Temperature Dependence of Activation Parameters in the Neutral Ester Hydrolysis in Methanol–Water Solutions

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The kinetic behaviour of the uncatalysed reactions of methyl trifluoroacetate and chloromethyl dichloroacetate in MeOH-water solutions have been studied. In the water-rich region, the plots of $\Delta H^{\ne}$ vs. x_w for the hydrolysis of methyl trifluoroacetate have a maximum at lower and a minimum at higher temperatures. The plots of $T\Delta S^{\ne}$ vs. x_w have no extreme points in the temperature range studied. In the case of chloromethyl dichloroacetate, the values of activation parameters represent the simultaneous hydrolysis and methanolysis.

The heat capacity of activation has a minimum value -324 ± 6 J mol^{-1} K^{-1} at x_w 0.843 for methyl trifluoroacetate and -244 ± 13 J mol^{-1} K^{-1} at x_w 0.950 for chloromethyl dichloroacetate. For the same reactions in water the values of $\Delta C_p^{\ne}$ are -245 ± 5 and -182 ± 8 J mol^{-1} K^{-1}, respectively. The positions of the minima of $\Delta C_p^{\ne}$ are in accord with the anticipated effects of the substrate at the "magic" mole fraction 0.85 of water, but in the case of chloromethyl dichloroacetate the value of $\Delta C_p^{\ne}$ at the minimum may be too positive owing to the effects of the simultaneous methanolysis and hydrolysis.

Liquid water has a random, three-dimensional structure in which each water molecule attempts to form four tetrahedrally-disposed hydrogen bonds with its nearest neighbours.[1] If an organic co-solvent is added to water it is possible to change this hydrogen-bonded network continuously. Considerable information is available on the properties of dilute aqueous solutions of alcohols[2] which, according to their thermodynamic properties, belong to a class of typically aqueous (TA) solutions.[3–5] It is known that small amounts of a monohydric alcohol promote the formation of hydrogen bonds between the surrounding water molecules in a co-operative manner but larger amounts break the enhanced water structure. Thus, in the water-rich region, there is an alcohol concentration where a maximal water structure is reached. This "magic" mole fraction of water is determined by the nature of the added organic co-solvent. In alcohol–water solutions it has been found that the maximal water structure is reached when the mole fraction of water (x_w) is about 0.85, 0.91, 0.94, 0.96 and 0.98 in the case of methanol (MeOH), ethanol (EtOH), isopropyl alcohol (i-PrOH), tert-butyl alcohol (t-BuOH), and 2-butoxyethanol (2-BE), respectively.[3,6]

The thermodynamic activation parameters, activation enthalpy ($\Delta H^{\ne}$), activation entropy ($\Delta S^{\ne}$), and especially the heat capacity of activation ($\Delta C_p^{\ne}=d\Delta H^{\ne}/dT$)) have been widely employed as probes for the study of solvent effects in aqueous binaries.[3,5,7–12] The heat capacity of activation, found to differ from zero in most ionogenic solvolytic reactions, is usually assumed to be a genuine rate parameter of a single-step reaction.[7,13,14] Its value may depend on temperature and is mainly determined by the solvation differences between the initial and transition states. Another explanation for $\Delta C_p^{\ne}$ is based on a two-step mechanism with a tetrahedral intermediate, the first step of the reaction being reversible.[15–23] It has been, however, recently concluded that the heat capacity of activation and its derivatives are real rate parameters which may include a "spurious" contribution caused by the partitioning of a possible intermediate.[14]

The aim of the present work was to study the behaviour of the reactions of methyl trifluoro-

acetate and chloromethyl dichloroacetate in different MeOH–water solutions over a wide temperature range. The reactions are assumed to take place as a general base catalysed ester hydrolysis, $B_{AC}3$.[9,10,24]

EXPERIMENTAL

Methyl trifluoroacetate, a commercial product (E. Merck AG, zur Synthese), was redistilled before use. Chloromethyl dichloroacetate was prepared by chlorinating methyl dichloroacetate with gaseous chlorine.[25] The solvent mixtures were prepared by diluting a known weight of distilled water with MeOH (E. Merck AG, getrocknet, *pro analysi*) to a known volume in a volumetric flask. The initial ester concentrations were about 10^{-4} M. The temperature was stable to about 0.01 K.

The reactions were followed conductometrically as described earlier.[11] Actually the concentrations of trifluoroacetic acid in the hydrolysis of methyl trifluoroacetate and that of hydrochloric and dichloroacetic acids in the reactions of chloromethyl dichloroacetate were measured.[9-11]

The rate constants were calculated by Guggenheim's method.[26] In some cases also final values were measured, and the obtained rate constants were essentially the same. The accuracy of the kinetic data was as described earlier.[11] The thermodynamic activation parameters were calculated by an extended Arrhenius equation, eqn. (1), employing the method of Clarke and Glew[27] after an orthogonalization procedure.

$$\ln k = A + B/T + C \ln T + DT + ET^2 + \ldots + \varepsilon \qquad (1)$$

According to Student's t-test only the first three parameters of eqn. (1) were significant at the 95 % level. Exceptions to this are the reactions of methyl trifluoroacetate at $x_w = 0.740$ and that of chloromethyl dichloroacetate at $x_w = 0.599$ where also the fourth parameter was significant, probably because of, *e.g.*, systematic errors in rate measurements. In the following treatment, eqn. (1) has been used in its three-parametric form.

When studying the reaction of chloromethyl dichloroacetate in MeOH–water solutions, the possibility that both hydrolysis and methanolysis reactions take place concurrently cannot be ignored. In fact, a gas-chromatographic product analysis from the uncatalysed reaction of chloromethyl dichloroacetate revealed that the methanolysis product, methyl dichloroacetate, was formed during the reaction when x_w was about 0.9 or smaller. On the other hand, it was found that the esterification of the hydrolysis product, dichloroacetic acid, did not produce methyl dichloroacetate under the reaction conditions used. These results are in agreement with those from the uncatalysed reaction of chloromethyl chloroacetate in MeOH–water solutions when it has been possible to separate the simultaneous hydrolysis and methanolysis reactions.[31] Further, it has been found that when x_w is gradually lowered, MeOH decreases the hydrolysis rate of chloromethyl chloroacetate but water accelerates the rate of the alcoholysis so that at about x_w 0.72 the rate of the methanolysis exceeds that of the hydrolysis.

Table 1. Temperature range (K), number of kinetic runs, calculated values of k (s^{-1}), and activation parameters $\Delta H^{\neq}$ (J mol^{-1}), $\Delta S^{\neq}$ (J mol^{-1} K^{-1}), and $\Delta C_p^{\neq}$ (J mol^{-1} K^{-1}) at 298.15 K in the reactions of methyl trifluoroacetate in MeOH–water mixtures at the mole fraction x_w of water.

x_w	Temp. range	No. of runs	$10^3 k$	$\Delta H^{\neq}$	$-\Delta S^{\neq}$	$-\Delta C_p^{\neq}$
1.000	273–313	24	8.459	39700(40)	151.4(1)	245(5)
0.994	273–313	26	8.196	39950(40)	150.9(1)	250(5)
0.991	273–313	20	7.987	39810(30)	151.6(1)	242(4)
0.972	273–316	23	7.138	39770(20)	152.6(1)	252(4)
0.930	273–320	24	5.474	39300(20)	156.4(1)	281(3)
0.922	273–318	11	5.168	39190(50)	157.3(2)	294(8)
0.875	273–318	11	3.747	38750(60)	161.4(2)	322(8)
0.843	273–318	11	3.016	38580(40)	163.8(1)	324(6)
0.777	273–320	12	1.827	37870(50)	170.3(2)	292(7)
0.740	273–320	11	1.372	37770(40)	173.0(1)	265(6)
0.690	273–320	18	0.949	37760(60)	176.2(2)	250(8)

Table 2. Temperature range (K), number of kinetic runs, calculated values of k (s^{-1}), and activation parameters $\Delta H^{\ddagger}$ (J mol^{-1}), $\Delta S^{\ddagger}$ (J mol^{-1} K^{-1}), and $\Delta C_p^{\ddagger}$ (J mol^{-1} K^{-1}) at 298.15 K in the reactions of chloromethyl dichloroacetate in MeOH–water mixtures at the mole fraction x_w of water.

x_w	Temp. range	No. of runs	$10^2 k$	$\Delta H^{\ddagger}$	$-\Delta S^{\ddagger}$	$-\Delta C_p^{\ddagger}$
1.000	273–303	11	1.460	39180(90)	148.7(3)	182(8)
0.980	273–303	12	1.322	39040(100)	150.0(3)	189(8)
0.968	273–306	14	1.199	38080(140)	154.0(5)	230(15)
0.950	273–306	14	1.115	38130(130)	154.4(4)	244(13)
0.894	273–313	9	0.819	37900(80)	157.7(3)	266(10)
0.843	273–318	12	0.602	38340(60)	158.8(2)	197(9)
0.814	273–320	14	0.432	39140(40)	158.9(1)	166(6)
0.697	273–328	14	0.250	39940(60)	160.8(2)	133(8)
0.599	273–328	12	0.165	40000(100)	164.0(4)	174(12)
0.500	273–328	14	0.113	40130(80)	166.7(3)	162(11)

RESULTS AND DISCUSSION

Kinetic data at 298.15 K for the neutral reactions of methyl trifluoroacetate and chloromethyl dichloroacetate in the MeOH–water mixtures studied, are given in Tables 1 and 2, respectively. As can be seen from the Tables, MeOH decreases the rates of the hydrolyses. The retarding effect seems to be quite small when compared to the rate lowering effect caused by other organic co-solvents such as acetone,[28,29] 2-butanone,[30] 2-BE[9,10] and acetonitrile[28,29] in the hydrolyses of the same esters. This observation agrees with the fact that, of these co-solvents, MeOH is the most water-like solvent as it is a small molecule which can be hydrogen-bonded to other alcohol and water molecules.

In most neutral solvolytic reactions, organic co-solvents added to water, have been found to produce large and almost compensating changes upon $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$.[5,7–12,28–37] In solvent mixtures, rich in water, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ first decrease to a minimum, the occurrence and position of which in the solvent composition has been thought to be connected with the solvent structure. In the reactions of methyl trifluoroacetate and chloromethyl dichloroacetate in MeOH–water solutions there seems to be shallow minima in $\Delta H^{\ddagger}$ at x_w about 0.7 and 0.9 at 298.15 K (Tables 1 and 2; Figs. 1 and 2), respectively. However, when $\Delta H^{\ddagger}$ is plotted *vs.* x_w at different temperatures for the hydrolysis of methyl trifluoroacetate (Fig. 1), the plots show the unusual behaviour that $\Delta H^{\ddagger}$ has a maximum at $x_w = 0.875$

at 273 K and a minimum at x_w about 0.8 at 313 K. Although it is not possible to draw any far-reaching conclusions from the reaction of chloro-
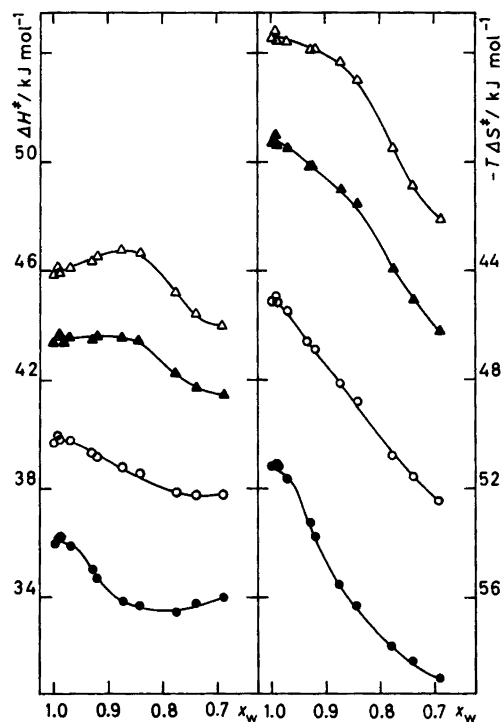

Fig. 1. Plots of $\Delta H^{\ddagger}$ and $T\Delta S^{\ddagger}$ *vs.* x_w for the neutral hydrolysis of methyl trifluoroacetate in methanol-water mixtures at the temperatures 273 K ($\triangle$); 283 K ($\blacktriangle$); 298 K ($\bigcirc$); 313 K ($\bullet$).
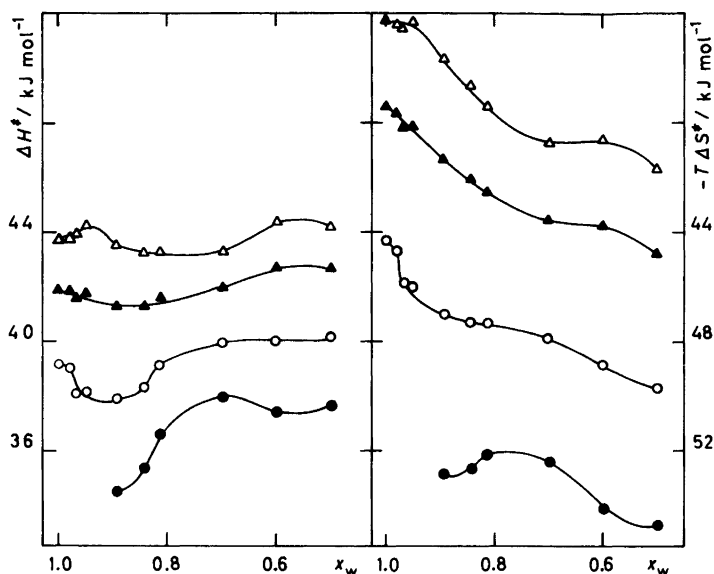
Fig. 2. Plots of $\Delta H^{\ddagger}$ and $T\Delta S^{\ddagger}$ *vs.* x_w for the neutral reaction of chloromethyl dichloroacetate in methanol-water mixtures at the temperatures 273 K ($\triangle$); 283 K ($\blacktriangle$); 298 K ($\bigcirc$); 313 K ($\bullet$).

methyl dichloroacetate in MeOH–water mixtures because the activation parameters then include the simultaneous hydrolysis and methanolysis, it seems that also in this case $\Delta H^{\ddagger}$ first increases when $x_w \geq 0.95$ at 273 K (Fig. 2). These unusual concentration dependences of $\Delta H^{\ddagger}$ for the present reactions at different temperatures may be understood by the solvation variation of the initial state, in accord with the results of Arnett *et al.*,[38] if it is expected that carbon dioxide can serve as a model compound for the present esters. It has been found that the solubility of carbon dioxide in MeOH–water solutions increases when x_w goes from 1.00 to about 0.95 and then decreases to x_w about 0.9 leading to a minimum in the enthalpy of solution in the highly water-rich MeOH solutions.[39] These properties are especially important at lower temperatures and gradually vanish when the temperature is raised from 277.9 to 333.4 K.

Contrary to the hydrolysis of chloromethyl dichloroacetate, it has been found that for the hydrolysis of methyl trifluoroacetate in aqueous binaries there are no minima in $\Delta S^{\ddagger}$ but the plots of $\Delta S^{\ddagger}$ *vs.* x_w have only an inflexion point.[7,8,28,29,34] This is also true for the neutral hydrolysis of methyl trifluoroacetate in the MeOH–water solutions studied (Fig.1), in spite

of the peculiar behaviour of the plots of $\Delta H^{\ddagger}$ *vs.* x_w at different temperatures.

Although in an aqueous binary the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ of solvolytic reactions are certainly connected with the solvent structure, the heat capacity of activation is the most valuable rate parameter for studying the specific role of the solvent reorganization during the activation process. In the water-rich region of an aqueous solution which belongs to the class TA, the values of $\Delta C_p^{\ddagger}$ decrease until a mimimum value is reached. The place and the depth of the minimum depend on the organic co-solvent used and the hydrophobic character of the reactant. Thus Robertson and Sugamori[33] have found that for the solvolysis of *tert*-butyl chloride, $\Delta C_p^{\ddagger}$ goes from the value -347 ± 19 J mol^{-1} K^{-1} in water to the minimum values -569 ± 33, -565 ± 17, and -812 ± 33 J mol^{-1} K^{-1} in EtOH–, i-PrOH–, and *t*-BuOH–water solutions at x_w 0.925, 0.95, and 0.95, respectively. In these cases the positions of the minima occur at the "magic" mole fractions of the binary systems studied[3] and further, within the limits of the experimental accuracy, the changes in the values of $\Delta C_p^{\ddagger}$ from water to the minimum values, $\Delta\Delta C_p^{\ddagger}=\Delta C_p^{\ddagger}(H_2O)-\Delta C_p^{\ddagger}$ (minimum), become greater when the alcohol component of the binary is changed from EtOH
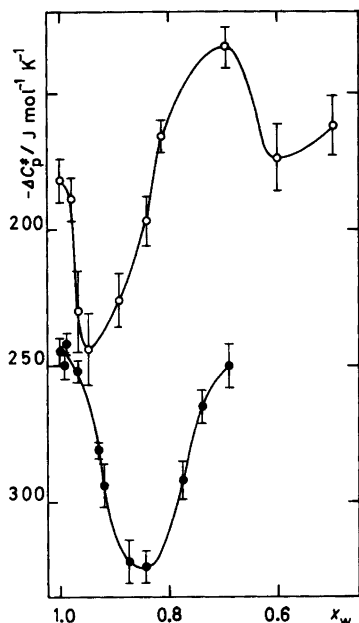
Fig. 3. Plots of $\Delta C_p^{\neq}$ vs. x_w for the neutral reactions of methyl trifluoroacetate (●) and chloromethyl dichloroacetate (○) in methanol-water mixtures at 298.15 K.

through i-PrOH to t-BuOH, $\Delta\Delta C_p^{\neq}$ being 222, 218 and 465 J mol^{-1} K^{-1}, respectively. In accordance with the above conclusions, $\Delta C_p^{\neq}$ is at a minimum at $x_w=0.843$ and 0.950 for the reactions of methyl trifluoroacetate and chloromethyl dichloroacetate, respectively, in the MeOH–water solutions studied (Tables 1 and 2; Fig. 3). It has been earlier found for the hydrolyses of the same esters that, if the organic component of an aqueous binary is the same, *e.g.*, acetone, $\Delta C_p^{\neq}$ reaches a minimum value at a lower x_w in the case of methyl trifluoroacetate than in that of chloromethyl dichloroacetate.[7,8,28,29] Thus when chloromethyl dichloroacetate reacts in aqueous methanol the effect of the substrate explains the fact that maximal water structure around the ester molecule is reached in a more water-rich region than could be expected on the basis of the "magic" mole fraction 0.85 of water. Further, according to the above-mentioned results for the solvolysis of *tert*-butyl chloride in alcohol–water solutions,[33] the depth of the minimum ($\Delta\Delta C_p^{\neq}=79$ J mol^{-1} K^{-1}) for the hydrolysis of methyl trifluoroacetate in MeOH–

water solutions seems to be quite natural. The conclusion that the co-solvent in water primarily determines the value of $\Delta\Delta C_p^{\neq}$, is further supported by the results from the hydrolysis of the same ester in t-BuOH–[40] and 2-BE–water solutions[9,10] the values of $\Delta\Delta C_p^{\neq}$ at 298.15 K being 254 and 378 J mol^{-1} K^{-1}, respectively. In the last-mentioned hydrolyses the values of $\Delta C_p^{\neq}$ depend considerably on temperature. On the other hand, the simultaneous hydrolysis and methanolysis in the reaction of chloromethyl dichloroacetate in water-rich methanol solutions may cause a positive contribution to the values of $\Delta C_p^{\neq}$ and thus the depth of the minimum ($\Delta\Delta C_p^{\neq}=62$ J mol^{-1} K^{-1}) may be too small.

In disagreement with the solvent effects on $\Delta C_p^{\neq}$ described above are the results of Huq[35] for the hydrolysis of *tert*-butyl chloride in MeOH–water solutions. In this case the values of $\Delta C_p^{\neq}$ decrease from -111 J mol^{-1} K^{-1} in water to a minimum value of -3046 J mol^{-1} K^{-1} at $x_w=0.935$. However, these results, based on only four experimental temperatures (from 273 to 293 K), do not fulfil all of the demands which are generally expected for heat capacity measurements.[11]

The present results show that the solvent effects, caused by a water-structure-making co-solvent, MeOH, on the activation parameters, especially on $\Delta C_p^{\neq}$, are small when compared to the solvent effects of the higher analogues in an alcohol series. This is in accordance with the small effect of added MeOH on water structure. Further, contrary to the high temperature dependence of $\Delta C_p^{\neq}$ found in t-BuOH–[40] and 2-BE–water solutions[9,10] in the hydrolyses of methyl trifluoroacetate and chloromethyl dichloroacetate, the values of $\Delta C_p^{\neq}$ for the reactions of the same esters in MeOH–water solutions do not seem to depend on temperature.

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