

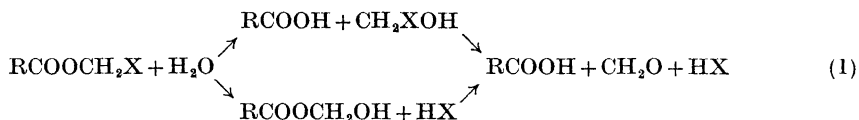
Concurrent Neutral Ester Hydrolysis and Bromine Displacement in the Hydrolysis of Bromomethyl Chloroacetate

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The rates of hydrolysis of bromomethyl chloroacetate in water at 0 to 75°C and in a 40 wt. % acetone-water mixture at -15 to 75°C have been measured. The uncatalysed hydrolysis was found to proceed concurrently by two mechanisms, the general base-catalysed mechanism ($B_{AC}3$) and the displacement of bromine (S_N). The contribution of the former reaction to the over-all rate is about 75 % in water at 25°C and about 45 % in the acetone-water mixture at 25°C. The rate coefficients of both concurrent reactions at different temperatures and the thermodynamic functions of activation were evaluated by a nonlinear iteration method.

Euranto¹ previously found that the uncatalysed hydrolysis of an α -haloalkyl ester may proceed by a general base-catalysed mechanism ($B_{AC}3$) or by a nucleophilic displacement of the α -halogen atom of the alkyl component ($S_N1,2$).*



The activation energy of the former reaction is about 10 kcal (1 cal = 4.184 J) per mol higher than that of the latter. The activation energies of both these reactions have a negative temperature coefficient of the order of 50 cal $K^{-1} \text{ mol}^{-1}$.^{2,3} However, the activation energy for the uncatalysed hydrolysis of chloromethyl chloroacetate² does not decrease above 65°C and hence it is possible that this reaction proceeds by both mechanisms concurrently so that the S_N mechanism begins to compete with the $B_{AC}3$ mechanism with rising temperature.

A change in mechanism is likely because the rate coefficient¹ ($0.153 \times 10^{-4} \text{ s}^{-1}$) of the uncatalysed hydrolysis of chloromethyl acetate taking place by the S_N mechanism in water at 25°C is only slightly lower than the rate coefficient² ($1.08 \times 10^{-4} \text{ s}^{-1}$) of the uncatalysed hydrolysis of chloromethyl chloroacetate

* This mechanism can be either a limiting unimolecular solvolysis (S_N1) or a borderline mechanism ($S_N1,2$); the notation S_N is therefore used in the following.

and because a distant chlorine substituent in the acyl group can have no large effect on the rate of an S_N reaction. Because the displacement of bromine is generally several tens of times as fast as that of chlorine from analogous compounds,¹ but substitution of bromine for chlorine in an ester probably does not appreciably alter the rate of neutral ester hydrolysis (*cf.* Ref. 10), the contribution of the displacement of halogen to the over-all reaction should be greater in the uncatalysed hydrolysis of bromomethyl chloroacetate than of chloromethyl chloroacetate at the same temperature. The difference should be even greater when the reactions proceed in 40 wt. % acetone-water because acetone retards the displacement of halogen from halomethyl esters less than it does ester hydrolysis.^{1,2}

For the above reasons, the rates of hydrolysis of bromomethyl chloroacetate in water and a 40 wt. % acetone-water mixture were measured at several temperatures to clarify the change in mechanism with rising temperature. At the same time, an attempt was made to determine how the occurrence of two concurrent reactions with different heat capacities of activation (ΔC_p^\ddagger) influences the dependence of the over-all rate coefficient on temperature and whether the rate coefficients of the concurrent reactions can be separately evaluated.

EXPERIMENTAL

Materials. Bromomethyl chloroacetate was synthesized as described earlier.⁴ Perchloric acid solutions were prepared by diluting concentrated perchloric acid (d 1.54, guaranteed reagent from Merck) with distilled water or a 40 wt. % acetone-water mixture. In the latter case, the necessary amount of acetone (guaranteed reagent from Merck) was added before dilution to correct for the water in the acid and maintain the ratio of acetone to water constant. The acid concentrations of the final solutions were checked by acid-base titration.

Kinetic experiments. The rates of the reactions in water were determined by titrating removed samples (10 ml) by a previously described argentometric method.^{1,2} The volatility of acetone from the 40 wt. % acetone-water mixture made it necessary to run the reactions in closed ampoules. The initial concentrations of bromomethyl chloroacetate were about 0.05 mol/l.

Calculation of rate coefficients of uncatalysed hydrolysis. Hydrogen ion was not found to catalyse the hydrolysis of bromomethyl chloroacetate in water. The calculated rate coefficients increased slightly as the reaction advanced in some runs, but the mean values of rate coefficients determined at different acid concentrations were equal within the limits of experimental error (Table 1). The rate coefficients of the uncatalysed reaction in water at different temperatures were calculated from the weighted means of the rate coefficients of the reactions at different acid concentrations. The weighting factor was the reciprocal of square of the standard deviation of the rate coefficient.

In the 40 wt. % acetone-water mixture, however, the reaction catalysed by the hydrogen ion had a considerable influence on the calculated first order rate coefficient k_t , which increased with hydrogen ion concentration c . The rate coefficients of the uncatalysed reaction (k_u) and the catalysed reaction (k_{HX}) were evaluated as described earlier.^{1,3} The contribution of chloroacetic acid to the hydrogen ion concentration is almost negligible even in the water solution that contained hydrogen bromide. For illustration, the experimental data for the hydrolysis of bromomethyl chloroacetate in 0.1065 M aqueous perchloric acid at 55°C (I), in water at 7.64°C (II), in 40 wt. % acetone-water mixture 0.0496 M in perchloric acid at 55°C (III), and in 40 wt. % acetone-water at -15°C (IV) are given below (c_t is the time-average of the hydrogen ion concentration calculated as described earlier^{1,3}).

I. t_s	0	90	204	282	384	492	612	720	918	1254	∞	
$10^5 x$	0	480	998	1313	1645	1958	2229	2440	2713	3036	3426	
$10^3 k_t$		1.677	1.688	1.714	1.703	1.723	1.719	1.730	1.710	1.734		
$10^3 \bar{k}_t = 1.711 \pm 0.006 \text{ s}^{-1}$												
II. t_{\min}	0	41.0	82.0	142.3	192.2	262.2	325.1	450.0	570.0	791.0	∞	
$10^5 x$	0	409	787	1269	1622	2056	2409	2869	3216	3640	4190	
$10^5 k_t$		4.182	4.229	4.225	4.246	4.289	4.387	4.275	4.267	4.278		
$10^5 \bar{k}_t = 4.264 \pm 0.019 \text{ s}^{-1}$												
III. t_{\min}	0	6.6	13.5	22.0	31.0	42.0	54.0	67.0	84.0	108.5	134.0	∞
$10^4 x$	0	40	78	121	162	204	244	276	314	351	377	422
$10^4 c_t$	560	580	600	623	646	671	696	720	747	780	807	
$10^4 k$		2.55	2.52	2.56	2.61	2.63	2.66	2.64	2.70	2.73	2.76	
$c_t = 0.0687 \text{ mol/l}; 10^4 \bar{k}_t = 2.64 \text{ s}^{-1}$												
IV. t_{days}	0	10.92	17.06	24.16	31.16	40.94	51.96	64.91	75.89	86.90	∞	
$10^4 x$	0	83	127	172	211	260	309	342	364	387	447	
$10^4 c_t$	21	63	86	111	133	163	193	224	245	265		
$10^7 k_t$		2.17	2.26	2.33	2.36	2.46	2.62	2.57	2.56	2.67		
$\bar{c}_t = 0.0165 \text{ mol/l}, 10^7 \bar{k}_t = 2.44 \text{ s}^{-1}$												

Experimental kinetic data for the hydrolysis of bromomethyl chloroacetate in water and in 40 wt. % acetone-water are given in Tables 1 and 2, which also include the values of the Arrhenius activation energy E_0 for the neutral ester hydrolysis calculated from data at three temperatures.

CALCULATION OF THE THERMODYNAMIC FUNCTIONS OF ACTIVATION

The dependence of the rate coefficient on temperature. If the heat capacity of activation does not vary with temperature, the temperature dependence of the rate coefficient can be expressed by the equation

$$\ln k = (A/T) + B \ln T + C \quad (2)$$

When two reactions, 1 and 2, proceed concurrently, the measured over-all rate coefficient is given by

$$k = k_1 + k_2 = e^{(A_1/T) + B_1 \ln T + C_1} + e^{(A_2/T) + B_2 \ln T + C_2} \quad (3)$$

where the coefficients A_i , B_i , and C_i are expressed by eqns. (4), (5), and (6).

$$A_i = -\frac{\Delta H_{i^\ddagger}}{R} + \frac{\Delta C_{p,i^\ddagger}}{R} \times T \quad (4)$$

$$B_i = \frac{\Delta C_{p,i^\ddagger}}{R} + 1 \quad (5)$$

$$C_i = \frac{\Delta S_{i^\ddagger}}{R} - \frac{\Delta C_{p,i^\ddagger}(\ln T + 1)}{R} - \ln \frac{h}{\bar{k}} \quad (6)$$

$$= \frac{(\Delta H_{i^\ddagger} - \Delta G_{i^\ddagger})}{RT} - \frac{\Delta C_{p,i^\ddagger}(\ln T + 1)}{R} - \ln \frac{h}{\bar{k}} \quad (6')$$

Table 1. Kinetic data for the hydrolysis of bromomethyl chloroacetate in water.

Temperature °C	c_0 mol/l	$10^4 k_t$ s ⁻¹	$10^4 k_0$ s ⁻¹	E_0 kcal/mol
0.00	0.0000	0.2124 ± 0.0008	0.2127	13.8
	0.0503	0.2123 ± 0.0006		
	0.1065	0.2139 ± 0.0009		
7.64	0.0000	0.4264 ± 0.0019	0.4245	
	0.0503	0.4236 ± 0.0017		
	0.1065	0.4241 ± 0.0013		
16.00	0.0000	0.8697 ± 0.0021	0.8697	
	0.0503	0.8699 ± 0.0025		
	0.1065	0.8685 ± 0.0053		
25.00	0.0000	1.750 ± 0.001	1.773	
	0.0000	1.771 ± 0.001		
	0.0503	1.790 ± 0.005		
	0.1003	1.777 ± 0.009		
	0.1065	1.800 ± 0.007		
35.00	0.0000	3.784 ± 0.011	3.802	
	0.0000	3.824 ± 0.019		
	0.0503	3.800 ± 0.006		
	0.1003	3.859 ± 0.014		
	0.1065	3.838 ± 0.020		
45.00	0.0000	8.230 ± 0.027	8.253	
	0.0000	8.182 ± 0.033		
	0.0503	8.377 ± 0.038		
	0.0503	8.357 ± 0.073		
	0.1065	8.397 ± 0.026		
	0.1065	8.093 ± 0.028		
55.00	0.0000	17.03 ± 0.08	17.02	
	0.0000	17.04 ± 0.08		
	0.0503	16.87 ± 0.08		
	0.1065	17.11 ± 0.06		
65.00	0.0000	36.73 ± 0.27	36.89	
	0.0503	36.94 ± 0.14		
	0.1065	36.87 ± 0.22		
75.00	0.0000	73.77 ± 0.27	73.77	

In these equations, i is 1 or 2, ΔH_i^\ddagger , ΔS_i^\ddagger , and $\Delta C_{p,i}^\ddagger$, are, respectively, the enthalpy, entropy, and heat capacity of activation of reaction i , h is Planck's constant, k Boltzmann's constant, and R the gas constant.

Optimization of values of the thermodynamic functions of activation by a Monte Carlo method. The thermodynamic functions of activation for the two concurrent reactions were evaluated from the measured rate coefficients at different temperatures both by a nonlinear iteration method and by a Monte Carlo method. In the latter method, the coefficients of eqn. (3) were expressed by eqns. (4), (5), (7), and (8). Eqns. (7) and (8)

Table 2. Kinetic data for the hydrolysis of bromomethyl chloroacetate in 40 wt. % acetone-water.

Temperature °C	\bar{c}_t mol/l	$10^5 k_t$ s ⁻¹	$10^5 k_0$ s ⁻¹	$10^5 k_{HX}$ l mol ⁻¹ s ⁻¹	E_0 kcal/mol
- 15.31	0.0164	0.0244	0.0228 ± 0.0006	0.109 ± 0.007	
	0.0648	0.0303			
	0.1156	0.0352			
- 15.17	0.0074	0.0246	0.0236 ± 0.0004	0.108 ± 0.005	
	0.0577	0.0296			
	0.1090	0.0356			
- 8.51	0.0175	0.0569	0.0532 ± 0.0003	0.215 ± 0.004	16.3
	0.0684	0.0682			
	0.1180	0.0785			
0.00	0.0146	0.144	0.137 ± 0.002	0.551 ± 0.030	16.2
	0.0661	0.175			
	0.1162	0.200			
7.53	0.0218	0.334	0.311 ± 0.004	1.05 ± 0.005	16.3
	0.0679	0.382			
	0.1208	0.438			
16.00	0.0192	0.765	0.723 ± 0.003	2.13 ± 0.04	16.3
	0.0672	0.864			
	0.1175	0.974			
25.00	0.0190	1.81	1.72 ± 0.01	4.46 ± 0.17	16.4
	0.0693	2.02			
	0.1177	2.25			
35.00	0.0185	4.36	4.20 ± 0.05	9.71 ± 0.64	16.7
	0.0685	4.90			
	0.1174	5.32			
45.00	0.0209	10.6	10.2 ± 0.03	21.6 ± 0.3	17.5
	0.0706	11.7			
	0.1183	12.7			
55.00	0.0223	24.6	23.9 ± 0.02	34.6 ± 2.5	17.3
	0.0687	26.4			
	0.1204	28.0			
65.00	0.0234	53.4	51.3 ± 0.04	90.6 ± 0.4	17.3
	0.0749	58.1			
	0.1228	62.4			
75.00	0.0340	115	110 ± 0.2	146 ± 3	
	0.0804	122			
	0.1297	129			

were derived by substituting in eqn. (6') the expressions $\Delta G_1^\ddagger = -RT \ln (kh/kT)$, and $k = k_1/s$, where s is the contribution of reaction 1 to the over-all reaction.

$$A_1 = \ln sk + \frac{\Delta H_1^\ddagger}{RT} - \frac{\ln T(\Delta C_{p,1}^\ddagger + R)}{R} - \frac{\Delta C_{p,1}^\ddagger}{R} \quad (7)$$

$$A_2 = \ln \frac{(1-s)}{k} + \frac{\Delta H_2^\ddagger}{RT} - \frac{\ln T(\Delta C_{p,2}^\ddagger + R)}{R} - \frac{\Delta C_{p,2}^\ddagger}{R} \quad (8)$$

Eqn. (6) has been replaced by eqns. (7) and (8) because the over-all rate coefficient, which has been directly determined and is hence relatively accurately known, then becomes one variable. In this method, the most probable values of ΔH^\ddagger and ΔC_p^\ddagger for each reaction at 25°C and the most probable contribution of reaction 1 to the over-all reaction and their ranges were chosen as initial values. The values of these five quantities were then independently varied within ranges determined by their standard deviations by choosing random numbers that are distributed according to the Gaussian curve with the maximum at each of the mentioned most probable values and extend to a distance that is six times the standard deviation on each side of the maximum. The best combinations were chosen by selecting those values for which the sum of squares

$$\varepsilon^2 = \sum (\Delta \log k)^2 \sim \left(\frac{k_{\text{obs}} - k_{\text{calc}}}{k_{\text{obs}} \times 2.30} \right)^2 \quad (9)$$

was smaller than a certain preselected value. Several tens of such combinations were averaged and their standard deviations were calculated. The average values were used as new starting values and new ranges were calculated by means of their standard deviations. Also the value of ε was diminished accordingly. The procedure was repeated 2 or 3 times. The aim of the procedure was to find a combination of the thermodynamic functions of activation that best corresponded to the measured rate coefficient values. For practical reasons, these calculations were not continued as far as the method would have been required because the values of the thermodynamic functions of activation in question could be calculated by an iteration method. This Monte Carlo method may, however, be of value in many cases where it is necessary to determine whether a certain model equation fits experimental data. It became evident during our calculations that several combinations of six parameters that give relatively good approximations of the experimental values can be chosen. Results obtained by this Monte Carlo method are given in Table 3.

The iteration method. In the iteration method, initial values of the thermodynamic functions of activation for both reactions were chosen on the basis of those for the hydrolysis of chloromethyl chloroacetate (B_{AC3}) and chloro-

Table 3. The values of the thermodynamic functions of activation for the hydrolysis of bromomethyl chloroacetate calculated by the Monte Carlo method at 25°C.

	In water		In 40 wt. % acetone-water	
	B_{AC3}	S_N	B_{AC3}	S_N
ΔH^\ddagger (kcal/mol)	11.5	21.3	12.5	18.8
ΔS^\ddagger [cal/(mol K)]	-37.5	-7.6	-40.2	-18.3
ΔC_p^\ddagger [cal/(mol K)]	-43	-40	-39	-31
$k_{B_{AC3}}/k_{S_N}$	0.81		0.41	
ε^2 (eqn. 9)	0.00034		0.00089	

Table 4. The thermodynamic functions of activation in the uncatalysed hydrolysis of bromomethyl chloroacetate in water at 25°C.

	ΔH^\ddagger kcal/mol	ΔS^\ddagger cal/(mol K)	ΔC_p^\ddagger cal/(mol K)	k_{BAC3}/k	ϵ^2 eqn. 9
B _{AC3}	10.2 ± 1.9	-41.9 ± 6.6	-110 ± 87	0.75	0.00015
S _N	21.7 ± 1.2	-5.7 ± 4.9	-79 ± 102		

Table 5. The thermodynamic functions of activation in the uncatalysed hydrolysis of bromomethyl chloroacetate in 40 wt. % acetate-water at 25°C.

	ΔH^\ddagger kcal/mol	ΔS^\ddagger cal/(mol K)	ΔC_p^\ddagger cal/(mol K)	k_{BAC3}/k	ϵ^2 eqn. 9
B _{AC3}	11.3 ± 1.1	-44.0 ± 3.7	-99 ± 37	0.45	0.00021
S _N	19.7 ± 1.1	-15.3 ± 3.4	-41 ± 33		

Table 6. The rate coefficients for the uncatalysed hydrolysis of bromomethyl chloroacetate taking place by the B_{AC3} and S_N mechanisms in water at different temperatures.

Temperature °C	$10^4 k_{BAC3}$ s ⁻¹	$10^4 k_{SN}$ s ⁻¹	k_{BAC3}/k_{obs} %	$(k_{obs} - k_{calc})/k_{obs}$ %
0.00	0.200	0.0124	94.2	0.23
7.64	0.386	0.0410	90.4	-0.58
16.00	0.729	0.137	84.2	0.43
25.00	1.32	0.450	74.6	0.06
35.00	2.32	1.49	60.9	-0.45
45.00	3.73	4.42	45.8	1.18
55.00	5.53	11.8	31.9	-1.85
65.00	7.62	28.7	21.0	1.50
75.00	9.84	64.2	13.3	-0.44

methyl acetate (S_N). In addition, the entropies of activation were chosen to correspond to the experimentally found values of the over-all rate coefficients. These values were varied according to eqns. (3), (4), (5), and (6') in the iteration. Eqn. (6') was used instead of eqn. (6) because ΔH^\ddagger and ΔS^\ddagger are interrelated. The minimisation was performed with respect to ΔH^\ddagger , ΔG^\ddagger , and ΔC_p^\ddagger applying the general minimisation programme VA04A of Powell.⁵ The standard deviations of the thermodynamic functions of activation were calculated by the method of Quenouille.⁹

Table 7. The rate coefficients for the uncatalysed hydrolysis of bromomethyl chloroacetate taking place by the $B_{AC}3$ and S_N mechanisms in 40 wt. % acetone-water at different temperatures.

Temperature °C	$10^4 k_{BAC3}$ s ⁻¹	$10^4 k_{SN}$ s ⁻¹	k_{BAC3}/k_{obs} %	$(k_{obs} - k_{calc})/k_{obs}$ %
-15.31	0.194	0.0358	84.4	-0.89
-15.17	0.198	0.0366	84.4	0.79
- 8.51	0.422	0.106	79.9	0.69
0.00	1.01	0.378	72.8	-1.34
7.53	2.01	1.07	65.2	0.74
16.00	4.02	3.20	55.7	0.09
25.00	7.69	9.37	45.1	0.79
35.00	14.4	28.1	33.8	-1.26
45.00	24.6	77.3	24.1	-0.31
55.00	38.8	196	16.5	1.74
65.00	57.2	462	11.0	-1.19
75.00	78.9	1020	7.2	0.27

The calculations were performed in both cases on an IBM 1130 computer at the Computer Centre of the University of Turku. The iteration method then led to a minimum value of the sum of squares that was smaller than that obtained with any other combination of the thermodynamic functions of activation for the reactions in water and in 40 wt. % acetone-water. Results obtained by the iteration method are given in Tables 4 and 5. The rate coefficients calculated using these values of the thermodynamic functions of activation and the experimental rate coefficients differed less than 1 % on average and even the largest differences were less than 2 % (Tables 6 and 7). Also the experimental rate coefficients varied within the same relative limits (Tables 1 and 2). As the differences between the calculated and experimental rate coefficients differed randomly in sign, the calculated values of the thermodynamic functions of activation can be considered to relate to the uncatalysed hydrolysis of bromomethyl chloroacetate.

DISCUSSION

Change in mechanism caused by temperature. The activation energy of the uncatalysed hydrolysis of bromomethyl chloroacetate in water at 25°C is about 13.8 kcal/mol. This value is slightly higher than the activation energies of halomethyl esters that hydrolyse by the $B_{AC}3$ mechanism. For example, the activation energy of the uncatalysed hydrolysis of chloromethyl chloroacetate² is 12.4 kcal/mol. Furthermore, as seen in Fig. 1, the activation energy for the hydrolysis of bromomethyl chloroacetate increases with temperature. The activation energy of the latter ester in 40 wt. % acetone-water at 25°C is about 16.5 kcal/mol and increases slowly with temperature (Fig. 2). The activation energy for the hydrolysis of chloromethyl chloroacetate⁷ under the same conditions is 13.9 kcal/mol and may also include a contribution of an S_N reaction. An increase in activation energy with rising temperature implies a

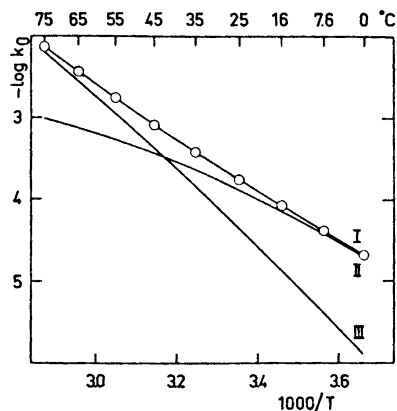


Fig. 1. Plots of $\log k_0$ versus $1/T$ for the uncatalysed hydrolysis of bromomethyl chloroacetate in water. Curve I plots eqn. (3), and the other curves plot eqn. (2) for the uncatalysed hydrolysis taking place by the $B_{AC}3$ (II) and S_N (III) mechanisms.

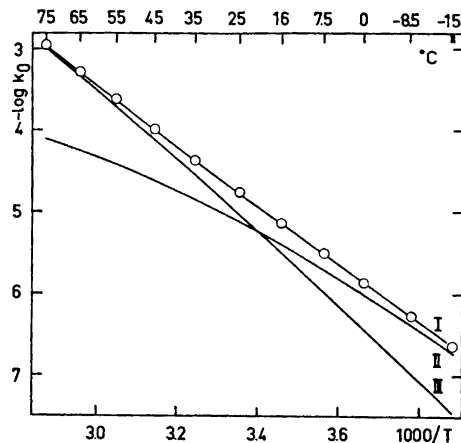


Fig. 2. Plots of $\log k_0$ versus $1/T$ for the uncatalysed hydrolysis of bromomethyl chloroacetate in 40 wt. % acetone-water. Curve I plots eqn. (3), the other curves plot eqn. (2) for the uncatalysed hydrolysis taking place by the $B_{AC}3$ (II) and S_N (III) mechanisms.

positive heat capacity of activation. However, the heat capacity of activation has been found to be negative for all uncatalysed hydrolyses of esters for which it has been evaluated.^{2,3,7-9} Hence it is obvious that the uncatalysed hydrolysis of bromomethyl chloroacetate proceeds concurrently by two mechanisms. The reaction that takes place by the $B_{AC}3$ mechanism predominates at low temperatures, but as the temperature rises, the contribution of the reaction taking place by the S_N mechanism becomes greater owing to its higher activation energy. The fact that the experimental activation energy of the uncatalysed hydrolysis of bromomethyl chloroacetate in 40 wt. % acetone-water is almost constant over a wide temperature range is due to the smaller difference between the activation energies of the two reactions in this solvent than in water. In addition, two opposing factors influence the activation energy. One is the change in mechanism which leads to an increase in the activation energy with rising temperature and the other is the negative heat capacity of activation which lowers the activation energy. When the influence of the latter factor outweighs that of the former, the activation energy should decrease. The activation energy should then have a maximum value at a certain temperature. Indications that this is the case are evident in the values of activation energy shown in Table 2, although the experimental error is of the same order as the variation in these values. The activation energy of the uncatalysed hydrolysis of bromomethyl acetate^{1,7} in the same solvent mixture is about 19 kcal/mol at 25°C. Taking into account the negative heat capacity of activation of the reaction, the value of the activation energy

at 65°C would be 17.0–17.5 kcal/mol, which is approximately the value obtained for the uncatalysed hydrolysis of bromomethyl chloroacetate (Table 2).

These observations indicate that the experimental rate coefficients may follow the Arrhenius equation closely "within the limits of experimental error" although a change in mechanism is taking place if both reactions have a negative heat capacity of activation. As shown, above evaluation of the rate coefficients of such two reactions is possible.

The thermodynamic functions of activation. The values of the thermodynamic functions of activation for the uncatalysed hydrolyses of bromomethyl chloroacetate are typical of reactions that proceed by the corresponding mechanisms in water and 40 wt. % acetone-water. Although the values of ΔC_p^\ddagger are slightly more negative than generally, their statistical significance is very low, almost negligible. The standard deviations of the thermodynamic functions of activation are relatively large. This is natural in a case like the present because several combinations of values of the six parameters, the thermodynamic functions for both reactions, can be chosen which all yield values that reproduce rate coefficient values that are approximately in agreement with the experimentally determined values. By fixing, for example, the value of the heat capacity of activation, values of the other thermodynamic functions of activation are obtained that have smaller standard deviations, but these values do not yield rate coefficient values that agree as well with the experimental values as with the values given in Tables 4 and 5. The change in the enthalpy of activation when water is replaced by 40 wt. % acetone-water as solvent is of the same magnitude as with other reactions proceeding by the same mechanism.^{1,7} For reactions taking place by the $B_{AC}3$ mechanism ΔH^\ddagger increases, and for reactions taking place by the S_N mechanism it decreases when water is replaced by 40 wt. % acetone-water.

Structural effects. The ratio of rate coefficients of the uncatalysed hydrolysis by the $B_{AC}3$ mechanism of bromomethyl chloroacetate (Tables 6 and 7) and chloromethyl chloroacetate at 25°C is 1.2 when water is the solvent and 1.3 when 40 wt. % acetone-water is the solvent, whereas the ratio of the rate coefficients of the alkaline hydrolysis of bromomethyl and chloromethyl acetates in water reported by Euranto and Moisio¹⁰ is 1.38. The ratio of the rate coefficients of uncatalysed hydrolysis of bromomethyl acetate¹ and bromomethyl chloroacetate by the S_N mechanism is 13 in water and 14 in 40 wt. % acetone-water. If it can be assumed that the rate of uncatalysed hydrolysis of chloromethyl chloroacetate by the S_N mechanism is 1/13 of the rate of the corresponding reaction of chloromethyl acetate, the rate coefficient of the former ester at 25°C would be $1.2 \times 10^{-6} \text{ s}^{-1}$. This would mean that the contribution of the uncatalysed hydrolysis by the S_N mechanism of chloromethyl chloroacetate to the over-all rate is only about one per cent at this temperature. At 75°C the contribution would be several per cent and the observed² increase in the activation energy of the uncatalysed hydrolysis of chloromethyl chloroacetate with temperature would be consistent with this.

Solvent effects. The retardation by acetone of the reactions of bromomethyl chloroacetate that proceed by the two mechanisms is typical for reactions that take place by these mechanisms. The slope of the plot of $\log k$ versus $\log c_{H_2O}$ is 5.0 for the hydrolysis of this ester by the $B_{AC}3$ mechanism and 5.1 for the

hydrolysis of chloromethyl chloroacetate ($B_{AC}3$).^{2,7} For the reaction of the former ester taking place by the S_N mechanism, the value of the slope is 2.7, whereas the value for the uncatalysed hydrolysis of bromomethyl acetate (S_N) is 2.6.¹

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