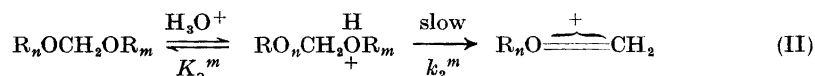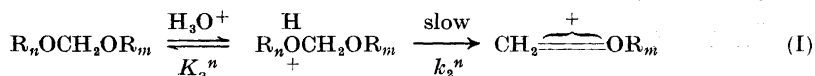# Basicities of the Oxygen Atoms in Symmetrical and Unsymmetrical Acetals. Part II. The Base Strengths and their Relation to the Rate Coefficients of the Different Partial Fission Reactions of Acetal Hydrolysis

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The rate coefficients of hydrolysis of acetals are products of two factors, the equilibrium constant of the protonation reaction and the rate coefficient of the rate-determining heterolysis of the protonated substrate. The effects of these two factors on the different partial fission reactions of hydrolysis of symmetrical and unsymmetrical acetals were determined. The rate coefficients of the rate-determining stages were evaluated.

Simultaneous routes in the hydrolysis of acetals by the A-1 mechanism are shown in schemes I and II:

$$R_nOCH_2OR_m \underset{K_a{}^n}{\overset{H_3O^+}{\rightleftharpoons}} \underset{+}{\overset{H}{R_nOCH_2OR_m}} \xoverset{slow}{\underset{k_2{}^n}{\longrightarrow}} CH_2\overset{+}{\rightleftharpoons}OR_m \qquad (I)$$

$$R_nOCH_2OR_m \underset{K_a{}^m}{\overset{H_3O^+}{\rightleftharpoons}} \underset{+}{\overset{H}{RO_nCH_2OR_m}} \xoverset{slow}{\underset{k_2{}^m}{\longrightarrow}} R_nO\overset{+}{\rightleftharpoons}CH_2 \qquad (II)$$

In a kinetic study, Salomaa[1] discussed structural effects in the hydrolysis of symmetrical and unsymmetrical acetals. R_n remains in the remnant of the molecule in the rate-determining stage of the hydrolysis II. The relative rate coefficients of reactions II when R_n is varied and R_m is held constant are determined by the structures of the remnants. Salomaa[1] deduced the following relative rate coefficients for these reactions (in the case of formaldehyde acetals):

R_n	FCH_2CH_2	$ClCH_2CH_2$	$CH_3OCH_2CH_2$	CH_3	CH_3CH_2	$(CH_3)_2CH$
$k_{nm}{}^m$ (relative)	0.0801	0.0480	0.201	1	4.48	22.1

The influence of R_n on the protonation reaction is in this case negligible due to its distant position (see Ref. 2). An increase in the electropositivity of R_n stabilizes the intermediate oxonium-carbonium ion which is formed in the rate-determining heterolysis of the protonated substrate, and thus increases the rate of hydrolysis.

The rate coefficients of reaction I as R_n is varied and R_m is held constant give rise to the leaving group effect in the hydrolysis of acetals. The relative rate coefficients deduced by Salomaa[1] for this reaction have been collected below:

| R_n	FCH_2CH_2	$ClCH_2CH_2$	$CH_3OCH_2CH_2$	CH_3	CH_3CH_2	$(CH_3)_2CH$
$k_{nm}{}^n$ (relative)	2.02	1.96	1.53	1	1.21	2.27

The effect of the leaving group on the rate coefficient is much smaller than the effect of the remnant and furthermore the rate coefficient is a minimum when R_n is a methyl group. Both of these observations are, however, in accordance with structural effects expected for reaction I; an increased electropositivity of R_n increases the basicity of the adjacent oxygen atom (see Fig. 1 in Ref. 2) and thus shifts the equilibrium to the right but at the same time it retards the heterolysis of the protonated substrate. To get a more detailed picture of the effect of these two factors, the equilibrium constants of the protonation and the rate coefficients of the rate-determining heterolysis of the protonated substrate were estimated for symmetrical and unsymmetrical acetals on the basis of the rate coefficients of the individual fission reactions[1] and the basicities of the oxygen atoms.[2]

Results and discussion. The rate coefficients of hydrolysis of symmetrical and unsymmetrical acetals at 25°C measured by Salomaa[1] are collected in Table 1. These overall rate coefficients were extrapolated from the values in 1 M hydrochloric acid solutions using the empirical eqn. (1):[1]

$$\log k_{\text{dil.acid}} = 1.008 \log k_{\text{1 M acid}} - 0.298 \tag{1}$$

The rate coefficients of the fission reactions, $k_{nm}{}^n$ and $k_{nm}{}^m$, are also collected in Table 1;[1] the upper index of k refers to the site of fission in question.

Let us denote by k_1, k_{-1}, and k_2 the partial rate coefficients of the acetal hydrolysis:

$$S \underset{k_{-1}}{\overset{H_3O^+ \quad k_1}{\rightleftharpoons}} SH^+ \xrightarrow[k_2]{\text{slow}} \text{products} \tag{2}$$
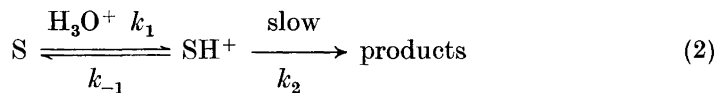
where S is the acetal. The steady state approximation leads to equation

$$k_{H_3O^+} = \frac{k_1 \times k_2}{k_{-1} + k_2} \tag{3}$$

$k_{H_3O^+}$ is the measured second-order rate coefficient. Because the protonation leads to a pre-equilibrium in acetal hydrolysis (scheme 2), $k_{-1} \gg k_2$. Thus eqn. 3 may be written

$$k_{H_3O^+} = k_1 \times k_2/k_{-1} \tag{4}$$

Table 1. The hydrolysis of symmetrical and unsymmetrical acetals $R_nOCH_2OR_m$ at 25°C in hydrochloric acid solutions. The constants of partial reactions have been deduced on the basis of kinetic and basicity data.

Substituents		Overall rate coefficients $10^5 k$ ($M^{-1}s^{-1}$)	Partial reactions of scheme I: Rate coefficients and equilibrium constants			Partial reactions of scheme II: Rate coefficients and equilibrium constants		
R_n	R_m		$10^{-4}K_a^n$ (M)	$10^5 k_{nm}^n$ ($M^{-1}s^{-1}$)	k_2^n (s^{-1})	$10^{-4}K_a^m$ (M)	$10^5 k_{nm}^m$ ($M^{-1}s^{-1}$)	k_2^m (s^{-1})
Methyl	Methyl	2.74	7.4	1.4	1.0			
Ethyl	Ethyl	15.1	2.7	7.6	2.0			
Isopropyl	Isopropyl	142	1.0	71	7.1			
tert-Butyl	tert-Butyl	10200	0.14	5100	72			
β-Fluoroethyl	β-Fluoroethyl	0.441	200	0.22	0.43			
β-Chloroethyl	β-Chloroethyl	0.253	420	0.13	0.53			
Methyl	Ethyl	7.87	7.4	6.2	4.6	2.7	1.7	0.45
Methyl	Isopropyl	34.9	7.4	32	24	1.0	3.3	0.33
Methyl	β-Chloroethyl	2.79	7.4	0.067	0.050	420	2.7	11
Ethyl	Isopropyl	50.8	2.7	37	9.8	1.0	14	1.4
Ethyl	tert-Butyl	417	2.7	420	110	0.14	1.3	0.019
Ethyl	β-Chloroethyl	12.4	2.7	0.082	0.022	420	12	51
Isopropyl	β-Fluoroethyl	65.4	1.0	0.26	0.026	200	65	130
Isopropyl	β-Chloroethyl	59.1	1.0	0.15	0.015	420	59	250
β-Fluoroethyl	β-Chloroethyl	0.346	200	0.13	0.26	420	0.22	0.90
Reference		1	2	1	This work	2	1	This work

Because the pre-equilibrium constant $K_a = k_{-1}/k_1$, the coefficient of the rate-determining stage can be expressed in the form

$$k_2 = K_a \times k_{H_3O^+} \tag{5}$$

The values of k_2 for the hydrolysis of the studied acetals can thus be calculated from the partial fission rate coefficients and the measured basicities of the different oxygen atoms in Table 1. The results are collected in the same table.

The k_2 values in Table 1 vary between 0.01 and 250 s⁻¹. Correction: The k_2 values in Table 1 vary between 0.01 and 250 s^{-1}. k_{-1} of reaction 2 has an upper limit of 10^{10} s^{-1}, the rate coefficient of the diffusion-controlled reaction, because it involves a proton transfer from a strong acid SH^+ to water.[3] Thus the calculated k_2 values are in accordance with a protonation equilibrium because they are much smaller than the k_{-1} values. This, of course, can be considered as additional and independent experimental evidence for the existence of a fast proton-transfer pre-equilibrium in the reactions studied.

Let us consider the effect of the structure of the leaving group on the rate coefficient of the rate-determining stage of acetal hydrolysis. The following relative rate coefficients can be calculated for the reactions with different leaving groups R_n:

R_n (in the leaving group)	$ClCH_2CH_2$	CH_3	CH_3CH_2	$(CH_3)_2CH$
k_2^n (relative)	11	1.0	0.44	0.31

These coefficients were calculated from the k_2 values using all the series with different groups R_m in the remnant. When this leaving group effect is compared with its effect on the overall fission reaction two differences are found: the structural effects are more marked in the rate-determining stage and a minimum overall rate is not observed. When the relative rate coefficients k_2^n are plotted against Taft's σ^*values, a linear plot with a slope of about 3 is obtained (Fig. 1, filled circles). Because the intermediate of the rate-determining stage remains constant in this series, the differences in the rate coefficients are largely due to differences in the stabilities of the protonated substrates, the initial states of the rate-determining stages. Thus the found linear free energy relationship is understandable on the basis of the previous study of acetals [2] in which a linear correlation was found between
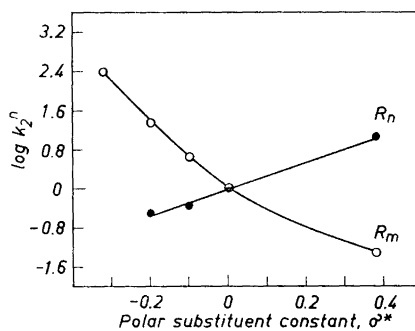

Fig. 1. The relation between the relative rate coefficients of the rate-determining heterolysis of protonated acetals and Taft's σ^* values of the alkyl groups adjacent to the oxygen atoms. ● The leaving group effect and ○ the effect of the remnant of the molecule.

the basicity of the oxygen atom and the polar substituent constant of the neighbouring substituent.

Similarly as above, we can compare the relative rate coefficients of the rate-determining heterolysis of the protonated substrate when the substituent R_m in the remnant is varied:

R_m (in the remnant)	$ClCH_2CH_2$	CH_3	CH_3CH_2	$(CH_3)_2CH$
$k_2{}^n$ (relative)	0.048	1.0	4.5	22

In this series the increase of the rate coefficient with increasing electron releasing power of R_m is largely due to the increasing stability of the intermediate ion because the leaving group remains constant and the pK_a values of the protonated forms are virtually equal. When the relative rate coefficients are plotted against Taft's σ^* values, a plot with a weak upward curvature is obtained with an average slope of approximately -7 (Fig. 1, open circles). Thus the inductive polar effects of the substituents are more marked when they are in the remnants than when they are in the leaving groups. Naturally, the change in the polarity of the substituents has an inverse effect to the rate coefficients in these cases.

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