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The Kinetics of the Solvolysis of Acid Chlorides

III.[1] The Influence of Solvent Composition on Reaction Rate, with Special Reference to the Solvolysis of Ethyl Chloroformate

ANTTI KIVINEN

Department of Chemistry, University of Helsinki, Helsinki, Finland

The rates of solvolysis of ethyl chloroformate in water, methanol and ethanol and in several binary solvent mixtures containing water, methanol or ethanol as one component have been measured. Ethyl chloroformate was found to react by the S_N2 mechanism in all the solvents. The rates of bimolecular solvolysis of carboxylic acid chlorides have been found to vary as the 1.5–2.5th power of the molar concentration of the hydroxylic solvent component over a wide range of solvent composition. In unimolecular solvolyses the order of the reaction with respect to the solvolysing component varies from 1.5 to 6 depending on solvent composition. No simple relationship was established between the reaction rate and the dielectric constant of the solvent. The variation of the rate with the structure of the solvent revealed the best correlation with the molar concentration of the solvolysing component. The variation of the activation parameters with solvent composition is discussed.

Various possible mechanisms for the solvolysis of acid chlorides are considered. It is concluded that at this state of our knowledge the solvolysis mechanisms can most conveniently be interpreted in terms of the S_N mechanisms. The variation of the reaction rate with the concentration of added alkali has been examined as a criterion of mechanism. It is concluded that one needs only two reference compounds (ethyl chloroformate and, *e.g.*, *p*-nitrobenzoyl chloride) to clarify the effect of solvent composition on the bimolecular solvolysis of acid chlorides in almost all solvent mixtures containing a hydroxylic component.

A new criterion is proposed for deciding whether an alcoholysis reaction proceeds by the S_N1 or the S_N2 mechanism.

An interesting aspect of solvolytic reactions is the influence that variations in the composition of the solvent have upon the courses of these reactions. A large number of studies have been carried out on the solvolysis of carboxylic acid chlorides in weakly or moderately polar solvent mixtures. The great reactivity of acid chlorides renders difficult the measurement of the rates of their reactions in water and other solvents of high polarity. As an example it may be mentioned that Hudson and Moss[2] measured the rate of hydrolysis of acetyl chloride in an acetone-water mixture containing 76.6 % water by volume by the "stopped flow" method and found the half-life of the reaction at 27°C to be 2.38×10^{-3} $\sec^{-1}$. The study of the solvolysis of aromatic acid chlorides in solvents of high water content is limited by their low solubility or low rate of dissolution and above all by the fact that only the rates of those derivatives of benzoyl chlorides that have a suitable substituent in the *ortho* position are so slow that they can be measured by conventional methods. The *ortho* substituents, on the other hand, may give rise to steric effects which render difficult an interpretation of their rates in relation to those of other acid chlorides.

The simplest aliphatic acid chloride, formyl chloride, is so reactive that its synthesis has succeeded only recently.[3] If, however, we substitute an alkoxy group for the hydrogen in formyl chloride, the reactivity decreases to such an extent, owing to the conjugation of the group $\mathrm{RO}\overset{\curvearrowright}{-}\mathrm{C}\overset{\curvearrowright}{=}\mathrm{O}$, that the rate of hydrolysis of the resulting acid chloride, an alkyl chloroformate, in water can be readily measured. At first sight the influence of the alkoxy group may seem surprising in view of the fact that when a hydrogen in methyl chloride is replaced by a methoxy group, the velocity of the solvolysis increases approximately 10^{14}-fold.[4] The different effect of the alkoxy group in these two types of compound is evidently due to the fact that there is no conjugation in chloromethyl alkyl ethers as there is in alkyl chloroformates.[5,6]

Alkyl chloroformates, RO·CO·Cl, can be considered as alkoxysubstituted formyl chlorides, esters of chloroformic acid, or ester chlorides of carbonic acid. In any study of the solvolytic reactions of these compounds it is therefore necessary to take into account that in addition to the heterolysis of the carbon-chloride bond there may occur acyl-oxygen or alkyl-oxygen bond fission. It is also possible that under favourable conditions alkyl chloroformates may react by the S_Ni mechanism.[7] The present study relates to the solvolysis of ethyl chloroformate as it was expected that the reactions of this compound would be influenced by relatively few complicating factors. Some earlier data exist on the solvolysis of ethyl chloroformate which provide suitable points of comparison with the data to be presented below.

EXPERIMENTAL

Chemicals. Ethyl chloroformate (Fluka AG, Switzerland) was distilled; b.p. 93.0 — 93.1°C at 761 mm Hg. Diethylamine (abs., *pro analysi*, Fluka AG) was used as received.

Ethanol (absolute alcohol from the State Alcohol Monopoly, Helsinki) was dried with aluminium ethylate[8] before distillation through a 30-cm Vigreux column. Methanol (E. Merck AG, Darmstadt) was dried with magnesium[8] and distilled through the 30-cm Vigreux column. Toluene (guaranteed reagent, E. Merck AG) was used as received. Acetone (guaranteed reagent, E. Merck AG) was dried with potassium carbonate, filtered and distilled from phosphorus pentoxide (guaranteed reagent, E. Merck AG) through the 30-cm Vigreux column. Some batches of acetone were dried with Drierite (W. A. Hammond Drierite Company, Xenia, Ohio) before distillation. The water was distilled in a Fontavapor-61 type B distillation unit (W. Büchi Glasapparatefabrik, Flawil, Switzerland) and boiled for 15 min to expel any carbon dioxide. Dioxan (guaranteed reagent for spectroscopy, E. Merck AG) was used as received.

Solvent mixtures. Most of the solvent mixtures were prepared by weighing the components, but in some cases appropriate volumes of the solvent components were mixed.

In the latter cases the compositions are expressed in parts by volume before mixing. The percentages given in connection with the solvent mixtures refer to the first-mentioned component; thus, for example, 20 wt. % acetone-water refers to the mixture containing 20 % acetone and 80 % water by weight. The densities of the dioxan-water, acetone-water, benzene-ethanol and diethyl ether-ethanol mixtures were taken from the handbook of Timmermans[9] and the densities of ethylene glycol dimethyl ether-water mixtures from a publication of Wallace and Mathews.[10] When necessary, the densities were estimated by graphical interpolation.

Kinetic measurements. (a) *Conductometric method.* The rates in water and solvent mixtures of high water content were measured by following the variation of the conductance of the solution in a Philips Type GM 4221 conductance cell with a Philips Conductance Bridge Type PR 9500. A number of comparative measurements were made using special conductance cells and an Impedance Bridge, Model 250-DA (Electro Scientific Industries, Inc., Portland, Oregon, USA). The concentration of hydrogen chloride in the employed solvents was found to be directly proportional to the conductance and the rate constants could hence be evaluated from the integrated first-order rate equation in the form

$$k_1 = \frac{1}{t} \ln \frac{a}{a-x} = \frac{1}{t} \ln \frac{\lambda_\infty - \lambda_0}{\lambda_\infty - \lambda_x} \tag{1}$$

where λ_0, λ_x and λ_∞ are the relative conductances at times $t = 0$, x and ∞, respectively. In a few cases Guggenheim's method[11] was employed.

(b) *Titrimetric method.* The other method used to determine the rates was the amine method which has been described in detail previously.[12] 5 ml of an about 0.1 N solution of diethylamine in toluene was measured into each of a series of 50-ml glass-stoppered erlenmeyer flasks (number equal to the number of samples that were to be taken from the reaction mixture). The titre of the diethylamine solution had been accurately determined beforehand. A 100-ml graduated flask containing 65—70 ml of the solvent was allowed to attain the desired temperature in a thermostat. A volume of ethyl chloroformate sufficient to give an approximately 0.04 M solution was added to the flask from a graduated pipette and the mixture was vigorously shaken 2—6 min depending on the temperature when water was the solvent. Böhme and Schürhoff[13] reported that ethyl chloroformate dissolves in water at 25°C to give only a 0.038 M solution and for this reason 0.02 M solutions of ethyl chloroformate in water were prepared. After the acid chloride had dissolved completely, 5-ml samples were taken at suitable intervals from the reaction mixture and added to the erlenmeyer flasks containing the diethylamine solution. The flask were then shaken vigorously; this is especially important when the solvent contains much water since two phases are formed. About 10 min later the excess diethylamine was titrated with standard 0.02 N hydrochloric acid employing chlorophenol red as indicator. The consumption of acid is proportional to the extent of reaction because the acid chloride in the sample that has not reacted consumes two equivalents of diethylamine, but the hydrogen chloride formed in the reaction only one equivalent.[12] The volumes of standard acid can be substituted directly in the first-order rate equation:

$$k_1 = \frac{1}{t} \ln \frac{a}{a-x} = \frac{1}{t} \ln \frac{v_\infty - v_0}{v_\infty - v_x} \tag{2}$$

where v_0, v_x, and v_∞ are the consumed volumes at times 0, x and ∞.

Satisfactory results are obtained with the amine method on two conditions. First, the diethylamine and acid chloride must react completely, and, second, this reaction must be so rapid that the solvolytic reaction no longer continues after the sample of the reaction mixture has been added to the diethylamine solution. Both these conditions were found to be fulfilled in the case of ethyl chloroformate. An idea of the high rates of reactions between acid chlorides and amines is given by the results of Hall[14] and Ugi and Beck[15] although these workers did not study the reactions of acid chlorides with diethylamine.

The first samples were withdrawn as soon as possible after the reactant had dissolved. Owing to their high rates, the reactions had usually progressed so far that the extrapolation of the consumed volume to zero time did not prove reliable and hence the rate constants were evaluated employing the first two or three volumes separately as the initial value v_0 in which case the time t_0 was the time when the respective sample was taken.

The thermostats used were electrically regulated water thermostats in which the temperature remained constant within ± 0.02°C. For 0°C, a 7-l Dewar flask filled with crushed ice and water was used.

Calculations. The values of the activation energy E and frequency factor log A_1 were computed by the method of least squares by fitting the Arrhenius equation $k_1 = A_1\exp(-E/RT)$ to the first-order rate constants. The values of the frequency factor log A_2 corresponding to the second-order (bimolecular) rate constants were computed from

$$\log A_2 = \log A_1 - \log [\mathrm{ROH}] \tag{3}$$

where [ROH] is the molar concentration of the hydroxylic solvent component in the solvent mixture at 25°C. The dimensions of A_1 and A_2 are hence sec^{-1} and l.mole^{-1}sec^{-1}, respectively. The values of the activation entropy at 25°C relating to the bimolecular rate constants were computed from the equation $\Delta S^* = \boldsymbol{R} \ln (A_2\boldsymbol{h}/e\boldsymbol{k}T)$. The dimension of the activation entropy is hence cal. mole^{-1} degree^{-1}.

Table 1. Solvolysis of ethyl chloroformate. Illustrative runs.

a. Solvent. Water. Conductivity method. 25°.

t, sec	%	$10^5\ k_1$
300	11.0	(38.9)
600	20.7	38.6
900	29.7	39.2
1200	37.5	39.2
1500	43.6	39.2
1800	49.5	39.0
2100	54.9	39.0
2400	59.8	39.0
2700	64.1	38.9
3000	68.4	38.4
3300	71.9	(38.5)
3600	74.8	(38.3)
	Mean	38.9

b. Solvent: 60 wt. % ethanol, 40 wt. % water. Conductivity method. 40°.

t, sec	%	$10^5\ k_1$
300	12.4	(43.8)
600	22.6	42.7
900	31.6	42.2
1200	39.4	41.8
1500	46.1	41.2
1800	53.5	42.6
2100	58.6	42.2
2400	63.5	42.0
2700	67.7	41.8
3000	71.7	(42.1)
3300	74.0	(40.8)
	Mean	42.1

c. Solvent: water. 25°. Titrimetric method.

t, sec	%	$10^5\ k_1$
475	16.4	37.7
835	27.3	38.2
1315	38.4	38.3
1855	50.7	38.1
2695	65.2	39.2
3655	75.4	38.9
	Mean	38.4

d. Solvent: 20 wt.% diethyl ether, 80 wt.% methanol. 0°. Titrimetric method.

t, sec.	%	$10^6\ k_1$
68880	25.5	4.27
79560	28.5	4.22
145440	44.9	4.09
235740	62.9	4.21
	Mean	4.20

Illustrative data. Data from two runs in which the conductometric method was employed and those from two runs in which the titrimetric method was employed are shown in Table 1. *p* denotes the extent of reaction from the moment when the first sample was taken. The rate constants in Tables 3, 4, 5, and 7 refer to relative conversions of 15—70 %; all values outside this range were omitted when computing the rate constants. The data in Table 1 show that the values of the rate constants exhibited no tendency to rise or fall. In order to determine whether both methods yield conforming results, the hydrolysis of ethyl chloroformate in water was followed by both methods; the results were equal with the limits of experimental error (Tables 1 and 3, Fig. 1).

According to reaction (10) one product of the solvolysis of ethyl chloroformate is carbon dioxide (p.853), which might influence the results obtained by the conductometric and titrimetric methods. It is somewhat surprising that no interference due to carbon dioxide was observed. One explanation may be that no gas bubbles adhered to the vertical electrodes of the conductance cell and another that the carbon dioxide escaped when the volumetric flask was opened to remove samples for titration. Other workers have not either observed that carbon dioxide gives rise to any interference.[2,6,16,18]

RESULTS AND DISCUSSION

Comparison with data reported earlier. The rate of hydrolysis of ethyl chloroformate in water has been previously measured by Böhme and Schürhoff[13] and Hall.[16] Values reported by Hall and those computed with the aid of the Arrhenius equation from the present data are shown in Table 2; the two sets of data are seen to be equal within the limits of experimental error (see Fig. 1). The neutral salts added to the solutions by Hall did not appreciably alter the magnitudes of the rate constants.

Table 2. Comparison of the data obtained in this work with those reported earlier for the hydrolysis of ethyl chloroformate.

Solvent	$10^6 k_1$ sec^{-1}			E kcal mole^{-1}	log A_1 (A_1 in sec^{-1})	Source
	20.1°	30.0°	39.7°			
Water	215	692	1670	19.0	10.50	Hall[16]
”	233	637	1600	17.94	9.733	This work

Böhme and Schürhoff[13] reported the rate constant of the hydrolysis of ethyl chloroformate in water at 25°C to be 2.1×10^{-4} sec^{-1}, which is much lower than the value 3.87×10^{-4} sec^{-1} obtained in this study and the value 3.63×10^{-4} sec^{-1} computed from the data of Hall.[16] To confirm the data of Böhme and Schürhoff, it might be worth while to study the hydrolysis of ethyl chloroformate in their solvent mixtures. Preliminary experiments indicate that the method employed in this study yields values of the rate constant of the reaction in dioxan-water mixtures that are higher than the values reported by these authors.

Grunden and Hudson[17] have reported the value 109×10^{-5} sec^{-1} for the rate constant of the hydrolysis of ethyl chloroformate in a mixture containing

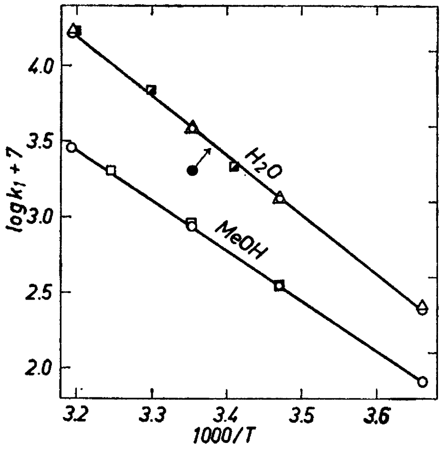


Fig. 1. Plots of log k_1 against $1/T$ for the solvolysis of ethyl chloroformate. ○, this work, titrimetric method; △, this work, conductivity method; ◪, Hall[16]; ●, Böhme and Schürhoff[13]; □, Leimu.[18]

65 % water and 35 % acetone by volume at 50°C. The corresponding value computed from the data of the present study by means of the Arrhenius equation is slightly lower, 99×10^{-5} sec^{-1}.

The kinetic data for the reaction in 15 % (v/v) acetone-water reported by Hudson and Green[6] deviate considerably from the data obtained in this study. Their values for the rate constant k_1 at 25°C are 208×10^{-6} sec^{-1} (acid-base titration) and 233×10^{-6} sec^{-1} (Volhard titration), mean 221×10^{-6} sec^{-1}, while those obtained in this study are 271×10^{-6} sec^{-1} (titrimetric method) and 272×10^{-6} sec^{-1} (conductometric method). The values obtained by Hudson and Green for the rate constant at 0°C by acid-base titration are 28.3×10^{-6}, 26.0×10^{-6} and 26.7×10^{-6} sec^{-1}, mean 27.0×10^{-6} sec^{-1}, and the value obtained by the conductometric method in this study 22.2×10^{-6} sec^{-1}. The value of the activation energy computed from the data of Hudson and Green is low, 13.61 kcal mole^{-1}, whereas the value computed from the present data is 16.35 kcal mole^{-1} (see Fig. 4).

Leimu[18] measured the rate of alcoholysis of ethyl chloroformate in methanol. Despite the different methods of analysis, his data may be considered identical with those obtained in the present study (Table 4; *cf.* Fig. 1).

The mechanism of solvolytic acylation. The mechanisms of acylation have been reviewed recently by Hudson,[5] Satchell,[19] Bender[20] and, primarily in relation to solvolytic reactions, by Kivinen.[12] The following discussion will be primarily limited to various possible reaction paths. The structures of various species (*e.g.* transition states), either established or assumed, occurring in various stages of the reactions will not be discussed in detail except in a number of special cases. These species have been discussed in detail by Bender,[20] Hudson and Green,[6] and others.

The solvolytic reactions of organic acid chlorides can be divided from the mechanistic standpoint into two main types, unimolecular and bimolecular, in the sense these terms were introduced by Ingold.[21] The terms unimolecular mechanism, ionization mechanism, and S_N1 (or "S_N1-like") mechanism are generally taken to be synonomous. In the case of bimolecular mechanisms two quite different points of view prevail; the mechanism may be either an S_N2 mechanism or an addition-elimination (AE) mechanism. A large number of subgroups have been proposed in connection with both unimolecular and bimolecular mechanisms (see, for example, the references in the paper of Kivinen[12]), but these will not be considered here as they are more likely to confuse than to clarify the following discussion.

In its simplest form, the S_N1 mechanism can be presented as scheme (4). The rate-determining step is the ionization of the acid chloride to an acylium ion R^+ and a chloride ion. The acylium ion formed reacts rapidly with a hydroxylic solvent.

$$\begin{array}{ll}\text{(a) } RCl \overset{\text{slow}}{\rightleftharpoons} R^+ + Cl^- & \\ \text{(b) } R^+ + R'OH \xrightarrow{\text{fast}} ROR' + H^+ & \end{array} \qquad (4)$$

The bimolecular S_N2 reaction is a one-step conversion of the reactants to the products by way of a transition state:

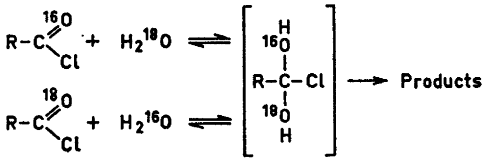
$$RCl + R'OH \longrightarrow ROR' + H^+ + Cl^- \qquad (5)$$

Recent reviews of S_N mechanisms may be found in the works of Bunton[4] and Streitwieser.[22; *cf.* 23, 24]

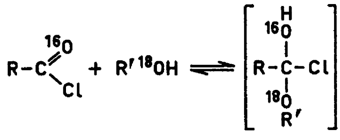
In order to explain the oxygen exchange observed in solvolytic reactions, the bimolecular reaction has been proposed as taking place not as a synchronous substitution reaction, but by way of a tetrahedral intermediate (see, *e.g.*, the review of Bender[20]):

$$RCl + R'OH \rightleftharpoons \text{Intermediate} \longrightarrow \text{Products} \qquad (6)$$

In the simplest case when water is the solvolytic agent (7 a), the hydroxyl groups in the intermediate are symmetrically located with respect to the plane R—C—Cl:



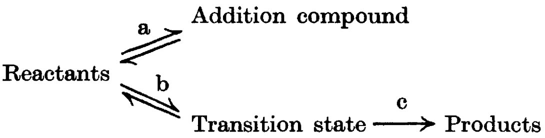
(7a)



(7b)

If the solvolysis takes place in water containing oxygen-18 the intermediate of eqn. (6) has an even chance of reverting to a reactant molecule containing ^{18}O or one containing ^{16}O (eqn. (7a)). There is also the possibility that the intermediate is so long-lived that it may not only change back into the reactants or decompose to the products but also participate in other reactions.

There are two possible reaction routes in addition to the S_N2 and addition-elimination (6) paths for the bimolecular reaction. We may first assume that both the S_N2 and addition-elimination reactions are concurrent. If so, it would seem that their contributions to the over-all reaction would vary greatly depending on the experimental conditions such as solvent composition. Studies of oxygen exchange have been restricted to date to a relatively few solvent mixtures and without more extensive investigation it is not possible to say whether oxygen exchange takes place in all solvent mixtures.



(8)

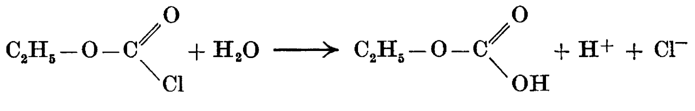
Second, it is possible that the reaction scheme is that given (in simplified form) by eqn. (8).

If the energy barrier between the addition compound and the products is high enough, the reaction will not take place *via* the addition compound, but the acid chloride will be in equilibrium (a) with its hydrated form and the actual reaction would take place by an S_N2-like mechanism (route b-c). The reaction route given by eqn. (8) explains also the observed oxygen exchange.

It was proposed above that the reactant becomes enriched with oxygen-18 in accordance with eqn. (7a). If the solvolytic reagent is not water, but an alcohol, the intermediate is not symmetric (7b). The intermediate should then be able to undergo internal rearrangement in some way to another intermediate which on changing back into the reactant yields an acid chloride containing oxygen-18. The hydrolysis and alcoholysis of an acid chloride may hence differ somewhat in mechanism. The present writer does not know whether kinetic exchange studies have been carried out with oxygen-labeled alcohols. It would be interesting to know whether the results would be identical with those obtained with water as solvent.

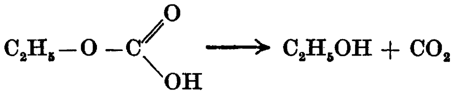
The mechanisms of solvolysis of acid chlorides have recently been discussed also by Bender and Chen. [25] It is reasonable in this connexion to expect that there may exist intermediates with varying degrees of stability also in connexion with S_N2 mechanisms at saturated carbon atoms. This point is discussed in detail by, *e.g.*, Streitwieser.[22]; Ref. 23, p. 367.

The hydrolysis of ethyl chloroformate. The primary products of the hydrolysis of ethyl chloroformate are monoethyl carbonate and hydrogen chloride.



$$C_2H_5-O-C\begin{matrix}\nearrow O\\ \searrow Cl\end{matrix} + H_2O \longrightarrow C_2H_5-O-C\begin{matrix}\nearrow O\\ \searrow OH\end{matrix} + H^+ + Cl^- \qquad (9)$$

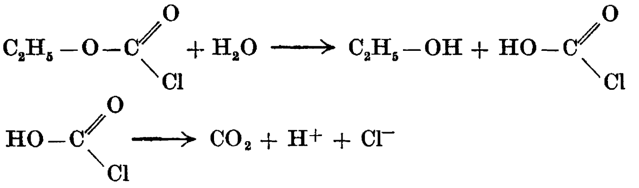
The monoethyl carbonate decomposes rapidly in neutral and acid solutions to ethanol and carbon dioxide.



$$C_2H_5-O-C(=O)OH \longrightarrow C_2H_5OH + CO_2 \qquad (10)$$

Because neither monoethyl carbonate (nor the dialkyl carbonates formed in the alcoholysis reactions) nor the carbon dioxide affected the data (p. 849), there is no point in considering in detail the last reaction step (10). The decomposition of alkyl carbonates has been thoroughly studied by Faurholt and Gjaldbæck[26] and Levin *et al.*[27]

Hudson and his co-workers[6,17] have concluded that the bimolecular solvolysis of ethyl chloroformate involves heterolysis of the carbon-chlorine bond and not heterolysis of the carbon-oxygen bond. In addition to their conclusion, it would be expected that the hydrogen chloride formed would catalyse the reaction if an ester hydrolysis were in question. No trends due to autocatalysis were noted in the calculated first-order rate constants for different runs (see p. 848). It is worth noting that the same reaction products would result regardless of whether the bond broken is the carbon-oxygen bond or the carbon-chlorine bond and an analysis of the products would not clarify the mechanism.



$$\begin{gathered} C_2H_5-O-C(=O)Cl + H_2O \longrightarrow C_2H_5-OH + HO-C(=O)Cl \\ HO-C(=O)Cl \longrightarrow CO_2 + H^+ + Cl^- \end{gathered} \qquad (11)$$

One of the products of the hydrolysis of ethyl chloroformate is ethanol. The amounts of ethanol formed in the reaction in the aqueous solvent mixtures employed in this work were so negligible compared with the water present that the reaction between acid chloride and ethanol could be disregarded. We believe further that the reaction can hardly take place by the S_Ni mechanism under the experimental conditions, for the hydrogen chloride formed in the reactions was equivalent to the ethyl chloroformate added to the reaction mixtures. If the S_Ni reaction took place, one of the reaction products would be an alkyl chloride, not hydrogen chloride.[7]

The data of Grunden and Hudson[17] show that the hydrolysis of ethyl chloroformate is a bimolecular reaction in water-acetone mixtures (*cf.* Ref. 6). Thus, they found, for example, that methyl cloroformate reacts about 2.2 times as fast as ethyl chloroformate in the mixture containing 65 % water by volume at 50°C, which is in agreement with the observed substituent effects in bimolecular reactions. Hydroxide ion greatly accelerates the reaction, the ratio of the rates of the hydroxide ion-catalysed and spontaneous hydrolysis is 3.1×10^7 in 18 % (v/v) water-acetone and 3.4×10^6 in 85 % (v/v) water-acetone. The catalysis by hydroxide ion in pure water was observed also by Hall.[16]

It is interesting to compare the data for ethyl chloroformate with data on the solvolysis of alkyl halides (for which the S_N mechanisms were originally proposed). As it was concluded that the hydrolysis of ethyl chloroformate takes place by the S_N2 mechanism, we shall compare it with the hydrolysis of ethyl bromide because this reaction has been thoroughly studied and is known to take place by the S_N2 mechanism. On the basis of the work of Grunden and Hudson [17] the ratio of the rates of the base-catalysed and spontaneous hydrolysis of ethyl chloroformate in water is of the order of 10^6. The value of this ratio derived from the data of Tommila and co-workers [28,29] for the hydrolysis of ethyl bromide is about 2000. The value of the ratio for ethyl chloroformate is hence about one thousand times the value for ethyl bromide.

The results of the study of the hydrolysis of ethyl chloroformate in water and in acetone-water mixtures are collected in Table 3. The value of the activation energy, 17.9 kcal/mole, for the reaction in water is 3.7 kcal/mole smaller than that for dimethylcarbamyl chloride (21.6 kcal/mole).[16] The former value is approximately equal to the activation energy (18.8 kcal/mole) of the hydrolysis of benzoyl chloride in 50 % acetone-water;[30] the activation energy of the latter reaction in water would be much higher (*cf.* Refs. 31, 32).

Table 3. Hydrolysis of ethyl chloroformate in acetone-water mixtures. A_1 in sec^{-1}, A_2 in l mole^{-1} sec^{-1}. Method: cond. = conductivity, titr. = titrimetric.

Vol.% acetone	x_{H_2O}	$10^6 k_1$ sec^{-1}				E kcal mole^{-1}	log A_1	log A_2	ΔS^* cal. mole^{-1} deg.$^{-1}$	Method
		0°	15°	25°	40°					
0	1.000	25.3	135	389	1700	17.88	9.702	7.959	−24.0	cond.
0	1.000	24.4	134	384	1660	17.94	9.733	7.990	−23.9	titr.
15[a]	0.959	22.2	108	272	1050	16.35	9.429	6.750	−29.6	cond.
15[a]	0.959			271						titr.
35[b]	0.883	11.7	53.0	131	456	15.56	7.523	5.954	−33.2	cond.
80[c]	0.504	0.91	4.00	9.40	30.6	14.93	5.912	4.857	−38.2	titr.

[a] 12.2 wt.%; [b] 30.0 wt.%; [c] 76.0 wt.%

It is noteworthy that the high rate of hydrolysis of ethyl chloroformate ($k_1 = 1680 \times 10^6$ sec^{-1}) at 40°C as compared with the rate of ethyl bromide ($k_1 = 2.17 \times 10^6$ sec^{-1}) [28] is due to a lower activation energy, although the effect of the frequency factor is the opposite. The activation energy of the hydrolysis of ethyl bromide is 24.9 kcal/mole and that of ethyl chloroformate 17.9 kcal/mole and the logarithms of the frequency factors 9.96 and 7.98. The large negative value, −23.9, cal mole^{-1} degree^{-1} (Table 3), of the activation entropy of the hydrolysis of ethyl chloroformate (ethyl bromide: −14.9 cal mole^{-1} degree^{-1}) [28] is a strong indication that the hydrolysis of ethyl chloroformate takes place by the S_N2 mechanism also in pure water.

One way of illustrating the variation of the rates of solvolytic reactions with solvent composition is to plot the logarithm of the first-order rate con-

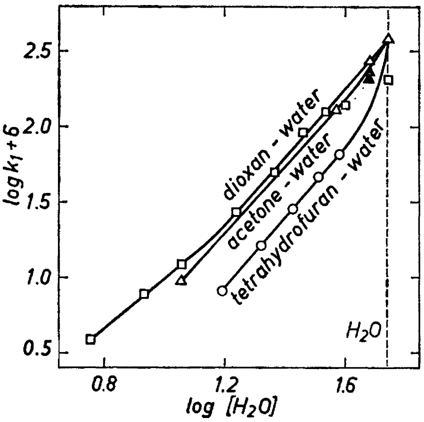


Fig 2. Plots of log k_1 against log [H_2O] for the hydrolysis of ethyl chloroformate. △, this work, acetone-water; ▲, Hudson and Green [6], acetone-water; □, Böhme and Schürhoff,[13] dioxan-water; ○, Böhme and Schürhoff,[13] tetrahydrofuran-water. 25°C.

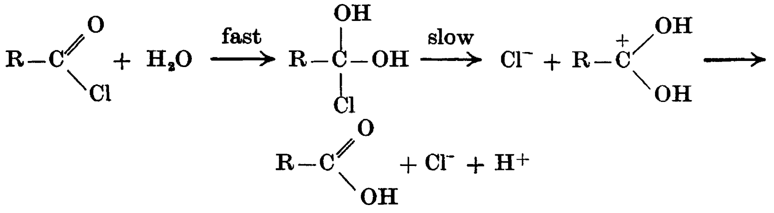
stant as a function of the logarithm of the molar concentration of the hydroxylic solvent component. Such plots for the hydrolysis of ethyl chloroformate are drawn in Fig. 2. The slope of the curve gives the apparent order of the reaction with respect to water. The value of the slope is a criterion of mechanism of S_N-type reactions, for it has been found that the value of the slope is 6—7 for S_N1 reactions, but much lower, 2—3, for S_N2 reactions in dioxan-water and acetone-water mixtures (see, *e.g.*, Refs. 28, 33).

The curves in Fig. 2 were drawn by taking the value of the rate in water to be that determined in this work and not the value reported by Böhme and Schürhoff.[13] The plot is practically linear for acetone-water mixtures except those of low acetone content. If we disregard the value of the rate in 30 % dioxan-water, the plot is linear also for dioxan-water mixtures in the dioxan range from 0 to 70 % by weight. A linear relationship has been found for the reaction in tetrahydrofuran-water mixtures containing 30—75 % tetrahydrofuran, but the slope of the plot changes rapidly when the water content is high. For all three series of solvent mixtures the slopes of the linear sections of the plots are equal, about 2.3—2.4, in accordance with the S_N2 mechanism; the value of the slope reported by Tommila *et al.*[28] for the hydrolysis of ethyl bromide in acetone-water mixtures is 2.3.

The slope of the plot for the reaction in dioxan-water mixtures decreases slightly to the value 1.65 when the weight percentage of dioxan exceeds 70. This value is of the same magnitude as the value found for the hydrolysis of acetyl chloride in binary solvent mixtures of low water content, for Zimmerman and Yan [34] found the rate of hydrolysis of acetyl chloride in acetone-water mixtures to be proportional to the 1.92th power of the water concentration when the water concentration increased from 0.547 to 2.83 moles/l and Koskikallio [35] to the 1.9th power in dioxan-water mixtures when the water concentration increased from 0.180 to 2.22 moles/l.

On the basis of his own data and the value of the rate of hydrolysis of acetyl chloride in water reported by Gold and Hilton,[36] Koskikallio has estimated that the rate is proportional to the 1.6th power of the water concentration over the whole range of dioxan-water mixtures. It may, however, be concluded from the work of Hudson and Moss[2] and Ugi and Beck[15] that the value reported by Gold and Hilton is incorrect. The true value of the rate constant of the hydrolysis of acetyl chloride is probably several powers of ten greater than the value reported by Gold and Hilton. From the data of Hudson and Moss it may be estimated that the value of the slope is approximately 5 when the water content of dioxan-water mixtures increases from 19.6 to 75.6 % by volume.

Hudson and Moss[2] have, in fact, concluded that the hydrolysis of acetyl chloride takes place by the ionisation mechanism, which is possibly preceded by hydration of the reactant. (In dioxan-water mixtures containing only a few per cent water, the hydrolysis of acetyl chloride is obviously, as Koskikallio[35] has claimed, a bimolecular reaction). The reaction mechanism is hence the following.



$$\mathrm{R{-}C(=O)Cl} + \mathrm{H_2O} \xrightarrow{\text{fast}} \mathrm{R{-}C(OH)_2Cl} \xrightarrow{\text{slow}} \mathrm{Cl^-} + \mathrm{R{-}\overset{+}{C}(OH)_2} \longrightarrow \mathrm{R{-}C(=O)OH} + \mathrm{Cl^-} + \mathrm{H^+} \qquad (12)$$

From the preceding it is obvious that the solvolysis of ethyl chloroformate takes place by the S_N2 mechanism in water and solvent mixtures of weaker ionising power. This does not exclude the possibility that the hydrolysis of ethyl chloroformate takes place by the S_N1 mechanism in solvents that greatly retard the bimolecular reaction. Grunden and Hudson[17] have presented evidence which shows that ethyl chloroformate hydrolyses by the ionisation mechanism in formic acid containing at most 4 % (v/v) water. When the water content of the formic acid increases over 4 %, the reaction mechanism gradually changes into the bimolecular mechanism. In a later paper Green and Hudson[37] examined the nature of the ionisation mechanism in connection with the hydrolysis of secondary alkyl chloroformates and concluded that the data are best in accord with a mechanism where the rate-determining stage is the formation of the acylium ion (scheme (4), p.851). It seems that Hudson *et al.*[2,17,37] are of the opinion that hydration (eqn. (12)) precedes the ionisation in the hydrolysis of acetyl chloride, whereas the hydrolysis of alkyl chloroformates takes place *via* the acylium ion (4), without, however, definitely excluding the other alternative in either case.

The formation of the acylium ion in the hydrolysis of acid chlorides was studied recently by Hall and Lueck[38] by two methods, one in which the hydrolysis was allowed to take place in the presence of the strongly electrophilic reagent mercury perchlorate and another in which they attempted to trap the unstable intermediates. No appreciable electrophilic catalysis as is observed in the case of reactions that take place by the ionisation mechanism[1,38] was observed when butyl chloroformate underwent hydrolysis in 50 % (v/v) dioxan-water and we may conclude that, like ethyl chloroformate, butyl chloroformate hydrolyses by the S_N2 mechanism in this solvent mixture.

It is of interest in this connection to note the work of Bartlett and Minato[39] with a chloroformate of unusual structure, *tert*-butylperoxy chloroformate. They studied the decomposition of this compound under widely varying experimental conditions and concluded that it decomposes by the ionisation mechanism in formic acid, 60 % dioxan-water and methanol. They observed further that the Criegee rearrangement[40] predominates in formic acid and simple methanolysis takes place in methanol with very little loss of peroxidic oxygen, whereas both reactions proceed concurrently in the aqueous dioxan.

The methanolysis of alkyl chloroformates. Kinetic data for the methanolysis of ethyl chloroformate in methanol and in some binary solvent mixtures containing methanol as one component are shown in Table 4. Data reported by Leimu[18] for several alkyl chloroformates and values of the activation parameters calculated from them by the present writer are included in the table.

Since the solvolysis of ethyl chloroformate takes place by the S_N2 mechanism in water, it is obvious that the mechanism is the same in the less polar solvent methanol (in alcoholysis reactions one of the products is dialkyl carbonate $C_2H_5O{\cdot}CO{\cdot}OR'$). It may be noted that the rate decreases in the sequence MeO·COCl > EtO·COCl > i-PrO·COCl in water, which is the reverse of the sequence in formic acid containing 1 % water.[17] In 35 % (v/v) acetone-water, the rate sequence is i-PrO·COCl > MeO·COCl > EtO·COCl. It is probable that also the solvolysis of isopropyl chloroformate takes place by the S_N2 mechanism in methanol, but that the ionisation mechanism makes a large contribution to the over-all rate already in the 35 % acetone-water mixture.

As stated above, Bartlett and Minato found that the alcoholysis of *tert*-butylperoxy chloroformate in anhydrous methanol is a simple methanolysis that yields methyl *tert*-butylperoxy carbonate. The contribution of ionic

Table 4. Methanolysis of chloroformates R·O·COCl in methanol and in diethyl ether-methanol and benzene-methanol mixtures. Titrimetric method. A_1 in sec^{-1}, A_2 in l mole^{-1} sec^{-1}.

Solvent	R	$10^6 k_1$					E kcal mole^{-1}	log A_1	log A_2	ΔS^* cal. mole^{-1} deg^{-1}	Source
		0°	15°	25°	35°	40°					
Methanol	C_2H_5	8.15	35.4	86.8		293	15.22	7.089	5.697	−34.4	This work
»	C_2H_5		35.7	90.3	203		15.34	7.192	5.800	−33.9	Leimu[18]
»	CH_3		66.0	164	363		15.05	7.236	5.844	−33.7	»
»	$(CH_3)_2CH$		15.8	41.0	101		16.39	7.630	6.238	−31.9	»
»	CH_2ClCH_2		215	512	1100		14.37	7.233	5.841	−33.7	»
20 wt.% ether	C_2H_5	4.20	18.5	44.7		153	15.27	6.843	5.556	−35.0	This work
40 wt.% ether	C_2H_5			26.5							»
59.5wt.% benzene	C_2H_5			28.2							»

rearrangement [40] to the over-all rate they estimated to be 5 %. *tert*-Butylperoxy chloroformate is much more reactive than ethyl chloroformate, the reaction rate of the former at 25° being about 91 times the rate of the latter. The authors studied also the influence of carbon tetrachloride added to methanol on the over-all rate. From their data one can estimate that the slope of the plot of log k_1 against log [MEOH] varies from about 2.3 to 1.1 when the concentration of methanol diminishes from 24.8 mole/l (pure methanol) to 4.96 mole/l.

It is seen from Tables 4 and 5 that the activation entropy is the same for both methanolysis and ethanolysis of ethyl chloroformate within the limits of experimental error and that the value of the activation energy is less than 1 kcal/mole smaller for the former than for the latter reaction. The addition of 20 % diethyl ether does not effect any greater change in the activation energy or in the activation entropy in contrast to the effect of acetone on the hydrolysis (Table 3). The slope of the log k_1 *vs.* log [ROH] curve is 2.7 in methanol and 2.5 in ethanol. Because more information is available on the alcoholysis of acid chlorides in ethanol-containing mixtures,[12] the ethanolysis of ethyl chloroformate will be discussed in more detail.

Ethanol is a more suitable solvent in several respects than methanol in kinetic studies of the alcoholysis reaction. First, if hydrogen halides are present or are produced in methanol, their esterification must be taken into account. The reaction between ethyl chloroformate and methanol is, however, so rapid that the esterification of the formed hydrogen chloride does not essentially alter the results. For example, Leimu [18] estimated the error in the rate constant due to the esterification of hydrogen chloride at 25°C in pure methanol to be about 0.2 %, which is less than the experimental uncertainty of the method used in this work. On the other hand, even "dry" alcohols often contain water due to the equilibrium $2\ ROH \rightleftharpoons ROR + H_2O$, and especially methanol is difficult to dehydrate completely.[41]

Table 5. Ethanolysis of ethyl chloroformate in diethyl ether-ethanol and benzene-ethanol mixtures. Titrimetric method. A_1 in sec^{-1}, A_2 in l mole^{-1} sec^{-1}.

Solvent	x_{EtOH}	$10^7 k_1$					E kcal mole^{-1}	log A_1	log A_2	ΔS^* cal.mole^{-1} deg^{-1}
		0°	15°	25°	40°	50°				
Ethanol	1.000	17.6	81.7	211	764		16.04	7.075	5.841	−33.7
Diethyl ether										
20 wt.%[a]	0.866	10.2	45.9	118	423		15.84	6.681	5.572	−35.0
40 wt.%[a]	0.707			58.0						
Benzene										
40 wt.%[a]	0.718			116						
60 wt.%[a]	0.531		28.9	67.5	228	465	14.75	5.643	4.781	−38.6

[a] Reaction in sealed ampoules.

The ethanolysis of ethyl chloroformate. The rates of ethanolysis of ethyl chloroformate in several solvent mixtures were measured to permit a comparison of the rates with the rates of ethanolysis of monosubstituted benzoyl chlorides[12] and by this means to obtain a general picture of the influence of solvent composition on the course of acid chloride solvolysis.

Kinetic data on the solvolysis of ethyl chloroformate are shown in Table 5. The rate of the solvolysis in ethanol is about one-fourth of the rate in methanol and slightly over one-sixth of the rate in water at 25° (Tables 3 and 4). The former ratio is mainly due to a difference of about 0.8 kcal/mole in the activation energy since the values of log A_1 do not differ singificantly. As the solvolysis of ethyl chloroformate takes place by the S_N2 mechanism in water and methanol, there is no doubt that the same mechanism applies when ethanol is the solvent. We may nevertheless examine whether the data for ethyl chloroformate fulfill the criteria for deciding the reaction mechanism that were employed in connection with the ethanolysis of benzoyl chlorides.[12]

Slopes of the plots of log k_1 against log [ROH] for the ethanolysis of ethyl chloroformate and the previously studied benzoyl chlorides are given in Table 6. The value of the slope (2.4) for ethyl chloroformate in diethyl ether-ethanol mixtures is in agreement with the values of the slope for the benzoyl chlorides that react by the S_N2 mechanism (*i.e.*, all other substituted benzoyl chlorides in Table 6 except *p*-methoxybenzoyl chloride). The values of the slope were previously concluded to be 1.9—2.1 for substituted benzoyl chlorides that react solely by the S_N2 mechanism, whereas values between 2.3 and 2.5 were taken, in agreement with other mechanistic criteria, to indicate a weak contribution of the ionisation mechanism. These small differences in slope are, however, of the order of magnitude of the experimental uncertainty, and hence a value of the slope between 1.9 and 2.5 is strong evidence for a bimolecular mechanism.

The values of the slope for the solvolysis of *p*-methoxybenzoyl chloride, the mechanism of which changes into the S_N1 mechanism as the ethanol

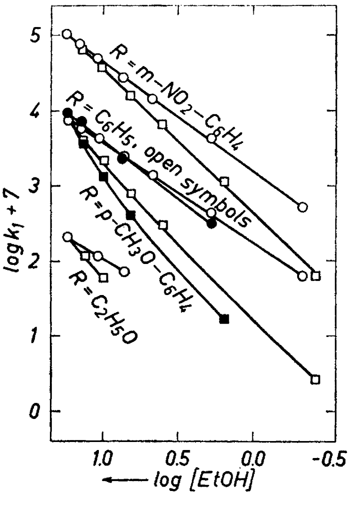


Fig. 3. Plots of log k_1 against log [EtOH] for the ethanolysis of acid chlorides RCOCl. ○, benzene-ethanol; □, diethyl ether-ethanol. 25°C.

Table 6. Mean values of n obtained for the ethanolysis of acid chlorides R·COCl with the aid of the equation $\log k_1 = n \log [EtOH] + \text{const.}$ 25°C.

R	Benzene-ethanol mixtures	Wt.% diethyl ether in diethyl ether-ethanol mixtures			Source
		0–20	20–60	60–90	
C_2H_5O	1.5	2.4	2.3		This work
p-$NO_2-C_6H_4$	1.4	1.9	1.9	1.9	Kivinen[12]
m-$NO_2-C_6H_4$	1.5	2.0	2.0	2.0	»
m-$Br-C_6H_4$	1.4	2.2	2.0	2.0	»
m-$CH_3O-C_6H_4$	1.3	2.5	2.1	2.0	»
C_6H_5	1.3	2.3	2.2	2.0	»
m-$CH_3-C_6H_4$	1.3	2.5	2.4	2.0	»
p-$CH_3O-C_6H_4$	1.5	4.1	2.7	2.4	»

content of the solvent increases,[1,12] are of a different magnitude in diethyl ether-ethanol mixtures. The mean slope is 4.7 for 0 — 20 % diethyl ether-ethanol mixtures and may be expected to rise to about 5 in pure ethanol.[12] As it is possible that the mechanism of the solvolysis of p-methoxybenzoyl chloride is not identical with the S_N1 limiting mechanism in pure ethanol, it is probable that the values of the slope for acid chlorides that have a greater tendency than p-methoxybenzoyl chloride to react by an ionisation mechanism are somewhat larger, possibly 6 or 7, in ethanol. No confirmative experimental data are, however, available.

It is thus evident that the value of the slope of the curve plotting $\log k_1$ against log [ROH] provides an additional criterion for judging whether a reaction is of the S_N1 or S_N2 type in diethyl ether-ethanol mixtures.

The situation is quite different with respect to the reactions in benzene-ethanol mixtures. It is seen from Table 6 that the mean values of the slope are between 1.3 and 1.5 irrespective of whether the mechanism is of the S_N1 or S_N2 type, and hence the values of the slope for reactions in benzene-ethanol mixtures give no indications of the mechanisms. The difference between the rates in diethyl ether-alcohol mixtures on one hand and in many other alcohol-containing mixtures (*e.g.*, benzene-ethanol) on the other seems to be quite general. Various solvolytic reactions in alcohol-containing mixtures have been systematically studied previously by, *e.g.*, Salomaa,[42] Hudson and Saville [43–45] and Tommila and Nieminen.[46] As examples of the values of the slope of the plot of $\log k_1$ against log [ROH], the following may be mentioned. Salomaa [42] found that the slopes are 1.5—2.0 for several 1-halogenoethers in benzene-ethanol mixtures; all the reactions he studied take place by the S_N1 mechanism. Hudson and Saville [45] have noted that the value of the slope for the ethanolysis of triphenylmethyl chloride increases from a value of about 2 at low alcohol contents to a value of about 6 at high alcohol contents in diethyl ether-ethanol mixtures. There is good reason to believe that the ethanolysis of triphenylmethyl chloride takes place by the S_N1 mechanism in pure ethanol. Tommila and Nieminen [46] have reported the value of the slope to be 1.7 for

Table 7. Rates of solvolysis of ethyl chloroformate in ethanol-water mixtures.

Wt.% ethanol	x_{H_2O}	$10^6 k_1$				E kcal mole^{-1}	log A_1 (A_1 in sec^{-1})	Method
		0.0°	15.0°	25.0°	40.0°			
0	1.000	25.3	135	389	1700	17.88	9.702	conductivity
0	1.000	24.4	134	384	1660	17.94	9.733	titrimetric
20	0.911	29.6	142	366		16.31	8.520	conductivity
30	0.856	29.6	115	285	909	14.61	7.152	»
30	0.856			274				titrimetric
60	0.630	11.0	49.2	121	421	15.49	7.432	conductivity
100	0.000	1.76	8.17	21.1	76.4	16.04	7.075	titrimetric

the ethanolysis of ethyl benzenesulphonate in benzene-ethanol mixtures; the mechanism is S_N2 in this case.

It may be noted that the effect of added dioxan on the reaction rates of alcoholysis reactions is somewhat similar to the effect of added diethyl ether (see *e.g.* Ref. 42). It is also important to note that the above discussion concerns only those cases where the reaction mixture contains the alcoholic component in a concentration of at least, say, ten times the concentration of the reactant. If the alcohol concentration is very low, the situation may be quite different.[47]

Ethanol-water mixtures. Solvolytic reactions in ethanol-water mixtures (in neutral conditions) have been studied in great detail by, *e.g.*, Kohnstam *et al.*[48,49] and Hyne *et al.*[50-52] In most cases the activation energy has been found to be a minimum when the mole fraction of ethanol is approximately 0.1.[49] In order to clarify the main features of the solvolysis of acid chlorides in ethanol-water mixtures, the rates of solvolysis of ethyl chloroformate were measured in several solvent mixtures. The results are shown in Table 7.

It is seen from Table 7 (*cf.* Fig. 4) that the activation energy decreases abruptly when ethanol is added to water until its mole fraction is about 0.1, but then changes very little with increasing alcohol content. There is a deep minimum in the curve plotting E against x_{H_2O} where the mole fraction of ethanol is 0.1—0.2. The variation of the rate constants, is however small in water-rich solvent mixtures.

The influence of dielectric constant on reaction rates. Many attempts have been made to find correlations between reaction rates and macroscopic properties of solvents and much attention has been paid from both experimental and theoretical standpoints to find the relationship between rate and dielectric constant of the solvent. Recent papers on this subject have been written by Laidler,[53] Tommila and his co-workers [54] and Wiberg.[24] When a linear relationship has been found to exist between the logarithm of the rate constant and the expression $(\varepsilon-1)/(2\varepsilon+1)$ (or $1/\varepsilon$ when the dielectric constant ε exceeds 7 in value), the slope of the plot assumes different values for different series of solvent mixtures.[24] A linear relationship of this kind has been established for the hydrolysis of acetyl chloride in dioxan-water mixtures (Gold and Hilton [55]) and for the hydrolysis of benzoyl chloride in acetone-water mixtures (Archer and Hudson [31]). Böhme and Schürhoff [13] found the logarithm of the rate of hydrolysis of ethyl chloroformate to vary linearly as $1/\varepsilon$ in a number of binary solvent mixtures and the present writer [12] found a linear relationship between log k_2 (k_2 = the second-order rate constant) and log ε for the ethanolysis of monosubstituted benzoyl chlorides in benzene-ethanol mixtures containing 100—20 % ethanol by weight. However, the solvent composition was varied to only a limited extent in these studies. The plots of log k_2 against $(\varepsilon - 1)/(2\varepsilon + 1)$ for the ethanolysis of monosubstituted benzoyl chlorides [12] over wide ranges of solvent composition have been found to be slightly S-shaped as predicted by Laidler [53] on theoretical grounds.

There exists, on the other hand, much evidence that the dielectric constant is not a factor that decisively determines the variation of the rate of solvolysis of an acid chloride when the solvent composition changes. The dielectric constant decreases from a value of about 25 in ethanol to 21 in the 50 % acetone-ethanol mixture and then remains practically constant at about 21 when the acetone content increases further, and yet the rate of ethanolysis of benzoyl chlorides decreases as the 1.5-2.0th power of the molar concentration of ethanol also in mixtures that contain more than 50 % acetone.[12] The lowering of the rate is nearly the same when acetone or benzene is added to ethanol in spite of the great difference in the dielectric constants of benzene ($\varepsilon = 2.27$) and acetone ($\varepsilon = 21$). Another extreme case is the rate of hydrolysis of ethyl chloroformate in dimethyl sulphoxide-water mixtures, which increases with increasing dimethyl sulphoxide content although the dielectric constant of this solvent is much smaller than that of water.[57]

Even these examples lead to the conclusion that no simple correlation exists between the rate of solvolysis of acid chlorides and the dielectric constant of the solvent. This conclusion was also drawn by Hudson,[47] who stressed the importance of hydrogen bond formation between the solvent and the solute or between the solvent and the transition state which is disregarded when the theory of electrostatics is applied.

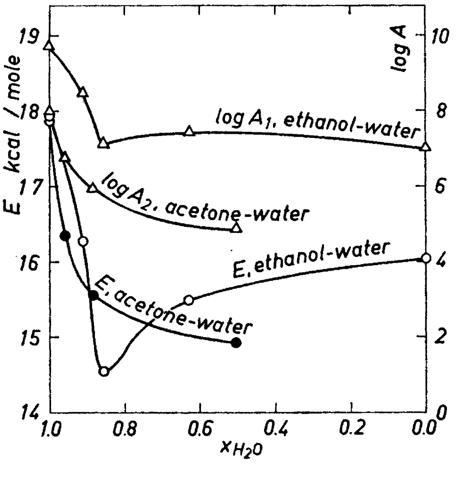


Fig. 4. E and log A for the solvolysis of ethyl chloroformate as functions of the mole fraction of water. A_1 in sec^{-1}; A_2 in l mole^{-1} sec^{-1}.

The dependence of the activation parameters on solvent composition. The computed values of the activation parameters E and log A_2 (or log A_1 for reactions in ethanol-water mixtures) are plotted as functions of the mole fraction of water in Fig. 4.

The addition of acetone to water leads at first to an abrupt decrease in the activation energy; the latter is nearly 3 kcal/mole lower when the mole fraction of water is 0.883 (35 % (v/v) acetone) than when water alone is the solvent. The limited number of data points does not permit conclusions as to whether or not the curve has a minimum (and perhaps also a maximum) as has often been found for reactions in acetone-water mixtures.[28] Tommila *et al.*[28] have found that the activation parameters are often complex functions of solvent composition. This is revealed also by the work of Salomaa [58] and Winstein and Feinberg.[59] It is a general observation that the dependence of the activation parameters on solvent composition cannot be used to draw conclusions about reaction mechanisms as this dependence is determined by specific properties of the reactants and solvent mixtures.

The variation of the activation parameters of the reactions in ethanol-water mixtures was discussed already on p. 861.

The variation of the activation parameters with the composition of mixtures containing ethanol is much simpler than their variation with the composition of aqueous mixtures. The activation energies of the ethanolysis of acid chlorides vary linearly as the mole fraction of ethanol between 1.0 and 0.04 (diethyl ether content 97.5 wt. %) in diethyl ether-ethanol mixtures (Fig. 5). The same applies to the reactions in benzene-ethanol mixtures when the ethanol mole fraction varies from 1.0 to about 0.2, but the curves slope abruptly downward when the weight ratio of benzene exceeds 90 % (ethanol mole fraction 0.16).

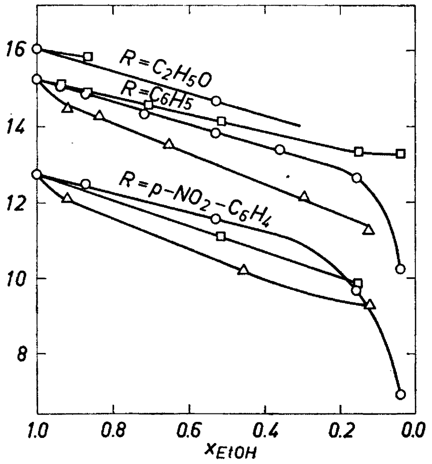


Fig. 5. Plots of activation energy against mole fraction of ethanol for the ethanolysis of acid chlorides RCOCl. ○, benzene-ethanol; □, diethyl ether-ethanol; △, acetone-ethanol.

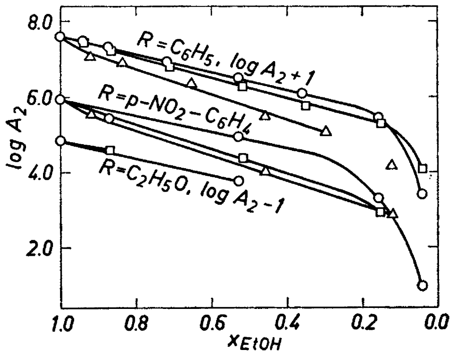


Fig. 6. Plots of log A_2 (A_2 in l mole^{-1} sec^{-1}) against mole fraction of ethanol. Symbols as in Fig. 5.

Table 8. Values of the activation entropy ΔS^* (in cal.mole^{-1} deg^{-1}) in the ethanolysis of ethyl chloroformate (this work), substituted benzoyl chlorides (Kivinen [12]), methyl chloromethyl ether (Salomaa [42]) and isopropyl benzenesulphonate (Tommila and Nieminen [46]) in benzene-ethanol and diethyl ether-ethanol mixtures at 25.0°C.

Solvent	x_{EtOH}	Ethyl chloroformate	Substituent in benzoyl chloride						Methyl chloromethyl ether	Isopropyl benzenesulphonate
			p-NO$_2$	m-NO$_2$	m-Br	m-CH$_3$O	H	p-CH$_3$O		
Ethanol	1.000	−33.7	−33.2	−32.9	−31.9	−29.5	−29.1	−16.7	−21.2	−17.2
Benzene										
20 wt.%	0.872		−34.6	−34.2	−34.6	−31.7	−30.5	−17.1	−25.9[a]	−20.0[b]
60 »	0.531	−38.4	−36.8	−37.2	−36.8	−34.5	−34.4	−22.9	−31.7	−21.3[c]
90 »	0.159		−44.1	−43.4	−42.4	−39.4	−39.1	−31.2	−40.5[d]	
Diethyl ether										
20 wt.%	0.866	−35.0		−34.6	−33.7	−31.3	−31.1	−17.5		
60 »	0.517		−39.4	−39.3	−38.1	−35.6	−35.4	−24.8		
90 »	0.152		−45.9	−45.9	−45.5	−41.5	−41.2	−32.6		
97.5 »	0.040			−51.5			−45.4			

[a] 40 wt.% benzene; [b] 32.6 wt.% benzene; [c] 52.8 wt.% benzene; [d] 95 wt.% benzene.

The dependence is also linear in acetone-ethanol mixtures when the weight percentage of acetone increases from 0 to 90 (except for a small abrupt decrease of the order of 0.2 kcal/mole caused by the addition of a small amount of acetone; *cf.* Fig. 5). It may be concluded from the data of Salomaa [42] (*cf.* Ref. 60) and Tommila and Nieminen [46] that the variation of the activation parameters with solvent composition in alcoholic media for other reactions which take place by mechanisms of the S_N type are quite similar to the variation found for acid chlorides. As for reactions such as the alcoholysis of acid anhydrides which are more complex by nature (Koskikallio [61]), the relationships between the activation parameters and solvent composition are described by fairly simple curves although the latter differ greatly in form from those in Figs. 5 and 6.

The curves plotting the variation of the frequency factor are similar to those plotting the variation of the activation energy (Figs. 5 and 6) except that the frequency factor diminishes abruptly in the same ethanol mole fraction range in diethyl ether-ethanol and benzene-ethanol mixtures.

Values of the activation entropy ΔS^* for the reactions of several acid chlorides, methyl chloromethyl ether and isopropyl benzenesulphonate at various mole fractions of ethanol are given in Table 8. The activation entropy for the solvolysis of ethyl chloroformate in pure ethanol is of the same magnitude as the activation entropies of monosubstituted benzoyl chlorides that react by the S_N2 mechanism in this solvent. The value for p-methoxybenzoyl chloride in ethanol, −15.7 cal mole^{-1} deg^{-1}, is not as negative as the values for the other acid chlorides, but the difference becomes smaller as the ethanol content of the solvent decreases, obviously because the mechanism of the reaction of *p*-methoxybenzoyl chloride changes gradually to the S_N2 mechanism.

When expressed in calories per degree, the activation entropies are −10.1 for *p*-methoxybenzoyl chloride, −11.6 for isopropyl benzenesulphonate[46] and −15.6 for methyl chloromethyl ether,[42] all in ethanol. Accordingly, the activation entropy values thus differ for reactions that take place by the S_N1 and S_N2 mechanisms. It should be noted, however, that, as Schlager and Long[62] have stated, a mechanistic interpretation can be given to ΔS^* for the reaction of a given compound only if there exists a body of thermodynamic data for series of reactions for which the mechanisms are known independently; examples are the reactions taking place by the S_N1 and S_N2 mechanisms.

The relationship between the activation energy and frequency factor (or between ΔH^* and ΔS^*) will not be discussed in detail here as several excellent surveys and discussions of the subject have appeared recently.[63—66, *cf.* 67, 68] A linear relationship has been found to exist between these parameters for the alcoholysis reactions of acid chlorides in benzene-ethanol mixtures (over such a wide range of solvent composition that the linearity cannot be due to systematic experimental errors (*cf.* Ref. 28, p.p. 377—379) but not when diethyl ether-ethanol mixtures are the solvents.[12]

The effect of alkali as a mechanistic criterion. A pronounced acceleration of reaction rate by hydroxide (or alkoxide) ion is generally considered to point to a mechanism of S_N2 type. A sufficiently high ratio (of the order of 10^5) of the rate constant of a reaction in the presence of a base to the rate constant of the uncatalysed reaction has often been taken as sufficient evidence that the reaction is bimolecular.

Quite recently, Bender and Chen[25] obtained interesting and in some degree unexpected results in a study of the hydrolysis of 4-substituted 2,6-dimethylbenzoyl chlorides in acetonitrile containing 1 % water. They found that the acid chlorides reacted by the unimolecular mechanism (with the acylium ion as an intermediate) in neutral and acid solvents. The values of the Hammett reaction constant for both the neutral hydrolysis ($\varrho = -3.85$) and acid hydrolysis ($\varrho = -3.73$) are highly negative. Tetramethylammonium hydroxide, on the other hand, greatly accelerates the reactions and the value of the reaction constant for the base-catalysed reaction is positive ($\varrho = +1.2$). The mechanistic criteria Bender and Chen have applied in their studies are substituent effects, salt effects and isotope exchange. (Ladenheim and Bender[69] have stated that carbonyl oxygen exchange during hydrolysis is a good indication of a tetrahedral intermediate, and its absence is a reasonable, although not infallible, indication of an acylium ion intermediate). The authors have concluded that the neutral (and acid) solvolysis and the base-catalysed solvolysis proceed by quite different mechanisms.[70] If this is true, base catalysis is not a reliable mechanistic criterion. Hall and Lueck[38] have suggested that probably only a large ratio *k*(nucleophile)/*k*(water) is a satisfactory indication of a bimolecular hydrolysis. It must, however, be noted that the solvent mixture employed by Bender and Chen[25] differs considerably from those usually employed in studies of the solvolysis of acid chlorides. Without further experimentation one cannot say whether their results can be extended to the solvolysis of acid chlorides in solvent mixtures containing high proportions of hydroxylic components. For example, the work of Hudson *et al.*[17,32,71] shows that the effect of hydroxide ion is generally in agreement with other mechanistic criteria although the effect is not always of the expected magnitude.[32] Furthermore, the acid chlorides studied by Bender and Chen [25] are sterically hindered to a certain extent and, as Cason and Kraus [72] have shown, the solvolysis of acid chlorides is highly sensitive to steric effects.

In addition to the unusual base catalysis, the work of Bender and Chen [25] reveals another significant feature, the catalysis of the solvolysis of acid chlorides by acids. Acid catalysis of the solvolysis of an acid chloride has been reported only once previously,[45] although the solvolysis of acid fluorides is known to be catalysed by acids.[73] At the same time as the paper of Bender and Chen appeared, Satchell [74] reported the results of a study of the solvolysis of acyl fluorides (acetyl, butyryl and benzoyl fluorides) from which he concluded that acid fluorides do not differ in kind but only in degree from other acid halides in their acid solvolysis. The work of Bender and Chen supports Satchell's conclusion. When he discussed the mechanism of the acid-catalysed solvolysis of acid fluorides, Satchell proposed two different reaction routes [75] in one of which a tetrahedral intermediate is formed. Without considering Satchell's elegant approach to the question in detail, we may note his statement that the reaction may take place by both routes concurrently (*cf.* p. 852). Even in cases where the reaction route does not involve a tetrahedral intermediate, at least some degree of oxygen exchange is likely to occur under similar conditions.

In this connection it is worth noting the work of Bunton *et al.*,[76] Butler and Gold,[77] and Bender and Feng,[78] who have employed the deuterium isotope effect as a means of clarifying the mechanisms of acid chloride solvolysis. Although their work has contributed much new information on these solvolytic reactions, various unexplored structures of the transition state may still be envisaged.

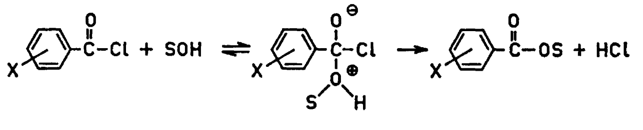
Conclusions. As a summary of the preceding discussion, it may be stated that the solvolysis of ethyl chloroformate proceeds by the S_N2 mechanism in a wide range of binary solvent mixtures and that the rate can be measured by conventional methods even when the solvent mixture is such that acid chlorides react in it much faster than in water. In highly ionising solvents such as moist formic acid, the solvolysis of ethyl chloroformate may proceed by the ionisation mechanism. The solvolytic reactions of aliphatic and aromatic acid chlorides do not differ in their kinetics. When the solvent mixtures are such (containing, say, less than 70—80 % alcohol or less than 20—30 % water) that the rate of solvolysis is low, a more reactive substrate, *e.g.* *p*-nitrobenzoyl chloride, than ethyl chloroformate is more suitable a type compound than ethyl chloroformate in the study of the bimolecular solvolysis of acid chlorides. The rate of solvolysis of *p*-nitrobenzoyl chloride can be conveniently measured even when the concentration of the hydroxylic component in the solvent mixture is of the order of 0.01 mole/l. In studies of the effect of the medium on bimolecular solvolyses of acid chlorides, only two standard substrates are thus required to permit the performance of kinetic measurements in almost all possible solvent mixture combinations; these substrates are ethyl chloroformate and *p*-nitrobenzoyl chloride.

The detailed mechanisms of solvolytic reactions of acid chlorides have not been fully clarified and there are still many aspects that merit investigation. It may be stated, however, that the macroscopic kinetic behaviour of acid chlorides is in practically all aspects closely similar to the kinetic behaviour of compounds in which the reaction centre is a saturated carbon atom. The similarities are evident in the variation of the rate and activation parameters with solvent composition, in the salt effects, in electrophilic catalysis and in base catalysis. In view of this, it seems that at this state of our knowledge the mechanisms of solvolysis of acid chlorides can, without going to the intimate details of mechanisms, be profitably examined in terms of the mechanisms of nucleophilic substitution reactions (S_N1 and S_N2).

When the manuscript of this paper was in the course of preparation, there appeared some interesting papers, which may with good reason be mentioned here.

Johnson [79] has presented evidence that a tetrahedral intermediate exists on the reaction path in the solvolysis of carboxylic esters. Johnson studied the pyridine-catalysed ethanolysis of ethyl trifluoroacetate in deuterated ethanol and concluded that the reaction occurs by way of an anionic tetrahedral intermediate.

Cocivera [80] has examined the role of the solvent in solvolysis and studied the contributions of two competitive mechanisms to the over-all rates of solvolysis of substituted benzoyl chlorides under different conditions. One of the mechanisms is a nucleophilic substitution of the S_N type (eqn. (5)) and the other an addition mechanism in which a solvent molecule adds to the carbonyl carbon atom of the acid chloride and hydrogen chloride is then eliminated:



(13)

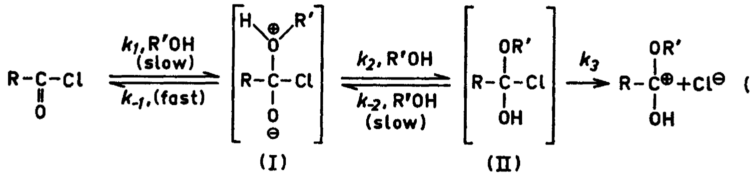
From the data of Swain *et al.*[81,82] and Hudson *et al.*[31,83,84] on the hydrolysis of benzoyl chloride in acetone-water mixtures, Cocivera [80] concluded that the addition reaction is about 165 times as fast as the bimolecular substitution (which may be a "merged" S_N1-S_N2 mechanism) in 90 vol. % acetone-water, that both reactions proceed at the same rate in about 55 vol. % acetone-water, and that the bimolecular substitution is about 12 times as fast as the addition reaction in 30 vol. % acetone-water.

From the data of Kivinen [12] for the ethanolysis of substituted benzoyl chlorides in various solvent mixtures, Cocivera [80] concluded that all the acid chlorides react by the addition mechanism in ethanolic solvents (the solvolysis of *p*-methoxybenzoyl chloride, however, proceeds by a unimolecular mechanism in ethanol and ethanol-rich solvent mixtures [1,12]). It is of interest that Cocivera found that the solvolysis reactions of *p*-nitro, *m*-nitro-, *m*-methoxy- and *m*-bromobenzoyl chlorides in benzene-ethanol mixtures are of the type

$_5A_{100}$ in the classification of Winstein and Fainberg,[59] *i.e.* of the same type as the solvolysis of methyl chloromethyl ether.[42,59]

Sims [85] has studied the effect of solvent on the esterification of benzoyl chloride in carbon tetrachloride-methanol mixtures by examining the relationship between the rate constant and the thermodynamic excess functions of the solvent mixtures.

Minato [86] reviewed the details of the solvolysis mechanisms proposed for acid chlorides by various writers and presented the following mechanism:



(14)

Without taking any stand as to the conclusions of Minato, it may be noted that mechanism (14) explains many experimental observations made in studies of the solvolysis of acid chlorides. On the other hand, as Minato himself pointed out, the mechanism (14) may not be in accordance with the observed linear dependence between σ^+ and ϱ. The common-ion effect [14,87] and electrophilic catalysis [1,38] observed in the solvolysis reactions of acid chlorides that take place by the ionisation mechanism would possibly be more easily explained by a simpler mechanism such as the S_N1 or the hydration-ionisation mechanism (p. 856).

In his discussion of the ethanolysis of acid chlorides Minato [86] partly based his conclusions on different rates of solvolysis of acid chlorides in diethyl ether-ethanol and carbon tetrachloride-ethanol mixtures. The present writer cannot, however, accept Minato's view that different orders of reaction rate with respect to ethanol in these solvent mixtures can be used as a criterion when detailed mechanisms are being considered because the apparent order is largely independent of mechanism in carbon tetrachloride-ethanol mixtures (and also in benzene-ethanol mixtures, see p. 860). Salomaa [42] has, for instance, found that the apparent order with respect to ethanol of the rate of alcoholysis of methyl chloromethyl ether, which is an S_N1 reaction, is 1.5—2.0 in carbon tetrachloride-ethanol mixtures; this is the same order as has been observed in the solvolysis of acid chlorides.As a whole, Minato's work is a very interesting contribution to the discussion of the mechanisms of solvolysis of acid chlorides.

In a recently published paper on salt effects in the hydrolysis of acid chlorides, Hudson and Moss [87] drew attention primarily to the hydrolysis of 2,4,6-trimethylbenzoyl chloride which they found to take place by the ionisation mechanism in acetone-water mixtures. Their conclusions are in agreement with the views of the present writer.[1]

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