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Kinetics of Alkaline Hydrolysis of Esters. III. Acyl Acetals

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The kinetics of the alkaline hydrolysis of some acyl acetals (liquid and solid) was studied in 90 parts (wt/wt) aqueous ethanol medium. Steric and inductive effects were found to play an important role. A straight line relationship was observed between the rate constants for the alkaline hydrolysis of benzylidene-, and *m*- and *p*-nitrobenzylidene diacetates and Hammett's substitution constant, σ. In the case of *n*-butylidene and benzylidene diacetates the theory of mass transfer accompanied by fast pseudo first-order reaction was employed for the determination of rate constants in an aqueous medium.

There is a limited information available in the literature on the kinetics of the alkaline hydrolysis of acyl acetals. The reaction can be written as:

$$R'CH(OAC)_2 + OH^- \xrightarrow[\text{slow}]{k_2} R'\underset{\displaystyle OH}{\underset{|}{C}}H(OAC) + CH_3COO^- \quad (1)$$

$$R'\underset{\displaystyle OH}{\underset{|}{C}}H(OAC) + OH^- \xrightarrow{\text{fast}} RCHO + H_2O + CH_3COO^- \quad (2)$$

The first step of the hydrolysis has been reported to be first order with respect to the ester and first order with respect to hydroxyl ions.[1,2] The second step is very fast.[3] There are some discrepancies in the data reported in the literature concerning the rate constants of the alkaline hydrolysis of acyl acetals. Skrabal and Schiffrer[1] and Skrabal and Belavic[2] have reported the value of the rate constant for the alkaline hydrolysis of methylene diacetate to be 18 and 16 *l*/g·mol·sec at 25°C, respectively. Salmi and Kantola[3] have, however, reported a value of 5.3 *l*/g·mol·sec for methylene diacetate and 2.33 *l*/g·mol·sec for ethylidene diacetate. Most recently Euranto and Moisio[4] reported the rate constant for methylene diacetate as 5.85 *l*/g·mol·sec. It was thought desirable to study a series of typical acyl acetals like ethylidene-, *n*-butylidene- and benzylidene diacetates. The effect of an electronegative group, $-NO_2$, in the benzene ring of benzylidene diacetate was also studied in this work.

Mechanism

An acyl acetal is an acetic ester with the group $-OCOCH_3$ at the α-carbon atom of the alkyl part.

$$CH_3COO\underset{\displaystyle OCOCH_3}{\underset{|}{C}}H-R'$$

The alkaline hydrolysis of an acyl acetal probably involves acyl-oxygen fission ($B_{AC}2$)[5] and the following mechanism is likely to hold:

$$HO^- + \underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle O}{\overset{\|}{C}}}}-O-\underset{\displaystyle R'}{\underset{|}{C}}-OCOCH_3 \underset{\text{I}}{\overset{\text{Slow}}{\rightleftharpoons}} \left[HO-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle O}{\overset{|}{C}}}}-O-\underset{\displaystyle R'}{\underset{|}{C}}-OCOCH_3 \right]^- \quad (3)$$

$$\left[\quad \right] \overset{\text{fast}}{\underset{\text{II}}{\rightleftharpoons}}$$

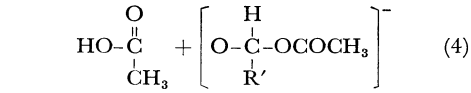
1) A. Skrabal and A. Schiffrer, *Z. Phys. Chem.*, **99**, 290 (1921).

2) A. Skrabal and M. Belavic, *ibid.*, **103**, 451 (1923).

3) E. J. Salmi and K. K. Kantola, *Ann. Acad. Sci., Fennicae, Ser.* A, XLVI, No. 2 (1936).

4) E. K. Euranto and A. Moisio, Suomen Kemistilehti, **37B**, 92 (1964).

5) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Holt, Richard and Winston, N. Y., Chicago, San Francisco, Toronto, London (1964), p. 314.



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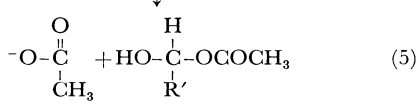

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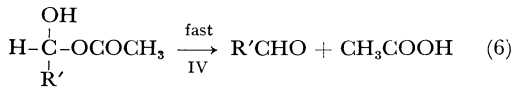

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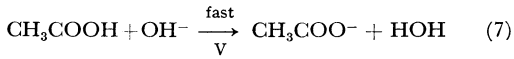

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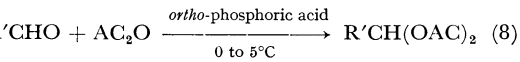
Materials

Ethylidene-, *n*-butylidene- and benzylidene diacetates were prepared by the reaction of the relevant aldehyde with acetic anhydride at a temperature of about 0 to 5°C in the presence of 0.5 per cent *ortho*-phosphoric acid as a catalyst.[6]



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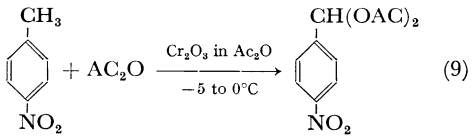
o-, *m*- and *p*-Nitrobenzylidene diacetates were synthesized by the method reported in the literature.[7]



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Ethylidene-, *n*-butylidene-, and benzylidene diacetates were purified by fractional distillation at a reduced pressure (10 to 50 mmHg). *o*-, *m*-, and *p*-Nitrobenzylidene diacetates were purified by recrystallization using 95 per cent ethanol as a solvent. For all the esters, studied in this work, except *n*-butylidene diacetate, the physical properties are reported in the literature. The boiling point of *n*-butylidene diacetate was 106°C at 25 mmHg.

Commercial ethanol was purified by the standard method. The amount of alcohol was estimated by the dichromate method.[8]

Kinetic Measurements

The kinetics of alkaline hydrolysis of acyl acetals was studied in 90 per cent (wt/wt) aqueous ethanol as some of the esters have very low solubility in water. Further, the rate constant of some of fast reacting acyl acetals can be conveniently studied in the alcoholic medium as rate constants in 90 per cent (wt/wt) aqueous ethanol medium are substantially lower than in water. In addition, experiments were carried out at lower temperatures so that the homogeneous method could be used.

Appropriate amounts of sodium hydroxide and ester solutions were taken separately in two conical flasks and brought to the experimental temperature in the thermostatic bath where temperature could be controlled to within ±0.05°C of the desired temperature. The reactants were mixed at a noted time and aliquots were withdrawn periodically into flasks containing a known excess of standard hydrochloric acid solution to arrest the reaction. The excess acid was back titrated with standard sodium hydroxide solution to a phenolphthalein end point. The following equation was used to calculate the rate constant:

$$k_2 = \frac{2.303}{t(2a-b)} \log_{10} \frac{b(a-x)}{a(b-2x)} \cdot \frac{V}{N} \qquad (10)$$

where, a and b are the initial concentrations of the ester and alkali, in terms of m*l* of sodium hydroxide of N normality used as titrant, respectively; $(a-x)$ and $(b-2x)$ are the concentrations of these reactants at time t. V is the volume of sample withdrawn from the reaction mixture, m*l*. A plot of $\log_{10}(a-x)/(b-2x)$ against t, should give a straight line with a slope of $k_2(2a-b)/2.303 \cdot N/V$ from which the value of the rate constant, k_2, can be calculated.

For fast reacting esters which are sparingly soluble in water, the theory of diffusion accompanied by fast pseudo first order reaction was employed for studying the kinetics. The details of this method have been reported in the previous paper.[9]

Results and Discussion

In Table 1 are reported the second order rate constants for the alkaline hydrolysis of some acyl acetals. The values are very much higher than that for simple acetic esters. The higher values are due to the presence of a highly electron attracting group, $-O-\overset{\overset{O}{\|}}{C}-CH_3$, at the α-carbon atom of the alkyl part of the ester. The nature of R′ of an acyl acetal would also influence the rate of the reaction as it is also attached to the α-carbon atom of the alkyl part. The rate would increase with an increase in the electronegativity of R′ and decrease when R′ is a bulky group.

The most recent value of rate constant for alkaline hydrolysis of methylene diacetate, reported by Euranto and Moisio[4] is 5.85 *l*/g mol sec in water at 25°C. It would be expected that the rate constant for ethylidene diacetate would be about 4.0 *l*/g·mol·sec in water at 25°C as the rate constant decreases

6) W. Davy and B. R. Gwilt, *J. Chem. Soc.*, **1955**, 1385.

7) B. M. Nordlender and W. E. Cass, *J. Amer. Chem. Soc.*, **69**, 2679 (1947).

8) N. R. Kamath and M. M. Sharma, *J. Sci. Ind. Res.*, **20D**, 200 (1961).

9) R. C. Sharma and M. M. Sharma, *J. Appl. Chem.*, **19**, 162 (1969).

TABLE 1. RATE CONSTANTS FOR THE ALKALINE HYDROLYSIS OF ACYL ACETALS IN 90 PER CENT (wt/wt) AQUEOUS ETHANOL

No.	$R'CH(OAC)_2$ R′	k_2, l/g·mol·sec, temperature, °C							E kcal/g·mol
		−5.5	0.2	5	10	15	25	30	
1	$-CH_3$	0.118	0.166	0.256	0.328	0.495	1.08*	1.38*	11.0
2	$-CH_2CH_2CH_3$	0.089	0.128	0.182	0.301	0.372	0.75*	0.871*	10.3
3		0.275	0.357	0.479	0.76	—	2.51*	3.16*	12.1
4		0.234	0.3	0.394	0.602	0.77	1.78*	2.2	11.2
5		0.953	—	—	—	—	—	—	—
6		1.15	—	—	—	—	—	—	—

* Extrapolated

by a factor of about 1.5 when ethyl group is substituted at the alkyl portion instead of methyl group.[10] The value of the rate constant obtained in this work is 1.08 l/g·mol·sec in 90 per cent (wt/wt) aqueous ethanol at 25°C (extrapolated). It is likely that the rate constant increases by a factor of about 4 when water is used instead of 90 per cent (wt/wt) aqueous ethanol. Thus the estimated rate constant would be about 4.3 l/g·mol·sec.

n-Butylidene diacetate reacts at a rate lower than that of ethylidene diacetate because of the steric effect. The extrapolated value of the rate constant in 90 per cent (wt/wt) aqueous ethanol is 0.75 l/g·mol·sec at 25°C. The value of the ratio of the rate constants for ethyl and butyl acetates of about 1.35[11] may be compared with the ratio of rate constants for ethylidene and butylidene diacetates of about 1.4. Apparently the effect of steric factors for the alkaline hydrolysis of acetic esters and the corresponding acyl acetals is comparable.

The rate constant for the alkaline hydrolysis of benzylidene diacetate is nearly twice that of ethylidene diacetate. The higher rate is due to the electronegative nature of the phenyl group. The inductive effect is of the same order of magnitude as observed in the case of benzyl acetate.[12] The values of the rate constant for ethyl and benzyl acetates are 0.11 and 0.2 l/g·mol·sec, respectively, in water at 25°C.

It is obvious that substitution on the benzene ring of benzylidene diacetate would affect the value of the rate constant. Tommila and Hinshelwood[13] have studied the influence of substitution on the alkaline hydrolysis of benzoic, phenyl and benzyl esters.

The values of the rate constants for the alkaline hydrolysis of benzylidene diacetates were obtained at −5.5°C as these esters are relatively fast reacting. These values are 1.153 and 0.953 l/g·mol·sec

TABLE 2. RELATIVE INFLUENCE OF *m*- AND *p*-NITRO SUBSTITUENTS ON THE ALKALINE HYDROLYSIS OF ESTERS

No.	Ester	Solvent	Temperature °C	k_2, l/g·mol·sec			Ratio (m/p)	References
				Unsubstituted	*m*-Nitro substituted	*p*-Nitro substituted		
1	Ethyl benzoate	60% (wt/wt) aq. acetone	25	0.00289	0.1365	0.2465	0.554	13
2	Phenyl acetate	60% (wt/wt) aq. acetone	25	0.537	5.49	8.05	0.7	13
3	Benzyl acetate	60% (wt/wt) aq. acetone	25	0.0697	2.13	2.685	0.682	13
4	Benzylidene diacetate	90% (wt/wt) aq. ethanol	−5.5	0.275	0.953	1.15	0.828	This work

10) A. I. Kravchenko and U. E. Penzova, *Zh. Obsch. Khem.*, **20**, 2076 (1951); *Chem. Abstr.*, **45**, 1296 (1951).

11) M. M. Sharma and R. C. Sharma, unpublished work.

12) A. Skrabal and M. A. Hugetz, *Monatsh*, **47**, 17 (1926).

13) E. Tommila and C. N. Hinshelwood, *J. Chem. Soc.*, **1938**, 1801.

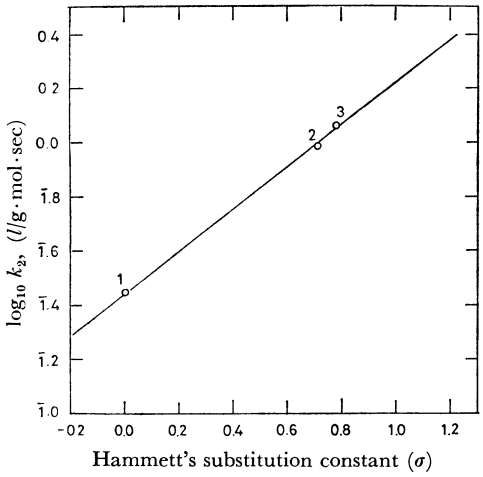

Fig. 1. Hammett's plot.
○(1) Benzylidene diacetate
○(2) *m*-Nitrobenzylidene diacetate
○(3) *p*-Nitrobenzylidene diacetate

for *p*- and *m*-nitrobenzylidene diacetates, respectively. The ratios of *m*- and *p*-substituted esters of different types are compared in Table 2.

A straight line relationship is obtained when the logarithms of the rate constants for the alkaline hydrolysis of benzylidene and *m*- and *p*-nitrobenzylidene diacetates in 90 per cent (wt/wt) aqueous ethanol at −5.5°C are plotted against the Hammett's substitution constant,[14] σ (Fig. 1). It would be necessary to investigate the kinetics of alkaline hydrolysis of some more related substituents, notably chloro- and bromo-, before it can be said that the Hammett's correlation is really applicable. Fife and Jao[15] have studied the acid catalyzed hydrolysis of acetals containing substituted benzene ring and found a straight line correlation between the logarithms of the rate cnstants and the substitution constant, σ.

Ortho Effect

It was thought desirable to investigate the effect of *ortho*-substitution on the kinetics of the alkaline hydrolysis of benzylidene diacetate. For this purpose, *o*-nitrobenzylidene diacetate was considered. *Ortho* effects arising from the proximity of the substituents to the reaction center vary with the reaction as well as with the substituents and this makes it almost impossible to represent the effect of *ortho*-substituents in the same manner as those of *m*- and *p*-substituents. The rate constant for the alkaline hydrolysis of *o*-nitro-benzylidene diacetate was found to be 0.23 l/g·mol·sec in 90 per cent (wt/wt) aqueous ethanol at −5.5°C which is lower than the value of 0.275 l/g·mol·sec for benzylidene diacetate.

Watkinson *et al.*[16] have investigated the *Ortho* effect in the alkaline hydrolysis of *Ortho* substituted ethyl phenyl acetate. The ratio of the rate constants of the unsubstituted and *o*-substituted benzylidene diacetates of 1.18, may be compared with that reported by Watkinson *et al.*[16] for unsubstituted and *o*-substituted ethyl phenyl acetates of 1.28.

Some of the acyl acetals satisfy the conditions for the applicability of the theory of mass transfer accompanied by fast pseudo first-order reaction for the determination of the rate constant for the alkaline hydrolysis of esters.[9] Solubilities of esters in water and aqueous solution of sodium chloride were determined experimentally in this work as such data are not available in literature. The results were correlated by the methods reported in the literature,[17-19] and are given in Table 3. Diffusivities of esters were estimated by the method of Wilke and Chang[20] and are reported in Table 4. The rate constants determined by the diffusion method are also reported in Table 4.

The rate constant for the alkaline hydrolysis of *n*-butylidene diacetate was found to be 2.58 l/g·mol·sec in the aqueous medium at 30°C (2M NaCl+1N NaOH). The value of the rate constant in alkaline solution at vanishing concentration of OH^- would be higher because of the negative salt effect. The value of the rate constant for the alkaline hydro-

Table 3. Solubilities of acyl acetals in water and aqueous sodium chloride solutions (1 to 4M)

No.	Acyl acetal	Temperature °C	Solubility, in water g·mol/cm³ $[E]_w \times 10^5$	K_s* (l/g ion)
1	Ethylidene diacetate	30	46	0.175
2	*n*-Butylidene diacetate	30	3.02	0.192
3	Benzylidene diacetate	30	0.139	0.265
		50	0.802	0.269
		60	1.026	0.266

* $\log_{10} \frac{[E]_w}{[E]} = K_s I$[9];
[E]=Solubility of the ester in aqueous sodium chloride solution, g·mol/cm³
I=Ionic strength, g·ion/l

14) R. W. Taft, Jr., "Steric Effect in Organic Chemistry," ed. by M.S. Newman John Wiley & Sons, Inc., N. Y. (1956), p. 556.
15) T. H. Fife and L. K. Jao, *J. Org. Chem.*, **30**, 1492 (1965).
16) J. K. Watkinson, W. Watson and B. L. Yates, *J. Chem. Soc.*, **1963**, 5437.
17) F. A. Long and W. F. McDevit, *Chem. Rev.*, **51**, 119 (1952).
18) D. W. Van Krevelen and P. J. Hoftizer, *Chem. Ind.* (London), **1948**, 168.
19) P. J. Kothari and M. M. Sharma, *Chem. Eng. Sci.*, **21**, 391 (1966).
20) C. R. Wilke and P. Chang, *A. I. Ch. E. J.*, **1**, 264 (1955).

TABLE 4. SPECIFIC RATES OF EXTRACTION, DIFFUSIVITIES AND RATE CONSTANTS FOR ALKALINE HYDROLYSIS OF ACYL ACETALS IN AQUEOUS SOLUTIONS

No.	Acyl acetal	Concentration of electrolytes, g·mol/*l*		Temp. °C	Specific rate of extraction, g·mol/cm²·sec ×10⁸	Diffusivity ×10⁶, cm²/sec	k_2 *l*/g·mol·sec
		NaCl	NaOH				
1	*n*-Butylidene diacetate	2	1	30	2.97	5.15	2.58
2	Benzylidene diacetate	0	0.5	30	2.94	6.46	11.5
		0	0.5	50	7.65	10.0	51.3
		0	0.5	60	14	12.1	93.6

lysis of *n*-butylidene diacetate at 30°C in 90% (wt/wt) aqueous ethanol is 0.87 *l*/g·mol·sec (Table 1). It would be expected that the rate constant in the aqueous medium would be about four times that in the aqueous medium containing 90% (wt/wt) alcohol. Thus the value of the rate constant in the aqueous medium would be expected to be about 3.5 *l*/g·mol·sec.

As the melting point of benzylidene diacetate is 46°C, the kinetics of alkaline hydrolysis was studied by the extraction of molten ester in the stirred cell at 50 and 60°C. Benzaldehyde, the hydrolysis product of benzylidene diacetate, may further react with sodium hydroxide (Cannizzaro's reaction).

$$2R'CHO + NaOH \rightarrow R'COONa + R'CH_2OH \quad (11)$$

Therefore, it was necessary to study the specific rate of extraction in aqueous sodium hydroxide for a short period (say 5 min) so that the possibility of the Cannizzaro's reaction was minimised. The rate constant was also determined at the room temperature (30°C) by the solid dissolution technique. The value of the rate constant for the alkaline hydrolysis of benzylidene diacetate was found to be 11.4 *l*/g·mol·sec at 30°C in water (Table 4). This value is about four times greater than the extrapolated value obtained by the conventional method in 90 per cent (wt/wt) aqueous ethanol at 30°C (3.16 *l*/g·mol·sec, Table 1). The energy of activation was found to be 13 kcal/g·mol.

Ethylidene diacetate did not satisfy the necessary conditions for the validity of the diffusion method as its solubility is relatively high. *o*-, *m*- and *p*-Nitrobenzylidene diacetates, on the other hand have too low a solubility to be determined accurately. In view of the above the diffusion method could not be used for these esters and conventional method was used employing 90 per cent (wt/wt) aqueous ethanol as the medium.

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