Nucleophilic Substitution at Trigonal Carbon. Part II.[1] Ethanolysis of Aliphatic Acyl Chlorides

By **Dennis N. Kevill,* Peter H. Daum,*** and **Rekha Sapre,** Department of Chemistry, Northern Illinois University, DeKalb, Illinois 60115, U.S.A.

A bipolar current method for the measurement of rapidly changing resistance has been used to study the rates of solvolysis of a series of aliphatic acyl chlorides in ethanol. Although polar and steric factors are of importance in determining the rate, the substituent effects cannot be satisfactorily correlated by the two-term Taft equation. The results are consistent with a bimolecular reaction, and are best explained by a synchronous displacement mechanism or a combination of this and an addition–elimination mechanism.

KINETIC studies on the solvolysis rates of acyl chlorides are numerous.[2,3] Because the rates are fast in pure hydroxylic solvents most of the studies on aliphatic compounds have been in mixed solvents containing low proportions of hydroxylic reagent. Very few studies have been reported of substituent effects within the alkyl group: Leimu has studied alcoholysis rates with dioxan as diluent;[4] Ugi and Beck have reported hydrolysis rates in aqueous acetone.[5] No linear free energy correlations[6,7] were attempted. In pure hydroxylic solvents studies of aliphatic acyl chlorides appear to have been limited to the ethanolyses of acetyl[8–10] and pivaloyl[11] chlorides. We have extended these studies to other acyl chlorides in the hope of correlating substituent effects.

EXPERIMENTAL

Ethanol was purified as described previously.[12] Commercial samples of the acyl chlorides were distilled at appropriate pressure immediately prior to use. The design of the instrument used to monitor the rapid changes in conductivity, the experimental techniques, and typical kinetic data for the ethanolysis of acetyl chloride have been described in detail.[10] The data obtained, in identical fashion, for six additional aliphatic acyl chlorides are presented in Table 1.

DISCUSSION

Using the data of Table 1, together with the previously obtained data for acetyl chloride,[10] interpolated specific ethanolysis rates ($k^{25.0}$) (extrapolated for chloroacetyl chloride) and enthalpies ($\Delta H^{\ddagger}$) and entropies ($\Delta S^{\ddagger}$) of activation were computed at 25.0°; the values are reported in Table 2. The agreement between the results for acetyl chloride and earlier determinations has been discussed previously.[10] The values for pivaloyl chloride are in good agreement with those previously obtained by different techniques.[11]

Acyl halides have been believed to react with ethanol by a bimolecular mechanism[2] and the relatively large negative entropies of activation observed in the present study (-18 to -28 cal mol^{-1} K^{-1}) are consistent with this viewpoint. Ethanolyses of ethyl chloroformate,[13] benzoyl chloride, and several monosubstituted benzoyl chlorides[14] have corresponding values in the range of -28 to -34 cal mol^{-1} K^{-1}. However, *p*-methoxybenzoyl chloride, which is believed to have a substantial unimolecular contribution,[14] has a higher value of -16 cal mol^{-1} K^{-1}. Rather more convincing evidence comes from the trend of reactivities as the substituent R of RCOCl is varied: $ClCH_2 \gg Me \sim Et > Pr^i \gg Bu^t$. This order can be rationalized in terms of bimolecular reaction and it is not compatible with a unimolecular ionization mechanism.

A survey of the specific rates reported within Table 2 shows that both polar and steric factors are of importance. In going from acetyl to chloroacetyl chloride, there is a 5.8-fold increase in rate, evidence that on introduction of the chlorine atom a facilitating, electron-withdrawing polar effect outweighs the steric hindrance effect. Consideration of the α-methylated series shows that relatively small rate decreases are observed as the first and second methyl groups are introduced and then a relatively large fall off in the rate accompanies introduction of the third, indicative of the importance of steric effects.

For an aliphatic series in which both polar and steric factors are believed to be of importance, the two-term Taft equation (1)[15,16] may be applicable. k Is the

$$\log (k/k_0) = \rho^*\sigma^* + \delta E_s, \qquad (1)$$

appropriate rate coefficient for reaction of a member of the series, k_0 is the corresponding rate coefficient for reaction of the standard substrate, ρ^* is the polar reaction constant, σ^* is the polar substituent constant, δ is the steric susceptibility constant, and E_s is the steric substituent constant. It should be emphasized that the tabulated substituent constants[17] would only be expected to be valid for a mechanism which resembles that for

---

[1] Part I, D. N. Kevill and F. D. Foss, *J. Amer. Chem. Soc.* 1969, **91**, 5054.

[2] For a recent review, see A. Kivinen in 'The Chemistry of Acyl Halides,' ed. S. Patai, Interscience, New York, 1972, pp. 179—210.

[3] For a recent review, see R. J. E. Talbot in 'Comprehensive Chemical Kinetics,' eds. C. H. Bamford and C. F. H. Tipper, Elsevier, Amsterdam, 1972, vol. 10, pp. 226—257.

[4] R. Leimu, *Ber.*, 1937, **70**, 1040.

[5] I. Ugi and F. Beck, *Chem. Ber.*, 1961, **94**, 1839.

[6] R. W. Taft, jun., in 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, London, 1956, ch. 13.

[7] R. W. Taft, jun., *J. Amer. Chem. Soc.*, 1953, **75**, 4538.

[8] E. Euranto and R. Leimu, *Acta Chem. Scand.*, 1966, **20**, 2028.

[9] D. E. Johnson and C. G. Enke, *Analyt. Chem.*, 1970, **42**, 329.

[10] P. H. Daum and D. F. Nelson, *Analyt. Chem.*, 1973, **45**, 463.

[11] A. Kivinen, *Suomen Kemi.*, 1965, **38B**, 209.

[12] H. Lund and J. Bjerrum, *Ber.*, 1931, **B64**, 210.

[13] A. Kivinen, *Acta Chem. Scand.*, 1965, **19**, 845.

[14] A. Kivinen, *Ann. Acad. Sci. Fenn. Ser. A2*, 1961, No. 108.

[15] W. A. Pavelich and R. W. Taft, jun., *J. Amer. Chem. Soc.*, 1957, **79**, 4935.

[16] For a recent review, see J. Shorter in 'Advances in Linear Free Energy Relationships,' eds. N. B. Chapman and J. Shorter, Plenum Press, London, 1972, ch. 2.

[17] For example, in J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions,' Wiley, New York, 1963, pp. 222 and 228.

the standard system, ester hydrolysis. Attempts are being made to develop a new set of polar and steric substituent constants for use in S_N2 reactions.[18]

TABLE 1

Specific rates of ethanolysis, in 100% ethanol, of aliphatic acyl chlorides (RCOCl) at various temperatures

R	T/°C	k/s^{-1} [a]	Number of runs
$ClCH_2$	−19.1	0.0630 ± 0.0042	7
	−9.8	0.1016 ± 0.0089	12
	0.2	0.207 ± 0.022	20
	10.2	0.419 ± 0.035	22
	21.7	0.799 ± 0.052	13
$PhOCH_2$	0.9	0.0342 ± 0.0026	14
	10.4	0.0684 ± 0.0050	8
	10.7	0.0743 ± 0.0028	11
	20.9	0.1381 ± 0.0053	12
	30.2	0.242 ± 0.014	9
Et	2.0	0.0224 ± 0.0014	3
	4.9	0.0291 ± 0.0009	3
	9.9	0.0443 ± 0.0013	3
	12.2	0.0537 ± 0.0007	3
	15.8	0.0696 ± 0.0006	3
	20.8	0.1047 ± 0.0023	4
	25.3	0.1546 ± 0.0001	2
	25.9	0.1588 ± 0.0012	2
	27.4	0.1773 ± 0.0064	3
	32.2	0.256 ± 0.013	5
	40.1	0.444 ± 0.013	3
	46.8	0.670 ± 0.010	3
Pr^i	−2.1	0.01267 ± 0.00046	12
	4.0	0.0213 ± 0.0002	7
	12.1	0.0425 ± 0.0044	9
	18.3	0.0612 ± 0.0020	9
	28.8	0.138 ± 0.010	8
$PhCH_2$	−2.2	0.01425 ± 0.00113	11
	2.9	0.0210 ± 0.0008	8
	11.9	0.0423 ± 0.0013	9
	16.3	0.0586 ± 0.0016	11
	22.2	0.0813 ± 0.0028	5
	32.2	0.1618 ± 0.0085	14
Bu^t	0.4	0.00278 ± 0.00027	7
	9.9	0.00571 ± 0.00024	2
	16.7	0.01020 ± 0.00069	4
	27.6	0.0233 ± 0.0005	5
	35.8	0.0411 ± 0.0004	5
	42.8	0.0676 ± 0.0012	4
	49.1	0.0993 ± 0.0014	3

[a] With associated standard deviation.

The formal similarity of the solvolyses of acid chlorides and esters suggests that equation (1) might be applicable to the present results. Support for this prediction comes from previous observations that both acid [19] and base [20] catalysed hydrolysis of amides can be correlated by the equation.

In actual fact, a consideration of the specific rates reported, within Table 2, for ethanolyses of seven aliphatic acyl chlorides leads to the conclusion that the data cannot be satisfactorily correlated by the two-term Taft equation. Introduction of a chlorine into acetyl chloride gives a situation where the polar and steric effects must be opposed and, by neglecting the steric term, we can calculate a *minimum* value for the polar reaction constant (ρ^*) of 0.73. On the other hand, we would predict that in going from acetyl to propionyl chloride both polar and steric factors will tend to decelerate the reaction and, if we neglect the steric term, a *maximum* value for ρ^* of 0.26 can be calculated. While the electron-withdrawing group has quite a powerful facilitating polar influence upon the reaction, the polar influence of electron supplying groups is considerably smaller.

TABLE 2

Specific rates of ethanolysis, in 100% ethanol, of aliphatic acyl chlorides (RCOCl) and enthalpies and entropies of activation, at 25.0°

R	$k^{25.0}$/s^{-1}	$\Delta H^‡$/ kcal mol^{-1} [a]	$\Delta S^‡$/ cal mol^{-1} K^{-1} [a]
$ClCH_2$	0.947	9.1 ± 0.2	−28.1 ± 0.6
$PhOCH_2$	0.179	10.4 ± 0.2	−27.0 ± 0.7
Me [b]	0.163	13.1 ± 0.2	−18.2 ± 0.7
Et	0.153	12.8 ± 0.2	−19.5 ± 0.7
$PhCH_2$	0.111	10.7 ± 0.3	−27.0 ± 0.9
Pr^i	0.103	11.9 ± 0.2	−23.3 ± 0.6
Bu^t [c]	0.0191	12.3 ± 0.2	−25.2 ± 0.6

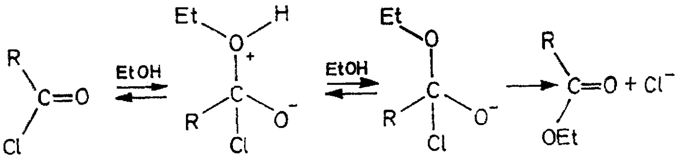
[a] With associated standard deviation. [b] Using data from ref. 10; from ref. 8, corresponding values of 0.147 s^{-1}, 12.6 kcal mol^{-1}, and −20.0 cal mol^{-1} K^{-1} are obtained. [c] From ref. 11, corresponding values of 0.0181 s^{-1}, 12.6 kcal mol^{-1}, and −24.4 cal mol^{-1} K^{-1} are obtained.

If a multiple regression analysis of log k on σ^* and E_s is carried out, expression (2) is obtained with a correlation coefficient of 0.933 and a standard deviation of 0.218.

$$\log k = -0.753 + 0.547\sigma^* + 0.527\,E_s \qquad (2)$$

While the value for the correlation coefficient could be regarded as reasonably significant, the standard deviation is unacceptably high for this kind of correlation. In particular, the expression compresses Δ log k of 0.72 between $ClCH_2COCl$ and $PhOCH_2COCl$ to a mere 0.15.

The failure of equation (1) satisfactorily to correlate the kinetic data for ethanolysis of our series of aliphatic acyl chlorides raises a serious question on the extent to which the addition–elimination (tetrahedral intermediate) mechanism, fairly well established for the solvolyses of esters (the standard system [15,16]) and amides [21] (which correlate [19,20]), applies to the solvolysis of acyl halides. One possibility, discussed by Cocivera,[22] is that the overall bimolecular reaction is a sum of contributions from addition–elimination (Scheme 1, or variation) and synchronous displacement (Scheme 2) mechanisms. Coci-



SCHEME 1

---

[18] K. Okamoto, I. Nitta, T. Imoto, and H. Shingu, *Bull. Chem. Soc. Japan*, 1967, **40**, 1905.

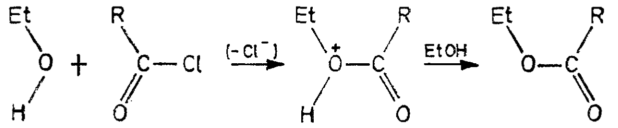
[19] P. D. Bolton and G. L. Jackson, *Austral. J. Chem.*, 1969, **22**, 527.

[20] A. Bruylants and F. Kedzy, *Rec. Chem. Progr.*, 1960, **21**, 213.

[21] Ref. 3, pp. 257—280.

[22] M. Cocivera, Ph.D. Thesis, University of California, Los Angeles, 1963.

vera concluded that, in ethanolic solvents, benzoyl chlorides solvolyse only by way of the addition–elimination mechanism. On the other hand, Haberfield and Trattner[23] have presented evidence that, in non-polar solvents, benzoyl chlorides react with alkoxide ions by a synchronous displacement mechanism.



Scheme 2

The present data can be rationalized quite well by a blending together of these two mechanisms. Especially if addition is rate determining, addition–elimination will be most important for the case of chloroacetyl chloride and polar factors will favour a fall off in rate as we decrease the σ^* value of the substituent. A direct substitution mechanism, involving bond-breaking as well as bond-making in the transition state, will be less dependent upon polar influences (which could be in either direction) and it will be primarily influenced by steric factors. These steric factors will be different in their relative magnitudes from those for a tetrahedral intermediate mechanism and also different to any which may be developed for synchronous displacement at a saturated carbon atom.[18] A change in the dominant mechanism at around acetyl chloride (σ^* 0.000) would be consistent with the observation that ρ^* changes over from >0.73 to <0.26 in this region. While one must be extremely cautious concerning the interpretation of activation parameter values, it is worthy of note that the enthalpy of activation passes through a maximum and the entropy of activation through a minimum within the region where a change in mechanism may occur.

A plausible alternative would be if a single direct synchronous displacement mechanism operated throughout the series but with variable transition state structure leading to corresponding variations in the importance of polar and steric factors and in the values for ρ^* and δ. Behaviour of this type has previously been claimed[24] as an explanation for non-linear Hammett ($\rho\sigma$) plots for certain bimolecular substitutions at a benzylic carbon atom. Yet another mechanism which might operate, especially with electron-supplying substituents, would be an S_N2C^+ type attack (3)[25] upon a preformed ion-pair.

$$\mathrm{RCOCl} \underset{\text{fast}}{\overset{\text{slow}}{\rightleftharpoons}} \mathrm{RCO^+,Cl^-} \xrightarrow[\text{EtOH}]{\text{fast}} \mathrm{RCO_2Et + HCl} \quad (3)$$

Steric hindrance factors would not be relevant until the attack upon the ion-pair. An acylium ion would be sp hybridized and linear and, contrary to the observations, steric hindrance effects should be considerably less for attack upon a species of this type than for attack at sp^2 hybridized carbon. This has previously been discussed for the analogous comparison of addition to alkynes and alkenes.[26] A S_N2C^+ type mechanism has, however, been proposed[27] for reactions of benzoyl chloride with water and *o*-nitroaniline in aqueous acetone.[28]

In principle, a change in mechanism can occur within the tetrahedral intermediate mechanism dependent upon whether addition or elimination is rate determining. This would, however, require very large influences upon the direction of elimination from the intermediate and it is difficult to see how these influences could arise from relatively minor variation within the substituent group.

It is concluded that the present kinetic data are best rationalized in terms of either a synchronous displacement mechanism, incorporating variable transition state structure, or as the sum of this type of mechanism with, especially for electron-withdrawing substituents, an addition–elimination mechanism. The data cannot be satisfactorily correlated by the modified Taft equation, which is based upon the sole operation of an addition–elimination mechanism.

[4/2274 *Received, 4th November,* 1974]

---

[23] P. Haberfield and R. B. Trattner, *Chem. Comm.*, 1971, 1481.

[24] C. G. Swain and W. P. Langsdorf, jun., *J. Amer. Chem. Soc.*, 1951, **73**, 2813.

[25] C. K. Ingold, ' Structure and Mechanism in Organic Chemistry,' Cornell University Press, Ithaca, New York, 1969, 2nd edn., p. 470.

[26] M. S. Newman in ' Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, London, 1956, p. 247.

[27] R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, 1969, **91**, 6031.

[28] V. Gold, J. Hilton, and E. G. Jefferson, *J. Chem. Soc.*, 1954, 2756.