

On the Accuracy and Significance in Determination of the Temperature Dependence of Activation Energy in Neutral Ester Hydrolysis and Solvolytic Substitution Reactions

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Various experimental methods (conductometry, spectrophotometry, titrimetry and polarimetry) employed for the accurate rate determinations required in the investigation of the temperature dependence of activation energy are discussed. A conductometric method which requires only simple apparatus in addition to an accurate conductometer and a reaction cell is described. The theoretical non-linearity between the degree of reaction and conductance, caused by the effect of ionic strength in the case of strong electrolytes and by the changes in the degree of dissociation of weaker electrolytes, are shown to lead only to minor errors in the rate parameters, provided that the initial ester concentration is sufficiently low.

The neutral hydrolysis of methyl trifluoroacetate in 7 different dimethyl sulfoxide-water mixtures at a wide temperature range have been studied. For ΔC_p^\ddagger a precision better than $10 \text{ J mol}^{-1} \text{ K}^{-1}$ is achievable and reproducible. Further, it is concluded that ΔC_p^\ddagger , as the derivative of ΔH^\ddagger , gives information, *e.g.*, about solvent effects not available from ΔG^\ddagger , ΔH^\ddagger and ΔS^\ddagger alone.

It is well known that many solvolytic reactions do not exactly follow the Arrhenius equation. In this respect especially the S_N solvolyses of organic halides and sulfonates¹ and the neutral ester hydrolysis²⁻⁶ have been thoroughly studied. Recently Albano and Wold criticized the methods employed in these studies, questioning their accuracy⁷ and even their significance in general.⁸ As our experience of ester hydrolysis, gained during two decennaries, gives evidence of sufficient accuracy in such measurements and because we

believe that valuable new information, *e.g.*, on solvent structure can be obtained from them, we want to describe our experimental method, compare it with other methods, and consider the significance of such studies. In the following, we use the terminology of the transition-state theory and discuss the deviations from the Arrhenius equation in terms of the heat capacity of activation $\Delta C_p^\ddagger = d\Delta H^\ddagger/dT$ and its derivatives. In this connection we will not consider the question of whether they are caused by a true temperature dependence of activation energy or by a complex reaction mechanism nor how these phenomena are connected with solvent structure.

DETERMINATION OF RATE CONSTANTS

Conductometric method. The calculation of ΔC_p^\ddagger requires an accurate determination of rate constants over a large temperature range. Conductometry is by far the most commonly employed experimental method in this connection. The method requires that the conductance of the solution changes regularly during the reaction. This is the case in the hydrolysis of, *e.g.*, organic halides and sulfonates. Robertson *et al.*^{1a,9} have developed an accurate conductometric method widely employed for these solvolyses. In the case of the neutral hydrolysis of carboxylic esters, the method can be applied only in the case of esters like 1-haloalkyl carboxylates or alkyl trihaloacetates when a sufficiently strong acid is produced in the reaction.^{2,5,10,11}

In theory, the conductance G is proportional to $c\Lambda$ and is not a precisely linear function of the concentration c , because for dilute solutions of strong electrolytes as given by eqn. (1), the limiting

$$\Lambda/\Lambda_0 = 1 - (\alpha^* + \beta^*/\Lambda_0)\sqrt{c} \quad (1)$$

equivalent conductance Λ_0 depends on the solvent, electrolyte and temperature, and the coefficients α^* and β^* on the solvent and temperature.¹² If $(\alpha^* + \beta^*/\Lambda_0)\sqrt{c}$ is not $\ll 1$, an error is introduced into the rate constants calculated from conductances. On the basis of the available data for HCl in water¹² it can be estimated that the rate constants are less than 0.1 % too high, provided that the reaction is followed conductometrically as described in the Experimental section and that the initial ester concentration is $\leq 10^{-4}$ M. Further, the effect is quite similar at different temperatures and introduces to ΔC_p^{\ddagger} an error which is less than $0.5 \text{ J mol}^{-1} \text{ K}^{-1}$.

In the case of weaker acids also the changes in dissociation must be taken into account. The hydrolysis of chloromethyl dichloroacetate, extensively studied by us, produces equal amounts of hydrochloric and dichloroacetic acids. From the dissociation constants of dichloroacetic acid in water at different temperatures¹³ it can be calculated that its degree of dissociation varies between 0.999 and 0.997 during the reaction if the initial ester concentration is 10^{-4} M. With the aid of synthetic model runs, it can be estimated that the errors introduced to the rate constants and ΔC_p^{\ddagger} values are less than 0.1 % and $0.5 \text{ J mol}^{-1} \text{ K}^{-1}$, respectively. Trihaloacetic acids formed in the hydrolysis of alkyl trihaloacetates are moderately strong acids and thus almost wholly dissociated in dilute solutions. *E.g.*, from the ionization constant 0.23 for trichloroacetic acid in water at 298 K the value 0.9996 is obtained for its degree of dissociation in a 10^{-4} M solution. In accordance with the consideration by Winter and Scott,¹⁴ it can be concluded that also in this case the small variation in the degree of dissociation during the reaction does not affect the calculated rate parameters, including ΔC_p^{\ddagger} .

Although the use of sufficiently low concentrations of the reactant (10^{-4} M or below) usually precludes significant errors, it is possible that deviations from linearity between concentration and conductivity cannot be avoided, *e.g.*, in the case of weaker acids. The use of a calibration

procedure is then possible,^{10,11} but it makes the measurements more elaborate and may decrease the accuracy essentially. Our conductometric method, based on the use of low concentrations and an accurate conductometer, is described in the Experimental section.

According to Albano and Wold⁷ an important objection against the conductometric method is that "in order to get good results, the experimental solution must be buffered with salt to give a salt concentration which is almost constant during the reaction". However, the above considerations show that good results will be achieved by using sufficiently low substrate concentrations without salt buffering. Robertson *et al.*^{1a,15} have used salt solutions as backing electrolytes but the concentrations they used were only from 0.0001 to 0.003 M. In our case the only "salt buffering" has been caused by the electrolyte produced in the reaction and left in the cell after most of the solution was poured out without flushing, because in our experience a high salt concentration only decreases the accuracy. In their attempts to show the disadvantages of salt buffering, Albano and Wold employed a salt concentration of 0.2 M.⁷ Such buffering with salt really changes the structure of the solvent and thus makes the interpretation of the activation parameters obscure.

Spectrophotometric method. Spectrophotometric methods have only seldom been employed in ΔC_p^{\ddagger} determinations,^{16,17} evidently because accurate temperature control over a large temperature range is not easily achieved. If the substrate has a good chromophoric group, as vinyl and phenyl esters have, this method is useful although less accurate than the conductometric method; also similar initial concentrations can be used.

Titrimetric method. Analysis by titrating samples, taken at intervals from the reaction mixtures, has been employed by us for sufficiently slow reactions and was found to produce ΔC_p^{\ddagger} values which compare well with those obtained by other methods. Especially argentometric titration of halide ions from halomethyl esters was found to be useful.¹⁸

Polarimetric method. Albano and Wold⁷ employed a polarimetric method, which in principle has many advantages although its use is limited to optically active compounds and seems to require a high initial substrate concentration (0.2 M) which inevitably leads to major changes in the medium during the reaction.

Differential method. Albery and Robinson¹⁹

developed a differential method of measuring small differences in reaction rate which allows the variation of ΔH^\ddagger with T to be measured. Thus, values of ΔH^\ddagger could be found at different temperatures directly and ΔC_p^\ddagger could be obtained more accurately. This method was applied both in spectrophotometry and conductometry. The method seems not to have been applied later to ΔC_p^\ddagger determinations.

Calculation of rate constants. A prerequisite for accurate rate constants is that the kinetic form is known and that the rate equation is strictly obeyed. Solvolytic reactions mostly follow first-order kinetics, although, *e.g.*, the common ion effect in S_N1 solvolyses may lead to exceptions from it. Most often the integrated first-order eqn. (2) is used in the

$$k_t = \frac{1}{t} \ln \frac{c_0}{c_t} = \frac{1}{t} \ln \frac{y_0 - y_\infty}{y_t - y_\infty} \quad (2)$$

calculation of the rate constants. Here y can be any quantity directly proportional to the concentration c of the reactant or product. Because y_0 and y_∞ are included in every k_t value and are often the most inaccurate y values (*e.g.*, in the case of conductometry, adsorption or desorption may cause some drift in longer time periods thus effecting an error mostly in y_∞), their elimination is preferable. Adams and Sheppard²⁰ recommend non-linear least-squares fitting of data to an equation of the form $y = A - B e^{-kt}$. We have preferred Guggenheim's method,²¹ when also the possible errors in rate constants caused by the non-linearity between conductance and concentration are partly compensated. However, systematic errors may be masked in the calculated k value and lead to a too low error estimate. Therefore we always draw a large-scale plot of $\ln(y_{t+\Delta} - y_\infty)$ vs. t , if the calculated standard deviation of k exceeds 0.05%, and the run in question is rejected if any curvature can be seen. Albano and Wold⁷ have employed a "local determination of rate constants" using spline functions, but also it suffers from the fact that every k_t includes y_∞ (see eqn. (4) in Ref. 7).

If there is any drift in the calculated rate constants, *e.g.*, due to catalysis or retardation by reaction products, extrapolations are sometimes performed. They may cause diminished accuracy and even give erroneous rate constants. The extrapolations should be performed as similarly as possible for all of the constants to be compared with each other. When the temperature dependence is studied, the

extrapolation must be done from the same stages of the reaction, not from the same time intervals at different temperatures as Albano and Wold⁷ did, thus probably getting uncomparable and inaccurate k_0 values.

EXPERIMENTAL

Apparatus. Conductances were measured with a Beckman RC-18 Conductometer. The readings of conductances (G) in μS are indicated directly on decade dials and the accuracy is $\pm 0.05\%$ of the reading. The advantage of the conductometer used by us is its great accuracy, but it has the disadvantage that the compensation of capacitance changes and the balancing of the bridge must be made by hand. Thus very fast reactions ($t_{1/2} < 40$ s) cannot be measured. The times were measured with a Casio CQ-2 digital clock. The time accuracy was 0.1 s.

Since the aim of our work is to determine the temperature dependence of the rate with a great accuracy, the temperature stability and its measurement during the reaction are very important. At reaction temperatures from 273 K to 293 K the thermostat used was Lauda GP S15/17 and the bath was filled with glycol-water. The cooling was done by Lauda DLK 15. At higher temperatures the thermostat was Heto 02 PT 623 and the cooling, if necessary, was done with thermostated water; the bath was filled with water. The temperature was stable to about 0.01 K. Temperatures were measured with mercury thermometers graduated in hundredths of a degree and calibrated with a Hewlett-Packard quartz crystal thermometer.

Conductivity cell. The cell was a "glass bottle" with platinum electrodes (Fig. 1). The cell constant was about 1. Before use, electrocleaning was accomplished with HCl solution. Then the electrodes were platinized with a solution of hexachloroplatinic acid and lead acetate in distilled water so that the electrodes looked velvety black. Thereafter the reaction cell was treated with water or with the water-organic cosolvent mixture in which the ester was hydrolysed, to produce a similar concentration of ions as in the kinetic runs. When the cell was properly accommodated to reaction conditions it could be used repeatedly for the same ester and solvent composition without any salt buffering. The cell was never allowed to dry, and between the kinetic experiments the reaction solution was left in the cell.

Performance of kinetic measurements. Before beginning the reaction, 15 ml of the solvent was placed in the reaction vessel A (see Fig. 1) from where it was pumped into the cell B till it was full.

Table 1. Example of experimental data for the neutral hydrolysis of methyl trifluoroacetate in a dimethyl sulfoxide–water mixture with the mole fraction 0.973 of water at 298.19 K.

t/s	$G_t/\mu S$	$G_{t+\Delta}/\mu S^a$	t/s	$G_t/\mu S$	$G_{t+\Delta}/\mu S$
0.0	30.00	82.77	88.4	58.00	86.40
4.9	32.00	83.02	97.4	60.00	86.66
9.9	34.00	83.28	107.0	62.00	86.92
14.9	36.00	83.54	117.4	64.00	87.18
20.2	38.00	83.80	128.4	66.00	87.44
25.8	40.00	84.06	140.5	68.00	87.70
31.5	42.00	84.32	153.7	70.00	87.96
37.5	44.00	84.58	168.3	72.00	88.22
43.9	46.00	84.85	184.4	74.00	88.48
50.4	48.00	85.11	202.7	76.00	88.74
57.2	50.00	85.37	223.7	78.00	89.00
64.5	52.00	85.63	248.1	80.00	89.26
72.1	54.00	85.89	277.8	82.00	89.51
80.0	56.00	86.15			

$$^a \Delta = 290 \text{ s}; k = (7.018 \pm 0.002) \times 10^{-3} \text{ s}^{-1}.$$

The solvent was allowed to thermostate for 30 min at the reaction temperature and then sucked back into A. The neat ester or, in the case of sparingly soluble or highly volatile esters, its about 10% solution in acetonitrile or methanol was injected with a microsyringe into the reaction vessel below

the surface of the solvent so that the initial ester concentration was about 10^{-4} M or less. The solution was then shaken thoroughly and pumped to and fro between A and B. In the case of slightly soluble esters shaking and pumping were repeated. Finally B was filled with the reaction mixture. To

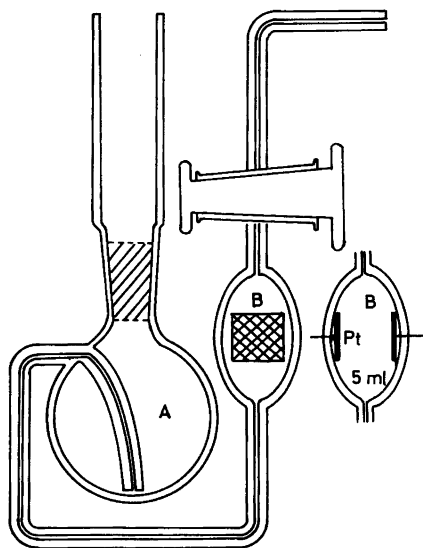


Fig. 1. The cell used in conductometric measurements. A is the reaction vessel and B the cell with platinum electrodes. Parts A and B are connected with a capillary tube so that diffusion is at minimum during the reaction.

Table 2. First order rate constants k for the neutral hydrolysis of methyl trifluoroacetate in a dimethyl sulfoxide–water mixture with the mole fraction 0.973 of water.

T/K	$10^3 k/s^{-1}$
273.22	1.3252 ± 0.0006
275.69	1.6106 ± 0.0004
278.16	1.9317 ± 0.0010
280.70	2.3261 ± 0.0007
283.22	2.7558 ± 0.0005
283.32	2.7785 ± 0.0004
285.44	3.2124 ± 0.0011
288.14	3.8269 ± 0.0010
290.61	4.493 ± 0.002
293.14	5.226 ± 0.002
295.81	6.121 ± 0.003
298.19	7.018 ± 0.002
300.78	8.108 ± 0.005
303.13	9.196 ± 0.007
305.73	10.576 ± 0.007
308.17	11.950 ± 0.005
310.77	13.631 ± 0.009
313.16	15.318 ± 0.008
315.68	17.200 ± 0.007

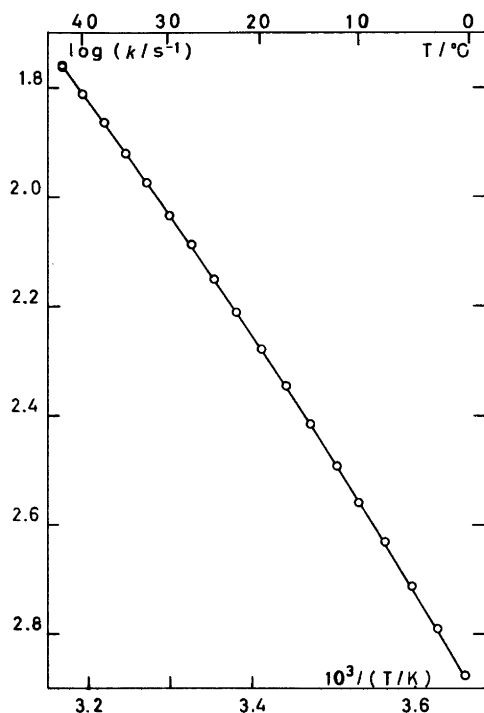


Fig. 2. Arrhenius plot for the neutral hydrolysis of methyl trifluoroacetate in a dimethyl sulfoxide–water mixture with the mole fraction 0.973 of water.

confirm the highest possible similarity between runs at different temperatures the conductance measurements were begun after about one half of the half-life of the reaction. The measurements were arranged for Guggenheim's calculation method²¹ so that the first period was 2.5 to 3 times the half-life of the reaction ($=\Delta$) and the successive conductance changes were constant. In the second period the timetable of the first period was followed as seen from the example presented in Table 1. The rate constants were calculated by the method of least squares, the error estimates being the standard deviations of k . The above-mentioned theoretical and other possible systematic errors are, of course, not included in this estimate.

Materials. Methyl trifluoroacetate (zur Synthese, E. Merck AG.) was distilled before use. Dimethyl sulfoxide (zur Analyse, E. Merck AG.) was a commercial product, which was used without further purification. The solvent mixtures were prepared by diluting a known weight of distilled water with dimethyl sulfoxide to a known volume in a volumetric flask at 293 K and the resulting solvent mixture was weighed.

Experimental data. The first-order rate constants for the hydrolysis of methyl trifluoroacetate in a dimethyl sulfoxide–water mixture are given in Table 2. It is seen that the standard deviations of the calculated rate constants vary from 0.014 to 0.076%. In general in our experiments they are found to be less than 0.05% but sometimes at higher temperatures about 0.1%.

CALCULATION AND ACCURACY OF ΔC_p^\ddagger

When the deviations from the Arrhenius equation are studied it is customary to measure accurate rate constants over as large a temperature range as possible at a high number of temperatures. From an Arrhenius plot one can control the regularity of the experimental points (as an example, see Fig. 2). Then an appropriate equation is fitted to the data employing a suitable calculation method, e.g., an extended Arrhenius equation,² eqn. (3), after

$$\ln k = A + B/T + C \ln T + DT + ET^2 + \dots + \varepsilon \quad (3)$$

orthogonalization by the method of Clarke and Glew.²² By studying the standard errors and residuals the suitability of the equation and the required number of parameters can be tested (cf. Table 3).

Albano and Wold⁷ measured the rate constants at 3 temperatures only. As there are then no degrees of freedom, the calculated value of ΔC_p^\ddagger is questionable and no true estimation of its accuracy is possible. Adams²³ has described a technique for assessing the stability of ΔC_p^\ddagger and $d\Delta C_p^\ddagger/dT$.

Blandamer *et al.*²⁴ have examined the temperature dependence of ΔC_p^\ddagger using a "new" equation, which is, in fact, the basic equation of the method of Clarke and Glew.^{2,22} By using in succession every experimental temperature as fixed, the equation was "capable of correctly sensing changes in ΔC_p^\ddagger with temperature". We fitted some synthetic data, calculated from eqn. (3) with 4 appropriately selected parameters, to their equation. A representative case is presented in Fig. 3. It can be seen, as already stated by Blandamer *et al.*,²⁴ that the method underestimates the true value of the temperature effect on ΔC_p^\ddagger , but in some cases it may be useful, although only of limited value. Being a linear equation, it is much simpler to use than eqn. (3) with 4 or 5 parameters. Because the error of ΔC_p^\ddagger calculated by the new method²⁴ arises

Table 3. Temperature range (K), number of kinetic runs, calculated values of k (s^{-1}), activation parameters ΔG^\ddagger ($J\ mol^{-1}$), ΔH^\ddagger ($J\ mol^{-1}$), ΔS^\ddagger ($J\ mol^{-1}\ K^{-1}$), ΔC_p^\ddagger ($J\ mol^{-1}\ K^{-1}$), and first two derivatives of the heat capacity of activation, $d\Delta C_p^\ddagger/dT$ ($J\ mol^{-1}\ K^{-2}$) and $d^2\Delta C_p^\ddagger/dT^2$ ($J\ mol^{-1}\ K^{-3}$) at 298.15 K in neutral hydrolysis of methyl trifluoroacetate in dimethyl sulfoxide–water mixture at the mole fraction x_{H_2O} of water.

A. (The present work)							
x_{H_2O}	0.984	0.973	0.951	0.920	0.849	0.790	0.681
Temperature range	273–316	273–316	273–321	273–338	273–338	273–338	273–338
Number of runs	25	19	22	30	27	28	35
$10^3 k$	7.588	7.010	6.049	4.831	2.750	1.571	0.450
ΔG^\ddagger	85120	85330	85680	86250	87650	89040	92130
ΔH^\ddagger	39590(20)	39560(40)	39020(40)	38840(40)	37770(30)	37370(40)	37990(50)
$-\Delta S^\ddagger$	152.7(1)	153.5(1)	156.5(1)	159.0(1)	167.3(1)	173.3(1)	181.6(2)
$-\Delta C_p^\ddagger$	245(4)	249(6)	272(6)	257(3)	233(3)	205(4)	179(4)
$d\Delta C_p^\ddagger/dT$	0.4(10)	4.5(11)	0.2(14)	-0.7(6)	-0.3(5)	0.2(7)	-0.7(7)
$d^2\Delta C_p^\ddagger/dT^2$	-0.2(4)	-0.2(4)	-1.0(4)	0.04(15)	0.1(1)	-0.2(2)	0.3(2)
B. (Cleve ²⁵)							
x_{H_2O}			0.950	0.920		0.790	0.681
Temperature range			268–328	268–338		268–348	268–348
Number of runs			9	12		18	12
$10^3 k$			6.04	4.83		1.57	0.468
ΔG^\ddagger			85700	86230		89050	92030
ΔH^\ddagger			39160(70)	38760(80)		37770(170)	38330(70)
$-\Delta S^\ddagger$			156.1(2)	159.2(3)		172.0(6)	180.1(3)
$-\Delta C_p^\ddagger$			270(8)	264(8)		229(15)	183(6)

mainly from the use of the “wrong equation”, it cannot be a true measure of the precision of ΔC_p^\ddagger as claimed by Albano and Wold.⁷

The calculated kinetic parameters for our experimental case are given in Table 3A. For the sake of comparison the corresponding data²⁵ obtained about ten years ago are given in Table 3B. It is seen that the independent new results obtained by the improved conductometric method are in good agreement with the older ones (differences in ΔC_p^\ddagger 2 to 7 $J\ mol^{-1}\ K^{-1}$), except in the mol fraction 0.790 of water. This small disagreement (difference in the ΔC_p^\ddagger values is 24 $J\ mol^{-1}\ K^{-1}$, sum of their standard deviations being 19 $J\ mol^{-1}\ K^{-1}$) may arise from the fact that the older data include two k values at 280.09 K which deviate more than usual (3%). Further, it is seen from Table 3 that the values of ΔC_p^\ddagger differ from zero at a very high level of probability (>0.999999 according to Student's t -test). On the other hand, only in one case $d\Delta C_p^\ddagger/dT$

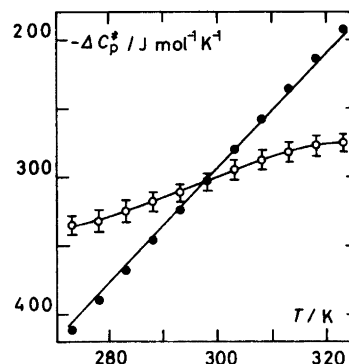


Fig. 3. Plots of ΔC_p^\ddagger vs. T for synthetic data ($\Delta C_p^\ddagger = -293\ J\ mol^{-1}\ K^{-1}$ at 298.15 K, $d\Delta C_p^\ddagger/dT = 4.184\ J\ mol^{-1}\ K^{-2}$; straight line). ○ Calculated with the aid of eqn. (7) in Ref. 24; standard deviations indicated by bars. ● Calculated by the method of Clarke and Glew²² with 4 parameters.

differs from zero at an 80% level. Therefore eqn. (3) with three parameters A, B and C, as modified by Clarke and Glew,²² was used. This situation is typical also in other cases studied by us. Another comparison of independent ΔC_p^\ddagger determinations can be obtained from the neutral hydrolysis of ethyl trichloroacetate in water: Kurz and Ehrhardt⁶ got the value $-230 \pm 4 \text{ J mol}^{-1} \text{ K}^{-1}$, which compares well with the value -238 ± 17 previously determined by Cleve.²⁶

DISCUSSION

We have developed a conductometric method which requires only simple apparatus in addition to an accurate conductometer or conductivity bridge. As manual operations are needed, the measurements are time-consuming and in fast reactions two operators are required. The rate coefficients calculated by Guggenheim's method are accurate, the standard deviation of k being about 0.05%. As usual in kinetic measurements, the reproducibility of k is lower, in extreme cases parallel runs may differ by 0.5%. The method compares, however, well with other conductometric methods and evidently is superior to other available kinetic methods for solvolytic reactions.

In our opinion, the best method for the calculation of the heat capacity of activation is that described by Clarke and Glew.²² It has been recently criticized,²⁴ but in principle it is entirely correct, if the reaction rate is controlled by one step. The numerical difficulties sometimes met have their basis in the fact that the small deviations from the Arrhenius equation (*cf.* Fig. 2), in an inevitable limited temperature range, do not allow accurate determination of too many parameters whatever the functional form is. Because experimental data always have random and often also systematic errors, the only way is to extend the temperature range and to make measurements at a high number of temperatures. Neutral ester hydrolysis is an advantageous object because of its low activation energy.

Our experience has led to the impression that for ΔC_p^\ddagger a precision better than $10 \text{ J mol}^{-1} \text{ K}^{-1}$ (*ca.* 2 cal mol⁻¹ K⁻¹) is achievable and reproducible. This is comparable with the accuracy obtained by Robertson *et al.* It is therefore sure that $\Delta C_p^\ddagger \neq 0$ for most solvolytic reactions and that the effects of temperature, structure of the reactant and composition of solvent mixture on ΔC_p^\ddagger can be

considered. Although the above discussion is in terms of ΔC_p^\ddagger , it is possible, on the basis of more complicated mechanistic models, to explain the found deviations from the Arrhenius equation without assuming that the activation energy of any single step depends on temperature.²⁷

Albano and Wold⁸ have performed a multivariate data analysis of ΔG^\ddagger and ΔH^\ddagger for solvolysis reactions in H₂O and D₂O and investigated the possibility to substitute ΔC_p^\ddagger by parameters derived from them. They claim that it is sufficient to use only ΔG^\ddagger and ΔH^\ddagger from runs in water to get the same information as from ΔC_p^\ddagger . Furthermore, they say that $\Delta G^\ddagger + \Delta H^\ddagger$ is correlated to ΔC_p^\ddagger and "that it is unnecessary to use the parameter ΔC_p^\ddagger to probe the solvent participation in hydrolysis reactions". Because of our interest in solvent effects, we have studied whether similar correlations could be found in these, too (Fig. 4). No simple correlation can be seen from the plots. It must also be noted that activation parameters have strongly different temperature dependences and therefore such plots will be of

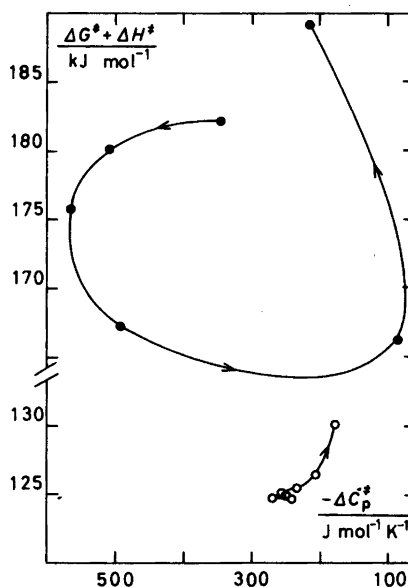


Fig. 4. Plots of $\Delta G^\ddagger + \Delta H^\ddagger$ vs. ΔC_p^\ddagger for the neutral hydrolysis of methyl trifluoroacetate in dimethyl sulfoxide-water mixtures with the mole fraction of water, $x_{\text{H}_2\text{O}}$, from 0.984 to 0.684 at 298.15 K (○) and for the solvolysis of *tert*-butyl chloride⁹ in isopropyl alcohol-water mixtures with $x_{\text{H}_2\text{O}}$ from 1 to 0.80 at 283.15 K (●).

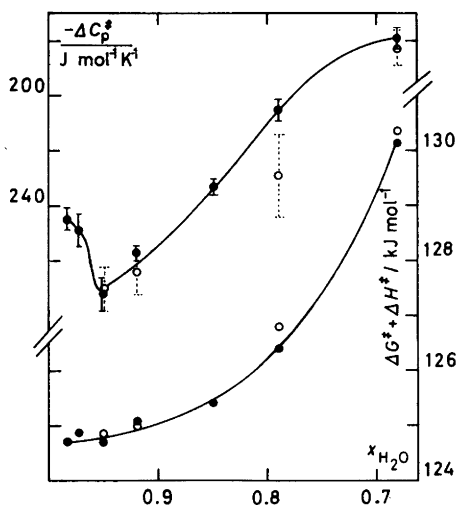


Fig. 5. Plots of ΔC_p^\ddagger and $\Delta G^\ddagger + \Delta H^\ddagger$ vs. the mole fraction of water, x_{H_2O} , for the neutral hydrolysis of methyl trifluoroacetate in dimethyl sulfoxide-water mixtures at 298.15 K: \circ Cleve,²⁵ \bullet this work.

variable complexity at different temperatures.²⁸ We therefore conclude that ΔC_p^\ddagger as the derivative of ΔH^\ddagger gives information that is not available from ΔG^\ddagger , ΔH^\ddagger and ΔS^\ddagger alone and we are convinced that ΔC_p^\ddagger is a more sensitive indicator of solvent effects than the other parameters (see Fig. 5). Unfortunately, it does not seem to be true that " ΔC_p^\ddagger is redundant and the demanding experiments for its determination are not necessary" and that "the difficulties in determining ΔC_p^\ddagger are avoided".⁸

Acknowledgement. A grant from the Emil Aaltonen Foundation to one of us (L.T.K.) is gratefully acknowledged.

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Received April 22, 1982.