# The Hydrolysis of Alkyl Salicylates in Alkaline Solutions

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The alkaline hydrolysis of methyl, ethyl and *iso*propyl salicylates has been investigated in pure water and in various methanol-water, ethanol-water, *iso*propanol-water and acetone-water mixtures at different temperatures. All facts sustain the proposition suggested by Goldschmidt and Scholtz in 1907 that in solutions the reacting substance is the free ester, which is in equilibrium with its ionized form. Beside this reaction, a simple bimolecular process between the ester ion and hydroxyl ion has a subordinate importance. The alkaline hydrolysis of *p*- and *m*-hydroxybenzoates takes place practically solely as a reaction between the ester ion and hydroxyl ion.

In 1907, Goldschmidt and Scholtz[1] observed that methyl salicylate in alkaline solution undergoes hydrolysis by first-order kinetics. On the basis of Goldschmidt's earlier investigations on the hydrolysis of sodio-acetoacetate[2], they concluded that the reacting substance is not the sodium compound but the free ester with which the former is in equilibrium:

I

II

III
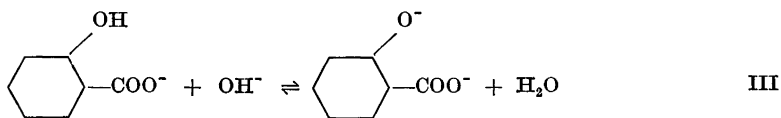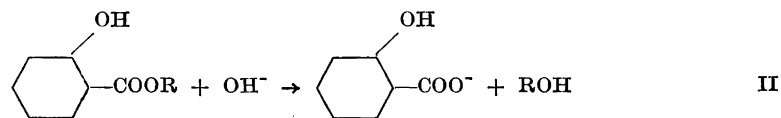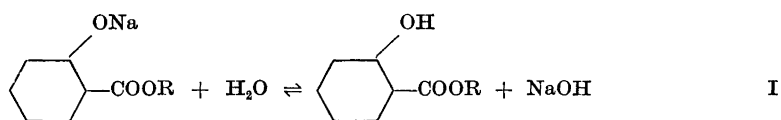
They showed mathematically that this mechanism leads to first-order kinetics. Suppose that a is the initial total concentration of the ester and b that of the alkali hydroxide, ξ the concentration of the free ester and η that of the disodi-

um salt at any instant, and x the decrease in the concentration of the ester after a lapse of time t. Then according to the law of mass action, since the concentration of water can be taken as constant, we have

$$\frac{\text{[Free ester]} \times \text{[OH}^-]}{\text{[Ester ion]} \times \text{[H}_2\text{O]}} = \frac{\xi \ (b+\xi-\eta)}{(a-x-\xi)} = K \tag{1}$$

The velocity equation is then given by

$$\frac{dx}{dt} = k\xi[\text{OH}_a^-] = kK(a-x-\xi) \tag{2}$$

Taking into account that $\xi \ll (a-x)$, and writing $kK = k_1$, we obtain

$$\frac{dx}{dt} = k_1(a-x) \tag{3}$$

i.e. an equation of the first order.

There is a considerable body of evidence in support of Goldschmidt's hypothesis. To-day, however, the well-known ability of salicylic acid and its esters to form chelate rings must be taken into account. The purpose of the present investigation is to study this reaction from different points of view and so gain insight into its mechanism. The reaction was investigated with different salicylic esters and under various conditions, and some kinetic measurements were also carried out with ethyl *m*- and *p*-hydroxybenzoates.

EXPERIMENTAL

Esters. The esters were prepared from the corresponding acid and alcohol by the usual method. The salicylic esters were purified by repeated distillation at reduced pressure. Their refractive indices were identical with the best values reported in the literature. The *m*- and *p*-hydroxybenzoates were crystallized from ethanol. Their melting points (72° and 115.2°) agreed with those given in the literature.

The alkali hydroxides were of a high degree of purity. The alkali solutions used were as carbonate-free as possible.

Solvents. The water used in the kinetic experiments was freshly distilled and freed from carbon dioxide by brief boiling. The methanol and ethanol were purified by the method of Walden [3]. The *iso*propanol was treated with solid sodium hydroxide and distilled. Merck's acetone "pro analysi" was used as received.

Method. The reaction vessels and method used in most of the kinetic experiments have been previously described [4]. In general, equal volumes of an *a* M ester solution and an $(a + b)$ M alkali hydroxide solution were used, so that after mixing the concentration of the ester salt was $a/2$ and that of the hydroxyl ions $b/2$. The reaction was stopped with an excess of 0.02 N HCl and the mixture titrated back with 0.02 N baryta solution, cresol red being used as indicator. For ethyl *m*- and *p*-hydroxybenzoates, however, methyl red was used as indicator, and the titration carried to a standard tint. The experiments at the greatest dilution were conducted in large flasks from which the samples were withdrawn with a pipette. The experiments in methanol-water and ethanol-water at 50° were carried out in sealed ampoules of Pyrex glass and filled with nitrogen. The reaction mixtures were carefully protected from atmospheric carbon dioxide.

The electrically controlled thermostats were constant to within ±0.01°. The thermometers were checked against a thermometer calibrated at the National Bureau of Standards (U.S.A.).

RESULTS AND DISCUSSION

1. The order of the reaction. Goldschmidt's observation concerning the order of the reaction was confirmed. The first-order formula gave a good constancy for k, as is exemplified by the following run (solvent: water; [sodium salt of the ester] = [NaOH] = 0.04 mole/l; temperature 25°):

| Time, min.	50	82	100	120	144 ½	195	272	346
Change, %	19.0	29.5	34.5	38.5	45.5	55.5	68.5	76.5
$10^7 k$, s^{-1}	725	710	705	680	700	690	700	697

Moreover, within the limits of experimental error, in dilute solutions, the time of half completion of the reaction is independent of the initial concentrations, as the following figures show (water, 25°):

$[C_6H_4(ONa)COOEt]$ = [NaOH], mole/l	0.001	0.0025	0.005	0.01	0.02	0.04
t, min.		175	174	171	165	168	165

For the alkaline hydrolysis of ethyl *p*-hydroxybenzoate ion and ethyl *m*-hydroxybenzoate ion, the second order formula always gave a good constancy for k.

The results obtained with the ester salts are summarised in Tables 1—3.

2. The mechanism of the reaction. As already mentioned, many facts are in conformity with the reaction mechanism proposed by Goldschmidt according to which the reaction occurs between the free ester and hydroxyl ion. As is easily seen, a reaction between the ester ion (or chelate) and hydroxyl ion would exhibit second-order kinetics. The experimental results, however, as we have seen, reveal that the reaction follows a first-order rate law. In fact, the free charge on the oxygen atom of the ionized phenol group in the *ortho*-position generates a large negative charge on the carbonyl carbon in the ester ion, and this causes a very powerful repulsion between this carbon atom and the attacking hydroxyl ion:

$$\text{HO}^- \rightarrow \underset{\underset{\bigcirc\!-\text{O}^-}{|}}{\overset{\overset{\text{OR}}{|}}{\text{C}}} = \text{O}$$
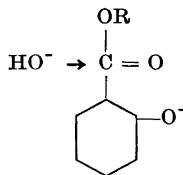
This results in a high activation energy and small reaction velocity. A similar case occurs in the alkaline hydrolysis of ethyl *p*-hydroxybenzoate [5]. In the case of the ethyl *m*-hydroxybenzoate, the negative charge on the carbonyl carbon is less, because only the inductive effect is operative, and the effect on the activation energy is correspondingly weaker. The values in pure water [6] and in 56 % aqueous acetone [5] are seen from the following figures:

	Water			*56 % acetone*		
	$10^4 k_{25}$	E cal	log A	$10^4 k_{25}$	E cal	log A
(H)	293	12 680	7.76	26.9	14 560	8.18
p-O⁻	2.63	13 510	6.32	0.0870	17 300	7.61
m-O⁻	40.2			4.73	15 450	8.04

Table 1. Alkaline hydrolysis of ethyl salicylate. A = acetone, E = ethanol, % = per cent by weight; a = initial concn. of the ester, b = excess of alkali, c = concn. of added salt, mole/l.

Solvent	a	b	c	$10^6\,k_1$ s^{-1}					E_a cal	log A
				0.00°	15.00°	25.00°	40.00°	50.00°		
Water	0.02	0.02 NaOH	—	4.12	13.6 (10°)	69.2	323	—	18 500	9.416
»	0.02	0.06 »	—	—	—	70.4	—	—	—	—
»	0.02	0.02 »	0.1 LiCl	—	—	60.4	—	—	—	—
»	0.02	0.02 »	0.1 NaI	—	—	68.0	—	—	—	—
»	0.02	0.02 KOH	0.9 KCl	—	—	58.8	—	—	—	—
»	0.05	0.2 »	—	—	—	84.7	—	—	—	—
»	0.10	0.4 »	—	—	—	111	—	—	—	—
»	0.15	0.6 »	—	—	—	133	—	—	—	—
»	0.20	0.8 »	—	—	—	164]	—	—	—	—
»	0.20	1.1 »	—	—	—	188	—	—	—	—
»	0.30	1.4 »	—	—	—	240	—	—	—	—
»	0.40	1.6 »	—	—	—	244]	—	—	—	—
20 % A	0.02	0.02 NaOH	—	2.13	7.41 (10°)	43.4	210	—	19 540	9.959
»	0.04	0.04 »	—	—	—	45.3	—	—	—	—
»	0.04	0.02 »	—	—	—	44.9	—	—	—	—
50 % A	0.02	0.02 »	—	0.880	6.61	21.4	115	—	20 680	10.502
»	0.04	0.04 »	—	—	—	19.6	—	—	—	—
»	0.04	0.02 »	—	—	—	20.5	—	—	—	—
20 % E	0.02	0.02 »	—	2.84	16.6	49.9	226	—	18 600	9.339
50 % E	0.02	0.02 »	—	—	6.69	22.2	118	298	20 170	10.136
80 % E	0.02	0.02 »	—	—	2.58	8.73	46.7	131	20 740	10.145
»	0.02	0.04 »	—	—	—	—	45.4	—	—	—
»	0.02	0.02 »	0.1 NaI	—	—	—	29.0	—	—	—
»	0.02	0.02 »	0.5 »	—	—	—	15.5	—	—	—
80 % E	0.02	0.02 NaOH	0.1 KBr	—	—	—	36.9	—	—	—
»	0.02	0.02 KOH	—	—	—	—	51.1	—	—	—
»	0.02	0.02 »	0.069 KBr	—	—	—	43.1	—	—	—
95 % E	0.02	0.02 NaOH	—	—	—	1.04	5.60	15.4	20 620	9.142
»	0.02	0.04 »	—	—	—	—	—	15.7	—	—
»	0.02	0.02 »	0.1 NaI	—	—	—	—	11.2	—	—
»	0.01	0.02 »	—	—	—	—	—	16.3	—	—
»	0.01	0.03 »	—	—	—	—	—	15.0	—	—
»	0.02	0.02 »	0.05 NaI	—	—	—	—	12.2	—	—
»	0.02	0.02 »	0.3 »	—	—	—	—	9.16	—	—
»	0.02	0.02 »	0.5 »	—	—	—	—	7.99	—	—
»	0.02	0.04 »	0.5 »	—	—	—	—	10.4	—	—
»	0.02	0.04 »	0.3 »	—	—	—	—	10.6	—	—
»	0.02	0.04 »	0.05 »	—	—	—	—	13.4	—	—
»	0.01	0.02 KOH	—	—	—	—	—	30.8	—	—
»	0.02	0.02 »	—	—	—	—	—	30.2	—	—
»	0.02	0.04 »	—	—	—	—	—	27.9	—	—
»	0.02	0.02 LiOH	—	—	—	—	—	2.83	—	—
»	0.02	0.04 »	—	—	—	—	—	4.50	—	—
»	0.02	0.02 »	0.1 LiCl	—	—	—	—	2.57	—	—
»	0.02	0.04 »	0.08 »	—	—	—	—	4.71	—	—
»	0.02	0.02 »	0.02 »	—	—	—	—	2.74	—	—
»	0.01	0.02 »	0.01 »	—	—	—	—	2.65	—	—
»	0.01	0.03 »	—	—	—	—	—	3.68	—	—

Table 2. Alkaline hydrolysis of methyl salicylate. A = acetone, M = methanol.

Solvent	a	b		c	$10^6\ k_1\ \mathrm{s^{-1}}$					E_a cal	log A
					0.00°	15.0°	25.00°	40.00°	50.00°		
Water	0.02	0.02	NaOH	—	4.23	25.7	78.1	363	—	18 910	9.759
»	0.02	0.04	»	—	—	—	76.8	—	—	—	—
20 % A	0.02	0.02	»	—	—	—	52.7	—	—	—	—
50 % A	0.02	0.02	»	—	—	—	30.8	—	—	—	—
»	0.02	0.04	»	—	—	—	32.0	—	—	—	—
20 % M	0.02	0.02	»	—	2.76	16.7	54.3	251	—	19 220	9.819
50 % M	0.02	0.02	»	—	—	7.94	26.9	140	370	20 060	10.331
95 % M	0.02	0.02	»	—	—	—	1.52	8.53	23.9	21 100	9.653
»	0.02	0.06	»	—	—	—	—	—	24.4	—	—
»	0.02	0.04	»	—	—	—	—	—	25.8	—	—
»	0.02	0.02	»	0.04 NaCl	—	—	—	—	21.0	—	—
»	0.02	0.02	LiOH	—	—	—	—	—	6.23	—	—
»	0.02	0.04	»	—	—	—	—	—	5.30	—	—

In the case of the *ortho*-compound, owing to the close proximity between the charged oxygen atom and the carbonyl carbon, the repulsion of the hydroxyl ion must be still greater than in the case of the *para*-compound. Further, the electromeric displacement $C\!=\!O$ will be somewhat hindered by the direct field effect of the charged oxygen atom. Thus the bimolecular reaction between the salicylate ion and hydroxyl ion must be very slow. This is clearly seen from the following argument. If we assume that part of the salicylic ester is hydrolysed by the Goldschmidt mechanism and part changed by a bimolecular reaction between the ester ion and hydroxyl ion, the total rate equation is, instead of (3)

$$\mathrm{d}x/\mathrm{d}t = k_1'(a\!-\!x) + k_2[\mathrm{OH^-}](a\!-\!x) \qquad (4)$$

or

$$\mathrm{d}x/\mathrm{d}t = (k_1' + k_2[\mathrm{OH^-}])(a\!-\!x) \qquad (5)$$

Table 3. Alkaline hydrolysis of *iso*propyl salicylate. A = acetone, P = *iso*propanol.

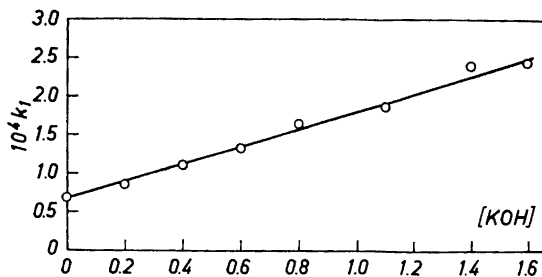| Solvent	a	b		$10^6\ k_1\ \mathrm{s^{-1}}$					E_a cal	log A
				0.00°	15.00°	25.00°	40.00°	50.00°		
Water	0.02	0.02	NaOH	2.08	11.8	35.3	155	—	18 340	8.982
»	0.02	0.04	»	—	—	34.8	—	—	—	—
20 % A	0.02	0.02	»	—	—	19.3	—	—	—	—
50 % A	0.02	0.02	»	—	—	7.47	—	—	—	—
»	0.02	0.0354	»	—	—	7.85	—	—	—	—
20 % P	0.02	0.02	»	—	6.97	19.4	85.5	212	18 090	8.562
50 » P	0.02	0.02	»	—	1.90	6.70	38.4	103	21 200	10.365
»	0.02	0.04	»	—	—	—	—	103	—	—
80 » P	0.02	0.02	»	—	0.763	2.32	13.2	37.6	20 720	9.586

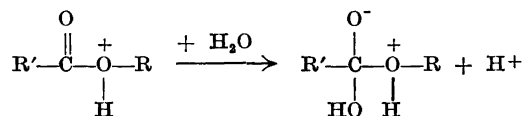*Fig. 1.* Plot of k_1 *vs.* KOH in water at 25°.

If the alkali is used in sufficient excess, the hydroxyl ion concentration remains practically constant during the reaction and the experimental rate constant, k_1, is

$$k_1 = k_1' + k_2[\text{OH}^-] \tag{6}$$

Accordingly, k_1 as a function of the hydroxyl ion concentration should yield a straight line. Fig. 1 shows that this is indeed the case. From the slope of this straight line we obtain for the bimolecular reaction in pure water at 25° $k_2 = 1.1 \times 10^{-4}$ litre mole^{-1} s^{-1}. The corresponding value for ethyl *p*-hydroxy-benzoic ester ion is 2.63×10^{-4} litre mole^{-1} s^{-1}. The result shows that, beside the hydrolysis of the free ester, the bimolecular reaction between the salicylic ester ion and hydroxyl ion also takes place, although its velocity is low. The result is further interesting in that it shows that the velocity of this reaction is of the same order of magnitude as that of the *para*-compound and also that the relation of the rate constants is in the direction to be expected. The experiments were carried out with potassium hydroxide, since in this case the salt effect is at a minimum (Section 3).

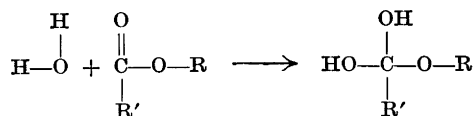Any possible role played by chelate formation is treated in Section 3.

Apart from Goldschmidt's mechanism, a "water hydrolysis" would also display first-order kinetics. It is now generally accepted that the acid-catalyzed hydrolysis begins with primary addition of a proton to the ethereal oxygen, and this step is followed by addition of hydroxyl from the water to the carbonyl carbon, which is now less negative,

$$\underset{\substack{|\\ \text{H}}}{\overset{\overset{\text{O}}{\|}}{\text{R}'\!-\!\text{C}\!-\!\overset{+}{\text{O}}\!-\!\text{R}}} \;\; \xrightarrow{+\ \text{H}_2\text{O}} \;\; \underset{\substack{|\\ \text{HO}}}{\overset{\overset{\text{O}^-}{|}}{\text{R}'\!-\!\text{C}\!-\!\overset{+}{\underset{|}{\text{O}}}\!-\!\text{R}}} + \text{H}^+$$

In the case of "water hydrolysis", the first step could correspondingly be assumed to be the transfer of a proton from the water to the ethereal oxygen,

$$\underset{\substack{\vdots\\ \text{H}\cdots\text{OH}}}{\overset{\overset{\text{O}}{\|}}{\text{R}'\!-\!\text{C}\!-\!\overset{+}{\text{O}}\!-\!\text{R}}}$$
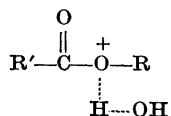
after which the reaction would proceed as in the acid-catalyzed hydrolysis. This mechanism, however, and likewise one with primary addition of water to the carbonyl group [cf. 7],

$$H\text{---}\overset{\displaystyle H}{\underset{\displaystyle }{O}} + \overset{\displaystyle O}{\underset{\displaystyle R'}{C}}\text{---}O\text{---}R \longrightarrow HO\text{---}\overset{\displaystyle OH}{\underset{\displaystyle R'}{C}}\text{---}O\text{---}R$$

is excluded by the fact that the acid-catalyzed hydrolysis of ethyl salicylate is extremely slow [8].

The bimolecular rate constant for the reaction $C_6H_4(OH)\cdot COOEt + OH^-$ in water at 25°, calculated from the measured first-order rate constant ($k_1 = 69.2 \times 10^{-6}$ s^{-1}) and the ionization constant of ethyl salicylate (log $K = -10.5$)[9], is $k_2 = 0.23$ l mole^{-1} s^{-1}. The corresponding value for methyl salicylate ($k_1 = 78.1 \times 10^{-6}$ s^{-1}, log $K = -10.19$) is $k_2 = 0.51$ l mole^{-1} s^{-1}. For ethyl benzoate in water at 25°, $k_2 = 0.0293$ [6]. As a comparison, it may be mentioned that the bimolecular rate constants for ethyl o-, m- and p-nitrobenzoates [5] in water at 25°, estimated from the measurements in 56 % acetone and supposing that the effect of the change of solvent is about the same as for ethyl benzoate [6], are $k_2 = 0.12$, 1.5 and 2.5, respectively. In the same manner, for ethyl p-chlorobenzoate and ethyl p-bromobenzoate we obtain $k_2 = 0.13$ and $k_2 = 0.15$, respectively. In 50 % ethanol the values at 25° are: ethyl salicylate ($k_1 = 22.2 \times 10^{-6}$ s^{-1}, log $K = -11.6$)[9] $k_2 = 0.0089$, ethyl benzoate $k_2 = 0.0017$ l mole^{-1} s^{-1}. We see that the unionized phenyl group acts as a rather powerful electron-attracting substituent. No doubt also the internal hydrogen bond formation [11]
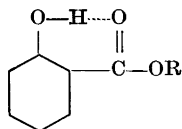

which makes the carbonyl carbon more positive, plays an important role here. However, it is noteworthy that ethyl lactate, in which internal hydrogen bond formation is very weak [11], is hydrolysed much faster [12] than ethyl propionate [13] or ethyl acetate [14].

The ionization constants of the ethyl esters of m- and p-hydroxybenzoic acids are appreciably larger (log $K = -9.1$ and -8.3, respectively [9]) than that of ethyl salicylate (log $K = -10.5$). This implies that the concentration of the free ester in their alkali salt solutions is much less than that in the salicylate solutions. Further, as mentioned above, the reaction of the free salicylic ester is favoured by internal hydrogen bond formation. We have also seen that the reaction between the ions of m- and p-hydroxybenzoic esters and hydroxyl ion is less hindered than in the case of salicylate. The result is that the esters of the m- and p-isomerides undergo alkaline hydrolysis mainly by a simple bimolecular process between the ester ion and hydroxyl ion.

In one experiment with water as solvent equal equivalents of the ester and sodium hydroxide were mixed, [ester] = [NaOH] = 0.02 mole/l, 25°. The result was as follows:

Time, min.	52.5	82	118	160	260	287	320	361	420
Change, %	18.5	27.0	35.5	44.5	61.5	65.0	68.5	72.5	77.5
$10^5 k_1$, s^{-1}	6.50	6.40	6.20	6.11	6.11	6.10	6.01	5.94	5.93

As is seen, first-order kinetics are approximately obeyed in this case also. Since the ester is a very weak acid, the solution now contains a considerable concentration of the free ester and hydroxyl ions:

$$C_6H_4(O^-)COOR + H_2O \rightleftharpoons C_6H_4(OH)COOR + OH^-$$
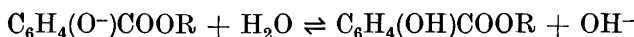
Consequently, ξ in eqn. (2) cannot now be ignored; the neglect of ξ in the calculations has caused a small continuous decrease in the rate constant and also made its value somewhat less than the value obtained in the presence of excess of alkali ($k_1 = 6.92 \times 10^{-5}$ s^{-1}, Table 1). Thus this result of Goldschmidt and Scholtz has likewise been confirmed.

The experimental activation energies and frequency factors, as given in Tables 1—3, are strikingly high. Their values, as is shown by the data given on p. 1021, are remarkably higher than the corresponding values for the reaction between hydroxyl ion and ethyl p-hydroxybenzoate ion or ethyl m-hydroxybenzoate ion. However, we must bear in mind that the activation energies, E_a given in Tables 1—3 are only apparent, as the rate constants from which they are obtained include the change of the equilibrium constant K of eqn. (1) with change in temperature. We have

$$\frac{d \ln k}{dT} = \frac{E}{RT^2} \quad \text{and} \quad \frac{d \ln K}{dT} = \frac{\Delta H}{RT^2}$$

Thus, if E and ΔH are independent of temperature,

$$\ln k_{exp.} = -E_a/RT + \ln A \text{ and } \ln K = -\Delta H/RT + \ln B$$

where k_{exp} is the experimental rate constant and E_a the (apparent) activation energy calculated from its dependence on temperature; ln A and ln B are integration constants. From (p. 1020) follows that

$$k_{exp.} = k_1 = kK, \ln k = \ln k_1 - \ln K = -(E_a - \Delta H)/RT + \ln (A/B)$$

or

$$k = (A/B)e^{-(E_a - \Delta H)RT} \tag{7}$$

We see that the true activation energy for the bimolecular reaction between the free ester and hydroxyl ion is

$$E' = E_a - \Delta H \tag{8}$$

The values of ΔH for the reaction I are not known, but it is, perhaps, legiti-
mate to assume that they do not differ essentially from those for phenol. For
phenol (log $K = -9.92$), e.g. in ethanol-water mixtures, the values of ΔH are
seen from the following table [15]:

wt. % of EtOH	0	20	50	80	95
ΔH, kcal	7.20	8.15	5.40	4.42	3.20
E', ethyl salic., kcal	11.3	10.5	14.8	16.3	17.4
E, ethyl benz., kcal	12.7	11.5	15.7	17.2	19.1

If the values of ΔH are substracted from E_a given in Table 1, the figures in
the third line are obtained for ethyl salicylate. These values are of the same
order of magnitude as those found for the alkaline hydrolysis of ethyl
benzoate [6]. Furthermore, in accordance with the fact that the unionized phenol
hydroxyl acts as an electron-attracting substituent, the activation energy for
ethyl salicylate is somewhat smaller than that for ethyl benzoate in the same
solvent. Corresponding results are obtained in other cases:

Methyl salicylate in methanol-water

wt. % of MeOH	0	20	50	95
ΔH for phenol, kcal	7.20	6.57	3.60	1.40
E', kcal	11.7	12.7	16.5	19.7

Isopropyl salicylate in isopropanol-water

wt. % of i-PrOH	0	20	50	80
ΔH for phenol, kcal	7.20	9.25	6.70	5.17
E', kcal	11.1	8.8	14.5	15.6

From the values of k_2 calculated on p. 1025 log A can also be estimated for
reactions in pure water and in 50 % ethanol. The values obtained are 7.65
and 8.80, respectively. The values of log A for the alkaline hydrolysis of ethyl
benzoate in the same solvents are 7.76 and 8.70, respectively. The result is
very striking, for it is known that in the alkaline hydrolysis of ethyl benzoates
the substituents exert their main influence on the rate of the reaction through
changes in the activation energy, whereas the frequency factor often remains
almost constant if the reactions are carried out in exactly the same solvent. All
this is in excellent agreement with earlier experiences concerning ester hydrolysis.
However, it must be reiterated that the results are based on the assumption
that ΔH for salicylates is equal to that for phenol in the same solvent.

The reaction mechanism propounded obtains additional support from
the fact that if the values of E' are plotted against the composition of the sol-
vent, the graphs have the form usual for alkaline ester hydrolysis; for instance,
they pass through a minimum, except in the case of methanol-water [13,14,16]
(Fig. 2). On the other hand, if E_a is plotted against the composition of the
solvent, the curves have a decidedly different shape.

3. Salt effects. The dependence of the rate constants of the alkaline hydr-
olysis of ethyl m- and p-hydroxybenzoates on the initial concentration of
the reactants in water at 25° is seen from the following experimental data obtain-
ed in reaction mixtures prepared by mixing equal volumes of a $2a$ molar ester
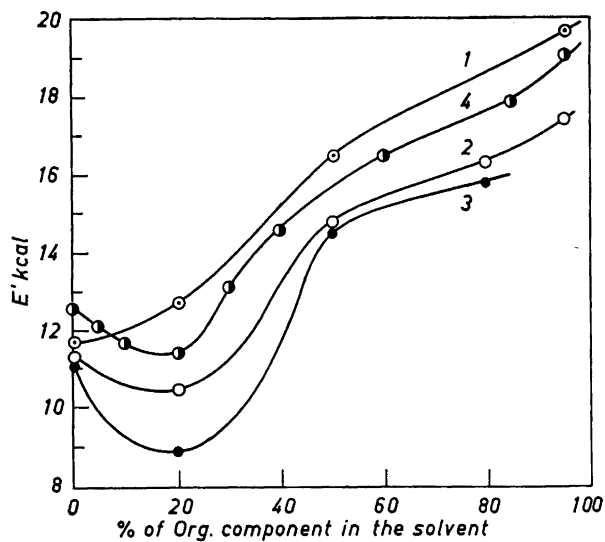solution and a $4a$ molar sodium hydroxide solution:

Fig. 2. Variation of the activation energy E' with the composition of the solvent.
1. Methyl salicylate in methanol-water
2. Ethyl salicylate in ethanol-water
3. *Iso*propyl salicylate in *iso*propanol-water
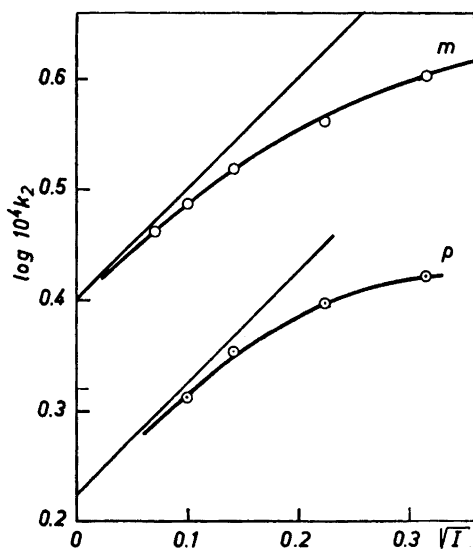4. Ethyl benzoate in ethanol-water.

Fig. 3. Influence of the ionic strength I on the rate of the alkaline hydrolysis of ethyl *m*- and *p*-hydroxybenzoates.
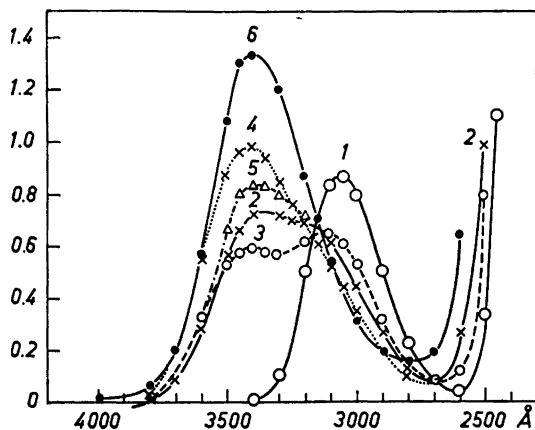
Fig. 4. Absorption curves, 95 wt. % ethanol, 1 cm cell. 1. $c_{est.}$ = 0.0002; 2. $c_{est.}$ = 0.0002, c_{KOH} = 0.002; 3. $c_{est.}$ = 0.0002, c_{LiOH} = 0.0004; 4. $c_{est.}$ = 0.0002, c_{LiOH} = 0.0004, c_{LiCl} = 0.0023; 5. $c_{est.}$ = 0.0002, c_{NaOH} = 0.0016, c_{NaI} = 0.0013; 6. $c_{est.}$ = 0.0002, c_{NaOH} = 0.15, c_{NaI} = 0.09.
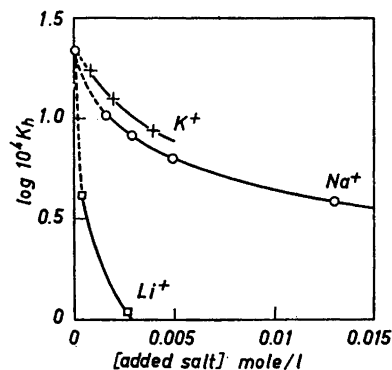
Fig. 5. The relative hydrolysis constants of the ester as a function of salt concentration.

a	0.0025	0.005	0.01	0.025	0.05
$\sqrt{I}$	0.071	0.1	0.142	0.224	0.316
m-, 10^5 k, 1 mole^{-1} s^{-1}	290	307	331	365	402
p-, 10^5 k, 1 mole^{-1} s^{-1}		20.5	22.6	25.0	26.3

Fig. 3 shows that these values approximate to the equation

$$\log k = \log k_0 + 1.02 \ z_A z_B \sqrt{I}$$

in a manner which shows that we have here a reaction between two univalent ions of the same sign. Thus this result also shows that the reaction takes place between the ester ion and the hydroxyl ion.

In the hydrolysis of alkyl salicylates the rate constants are only very slightly dependent on the initial concentration of the reactants, as is seen from Tables 1—3. (The effect of excess alkali concentration has been treated in Section 2). An increase in salt concentration always decreases the reaction velocity (Table 1). In water the salt effect is very weak, except in the case of lithium salts. In 95 % ethanol, for the initial concentration 0.02 mole/l of the ester and alkali, the rate constant at 50° is 30.2 × 10^{-6} s^{-1} when KOH is used and 15.4 × 10^{-6} s^{-1} when NaOH is used. The lithium ion reduces the reaction rate still more than the sodium ion. A very interesting point is that in aqueous alcohol even at a relatively low lithium ion concentration the reaction becomes sensitive to hydroxyl ions, and as the lithium salt concentration increases the reaction finally approaches one of second-order rate.

In general, addition of alkali metal ions shifts the equilibrium (I) towards the left, which causes a decrease in the reaction velocity. This shift of the equilibrium was spectrometrically verified with a Beckman spectrophotometer. Some typical absorption curves are presented in Fig. 4. The relative hydrolysis constants, K_h, of the ester as a function of salt concentration are graphically represented in Fig. 5. As is seen, the effect of lithium ion is much greater than that of potassium or sodium ions. This corresponds to the greater effect of the lithium ion on the reaction velocity *.

One possible explanation of the powerful effect of the lithium ion is that owing to its small size this ion can be fitted between the charged oxygen and the oxygen of the carbonyl group in the salicylic ester, thus forming a chelate. Chelate formation should render the carbonyl carbon more positive and also facilitate the electrometric displacement $C\!=\!\overset{\frown}{O}$ and thus facilitate the bimolecular reaction between the ester ion and hydroxyl ion. Thus chelate formation on the one hand reduces the part of the ester changed by the Goldschmidt mechanism, and on the other hand increases the amount changed by the reaction between the ester ion and hydroxyl ion.

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* The maximum for the salt form is shifted towards longer wave lengths in the order K, Na, Li, and furthermore, the extinction is greatest for the Li compound and weakest for the K compound. This was taken into account in estimating the concentration of the salt form.

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