Intermediates in the Reaction Path for the Unsymmetrically Acid-catalysed Hydrolysis of Carboxylic Esters with Electronegative Substituents

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The mechanism for the exceptional acid-catalysed $A\text{-}B_{AC}3$ hydrolysis is considered in detail on the basis of the estimated free energy levels of transition states and intermediates on the possible reaction paths for the hydrolyses of ethyl trichloroacetate and methyl acetate by the acid-catalysed $A_{AC}2$ and $A\text{-}B_{AC}3$ and the neutral $B_{AC}3$ mechanisms. It is concluded that the first step of the $B_{AC}3$ and $A\text{-}B_{AC}3$ reactions to the tetrahedral anionic intermediate T^- [$R^1C(OH)(O^-)(OR^2)$] is the same. T^- is assumed to be in equilibrium or in a steady-state condition with the neutral intermediate T^0 [$R^1C(OH)_2(OR^2)$]. It is proposed that, in the case of the $A\text{-}B_{AC}3$ mechanism, a concerted general base–general acid-catalysed decomposition of T^0 leads to the observed acid catalysis which thus follows the sequence of steps Ester $\longrightarrow T^- \longrightarrow T^0 \longrightarrow$ Products. Kinetic data for the acid hydrolyses of chloromethyl and 2,2-dichlorovinyl acetates together with other available data for exceptional, acid-catalysed hydrolyses were treated by a non-linear least-squares procedure.

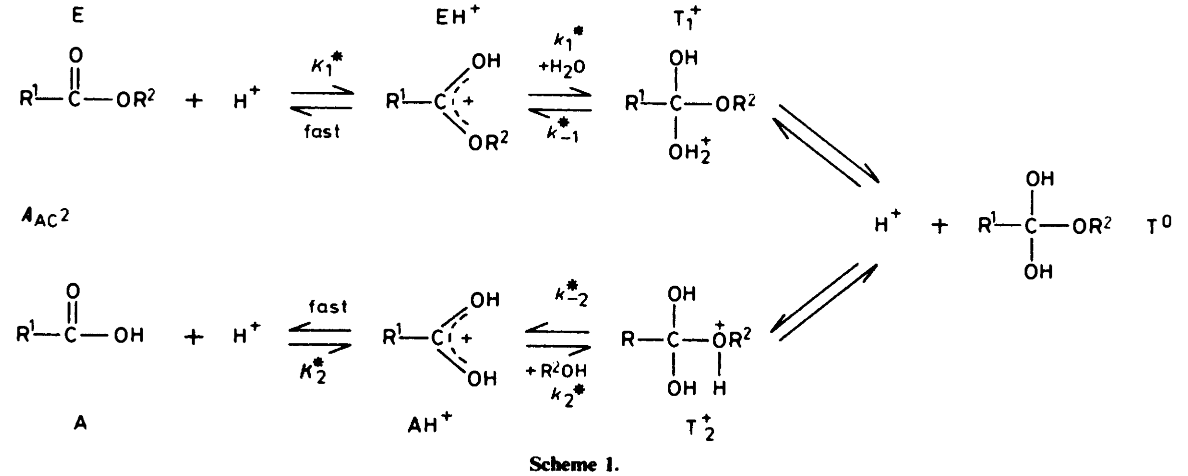
The hydrolysis of ordinary carboxylic esters is usually observable only in the presence of acidic or basic catalysts. However, significant neutral or water hydrolysis is of importance if the ester has electronegative substituents, especially in the acyl component.[1,2] Its mechanism ($B_{AC}3$) is believed to include the addition of water to the carbonyl group, catalysed by a second water molecule as a general base[1,2] in accord with the proton inventory which indicated that there are at least four exchangeable protons in the transition state[3] and with the observation that water falls on a plausible Brønsted slope.[1,2] The acid-catalysed hydrolysis of the same esters is often found to have a non-linear dependence on acid concentration.[1,2,4–10] Thus, *e.g.*, the rate of the hydrolysis of chloromethyl chloroacetate in water was found to go through a flat maximum at *ca.* 2M-perchloric acid followed by a minimum at *ca.* 4M-acid and a rapid increase at still higher acid concentrations.[4] It was concluded previously that this behaviour is a consequence of an unsymmetrically acid-catalysed partition of the intermediate formed in the neutral ester hydrolysis.[6,7] Therefore, the symbol $A\text{-}B_{AC}3$ was proposed by us[8–10] for this exceptional acid catalysis. The final rate increase is caused by a change in the mechanism.[5] Kurz and Farrar[7] proposed a detailed mechanism for the $A\text{-}B_{AC}3$ reaction in agreement with the proposal made by one of us.[6] However, the work of Guthrie *et al.*[11–14] led us to reconsider this mechanism in the light of the available data.

Kinetic Equations.—The following discussion is based on the accepted or proposed mechanisms for the neutral ($B_{AC}3$)[2] and the normal ($A_{AC}2$[2,15] and exceptional, acid-catalysed ($A\text{-}B_{AC}3$)[7–9] ester hydrolyses (Schemes 1 and 2). When the steady-state assumption is applied to the intermediates T^0 and T^- in the case of the $A\text{-}B_{AC}3$ mechanism (Scheme 2) and the inverse esterification is neglected the dependence of the rate coefficient k_ψ on $[H^+]$ can be expressed by equation (1), k_ψ being either the observed rate coefficient for the hydrolysis at constant ionic strength or $k_\psi = k_O + k_{HA} - k_{MA}$ where k_O, k_{HA}, and k_{MA} are the rate coefficients at zero electrolyte concentration and for a given acid (HA) and salt (MA, M = Li or Na) concentration, respectively.[5]

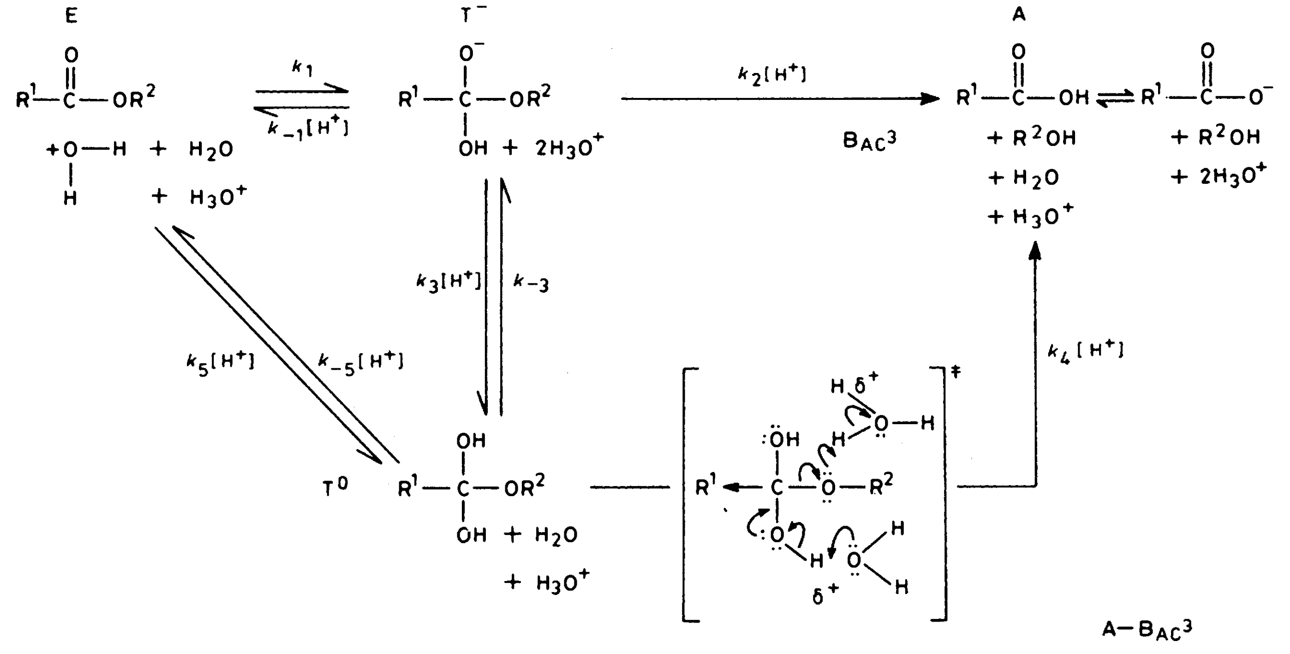
$$k_\psi = \frac{k_1k_{-3} + k_1(k_4 + k_{-5} + k_3k_4/k_2 + k_{-3}k_5/k_1)[H^+] + k_4k_5(1 + \alpha + k_3/k_2)[H^+]^2}{(1 + \alpha)k_{-3} + (k_4 + k_{-5})(1 + \alpha + k_3/k_2)[H^+]} \tag{1}$$

$$\text{Å}\,(k_a + k_c[H^+] + k_e[H^+]^2)/(1 + k_b[H^+]) \tag{1*}$$

As discussed below it can be assumed that the k_5,k_{-5} path



Scheme 1.



Scheme 2.

does not markedly contribute to the kinetics in the cases to be considered. By putting $k_5 = k_{-5} = 0$ one gets equation (2), also employed by Kurz and Farrar,[7] with expressions (3)—(6) for the rate parameters.

$$k_\psi = (k_a + k_c[H^+])/(1 + k_b(H^+]) \qquad (2)$$

$$k_a = k_1/(1 + \alpha) \qquad (3)$$

$$k_b = k_4[1 + k_3/(1 + \alpha)k_2]/k_{-3} \qquad (4)$$

$$k_c = k_1k_4(1 + k_3/k_2)/[(1 + \alpha)k_{-3}] \qquad (5)$$

$$\alpha = k_{-1}/k_2 \qquad (6)$$

If it is further assumed that there is an equilibrium (7) between T^0 and T^-, when the critical requirement is $k_3 \gg (1 + \alpha)k_2$, equations (4) and (5) will be simplified to equations (4*) and (5*), the acid-dissociation constant of the intermediate T^0 being K_{-3}. The rate constant k_1 and the partition coefficient α can then be calculated by equations (8) and (9).[7]

$$K_{-3} = [T^-][H^+]/[T^0] \qquad (7)$$

$$k_b = k_4/[(1 + \alpha)k_2K_{-3}] \qquad (4^*)$$

$$k_c = k_1k_4/[(1 + \alpha)k_2K_{-3}] \qquad (5^*)$$

$$k_1 = k_c/k_b \qquad (8)$$

$$\alpha = (k_c/k_ak_b) - 1 \qquad (9)$$

In dilute acid solutions the rate for the $A_{AC}2$ mechanism (Scheme 1) is known to follow equation (10).[2] Therefore, the term $k_d[H^+]$ ought to be added to equation (2) when the acid

$$-d[E]/dt = k_1^{\ddagger}K_1^{\ddagger}[H^+][H_2O][E]/(1 + \alpha^*) = k_d[H^+][H_2O][E] \qquad (10)$$

hydrolysis takes place simultaneously by the $A\text{-}B_{AC}3$ and $A_{AC}2$ mechanisms[5,7,9,10] thus leading to an equation formally similar to equation (1*).

Table 1. Kinetic data for the hydrolysis of chloromethyl chloroacetate in water solutions containing electrolytes at a constant ionic strength, μ, at 25 °C

μ/M	[NaClO$_4$]/M	[HClO$_4$]/M	$\bar{c}_t$/M	$10^5 k_t$/s^{-1}
1.0	1.00[a]	0.00	0.0202	5.66
	1.00	0.00	0.0227	5.81
	0.95	0.05	0.0665	6.27
	0.95	0.05	0.0689	6.24
	0.90	0.10	0.1171	6.81
	0.80	0.20	0.2182	7.83
	0.50	0.50	0.5172	10.59
	0.00[a]	1.00	1.017	14.72
	0.00[a]	1.02	1.038	14.59
4.0	3.98[a]	0.00	0.0185	0.839
	3.90	0.10	0.1168	1.33
	3.80	0.20	0.2191	1.95
	3.50	0.50	0.5162	3.47
	3.00	1.00	1.017	5.68
	2.00	2.00	2.012	9.44
	2.00	2.00	2.013	9.21
	1.00	3.00	3.008	12.20
	0.00[a]	3.98	4.001	14.51
	0.00[a]	3.98	4.001	14.57

[a] Ref. 5.

Results

As mentioned above, the general equation (1) includes a term second order in $[H^+]$ in the numerator. However, Kurz and Farrar[7] found that such a term did not improve the fit; k_d obtained was even negative and it was concluded that its value must be much less than 10^{-4} l mol^{-1} s^{-1} for the hydrolysis of ethyl trichloroacetate. Also our data for methyl and ethyl trichloroacetates,[9] methyl dichloroacetate,[9] chloromethyl chloroacetate (Table 1), and 2,2-dichlorovinyl chloroacetate (Table 2),

Table 2. Kinetic data for the hydrolysis of 2,2-dichlorovinyl chloroacetate in water solutions containing electrolytes at the constant ionic strength, μ, of 1.0 at 25 °C

[NaCl]/M	[HCl]/M	$10^3k/\mathrm{s}^{-1}$
1.00	0.00	1.340 ± 0.006
		1.356 ± 0.004
		1.357 ± 0.007
0.80	0.20	1.427 ± 0.006
		1.458 ± 0.003
0.60	0.40	1.503 ± 0.004
		1.539 ± 0.008
0.40	0.60	1.593 ± 0.007
		1.610 ± 0.005
0.20	0.80	1.659 ± 0.006
		1.687 ± 0.007
		1.694 ± 0.006
0.00	1.00	1.689 ± 0.005
		1.724 ± 0.005

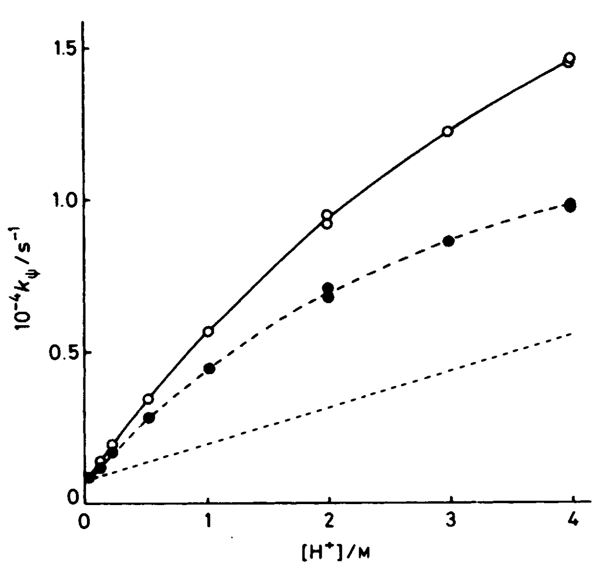


Figure 1. Plots of the rate coefficients k_ψ for the hydrolysis of chloromethyl chloroacetate *versus* $[\mathrm{H}^+]$ in aqueous solutions for the ionic strength 4M at 25 °C for experimental points (○) and for experimental points corrected for the estimated A_{AC^2} reaction (see text) (●). The curves are the best fits calculated for the experimental points by equation (1*) (full line) or for the corrected points by equation (2) (broken line). The estimate for the A_{AC^2} reaction is presented by the dashed line

up to 1M-acid, did not in most cases give significantly better fit when equation (1*) was employed instead of equation (2). Even when k_e was formally found to be statistically significant its value was almost as often negative as positive evidently because of the limited number of data points, small range of $[\mathrm{H}^+]$, and the relatively low experimental accuracy achievable under the reaction conditions. On the other hand, at an ionic strength of 4M, the data for the hydrolysis of chloromethyl chloroacetate (Table 1 and Figure 1) gave for k_d the value $(0.056 \pm 0.009) \times 10^{-4}$ l mol^{-1} s^{-1} which is comparable with the value 0.12×10^{-4} l mol^{-1} s^{-1} estimated for its A_{AC^2} reaction.[5] After correction for the above estimate, the experimental data gave the value $(-0.07 \pm 0.01) \times 10^{-4}$ l mol^{-1} s^{-1} for k_e. Specific salt effects evidently are substantial at high electrolyte concentrations. It is noteworthy that equation (1) assumes, at high acid concentrations, a linear dependence of k_ψ on $[\mathrm{H}^+]$ with slope $k_4k_5/(k_4 + k_{-5})$ whereas equation (2) gives a constant value for k_ψ (*cf.* Figure 1). In summary, it can be concluded that there is no experimental indication of a k_d or k_e term higher than expected to be caused by an A_{AC^2} reaction.

In the following discussion all the available experimental data on the exceptional, acid-catalysed hydrolysis of electronegatively substituted esters were taken into account.[4–9] The calculated values of the parameters k_a, k_b, and k_c of equation (2) together with the derived parameters k_1 and α are shown in Table 3. From equation (2) it is seen that k_a is the rate coefficient k_0 of the neutral hydrolysis under the experimental conditions in question; in the case of variable ionic strength k_a is its value at zero electrolyte concentration.

Free Energy Diagrams.—The free energy–reaction co-ordinate diagrams for the A_{AC^2}, A-B_{AC^3}, and B_{AC^3} hydrolyses of ethyl trichloroacetate and methyl acetate in aqueous solution at 25 °C on the standard state of a 1M-acid solution with an infinitely dilute reference state are presented in Figures 2 and 3. The rate coefficient for the A_{AC^2} hydrolysis of ethyl trichloroacetate was estimated by the Ingold–Taft equation[16] by using the value[17] 2 570 l mol^{-1} s^{-1} for its alkaline hydrolysis in water at 25 °C together with the data for ethyl acetate.[2] For σ* we used the value[18] 2.61, obtained by the aid of the acid-dissociation constants of carboxylic acids, instead of the value[16] 2.65 generally employed. The free energies for the transition states of the rate-limiting k_1, k_2, $k_1^{\ddagger}$, and $k_2^{\ddagger}$ steps in Figures 2 and 3 were obtained by using the observed[11,19] or the above-mentioned calculated rate coefficients together with the partition coefficients.[7,20,21] Unfortunately, the values of the partition coefficients, directly measured by the $^{18}\mathrm{O}$-exchange method, are scarce and their accuracy is insufficient for conclusions to be made about their dependence upon the reaction mechanism, the structure of the substrate, and reaction conditions. The values used in this work are 0.4 and 3 for the A_{AC^2} and B_{AC^3} hydrolyses, respectively, in accord with the data of Bender *et al.*[20] and Kurz *et al.*[7,21] for ethyl benzoate and ethyl trichloroacetate, respectively.

The free energy levels of the intermediates EH^+, $\mathrm{T_1}^+$, and T^0 (Schemes 1 and 2) were calculated by using the acid-dissociation and equilibrium constants as proposed by Guthrie and Cullimore[11] and by assuming that the substitution of EtO by MeO in the case of ethyl trichloroacetate has only a negligible effect on the values of these constants. Owing to the approximately three times higher basicity of the HO than the RO group[22] and to the statistical probability factor 2 the term $RT\ln 6$ was added to the free energy of the intermediate $\mathrm{T_1}^+$ to get that of $\mathrm{T_2}^+$. The free energies of the anionic intermediates T^- are based on the $\mathrm{p}K_a$ values of the neutral tetrahedral intermediate T^0.[12,21] Those for the protonated acids AH^+ were obtained by using the $\mathrm{p}K_{\mathrm{AH}^+}$ values of $\mathrm{RC(OH)_2}^+$ calculated from equation (11) as proposed by Guthrie.[13]

$$\mathrm{p}K_{\mathrm{AH}^+} = -7.08 - 2.39\,\sigma^* \qquad (11)$$

It has been further assumed that for every proton transfer the free energy change is[21] 6 kJ mol^{-1} although it is possible that, *e.g.*, $\mathrm{T_1}^+$ in Scheme 1 is not actually at an energy minimum at all.[23]

Discussion

According to the generally accepted A_{AC^2} mechanism (Scheme 1)[2,15] for the acid-catalysed hydrolysis of ordinary esters such as methyl acetate the free energy difference between the initial state E and the transition state of the $k_1^{\ddagger}$ step limits the rate of reaction. This free energy difference increases with increasing number of chlorine atoms in the ester, being 95, 100, 100, and

Table 3. Rate parameters k_a, k_b, and k_c and derived parameters k_1 and α with their standard deviations for the acid-catalysed hydrolysis of esters in water at 25 °C at an ionic strength μ

Ester	Solvent	μ/M	c_{H+}/M	Data points	10^4k_a/ s^{-1}	k_b/ l mol^{-1}	10^4k_c/ l mol^{-1} s^{-1}	10^4k_1/ s^{-1}	α
$CH_2ClCO_2CH_2Cl$[a]	H_2O	variable	0—1.0	5	1.082 ± 0.009	0.53 ± 0.07	1.95 ± 0.01	3.7 ± 0.2	2.4 ± 0.2
			0—4.0	9	1.054 ± 0.035	1.05 ± 0.12	2.99 ± 0.29	2.8 ± 0.4	1.7 ± 0.4
	D_2O	variable	0—1.0	4	0.316 ± 0.016	0.64 ± 0.19	1.20 ± 0.18	1.9 ± 0.6	5.0 ± 2.0
			0—4.0	6	0.326 ± 0.013	0.46 ± 0.04	1.03 ± 0.06	2.2 ± 0.2	5.8 ± 0.7
$CH_2ClCO_2CH_2Cl$[b]	H_2O	0.2	0—0.2	6	0.928 ± 0.007	0.57 ± 0.43	1.99 ± 0.55	3.5 ± 1.7	2.8 ± 1.8
		0.5	0—0.5	6	0.772 ± 0.004	0.20 ± 0.07	1.36 ± 0.10	6.6 ± 1.8	7.6 ± 2.9
$CH_2ClCO_2CH_2Cl$	H_2O	1.0	0—1.0	9	0.551 ± 0.006	0.25 ± 0.05	1.25 ± 0.07	5.1 ± 0.7	8.2 ± 1.3
		4.0	0—4.0	10	0.073 ± 0.004	0.16 ± 0.01	0.58 ± 0.01	3.6 ± 0.2	48 ± 4
$CHCl_2CO_2Me$[b]	H_2O	0.2	0—0.2	5	0.170 ± 0.005	0.61 ± 0.37	1.51 ± 0.17	2.5 ± 1.2	14 ± 7
CCl_3CO_2Me[b]	H_2O	0.5	0—0.5	7	7.57 ± 0.11	1.0 ± 0.5	16 ± 5	16 ± 3	1.1 ± 0.4
CCl_3CO_2Et[c]	H_2O	0			2.404			10.1 ± 2	3.18 ± 0.06
CCl_3CO_2Et[b]	H_2O	0.5	0—0.5	7	2.49 ± 0.05	0.58 ± 0.37	4.6 ± 1.4	8.0 ± 2.7	2.2 ± 1.1
CCl_3CO_2Et[c]	H_2O	1.0	0—1.0	6	1.24 ± 0.04	0.87 ± 0.07	4.4 ± 0.4	5.03 ± 0.11	3.06 ± 0.20
$CH_2ClCO_2CH{=}CCl_2$	H_2O	1.0	0—1.0	15	13.5 ± 0.2	0.41 ± 0.30	11 ± 5	27 ± 7	1.0 ± 0.5

[a] Experimental data from ref. 5 [b] Experimental data from ref. 9. [c] Ref. 7, 21, and 32.

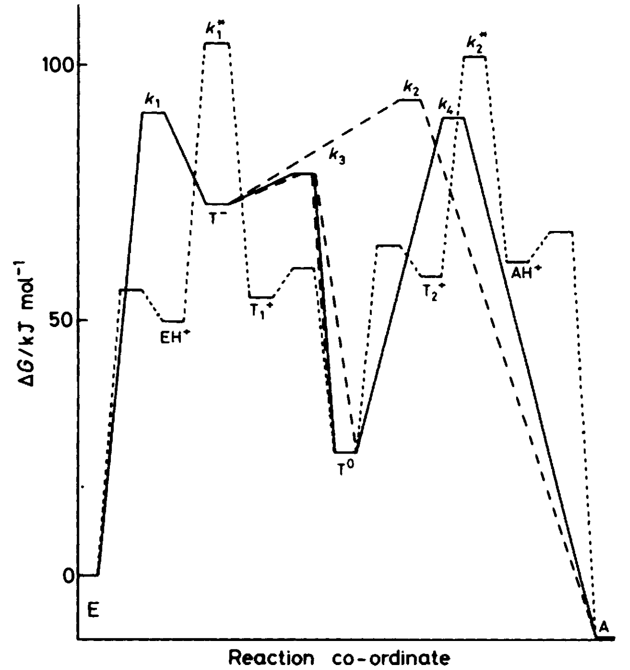


Figure 2. Free energy-reaction co-ordinate diagram for the $A_{AC}2$ (dashed lines), A-$B_{AC}2$ (full lines), and $B_{AC}3$ (broken lines) hydrolyses of ethyl trichloroacetate in water at 25 °C

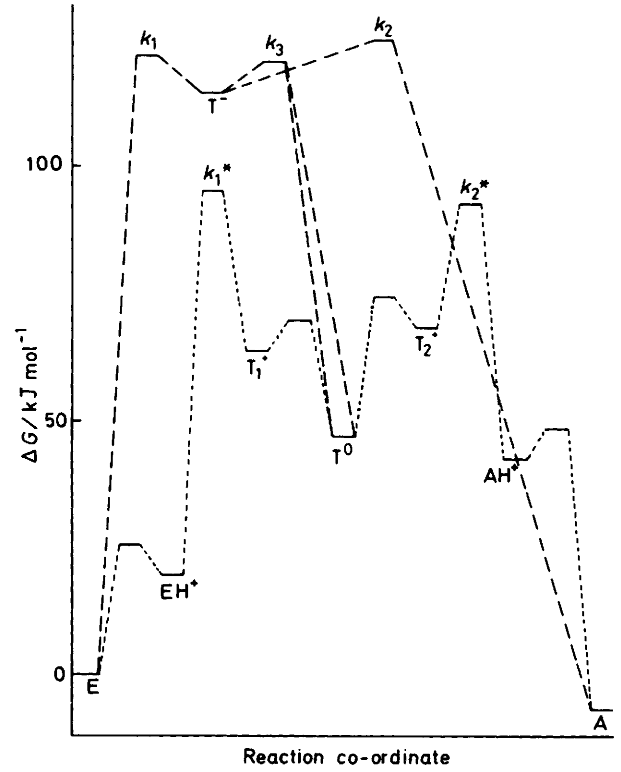


Figure 3. Free energy-reaction co-ordinate diagram for the $A_{AC}2$ (dashed lines) and $B_{AC}3$ (broken lines) hydrolyses of methyl acetate in water at 25 °C

107 kJ mol⁻¹ in water at 25 °C for the hydrolyses of methyl acetate (Figure 3), methyl dichloroacetate,[15,16] chloromethyl chloroacetate,[5,15] and ethyl trichloroacetate (Figure 2), respectively. This is in accord with the negative inductive effect of chlorine on the protonation step ($E \longrightarrow EH^+$), which, on the other hand, should facilitate the addition of water to the protonated ester EH^+ in spite of steric effects. The first mentioned effect is seen to be more important. The values of $\Delta G^\ddagger$ for $EH^+ \longrightarrow T_1{}^+$ are estimated to be 75, 57, and 56 kJ mol⁻¹ for methyl acetate, methyl dichloroacetate, and ethyl trichloroacetate, respectively.

The neutral hydrolysis of esters with electronegative substituents is generally known to take place by the $B_{AC}3$ mechanism (Scheme 2)[1,2] although in the case of 1-halogenoalkyl esters the S_N-type solvolysis of the α-halogen is also possible.[2] The free energy level for the transition state of the rate-limiting k_1 step decreases from the value 121 through 97 and 92 to 90 kJ mol⁻¹ when the ester is changed from methyl acetate (Figure 3) through methyl dichloroacetate[7,21,24] and chloromethyl chloroacetate[5,7,21] to ethyl trichloroacetate (Figure 2). This lowering of the free energy values is reasonable because the electronegative chloro-substituents facilitate the rate-limiting nucleophilic addition of water to the carbonyl group of the ester.

In acid solutions the water-catalysed neutral ester hydrolysis is often accompanied by an acid-catalysed A_{AC^2} or A-B_{AC^3} reaction or both. It has been proposed that the B_{AC^3} and A-B_{AC^3} mechanisms go through the same tetrahedral intermediate T^-.[2,6,7] In accord with this fact, Kurz and Farrar[7] proposed a mechanism for the A-B_{AC^3} hydrolysis of ethyl trichloroacetate in water which follows the sequence of steps $E \longrightarrow T^- \longrightarrow T^0 \longrightarrow T_2^+ \longrightarrow AH^+ \longrightarrow A$. The same sequence of steps should, of course, also hold for other polyhalogeno-substituted alkyl esters. Thus, the first step of the reaction to the intermediate T^- was thought to be common with the B_{AC^3} mechanism (Scheme 2). The next steps were proposed to lead to the cationic intermediate T_2^+, assumed to be the same as in the A_{AC^2} mechanism. The difference between the A_{AC^3} and A-B_{AC^3} mechanisms were then the timing of the protonation and addition steps[7] and the proposal that the A_{AC^2} mechanism leads directly from EH^+ to T_2^+ without the formation of T^0. Although subject to continuing investigation, the acid-catalysed A_{AC^2} hydrolysis is generally thought to proceed through the neutral intermediate T^0 (Scheme 1).[15,23] Thus, for the proposed[7] A-B_{AC^3} mechanism the steps from T^0 to the product A were common with the A_{AC^2} mechanism. As seen from the reaction co-ordinate diagram in Figure 2 the free energy level (ΔG 105 kJ mol^{-1}), now estimated for the transition state of the k_2^* step for the A_{AC^2} hydrolysis of ethyl trichloroacetate, is distinctly higher than the value found experimentally for the acid-catalysed reaction. Therefore, the reaction path from the intermediate T^0 to products cannot follow the A_{AC^2} way at least in 1M or more dilute acid solutions. Also, a mechanism where the alkoxy group of the first-formed intermediate T^- is protonated, leading through a zwitterion intermediate $T^\pm$ to products, is excluded because the sequence of steps $E \longrightarrow T^- \longrightarrow T^\pm \longrightarrow A$ does not lead to acid catalysis but represents a water-catalysed neutral reaction.[13,14,25]

Our proposal for the B_{AC^3} and A-B_{AC^3} mechanisms is given in Scheme 2. Thus, the neutral ester hydrolysis follows the accepted sequence of steps $E \longrightarrow T^- \longrightarrow A$, the k_1 step proceeding by general-base catalysis by H_2O and the k_{-1} and k_2 steps by the catalysis of H_3O^+ as a general acid.[1,2,7] However, there must be a rapid equilibrium between T^- and T^0 or a steady-state condition of T^0 because of the observed ^{18}O exchange[26] demanding that the majority of molecules go through the neutral intermediate T^0 which has two equivalent oxygen atoms. Direct evidence for the existence of T^0 or kinetic data for its decomposition do not exist, mainly because of its low steady-state concentration, but it is known that general acids and general bases catalyse the decomposition of hemi-orthoester tetrahedral intermediates, $R^1C(OR^2)(OR^3)(OH)$, which closely resemble the assumed intermediate T^0.[27] We therefore propose that, in the case of the A-B_{AC^3} mechanism, a concerted general base–general acid-catalysed decomposition of the tetrahedral intermediate T^0 leads to the observed acid catalysis which thus follows the sequence $E \longrightarrow T^- \longrightarrow T^0 \longrightarrow A$.

If acids and bases catalyse the decomposition of T^0 to the products they should also be expected to catalyse its decomposition to the starting materials, *i.e.*, there should exist the k_5 path $T^0 \longrightarrow E$. In fact, for a symmetric case, *e.g.* the ethanolysis of ethyl trichloroacetate, there should exist an acid-catalysed reaction with $k_4 = k_{-5}$ (Scheme 2). However, as shown above, in the case of hydrolysis there is no experimental evidence for the k_5, k_{-5} reaction which would lead to the kinetic form (1) with a second-order term in the numerator. Thus, the $E \longrightarrow T^- \longrightarrow T^0$ path must be more advantageous than the formation of T^0 *via* the k_5 path and the unsymmetric catalysis observed in the A-B_{AC^3} hydrolysis is in the first place a consequence of the existence of an easy formation of T^0 by the B_{AC^3} mechanism rather than a highly unsymmetric decomposition of T^0. The above conclusions are strongly supported by the fact that Kurz and Wexler[21] obtained the same value for $\alpha = k_{-1}/k_2$ by oxygen-18 exchange accompanying the water-catalysed hydrolysis and from the dependence of k_w on $[H^+]$ [*cf.* equation (9)]. Also the data[3] for the hydrolysis of chloromethyl chloroacetate in solutions of perchloric acid in H_2O–D_2O mixtures seem to be in accord with the proposed mechanism.

It can be seen from Table 3 that the calculated values of α are > 1, *i.e.* the breakdown of the intermediate T^- back to the ester takes place faster than the forward reaction to the products ($k_{-1} > k_2$). However, the low significance of the α values calculated by the indirect way from the approximate equation (9) should be borne in mind. The values of α obtained for ethyl trichloroacetate and chloromethyl chloroacetate are surprisingly similar in spite of the great differences in acidity and other properties of the corresponding leaving groups, OEt and CH_2Cl, compared with the leaving group, OH, of the backward reaction. This seems to indicate that the unsymmetric catalysis cannot in the first place be due to the properties of the leaving group.

In 1M-acid solution the free energy difference 20 kJ mol^{-1} (Figure 2) between the k_2 transition state and T^- corresponds to the k_2 value 2×10^9 l mol^{-1} s^{-1} for the hydrolysis of ethyl trichloroacetate at 25 °C. By using this k_2 value and the pK_{-3} value[21] 8.5 for the ionization of $CCl_3C(OH)_2(OEt)$ it can be roughly estimated from equation (4*) that in 1M-acid solution at 25 °C the value of k_4 is *ca.* 21 l mol^{-1} s^{-1}, corresponding to the free energy barrier of 90 kJ mol^{-1} (Figure 2) for the A-B_{AC^3} hydrolysis of ethyl trichloroacetate. This k_4 value may be compared with the rate constants 5×10^3 and 6×10^5 l mol^{-1} s^{-1} for the decomposition of methyl hemiorthoformate [$HC(OH)_2(OMe)$] and acetate [$CH_3C(OH)_2(OMe)$], respectively, as estimated by Guthrie.[28]

According to the above consideration, the acid-catalysed hydrolysis of ethyl trichloroacetate by the A_{AC^2} mechanism is unfavourable with respect to that by the B_{AC^3} and A-B_{AC^3} mechanisms in 1M and more dilute acid solutions. Thus, the free energy difference between the transition states of the k_1^* and k_1 steps for the A_{AC^2} and A-B_{AC^3} hydrolyses is 16 kJ mol^{-1} at 25 °C in 1M-acid solution (Figure 2). The hydrolysis by the A_{AC^2} mechanism may, however, become important when sufficiently concentrated acid solutions are used because the rate of the A_{AC^2} reaction increases even more rapidly than the acid concentration whereas k_1 for the A-B_{AC^3} hydrolysis decreases with increasing ionic strength (Table 3). This is in accord with the positive salt effects[2] found for the A_{AC^2} hydrolysis and with the negative electrolyte effects[29] for the B_{AC^3} and therefore also for the A-B_{AC^3} hydrolyses.

It has been estimated that the rate coefficient for the A_{AC^2} hydrolysis of chloromethyl chloroacetate[5] is 1.2×10^{-5} l mol^{-1} s^{-1}, while the value 1.3×10^{-5} l mol^{-1} s^{-1} was obtained for methyl dichloroacetate by the aid of the Ingold–Taft equation.[16] These rate coefficients are *ca.* 10% of the observed values 12.7×10^{-5} and 12.2×10^{-5} l mol^{-1} s^{-1}, respectively.[5,9] The estimated free energy differences between the transition states of the k_1^* and k_1 steps for these two esters are 8 and 3 kJ mol^{-1}, respectively, in favour of the A-B_{AC^3} hydrolysis, in 1M-perchloric acid solution at 25 °C. These estimates confirm the earlier proposal that in dilute acid solutions the acid-catalysed hydrolyses of these two esters proceed simultaneously by the A_{AC^2} and A-B_{AC^3} mechanisms.[5,9,10]

Conclusions.—On the basis of previous studies[2,6,7] it was concluded that the exceptional, acid-catalysed hydrolysis of carboxylic esters with electronegative substituents is a consequence of an unsymmetrically acid-catalysed partition of the tetrahedral intermediate formed also in their neutral hydrolysis. It is now shown that in slightly acidic solutions the decomposition of this intermediate cannot follow the same sequence of steps as does the normal A_{AC^2} pathway (Scheme 1), but is a concerted reaction catalysed by the oxonium ion and water as a general acid and a general base, respectively (Scheme 2). For the acid-catalysed hydrolyses of alkyl trihalogenoacetates this mechanism (A-B_{AC^3}) prevails (Figure 2), whereas, *e.g.*, for the hydrolyses of methyl dichloroacetate and chloromethyl chloroacetate the A_{AC^2} and A-B_{AC^3} mechanisms are energetically almost equally favourable. It remains unsolved whether the hypothetical general acid–general base-catalysed k_5,k_{-5} reaction path (Scheme 2) from the ester to the neutral intermediate T^0 and its reverse really exist and what is its relation to the k_4 path. The acid-catalysed hydrolysis of ordinary esters like methyl acetate by the A-B_{AC^3} mechanism is energetically unfavourable compared with the hydrolysis by the normal A_{AC^2} mechanism (Figure 3).

Experimental

Materials and Kinetic Measurements.—Chloromethyl chloroacetate,[29] 2,2-dichlorovinyl chloroacetate,[30] and the reaction solutions [9,29] were prepared as described previously. The hydrolysis of chloromethyl chloroacetate was followed by an argentometric method [5,29] by adding the ester (*ca.* 0.7 ml) into the reaction mixture (150 ml). The time-dependent first-order rate coefficients k_t and the time-averages c_t of the oxonium ion concentration were calculated as described previously.[9] The standard deviations of the means $\bar{k}_t$ were of the order of 0.2%. The hydrolysis of 2,2-dichlorovinyl chloroacetate was followed spectrophotometrically at 225 nm by a Perkin-Elmer–Coleman model 46 spectrophotometer equipped with a thermostatted cuvette. The initial ester concentration was 2×10^{-4}M. The first-order rate coefficients k were calculated by Guggenheim's method.

Calculations.—The kinetic data were fitted to equations (1*) and (2) by a non-linear least-squares procedure using the Minuit program.[31] The calculation of the rate constant k_1 [equation (8)] and the partition coefficient α [equation (9)] with their standard errors, obtained from the variances and covariances of k_a, k_b, and k_c, were included in the computer program. The Minuit calculations often failed, especially in the case of equation (1*), evidently because the minima were not sufficiently well defined as indicated by the high correlation between k_b, k_c, and k_e and shown by synthetic rate data. To check the calculations and to get proper starting values for the Minuit minimization the equations (1*) and (2) were linearized to the form (12) and the data were fitted to it by the method of least-squares with k_β as an adjustable parameter.

$$k_\psi(k_\beta + [H^+]) = k_\alpha + k_\gamma[H^+] + k_\varepsilon[H^+]^2 \quad (12)$$

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