Solvent Participation in Nucleophilic Displacement Reactions. Part II. The Reaction between Ethanol and Acid Chlorides.*

By R. F. Hudson and B. Saville.

[Reprint Order No. 5760.]

The kinetics of the reaction between alcohol and *p*-nitrobenzoyl and acetyl chlorides have been compared in a non-polar solvent (carbon tetrachloride) and a donor solvent (ether). In the former the order with respect to alcohol approaches three in dilute solutions and unity in concentrated solutions, whereas in ether the rate remains proportional to the square of the alcohol concentration.

These results are interpreted by assuming the reaction to occur with trimeric associates in carbon tetrachloride, the concentration of which may be obtained from infrared data, and with two alcohol molecules in ether. The relative reactivity of the assemblies $(ROH)_3$ and $(ROH)_2$ in carbon tetrachloride and ether respectively is shown to be given by the statistical factor for the different number of alcohol molecules in the two cases, simultaneous nucleophilic and electrophilic action being assumed.

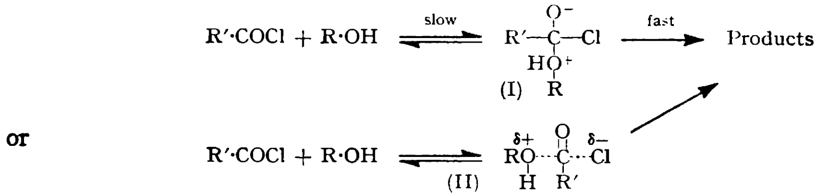
The results in the more concentrated solutions suggest a negligible (additional) solvent effect, which is supported by the similarity of the third-order velocity constants in ether and acetone.

The general considerations discussed in the preceding paper will now be examined experimentally for two extreme types of reaction controlled either by the bond-forming process (S_N2 type) or by the bond-breaking process (S_N1 type). The experiments now to be described deal exclusively with the alcoholysis of acid chlorides in solvents of varying polarity, as these reactions proceed at convenient speeds and are irreversible under these conditions. Although the exact mechanism of the alcoholysis is not known with certainty even in solvolytic media owing to the possibility of addition, it is generally agreed that the preliminary bond-forming process determines the rate (Hudson *et al.*, *J.*, 1950, 1729, 3259; 1953, 883, 888, 3352; Gold, Hilton, and Jefferson, *J.*, 1950, 3259; Baker, *Trans. Faraday*

---

* Part I, preceding paper.

Soc., 1941, **37**, 632; Hughes, *ibid.*, p. 613). Hence the process kinetically resembles an S_N2 substitution at a saturated carbon atom, although energetically stable intermediates may be formed in the subsequent steps of the reaction. As considerable solvation is necessary for reaction, charge separation must occur in the transition state. This may be due to the formation of a polar addition compound (I) as in the case of esters (Bender, *J. Amer. Chem. Soc.*, 1951, **73**, 1626; see Ingold, " Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, 1953, p. 775) or to the recurrence of an S_N2 mechanism (II). The rate sequence R·COBr > R·COCl > R·COF (Archer, Hudson, and Wardill, *J.*, 1953, 888; Bevan and Hudson, *J.*, 1953, 2187) with relative rates similar to those of the corresponding saturated halides, shows that considerable separation of the C–X bond occurs (II) and the transition state is probably best represented as an intermediate between (I) and (II). For present purposes it is sufficient to assume that such a transition state is stabilised by solvation as in the case of a corresponding reaction at a saturated carbon atom.



The reaction is followed first in a non-polar solvent, as under these conditions solvent–transition state interaction will be at a minimum, and the preferential solvation by the more polar molecules will provide most of the solvation energy. There is some uncertainty over the reaction mechanism and even the kinetic order of reactions leading to ionic products in completely non-polar media as the reactions are frequently heterogeneous (Pickles and Hinshelwood, *J.*, 1936, 1353). These reactions become homogeneous in more polar solvents (*idem, loc. cit.*). The small activation energies show that such reactions are energetically favourable when only small solvation forces are available.

In solvents of low polarity the preferential solvation by the more " active " molecules frequently leads to integral kinetic orders (Swain, *J. Amer. Chem. Soc.*, 1948, **70**, 1119; Swain and Eddy, *ibid.*, p. 2989) and this has led to some controversy over the molecularity of the process. Following the recent suggestions of Gelles, Hughes, and Ingold (*J.*, 1954, 2918) and of Swain (*J. Amer. Chem. Soc.*, 1955, **77**, 1122) it is proposed to refer to the number of molecules of one kind solvating the transition state as the kinetic order of the solvation process, and retain the original definition of molecularity (Hughes and Ingold, *J.*, 1935, 252), since this differentiates between two extreme kinds of substitution mechanism.

EXPERIMENTAL

Purification of Materials.—Carbon tetrachloride (Hopkin and Williams, " AnalaR " grade) was refluxed for 4 hr. over phosphoric oxide and distilled through a Vigreux column. Absolute alcohol was distilled from quicklime and finally treated with magnesium and iodine before further distillation in the manner described by Vogel (" Practical Organic Chemistry," Longmans, Green, 1948, 170). Acetone was stored over potassium carbonate, distilled in a Towers distillation unit, and finally refluxed over phosphoric oxide before redistillation. Only small amounts were distilled as required, since water slowly accumulates on standing as shown by titrations with Karl Fischer reagent. Freshly distilled samples usually contained a maximum of 0·05% of water; they had b. p. 56·5°.

Ether was stored over sodium wire for at least a week and decanted on to freshly prepared sodium sand, over which it was refluxed for 2 hr. The ether was finally distilled through a Vigreux column and had b. p. 34·5°. Acetyl chloride and *p*-nitrobenzoyl chloride were purified by fractional distillation (Brown and Hudson, *J.*, 1953, 3352).

Kinetic Measurements.—The reactions were initiated by weighing the required quantity of acid chloride into 100 ml. of ethanol solution in a stoppered flask in a thermostat after temperature equilibrium had been obtained. A stop-clock was started at the same time, and the flask was shaken vigorously for a few seconds. Portions of 5 ml. were extracted at convenient times and added to 40 ml. of pure cold acetone to stop the reaction. The liberated hydrogen chloride was titrated with 0·05N-triethylamine in toluene, Naphthylamine-orange being used as indicator.

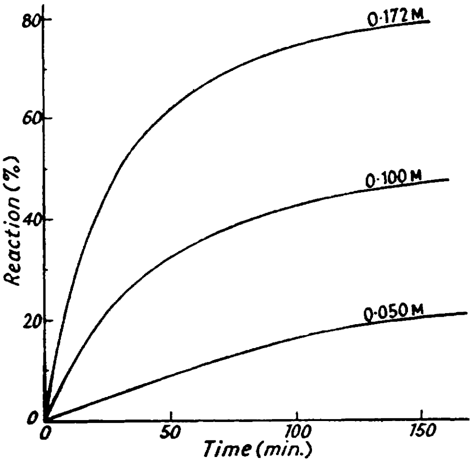
A modified procedure was used for reactions with half-lives of the order of 1 min. or less. A solution of the acid chloride in the solvent alone, and a solution of twice the required concentration of alcohol were brought to the thermostat temperature; 5 ml. of the acid chloride solution were pipetted into a clean dry flask, 5 ml. of the alcohol solution rapidly added, and a stop-watch was started when the pipette was half empty. After an appropriate time, 40 ml. of cold dry acetone were rapidly added, thus stopping the reaction. The reaction mixture was then titrated as before, and the measurement repeated for other reaction times.

When ether was used as solvent the reactions were carried out in specially constructed vessels to allow samples to be withdrawn for analysis with minimum liquid surface exposed to the atmosphere, thus reducing evaporation losses.

Treatment of Experimental Results.—In the more concentrated solutions, *i.e.*, above *ca.* 0·5M, the rate of reaction is given accurately by a first-order equation from which a pseudo-unimolecular constant can be obtained directly. Results so obtained are denoted by *L* in the following Tables. In the more dilute solutions (0·05—0·34N-EtOH) the rate, as estimated by the variation in hydrogen chloride concentration with time, varies in a complex manner with alcohol concentration (Fig. 1), which may be due to one or more of the following causes : (1) The change in degree of association of alcohol as the concentration decreases in the course of the reaction (see p. 4127). (2) The change in the degree of association by interaction of alcohol with the products of reaction. (3) The loss of hydrogen chloride from the solution (in particular when carbon tetrachloride was used as solvent). This effect can usually be detected qualitatively, and leads to a sharp decrease in rate (Fig. 1).

For these reasons, attention was paid to the first part of the rate curve. Values of the initial rates were obtained from the slope of the % reaction–time curves in the first few % of the total reaction. This was taken as the instantaneous rate at the mean concentration over which the extrapolation was made. This method (denoted by " I " in the following Tables) gives pseudo-unimolecular rate constants comparable with the values obtained for higher concentrations.

FIG. 1.



First-order rate constants for the reaction in carbon tetrachloride were also obtained graphically from the rate curves by assuming that over the initial part of the reaction the reaction rate is given by $dx/dt = (a - x)(b^* - x)$, where a is the initial concentration of chloride, b^* the effective initial concentration of alcohol, and x the concentration of hydrogen chloride produced at time t. Then

$$\ln a/(a - x) = k\int_0^t (b^* - x)dt$$

At time t_1 when $x = x_1$ it follows that

$$\ln a/(a - x_1) = kb^*t - k\int_0^{t_1} x \, . \, dt = k(b^*t_1 - s_1)$$

and at time t_2 when $x = x_2$

$$\ln a/(a - x_2) = k(b^*t_2 - s_2)$$

where s_1 and s_2 are the areas under the curves of x against t. As $k_1 = kb^*$ it follows that

$$k_1 = [s_2 \ln a/(a - x_1) - s_1 \ln a/(a - x_2)]/(s_2t_1 - s_1t_2)$$

By choosing several pairs of x and t the constancy of k_1 can be investigated. This method of calculating k_1 is referred to as " A " in the following tables.

Results.—The rate was found to be almost proportional to the concentration of chloride for a constant ethanol concentration as shown by the results in Table 1. The rate curves were almost superimposable for the first 15% of the reaction in 0·172M-alcohol solution, after which the rate reductions are more pronounced for the higher concentrations. This observation is important in that it indicates that the acid chloride does not form a complex with alcohol. If this were the case some change in the equilibrium constant with the concentration of acid chloride should be observed with a corresponding effect on the kinetics, unless of course the association is complete. In view of the incomplete association of the alcohol, this is unlikely, and in the following discussion preliminary association of alcohol and acid chloride will be neglected.

The effect of ethanol concentration on the rate of reaction of acetyl chloride is shown in Table 1, and of *p*-nitrobenzoyl chloride in Table 2. The internal consistency is of the order of 1—2% except in the most dilute solutions where the inaccuracy may be as high as 5%.

TABLE 1. *Rates of ethanolysis of acetyl chloride in carbon tetrachloride.*

[EtOH] (mole/l.)	[AcCl] (mole/l.)	Temp.	10^4k_1 (min.$^{-1}$)	Method	10^4k_1 (min.$^{-1}$), mean
0·050	0·0526	20·0°	23·8	A	23·2
			22·6	I	
0·050	0·0516	20·0	23·4	A	23·4
			23·4	I	
0·050	0·0520	0	15·4	I	15·4
			15·4	A	
0·100	0·0520	20·0	122·5	A	122·5
			124	I	
0·100	0·050	20·0	121	I	
0·100	0·0496	0	63·2	A	62·5
			61·8	I	
0·172	0·0510	20·0	369	A	369
			358	I	
0·172	0·0570	20·0	372	A	
0·172	0·0497	—	371	I	
0·172	0·0235	—	364	I	
0·172	0·0100	—	380	I	
0·172	0·0510	0°	114	A	114
0·345	0·0502	20·0	952	I	969
			969	A	
0·345	0·0638	20·0	979	I	
			979	A	
0·345	0·0506	0	245	A	245
0·690 *	0·0510	20·0	2290	L	2290
			2550	I	
0·690 *	0·0510	20·0	2310	I	
			2330	L	
0·690 *	0·0521	0	497	L	497
0·3193	0·0450	26·0	—	I	1170
0·3193	0·0450	13·0	—	I	593
0·2190	0·0436	26·0	—	I	701
0·2190	0·0438	13·0	—	I	375
0·1105	0·0430	26·0	—	I	189
0·1105	0·0430	13·0	—	I	135

* In the most concentrated ethanol solutions k_1 was obtained from the first-order equation.

TABLE 2. *Rates of ethanolysis of* p-*nitrobenzoyl chloride in carbon tetrachloride.*

[EtOH] (mole/l.)	[R·COCl] (mole/l.)	Temp.	10^4k_1 (min.$^{-1}$)	Method	*E* (kcal./mole)
0·100	0·0489	20·0°	6·89	I	
0·172	0·0485	20·0	20·5	I	
0·690	0·0462	20·0	139	L	10·25
0·690	0·0551	10·5	80	L	
0·690	0·0499	0·5	40	L	
5·175	0·0465	20·0	1264	L	10·73
5·175	0·0468	10·5	694	L	
5·175	0·0465	0·0	319	L	

TABLE 3. *Activation energies for the alcoholysis of acetyl chloride in carbon tetrachloride solutions of varying alcohol concentration.*

[EtOH] (mole/l.)	E_{0-20} (kcal./mole)	[EtOH] (mole/l.)	E_{0-20} (kcal./mole)	[EtOH] (mole/l.)	E_{13-26} (kcal./lmole)	[EtOH] (mole/l.)	E_{13-26} (kcal./mole)
0·050	3·30	0·345	10·8	0·3193	8·95	0·1105	4·40
0·100	5·35	0·690	12·1	0·2192	8·18	—	—
0·172	7·6						

TABLE 4. *Ethanolysis of acetyl chloride and* p-*nitrobenzoyl chloride in donor solvents at 20°.*

[EtOH] (mole/l.)	[R·COCl] (mole/l.)	10^4k_1 (min.$^{-1}$)	[EtOH] (mole/l.)	[R·COCl] (mole/l.)	10^4k_1 (min.$^{-1}$)	[EtOH] (mole/l.)	[R·COCl] (mole/l.)	10^4k_1 (min.$^{-1}$)
Acetyl chloride in ether						*p*-Nitrobenzoyl chloride		
0·089	0·049	2·1 †	1·00	0·0503	136	0·345	0·050	2·44
0·172	0·050	4·8 †	1·725	0·0496	460	0·690	0·050	10·0
0·345	0·053	16·85	6·90 *	—	*ca.* 7000	3·450	0·038	244
0·690	0·048	61·8, 61·9 †				6·90 *	—	900

* Extrapolated from Branch and Nixon's results (*J. Amer. Chem. Soc.*, 1936, **58**, 2499).

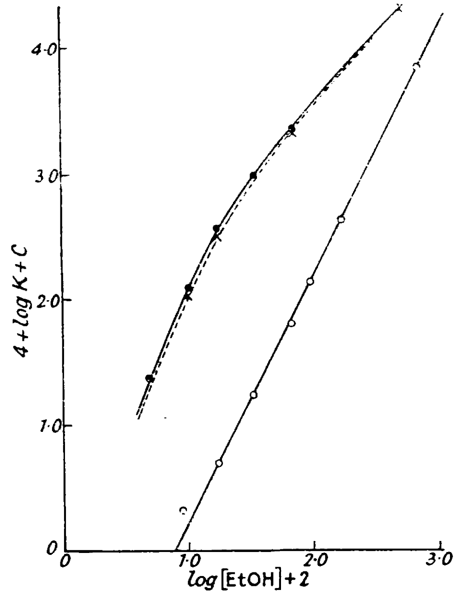
The activation energies were calculated from the Arrhenius equation (see Table 3), and the rate constants in ether and acetone are given in Table 4. The rate constants were obtained graphically from the first-order rate plots except when marked (†). The energy of activation for the ethanolysis of *p*-nitrobenzoyl chloride in 3·45M-ethanol in acetone was found to be 9·65 kcal.

DISCUSSION

(A) *Reaction in Carbon Tetrachloride.*—The most characteristic feature of the kinetic results recorded in Tables 1 and 2 and Fig. 2 is the rapid change in apparent reaction order as the concentration of alcohol changes. Thus as the concentration of alcohol decreases, the order with respect to alcohol approaches 3, whereas above *ca.* 0·7M the order is almost unity. Over the same concentration range the temperature coefficient changes from very low values as the concentration of alcohol approaches zero to reach an almost constant value above 0·7M (Table 3).

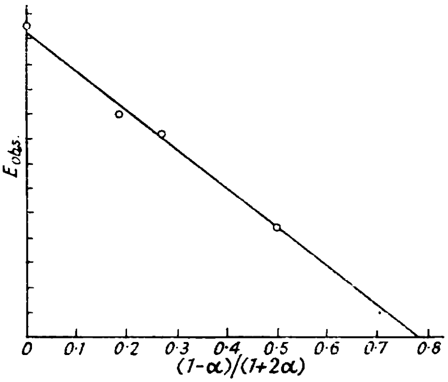
These regular changes are no doubt due to the association of alcohols in non-polar media. This association may be complex and the exact nature is not fully understood, but in the case of the simpler alcohols most measurements show that the smallest polymer which can be detected is the trimer (Hoffmann, *Z. phys. Chem.*, 1943, **53**, *B*, 179; Staveley and Spice, *J.*, 1952, 406; Mecke and Nückel, *Naturwiss.*, 1943, **31**, 348), and not the dimer as in the case of phenol and benzyl alcohol (Kreuzer and Mecke, *Z. phys. Chem.*, 1941, **49**, *B*, 309). Further association undoubtedly occurs as the alcohol concentration increases but the various equilibria may be represented by a common equilibrium constant (Lassettre, *Chem. Rev.*, 1937, **20**, 259; Kreuzer and Mecke, *loc. cit.*; Coggeshall and Saier, *J. Amer. Chem. Soc.*, 1951, **73**, 5414).

FIG. 2.



○ AcCl in Et$_2$O, $c = 0$.
● AcCl in CCl$_4$, $c = 0$.
× p-NO$_2$·C$_6$H$_4$·COCl in CCl$_4$, $c = 1{\cdot}25$.
– – – – Superimposition of log [Trimers] (ordinate) + constant.

FIG. 3.



In the more dilute solutions (up to *ca.* 0·2—0·3M), the association may be satisfactorily described in terms of the monomer–trimer equilibrium only (Hoffmann, *loc. cit.*; Staveley and Spice, *loc. cit.*). It is significant that the kinetic order of the reactions studied changes over the concentration range where this equilibrium changes from one side to the other, and comparison with Hoffmann's data (*loc. cit.*) shows that the rate is proportional to the concentration of alcohol *in the associated state* over a wide concentration range (Fig. 2). It follows therefore that in the more dilute solutions reaction involves a group of three alcohol molecules either in the form of monomers or as a trimeric associate. Owing to the dynamic equilibrium between monomers and trimers, these two possibilities cannot be differentiated by kinetic measurements, and it is doubtful if there is any significant theoretical difference.

In the following discussion, reaction will be assumed to occur with a decomposing aggregate rather than a group of monomers, because this leads to a slightly simpler treatment when the more concentrated solutions are considered, and involves a more plausible picture of the reaction mechanism. The change in activation energy may be interpreted quantitatively on this basis as follows. From the mass-action equation,

$$\underset{C(1-\alpha)}{3\mathrm{ROH}} \rightleftharpoons \underset{\alpha C/3}{(\mathrm{ROH})_3}$$

it follows that

$$\alpha/(1-\alpha)^3 = 3C^2K \qquad \text{(i)}$$

The reaction being assumed to occur between an aggregate and the alkyl or acyl halide, the rate is given by

$$-\mathrm{d}[\mathrm{R'X}]/\mathrm{d}t = k_1[(\mathrm{ROH})_3][\mathrm{R'X}]$$

If $(\mathrm{ROH})_3$ is sensibly constant over the initial part of the reaction the observed pseudo-unimolecular constant k_0 is given by

$$k_0 = k_1[(\mathrm{ROH})_3] = k_1\alpha C/3$$

Logarithmic differentiation leads to

$$\frac{-E_{\mathrm{obs.}}}{RT^2} = \frac{E}{RT^2} + \frac{\partial \ln \alpha}{\partial T} \qquad \text{(ii)}$$

It follows from equation (i) that $\ln \alpha - 3 \ln (1 - \alpha) = \ln K + \ln C^2$. Expanding $\ln (1 - \alpha)$ and differentiating with respect to T, we have

$$\frac{\partial \ln \alpha}{\partial T} + \frac{3\partial \ln \alpha}{\partial T}\sum_0^\infty(\alpha + \alpha^2 + \ldots\ldots) = \frac{-\Delta H}{RT^2}$$

so that

$$\frac{-\Delta H}{RT^2} = \frac{\partial \ln \alpha}{\partial T}\cdot\left(\frac{1+2\alpha}{1-\alpha}\right)$$

Rearrangement and substitution in (ii) leads to

$$E_{\mathrm{obs.}} = E - [(1-\alpha)/(1+2\alpha)]\,.\,\Delta H \qquad \text{(iii)}$$

where $E_{\mathrm{obs.}}$ is the experimental activation energy, E the true activation energy, and ΔH the heat of association of the trimer.

Values of $E_{\mathrm{obs.}}$ were obtained over the 13—26° range (a smaller temperature range could not be employed owing to the small temperature coefficient at the lower concentrations), and compared with the values of α obtained from Hoffmann's data (*loc. cit.*) at 20° (Table 5).

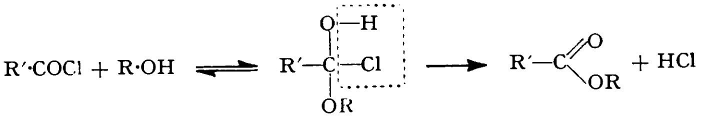
TABLE 5.

Ethanol (mole/l.)	—	0·3193	0·2192	0·1105
α	1	0·594	0·477	0·254
$(1-\alpha)/(1+2\alpha)$	0	0·186	0·267	0·495
E_0 (kcal./mole)	12·5	8·95	8·19	4·40

The value for $\alpha = 1$ was obtained by extrapolation of the E_0–[ROH] graph and is found to be equal to the value in 40% alcohol–ether solution (Branch and Nixon, *J. Amer. Chem. Soc.*, 1936, **58**, 2499). From the linear relation between $(1-\alpha)/(1+2\alpha)$ and $E_{\mathrm{obs.}}$ (Fig. 3) a value of ΔH of *ca.* 16 kcal./mole is obtained in agreement with the value of *ca.* 15 kcal./mole obtained spectroscopically by Mecke *et al.* (*loc. cit.*) and Hoffmann (*loc. cit.*) for simple alcohols.

A similar conclusion is reached if reaction is supposed to proceed with three monomers, the activation energy E' then being given by $E_{\mathrm{obs.}} = E' + [3\alpha/(1+2\alpha)]\Delta H$. The activation energy E' is negative in this case, and may be looked upon either as involving a pre-equilibrium as already considered, or alternatively as a result of the complexity of the transition state such that the heat content at this temperature is less than that of the reactants. In simple molecular terms this may be explained by regarding the nucleophilic attack and C–Cl bond stretching as activated processes assisted by an increase in temperature. The specific solvation will be non-activated in the sense that it is given approximately by simple electrostatic considerations. Hence increase in temperature will decrease this interaction by increasing thermal movement of the solvating molecules, and this effect may well be greater than the activation. The rate is measurable because of the very large entropy decrease accompanying a process of this kind.

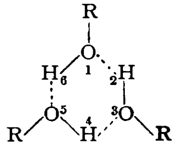
It should be noted in passing that the present data in the most dilute solutions show that reaction does not proceed by elimination of covalent hydrogen chloride from an addition intermediate :

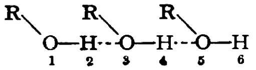


The results support the view already expressed (p. 4123) that the formation of the transition state is accompanied by considerable increase in polarity requiring further solvation.

The data given in Fig. 2 and Table 2 show that the rate of reaction of *p*-nitrobenzoyl chloride remains proportional to the concentration of alcohol in the associated state even though association proceeds beyond trimerisation. Before an explanation of this correlation is advanced, the properties and structure of the trimer will be briefly considered (see Davies, *Ann. Reports*, 1946, **43**, 17). The preferential trimerisation may be attributed to the hydrogen bonding of two ROH molecules to each central molecule to give a cyclic or micelle type of structure (I). This explains the low polarity of the aggregate in non-polar liquids (Harms, *Z. phys. Chem.*, 1939, **43**, *B*, 257), and the disappearance of the " free " OH frequency (Kempter and Mecke, *ibid.*, 1940, **46**, *B*, 229; Hoffmann, *loc. cit.*) which would be detected if the polymer were linear (II) as it probably is in more polar solvents (Harms, *loc. cit.*). Although further association increases the size of the aggregate, each molecule will still be bonded to two neighbours as shown by *X*-ray analysis (Pierce and MacMillan, *J. Amer. Chem. Soc.*, 1938, **60**, 779). Then if reaction involves only three of these molecules as in the case of reaction with a trimer, further association may have no effect on the kinetics, as shown by the following considerations.

(I)





(II)

Reaction may then be regarded as involving the activation of one of the alcohol molecules by disruption of the hydrogen bond, so that oxygen atom (1) interacts with the carbon atom. As the hydrogen bond is now broken the hydrogen atom (2) simultaneously solvates the chlorine atom while oxygen atom (5) assists in the removal of the proton as the O–H bond breaks. The tendency for the molecule carrying oxygen atom (1) to become energised will be proportional to the number of molecules in the aggregate. Thus the total rate $= \sum_{3}^{\infty} kn[(\mathrm{ROH}_n)]$.

The concentration of alcohol in the associated state is given by $\sum_{3}^{\infty} n[(\mathrm{ROH})_n]$, so that the total rate is proportional to the concentration of alcohol in the associated state, as experimentally observed. There is no doubt that alternative formulations of the reaction mechanism may explain the observations, but the one adopted here is probably the simplest. Reaction with a decomposing aggregate rather than with individual monomers is preferred as the entropy change is more reasonable, as already indicated.

It follows from the above interpretation that the reaction proceeds specifically with a group of three ROH molecules irrespective of the size of the aggregate, and that the influence of the remainder of the solvent is negligible. This may be partly fortuitous in the more concentrated solutions, but it should be realised that this close correlation is found for a chloride, the rate of which is controlled largely by bond formation. (*p*-Nitrobenzoyl chloride reacts strongly by an S_N2 type of mechanism.) Consequently, the life-time of the transition state is likely to be small compared with the time of relaxation of the alcohol molecules, as these are hydrogen-bonded to each other, thus reducing the probability of solvent molecules' orientating suitably. Moreover, the small general solvent effect may follow from the low polarity of the specifically solvated transition state as the charge separation in an S_N2 type of process may be relatively small (see Part I). This conclusion is supported by rate measurements in donor solvents which show that the rate of the third-order process * is only slightly affected by the polarity of the medium.

(B) *Reaction in Ether and Acetone.*—As seen from the results of Table 3 and Fig. 2, changes in alcohol concentration have an entirely different effect on rate when ether is used as solvent. Ether was chosen because of the low polarity compared with ethanol, and because the basicity enables strong hydrogen bonds to form with hydroxylic molecules (see Lassettre, *loc. cit.*), thus promoting the distribution of alcohol molecules in the medium. As the strength of an alcohol–ether bond is probably of the same order of magnitude as that of the hydrogen bond between two alcohol molecules, the latter may remain randomly distributed up to relatively high concentrations.

If this is the case, the observed kinetic order will be related directly to the number of molecules of a given kind (in this case ROH molecules) involved in the transition state. This is the case in polar solvents in which the hydroxylic molecules are separated by strong solvent–solute interaction. Thus the rate of the reaction between water and alkyl halides (Bateman and Hughes, *J.*, 1940, 942) and acyl halides (Crunden and Hudson, unpublished work) is proportional to the water concentration up to *ca.* 10% (v/v) in formic acid. Similarly the rate of solvolysis of Bu^tBr in nitromethane is proportional to the concentration of alcohol up to *at least* 10% (v/v) owing to electrophilic solvation (Gelles, Hughes, and Ingold, *J.*, 1954, 2918). These results suggest that changes in solvent structure (*e.g.*, as reflected in free volume, viscosity, etc.) produce relatively small effects on the rate, and may be regarded as secondary to the effect caused by concentration changes in the specifically solvating species.

The present results show that the rate of ethanolysis of acetyl chloride and *p*-nitrobenzoyl chloride in ether (and acetone) may be represented by the general expression

$$\text{Rate} = k_2[\text{R}'\cdot\text{COCl}][\text{R}\cdot\text{OH}] + k_3[\text{R}'\cdot\text{COCl}][\text{R}\cdot\text{OH}]^2 \quad . \quad . \quad . \quad \text{(iv)}$$

The first term is small in ether, so that the overall kinetics remain of third order over a wide range of concentration. This stoicheiometry supports the contention that the alcohol molecules remain more or less randomly distributed over a wide range of concentration.

The first term may be attributed to the rate of the bimolecular reaction with the transition state solvated by ether solvent. Owing to the shielding of the positive charges on the ether molecules, the electrophilic solvating power is small, so that $k_2 \ll k_3$. The second term represents the bimolecular rate with the transition state solvated by an alcohol molecule. A relation of this kind has been found to hold for other reactions in solvents where the specifically solvating molecules may be regarded as randomly distributed (Bartlett and Nebel, *J. Amer. Chem. Soc.*, 1940, **62**, 1345; Ashdown, *ibid.*, 1930, **52**, 268; Swain, *loc. cit.*).

Again, no decision can be made as to whether reaction proceeds with two ROH monomers coming together or with an activated aggregate of the kind R_2O–$(ROH)_2$. This difference is, however, trivial owing to the kinetic nature of liquid structure, and the rate may again be examined in terms of the concentration of these aggregates. In the more

---

* In donor solvents, *e.g.*, ether and acetone, solvation of the positive pole of the transition state can occur as readily as in alcohol, and hence the third alcohol molecule participating in non-polar media is not required. The overall kinetic order therefore decreases from 4 to 3. There is no evidence that removal or partial removal of the proton occurs in the transition state, and hence the third alcohol may not be necessary. If this is so it follows that reaction proceeds with trimers in carbon tetrachloride and not with three monomers, and that the third alcohol molecule is not involved in the rate-determining step. This point is being investigated.

dilute solutions, the probability of finding two ROH molecules together is given approximately by $(v_{\mathrm{ROH}})^2/V^2$, *i.e.*, $(46/800)N^2$, where N is the molar concentration of alcohol. This gives approximately the concentration of $R_2O,(ROH)_2$ aggregates. The rates of reaction in carbon tetrachloride and ether containing equal concentrations of aggregates of the kind $(ROH)_3$ and $R_2O,(ROH)_2$ respectively are compared in Table 6.

TABLE 6.

[ROH] in ether	[(ROH$_2$)] in ether	k_{20} in ether	[ROH] * in CCl_4	k_{20} in CCl_4	$\frac{1}{3}\frac{k_{CCl_4}}{k_{\mathrm{ether}}}$
Acetyl chloride					
0·345	0·0068	23·8	0·095	112·5	1·6
0·690	0·0270	123	0·187	405	1·1
1·00	0·575	369	0·300	825	0·8
1·725	0·170	949	0·670	2220	0·8
p-Nitrobenzoyl chloride					
0·345	0·0068	2·44	0·095	6·79	0·95
0·690	0·0270	10·0	0·187	24·2	0·8
Triphenylmethyl chloride					
0·828	0·0394	7·93	0·240	46	1·9
1·725	0·170	45·5	0·670	190	1·4

* Stoicheiometric concentration of alcohol in a solution in which the concentration of $(ROH)_3$ is equal to that of $R_2O,(ROH)_2$ in ether.

It is observed that in all cases where this comparison can be made, the rate of reaction with $(ROH)_3$ is of the order of three times as great as the rate with $R_2O,(ROH)_2$. A difference in reactivity of this order of magnitude may readily be attributed to the different number of alcohol molecules in the two aggregates. If it is assumed that simultaneous nucleophilic and electrophilic action are essential, the ratio of reactivities of the two aggregates is given simply by $2 \times 3 : 2 \times 1$, since the ether molecule can remove the proton as readily as the third alcohol molecule.

This close agreement supports the description of the reaction mechanism in carbon tetrachloride, and the conclusion that the effect of solvent on the specifically solvated transition state is negligible for these two reactions. The comparisons may be extended by comparing the rates of reaction of *p*-nitrobenzoyl chloride in acetone–alcohol and ether–alcohol mixtures. From the data given in Tables 3 and 4, it is readily seen that k_2 of equation (iv) is much greater in acetone than in ether, in agreement with the greater polarity of the medium. On the other hand, the value of k_3 in acetone is only approximately twice the value in ether, showing the small contribution of the solvent (other than the two alcohol molecules) to the solvation energy. This observation is in harmony with a previous observation that the rates of reaction of several acyl chlorides in 5% aqueous acetone and dioxan are almost equal in spite of the considerable difference in dielectric constant (Brown and Hudson, *J.*, 1953, 883). For this particular reaction, therefore, rates of reaction may be correlated over a wide range of solvents from non-polar to aqueous media.

It is considered that in such reactions the entropy decrease associated with the covalent interaction is sufficiently great to limit the specific solvation to one electrophilic group. It must be stressed, however, that the above simple treatment will only apply to suitable reactions, and that in general the stoicheiometry will not hold in concentrated solutions. For most bimolecular reactions, the stoicheiometry will break down in sufficiently polar solvents, *e.g.*, in highly aqueous solutions. Thus, although the present results suggest that the transition state structure of the alcoholysis of *p*-nitrobenzoyl chloride is unaffected by change in solvent over the range considered, a gradual change is observed in more aqueous solutions, accompanied by progressive increase in solvation (see Brown and Hudson, *J.*, 1953, 3352). This corresponds to a gradual change from the S_N2 type to the S_N1 type of mechanism which is considerably more advanced for other benzoyl chlorides (Brown and Hudson, *loc. cit.*; Gold *et al.*, *loc. cit.*; Crunden, M.Sc. Thesis, London, 1954).

QUEEN MARY COLLEGE, MILE END ROAD, LONDON, E.1.

[*Received, September 27th*, 1954.]