The Kinetics of the Uncatalyzed Hydrolysis of Aliphatic Acylals

PENTTI SALOMAA

Department of Chemistry, University of Turku, Turku, Finland

The hydrolysis of acylals has been the subject of several kinetic investigations.[1-4] However, the uncatalyzed hydrolysis of these compounds has been studied in the case of cyclic acylals only. The present paper reports experimental data for a number of aliphatic acylals along with supplementary values relating to the corresponding acid-catalyzed reaction.

The methoxymethyl esters of mono-, di- and trichloroacetic acids were prepared from the acids and methoxymethyl chloride, CH_3OCH_2Cl. The freshly distilled chloride was added in small proportions into a cooled solution of chloroacid and pyridine in diethyl ether. The reactants were used in equimolar quantities. To accomplish the reaction the solution was refluxed for 2 h. The solution was then separated from the salts in a centrifuge and the ether distilled off, after which the residue was distilled under reduced pressure in a Todd precision fractionation assembly. The following physical constants were obtained for the purified compounds:

Methoxymethyl chloroacetate, b.p. 96°C/39 torr, d_4^{20} 1.2503, n_D^{20} 1.4298, $[R]_D$ 28.65.

Methoxymethyl dichloroacetate, b.p. 102°C/40 torr, d_4^{20} 1.3630, n_D^{20} 1.4460, $[R]_D$ 33.85.

Methoxymethyl trichloroacetate, b.p. 116°C/18 torr, d_4^{20} 1.4672, n_D^{20} 1.4613, $[R]_D$ 38.82.

α-Methoxyethyl acetate was synthesized according to Hurd and Green.[5] B.p. 56°C/73 torr, d_4^{20} 0.9753, n_D^{20} 1.3873, $[R]_D$ 28.53.

The other acylals studied were prepared as described earlier.[1]

The experimental technique of the kinetic measurements and the method of calculation were those reported in connection with earlier studies of cyclic acylals.[2,3] In initially neutral solutions the reactions were autocatalytic and followed the rate law

$$dx/dt = (k_0 + k_a[H^+])\,(a-x)$$

in which k_0 and k_a are the rate coefficients of the uncatalyzed and hydrogen ion-catalyzed reactions, respectively. Two or three additional measurements were made in each case in 0.03 to 0.1 M hydrochloric acid solutions. Table 1 gives the values of the rate coefficients obtained along with derived kinetic quantities. The second is used as the dimension of time. E is in kcal/mole and S in cal/(degree × mole).

The experimental results obtained suggest that the mechanism of the uncatalyzed hydrolysis of the acylals studied is essentially similar to that proposed for the corresponding reaction of 2-alkyl-substituted 1,3-dioxolones,[3] *i.e.* that involving a rate-determining ionization of the acylal:

$$RCOOCHR'OCH_3 \rightarrow RCOO^-$$
$$+ CHR' \overset{+}{=} OCH_3$$
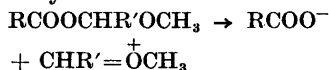
First, the magnitudes of the entropies of activation conform to this mechanism.[3,4] Second, the increasing acid strength of the parent acid will increase the tendency of the group RCOO to act as a leaving group, whereupon the rate coefficients of the esters increase in the sequence: acetic, formic, chloroacetic, dichloroacetic, and trichloroacetic acid. Moreover, when the logarithms of these rate coefficients are plotted against the pK values of the parent acids an approximately straight line is obtained, thus indicating a typical free-energy correlation. Third, the enhanced reactivity of α-methoxyethyl acetate when compared with methoxymethyl acetate is in general harmony with this mechanism.[3]

Considering the hydrogen ion-catalyzed hydrolysis, it was concluded earlier[1] that the mechanism of this reaction is *A1*. The present data allow some new observations to be made. As the transition state of the *A1*-hydrolysis of acylals differs from that of the uncatalyzed hydrolysis by a proton, the ratio of the rate coefficients of the uncatalyzed and acid-catalyzed hydrolyses is simply the acid dissociation constant of the critical complex of the acid-catalyzed reaction.[6] This gives the following pK values for these transition states, which may be contrasted with those of the parent acids:

	pK‡	pK (acid)
$CH_2ClCOOCH_2OCH_3$	0.9	2.8
$HCOOCH_2OCH_3$	2.3	3.8
$CH_3COOCH_2OCH_3$	2.7	4.7

As the pK values of the protonated substrate molecules involved must be negative by several units,[7] it may be concluded that the carbon-oxygen bonds are nearly broken in the transition states.

16

Table 1. Kinetic data for the hydrolysis of aliphatic acylals in water solution. I = $HCOOCH_2OCH_3$; II = $CH_3COOCH_2OCH_3$; III = $CH_2ClCOOCH_2OCH_3$; IV = $CHCl_2COOCH_2OCH_3$; V = $CCl_3COOCH_2OCH_3$; VI = $CH_3COOCH(CH_3)OCH_3$.

(A) *Uncatalyzed reaction*

	°C	$10^4 k_0$	E_0	$\Delta S_0^{\ddagger}$
I	35	0.982		
I	45	2.64	19.2	−16.7
I	54.9	6.53		
II	35	0.175		
II	45	0.505	21.8	−11.4
II	54.9	1.52		
III	25	1.64		
III	35	5.26	20.6	− 8.6
III	45	14.5		
IV	25	30^a		
V	25	$\sim 1000^a$		
VI	5	26.9		

(B) *Hydrogen ion-catalyzed reaction*

	°C	$10^3 k_a$	E_a	$\Delta S_a^{\ddagger}$
I[b]	25	6.90	21.8	+ 2.7
II[b]	25	2.52	22.6	+ 3.4
III	25	1.47		
III	35	4.63	20.7	− 4.0
III	45	13.2		
VI	5	1290		

[a] Extrapolated from measurements in acetone-water mixtures. [b] Data from Ref. 1.

The above further suggests that the transition states of the *A1*-hydrolyses of acetals must be less acidic than those of the related hydrolyses of acylals. This implies that the deuterium solvent isotope effect [8] should be somewhat lower on the latter reaction than on the former, taking into account that the acidic transition states under comparison are structurally of a very similar type. This was confirmed experimentally. The k_D/k_H value measured for methoxymethyl acetate at 25°C was 2.23. This may be compared with the values for acetals, which are about 2.8.

1. Salomaa, P. *Acta Chem. Scand.* **11** (1957) 132, 239.
2. Salomaa, P. and Laiho, S. *Acta Chem. Scand.* **17** (1963) 103.
3. Salomaa, P. *Suomen Kemistilehti* **B 37** (1964) 86.
4. Fife, T. H. *J. Am. Chem. Soc.* **87** (1965) 271.
5. Hurd, C. D. and Green, F. O. *J. Am. Chem. Soc.* **63** (1941) 2201.
6. Kurz, J. L. *J. Am. Chem. Soc.* **85** (1963) 987.
7. Arnett, E. M. In *Progress in Physical Organic Chemistry*, Vol. 1, Interscience Publishers, New York 1963, pp. 289−294.
8. Salomaa, P., Schaleger, L. L. and Long, F. A. *J. Am. Chem. Soc.* **86** (1964) 1.