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HYDROLYTIC CLEAVAGE OF THE C—C DOUBLE BOND IN ORGANIC LEWIS-ACIDS

ORGANIC LEWIS ACIDS[†][*]

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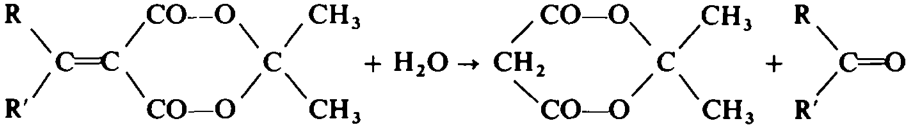
Abstract—The hydrolysis of various organic Lewis acids (I) in 10% MeOH at 25° is followed spectrophotometrically. The rate of hydrolysis depends on the pH-value and shows a maximum value at $pH = pK'_L$. The reaction is subject to general base catalysis.

A mechanism is proposed in accordance with the experimental results and the rate determining steps are discussed.

THE reaction of aldehydes or ketones with active methylene compounds, which leads to substituted olefins, is known in literature as the Knoevenagel-condensation;[1] its mechanism and kinetics have been investigated mainly by S. Patai, *et al.*[2] In the course of a research work about nucleophilic attack on carbon–carbon double bonds, S. Patai and Z. Rappoport[3] measured the kinetics of the hydrolysis of various arylmethylenemalononitriles in 95% EtOH; they proposed a mechanism, which presents the same steps in opposing sequence as for the carbonyl-methylene condensation and they concluded that the rate-determining step was the addition of H_2O to the C—C double bond.

During the measurement of acidity constants in aqueous solvent mixtures a hydrolytic decomposition of the Lewis-acid (I)[4,5] to Meldrum's acid and the corresponding carbonyl compound was observed (1).


(1)

Rates of hydrolysis were measured for various compounds of type I in H_2O with 10% CH_3OH at $pH = 1{\cdot}1$, in order to get an idea of the errors in the acidity constants. In one case, (**Ia**, $R = C_6H_5$, $R' = H$) the pH-dependence of the hydrolysis was investigated as well. At $pH = pK'_L$ a maximum was found in the $\bar{k}/p$H-plot. This complicated pH-dependence suggested a multistep hydrolysis mechanism, which seems to be of particular interest for a more general concept of Knoevenagel and Retro-Knoevenagel reaction. Accordingly we started a detailed investigation of the hydrolytic behaviour of various organic Lewis acids (**I**), which differ strongly in their pK'_L values. Hence a wide pH range could be covered by our measurements.

[†] 26th communication.

[*] 25th communication: H. Kisch, F. Mark and O. E. Polansky, Mh. f. Chemie.

RESULTS AND MECHANISM

The rates of hydrolysis of various Lewis acids (I) were measured spectrophotometrically as a function of pH in 10% aqueous MeOH at 25°; the measurements were extended from $pH = 1$ to $pH = 11$ ($\Delta pH = 1$). The pH of the solutions was adjusted by means of suitable buffer solutions. At pH-values, where $pH \leqslant pK'_L$ the decrease in concentration of I was measured directly; at higher pH-values, $pH > pK'_L$, we followed the formation of the carbonyl compound by means of the method described by E. L. King,[8] wherein the absorbance of the reaction solution is measured relative to the absorbance of another reaction solution, started at a different time. It turned out, that in all cases the pseudomonomolecular rate constant of hydrolysis shows a maximum at pH — pK'_L, and that the maximum rate of hydrolysis increases with increasing pK'_L-value of I; compound Ib (R = o-NO_2-C_6H_4, R' = H) makes an exception: the slower hydrolysis is caused by steric hindrance (Fig 1).

With the exception of high pH-values, where transesterification[9] occurs through direct attack of the base on the carbonyl-carbon atom of the acylal ring, the hydrolysis always follows a reaction rate of first order in the Lewis acid I. No intermediate stages of the decomposition reaction were observed, since the sum of the concentrations of Lewis acid and hydrolysis-products was always equal to the starting concentration of I.

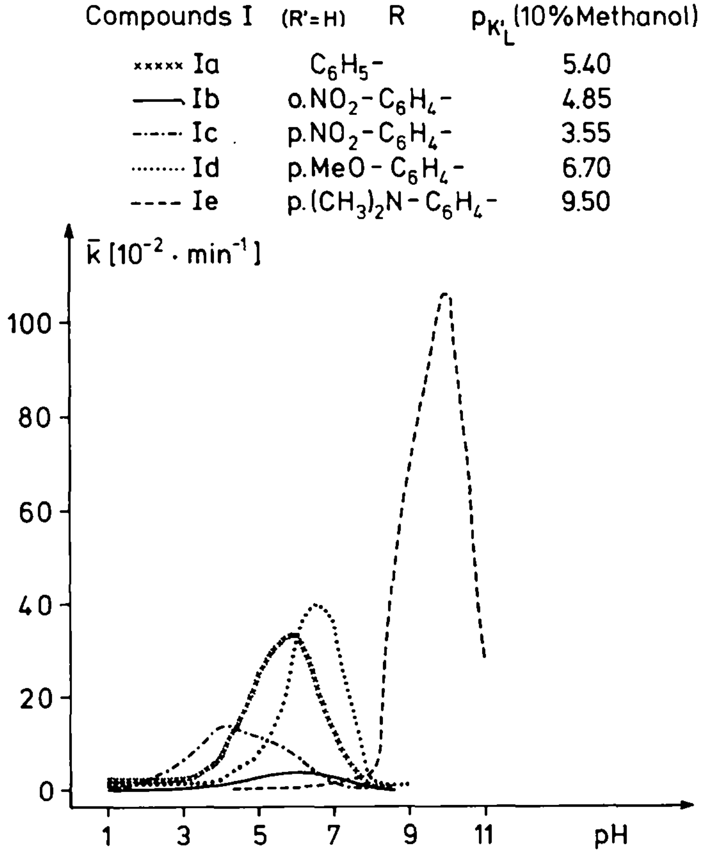


FIG 1. Hydrolysis rate constants of various organic Lewis acids I as function of the pH-value in 10% MeOH at 25°. (Buffer concentration not taken into consideration, ionic strength = 0·1).

TABLE 1. RATES OF HYDROLYSIS $\bar{k}\cdot10^2\cdot\text{min}^1$ OF VARIOUS ORGANIC LEWIS ACIDS I IN 10% MeOH aq AT 25° (*cf* Fig 1)

*p*H	Ia	Ib	Ic	Id	Ie
1·1	1·90	0·034	0·98	1·68	0·33
2·0	1·98	0·055	1·65	1·78	0·35
3·0	2·0	0·049	5·60	1·93	0·32
4·0	6·00	1·02	13·5	2·65	0·30
5·0	23·8	2·45	11·6	7·30	0·36
6·0	34·2	3·20	8·80	29·9	0·56
7·0	13·6	2·83	0·41	36·0	2·37
8·0	1·16	0·39	0·34	2·81	3·48
9·0	*	*	*	1·01	68·2
10·0	*	*	*	*	106
10·5	*	*	*	*	75·2
11·0	*	*	*	*	*

* No first order reaction any longer

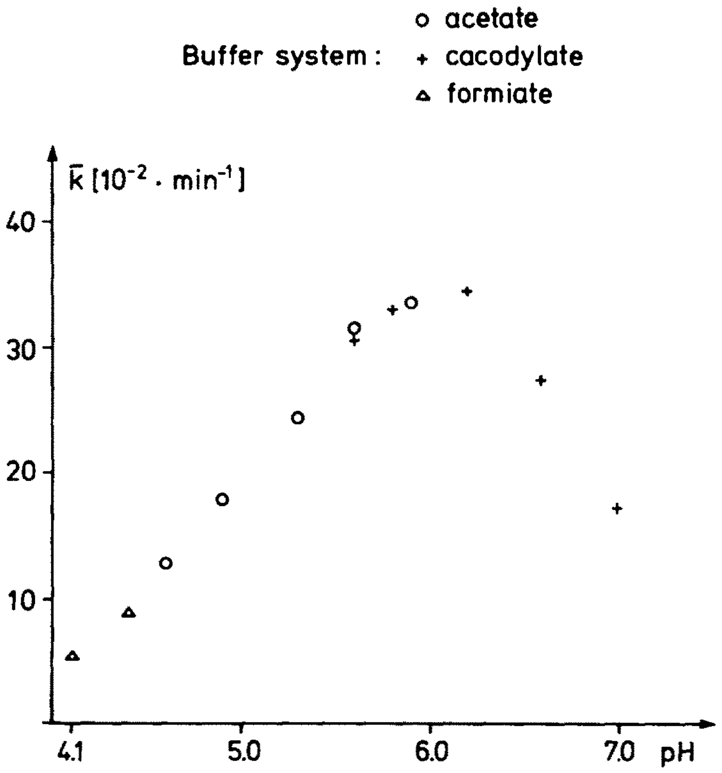


FIG 2. Extrapolated values of $\bar{k}$ for the hydrolysis of Ia; $c_{Buffer} \rightarrow 0$.

Table 2. Hydrolysis rate constants $\bar{k}\cdot 10^2\cdot \mathrm{min}^1$ of benzylidene meldrums acid Ia in 10% MeOH aq at 25° obtained from extrapolation of $c_{\mathrm{Buffer}} \rightarrow 0$ (*cf* Figs 2 and 3)

Buffer system	Formiate		Acetate		Cacodylate	
	pH	$\bar{k}$	pH	$\bar{k}$	pH	$\bar{k}$
$\bar{k}$:($10^{-2}\cdot\mathrm{min}^{-1}$)	3·5	3·0	4·6	13·0	5·6	30·4
	3·8	4·4	4·9	18·0	5·8	33·0
	4·1	5·5	5·3	24·5	6·2	34·2
	4·4	9·0	5·6	31·5	6·6	27·5
			5·9	33·5	7·0	17·2

The rate of hydrolysis depends on the ionic-strength of the solution, on the concentration of the buffer, and on the buffer-system. In order to determine the true pH-dependence of the hydrolysis, measurements with Ia in the range $p\mathrm{H} = 4{\cdot}0 - 7{\cdot}0$ were made and the above mentioned factors were eliminated.

Effect of the ionic strength. The hydrolysis rate of Ia in a 0·1 N KCl solution increases by 10% against the hydrolysis rate in pure H_2O; the corresponding values are $\bar{k} = 16{\cdot}5 \times 10^{-2}\ \mathrm{min}^{-1}$ and $15{\cdot}0 \times 10^{-2}\ \mathrm{min}^{-1}$. All the following measurements were undertaken at constant ionic strength ($I = 0{\cdot}1$).

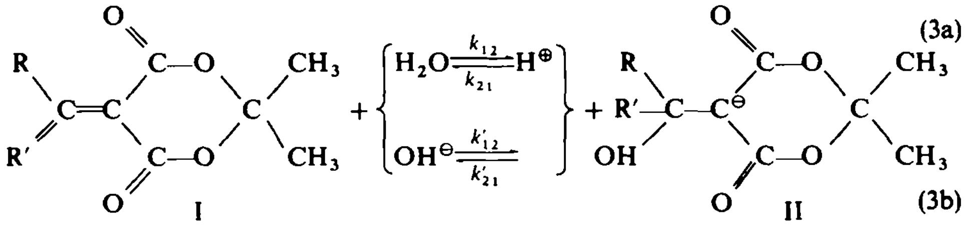
Effect of concentration and nature of the buffer. The buffer-concentration was varied at constant pH-values and constant ionic-strength; an extrapolation to the value $c_{\mathrm{Buffer}} = 0$ was made. Measurements in different buffer systems led to the same values of $\bar{k}$ for $c_{\mathrm{Buffer}} \rightarrow 0$. Hence the rate of hydrolysis becomes independent on the buffer system if the buffer concentration is strongly reduced (Fig. 2 Tab. 2).

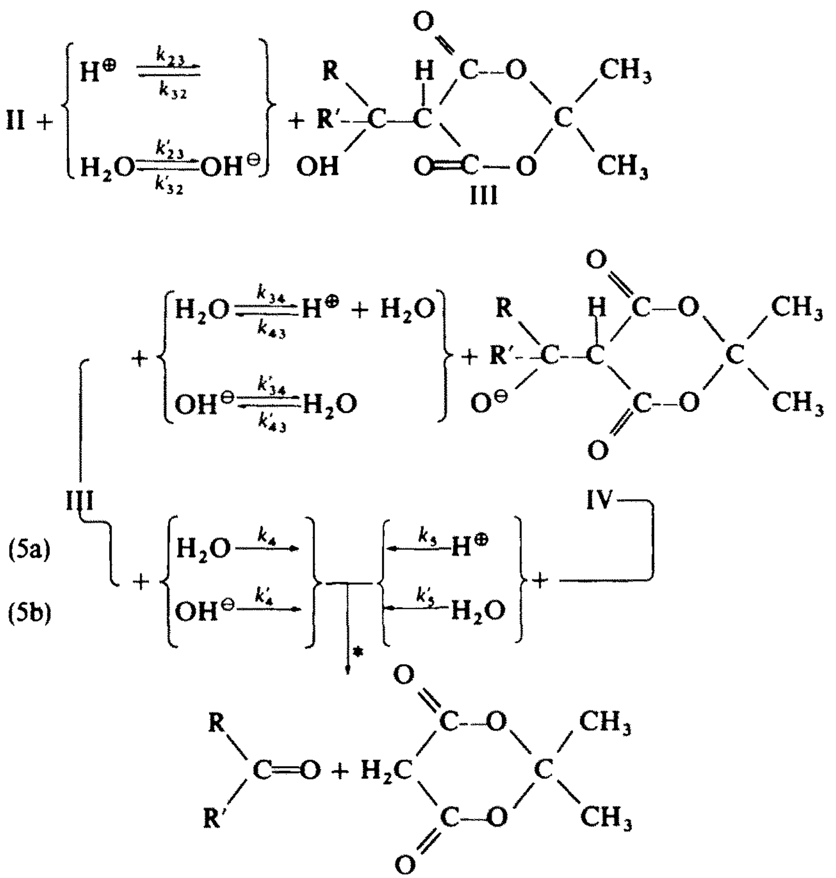
To investigate the catalytic action of the buffer system we employed Eq (2) described by Emmett[10] for the calculation of the catalytic coefficients of general acid and base catalysis.

$$\bar{k} = k_r + [\mathrm{HB}]\,(k_{\mathrm{B}^\ominus} + r^{-1})$$
$$r = \frac{[\mathrm{HB}]}{[\mathrm{B}^\ominus]};\ k_r = k_0 + k_{\mathrm{H}^\oplus}[\mathrm{H}^\oplus] + k_{\mathrm{OH}^\ominus}[\mathrm{OH}^\ominus] \qquad (2)$$

Fig 3 shows the results of these measurements; combination of 2 of the 5 r-values at a time leads to 10 equation systems for the calculation of k_{HB} and k_{B^-}. The mean values $k_{\mathrm{HB}} = 0{\cdot}0$ and $k_{\mathrm{B}^-} = 0{\cdot}57\ \mathrm{min}^{-1}\ (\mathrm{Mol/l})^{-1}$, obtained by means of least-square fitting, are in accordance with the presence of general base catalysis.

In the following reaction scheme (Eqs 3–7) the possible reaction steps are described. We tried to find out if the experimental results confirm or exclude some of the reaction steps.





(4a) (4b) (6a) (6b) (5a) (5b) (7a) (7b)

* Irreversible cleavage of the C—C bond under the experimental conditions; all other steps very fast.

Since the intermediates III and IV could not be detected in the UV-spectra, their concentrations are very small, and a steady state treatment is applied for both intermediates.

In order to facilitate the discussion the curve (Fig 1) is subdivided in 3 regions: (a) a region where $pH \ll pK'_L$, in the following called "strongly acidic region"; (b) a region where $pH — pK'_L$ "neutral region"; (c) a region where $pH \gg pK'_L$ "strongly alcaline region".

In the "strongly acidic region" the reaction steps 3a, 4a and 5a or 6a and 7a are predominant, since OH^- has no importance because of its low concentration. The concentration of the Lewis-acid-anion II is very low in this range as well. Therefore we can also apply steady state treatment to II. Considering the reaction steps mentioned we obtain:

$$\frac{d[I]}{dt} = -\frac{k_{12}[H_2O]}{\frac{k_{21}}{k_{23}}\left(\frac{k_{32}}{k_4[H_2O]} + 1\right) + 1}[I] = -\bar{k}[I] \qquad (8a)$$

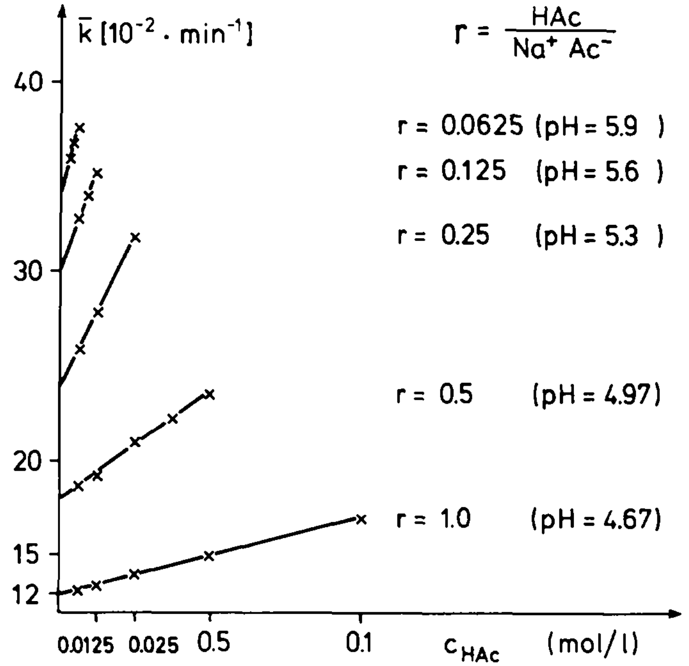


FIG 3. Hydrolysis of Ia in 10 MeOH at 25°; acetate buffer. (Investigation of general acid and base catalysis).

respectively

$$\frac{d[I]}{dt} = -\frac{k_{12}[H_2O]}{\frac{k_{21}}{k_{23}}\left\{\frac{k_{32}}{k_{34}[H_2O]}\left(\frac{k_{43}[H_2O]}{k_5}+1\right)+1\right\}+1}[I] \qquad (8b)$$

Eqs 8a and 8b are in accordance with the experimental results with regard to the reaction order; in our measurements first order in the Lewis acid **I** was always found. The rate constant varies only slightly as a function of *p*H as Eqs 8a and 8b indicate.

In order to find out if the reaction steps **5**, or the steps **6** and **7** are more important, the experimental results are correlated with other data. Since benzylidenemeldrums acid Ia has been examined most fully, it will be used as prototype compound.

The rate constants quotient of the Lewis acid-base reaction (3) is known from acidity-constant measurements.[4]

$$pK'_L\,(\text{Ia, 10\% MeOH}) = 5{\cdot}4 \qquad \frac{k_{12}}{k_{21}} = \frac{10^{-5\cdot4}}{[H_2O]} = 10^{-7\cdot1}$$

The equilibria are established faster than a few seconds, since no delay of the potential adjustment at the glass-electrode due to acid base reaction could be observed.[5]

The second intermediate equilibrium (4) corresponds to the acid-base reaction of a hydroxyalkylmeldrums acid; alkylmeldrums acids have *p*K-values of about 5 in 10% MeOH;[11] Eigen *et al.*[12] determined a value of 5×10^5 for k_{23}, so that we obtain: $k_{32} = 5 \times 10^0$.

Regarding the molecular structure of **III**, its dissociation constant (**6**) should lie in the order of magnitude of the acidity constants of secondary alcohols, hence $k_{34}/k_{43} < 10^{-14}$.

Inserting the experimental values in Eq 8a one obtains:

$$\frac{1}{\bar{k}} = 50 = \frac{5.10^{-2}}{k_4} + \frac{2{\cdot}5.10^5}{k_{23}} + \frac{2.10^{-2}}{k_{12}}$$

Substitution of k_{23} by its numerical value shows, that step 4a cannot be rate-determining; since k_{12} is expected, from equilibrium measurements, to be adequately fast, we conclude that k_4 represents the rate-determining constant, $k_4 \sim 10^{-3}$.

Proceeding analogously with Eq 8b one obtains:

$$\frac{1}{\bar{k}} = 50 = \frac{2{\cdot}5.10^{14}}{k_5} + \frac{5.10^{-2}}{k_{34}} + \frac{2{\cdot}5.10^5}{k_{23}} + \frac{2.10^{-7}}{k_{12}}$$

To fit into this equation, k_5 must have the value $k_5 > 10^{12}$; since this value exceeds even the numerical values for diffusion-controlled processes, we find that the hydrolysis in the "strongly acidic region" proceeds only through reaction step **5** and the steps **6** and **7** are excluded.

In the "strongly alkaline region" the equilibrium between **I** and **II** is completely shifted towards **II**, and the first "pre equilibrium" **I** $\rightleftharpoons$ **II** need not be considered further. One obtains a first order rate law in **II**, which does not depend on *p*H. No significant measurements with **Ia** could be made in this range, since, as mentioned before, transesterification of the acylal ring takes place. With compounds **Ib** and **Ic** a few measurements were made in this region; the experimental data confirm the beginning of a flat branch of the *k*/*p*H curve, as we would expect for a *p*H-independent rate at high *p*H.

While in the "strongly acidic region" one can use the steady state treatment for **II**, this is not possible at first in the "neutral region". A system of two coupled first order differential equations of the type $x'(t) = ax + by$ and $y'(t) = cx + dy$ is obtained for **I** and **II**. The solutions of such a system[13] correspond with a first order rate law for **I**. The calculation of the *p*H-dependence of the rate constant leads to an expression of the form:

$$\bar{k} = \frac{A[\mathrm{H}^{\oplus}]^2 + B[\mathrm{H}^{\oplus}] + C}{D[\mathrm{H}^{\oplus}]^2 + E[\mathrm{H}^{\oplus}] + F}$$

Reliable values for the coefficients *A*–*F* in our system cannot be given, because we need additional data for the individual rate constants.

The "neutral region" must therefore be regarded by means of a simplifying model; we assume, that in all steps the H_2O-molecule is the only reacting species, i.e. the hydrolysis proceeds through the steps **3a**, **4b** and **5a** or **6a** and **7b**; in addition the "neutral region" is subdivided into 2 parts: one, where $p\mathrm{H} < p\mathrm{K}'_{\mathrm{L}}$ and the other one, where $p\mathrm{H} > p\mathrm{K}'_{\mathrm{L}}$.

In the range $p\mathrm{H} < p\mathrm{K}'_{\mathrm{L}}$ we again use the stationary state treatment for **II**, this leads to:

$$\frac{\mathrm{d}[\mathrm{I}]}{\mathrm{d}t} = -\frac{k_{12}[\mathrm{H_2O}]}{\dfrac{k_{21}[\mathrm{H}^{\oplus}]}{k'_{23}[\mathrm{H_2O}]}\left(\dfrac{k'_{32}[\mathrm{OH}^{\ominus}]}{k_4[\mathrm{H_2O}]} + 1\right) + 1}[\mathrm{I}] \qquad (9a)$$

resp.

$$\frac{\mathrm{d}[\mathrm{I}]}{\mathrm{d}t} = -\frac{k_{12}[\mathrm{H_2O}]}{\dfrac{k_{21}[\mathrm{H}^{\oplus}]}{k'_{23}[\mathrm{H_2O}]}\left\{\dfrac{k'_{32}[\mathrm{OH}^{\ominus}]}{k_{34}[\mathrm{H_2O}]}\left(\dfrac{k_{43}[\mathrm{H}^{\oplus}]}{k'_5} + 1\right) + 1\right\} + 1}[\mathrm{I}] \tag{9b}$$

These relations are in agreement with the observed behaviour, that the decomposition rate decreases with decreasing pH.

In this range $p\mathrm{H} > p\mathrm{K}'_{\mathrm{L}}$ the equilibrium between **I** and **II** is almost completely shifted towards **II**, which therefore represents the real starting species of the hydrolysis; one obtains:

$$\frac{\mathrm{d}[\mathrm{II}]}{\mathrm{d}t} = -\frac{k'_{23}[\mathrm{H_2O}]}{\dfrac{k'_{32}[\mathrm{OH}^{\ominus}]}{k_4[\mathrm{H_2O}]} + 1}[\mathrm{II}] \tag{10a}$$

resp.

$$\frac{\mathrm{d}[\mathrm{II}]}{\mathrm{d}t} = -\frac{k'_{23}[\mathrm{H_2O}]}{\dfrac{k'_{32}[\mathrm{OH}^{\ominus}]}{k_{34}[\mathrm{H_2O}]}\left(\dfrac{k_{43}[\mathrm{H}^{\oplus}]}{k'_5} + 1\right) + 1}[\mathrm{II}] \tag{10b}$$

In spite of the approximative character of equations **9** and **10**, it is possible to correlate the experimental results with the kinetic data in the same way as it was done for eq. **8**; for eq. **9a** one obtains:

$$\frac{1}{\bar{k}}(p\mathrm{H} = 4{\cdot}0) = 17 = \frac{5.10^{-2}}{k_4} + \frac{5.10^{-1}}{k'_{23}} + \frac{2.10^{-2}}{k_{12}}$$

Neglecting the contribution of $1/k_{12}$ one obtains:

$$k_4 > 3.10^{-3} \quad \text{or} \quad k'_{23} > 2{\cdot}5.10^{-2}.$$

In this range it is not possible any more to regard with certainty one of the steps **4a** or **5b** as being rate-determining. In the same way one obtains $k'_5 > 10^7$ for eq. **9b**, a value, which still seems to be much too high.

Accordingly one obtains from Eqs 10a and 10b:

$$\frac{1}{\bar{k}}(p\mathrm{H} = 8{\cdot}0) = 100; \quad k_4 > 2.10^{-1}; \quad k'_5 > 2{\cdot}5.10^5$$

DISCUSSION

All our data are in good agreement with the multistep mechanism for the "Retro-Knoevenagel reaction" proposed above. In the strongly acidic "region" the rate determining step is the cleavage of the carbon–carbon bond ($k_4 \sim 10^{-3}$). In contrast to Patai's results[2c] the alcoholate anion (**IV**) can be excluded as intermediate in our case.

In the "strongly alkaline region" no analysis of the data is possible because of the transesterification reaction mentioned above.

In the "neutral region" the correlation is only partly satisfying; the experimental graph $\bar{k}$ as function of the pH (Fig 1) cannot be described by a simplified solution of the differential equations of the entire system; with the help of simplifying assumptions, there is the possibility of reproducing the ascending and descending branches of the curve and thus to prove the existence of a maximum. In this range, where the reaction steps involving OH^- ion become more important, the cleavage of the carbon–carbon bond is not the exclusively rate-determining process. In the alkaline range the rate determining step will certainly be **4b** (k'_{23}). Reaction step **3a** (k_{12}) can be excluded as being rate-determining, in every case.

Concerning the reaction paths 6 and 7, we found that rate constants of $k'_5 > 10^5$ are necessary, to fulfill the kinetic equations; this value seems much too high for the cleavage of a carbon–carbon bond, so that we may say, that IV will only be an intermediate of the hydrolysis at extremely high *p*H-values.

Finally, a critical comment. Our kinetic investigations of the hydrolytic cleavage of C—C double bonds were restricted to one type of electrophilic olefins—the organic Lewis acids. Our results differ in pathway and rate determining step from Patai's measurements and show one alternative mechanism. The reason for the change in mechanism has to be found in the different *p*H ranges where the hydrolysis occurs. For a detailed and generalized mechanism of the "Retro-Knoevenagel reaction" other systems with C—C double bonds varying extensively with respect to their substituents have to be investigated.

EXPERIMENTAL

The compounds of type I were synthetized as described in literature [6] and purified by recrystallisation or sublimation. Distilled H_2O and MeOH (p.a. Merck) were used as solvents.

The buffer solns were prepared from p.a. grade materials according to "Biochemists Handbook".[7]

The UV spectra were recorded on a Bausch and Lomb "Spectronic 505".

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