.

Marked differences would be expected in the free energy curves of the acetals studied in this work due to the low basicities of the oxygen atoms. The following discussion is based on measured and estimated data for these acetals.

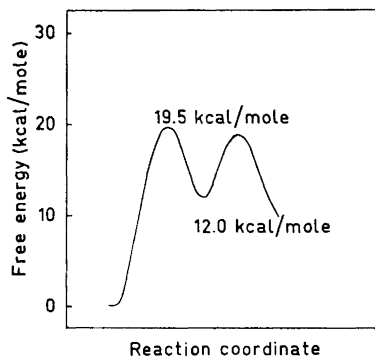
From the  $pK_a$  values of Table 1, we can estimate that protonated 1,1-di-(2,2,2-trichloroethoxy)ethane is 10.8 kcal/mole less stable than the unprotonated acetal in water. Thus the transition state of the proton transfer reaction must be on a higher energy level than in the case of diethyl acetal. The rate coefficient of hydrolysis of 1,1-di-(2,2,2-trichloroethoxy)ethane at 25°C in the 65 % dioxane-water mixture is  $6.87 \times 10^{-6} \text{ M}^{-1}\text{s}^{-1}$ . To estimate the value in pure water, the rates of hydrolysis of water-soluble acetals in water and in the 65 % dioxane-water mixture were measured; it was found that the rate coefficients of hydrolysis of 2,2-dimethyl-1,3-dioxolane and 2-methyl-2-ethyl-1,3-dioxolane in water are about five times the coefficients in the 65 % dioxane-water mixtures. Thus it can be estimated that the rate coefficient of 1,1-di-(2,2,2-trichloroethoxy)ethane in water solution is  $3 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1}$ ; the transition state of the hydrolysis is hence on an energy level 23.5 kcal/mole higher than the initial state. The free energy barrier of the partial reaction in which the proton is transferred from a hydronium ion to an oxygen atom of this acetal must be markedly lower as will be shown later. Thus, as seen in Fig. 3, the heterolysis of the protonated substrate must be the rate-determining stage in the hydrolysis of trichloroethyl and trifluoroethyl acetals of acetaldehyde.

The transition state is relatively more stable in the heterolysis of the protonated trichloroethyl acetal of acetone than in the heterolysis of the corresponding acetaldehyde derivative because the second methyl group attached to the reaction center greatly stabilizes both the formed oxonium-carbonium ion and the transition state in the case of acetone derivative. Thus it would be expected that the proton transfer becomes the rate-determining stage in the hydrolysis of the acetone acetal. The rate coefficient of hydroly-

ysis of this compound in water can be estimated to be  $3 \times 10^{-2} \text{ M}^{-1}\text{s}^{-1}$  at  $25^\circ\text{C}$ ; thus the energy level of the transition state of the hydrolysis is 19.5 kcal/mole higher than that of the initial state. The  $\text{p}K_{\text{a}}$  value of the protonated form



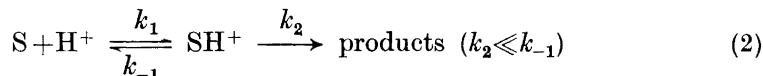
*Fig. 3.* Free energy profile for the hydrolysis of 1,1-di-(2,2,2-trichloroethoxy)ethane. The free energy level of the transition state of the proton transfer reaction is estimated to lie between 15 and 20 kcal/mole.



*Fig. 4.* Estimated free energy profile for the hydrolysis of 2,2,2-trichloroethyl acetal of acetone. Rate-determining proton transfer mechanism.

of trichloroethyl acetal of acetone reveals that the free energy difference between the protonated and unprotonated species is 12.0 kcal/mole. To obtain an approximate value for the height of the barrier between the initial state and the protonated form of the substrate, the rate coefficients of orthoesters and orthocarbonates were compared. In previous studies<sup>22</sup> it has been shown that the hydrolysis of orthoesters and orthocarbonates is a general acid-catalyzed reaction. Hence the proton transfer to the oxygen atom must be the rate-determining stage of the hydrolysis. In this work the  $\text{p}K_{\text{a}}$  of the conjugate acid of ethyl orthoacetate was measured by the IR method and was found to be  $-4.72$ . The basicity of methyl orthocarbonate was estimated from the band shift measured by Pletcher and Cordes;<sup>23</sup>  $\text{p}K_{\text{a}}$  was calculated from eqn. (1) to be  $-6.31$ . The basicity of ethyl orthocarbonate is virtually of the same magnitude. The rate coefficient of ethyl orthoacetate,  $k_{\text{H}_3\text{O}^+}^{25} = 1.31 \times 10^4 \text{ M}^{-1}\text{s}^{-1}$ , and that of ethyl orthocarbonate,  $k_{\text{H}_3\text{O}^+}^{25} = 9.15 \times 10^2 \text{ M}^{-1}\text{s}^{-1}$ ,<sup>24</sup> give free energy barriers of 11.8 kcal/mole and 13.4 kcal/mole, respectively. If these  $\Delta G^\ddagger$  values are plotted against the  $\text{p}K_{\text{a}}$  values of the conjugate acids of ethyl orthoacetate and ethyl orthocarbonate, the free energy of activation for the proton transfer to trichloroethyl acetal of acetone can be estimated from the plot using the measured  $\text{p}K_{\text{a}}$  value of the conjugate acid; the value found is  $\Delta G^\ddagger = 16-20$  kcal/mole. The measured free energy of activation of the hydrolysis is of the same magnitude. Thus the proton transfer reaction may be rate-determining stage in the hydrolysis of this compound as shown in Fig. 4. The situation in which both the barriers are on nearly the same energy level cannot however be excluded on the basis of the experimental data.

The *A*-1 hydrolysis of acetals can be expressed in the form



Using the steady state approximation, the following equation can be written for the second-order rate coefficient of this reaction:

$$k_{H_3O^+} = \frac{k_1 k_2}{k_{-1} + k_2} = \frac{k_1 k_2}{k_{-1}} = \frac{k_2}{K_a} \quad (3)$$

$K_a$  is the equilibrium constant of the protonation reaction. Thus the  $k_2$  values of the studied acetals can be estimated and their validity in the determination of the reaction pathways can be determined.

The value of the rate coefficient  $k_2$  for the hydrolysis of trichloroethyl acetal of acetaldehyde calculated from eqn. (3) is  $2 \times 10^3 \text{ s}^{-1}$ . The value of the partial rate coefficient  $k_{-1}$  is very high because it relates to proton transfer from a strong acid to water. An estimated maximum value of  $k_{-1}$  is the rate coefficient of the diffusion-controlled reaction ( $10^{10} \text{ s}^{-1}$ ).<sup>25</sup> Thus  $k_2$  is much smaller than  $k_{-1}$  and gives thus further evidence for the *A*-1 mechanism of hydrolysis of trichloroethyl and trifluoroethyl acetals of acetaldehyde.

The situation is very different in the hydrolysis of the studied acetone derivative. In this case the experimental data give a  $k_2$  value of  $2 \times 10^7 \text{ s}^{-1}$ , which is apparently smaller than the maximum value of  $k_{-1}$ . Actually,  $k_{-1}$  must, however, be much smaller than  $10^{10} \text{ s}^{-1}$ ; for instance, the rate coefficient of proton transfer from the protonated alcohol to the alcohol itself is of the order of  $10^6$ – $10^8 \text{ s}^{-1}$ .<sup>26</sup> Thus it can be concluded from these estimates that a rate-determining proton transfer mechanism ( $k_{-1} \leq k_2$ ) is possible for the hydrolysis of 2,2-di-(2,2,2-trichloroethoxy)propane, although the *A*-1 mechanism of acetal hydrolysis ( $k_{-1} > k_2$ ) cannot be fully excluded.

*Solvent deuterium isotope effect.* The rate coefficient of hydrolysis of the acetone derivative was determined also in a 65 wt. % dioxane- $D_2O$  mixture. The value  $1.04 \times 10^{-2} \text{ M}^{-1}\text{s}^{-1}$  was obtained for the rate coefficient at 25°C. When this value is compared with the data in Table 3, it is seen that a 1.80-fold increase in rate occurs when the solvent changes from light to heavy water. If the experiments had been performed in the pure waters, the ratio  $k_{D_2O}/k_{H_2O}$  would have been even smaller, as shown by earlier results.<sup>27</sup> The solvent deuterium isotope effect in the hydrolysis of 2,2-di-(2,2,2-trichloroethoxy)propane is thus much smaller than is usually found for acetals hydrolyzing by the *A*-1 mechanism.<sup>27-30</sup> This difference in isotope effect gives thus evidence for an exceptional mechanism of acetal hydrolysis.

It has been assumed previously<sup>31</sup> that only the rate coefficients of proton pre-equilibrium reactions (*A*-1 and *A*-2 mechanisms) are larger in  $D_2O$  than in  $H_2O$ . It has been shown, however, that also the  $k_{D_2O}/k_{H_2O}$  values for rate-determining proton transfer reactions may be larger than unity. For the *A*- $S_E2$  hydrolysis of orthoesters, which also are alkoxy-substituted alkanes like acetals, the deuterium solvent isotope effect varies between 2.2 and 2.4.<sup>20,29,32,33</sup> In the *A*- $S_E2$  hydrolysis of tetraalkoxyalkanes, the ortho-carbonates, the solvent deuterium isotope effect is slightly smaller, 1.4.<sup>34</sup>



The isotope effect 1.80 found for the hydrolysis of the studied acetone derivative lies between these values.

*General acid catalysis.* To get further evidence for the alternative mechanism in the hydrolysis of acetals the kinetic experiments were also performed in buffer solutions with a constant hydronium ion concentration. When the rate coefficients of the hydrolysis of the acetone derivative are compared (Fig. 5) an increase is to be found with the concentration of the undissociated

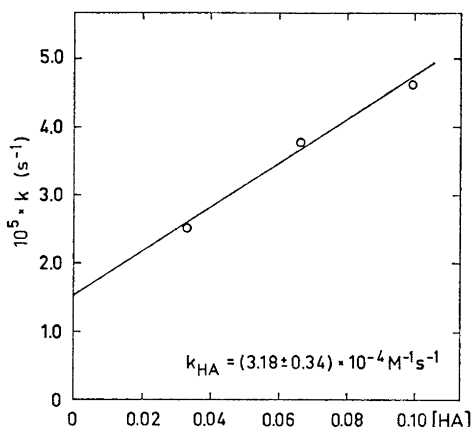


Fig. 5. Rate coefficients for the hydrolysis of the trichloroethyl acetal of acetone versus concentration of undissociated trichloroacetic acid at 25°C in dioxane-water mixture (65/35 w/w).

trichloroacetic acid. Thus the hydrolysis of this compound cannot be specifically hydronium ion catalyzed which is the case in the normal hydrolysis of acetals. In the  $A-S_E2$  reaction, however, general acid catalysis should be detected.

All the kinetic data of this work point out that the hydrolysis of the trichloroethyl acetal of acetone is exceptional; as a result of the low basicity of the acetal the proton transfer to the oxygen atom is the rate-determining stage of the hydrolysis.

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Received January 4, 1969.