

Studies in solvolysis. Part I. The neutral hydrolysis of some alkyl trifluoroacetates in water and deuterium oxide

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Received March 5, 1968

The temperature dependence of the rates of neutral hydrolysis of a series of alkyl trifluoroacetates (CF_3COOR ; R = methyl, ethyl, *s*-propyl, *t*-butyl) has been determined in both light and heavy water. From these studies the thermodynamic parameters (ΔH^\ddagger , ΔS^\ddagger) which characterize the activation process have been calculated. Sufficient rate data have been obtained in the case of the ethyl ester to calculate the heat capacity of activation (ΔC_p^\ddagger) for the hydrolysis of this compound in light water. Both the entropies and enthalpies of activation as well as the solvent isotope effects are consistent with the proposal that the primary and secondary esters react by an acyl-oxygen $\text{B}_{\text{Ac}2}$ mechanism, in contrast to the tertiary ester, which appears to react either by a carbonium ion ($\text{S}_{\text{N}}1$) process or by a route which combines both the $\text{B}_{\text{Ac}2}$ and $\text{S}_{\text{N}}1$ paths.

Canadian Journal of Chemistry, 46, 2887 (1968)

Introduction

The rate of neutral or spontaneous hydrolysis of simple alkyl esters related to the halogenoacetic acids has frequently been studied (1-11), although no systematic body of rate data is currently available concerning the reactivity of these substances in pure water and deuterium oxide. The present study surveys the temperature dependence of the rates of hydrolysis in pure water and deuterium oxide of four esters derived from trifluoroacetic acid (CF_3COOR ; R = Me, Et, *s*-Pr, and *t*-Bu).

On the basis of ^{18}O tracer studies Bunton and Hadwick (8) have concluded that the spontaneous hydrolysis of methyl trifluoroacetate in pure water takes place by an acyl-oxygen fission mechanism ($\text{B}_{\text{Ac}2}$). On the other hand, Moffat and Hunt (1) consider that *t*-butyl trifluoroacetate reacts in acetone-water mixtures by a carbonium ion ($\text{S}_{\text{N}}1$) mechanism since the extent of olefin formation in this reaction is similar to that produced by the *t*-butyl halides reacting in the same media. These separate observations suggest that a change in mechanism ($\text{B}_{\text{Ac}2} \rightarrow \text{S}_{\text{N}}1$) is to be anticipated in the hydrolysis reactions of the series of trifluoroacetates mentioned above. A further aim of the present study was to locate the point or region of mechanistic change using the thermodynamic parameters (ΔG^\ddagger , ΔH^\ddagger , ΔS^\ddagger , and ΔC_p^\ddagger), as well as the ratio of the rates of hydrolysis of each substrate in light and heavy water.

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Experimental

General

Nuclear magnetic resonance (n.m.r.) spectra were recorded on a Varian A-60 spectrometer and peaks are recorded on the τ scale relative to tetramethylsilane as an internal reference. Carbon tetrachloride was used as a solvent. Infrared spectra were recorded on a Perkin-Elmer model 225 spectrometer using the liquid cell technique with solvent carbon tetrachloride.

Materials

The methyl and ethyl trifluoroacetates were Fluka A.G. purum grade and were distilled prior to use. The *s*-propyl and *t*-butyl trifluoroacetates were prepared from the corresponding alcohols and trifluoroacetic anhydride in the presence of a small amount of silver trifluoroacetate (12). The boiling points and refractive indices agreed with the literature values (1-3, 12) and saponification values indicated that the esters were better than 98% pure. The τ values and carbonyl stretching frequencies for these esters are recorded in Table I. The excellent first order plots obtained from the kinetic studies also demonstrate the kinetic homogeneity of each sample used.

Solutions

(a) Light Water

Solutions in the range 10^{-5} - 10^{-4} M of each ester were prepared by injecting the appropriate volume of

TABLE I
Physical properties of some esters
derived from trifluoroacetic acid

Ester	Nuclear magnetic resonance (τ)	Infrared $\nu(\text{C}=\text{O})$ (cm^{-1})
—Me	6.02	1788
—Et	8.58, 5.54	1784 (1786)*
— <i>s</i> -Pr	8.64, 4.83	1787
— <i>t</i> -Bu	8.45	1782 (1777)*

*Literature values in parentheses are given in ref. 12.

ester from a micro syringe into stirred cells of a design similar to that originally described by Hyne and Robertson (13). The cells had been previously filled with backing electrolyte which was prepared by allowing a suitable amount of the appropriate substrate to react with deionized water so as to reduce the initial resistance of the solution to a convenient value. In situations where supersaturation was prevalent, a saturated solution of the appropriate ester was prepared at the required temperature. An aliquot of this solution (1 ml) was then withdrawn and injected into a suitable volume of backing electrolyte already in the cell.

(b) *Heavy Water*

Deuterium oxide (ca. 11) was obtained from Atomic Energy of Canada and was used several times with no appreciable decrease in purity. Solutions were prepared as for light water. Following each set of runs the contaminated heavy water was redistilled from a small amount of anhydrous sodium carbonate in an all glass apparatus. Subsequent analysis of the distillate using n.m.r. with purified acetonitrile as an internal standard, showed that the hydrogen content of the solvent collected from these distillations did not exceed 0.5% by weight.

Rate Measurements

The rate measurements were made using the conductance method, based on the Guggenheim treatment (14) in a form originally elaborated by Robertson (15). The equipment that was used was essentially that described in ref. 15 with minor modifications (16). Temperatures were measured by means of a Tinsley platinum resistance thermometer and bridge. The former was calibrated by the National Physical Laboratory, Teddington, England.

The excellence of the Guggenheim-Robertson Method (G.R.M.) for determining solvolytic rates in pure water is now well established in cases where the acid related to the leaving group is strong (14). Since trifluoroacetic acid is relatively weak, ($pK_a = 0.23^2$ at 25 °C (18)) the use and validity of the G.R.M. in this study requires further comment. For strong acids the reliability of the G.R.M. rests on the existence of a linear relationship between the conductance and concentration of the acid in a given reaction vessel. In the case of a weak acid (because of incomplete dissociation), this may not be correct and a quantitative assessment of the possible influence on this factor is required.

Ives (20) has suggested that the classical Ostwald Dilution Law stated in terms of conductance parameters, in a form which neglects the effect of ionic strength on both the activity and mobility of the ions of the weak electrolyte, accurately represents the variation of the equivalent conductance of the weak electrolyte as a function of concentration at high dilution ($< 10^{-4} M$). For our present purpose Ives' proposal means that the variation of the equivalent conductance (Λ) of the weak electrolyte with concentration (C) is accurately represented by the equation

$$[1] \quad 1/\Lambda = 1/\Lambda_0 + \Lambda C/K_c \Lambda_0^2$$

²An alternative pK_a value of -0.26 has been quoted for trifluoroacetic acid by O. Redlich and G. C. Hood (19). There appears to be some uncertainty concerning the pK_a of this acid.

where Λ_0 is the limiting equivalent conductance of the weak electrolyte and K_c is the classical dissociation constant which has not been corrected for either the variation of activities or mobilities with ionic strength. The equivalent conductance Λ is related to the experimental parameters by the equation

$$[2] \quad \Lambda = 10^3 K/RC$$

where R is the resistance, in ohms, of a solution of the electrolyte containing C moles/l in a cell of cell constant K .

Combining eqs. [1] and [2] gives after some manipulation

$$[3] \quad C = P/R + P^2/K_c R^2$$

where P is defined by the equation

$$[4] \quad P = 10^3 K/\Lambda_0$$

This latter quantity at a fixed temperature will be a constant, for a given electrolyte and reaction vessel (cell). Equation [3] shows that the simple relationship between the concentration of the acid and the reciprocal of the resistance used by Robertson (15) for strong acids, is modified in the case of a weak acid by a further term $P^2/K_c R^2$.

The Guggenheim equation for the evaluation of the pseudo first order rate constant in a solvolysis experiment is

$$[5] \quad C_{t+\tau} - C_t = C_0 \exp -kt [1 - \exp (-k\tau)]$$

where $C_{t+\tau}$ is the concentration of the product (acid) at time $t+\tau$ and C_t is the concentration at time t ; C_0 is the initial concentration of ester, k is the pseudo first order rate constant and τ is the arbitrary time interval between the two sets of observations required in a Guggenheim first order rate constant determination. Combining eqs. [3] and [5] gives after some manipulation

$$[6] \quad \log (1/R_{t+\tau} - 1/R_t) + \frac{\log [1 + P(1/R_{t+\tau} + 1/R_t)/K_c]}{= \log C_0 [1 - \exp (-k\tau)]/P - kt/2.3026}$$

Since the first term on the RHS of eq. [6] is a constant in any given experiment, a plot of $\log (1/R_{t+\tau} - 1/R_t)$ versus time will only be linear if the second term on the LHS of eq. [6] is negligible. If, Λ_0 and K_c for the weak acid are known it is possible to calculate the magnitude of this particular term and hence estimate the importance of the second term in eq. [6]. A typical calculation of this sort is displayed in Table II (see columns 6 and 7). The effect of the second term on the LHS of eq. [6] is clearly very small and well outside the limits of reproducibility offered by the G.R.M. (see ref. 17).

A further requirement of any precise determination of a rate constant is that this parameter should be constant over the complete reaction. Since the hydrolyses of trifluoroacetates are known to be acid catalyzed (6-8) it was important to demonstrate that no autocatalysis occurred with the present systems. The G.R.M. requires at least three half-lives for the determination of a rate constant since the parameters $R_{t+\tau}$ and R_t are each observed over the period of one half-life ($t_{1/2}$) and ideally the interval between the two sets of observations should satisfy the condition $\tau > 2t_{1/2}$. This means that the rate constants as usually determined represent at least 87.5% of a complete reaction. This period was deliberately extended in

TABLE II

Typical calculation for the determination* of a first order rate constant using eq. [6], $T = 14.95^\circ\text{C}$

Time (s)	R_t	$R_{t+\tau}$	$(1/R_{t+\tau} - 1/R_t) \times 10^5 = D$	$(1/R_t + 1/R_{t+\tau})P/K_c + 1 = M$	$\log D$	$\log D + \log M$
0	7710.0	4173.0	10.993	1.0003	4.0401	4.0402
41	7170.0	4137.5	10.222	1.0003	4.0095	4.0096
80	6760.0	4107.0	9.5558	1.0004	5.9803	5.9805
119	6410.0	4079.5	8.9122	1.0004	5.9500	5.9502
161	6100.0	4052.2	8.2845	1.0004	5.9183	5.9185
202	5840.0	4027.4	7.7066	1.0004	5.8869	5.8871
240	5630.0	4006.2	7.1993	1.0004	5.8573	5.8575
280	5440.0	3985.8	6.7067	1.0004	5.8265	5.8267
321	5270.0	3966.6	6.2352	1.0004	5.7949	5.7951
360	5130.0	3949.4	5.8271	1.0004	5.7655	5.7657
401	5000.0	3933.0	5.4259	1.0004	5.7345	5.7347

* $P = K \times 10^3/\Lambda_0$ calculated from $\Lambda_0(\text{CF}_3\text{COOH})^* = 332$ and $K_c = 0.652$, $K = 0.1966$; cell constant obtained via a solution of known equivalent conductance. The former parameters were extrapolated to 15°C using data from ref. 21.

TABLE III

Rates of hydrolysis of ethyl trifluoroacetate

T ($^\circ\text{K}$)	$k_{\text{obs}} \times 10^4$ (n)*	$k_{\text{calcd}} \times 10^4$ (s^{-1})	$k_{\text{obs}} - k_{\text{calcd}}$
273.34	6.120 ± 0.027 (4)	6.093	+0.027
274.26	6.524 ± 0.018 (4)	6.545	-0.021
275.54	7.193 ± 0.010 (5)	7.230	-0.037
276.16	7.565 ± 0.008 (4)	7.579	-0.014
277.03	8.134 ± 0.023 (5)	8.094	+0.040
278.14	8.772 ± 0.027 (4)	8.788	-0.016
279.14	9.489 ± 0.044 (4)	9.463	+0.026
280.10	10.14 ± 0.01 (4)	10.15	-0.01
281.14	10.90 ± 0.05 (4)	10.93	-0.03
282.13	11.75 ± 0.04 (4)	11.72	+0.03
283.11	12.53 ± 0.03 (5)	12.56	-0.03
284.17	13.49 ± 0.06 (4)	13.50	-0.01
285.15	14.54 ± 0.02 (4)	14.44	+0.10
286.11	15.39 ± 0.06 (4)	15.40	-0.01
287.14	16.53 ± 0.05 (4)	16.49	+0.06
288.11	17.57 ± 0.05 (4)	17.57	0.00
289.14	18.70 ± 0.07 (4)	18.78	-0.08
290.12	20.04 ± 0.07 (4)	20.00	+0.04
291.17	21.31 ± 0.07 (4)	21.36	-0.05
292.16	22.80 ± 0.06 (5)	22.71	+0.09
293.18	24.16 ± 0.06 (4)	24.18	-0.02
294.21	25.55 ± 0.05 (4)	25.73	-0.18
295.18	27.35 ± 0.12 (4)	27.27	+0.08

* n = number of separate runs at given temperature.

the present study by measuring the resistances of a reacting solution over four separate half-lives and observing the resistances at identical time intervals. The separation between the individual sets of observations was small, i.e. as soon as one set of measurements was complete the next set was started. From the four sets of resistances obtained in this way, three rate constants may be obtained and one of these covers at least 93.3% of the reaction. The average rate constant from the four sets of observations was $1.762 (\pm 0.004) \times 10^{-3} \text{ s}^{-1}$. This particular experiment confirms that there is no perceptible acid catalysis in these reactions and that the linear relationship between the conductance and the concentration of the product (acid) is valid over the range of substrate concentrations used.

The rate constants which have been measured in light and heavy water for the esters ($R = \text{Me, Et, } s\text{-Pr, and } t\text{-Bu}$) are recorded in Tables III and IV, together with the r.m.s. deviation obtained from 'n' separate large scale first order plots. For the ethyl ester the temperature dependence of the rates could be expressed within the experimental error by the equation

$$[7] \log k = -6439.0409/T - 32.7141 \log T + 100.0558$$

The numerical coefficients in eq. [7] were established by a least squares treatment (the individual rates were used; not the average experimental rates reported in Table III), and were converted to the thermodynamic quantities ΔH_0^\ddagger , ΔS_0^\ddagger , ΔC_p^\ddagger , ΔH^\ddagger , and ΔS^\ddagger , using the procedure originally proposed by Robertson (17) (see Table VI).

The temperature dependence of the methyl, *s*-propyl, and *t*-butyl esters over a shorter temperature interval reacting in light water was adequately represented by the equation

$$[8] \log k/T = A/T + B$$

and the same equation was also used to represent the temperature dependence of each ester reacting in heavy water. Values of A and B for each ester were determined by a least squares procedure (without averaging the individual rate constants at each temperature) and converted to the thermodynamic parameters ΔH^\ddagger and ΔS^\ddagger via the relationships,

$$[9] A = -\Delta H^\ddagger/2.3026R$$

and

$$[10] B = \Delta S^\ddagger/2.3026R + \log(k/h)$$

The symbols R , k , and h in eqs. [9] and [10] have their usual significance. The enthalpies and entropies of activation calculated in this way are detailed in Table V for both light and heavy water. The $k(\text{H}_2\text{O})/k(\text{D}_2\text{O})$ ratios for each ester are reported in Table IV and are probably accurate to ca. $\pm 1.0\%$.

Discussion

Relative Rates — Free Energies of Activation

It is generally accepted that free energies of activation provide the most useful parameters

TABLE IV
Rate constants and isotope effects for the solvolysis of trifluoroacetates in water and deuterium oxide

Ester	T (°C)	$k(\text{H}_2\text{O}) \times 10^4$ (s ⁻¹) (n)	$k(\text{D}_2\text{O}) \times 10^4$ (s ⁻¹) (n)	$k(\text{H}_2\text{O})/$ $k(\text{D}_2\text{O})^*$
—Me	4.98	23.09 ± 0.10 (4)	6.486 ± 0.008 (4)	3.54
	9.96	32.80 ± 0.05 (4)	9.420 ± 0.027 (4)	3.51
	14.95	46.42 ± 0.13 (3)	13.24 ± 0.05 (4)	3.48
—Et	4.98	8.777 ± 0.026 (4)	2.390 ± 0.009 (4)	3.67
	9.96	12.53 ± 0.04 (5)	3.468 ± 0.010 (4)	3.60
	14.95	17.57 ± 0.05 (4)	4.956 ± 0.017 (4)	3.54
— <i>s</i> -Pr	4.98	2.433 ± 0.008 (4)	0.6339 ± 0.019 (4)	3.83
	9.96	3.494 ± 0.012 (3)	0.9194 ± 0.028 (5)	3.79
	14.95	4.864 ± 0.022 (4)	1.296 ± 0.002 (4)	3.74
— <i>t</i> -Bu	4.98	0.5723 ± 0.030 (3)	0.4623 ± 0.030 (3)	1.24
	9.96	1.296 ± 0.004 (4)	1.076 ± 0.008 (4)	1.21
	14.95	2.915 ± 0.012 (3)	2.450 ± 0.007 (3)	1.19

*Values calculated from rate constants which have been smoothed using eq. [8].

TABLE V
Thermodynamic parameters for the solvolysis of trifluoroacetates in water and deuterium oxide (derived from the rates reported in Table IV)

Ester	ΔH^\ddagger (H ₂ O) (kcal/mole)	ΔH^\ddagger (D ₂ O) (kcal/mole)	ΔS^\ddagger (H ₂ O) (e.u.)	ΔS^\ddagger (D ₂ O) (e.u.)
—Me	10.60 ± 0.03	10.48 ± 0.05	-32.3 ± 0.3	-34.0 ± 0.4
—Et	10.53 ± 0.03	11.08 ± 0.03	-34.5 ± 0.3	-35.1 ± 0.3
— <i>s</i> -Pr	10.51 ± 0.05	10.87 ± 0.05	-37.1 ± 0.6	-38.5 ± 0.7
— <i>t</i> -Bu	25.44 ± 0.06	26.08 ± 0.05	13.7 ± 0.5	15.5 ± 0.0

TABLE VI
Thermodynamic parameters for the hydrolysis of ethyl trifluoroacetate in water at various temperatures

T (°K)	ΔH_T^\ddagger (kcal/mole)*	ΔS_T^\ddagger (e.u.)*
273.16	11.16	-32.2
298.16	9.486	-38.1
323.16	7.811	-43.5
348.16	6.137	-48.5
373.16	4.462	-53.1

*Calculated using the usual thermodynamic expressions with $\Delta C_p^\ddagger = -66.95$ cal mole⁻¹ deg⁻¹.

for discussing the influence of structure on the reactivity of organic molecules and much has been written to substantiate this point of view (22–26). The present series of solvolytic substrates would appear to offer an interesting exception to this principle. Thus the relative rates of hydrolysis of the four esters follow the sequence Me > Et > *s*-Pr > *t*-Bu at 3.37 °C and give an acceptable Taft (27) linear free energy relationship at this temperature (see Fig. 1).

This correlation suggests that a common mechanism is operating and that the reactivities of the esters are dominated by the inductive effect of the alkyl group. Further inspection, however, reveals that these ideas are untenable.

Thus extrapolation of the rates of solvolysis to 25 °C gives a sequence of reactivity Me > Et > *t*-Bu > *s*-Pr leading to the breakdown of the Taft correlation for the tertiary ester (see Fig. 1). Moreover, the sequence of reactivity observed at 3.37 °C is typical of S_N2 processes but the range of reactivity is rather small when compared with better established S_N2 reactions (28). On the other hand, the trend in reactivities at 25 °C is typical of an S_N2–S_N1 sequence with the change in mechanism occurring in the region of the *s*-Pr ester, but again the range of reactivity is relatively small. However, these mechanistic conclusions based solely on relative rates are inconsistent with the H₂¹⁸O and olefin production studies mentioned in the introduction. These latter experiments are best interpreted in terms of acyl–oxygen fission for the methyl ester

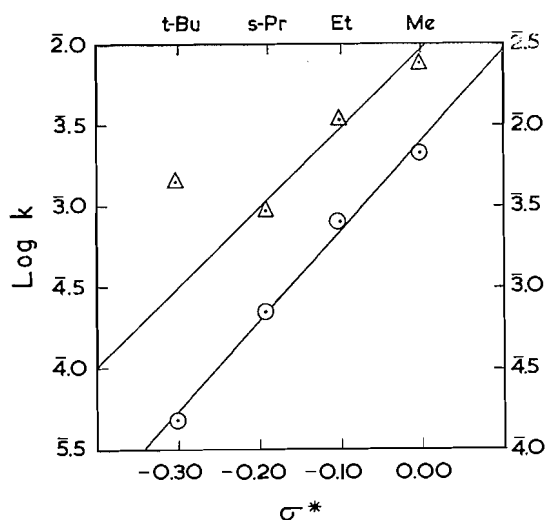


FIG. 1. Correlation of rates of hydrolysis of alkyl trifluoroacetates with the Taft σ^* parameter. Δ extrapolated rates at 25 °C; \circ extrapolated rates at 3.73 °C; the scale on right hand side is for rates at 25 °C.

and alkyl oxygen fission (S_N1 ?)³ for the tertiary ester. The point of change in mechanism ($B_{Ac}2 \rightarrow S_N1$) for the complete series of substrates clearly remains to be established.

The observation that the rates of hydrolysis of a series of ethyl esters derived from a sequence of halogenoacetic acids decrease as the pK_a of the related acid increases (see Table VII), suggests that nucleophilic attack at the carbonyl carbon is the main driving force for the ethyl

TABLE VII

Rates of neutral hydrolysis of a series of ethyl esters related to acetic acid

Ester	pK_a^*	k (s^{-1} at 25 °C)
CF_3COOEt	0.23 (-0.26)	$3.29 \times 10^{-3}\dagger$
CCl_3COOEt	0.65	$2.41 \times 10^{-4}\dagger$
CHF_2COOEt	1.24	$8.7 \times 10^{-5}\S$
$CHCl_2COOEt$	1.29	$7.7 \times 10^{-6}\S$
CH_3COOEt	2.86	$1.7 \times 10^{-7}\S$

*Taken from ref. 18, value in parentheses from ref. 19.

\dagger This work.

\S Reference 29.

\S From ref. 4, with a rough correction for ionic strength effects.

³The possibility of a mechanistic trichotomy has not been overlooked. If mixed kinetics is a valid concept it is feasible to assume that the tertiary ester might react by three routes, i.e. $B_{Ac}2$, S_N1 , and S_N2 . The problem of deciding between the S_N1 - S_N2 description for the tertiary ester is outside the scope of the present study but the problem is recognized. The incursion of a mixed $B_{Ac}2$ - S_N1 process will, however, be discussed here below.

esters and we therefore conclude that ethyl trifluoroacetate also reacts by the $B_{Ac}2$ mechanism. This is the limit of useful information which can be gleaned from a consideration of relative rates alone, but we wish to emphasize again that without ancillary information, these quantities are mechanistically ambiguous.

Enthalpies and Entropies of Activation

If the free energies of activation prove to be mechanistically equivocal, the same cannot be said of the entropies and enthalpies of activation. These parameters fall into two distinct categories, the primary and secondary esters which have enthalpies of activation which are virtually constant at 10.5 kcal/mole, and the entropies of activation which are relatively constant in the vicinity of 35 e.u. The second category is provided by the tertiary ester which shows dramatic changes from the parameters listed above. For this ester the enthalpy of activation is ca. 15 kcal/mole higher than that observed for the primary and secondary esters and the entropy of activation is ca. 50 e.u. more positive. The above considerations are consistent with the $B_{Ac}2$ description for the primary and secondary esters and alkyl-oxygen fission (S_N1) for the tertiary ester. The actual magnitude of the enthalpies and entropies of activation are also comparable with the 'average values' of thermodynamic parameters which characterize these two mechanisms (for a detailed discussion, see refs. 30, 31, and 16).

Solvent Isotope Effect

Further substantiation of these mechanistic conclusions obtained from the response of ΔH^\ddagger and ΔS^\ddagger to structure is provided by the solvent isotope effect (s.i.e.) studies. Thus the primary and secondary esters give s.i.e. ratios in the range 3.4-3.8, which have predicted to be characteristic of spontaneous $B_{Ac}2$ processes (32). On the other hand, the tertiary ester gives a s.i.e. ratio of 1.2 which is typical of a wide range S_N1 - S_N2 substrates studied by Laughton and Robertson (33-36). The s.i.e. is considered to be a rather blunt tool for distinguishing between S_N1 and S_N2 solvolytic processes (37). The data in Table V shows that the s.i.e. arises from concomitant changes in both the enthalpies and entropies of activation, but any attempt to rationalize such a dissection of the isotope effect would seem premature. These observations

do, however, suggest that the zero-point energy model used by Bunton and Shiner (32) is oversimplified. Some further points concerning the solvent isotope effects are discussed in the section (given below) dealing with heat capacities of activation.

The Heat Capacities of Activation

The heat capacity of activation for ethyl trifluoroacetate ($-66.95 \text{ cal mole}^{-1} \text{ deg}^{-1}$) approximately bisects the range of values ($-30 \rightarrow -100 \text{ cal mole}^{-1} \text{ deg}^{-1}$) obtained by Laughton and Robertson (33) and others (38) who have measured this parameter in water and mixed solvents for a wide range of solvolytic substrates and attempted to use it to build a more complete description of solvolytic displacement reactions. A detailed understanding of the magnitude of the heat capacity of activation for any particular substrate seems out of the question at the present time, but several qualitative points arising from the present study are worthy of mention. Since the evidence presented above indicates that the ethyl ester solvolyses by a $B_{AC}2$ mechanism it is clear that heat capacities of activation alone will not distinguish between this path and the S_N1-S_N2 type mechanisms. However, it may be possible to distinguish between the $B_{AC}2$ mechanism and the S_N1-S_N2 type via ΔC_p^\ddagger within a series of trifluoroacetates. A decision with regard to this matter must await further work in progress in the laboratory.

The strongly negative entropies and heat capacities of activation which appear to characterize the $B_{AC}2$ process (30) suggest that activation involves the cooperation of several solvent molecules. Similar proposals with regard to the composition of the activated complex have been put forward for S_N1-S_N2 reactions although the entropies of activation for these substrates may be both positive and negative (17) contrasting with the heat capacity of activation, which is invariably negative. The latter presents some rather awkward interpretative problems. It has been cogently argued (37) that the magnitude and sign of the heat capacity of activation is primarily a consequence of the variable heat content of the initial state solvation shell which is generally expected to show a maximum stability as the interaction of the water envelope with the substrate decreases. This rather curious conclusion is a consequence of the peculiar properties of aqueous solutions of neutral

molecules. Substances which contain no lyophilic groups, e.g. carbonyl or sulfoxide, induce the solvent to interact more strongly with itself and form a stronger 'iceberg'. Those substrates which contain hydrogen bonding groups such as those mentioned above, tend to reduce the stability of the 'iceberg' by providing centers of interaction between the solvent and solute, which partially 'liberates' the surrounding water molecules from the 'frozen' structure of the water in the immediate vicinity of the substrate. Arguments of this kind provide a qualitative explanation of the more positive heat capacities of activation observed for the sulfonates as compared with the halides (39). However, the heat capacity of activation for ethyl trifluoroacetate is approximately $30 \text{ cal mole}^{-1} \text{ deg}^{-1}$ more negative than the sulfonates although both series of compounds evidently contain hydrogen-bonding groups. This is presumably a consequence of an intrinsically more negative heat capacity of activation for the $B_{AC}2$ mechanism, and this proposal is in line with the shift in the entropy of activation between the sulfonates (17) and structurally related trifluoroacetates.

For the S_N1-S_N2 solvolytic displacements Robertson and Laughton (40) have proposed that the magnitude of the s.i.e. is a manifestation of the same factors which determine the magnitude of the heat capacity of activation, i.e. the stability of the initial state solvation shell.⁴ Thus the more positive heat capacities of activation of the sulfonates compared with the halides correlate with a reduced s.i.e. for the former series of compounds. The limited heat capacity data reported here do not confirm this correlation since a marked increase in the s.i.e. which characterizes the $B_{AC}2$ mechanism is accompanied by only a moderate shift in the heat capacity of activation.

It is worth pointing out at this juncture that if solvent isotope effects are to be rationalized in terms of zero-point energies (32) the statistical theory of equilibria vitiates any fundamental correlation between the s.i.e. and ΔC_p^\ddagger since zero-point energies make no contribution to heat capacities.

Some Further General Comments

In the present communication we have attempted to assign the mechanism of four rate

⁴For another point of view, however, see refs. 41 and 42.

processes on the basis of the thermodynamic parameters and solvent isotope effects which characterize the thermal activation of these molecules. We are fully aware of the limitations of such a procedure and in the present section we wish to examine these limitations more closely. Although the response of ΔH^\ddagger and ΔS^\ddagger to structural changes in the present series of substrates is marked, the question arises as to just how different such parameters must be before a change in mechanism can be legitimately inferred. We are forced to the conclusion that there is no satisfactory answer to this question at the present time and it must be admitted that without the product and tracer studies mentioned earlier in this paper the present data would only be marginally convincing. Taken together, however, the two types of evidence make the case for a change in mechanism that much stronger. The possibility that the tertiary ester reacts by a mixed $B_{AC}2/S_N1$ mechanism cannot be ruled out. Bunton and Hadwick (7) have shown that benzhydryl trifluoroacetate has an activation energy which increases with temperature and the present data for the tertiary ester also manifests an activation energy which increases with temperature, but the range of temperatures studied is too small to warrant any definite conclusion concerning this matter at the present time. If this trend is verified by future studies which are now underway, then the thermodynamic parameters reported for the tertiary ester will not be appropriate to a single process. Nevertheless, a change of mechanism in these circumstances is still evident but the change is not complete. Such a description is consistent with the sensitivity of the Taft correlation to temperature.

There are several reasons for expecting a change of mechanism in the hydrolysis reaction of the four esters studied. The most important of these is the increased stability of the trimethyl carbonium ion compared with the corresponding carbonium ions derived from the primary and secondary esters. However, other factors will tend to decrease the stability of the transition state for the $B_{AC}2$ process as the size of the alkyl group increases. The formation of a tetrahedral intermediate (43) will involve a decrease in the CF_3 -alkyl group distance and this would be expected to raise the energy of the transition state in the order $t\text{-Bu} > s\text{-Pr} > \text{Et} > \text{Me}$. Although the inductive effect of the alkyl groups

is attenuated by the intervening oxygen atom, this effect will also follow the steric effect mentioned above and will raise the energy of the transition state by reducing the positive charge at the carbonyl carbon atom. All of the factors mentioned above will decrease the stability of the $B_{AC}2$ transition state with increasing α -methylation and it is reasonable to deduce that alkyl-oxygen fission becomes an important reaction path for the tertiary ester.

Acknowledgments

We wish to thank the Technical Services Division at Memorial University, especially Mr. W. Gordon and Mr. R. Parsons, for their help in the construction of the apparatus. We also wish to express our gratitude to Dr. R. E. Robertson for arranging the construction of the conductance cells and to Mr. M. Jones for assisting with the least squares calculation. Finally our thanks are offered to the National Research Council of Canada for financial assistance and one of us (J. G. W.) acknowledges the award of an NRCC postgraduate bursary.

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