# Neutral Solvolysis of Acyl Carbon and the Temperature Dependence of the Kinetic Solvent Isotope Effect

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The temperature dependence of the rate of hydrolysis of benzoic, phthalic, and succinic anhydrides have been determined in  $H_2O$  and  $D_2O$  under "neutral" conditions. Corresponding data have been obtained for methyl trifluoroacetate. While both series supposedly react by the same  $B_{Ae}2$  mechanism, remarkable differences are made obvious by this investigation. Possible sources of such differences are proposed.

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On a déterminé, dans  $H_2O$  et  $D_2O$ , dans des conditions neutres, l'influence de la température sur la vitesse d'hydrolyse des anhydrides benzoique, phtalique et succinique. On a obtenu les données correspondantes pour le trifluoroacétate de méthyle. Alors que l'on suppose que les deux séries réagissent par le même mécanisme  $B_{Ac}2$ , des différences importantes découlent de la présente étude. On propose diverses sources possibles pour de telles différences.

[Traduit par le journal]

#### Introduction

The unexpected changes in the kinetic solvent isotope effects (k.s.i.e.) with temperature found for the hydrolysis of acetic and propionic anhydrides (1) were without precedent (2-4) and did not appear to resemble the results published by Winter and Scott (5) for the methyl, ethyl, and isopropyl trifluoroacetates which, like the anhydrides and other haloacetates, are considered to react by a  $B_{Ac}2$  mechanism (6). No satisfactory cause for such variation in k.s.i.e. with temperature was apparent for acetic and propionic anhydrides; hence in the hope of discovering some structural influence, the rates of hydrolysis for three other anhydrides with quite different structural features were determined in  $H_2O$  and  $D_2O$ . Rate measurements were made over a sufficient range of temperatures to permit a determination of the shape of the k.s.i.e. vs. T curve and to examine the temperature coefficient of  $\Delta H^{\dagger}$ . Since Winter and Scott (5) had determined the k.s.i.e. for alkyl trifluoroacetate at three temperatures only, and had determined  $\Delta C_p^{\dagger}$  for ethyl trifluoroacetate, we undertook a more complete study of temperature effects on the rate of hydrolysis of methyl trifluoroacetate in both  $H_2O$  and  $D_2O$ .

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# Experimental

Commercial samples of benzoic anhydride, succinic anhydride and phthalic anhydride were purified by recrystallization to constant melting point (Table 1).

Methyl trifluoroacetate was prepared by reaction of silver trifluoroacetate with methyl iodide in freshly distilled benzonitrile (8). The ester was isolated by distillation and purified by redistillation b.p.  $40-41^{\circ}$ , literature b.p.  $43^{\circ}$ .

b.p. 43°. Water and D<sub>2</sub>O were purified by methods reported previously (1). In all D<sub>2</sub>O experiments the %D exceeded 99.7% D.

First order rate constants for the reaction of each substrate in  $H_2O$  and  $D_2O$  were determined over the widest conveniently attainable temperature range by the conductance method used in the previous study (1) and treatment of the temperature dependence of these rates and derivation of pseudo-thermodynamic parameters followed previous formalism.

# **Results and Discussion**

Rate determination for the solvolysis of organic substrates which produce weak electrolytes and the interpretation of the conductance-time data for these reactions present special problems which we solved previously (1). The observed pseudo first order rate constants were determined using the Guggenheim method (9) modified for weak electrolytes. The procedure may be summarized as follows: resistance readings were collected in pairs at a constant time interval,  $\Delta t$ apart. In addition the acid ionization constant,  $K_a$ , limiting equivalent ionic conductance,  $\Lambda_0$ , were required for application of the following

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Melting point (°C) Anhydride Recrystallization solvent This work Literature (7) Benzoic Aqueous ethanol 42.6 42 118.7 Succinic 120 Chloroform Phthalic Benzene 131.7 132

TABLE 1. Melting points and recrystallization solvents for acid anhydrides

TABLE 2. Empirical constants for the rate-temperature relation (2)for the solvolysis of acyl carbon in  $H_2O$ 

Substrate	$A_2$	$-A_2$	$-A_{3}$	$n_{T_1}^{T_2}$
Benzoic anhydride	8.25593	2524.3274	1.2872	$24_{16}^{50}$
Succinic anhydride	33.88575	4054.6759	9.2282	$30_{1}^{27}$
Phthalic anhydride	185.94917	10654.3206	61.5189	261 <sup>16</sup>
Methyl trifluoroacetate	126.02044	7466.7501	41.6549	291 <sup>18</sup>

TABLE 3. Empirical constants for the rate-temperature relation (2) for the solvolysis of acyl carbon in  $D_2O$ 

Substrate	 A1	$-A_2$	$-A_3$	$n_{T_1}^{T_2}$
Benzoic anhydride	88.85618	6367.8447	28.8520	$22_{25}^{60}$ $23_{5}^{30}$ $17_{4}^{20}$ $20_{4}^{28}$
Succinic anhydride	2.29799	2642.6448	1.4460	
Phthalic anhydride	45.57871	4674.4670	13.0220	
Methyl trifluoroacetate	122.53008	7415.0428	40.5306	

equation. In (1) where  $C_0$  = stoichiometric concentration of anhydride at time t = 0;  $C_t$  = concentration of acid at time t;  $C_{t+\Delta}$  = concentration of acid at time  $t + \Delta$ ;  $\Delta$  = constant time interval, approximately  $2t_{1/2}$ ,  $k^0$  = observed first order rate constant,  $C_K$  = cell constant.

[1] 
$$\log\left\{\frac{1}{R_{t+\Delta}} - \frac{1}{R_t}\right\}$$
  
+  $\log\left[1 + \frac{10^3 C_{\mathrm{K}}}{\Lambda_0 K_{\mathrm{a}}} \left(\frac{1}{R_{t+\Delta}} + \frac{1}{R_t}\right)\right]$   
=  $\log\left[\frac{C_0 \Lambda_0}{2 \times 10^3 C_{\mathrm{K}}} \left(1 - \mathrm{e}^{-k\Delta}\right)\right] - \frac{k^0 t}{2.3026}$ 

Least-squares fit to eq. 1 provided  $k^0$ , the observed rate constant, and its standard deviation. For derivation of eq. 1, see ref. 1.

 $K_a$  values used were for benzoic acid in H<sub>2</sub>O (10), benzoic acid in D<sub>2</sub>O (11), succinic acid in H<sub>2</sub>O (12), succinic acid in D<sub>2</sub>O (13), phthalic acid in H<sub>2</sub>O (14), trifluoroacetic acid in H<sub>2</sub>O (15).  $K_a$  for phthalic acid and trifluoroacetic acid in D<sub>2</sub>O were not available, therefore values

were estimated using Rule and LaMer's law (16) and the data of Bates *et al.* (13). In order to test the reliability of the assumptions, tests of variation in observed  $k^0$  values with changes in  $K_a$ values were made. If  $K_a$  was estimated to within  $\pm 10\%$ , then the error introduced into  $k^0$  was less than 0.1%. For the cyclic anhydrides which produced dicarboxylic acids the effective ionic concentration was estimated by using the  $K_a$  (1) values, hereto, tests indicated this approximation produced no significant error in  $k^0$ .

Calculated standard deviations in  $k^0$  were usually  $<\pm 0.25\%$  and the agreement between the four experimental values for each temperature were within  $\pm 0.5\%$ .

The observed rate constants were fitted to the following empirical equation  $(k^0 = k_{observed})$ :

[2] 
$$\log k^0 = A_1 + A_2/T + A_3 \log T + A_4T + \dots$$

Using only a three parameter fit to eq. 2 the empirical constants  $A_1$ ,  $A_2$ , and  $A_3$ , see Table 2 for H<sub>2</sub>O and Table 3 for D<sub>2</sub>O were calculated

		ΤΑΒ	BLE 4. Ki	netic solve	ent isotope	effect as a	function	of tempera	ture				
	k.s.i.e. at												
Substrate	0 °C	5 °C	10 °C	15 °C	20 °C	25 °C	30 °C	35 °C	40 °C	45 °C	50 °C	55 °C	60 °C
Acetic anhydride*	2.837	2,892	2.927	2.941	2.937	2.916	2.878						
Propionic anhydride*	3.188	3.024	2.903	2.818	2.764	2.737	2.736	2.757	2.801	2.866	2.954		
Benzoic anhydride			3.658	3.445	3.279	3.151	3.053	2.985	2.941	2.917	2.917	2.934	2.970
Succinic anhydride	2.579	2.633	2.676	2.709	2.733	2,748	2.754	2.753	2.744			_	
Phthalic anhydride	2.257	2.314	2.335	2.319	2,272	2.197	_		_	_	_		
Methyl trifluoroacetate	3.645	3.600	3.555	3.511	3,468	3.426							

\*Data included from (1).

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TABLE 5. Pseudothermodynamic parameters of activation for solvolysis of acyl carbon in H<sub>2</sub>O at 25 °C

Substrate	$\frac{10^3 k^0}{(s^{-1})}$	$\Delta H^{\pm}$ (cal mol <sup>-1</sup> )	$-\Delta S^{\pm}$ (cal deg <sup>-1</sup> mol <sup>-1</sup> )	$-\Delta C_p^{+}$ (cal deg <sup>-1</sup> mol <sup>-1</sup> )
Benzoic anhydride	0,4021	10195+37	39.88 + 0.12	$\frac{5+3}{5+3}$
Succinic anhydride	2,829	$12493 \pm 41$	$28.30 \pm 0.14$	$20 \pm 4$
Phthalic anhydride	10.47	11668 + 274	$28.46 \pm 0.94$	124 + 16
Methyl trifluoroacetate	8.025	8 893 + 141	38.30 + 0.49	85 + 8
Ethyl trifluoroacetate*	3.29	11 530	35	67
Acetic anhydride†	2.6	9 600	38	74
Propionic anhydride†	1.5	9 510	40	31

\*Reference 5. †Reference 1.

TABLE 6. Pseudothermodynamic parameters of activation for solvolysis of acyl carbon in D<sub>2</sub>O at 25 °C

Substrate	$10^{3} k^{0}$ (s <sup>-1</sup> )	$\Delta H^{+}$ (cal mol <sup>-1</sup> )	$-\Delta S^{\dagger}$ (cal deg <sup>-1</sup> mol <sup>-1</sup> )	$\frac{-\Delta C_p^{+}}{(\text{cal deg}^{-1} \text{ mol}^{-1})}$
Benzoic anhydride Succinic anhydride Phthalic anhydride Methyl triffuoroacetate	0.1276 1.030 4.767 2.343	$ \begin{array}{r} 11 \ 451 \ \pm \ 90 \\ 12 \ 356 \ \pm \ 59 \\ 13 \ 081 \ \pm \ 91 \\ 9 \ 323 \ \pm \ 51 \end{array} $	$\begin{array}{r} 37.95 \pm 0.30 \\ 30.76 \pm 0.20 \\ 25.29 \pm 0.31 \\ 39.30 \pm 0.17 \end{array}$	$59 \pm 5 \\ -1 \pm 7 \\ 28 \pm 7 \\ 83 \pm 5$

for each reaction and could be used to recalculate smoothed curve values of  $k^0$  at 5° intervals throughout the experimental temperature range. While a fourth term in T might seem to be desirable formally, the accuracy of the rate data did not justify such an extension. The kinetic solvent isotope effect, k.s.i.e.  $= k_{H_2O}^0/k_{D_2O}^0$ , was determined as a function of temperature, see Table 4.

An error estimate in k.s.i.e. values is provided by assuming that the error in each individual observed  $k^0$  values was  $\pm 0.25\%$ , then the same error was appropriate for the smoothed curve  $k^{0}$  values. Consequently an error estimate on k.s.i.e. values would be  $\pm 0.5\%$  or less.

A formal interpretation of the temperature effect on  $k^0$  in terms of transition state assumptions permits the calculation of pseudo-thermodynamic quantities from the empirical constants  $A_1$ ,  $A_2$ , and  $A_3$  (17). The enthalpy,  $\Delta H^{\dagger}$ , entropy,  $\Delta S^{*}$ , and heat capacity of activation,  $\Delta C_{p}^{*}$ , for each reaction is given in Table 5 for  $H_2O$  and in Table 6 for  $D_2O$ .

# Discussion

Where comparisons are possible, our values of k.s.i.e. and of  $\Delta H^{\pm}$  and  $\Delta S^{\pm}$  for the hydrolysis of anhydrides agree with those published previously and lie in the range expected for a  $B_{Ac}2$ mechanism (18-22). However, because we have examined the temperature dependence of the rate in both  $H_2O$  and  $D_2O$ , it is evident that these k.s.i.e. values, like those for acetic and propionic anhydrides (1), do not decrease smoothly with increasing temperature (see Fig. 1) as had been found in the hydrolysis of halides (2), sulfonyl chlorides (23), nitrates (24), and alkyl trifluoroacetates (5); the last presumably reacting by a  $B_{Ac}2$  mechanism.

This departure from linearity was not uniform; the plot of log (k.s.i.e.) vs.  $10^3/T$  for benzoic and acetic anhydrides passing through minima, while that for succinic and phthalic, like that for propionic anhydride, passed through flat maxima. Winter and Scott (5) had determined k.s.i.e. for methyl, ethyl, and isopropyl trifluoroacetate at three temperatures and had found an apparent linear decrease with temperature. We have determined the rate of hydrolysis for methyl trifluoroacetate over a wider range of temperatures in both  $H_2O$  and  $D_2O$  and found no evidence of departure from linearity of the above plot. The slope (0.88) being about the same as that found by the previous investigators.

Further empirical evidence of differences in the detailed mechanism of hydrolysis of the anhydrides and of the alkyl trifluoroacetates becomes apparent if we compare the nominal values of the temperature coefficient of the enthalpy of activation  $(\Delta C_p^*)$  for the two series

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TABLE 7. Kinetic solvent isotope effects as pseudothermodynamic differences\*

for solvolysis of acyl carbon at 25 °C  $\delta_1 \Delta C_p^*$ (cal deg<sup>-1</sup> mol<sup>-1</sup>)  $\delta_1 \Delta H^+$  $\delta_1 \Delta S^{\dagger}$ Substrate (cal mol<sup>-1</sup>)  $(cal deg^{-1} mol^{-1})$  $-0.91\ \pm\ 0.22$  $42 \pm 6$ Acetic anhydride  $362 \pm 64$ 

 $-1.40 \pm 0.38$ 

 $1.93 \pm 0.42$ 

Succinic anhydride	$-137 \pm 100$	$-2.46 \pm 0.34$
Phthalic anhydride	$1413 \pm 365$	$3.17 \pm 1.25$
Methyl trifluoroacetate	430 ± 192	$-1.00 \pm 0.66$

179 ± 113

 $1256 \pm 127$ 

\*By definition  $S_{I}\Delta X^{\ddagger} = \Delta X^{\ddagger}{}_{D_{2}O} - \Delta X^{\ddagger}{}_{H_{2}O}$ 

Propionic anhydride

Benzoic anhydride



FIG. 1. The effect of temperature on the kinetic solvent isotope effect: (1) methyl trifluoroacetate, (2) benzoic anhydride, (3) acetic anhydride, (4) propionic anhydride, (5) succinic anhydride, (6) phthalic anhydride.

in light and heavy water. The values of  $\delta_1 \Delta C_p^{\dagger}$ (Table 7) found for the anhydrides are seen to be large and variable while the corresponding term for the methyl trifluoroacetate is less than the combined experimental error. The latter condition is normal for the hydrolysis of alkyl halides (2) and is found also for the ionization of acetic acid  $\Delta C_p^{0} = -36.6$  cal deg<sup>-1</sup> mol<sup>-1</sup> in H<sub>2</sub>O and -38.6 cal deg<sup>-1</sup> mol<sup>-1</sup> in D<sub>2</sub>O (25). The difference for the autoprotolysis of water is somewhat larger,  $\Delta C_p^{0} = -47$  cal deg<sup>-1</sup> mol<sup>-1</sup> in H<sub>2</sub>O and -55 cal deg<sup>-1</sup> mol<sup>-1</sup> in D<sub>2</sub>O (26). These



 $-63 \pm 12$  $-54 \pm 8$ 21 ± 11

96 ± 23

 $2 \pm 13$ 

FIG. 2. A comparison of  $\delta_I \Delta H^{\pm} vs. T \Delta S^{\pm}$  values for a series of anhydrides and methyl trifluoroacetate: (1) a series of aninytrides and mentyl transference (3) acetic anhydride, 25 °C; (2) propionic anhydride, 25 °C; (3) benzoic anhydride, 25 °C; (4) phthalic anhydride, 25 °C; (5) succinic anhydride, 25 °C; (6) methyl trifluoroacetate, 25 °C; (7) acetic anhydride, 15 °C; (8) propionic anhydride, 35 °C.

relatively small differences bear but accidental resemblance to those recorded in Table 7.

We could discern no relationship between the variation in  $\delta_I \Delta H$ ,  $\delta_I \Delta S^{\dagger}$ , or  $\delta_I \Delta C_p^{\dagger}$  and the  $pK_a$  of the derived acids. However, it was found that if  $\delta_{I}\Delta H^{\dagger}$  was plotted against  $T\delta_{I}\Delta S^{\dagger}$ , (see Fig. 2), the values for benzoic and phthalic anhydride (the aromatic anhydrides) are separated from values for the saturated members along the usual linear plot and this in spite of the fact that k.s.i.e. for the benzoic anhydride is the highest and the k.s.i.e. for the phthalic anhydride is among the lower values. In the  $\delta_1 \Delta H^{\dagger}$  vs.  $T \delta_1 \Delta S^{\dagger}$  plot, the point for succinic anhydride, also cyclic, is found with the saturated anhydrides. The differences noted probably relate in some way to the effect of conjugation between the phenyl and carboxyl group and such factors as

the approach of the nucleophilic water and solvation of the charged transition state but the exact relationship is not clear.<sup>2</sup>

One other observation, as yet unexplained, is that whereas k.s.i.e. decreases from 2.9 to 2.6 on passing from pure water to 40 vol% dioxane for acetic anhydride, and an even larger decrease occurs for methyl trifluoroacetate, benzoic anhydride shows a slight increase (20). While the decrease can be rationalized in terms of a decrease in water structure obviously the same argument will not apply for an increase. Since we are comparing results from various laboratories some allowance must be made for error, but the presence of a remarkable difference can hardly be doubted.

The changes in k.s.i.e. with T and in  $\delta_{I}\Delta C_{p}^{*}$ may be related. If the  $\Delta C_p^{+}$  is more negative in D<sub>2</sub>O than in H<sub>2</sub>O which might well be expected from a simple interpretation of the effect of temperature on the water structures, then k.s.i.e. would be expected to decrease as temperature increases. This in fact is found even though  $\delta_{I}\Delta C_{p}^{+} \rightarrow 0$  under normal conditions e.g., the case of the trifluoroacetates, Fig. 1. However, the decrease in k.s.i.e. with temperature for benzoic anhydride is far steeper than a  $\delta_{I}\Delta H^{*}$ argument would require and points to an unusual influence. Moreover it should be noted that the extrema which characterize the log (k.s.i.e.) vs.  $10^3/T$  plots for the anhydrides (Fig. 1) would not arise simply from the temperature effects on solvent structure. Some temperature dependent mechanistic change must occur which is dependent on the structure of the anhydride, the properties of D<sub>2</sub>O and H<sub>2</sub>O, and the wide range of mechanistic differences presently included under the definition of general acid base catalysis.

The relationship between structure and mechanism for general base catalyzed reactions has been investigated and discussed previously (21, 27-30) but not in terms of the distinction made evident in this paper. Here, a study of the temperature dependence of the k.s.i.e. and  $\Delta H^{*}$ reveals characteristic differences attributable to differences in mechanism even though both series insofar as conventional tests go, hydrolyze by the same  $B_{Ac}2$  mechanism (if we regard the mechanism for *t*-butyl trifluoroacetate and similar compounds as exceptional (5)).

One possible hypothesis would be the intrusion of various degrees of nucleophilic attack by OH<sup>-</sup> or indeed the direct attack of H<sub>2</sub>O in competition with general base catalyzed mechanism. Such a hypothesis is inconsistent with the fact that the reaction is pH-independent over the experimental range of temperature. Nor would a hypothesis based on the incursion of some degree of nucleophilic interaction appear to be satisfactory (31). Of course, competing reactions with different values of  $\Delta H^{\dagger}$  will give rise to changes in  $\Delta C_p^{\dagger}$  which may seem unusual (32, 33, 39). Winter and Scott (5) have shown that a change in mechanism from  $B_{Ac}2$  to  $S_N1$  probably does occur in the case of the alkyl trifluoroacetates, but this change is signalled by a dramatic change in the k.s.i.e. and in  $\Delta H^{\pm}$  and  $\Delta S^{\pm}$ . Such changes are not at all evident as between the anhydrides and the trifluoroacetates under investigation here. Rather we are faced by a more subtle temperature dependent distinction.

$$CH_3 - C - O - X + 2H_2O \xrightarrow{1}$$

$$\begin{bmatrix} O \\ CH_3 - C - O - X \\ \vdots \\ O - H - OH_2 \\ H \end{bmatrix} \xrightarrow{Q - C} CH_3 - C - O - X \xrightarrow{3} \\ \vdots \\ O + H_3 O^+ \\ H \\ H \end{bmatrix}$$



SCHEME 1. Generalized  $B_{Ac}^2$  mechanism for neutral hydrolysis (27).

<sup>&</sup>lt;sup>2</sup>One referee drew attention to the possibility of differences arising from initial state differences as a possible contributing factor here. Such a possibility is difficult to disprove or to prove but we do not consider it a strong possibility. The major contribution to  $\Delta C_p^+$  appears to arise in the vicinity of the anion and further appears to arise from solvation changes localized near the seat of reaction. For example,  $\Delta C_p^+$  for the hydrolysis of both methanesulfonyl chloride and benzenesulfonyl chloride are the same (-55 cal deg<sup>-1</sup> mol<sup>-1</sup>).

If we accept Scheme 1 (27) as approximating the  $B_{Ac}^2$  mechanism then it might seem remarkable that complex temperature dependency was not observed in all cases and in fact the hydrolysis of the trifluoroacetates actually represent some kind of limiting case. We know that the latter (34-36) as well as the benzoic anhydride give evidence of <sup>18</sup>O exchange to a much greater degree than acetic anhydride, for example. However, if the rate of return  $k_{-1}$  and product formation,  $k_2$ , are fast compared to the rate at which the two oxygens become equivalent by proton transfer, significant <sup>18</sup>O exchange may not be observed. Support for such a possibility may be seen in the fact that the k.s.i.e. and the large negative values of  $\Delta S^{\dagger}$  are very similar for both series while significant differences in <sup>18</sup>O are observed. Bunton, Fuller, Perry and Shiner (21) proposed a pre-equilibrium involving a charged intermediate, as shown above, followed by partitioning between a pathway leading to a dihydroxy intermediate, admitting <sup>18</sup>O exchange, expulsion of the leaving group, and return to starting reactants. In attempting to account for the k.s.i.e. found for the spontaneous hydrolysis of acetic anhydride Bunton and Shiner (37, 38) show that differences in hydrogen bonding to such an intermediate so far exceed hydrogen bonding in bulk water as to account for observed k.s.i.e. values. It is an interesting fact that the same arguments applied to the prediction of the k.s.i.e. for methyl trifluoroacetate gave a value of 2.7, far closer to that obtained by Winter and Scott (5) and to our value for methyl trifluoroacetate, than the value which they used for comparison (21). While we regard their calculation as an oversimplification, we agree with the rather obvious principle on which it is formulated *i.e.*, that where electronic displacements develop centers of high local acidity or basicity, there will be an increase in the strength of the hydrogen bonds between these centers and the solvent water molecules.

These results point to questions which deserve further study. There is the remarkable difference in the temperature dependence of the k.s.i.e. found for the trifluoroacetates and for the anhydrides, both of which are considered to react by a  $B_{Ac}^2$  mechanism but which, on the basis of this evidence must differ in some significant manner. There is the difference in the temperature dependence of the same ratio among the various anhydrides as well as the existence of remarkable differences in the *apparent*  $\Delta C_p^{+}$  values. There is the unprecedented difference in the *apparent*  $\Delta C_p^{+}$  value for the various anhydrides in D<sub>2</sub>O and H<sub>2</sub>O, a fact which points to complexities in the mechanism of neutral solvolysis of the anhydrides not present in the hydrolysis of the alkyl trifluoroacetates.

The differences in  $\Delta C_p^{+}$  values in H<sub>2</sub>O and D<sub>2</sub>O for the anhydride and trifluoroacetate series are not inconsistent with the important similarities which have led to both series being classed as reacting by general base catalysis (29). Whether this reaction is to be regarded as a single dominating concerted process (39, 40) or several stages involving pre-equilibria has been argued by several authors (27–29). We find no good reason to reject the formation of an intermediate of variable lifetime. That the trifluoroacetates are a better leaving group than the weak acid anions is accepted and this difference provides both for the difference in temperature dependency and in <sup>18</sup>O-exchange.

Scott and Robertson (41), in studying the effect of an intermediate on derived temperature coefficients for the hydrolysis of t-butyl chloride showed for the general mechanism

$$A \xrightarrow[k_2]{k_2} B \xrightarrow[k_4]{k_4} C$$

where

[5]

[6]

[4]

$$k_{obs} = \frac{k_1}{1 + \frac{k_2}{k_2}} = \frac{k_1}{1 + \alpha}$$

that for the region I where  $\alpha < 0.01$ 

 $\Delta C_p^{\dagger}_{calc} = \Delta C_{p_1}^{\dagger}$ 

and for region III where  $\alpha > 100$ 

[7] 
$$\Delta C_{p}^{*}_{calc} = \Delta C_{p_1}^{*} - \Delta C_{p_2}^{*} + \Delta C_{p_3}^{*}$$

For the intermediate region II where  $0.01 < \alpha < 100$  a much more complicated expression results *viz* 

[8] 
$$\Delta C_{\text{calc}}^{\dagger} = \Delta C_{p_1}^{\dagger} + \frac{\alpha}{\alpha + 1} (\Delta C_{p_{2n}}^{\dagger} - \Delta C_{p_2}^{\dagger}) - \frac{\alpha}{(1 + \alpha)^2} \frac{(\Delta H_{2n}^{\dagger} - \Delta H_2^{\dagger})^2}{RT^2}$$

The spurious heat capacity term on the r.h.s. will always be positive, hence will act to reduce  $\Delta C_{p}^{\dagger}_{calc}$  and  $\Delta C_{p_3}^{\dagger} - \Delta C_{p_2}^{\dagger}$  will probably be positive. Further complications arise since  $\alpha$  will be temperature dependent.

In principle such a scheme could provide the basis for understanding the differences in  $\Delta C_p^*$  characteristics between the alkyl trifluoroacetates and the anhydrides, and the differences within these series. Queen (42) has used pre-equilibria and partitioning to account for the more extreme changes in  $\Delta H^*$  with temperature found for the hydrolysis alkyl chloroformates some of which, like the above, display general characteristics of the  $B_{Ac}^2$  mechanism.

The above scheme provides for complex changes in  $\Delta C_p^{\pm}$  depending on the solvent, and on the electronic nature of the reactants. As we have shown already, these can lead to differences in k.s.i.e. with changing temperature where  $\delta_{I}C_{p}^{+}$  is large. In this connection there is a related factor which deserves comment. In an investigation of the hydrolysis of substituted benzenesulfonyl chlorides (43) it was found that the  $\Delta C_p^{\dagger}$  for the *p*-methoxy member was less negative than expected by comparison with other members of the series. This was attributed to a temperature dependent interaction of the water with the methoxy group, an effect which increased with increasing temperature as the equilibrium in cooperative water structure moved toward a greater number of unbonded water molecules (44). In support of this working hypothesis we noted that  $\Delta C_p^{\dagger}$  for the hydrolysis of 2-chloro-2methoxymethylpropane was 18 cal mol<sup>-1</sup> deg<sup>-1</sup> more positive than the corresponding value for *t*-butyl chloride. The  $\Delta C_p^0$  for the ionization of 4-methoxybenzoic acid was more negative than the value for other benzoic acids (45), the change in sign in the latter case being consistent with this hypothesis and the electronic requirements as applied to the benzoic acid system. Recently Koshy (20) found values of  $\Delta C_p^{\pm}$  for the hydrolysis of 3-methoxybenzyl nitrate in accord with this hypothesis. This same temperature dependent solvation effect must surely be present in the general base catalyzed hydrolysis involving displacement from esters, anhydrides and acid chlorides where hydrogen bonding is important. In the trifluoroacetate system  $\Delta C_p^{\pm}$  becomes less negative by 16 cal mol<sup>-1</sup> deg<sup>-1</sup> on changing from Me  $\rightarrow$  Et and at isopropyl (for which no

 $\Delta C_p^*$  is available) the  $\Delta H^*$  and  $\Delta S^*$  values resemble those for  $B_{Ac}^2$  displacement, while at *t*-butyl, the reaction is  $S_N^1$  (5). These changes clearly follow changes in electron density on the ether oxygen with increasing solvation and decreased positive charge on the carbonyl carbon. A similar trend is apparent in the chloroformate series studied by Queen (42). Phenyl and methyl chloroformates appear to have an intermediate in which  $\alpha$  lies outside the midrange while ethyl and propyl show large changes in  $\Delta C_p^*$  with temperature. For isopropyl chloroformate mixed mech-

anism is suspected while for *t*-Bu—O—C—Cl the reaction is claimed to be  $S_N 1$ . These changes in the alkyl group have a direct effect on the hydrogen bonding of the ether - oxygen and these effects are reflected in changes in  $\Delta C_p^{\pm}$ ,  $\Delta H^{\pm}$ , and in mechanism. The changes noted above were in the leaving group and the consequences in terms of mechanism were marked. Similar changes adjacent to the carbonyl carbon can change the mechanism from  $B_{Ac} 2$  to  $S_N 2$  or  $S_N 1$ (4, 42). These too represent extremes.

The results reported here for the anhydrides do not show such wide variation in  $\Delta H^{\pm}$ ,  $\Delta S^{\pm}$  or in k.s.i.e. as reported by Scott and Winter and by Queen but rather, differences best explained in terms of changing solvation with temperature combined with related changes in partitioning. If the structure of acetic anhydride in solution is similar to that in the gas phase (46) the ether oxygen is exposed to potential hydrogen bonding before, and in the activated state. Models suggest similar comments apply to other anhydrides. The influence of potential hydrogen bonding on the leaving group is thus a factor which may vary with the degree of bond breaking at the transition state, and as between H<sub>2</sub>O and D<sub>2</sub>O.

Summarizing the above qualitative arguments, we attribute the unusual temperature dependence of the k.s.i.e. to temperature dependent solvation effects and to the related effect on partitioning both of which are made evident by surprising differences in the temperature coefficients of  $\Delta H^{\pm}$ in H<sub>2</sub>O and D<sub>2</sub>O. The difference in the basicity of the leaving group probably contributes to an important degree to the rate of formation of the intermediate and breakup of same. Our results reveal an unexpected problem. We trust they may contribute to its solution.

- 1. R. E. ROBERTSON, B. ROSSALL, and W. A. REDMOND. Can. J. Chem. 49, 3665 (1971).
- 2. R. E. ROBERTSON. Prog. Phys. Org. Chem. 4, 213 (1967).
- L. TREINDL, R. E. ROBERTSON, and S. E. SUGAMORI, Can. J. Chem. 47, 3397 (1969).
- P. M. LAUGHTON and R. E. ROBERTSON. Solutesolvent interactions. *Edited by* J. F. Coetzee and C. D. Ritchie. Marcel Dekker, New York. 1969. Chapt. 7.
- 5. J. G. WINTER and J. M. W. SCOTT. Can. J. Chem. 46, 2887 (1968).
- 6. W. P. JENCKS. Prog. Phys. Org. Chem. 2, 63 (1964).
- I. HEILBRON. Dictionary of organic compounds. 4th ed. Eyre and Spottiswoode, London. 1965.
- A. J. VOGEL. Practical organic chemistry. Longman, London. 1967. p. 381.
- 9. E. A. GUGGENHEIM. Phil. Mag. 2, 538 (1926).
- R. A. ROBINSON and R. H. STOKES. Electrolyte solutions, 2nd ed. Butterworth, London. 1959. p. 518.
- 11. E. L. WEHRY and L. B. ROGERS. J. Am. Chem. Soc. 88, 351 (1966).
- 12. G. D. PINCHING and R. G. BATES. J. Res. Nat. Bur. Standard, 45, 322 (1950).
- R. A. ROBINSON, M. PAABO, R. G. BATES. J. Res. Nat. Bur. Standard, 73A, 299 (1969).
- 14. H. J. HAMER, G. D. PINCHING, and S. F. ACREE. J. Res. Nat. Bur. Standard, **35**, 539 (1945).
- A. L. HENNE and C. J. Fox. J. Am. Chem. Soc. 73, 2323 (1951).
- C. K. RULE and V. K. LAMER. J. Am. Chem. Soc. 60, 1974 (1938).
- 17. E. C. W. CLARKE and D. N. GLEW. Trans. Faraday Soc. 62, 539 (1966).
- 18. M. L. BENDER. Chem. Rev. 60, 53 (1960).
- 19. W. P. JENCKS and J. CARRIOLO. J. Am. Chem. Soc. 83, 1743 (1961).
- 20. A. R. BUTLER and V. GOLD. J. Chem. Soc. 2305 (1961).
- 21. C. A. BUNTON, N. A. FULLER, S. Y. PERRY, and V. J. SHINER, JR. J. Chem. Soc. 2918 (1963).
- 22. J. KOSKIKALLIO, D. PAULI, and E. WHALLEY. Can. J. Chem. 37, 1360 (1959).
- 23. R. E. ROBERTSON, B. ROSSALL, S. E. SUGAMORI, and L, TREINDL, Can. J. Chem. 47, 4199 (1969).

- 24. K. M. KOSHY and R. E. ROBERTSON. Can. J. Chem. 52, 2485 (1974).
- 25. R. GARY, R. G. BATES, and R. A. ROBINSON. J. Phys. Chem. 69, 2750 (1965).
- 26. A. K. COVINGTON, R. A. ROBINSON, and R. G. BATES. J. Phys. Chem. 70, 3820 (1966).
- 27. A. KIVINEN. Suomen Kemistilehti, B38, 159 (1965).
- 28. S. L. JOHNSON. Advan. Phys. Org. Chem. 5, 237 (1967).
- 29. W. P. JENCKS and M. GILCHRIST. J. Am. Chem. Soc. 90, 2622 (1968).
- T. C. BRUICE and U. K. PANDIT. J. Am. Chem. Soc. 82, 5858 (1960).
- J. F. KIRSCH and W. P. JENCKS, J. Am. Chem. Soc., 86, 837 (1964).
- 32. J. R. HULETT. Quart Rev. London, 18, 227 (1964).
- 33. G. KOHNSTAM. Advan. Phys. Org. Chem. 5, 121 (1967).
- 34. C. A. BUNTON, T. A. LEWIS, and D. R. LLEWELLYN. Chem. Ind. 11, 54(1954).
- 35. C. A. BUNTON and T. HADWICK, J. Chem. Soc. 3248 (1958).
- H. LUDENHEIM and M. L. BENDER, J. Am. Chem. Soc. 82, 1895 (1960).
- C. A. BUNTON and V. J. SHINER, JR. J. Am. Chem. Soc. 83, 42 (1961).
- C. A. BUNTON and V. J. SHINER, JR. J. Am. Chem. Soc. 83, 3207 (1961).
- 39. J. KOSKIKALLIO. Acta. Chem. Scand. 13, 665 (1959).
- J. HIPIN and D. P. N. SATCHELL, J. Chem. Soc. 1057 (1965).
- 41. J. M. W. SCOTT and R. E. ROBERTSON. Can. J. Chem. 50, 167 (1972).
- 42. A. QUEEN. Can. J. Chem. 45, 1619 (1967).
- 43. R. E. ROBERTSON and B. ROSSALL. Can. J. Chem. 49, 1441 (1971).
- 44. G. NEMETHY and H. A. SCHERAGA, J. Chem. Phys. 36, 3382 (1962).
- 45. J. W. LARSEN and L. G. HEPLER. In Solute-solvent interactions, *Edited by* J. F. Coetzee and C. D. Ritchie. Marcel Dekker. New York. 1969. Chapt 1.
- 46. H. J. V. LEDDER, F. C. MIJILHOFF, J. C. LEYTE, and C. ROMERS. J. Mol. Struct. 7, 421 (1971).

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