# Hydrolysis of Protolytic Esters

ALLAN ÅGREN, ULLA HEDSTEN and BRITTA JONSSON

Department of Chemistry, Royal Pharmaceutical Institute, Stockholm, Sweden

The hydrolysis of several esters with protolytic groups has been investigated in alkaline and acidic solution. The relation between reaction velocity and pH is discussed together with the best conditions for the determination of the activation energies of such esters.

In the alkaline hydrolysis of an ester of a carboxylic acid the following equation is valid

$$R_1 \cdot COOR_2 + OH^- = R_1 \cdot COO^- + R_2OH$$
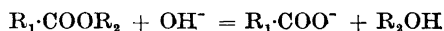
where R_1 and R_2 are radicals. This process has been studied with a great number of esters, both aliphatic and aromatic. Almost always the process has been found to be a second order one, and thus the following equation is valid

$$-dc/dt = k_{oh} \cdot c \cdot [OH^-]$$

where c is the concentration of the ester at the time t and $[OH^-]$ is the concentration of hydroxyl ion at the same time.
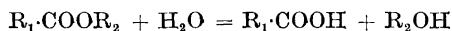
If the hydrolysis is performed at a constant pH value the process is pseudo monomolecular

$$-dc/dt = k'_{oh} \cdot c$$

where

$$k'_{oh} = k_{oh} \cdot [OH^-] \tag{1}$$

In the acidic hydrolysis of the ester the reaction may be written

$$R_1 \cdot COOR_2 + H_2O = R_1 \cdot COOH + R_2OH$$

This process is catalyzed by hydrogen ions, and often the following equation is found to be valid

$$-dc/dt = k_h \cdot c \cdot [H^+]$$

As the hydrogen ions are not consumed in the process and the acid formed is weak, $[H^+]$ is constant and thus the equation may be written

$$-dc/dt = k'_h \cdot c$$

where

$$k_h' = k_h \cdot [\text{H}^+] \tag{2}$$

Taking logarithms, eqns. (1) and (2) may be written

$$\log k_{oh}' = \log k_{oh} + \text{pH} - \text{p}K_w$$

and

$$\log k_h' = \log k_h - \text{pH}$$

respectively, where $\text{p}K_w$ is the negative logarithm of the ion product of water. Thus, k_{oh}' and k_h' change with varying pH as shown in Fig. 1. In this figure $\log k'$ refers to $\log k_h'$ in the left part of the figure, and to $\log k_{oh}'$ in the right part. The two lines cross at a pH value where the two processes are equally fast. Near this point the curved line shows the true velocity of the hydrolysis. (*Cf.* Tammelin and Larsson [1].)

Sometimes R_1 or R_2 in the ester, is a protolytic group. Depending on the pH of the solution, ethyl salicylate for example, exists as a molecule or as an ion:
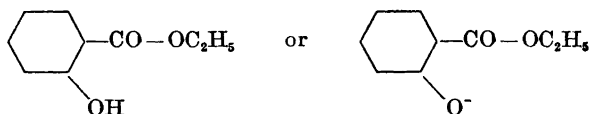
In a similar manner diethyl amino ethyl benzoate can exist as
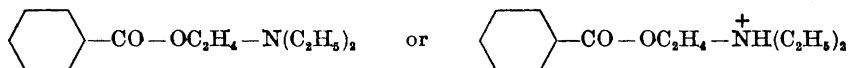
In the first example the ester may exist as an anion ester, in the second example as a cation ester.

Is such cases one may expect that the acidic form and the basic form of the ester may be hydrolyzed with different velocities. This is true in alkaline hydrolysis at least. In acidic hydrolysis there seems to be another situation. In the following, alkaline and acidic hydrolysis will be discussed separately.

ALKALINE HYDROLYSIS

In alkaline hydrolysis the reaction mechanism may be formulated in the following manner:
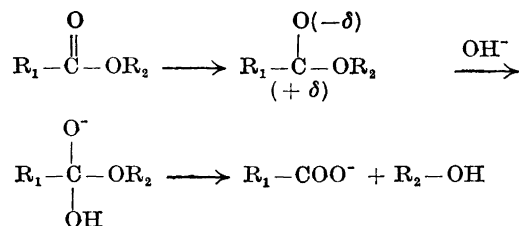
The carbonyl carbon has a partial positive charge, which attracts the hydroxyl ion. If R_1 or R_2 is a group which is electron attracting the process will be favoured. If the group is electron releasing the process will be slower. If the groups R_1 or R_2 have a positive or negative ionic charge this effect will be still more pronounced.

If the acidic and basic forms of the ester are called e_a and e_b, the reaction velocity may be written:

$$-\mathrm{d}c/\mathrm{d}t = k_{boh} \cdot [e_b] \cdot [OH^-] + k_{aoh} \cdot [e_a] \cdot [OH^-] \qquad (3)$$

where

$$c = [e_b] + [e_a]$$

and

$$[e_a] \cdot [OH^-] = [e_b] \cdot K_b \qquad (4)$$

K_b is the base constant of the ester. By combining these equations one obtains

$$-\frac{\mathrm{d}c}{\mathrm{d}t} = \frac{k_{boh} \cdot [OH^-]^2 + k_{aoh} \cdot K_b \cdot [OH^-]}{K_b + [OH^-]} \cdot c$$

If the hydroxyl ion concentration is constant this equation may be written

$$-\mathrm{d}c/\mathrm{d}t = k'_{oh} \cdot c$$

where

$$k'_{oh} = \frac{k_{boh} \cdot [OH^-]^2 + k_{aoh} \cdot K_b \cdot [OH^-]}{K_b + [OH^-]} \qquad (5)$$

The reaction is pseudo monomolecular. Three different cases may be distinguished.

1. $[OH^-] \gg K_b \cdot k_{aoh}/k_{boh}$. Eqn. (5) may be transformed to

$$k'_{oh} = k_{boh} \cdot [OH^-]$$

or by taking logarithms

$$\log k'_{oh} = \log k_{boh} + \mathrm{pH} - \mathrm{p}K_w$$

2. $[OH^-] \ll K_b \cdot k_{aoh}/k_{boh}$. Eqn. (5) may be written

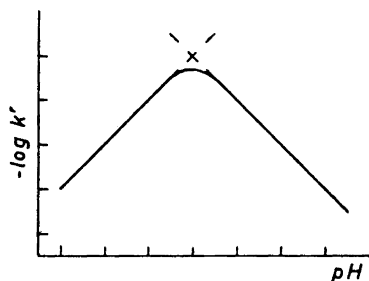$$\log k'_{oh} = \log k_{aoh} + \mathrm{pH} - \mathrm{p}K_w$$

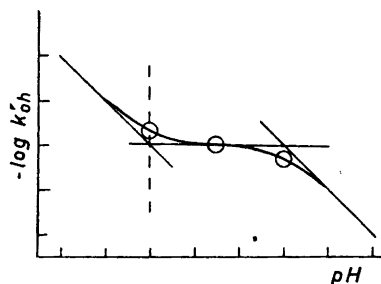Fig. 1. $\log k'_h$ and $\log k'_{oh}$ (to the left and to the right) $vs.$ pH.

Fig. 2. $\log k'_{oh}$ $vs.$ pH. Theoretical curve when $\log k_{aoh} = \log k_{boh} + 3$.

In both cases a straight line is formed when log k'_{oh} is plotted *vs.* pH. The two lines are identical only if $k_{aoh} = k_{boh}$. As has been noted before, this will not be the case in practice.

In the range where $[OH^-]$ is of the same order as $K_b \cdot k_{aoh}/k_{boh}$ the curve is bent and here the third case may be of interest.

3. $[OH^-] = K_b$. Eqn. (5) may be written

$$k'_{oh} = \frac{k_{boh} + k_{aoh}}{2} \cdot K_b$$

But k_{aoh} always is bigger than k_{boh}, and thus

$$\log k'_{oh} = \log k_{aoh} + \log K_b - \log 2$$

Now the line may be drawn for the whole range of pH as is shown in Fig. 2. The curved part of the line has its mid point at

$$\begin{cases} pH = pK_a + \tfrac{1}{2}(\log k_{aoh} - \log k_{boh}) \\ \log k'_{oh} = \log k_{aoh} + \log K_b \end{cases}$$

and if the distance between the straight lines is big enough (> 3 log units) the curve will be horizontal in this range, that is the reaction velocity is independent of pH.

This can be shown in a simpler manner from eqns. (3) and (4). By combining them one obtains

$$-dc/dt = k_{boh} \cdot [e_b] \cdot [OH^-] + k_{aoh} \cdot [e_b] \cdot K_b$$

or

$$-dc/dt = (k_{boh} \cdot [OH^-] + k_{aoh} \cdot K_b) \cdot [e_b]$$

If $k_{boh} \cdot [OH^-] \ll k_{aoh} \cdot K_b$ the expression in the brackets will be constant. Further, if $[OH^-] \gg K_b$ then $[e_b] = c$. That is, the reaction velocity will be independent of pH within a range where the following conditions are fulfilled

$$K_b \ll [OH^-] \ll K_b \cdot k_{aoh}/k_{boh}$$

This has been shown by Pekkarinen and Tommila [2], who studied alkyl salicylates.

That the reaction velocity is not a linear function of pH in alkaline hydrolysis of some esters has also been shown by Higuchi *et al.*[3].

As already noted, an ester of the type

$$R_1-CO-OC_2H_4-N(R_2)_2$$
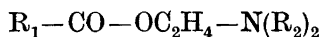
may add a proton and form the corresponding ammonium compound

$$R_1-CO-OC_2H_4-\overset{+}{N}H(R_2)_2 \tag{I}$$
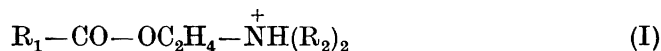
and this compound is more easily hydrolyzed in alkaline solution than the uncharged ester. The nitrogen atom may also acquire a positive charge by transformation to a quaternary compound of the following type

$$R_1-CO-OC_2H_4-\overset{+}{N}(R_2)_3 \tag{II}$$
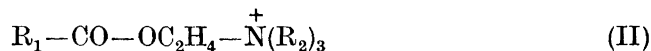
This product, as one might expect, is also more easily hydrolyzed than the primary ester. Such a case has been investigated by Butterworth et al.[4] who studied acetyl choline and ethyl acetate.

In order to compare reaction velocities of the different esters the bimolecular velocity constants k_{boh} and k_{aoh} must be calculated. These constants are independent of pH. This calculation can be made using eqn. (1). The effect of the positive charge is not, however, the same in both cases (I and II). A similar effect was found by Hansen [5]. The addition of a proton results in an increase of the velocity constant by about 1 000 (see for example esters Nos. 1, 4, and 10 in the experimental part of this work). The quaternary ester is hydrolyzed only about 15 times as fast as the primary ester without any ionic charge (compare esters Nos. 1 and 2 or 4 and 5). This may be explained by the following formulas

$$\text{(I)} \qquad\qquad\qquad \text{(II)}$$

In formula I there is a hydrogen bond because of which the charge of the carbonyl carbon is more pronounced than in formula II.

Esters which have two or more protolytic groups have also been studied in this work. An example of this type is

$$\text{—CO—OC}_2\text{H}_4\text{—}\overset{+}{\text{N}}\text{H(C}_2\text{H}_5)_2$$
$$\text{OH}$$
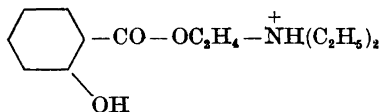
This compound is a dibasic acid and the difference between the pK_a values is relatively small. In this case the velocity constant of the positively charged ester was found to be about 10 [5] times as great as that of the negatively charged ester. (Compare esters Nos. 3, 7, and 8.)

ACIDIC HYDROLYSIS

The mechanism of acidic hydrolysis of esters is usually described in the following manner

$$R_1\text{—C—OR}_2 + H^+ \longrightarrow R_1\text{—C—OR}_2 \xrightarrow{H_2O}$$

$$R_1\text{—C—OR}_2 \longrightarrow R_1\text{—C}^+ + R_2\text{—OH}$$

$$R_1\text{—C—OH} + H^+$$
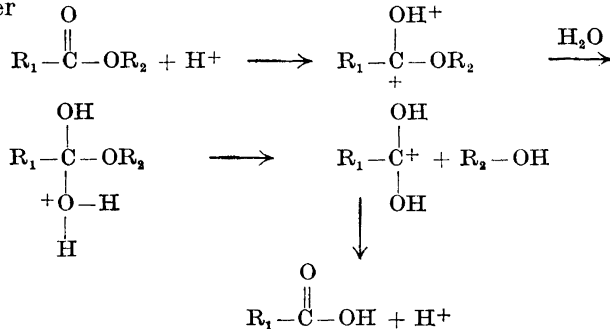
The reaction velocity is often, but not always, proportional to the hydrogen ion concentration.

In the acidic hydrolysis also, different substituents in R_1 and R_2 influence the reaction velocity. It has been found that electron attracting substituents favour the process and electron releasing substituents make the reaction slower.

However, in some cases the mechanism seems to be of another kind. Thus, when the mono ethyl ester of phthalic acid is studied there is found to be a relationship between the reaction velocity and the acid constant, of the same kind as has been described for alkaline hydrolysis. Bender [6] explains this fact by the assumption that the process is catalyzed internally by the carboxylic group. Phthalic acid anhydride is formed as an intermediate.

No matter what the mechanism may be, the experimental results (ester No. 11) show that the reaction velocity may be expressed by the following equation

$$-\mathrm{d}c/\mathrm{d}t = k_{\mathrm{bh}} \cdot [e_b] \cdot [H^+] + k_{\mathrm{ah}} \cdot [e_a] \cdot [H^+] \tag{6}$$

where

$$c = [e_b] + [e_a]$$

and

$$[e_b] \cdot [H^+] = [e_a] \cdot K_a \tag{7}$$

K_a is the acid constant of the ester. By transformations quite analogous to those shown for alkaline hydrolysis, one obtains

$$-\mathrm{d}c/\mathrm{d}t = k_{\mathrm{h}}' \cdot c$$

where

$$k_{\mathrm{h}}' = \frac{k_{\mathrm{ah}} \cdot [H^+]^2 + K_a \cdot k_{\mathrm{bh}} \cdot [H^+]}{K_a + [H^+]} \tag{8}$$

Thus, the reaction is monomolecular when the pH is constant. It can easily be shown that $\log k_{\mathrm{h}}'$ varies with varying pH as is shown in Fig. 3.
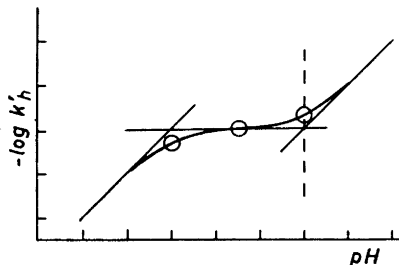

Fig. 3. $\log k_{\mathrm{h}}'$ *vs.* pH. Theoretical curve according to eqn. (8) when $\log k_{\mathrm{ah}} + 3 = \log k_{\mathrm{bh}}$.
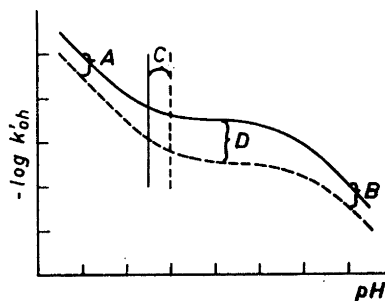
Fig. 4. $\log k_{\mathrm{oh}}'$ *vs.* pH at temp. T_1 (——) and T_2 (– – –). See text.

THE TEMPERATURE DEPENDENCE

The change of reaction velocity with temperature is given by the Arrhenius formula

$$\frac{d \ln k}{dT} = \frac{E}{RT^2}$$

or

$$\log k = A - \frac{E}{2.303 \; RT} \tag{9}$$

where k is the velocity constant, T the absolute temperature, A is the frequency factor and E is the activation energy. A and E may be calculated when k is determined at at least two temperatures.

In the hydrolysis of an ester possessing protolytic groups, the value of the velocity constant is different for the acidic and the basic forms, that is k_{aoh} and k_{boh} in alkaline solution and k_{ah} and k_{bh} in acidic solution (at least in some cases). Each of these constants varies with T according to eqn. (9). Further, the acid constant, K_a, varies with temperature

$$\frac{d \ln K_a}{dT} = \frac{\Delta H}{RT^2} \tag{10}$$

where ΔH is the enthalpy increase in the dissociation.

According to eqn. (5) the monomolecular velocity constant, k'_{oh}, depends on k_{boh}, k_{aoh}, and K_b (or K_a) and further on pH. In the same manner k'_h depends on k_{bh}, k_{ah}, and K_a. Thus, the correlation between k'_{oh} (or k'_h) and the temperature is rather complicated, but it is possible to deduce the relation by differentiating eqn. (5) or (8).

These relations may be understood more simply by using graphs*. This will be illustrated only for the case of alkaline hydrolysis. Fig. 4 shows how log k'_{oh} varies with pH. The full line corresponds to the temperature T_1 and the broken line to T_2. The same figure shows the variation of k_{aoh}, k_{boh}, and K_a when the temperature is changed from T_1 to T_2:

$$A = \frac{\Delta \log k_{aoh}}{\Delta T} \qquad\qquad B = \frac{\Delta \log k_{boh}}{\Delta T}$$

$$C = \frac{\Delta \log K_a}{\Delta T} \qquad\qquad D = A + C$$

It may be seen from the figure that in the range where log k'_{oh} vs. pH is a straight line, eqn. (9) may be used and from the experimental results at these pH values, the activation energy (E_a or E_b, resp.) and the frequency factor (A_a or A_b, resp.) of the ester acid and the ester base may be calculated. But if the measurements are made in that range, where the lines are curved the value

---

* In this description the change of pK_w with T is neglected.

$$\frac{d \ln k'_{oh}}{dT}$$

(that is D in Fig. 4) depends upon at least two of the expressions

$$\frac{d \ln k_{aoh}}{dT}, \quad \frac{d \ln k_{boh}}{dT} \quad \text{and} \quad \frac{d \ln K_a}{dT}$$

In this range the values E_a and E_b can not easily be calculated. If the difference between log k_{aoh} and log k_{boh} is big enough (as is the case in Fig. 4) it can be seen that within a certain range the following equation is valid

$$\frac{d \ln k'_{oh}}{dT} = \frac{d \ln k_{aoh}}{dT} + \frac{d \ln K_a}{dT}$$

or

$$E' = E_a + \Delta H$$

where E' is the apparent activation energy. One concludes that the measurements have to be made in carefully chosen pH ranges, when E_a and E_b are to be estimated.

Table 1. Survey of the esters studied.

$$R_1 - \text{[benzene ring]} - COO \cdot C_2H_4 \cdot R_3$$
$$R_2$$
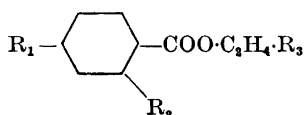
Ester No.	R_1	R_2	R_3
1	H	H	$N(C_2H_5)_2$
2	H	H	$\overset{+}{N}(C_2H_5)_3$
3	H	OH	$N(C_2H_5)_2$
4	NH_2	H	$N(C_2H_5)_2$
5	NH_2	H	$\overset{+}{N}(C_2H_5)_3$
6	NHC_4H_9	H	$N(C_2H_5)_2$
7	NH_2	OH	$N(C_2H_5)_2$
8	OH	H	$N(C_2H_5)_2$
9	OH	H	H
10	H	OH	H
11	H	COOH	H
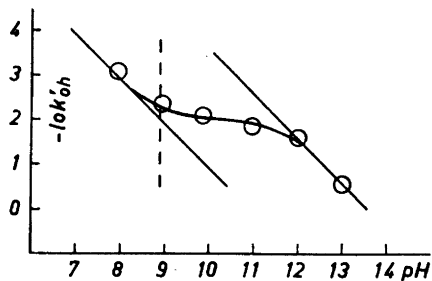
Fig. 5. Diethylaminoethyl benzoate.
$pK_a = 8.84$.
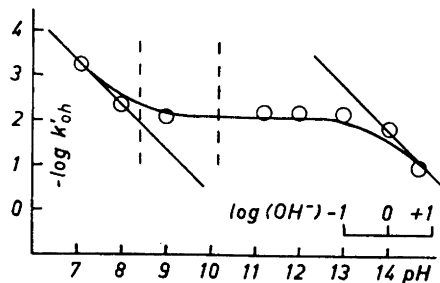
Fig. 6. Diethylaminoethyl salicylate.
$pK_{a1} = 8.41$, $pK_{a2} = 10.14$.

Table 2. Diethylaminoethyl benzoate.
25.0°C. *Cf.* Fig. 5.

pH	k'_{oh} (min^{-1})
7.96	8.2×10^{-4}
8.94	4.5×10^{-3}
9.86	8.2×10^{-3}
10.95	1.40×10^{-2}
13.0	2.75×10^{-1}

Table 3. Diethylaminoethyl salicylate.
25.0°C. *Cf.* Fig. 6.

pH	k'_{oh} (min^{-1})
7.08	5.7×10^{-4}
8.00	4.4×10^{-3}
9.00	8.0×10^{-3}
11.20	6.3×10^{-3}
12.0	6.4×10^{-3}
13.0	6.8×10^{-3}
14.0	1.3×10^{-2}
14.7	1.1×10^{-1}

Fig. 7. Procaine. $pK_a = 8.53$.
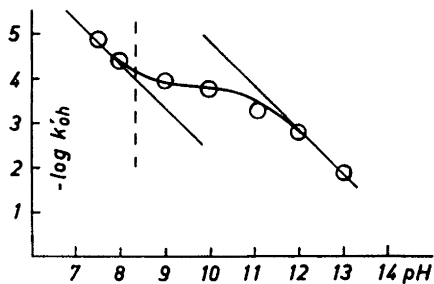
Fig. 8. Tetracaine. $pK_a = 8.33$.

Table 4. Procaine. 35.0°C. Cf. Fig. 7.

pH	k_{oh}' (min^{-1})
8.05	2.21×10^{-4}
8.52	5.46×10^{-4}
9.02	8.45×10^{-4}
9.52	1.48×10^{-3}
9.76	1.79×10^{-3}
10.90	3.54×10^{-3}
12.0	6.80×10^{-3}
13.0	4.82×10^{-2}

Table 5. Tetracaine. 25.0°C. Cf. Fig. 8.

pH	k_{oh}' (min^{-1})
7.50	1.34×10^{-5}
8.00	3.99×10^{-5}
9.00	1.15×10^{-4}
9.98	1.66×10^{-4}
11.08	5.47×10^{-4}
12.0	1.73×10^{-3}
13.0	1.43×10^{-2}

Fig. 9. Hydroxyprocaine.
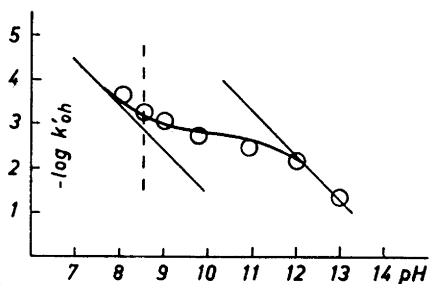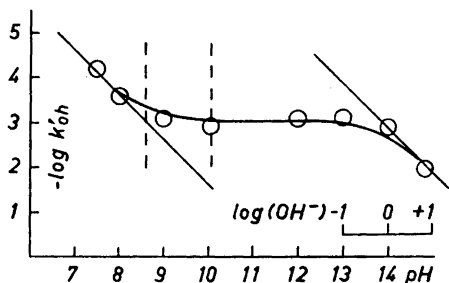$pK_{a1} = 8.61$, $pK_{a2} = 10.07$.
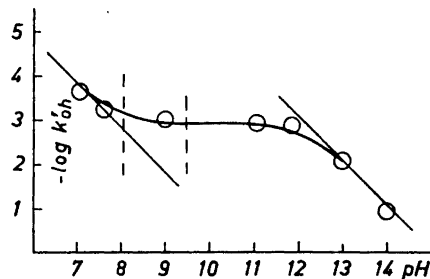
Fig. 10. Diethylaminoethyl(p-hydroxy)
benzoate. $pK_{a1} = 8.07$, $pK_{a2} = 9.5$.

Table 6. Hydroxyprocaine. 25.0°C. Cf.
Fig. 9.

pH	k_{oh}' (min^{-1})
7.54	2.40×10^{-4}
8.00	2.55×10^{-4}
9.00	8.52×10^{-4}
10.05	1.26×10^{-3}
12.0	8.25×10^{-4}
13.0	8.14×10^{-4}
14.0	1.69×10^{-3}
14.7	1.12×10^{-2}

Table 7. Diethylaminoethyl(p-hydroxy)-
benzoate. 45.0°C. Cf. Fig. 10.

pH	k_{oh}' (min^{-1})
7.04	2.36×10^{-4}
7.60	5.87×10^{-4}
9.01	1.03×10^{-3}
11.08	1.20×10^{-3}
11.84	1.38×10^{-3}
13.0	8.96×10^{-3}
14.0	1.27×10^{-1}

Fig. 11. Ethyl salicylate.
$pK_a = 10.1$.

Fig. 12. Phthalic acid monoethyl ester.
60°C. $pK_a = 3.24$ (at 25°C).

Table 8. Ethyl salicylate. 25.0°C. Cf. Fig. 11.

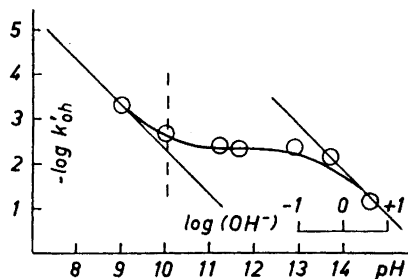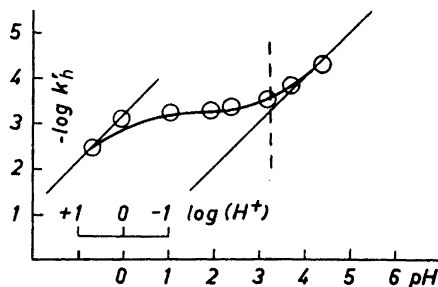| pH	k'_{oh} (min^{-1})
8.02	6.31×10^{-5}
9.02	4.78×10^{-4}
9.95	2.22×10^{-3}
11.23	3.95×10^{-3}
11.64	4.15×10^{-3}
12.89	4.33×10^{-3}
13.7	7.37×10^{-3}
14.6	7.29×10^{-2}

Table 9. Phthalic acid monoethyl ester. 110°C (the pH measurements were made at 25°C). Cf. Fig. 12.

pH	k'_h (min^{-1})
− 0.7	1.87×10^{-1}
0.0	5.16×10^{-2}
1.0	3.60×10^{-2}
2.0	3.59×10^{-2}
3.00	2.91×10^{-2}
4.02	1.02×10^{-2}
5.04	2.70×10^{-3}
6.01	1.29×10^{-3}
7.10	1.21×10^{-3}
8.00	2.16×10^{-3}
9.00	1.19×10^{-2}
10.00	6.62×10^{-2}

EXPERIMENTAL

Methods. The photometric method used by Karlén and Ågren [7] has been used in this work. The extinction curve of the ester and the hydrolysis products was taken and that wave length chosen where the extinction changes are greatest. In some cases the solution was buffered to a pH value where the reaction velocity was very low.

In strongly acidic solution (pH < 2) hydrochloric acid was used, in strongly alkaline solution (pH > 12) NaOH was used. In these solutions the stoichiometric concentration of hydrogen ion or hydroxyl ion was calculated. In the pH range between 2 and 12 buffer solutions were used and pH was measured with a glass electrode and a valve potentiometer (type Radiometer PHM 4). The buffer solutions recommended in the *Swedish Pharmacopeia Ed. XI* were used and between pH 10 and 12 carbonate buffers were employed.

Table 10. Determination of the activation energies. Velocity constants (l^{-1}.mole.min^{-1}).

Ester No.	1		3		7		8	
Temp.(°C)	pH	k_{boh}	pH	k_{aoh}	pH	k_{aoh}	pH	k_{aoh}
15.0	12.00	0.975	—	—	—	—	—	—
25.0	12.00	2.48	7.08	8.26×10^3	7.50	200	7.04	170
35.0	12.00	5.50	7.08	9.92×10^3	7.50	380	7.04	310
45.0	—	—	7.08	19.05×10^3	7.50	780	7.04	540

Ester No.	8		9		10	
Temp.(°C)	pH	k_{boh}	pH	k_{boh}	pH	k_{aoh}
25.0	13.0	2.17×10^{-2}	13.0	1.90×10^{-1}	9.00	48
35.0	13.0	4.65×10^{-2}	13.0	3.77×10^{-1}	9.00	74
45.0	13.0	8.96×10^{-2}	13.0	7.57×10^{-1}	9.00	118

Table 11. Survey of the results.

Ester No.	Temp.	log k_{aoh}	log k_{boh}	E_a kcal.	A_a	E_b kcal.	A_b
1	25.0	3.20	0.40	—	—	15.3	11.6
2	25.0	1.84	—	—	—	—	—
3	25.0	3.67	−2.0	13.2	13.4	—	—
4	35.0	2.65	−0.20	—	—	—	—
5	25.0	0.60	—	—	—	—	—
6	25.0	1.63	−0.84	—	—	—	—
7	25.0	2.50	−2.62	12.8	11.7	—	—
8	45.0	2.73	−1.05	10.9	10.2	13.4	8.1
9	25.0	—	−1.72	—	—	13.0	7.8
10	25.0	1.50	−1.73	8.5	7.9	—	—
11	110	−1.40 *	+ 2.1 **	—	—	—	—

* log k_{ah} ** log k_{bh}

The temperature was determined with an accuracy of 0.1°.

Chemicals. The chemicals used were of analytical grade. The esters which were investigated are tabulated in Table 1. Ester No. 1 was synthesized from benzoyl chloride and diethyl amino ethanol according to Vanderhaeghe [8]. Melting point 124.5 — 125°. Esters Nos. 2 and 5 were synthesized as iodides by boiling diethyl amino ethyl benzoate resp. procaine with ethyl iodide according to Jones [9]. Melting points 146 — 150°, resp. 135 — 137°. Esters Nos. 3 and 8 were made according to Ref.[10]. Melting points 147°, resp. 184 — 186°. Ester No. 9 was made according to Cavill and Vincent [11]. Melting point 114 — 115°. The synthesis of ester No. 7 is given by Karlén and Ågren [7]. The other esters were commercial materials, which were purified by distillation or recrystallisation.

Results. The results are given in Tables 1 — 10 and Figs. 5 — 12. The curves are the theoretical ones from eqn. (5) or (8) which best agree with the experimental points. In the figures the pK_a values of the ester are marked by vertical lines.

Ethyl salicylate (ester No. 10) has been studied earlier by Pekkarinen and Tommila [2] who, however, worked in an acetone-water mixture. Their results agree rather well with ours. Phthalic acid mono methyl ester has been studied by Bender [6] whose results the present authors could not reproduce (in this work the ethyl ester was used). The reason for the discrepancy is not known as the experimental conditions used by Bender are very briefly described. It may be that the buffer substances used by him had a catalyzing effect. The buffers used by us had no marked catalyzing effect as was proved by varying the buffer concentration (without changing pH) between wide limits.

REFERENCES

1. Tammelin, L. E. and Larsson, L. *Svensk Farm. Tidskr.* **59** (1955) 229.
2. Pekkarinen, L. and Tommila, E. *Acta Chem. Scand.* **13** (1959) 1019.
3. Higuchi, T., Havinga, A. and Busse, L. W. *J. Am. Pharm. Assoc., Sci. Ed.* **39** (1950) 405.
4. Butterworth, J., Eley, D. D. and Stone, G. S. *Biochem. J.* **53** (1953) 30.
5. Hansen, B. *Acta Chem. Scand.* **12** (1958) 324.
6. Bender, M. L. *Chem. Revs.* **60** (1960) 53.
7. Karlén, B. and Ågren, A. *Acta Chem. Scand.* **14** (1960) 197.
8. Vanderhaeghe, H. *J. Pharm. Pharmacol.* **6** (1954) 55.
9. Jones, M. *J. Am. Chem. Soc.* **49** (1927) 1534.
10. Brit. Pat. 739, 210.
11. Cavill, G. W. K. and Vincent, J. M. *J. Soc. Chem. Ind.* **66** (1947) 175.