Kinetic studies of neighbouring group participation in organic halides and sulphonates

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KINETIC STUDIES OF NEIGHBOURING GROUP PARTICIPATION IN ORGANIC HALIDES AND SULPHONATES

By

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MEMORANDUM

The work described in this thesis was carried out at the University of Durham, between September 1966 and July 1969. The thesis has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

The computer programs used in the calculation of most of the results were all written by Dr. G. Kohnstam.

Part of this work has been the subject of the following publication :

G. Kohnstam and M. Penty, in "Hydrogen-Bonded Solvent Systems", Taylor and Francis Ltd., London, 1968, p.275.

ABSTRACT

The effect of anchimeric assistance by neighbouring groups on the rates and products for the solvolysis of organic halides and sulphonates has been widely studied,[1] but the activation parameters of such internal nucleophilic substitutions (S_Ni) have received relatively little attention. This thesis describes experiments aimed at obtaining this information for the effect of neighbouring hydroxyl, methoxyl and phenyl groups on reactions with aqueous acetone. Compounds containing these substituents but reacting by the normal bimolecular mechanism (S_N2) were also examined, and data[2] for the unimolecular reactions (S_N1) of substrates with structurally similar reaction centres allowed a comparison to be made of the entropies and heat capacities of activation associated with these three mechanisms.

The chlorohydrins, $HO(CH_2)_nCH_2Cl$, (I; n = 1-5) showed the enhanced rates and the abnormal reaction products expected for the S_Ni mechanism when n = 3,4, as previously reported for reaction in water.[3] Entropies and heat capacities of activation for these compounds were intermediate between the values of the parameters for the solvolysis of structurally similar substrates by mechanisms S_N1 and S_N2.

The corresponding methoxy-bromides, $MeO(CH_2)_nCH_2Br$, (II; n = 1-5) showed very similar kinetic features when initial rates were measured, but subsequent reactions of the intermediate produced in the first step of the S_Ni process (n = 3,4) made it difficult to obtain rate coefficients with sufficient accuracy for the determination of accurate activation parameters. Similar results[4] had already been reported for the reactions of $MeO(CH_2)_nCH_2OBs$, (III; n = 1-5) but approximate rate coefficients could be assigned to the individual reaction steps in the present work.

Anchimeric assistance by a phenyl group in the reactions of $(C_6H_5)_3CCH_2Cl$ and $(C_6H_5)_3CCH_2OTs$ was accompanied by more positive activation parameters than in similar S_N1 and S_N2 reactions. The results allowed some estimate to be made of the effect of individual leaving groups on the values of the entropies and heat capacities of activation for reaction by mechanism S_Ni.

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CONTENTS

Page

CHAPTER 7.

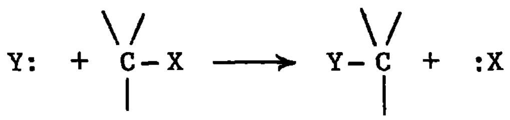
CHAPTER 1

INTRODUCTION

1.1 Nucleophilic Substitution Reactions

This thesis describes a study of the solvolytic reactions of selected organic chlorides, bromides and sulphonates in aqueous acetone. In each case the leaving group is attached to a saturated carbon atom and the reactions studied are nucleophilic substitutions.

A nucleophilic substitution (S_N)[1] at a saturated carbon atom is a heterolytic reaction, in which a group X (the leaving group) is displaced from the reaction centre by a reagent Y (the nucleophile) with transfer of a pair of electrons from Y to the reaction centre, and from the reaction centre to X. e.g.,



1.2 Mechanisms S_N1, S_N2 and S_Ni

Nucleophilic substitution reactions have for many years been considered to proceed by one of two reaction mechanisms, both of which were originally proposed and established by Hughes, Ingold and their co-workers:[1]

(a) The products may be formed in a single rate-determining step in which two molecules, the substrate and the nucleophile, undergo simultaneous covalency change. This reaction is bimolecular and designated S_N2. The mechanism can be written as:

$$Y + R{-}X \longrightarrow \underset{\text{(transition state)}}{\overset{\delta+}{Y} \text{-----} R \text{----} \overset{\delta-}{X}} \longrightarrow \overset{+}{Y}{-}R + X^-$$

(b) The second mechanism involves two stages. In the first and rate-determining step, the substrate, RX, ionises to give a highly reactive carbonium ion, R^+. This reacts rapidly with the nucleophile in a second step, to form the reaction products. In the rate-determining step only the substrate, RX, undergoes a covalency change and the reaction is therefore unimolecular and designated S_N1.

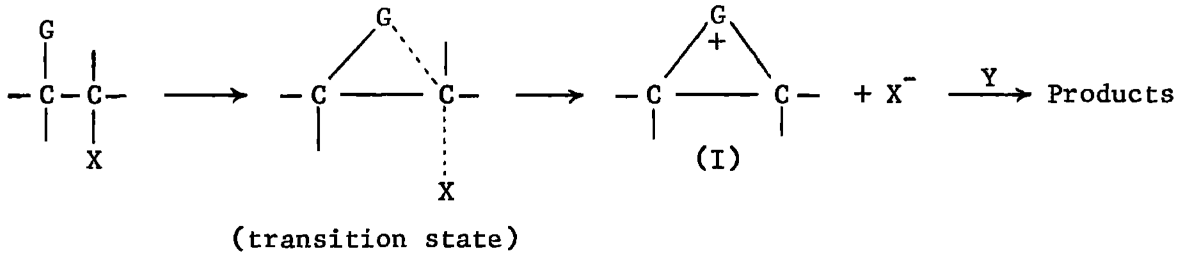
$$R\text{—}X \xrightarrow{\text{slow}} \underset{\text{(transition state)}}{R^{\delta+}\text{--------}X^{\delta-}} \longrightarrow R^+ + X^- \xrightarrow[\text{fast}]{Y} RY^+$$

Mechanism S_N2 as outlined above involves a rate-determining attack by an "external" nucleophile. The possibility also arises, however, of a third mechanism in which the nucleophile (Y) is "internal", being already attached to the substrate. e.g.

$$Y\text{—}(CH_2)_3\text{—}CH_2\text{—}X$$

This situation, called "internal nucleophilic substitution" (S_Ni), has been envisaged for some time, but evidence for the process has only been forthcoming more recently. On the other hand, there is now much evidence that groups which do not normally act as nucleophiles can act as internal nucleophiles and thus facilitate the heterolysis of the C-X linkage, e.g. the phenyl group.

In its simplest terms, the process can be represented in the following manner; G is the internal nucleophile.



The carbonium ion (I), formed in the rate-determining step, undergoes subsequent rapid reaction.

Much of the work has been done by Winstein and his co-workers, who describe such systems in terms of anchimeric assistance by a neighbouring group.[2]

An important consideration in the mechanism of S_N reactions is the possibility of ion-pair intermediates. The intervention of these species is briefly discussed in the following subsection, before further details of mechanism S_Ni are introduced.

1.3 Ion-Pair Intermediates in Solvolysis

The presence of ion-pairs during the dissociation of a neutral molecule into two free ions, and their intervention in organic reactions has often been postulated, although the meaning of an ion-pair is rather obscure and can be defined in various ways. Bjerrum[3] suggested that the term could be applied to two counter-ions whose electrostatic attraction is greater than their mean thermal energies. The interionic distance of an ion-pair on this definition would be ca. 3•5Å in water, but over 100Å in a non-polar solvent such as benzene.[4] Another extreme definition of an ion-pair, due to Fuoss,[5] requires the counter-ions to be in physical contact.

Winstein[6] has proposed that for the S_N1 solvolysis of certain substrates in solvents of low dielectric constant, the dissociation of a neutral molecule RX into R^+ and X^- is complicated by the intervention of ion-pairs and occurs essentially in three stages:

$$R-X \rightleftharpoons \underset{A}{R^+X^-} \rightleftharpoons \underset{B}{R^+/\!/X^-} \rightleftharpoons \underset{C}{R^+ + X^-}$$

The above reaction scheme was suggested in a discussion of the information gained from a detailed kinetic study of acetolysis.[7] Species A and B are ion-pairs and are formed in the progressive stages of ionisation-dissociation. A is an "intimate" ion-pair in which the two incipient ions share the same solvation shell. B is a "solvent separated" ion-pair, the two ions having penetrated the solvation cage.

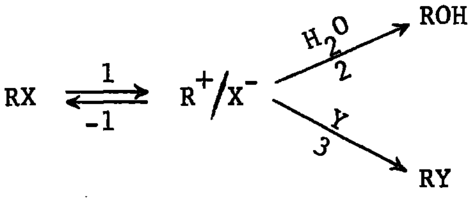
There is not much direct evidence for the existence of intermediate ion-pairs, but the assumption of their intervention in many reactions is consistent with much experimental evidence. In fact, the assumption consistent with ion-pairs rests largely on the fact that processes accompanying nucleophilic substitution (e.g. racemisation of an optically active substrate) occur more rapidly, and sometimes very much more rapidly, than the substitution reaction. Thus, in the acetolysis of norbornyl p-bromobenzenesulphonate (ROBs), which was one of the first examples of a system explained with the aid of ion-pairs,[8] the first-order polarimetric rate constant based on the disappearance of optical activity was found to be several times greater than the corresponding titrimetric rate constant. This discrepancy was explained with the aid of ionised, but undissociated R^+OBs^- ion-pairs, most of which returned to covalent racemic ROBs, the rest separating further and giving rise to product.

According to Winstein's scheme chemical capture by nucleophiles can in principle occur with A, B or C, but there is no evidence that species A can react with external nucleophiles.[6] To probe for the intervention of the "free" carbonium ion, C, one can employ the technique of isotopic exchange.[6] If a return to RX is occurring from C, inclusion of labelled common-ion salt should give rise to exchange via "external return". Information about ion-pairs A and B is provided by salt effects.[6] In particular, the addition of a non-common-ion salt such as lithium perchlorate often gives rise to a "special salt effect", the characteristics of which have been interpreted on the basis that the special salt traps the second ion-pair, B, preventing its return, but still permits return from the first ion-pair, A.

As discussed above, ion-pairs can intervene, under certain conditions, in S_N1 processes. On the other hand, S_N2 reactions have always been considered to involve direct nucleophilic attack on the substrate. However, Sneen and Larsen have recently argued[9] that both unimolecular and bimolecular solvolyses can be considered in terms of an ion-pair mechanism, and this is discussed in the next sub-section.

1.3.1. The Ion-Pair Mechanism

Sneen and Larsen[9a,b] have explained some results obtained from selected nucleophilic substitutions of 2-octyl sulphonates in 25 and 30 per cent aqueous dioxan, by suggesting that an intermediate ion-pair is involved in the reactions. Further, these workers have postulated that a single mechanism, involving ion-pairs, is operative over the entire range of nucleophilic substitution reactions, and that this mechanism becomes indistinguishable from S_N1 and S_N2 at the structural extremes. The central feature of this mechanism (see below) requires the intermediacy of an ion-pair whose formation is rate-determining at the S_N1 end and whose destruction by nucleophilic attack is rate-determining at the S_N2 end. "Borderline" behaviour is presumed to result when the rates of formation and destruction



by nucleophilic attack of the intermediate ion-pair are approximately the same.

Sneen and Larsen[9c] have extended their conclusion to results previously reported for the hydrolysis in 70 per cent aqueous acetone of 4-methoxybenzyl chloride,[10] and they have considered that these data are also consistent with their reaction scheme. This is contrary to the previous interpretation[10] which suggested concurrent S_N1 and S_N2 processes for this system.

However, the reactions of 2-octyl sulphonates like those of 4-methoxybenzyl chloride occur in the neighbourhood of the mechanistic borderline region and a re-examination[11] has recently shown that both sets of results are equally consistent with both the concurrence of S_N1 and S_N2 processes and the ion-pair mechanism.

Sneen and Larsen have considered their scheme to be of general validity, but a detailed investigation[11,12] has shown that it leads to serious inconsistencies, mainly because of the assumption that direct nucleophilic attack (S_N2) on the substrate does not occur, and also because the existence of free carbonium ions is not envisaged. Some examples of these inconsistencies are given below.

If Sneen's scheme is valid, the principle of microscopic reversibility requires that any reaction with a common-ion X^-, can only occur with the ion-pair R^+/X^- to produce the ion-pair, and will therefore have no effect on the rate of hydrolysis (no mass-law effect). Retardation by common-ion has, however, been observed on a large number of occasions, and though it could be argued that a small effect arises from a negative salt effect by added X^- anions, such an explanation could not account for the substantial retardations which frequently require mass-law constants in excess of 100.[13] Similarly, the observed retardations of the hydrolysis of benzhydryl chloride and bromide by lithium chloride and bromide, respectively,[14] and the acceleration of the organic chloride by lithium bromide,[14] are perfectly consistent with reaction by mechanism S_N1. The ion-pair scheme would require an explanation of why lithium bromide retards the ionisation of the organic bromide, but accelerates the ionisation of the structurally similar chloride.

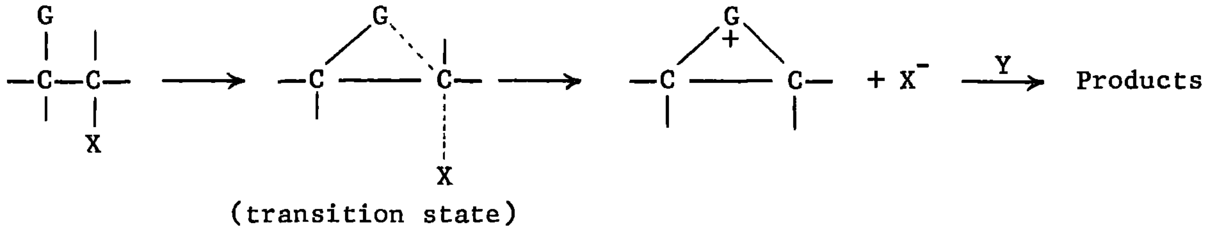
In addition, the activation parameters for the hydrolysis of 4-methoxy- and 4-phenoxybenzyl chloride in aqueous acetone[15] strongly suggest an entirely S_N1 process. Reaction by the ion-pair mechanism would require $k_{-1}/k_2 \ll 1$,[9b] but results in the presence of added azide ions then require k_{-1}/k_2 = ca.2 for the methoxy compound,[9c] and >10 for the phenoxy compound.[12] These apparent inconsistencies disappear if the strongly nucleophilic azide ions also undergo bimolecular (S_N2) reaction with the substrate. Since the reaction centres are sterically favourable to S_N2 attack[15] this explanation appears to be reasonable.

The considerations outlined in this and the preceding subsection, cast considerable doubts on the existence of any significant reactions between intermediate ion-pairs and external reagents in aqueous organic solvents. No such disadvantages arise on the basis of mechanisms S_N1 and S_N2 in their original form and it is therefore proposed to discuss the present reactions in these terms.

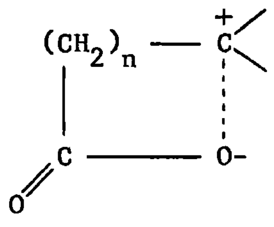
1.4 The Effects of Neighbouring Group Participation on Experimental Observations

Participation by a neighbouring group in a solvolysis reaction can be indicated in two main ways. An anchimerically assisted process usually exhibits an enhanced rate relative to that expected for S_N2 attack by solvent or S_N1 dissociation, and secondly there is the possibility of the formation of "abnormal" products, although this is not a requirement of the mechanism. Examples are given below of both types of observation and many more are included in a review by Capon.[16]

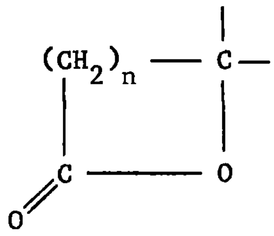
The simple diagramatic representation of mechanism S_Ni can be usefully included again at this point; G is the "internal" nucleophile or neighbouring group.



The effect was elucidated not as a result of an enhanced reaction rate, but through experiments involving the carboxylate group, where different products were formed depending on reactant concentrations. Cowdrey, Hughes and Ingold[17] hydrolysed the optically active α-bromopropionate ion (CH_3-CHBr-COO^-) in the presence of different concentrations of added alkali. Hydrolysis in concentrated alkali gave complete inversion of configuration by a bimolecular reaction, whereas with dilute base a unimolecular process resulted in a product with a predominantly retained configuration. It was originally proposed[17] that the rate-determining step in the hydrolysis with dilute base involved the formation of a carbonium ion (II) which is stabilised by direct electrostatic interaction between the oppositely charged centres, but a little later, anchimeric assistance by the carboxylate group leading to


(II)

an intermediate lactone (III), was proposed.[18]


(III)

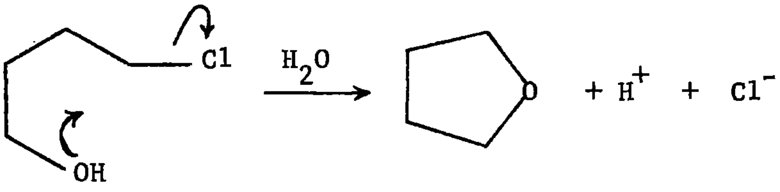
The enhanced rate which results when participation by a neighbouring carboxylate group occurs is clearly seen in Table 1.4 (see section 1.6), where the sequence of figures argues strongly in favour of this mechanism when n = 1,2,3,4, i.e. reaction via the lactones (III). As in the reactions of other compounds which are facilitated by the formation of a ring system containing an oxygen atom (see ref.16) neighbouring group participation in the ω-halogeno-carboxylate ions appears to be most efficient when it leads to a five- or six-membered ring (n = 2,3 in III).

Rings with five and six atoms, including an oxygen, are also formed as the products of hydrolysis of IV (n = 3,4).[19,16] The reactions of these two

$$HO(CH_2)_nCH_2Cl \qquad\qquad (IV)$$

substrates involve anchimeric assistance by a neighbouring hydroxyl group, and tetrahydrofuran and tetrahydropyran, respectively, have been isolated as the products of the hydrolysis of IV (n = 3,4),[19,16]

e.g.



(IV; n = 3) (tetrahydrofuran)

The enhanced rates accompanying solvolysis by mechanism S_Ni for IV (n = 3,4) are clearly seen in Table 1.1, which gives the rates of reaction for the series of chlorohydrins (IV; n = 2-5).

Table 1.1

Hydrolysis of $HO(CH_2)_nCH_2Cl$

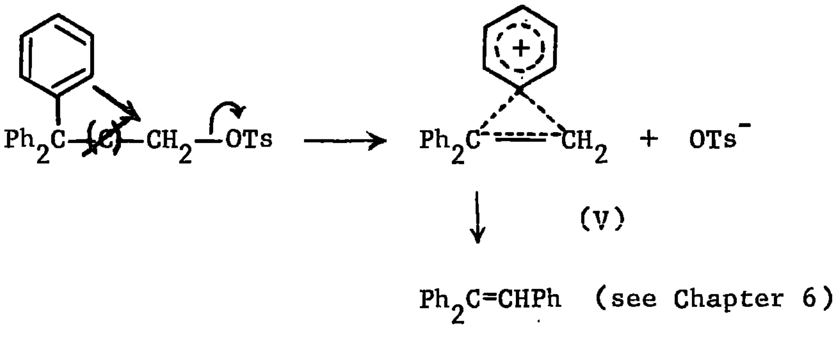
(IV; n = 2-5) in water at 70•5°.[16,19]

n	10^5k (min^{-1})
2	1•82
3	7•79
4	1710
5	70

A phenyl substituent can also act as a neighbouring group, although in this case the anchimeric assistance afforded is not always large and the data in Table 1.7 (see section 1.6) show that three phenyl groups on one carbon atom are required to give a greatly enhanced rate in the acetolysis of a series of substituted ethyl p-toluenesulphonates. However, recent work in solvents of very low nucleophilicity such as trifluoroacetic acid has shown that substantial rate enhancements do occur in the reactions of substrates which contain only one phenyl group. For example, the trifluoroacetolysis of 2-phenylethyl p-toluenesulphonate occurs about 3000 times more quickly at 75° than the similar reaction with ethyl p-toluenesulphonate.[20] This effect is briefly discussed in section 1.5.

Phenyl groups which provide anchimeric assistance usually migrate during reaction, resulting in molecular rearrangement. Elimination may also occur:

e.g.



This example suggests an intermediate "phenonium ion"[21] (V) with a three-membered ring (a non-classical carbonium ion), although some workers have doubted the existence of such species and prefer to regard the intermediate in terms of a rapidly equilibrating set of classical carbonium ions.[22] The two opposing views are discussed in section 6.3.3.

A cyclic transition state is automatically involved in anchimerically assisted reactions, irrespective of the nature of the carbonium ion, although the presence of a suitable nucleophile in a molecule does not necessarily mean that participation will occur. The reaction path for mechanism S_Ni must be energetically favourable compared with that for the S_N1 and S_N2 processes, if anchimeric assistance is to take place.

When describing participation it is convenient to employ the notation "G-n", where G is the participating group and <u>n</u> the size of the ring formed in the transition state.[23] Thus, assistance by a neighbouring hydroxyl group to form a 5-membered ring, can be represented by "HO-5".

1.5 The Influence of the Solvent on Reaction Mechanism

At this point, it is necessary to discuss briefly some of the factors which control the mechanism of reaction in a particular solvent, especially as a situation can be envisaged in which a solvolysis process will occur by mechanism S_N2 or S_Ni, depending on the solvent used.

The influence of the solvent in determining the mechanism of nucleophilic substitutions is most important in the reactions of organic halides, as the magnitude and direction of the solvent effect on velocity is different for the two mechanisms S_N1 and S_N2.[24] Hughes and Ingold[25] predicted a change of mechanism consequent on a change of solvent and this has since been realised in reactions such as the solvolysis of 2-phenylethyl p-toluenesulphonate, which is bimolecular in ethanol but unimolecular in trifluoroacetic acid.[20]

The two properties of solvents which are important in determining whether the solvolysis of an organic halide proceeds via mechanism S_N2 or S_N1 are loosely termed ionising power and nucleophilic power.

Bimolecular reactions require a good nucleophilic solvent, but ionising power is not an important factor. These processes are also considerably influenced by unfavourable steric effects which hinder the approach of a nucleophile. Unimolecular reactions, on the other hand, are favoured by a good ionising solvent. The nucleophilicity of the solvent is irrelevant, and to a first approximation, steric factors in the substrate are relatively unimportant.

The above terms are rather vague, but useful conclusions can be drawn from them. Water is a good nucleophile, and an ionising medium. In aqueous solvents simple alkyl halides react by mechanism S_N2 and tertiary compounds by mechanism S_N1.[26] Neopentyl halides are sterically blocked to S_N2 attack and therefore react by mechanism S_N1, although the rate is slow as the polar factors in the substrate are not favourable for this process.[27] With a change from water to a poorer nucleophilic solvent such as formic acid, bimolecular reaction becomes less favourable, and there is evidence that even the simple alkyl halides react by a mechanism which is similar to that of an S_N1 process.[28]

As was mentioned at the beginning of this section, a situation may arise where a reaction can proceed by mechanism S_N2 or S_Ni depending on the solvent. A poor nucleophilic solvent is required for the S_Ni process, and suitable internal nucleophiles must, of course, be present. This state of affairs also presupposes that the solvent has a reasonable ionising power and that the substrate is not likely to react by a conventional unimolecular process. Behaviour of this kind has been observed on a number of occasions where a change to a poorer nucleophilic solvent showed substantial rate enhancements for substrates where neighbouring group participation was possible, compared to substrates where this was not the case. For example, the trifluoroacetolysis of 2-phenylethyl p-toluenesulphonate occurs about 3000 times more quickly at 75° than the similar reaction with ethyl p-toluenesulphonate,[20] indicating that phenyl participation through mechanism $S_N i$ asserts itself forcefully in the phenyl compound. Thus, other factors apart; $S_N i$ processes are favoured over those by mechanism $S_N 2$, in the poorer nucleophilic solvents.

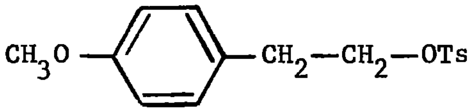
Table 1.2 gives the relative rates for the solvolysis of several 2-arylethyl p-toluenesulphonates ($ArCH_2CH_2OTs$) in three different solvents at 75°.

Table 1.2.[2]

Relative rates for the decomposition of $ArCH_2CH_2OTs$ at 75°

Solvent	C_2H_5OH	CH_3COOH	HCOOH
ethyl-OTs	1	1	1
2-phenylethyl-OTs	0•24	0•37	2•0
2-o-anisylethyl-OTs	0•28	8•9	93
2-p-anisylethyl-OTs	0•45	10•0	94

The relative rate of 2-phenylethyl p-toluenesulphonate is seen to be slower in ethanol and acetic acid but faster in formic acid than ethyl p-toluenesulphonate, suggesting that phenyl participation in the rate-determining step may be prominent in formic acid, which is the least nucleophilic of the three solvents. However, recent work by Coke[29] has shown that even in acetic acid, some phenyl participation and migration does occur. The anisyl compounds react much more rapidly than the phenyl compound in the poorer nucleophilic solvents (Table 1.2). This factor does not arise as a result of reaction by mechanism S_N1 for the more reactive compounds, since all the groups are insulated from the reaction centre, as shown in compound VI, and if mechanism S_N1 applies, all three compounds would solvolyse by this process, with relative rates not very far from unity. As this is not the case, the substantial rate increase on the successive introduction of electron-donating groups at some distance from the reaction centre, must result from the operation of mechanism S_Ni. However, it is likely that the S_Ni route is relatively unimportant for the reaction, in aqueous acetone, of the monosubstituted phenyl compound used in the present study.



(VI) (2-p-anisylethyl p-toluenesulphonate)

1.6 Previous Kinetic Studies Involving Neighbouring Group Participation

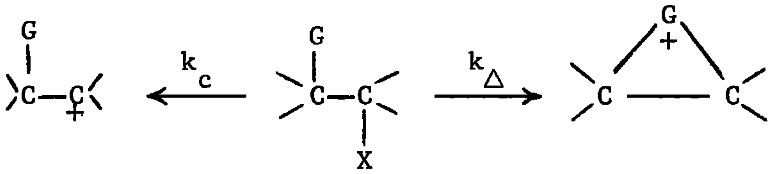
The incursion of neighbouring group participation must inevitably result in a reaction rate which is considerably greater than that expected in the absence of anchimeric assistance. In an attempt to express these rate enhancements quantitatively, Winstein[30] has used three different kinds of rate constant: k_Δ is the rate constant for anchimerically assisted ionisation; k_s applies to solvolyses which are not anchimerically assisted, but involve participation from the nucleophilic solvent, and k_c is for an idealised process involving neither anchimeric nor solvent participation. On this basis the ratio k_Δ/k_s is a measure of the competition between anchimerically assisted and unassisted processes and is usefully expressed as

$$k_\Delta/k_s = k/k_s - 1 \qquad 1.1$$

where k is the observed rate constant for the reaction studied. The driving force (L) due to the participation of a neighbouring group in the rate-determining process can be defined as

$$L = RT \ln (k_\Delta/k_c) \qquad 1.2$$

and is the free energy difference between the open and closed carbonium ions (VII) and (VIII).[31]



(VII) (VIII)

A knowledge of the reaction rate in the absence of neighbouring group participation is required before equations 1.1 and 1.2 can be used to measure anchimeric assistance, and the separation of this effect from steric and polar effects is often difficult,[30] particularly when the neighbouring group and reaction centre are at adjacent carbon atoms. Winstein has estimated the k_Δ and k_s portions of the observed solvolytic rates for a series of primary bromobenzenesulphonates[30] through the use of the $\rho^*\sigma^*$ correlation.[32] In this treatment, which takes account only of the polar effect of the R group of the substrate RCH_2OBs, the data for several compounds solvolysing without anchimeric assistance were fitted to the equation

$$\log(k_R/k_{CH_3}) = a + \rho^*\sigma^* \qquad 1.3$$

where k_R and k_{CH_3} are the rate constants for RCH_2OBs and CH_3CH_2OBs, respectively. This treatment fits anchimerically unassisted solvolysis of RCH_2OBs substrates with a probable error in $\log(k_R/k_{CH_3})$ of ca.0·05. With the aid of equation 1.3 the k_s portions of the solvolysis rate constants for substrates undergoing possible anchimeric assistance were estimated. A comparison of the rates of acetolysis of ω-methoxy-1-alkyl bromobenzenesulphonates is shown in Table 1.3.

Table 1.3.[30]

Rate data for the acetolyses of a series of ω-methoxy-1-alkyl bromobenzenesulphonates

Compound	Relative rates at 25°	Calculated k/k_s at 75°
$CH_3(CH_2)_3OBs$	1·00	0·81
$CH_3O(CH_2)_2OBs$	0·28	1·51
$CH_3O(CH_2)_3OBs$	0·63	1·20
$CH_3O(CH_2)_4OBs$	657	425
$CH_3O(CH_2)_5OBs$	123	47·2
$CH_3O(CH_2)_6OBs$	1·16	0·71

From the results in Table 1.3 it is evident that the ratio k_Δ/k_s is substantial for MeO-5 and MeO-6 participation, but essentially negligible for MeO-n participation, where n is 3, 4 or 7.

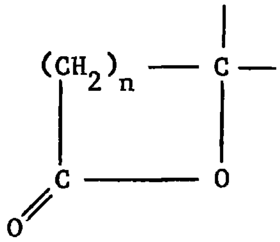
A large range of neighbouring groups have been shown to participate in several different types of reaction and these are summarised in a review by Capon.[16] Atoms which bond to the reaction centre include oxygen, nitrogen, sulphur, the halogens, hydrogen and carbon.

Much of the evidence for neighbouring group participation rests on the nature of the reaction products, and relatively few kinetic studies have been undertaken. At the beginning of this present study, activation parameters were available for only a small number of reactions involving anchimeric assistance. The relevant kinetic results of other workers will now be summarised. More recent kinetic work and studies involving reaction mechanisms and product distribution are discussed in later chapters.

The large rate enhancements which can be observed in the hydrolysis of ω-bromocarboxylate anions (IX), are shown in Table 1.4.[33] The largest effects are given when n = 2,3. In these compounds the CO_2^- group is a long

$BrCH_2(CH_2)_nCO_2^-$ (IX) (n = 0-5)

way from the reaction centre and would not affect the rate if mechanism S_N2 applied. These abnormal rate enhancements, therefore, are due to anchimeric assistance and the results show that this occurs substantially for IX (n = 2,3). Under these circumstances, the cyclic intermediate is a 5- or 6-membered ring (X; n = 2,3) containing an oxygen atom. Similar rings, formed



(X)

when an oxygen atom bonds to a remote carbon atom, occur when hydroxyl and methoxyl groups act as internal nucleophiles (see below). Cyclic species of

Table 1.4.[33]

The effect of an ω-CO_2^- group on the rates of hydrolysis of n-alkyl bromides, $H(CH_2)_nCH_2Br$, in water at 25°

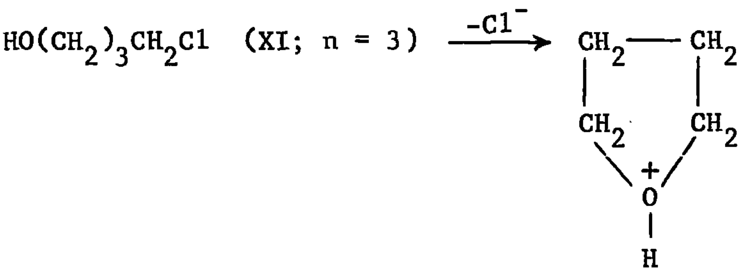
n	$k_{CO_2^-}/k_H$
0	0·139
1	9·14
2	272·1
3	226·5
4	6·23
5	1·62

this type, with 5 or 6 atoms are apparently fairly stable.[16]

Heine and his co-workers[19] determined the rates of hydrolysis in water of 3-chloro-1-propanol (XI; n = 2) and 4-chloro-1-butanol (XI; n = 3). It was found that the rate of hydrolysis as measured by the release of chloride

$$HO(CH_2)_nCH_2Cl \qquad \text{(XI)}$$

ions from XI (n = 2) and XI (n = 3) was 4 and 1000 times greater, respectively, than that of 2-chloro-1-ethanol (XI; n = 1; see Table 1.1). The large increase in the reactivity of XI (n = 3) was attributed primarily to the participation of the hydroxyl group in a transition state leading to the cyclic intermediate (XII). A substantial yield of tetrahydrofuran, the expected result of



(XII)

neighbouring hydroxyl participation (due to the easy loss of a proton from (XII)), was obtained on complete hydrolysis of XI (n = 3).[19]

Another study[16] showed that the rate of XI (n = 4) was <u>ca</u>. 40 times faster than XI (n = 2), but slower by a factor of <u>ca</u>. 25 than XI (n = 3). Tetrahydropyran was also isolated as a reaction product of XI (n = 4).[16] It therefore seems that anchimeric assistance by a neighbouring hydroxyl group occurs for XI (n = 4) but that the resulting 6-membered cyclic intermediate is not formed as readily as a 5-membered ring from XI (n = 3). This behaviour is analogous to that discussed above for carboxylate anions, where processes requiring 5- or 6-membered rings are energetically the most favourable.

Table 1.5.[19]

Enthalpies and entropies of activation at 70•5° for XI (n = 1-3)

Substrate	$\Delta H^\ddagger$ (kcal mole^{-1})	$\Delta S^\ddagger$ (cal deg^{-1}mole^{-1})	k(min^{-1})
2-chloro-1-ethanol (XI; n = 1)	24•5	-17•2	$1{\bullet}82 \times 10^{-5}$
3-chloro-1-propanol (XI; n = 2)	23•9	-16•2	$7{\bullet}79 \times 10^{-5}$
4-chloro-1-butanol (XI; n = 3)	21•9	-11•1	$1{\bullet}71 \times 10^{-2}$

The results of Heine's study[19] are quoted at 70•5° presumably because this is one of the experimental temperatures used. However, although it is claimed that the rates and activation parameters are compared at the same temperature, compound XI (n = 2) was studied at 3 temperatures between 72° and 97°, and XI (n = 3) at 3 temperatures between 50° and 70°, and the temperature dependence of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ is not considered. There is much reason for believing that $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are significantly dependent on temperature (see section 2.3). In the absence of values for the heat capacities of activation, calculated activation parameters must refer to the mean temperature of the experimental range and comparisons of the results for compounds studied at different ranges of temperature cannot be made with any accuracy. This point is further discussed in section 2.3. Even so, the relatively high entropy value for XI (n = 3) is noted and explained in terms of a freeing of the water molecules which were oriented stiffly around the hydroxyl group, a process which can only occur if the hydroxyl group itself effects the substitution.[19] However, this explanation[19] is unsatisfactory, as mentioned in the next section (1.7).

Most of the results for participation by the methoxyl group are due to Winstein and his co-workers, and some of these are summarised in Table 1.6.

Table 1.6.[30]

Relative rates at 25° and $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ for the acetolysis of

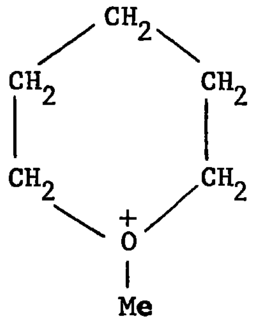
$CH_3O(CH_2)_nCH_2OBs$ (XIII; n = 1-5)

Compound	Relative rates at 25°	$\Delta H^{\ddagger}$(kcal mole^{-1})	$\Delta S^{\ddagger}$(cal deg^{-1}mole^{-1})
$CH_3(CH_2)_3OBs$	1•00	23•7	-17•4
$CH_3O(CH_2)_2OBs$	0•28	23•0	-22•1
$CH_3O(CH_2)_3OBs$	0•63	23•8	-17•9
$CH_3O(CH_2)_4OBs$	657	22•0	-10•4
$CH_3O(CH_2)_5OBs$	123	21•6	-15•1
$CH_3O(CH_2)_6OBs$	1•16	23•9	-16•5

These results show clearly the large rate enhancements which occur when the solvolyses are assisted by MeO-5 and MeO-6 participation, resulting once again in the ready formation of 5- and 6-membered rings containing an oxygen atom. Substrates XIII (n = 3,4) are associated with lower enthalpies and less negative entropies of activation than the other members of the series and this behaviour parallels that found for the chlorohydrins[19] (XI; n = 3,4) and discussed above.

Winstein's kinetic data[30] are presented in terms of relative rates, and details of the experimental temperatures are not included. However, heat capacities of activation are not reported, and as with the results for hydroxyl participation discussed above, the activation parameters presumably obtained from widely different rates measured over different temperature ranges, cannot be relied upon to support any more than the simplest deductions.

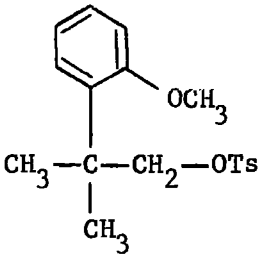
When anchimeric assistance is afforded by a neighbouring methoxyl group, the intermediate has been found to undergo a variety of reactions,[30] particularly in the case of XIII (n = 4), which gives rise to the intermediate XIV, and it is not quite clear to what extent the rate



(XIV)

measurements reflect the formation of the intermediate or products. Nevertheless, the rate enhancement is sufficient evidence of neighbouring group participation and its magnitude indicates the size of the effect. More recent work on the varied reactions of the intermediate (XIV) is discussed in section 5.5.

Participation by a methoxyl group attached to a benzene ring can sometimes occur. The nucleophilicity of the substituent is reduced by mesomeric interaction with the benzene ring but this is partly opposed by the increased rigidity of the system.[16] Solvolysis of o-methoxyneophyl p-toluenesulphonate (XV) was found to involve two competing anchimerically assisted ionisation processes, Ar-3 and o-MeO-5.[34]



(XV)

Winstein has also studied neighbouring phenyl participation and activation parameters have been obtained for several compounds which solvolyse by an anchimerically assisted route involving Ar-3 participation. The effect of β-phenyl substituents on the rate of acetolysis of ethyl p-toluenesulphonate at 75° is shown in Table 1.7.

Table 1.7

Rates of acetolysis at 75° of ethyl p-toluenesulphonate and its β-phenyl derivatives

Compound	$10^7k(\text{sec}^{-1})$
CH_3CH_2OTs[35]	7•7
$PhCH_2CH_2OTs$[2]	2•9
Ph_2CHCH_2OTs[36]	2.7
Ph_3CCH_2OTs[36]	3200

Activation enthalpies and entropies were determined for this series of compounds,[36] but they apply to the mean values of different temperature ranges and cannot usefully be compared.

The solvolyses of 2-o-anisylethyl- and 2-p-anisylethyl p-toluenesulphonate have been studied in ethanol, acetic acid and formic acid[2] and Table 1.2 (section 1.5) shows that these compounds react more quickly than 2-phenylethyl p-toluenesulphonate in the acid solvents. These relative rates are explained in section 1.5. Presumably, the o- and p-anisyl groups are more effective nucleophiles than the phenyl group because the methoxyl substituent donates electrons to the ring carbon atom which, as a result, can assist solvolysis more effectively.

Unlike the ring closures resulting from internal attack by an oxygen atom, anchimeric assistance by a phenyl group usually results in the formation of a 3-membered ring. This fact is mentioned in a little more detail in section 1.4 and the factors influencing the ease of ring closure are discussed in ref.16.

In an attempt to observe participation by more remote aryl rings, the rates of acetolysis and formolysis of 3-phenylpropyl, 4-phenylbutyl and 5-phenylpentyl p—bromobenzenesulphonates (XVI; n = 2-4) were determined[23] but found to be similar to those of the propyl and butyl esters, indicating that Ar-4, Ar-5 and Ar-6 participation are not very important. However, Winstein[23] studied the effect of introducing one and two methoxyl substituents into the phenyl group to increase the nucleophilicity of the ring. The relative rates showed that Ar-4 and Ar-6 participation are unimportant, but that Ar-5 participation is probably substantial for the methoxyl substituted 4-phenylbutyl esters.[23]

$$\mathrm{Ph(CH_2)_nCH_2OBs} \qquad \text{(XVI; } n = 2\text{-}4)$$

The main conclusion from this section is that although several kinetic studies involving reactions by mechanism S_Ni have been undertaken, the comparisons of rates and particularly activation parameters for compounds with widely differing reactivities are unavoidably inexact and superficial, since no account has been taken of the temperature dependence of these quantities. A knowledge of the heat capacities of activation for each substrate is required before accurate comparisons of data can be made (see section 2.3), and no kinetic study of neighbouring group participation including this extra parameter had been made at the beginning of the present work.

1.7 Activation Parameters for Solvolysis by Mechanism S_Ni

At the start of the present work, few activation parameters had been reported for reactions involving neighbouring group participation. Some of these are mentioned in the previous section.

An outstanding feature of all the results is that the entropy of activation for the compounds which show neighbouring group participation is invariably more positive than that expected for reaction by mechanism S_N2. Workers have pointed out that this is characteristic, but the explanations proposed are somewhat obscure, if not untenable, especially when it is borne in mind that any entropy change resulting from ring closure will be negative rather than positive.

The reactions which show neighbouring group participation are always the faster ones, and in general they are studied at considerably lower temperatures than reactions by mechanisms S_N1, S_N2. Hence because of the negative temperature coefficient of $\Delta S^\ddagger$, which is expected for reactions involving the creation of electric charges, there can be no guarantee that an increase in $\Delta S^\ddagger$ on the incursion of neighbouring group participation is genuine, and not just a result of the use of different temperature ranges.

The interpretation of the activation parameters and their temperature coefficients are discussed in detail in Chapter 2, but it is useful to mention at this point that the assumption of constant entropies and energies of activation means that the resulting values refer to the mean temperature of the experimental range.

1.8 The Present Study

It was decided, as a result of the above considerations, to study several series of compounds in which some members showed neighbouring group participation while others did not. The determination of heat capacities of activation (see section 2.3) made certain that all activation parameters could be compared at the same temperature.

The two series of compounds chosen first were the ω-hydroxyalkyl chlorides (XVII; n = 1-5) and the ω-methoxyalkyl bromides (XVIII; n = 1-5). This work

$HO(CH_2)_nCH_2Cl$ (XVII)

$MeO(CH_2)_nCH_2Br$ (XVIII)

was undertaken partly because it was known that certain members showed neighbouring group participation (see section 1.6), and partly in the hope that these compounds would give some information concerning reaction by an internal nucleophile, enabling a comparison to be made with mechanisms S_N1, S_N2. Information was also available[37] for the reactions of similar substrates, in the same solvents, with water as an external nucleophile. Results for the hydrolysis of XVII (n = 3), and XVIII (n = 3) in water[38] became available after the start of this study and are described in conjunction with the present results in section 4.3.

In addition, the effect of phenyl participation in the solvolyses of 2,2,2-triphenylethyl p-toluenesulphonate (XIX) and chloride (XX), was also studied, together with the reaction of 2-phenylethyl bromide (XXI) for comparison.

Ph_3CCH_2OTs	Ph_3CCH_2Cl	$PhCH_2CH_2Br$
(XIX)	(XX)	(XXI)

All reactions were studied in aqueous acetone and followed by the development of acidity. The main results are summarised and discussed in Chapters 4, 5 and 6. The methods of calculation of accurate rates and activation parameters are given in Chapter 3 and the experimental details in Chapter 7.

Before the results can be discussed it is necessary to consider the temperature dependence of the conventional activation parameters (E and $\Delta S^{\ddagger}$) and the interpretation of these quantities and their temperature coefficients.

CHAPTER 2

ACTIVATION PARAMETERS IN SOLVOLYTIC REACTIONS

2.1 The Arrhenius Law

In 1889, Arrhenius,[39] attempting to account for the influence of temperature on the rate of inversion of sucrose, suggested that an equilibrium existed between "inert" and "active" molecules of the reactant, and that only the latter could take part in the inversion. He showed that the variation of reaction rate with temperature could be expressed in an equation of the form

$$k = Ae^{-E/RT} \qquad 2.1$$

where E is the difference in energy between the activated and inert molecules and A is a quantity which is independent of or varies only slightly with temperature.

It is now generally accepted that this relationship represents the temperature dependence of the specific rates of most chemical reactions, provided that the temperature range is not large, so that the quantities A and E can be regarded as constant. The factor A, sometimes known as the "collision number" because of its role in the collision theory of reaction rates, has also been called the "frequency factor". The quantity E is termed the "experimental activation energy" and represents the energy that a molecule in the initial state of a process must acquire, before it can take part in a reaction.

The linear relation between lnk and 1/T, required by equation 2.1 has been found to be valid within the limits of the experimental error on many occasions. However, Hinshelwood[40] predicted that E would vary with the temperature if the additional energy of the activated molecules was distributed among more than two square terms, and a few years later, several workers[41] pointed out that any difference between the heat capacities of the normal and activated molecules would result in temperature-dependent values of

E. The transition state theory leads to similar conclusions, and has been successful, particularly for reactions in solution, in relating the experimental rate data to the activation parameters for a reaction under study.

2.2 The Transition State Theory

In its simplest terms, the use of the transition state theory[42] equations results in a calculation of the frequency factor, A, for a chemical reaction. The theory is based on the idea that a reaction can be represented by the continuous change of the co-ordinates of the initial state into the final state via a critical configuration called the "activated complex" or the "transition state". This intermediate configuration is situated at the point on the reaction path at which the potential energy of the system is a maximum. The activated complex is regarded as: "an ordinary molecule, possessing all the usual thermodynamic properties, with the exception that motion in one direction, i.e. along the reaction co-ordinate, leads to decomposition at a definite rate".[43] It is further assumed that the initial reactants are always in equilibrium with the activated complexes.

From the statistical treatment of reaction rates in the transition state theory, the rate coefficient of a single-step reaction is given in its most simple form by

$$k = \frac{\bar{k}T}{h} \exp(-\Delta G^{\ddagger}/RT) \qquad 2.2$$

where $\Delta G^{\ddagger}$ is the standard free energy change associated with the activation process. If $\Delta G^{\ddagger}$ is replaced by its equivalent, $\Delta H^{\ddagger} - T\Delta S^{\ddagger}$, equation 2.2 can be written in the form

$$\ln k = \ln \frac{\bar{k}T}{h} + \frac{\Delta S^{\ddagger}}{R} - \frac{\Delta H^{\ddagger}}{RT} \qquad 2.3$$

where $\Delta H^\ddagger$ and $\Delta S^\ddagger$ are the enthalpy and entropy of activation, respectively, and represent the changes in these functions for the activation process. Differentiation with respect to temperature and comparison with the definition of the activation energy by equation 2.1 shows that

$$E = \Delta H^\ddagger + RT \qquad 2.4$$

Equation 2.3 can then be written in the form

$$\ln k = \ln \frac{\bar{k}T}{h} + 1 + \frac{\Delta S^\ddagger}{R} - \frac{E}{RT} \qquad 2.5$$

This last equation is the form of the absolute rate equation usually used in the determination of entropies of activation for reactions in solution.

It is worth stressing at this point that the activation parameters E and $\Delta S^\ddagger$ are usually regarded as constant. However, this is not the case, as discussed in the following section. Comparisons of parameters for different reactions must therefore be made at the same temperature, and as different experimental temperature ranges are often involved, the temperature coefficient of E and $\Delta S^\ddagger$ is required, and this necessitates the determination of the heat capacity of activation ($\Delta C_p^\ddagger$) for each reaction.

2.3 Heat Capacities of Activation in Solvolysis Reactions

From Kirchhoff's equations and equation 2.4, the relations between the heat capacity of activation at constant pressure ($\Delta C_p^\ddagger$) and the other activation parameters, can be written as:

$$\Delta C_p^\ddagger = \frac{d(\Delta H^\ddagger)}{dT} = T\,\frac{d(\Delta S^\ddagger)}{dT} \qquad 2.6$$

$$\Delta C_p^\ddagger = dE/dT - R \qquad 2.7$$

The methods used for determining the activation parameters by the above relationships are discussed in Chapter 3 and section 7.4.

The difference between the heat capacities of normal and activated molecules was termed the heat capacity of activation by La Mer,[41b] who showed that its value was very close to that of the temperature coefficient of the experimental activation energy. Equation 2.7, resulting from the transition state theory is in agreement with this work.

Using the terms of the transition state theory, the heat capacity of activation is defined as the standard heat capacity change associated with the activation process, and can be expressed in the form

$$\Delta C^{\ddagger} = C^{\ddagger} - \sum_{R} C^{R} \qquad 2.8$$

where $C^{\ddagger}$ and C^{R} are the standard partial molar heat capacities of the activated complex and the reactants, the summation being carried out over all reactants.[37]

The heat capacity of activation at constant pressure, $\Delta C_p^{\ddagger}$, is numerically significant for solvolysis reactions, and most of these processes have negative values of this parameter in the range (-10 ⟶ -100 cal deg^{-1}).[37] A knowledge of $\Delta C_p^{\ddagger}$ is essential in any meaningful comparison of the energies and entropies of activation for reactions studied over different temperature ranges.[37] The values of E and $\Delta S^{\ddagger}$ as initially obtained, refer to a temperature near the mean of the experimental range, and if these parameters are assumed to be constant, they may lead to erroneous conclusions. Thus if $\Delta C_p^{\ddagger} = -30$ cal deg^{-1}, the entropies of activation at 0° and 50° differ by 5 cal deg^{-1}, a value well outside the limits of the experimental error[44] (ca. 0•1-0•2 cal deg^{-1} in accurate work).

In addition, $\Delta C_p^{\ddagger}$ serves as an extra parameter and provides useful information about the activation process of solvolysis reactions.

Heat capacities of activation can be determined at constant pressure ($\Delta C_p^{\ddagger}$) or constant volume ($\Delta C_v^{\ddagger}$) depending on the standard states chosen. Almost all the known values of this parameter refer to reactions in solution at constant pressure, and until very recently, corresponding constant volume parameters had not been accurately measured. However, Baliga and Whalley[45] have determined both $\Delta C_p^{\ddagger}$ and $\Delta C_v^{\ddagger}$ for the solvolyses of methyl and isopropyl bromide in water. The values of $\Delta C_v^{\ddagger}$ for both compounds were found to be numerically about twice as great as those which apply under constant pressure conditions. An interpretation of these results was not advanced, as $\Delta C_v^{\ddagger}$ was found unexpectedly to vary less with pressure but much more with temperature than $\Delta C_p^{\ddagger}$.[45]

Several workers[46] have argued that mechanistic interpretations might be made more easily from determinations at constant volume than from the corresponding data at constant pressure. Kohnstam[37] has summarised the arguments for and against this supposition. It is expected that further measurements of $\Delta C_v^{\ddagger}$ will be made in the near future, and clearly, results at constant pressure and constant volume for the same reaction will greatly aid the mechanistic interpretations.

As the techniques used in the measurement of reaction rates become more refined it is possible that the rate constants determined at different temperatures will be accurate enough to enable $d(\Delta C_p^{\ddagger})/dT$ to be calculated for solvolysis reactions. This parameter, a third differential of the rate with respect to temperature, can be expected to be non-zero if the structure of the transition state changes appreciably when the temperature is altered.[37]

Albery and Robinson[47] have recently claimed that for the solvolysis of tertiary butyl chloride in water, $d(\Delta C_p^{\ddagger})/dT$ is <u>ca.</u> 1 cal deg^{-2}. If valid, this would upset much previous work and interpretation. However, an examination and recalculation of the results[12] has shown that the error quoted for $d(\Delta C_p^{\ddagger})/dT$ ($\pm$ 0·18 cal deg^{-2}) is too small by a factor of 5. As a result, the quoted value of this parameter cannot be distinguished from zero within the limits of the experimental error.

The accuracy of the present results only allows the assumption that $\Delta C_p^{\ddagger}$ is constant i.e. $d(\Delta C_p^{\ddagger})/dT = 0$.

The methods of calculation of the activation parameters used in the present work are discussed in Chapter 3.

2.4 The Interpretation of Entropies and Heat Capacities of Activation in Solvolysis Reactions

2.4.1 Initial Considerations

It is generally agreed that negative heat capacities of activation in solvolysis reactions are due to the creation of electric charges during the solvolysis of a neutral substrate via a polar transition state.

Reactions which involve the creation of electric charges in the activation process have been discussed in terms of an electrostatic approach which considers the solvent to be a continuous dielectric and assumes that the Born relation applies.[48] Electrostatic contributions, ΔS_D, ΔC_D to $\Delta S^{\ddagger}$ and $\Delta C^{\ddagger}$ in S_N1 solvolysis can then be calculated,[48] using the Kirkwood equation.[49] However, the observed values of $\Delta C^{\ddagger}$ and $\Delta S^{\ddagger}$ bear no simple relation to the dielectric properties of the solvent, and it has been concluded that the electrostatic approach is quite inadequate to account for the experimental observations.[50]

Everett and Wynne-Jones[51] explained the values of ΔC_p^{o} for the ionisation of weak acids in terms of solvent reorganisation during ionisation, and this phenomenon is believed to be responsible for the observed values of $\Delta C_p^{\ddagger}$ which are applicable to the activation processes of solvolysis reactions.[37]

The basic hypothesis of increased solvation of the dipolar transition state relative to the initial state, for both S_N1 and S_N2 reactions, has been developed along two different lines to explain the observations for solvolysis in water and aqueous organic solvents. The two approaches are summarised in the following sections.

2.4.2 The Solvation Model for Solvolysis in Aqueous Organic Solvents

The solvation model approach[37] is due to Kohnstam, who proposed that for S_N1 reactions all the solvent-solvent and solvent-solute interactions in the initial and transition states are identical, except for the solvent-solute interactions arising from the increased charge of the transition state, a process assumed to involve only water, the more polar solvent component.

The entropy and heat capacity of activation can be expressed using the equations

$$\begin{aligned} \Delta S^{\ddagger} &= n_1(S_s - S_1) \\ \Delta C_p^{\ddagger} &= n_1(C_s - C_1) \end{aligned} \qquad 2.9$$

where n_1 is the difference between the number of water molecules solvated by the initial and transition states, S_s and C_s are the molar contributions of a solvated water molecule to the entropy and heat capacity of the activated complex, and S_1 and C_1 are the partial molar entropy and heat capacity of water in the solvent. For S_N1 solvolyses, the ratio $\Delta C_p^{\ddagger}/\Delta S^{\ddagger}$ has been found to be independent of the nature of the substrate,[37] a result predicted by equation 2.9.

Data for S_N2 solvolysis[37] in aqueous organic solvents shows that these reactions are associated, in general, with a more negative $\Delta S^{\ddagger}$, than for mechanism S_N1, presumably as a consequence of the covalent participation of water in the transition state. The results are consistent with the solvation model if a water molecule loses much more of its entropy when it forms a partial covalent bond than when it solvates a charged centre, while the reduction in its heat capacity is similar for the two processes. For S_N2 reactions the ratio $\Delta C_p^\ddagger/\Delta S^\ddagger$ is much less than for S_N1 processes, and is not independent of the nature of the substrate. Bensley and Kohnstam[52] have suggested that the difference between the values of this ratio for S_N1 and S_N2 solvolysis could be used to gain useful information about mechanism, particularly in the "borderline" region.

2.4.3 The Interaction Model for Solvolysis in Water

The interpretation of activation parameters for solvolysis in water was formed by Robertson,[38] using the basic hypothesis that a neutral organic solute is not involved in attractive solvent-solute interactions but enhances the structure of the solvent in its surroundings, resulting in increased solvent-solvent interactions. The activation process, with the formation of charges in the transition state promotes solvent-solute interactions near the reaction site at the expense of some of the solvent-solvent interactions operating in the initial state. This break-down of the "initial state solvation shell" reduces the heat capacity of the transition state relative to the initial state, and has been considered to be responsible for the observed values of $\Delta C_p^\ddagger$, although for S_N2 solvolysis a contribution resulting from covalent participation by water is expected.[38]

Solvent-solvent interactions reduce the entropy of a system, and a positive contribution to $\Delta S^\ddagger$ should result from the break-down of the initial state solvation shell. However, it seems that other factors influence the magnitude of $\Delta S^\ddagger$, as the predicted positive values have only been observed in some S_N1 reactions in water.

2.4.4 Conclusion

The results so far obtained suggest that the solvation and interaction models are successful, to a first approximation, in explaining the values of $\Delta C_p^{\ddagger}$ and $\Delta S^{\ddagger}$ for solvolysis in aqueous organic media and water, respectively. The important difference between the two types of solvent system probably arises from the fact that water is a highly ordered solvent, the structure of which is disturbed by the introduction of non-polar molecules. Aqueous organic media, on the other hand, have a much smaller degree of structure and attractive interactions between the solute and solvent (the organic component) are a favourable possibility.[37]

CHAPTER 3

THE DETERMINATION OF ACCURATE RATES AND ACTIVATION PARAMETERS FROM EXPERIMENTAL DATA

3.1 Introduction

This chapter considers the various methods of calculating rate constants and activation parameters and the errors of the resulting quantities.

It has already been pointed out that the present reactions were followed by noting the development of acidity (p). The concentration of the substrate (c) can therefore be expressed as

$$c = (p_\infty - p).\ \text{constant},$$

where p_∞ is the "infinity" value of the acidity, and the simplest form of the integrated first-order rate equation is

$$k_i = \frac{1}{t_i} \ln \frac{p_\infty - p_0}{p_\infty - p_i} \qquad 3.1$$

where k_i is the rate constant calculated from time t_i, and acidity p_i, and p_o is the "zero" value of the acidity.

In these laboratories, the rate constants used have usually been the mean values of individuals calculated from equation 3.1, but several workers, including Collins,[53] have pointed out that each k_i involves the values of p_o and p_∞, and hence errors in p_o and p_∞ lead to a systematic error in each k_i and therefore in the mean $\underline{k}$. However, errors in p_o and p_∞ are greatly reduced when several determinations of these quantities are made, and the systematic errors in the mean $\underline{k}$ become small.

Very accurate rate constants are required if accurate activation parameters are to be determined, and equation 3.1 can be written in several forms, each of which has a different reliability. The final mean $\underline{k}$ therefore depends on the equation used and the range of the reaction studied.

Kohnstam[12] has recently examined the problem of obtaining the most reliable rate constants from a set of rate data, and an outline of the approach and the conclusions are relevant to the present work, and discussed below.

3.2 Rate Equations

When the final mean k is calculated from equation 3.1, the principle of least squares is used to minimise errors in $\ln(p_\infty - p)$, although Collins[53] has noted that it is strictly more correct to minimise the errors in the experimental quantities, e.g. $(p_\infty - p)$, by writing equation 3.1 in the exponential form. Similar considerations apply to the alternative versions, and these are summarised in Table 3.1, which gives the expressions for the functions y_i and f_i in the general first-order rate equation:

$$y_i = f_i \qquad 3.2$$

Here, y_i is a function of concentrations (titres) and, occasionally, time (in 3.2.1a), and f_i is a function of k, other disposable parameters, and time (except in 3.2.1a).

Equations 3.2.1 a,b and 3.2.2a which all have one disposable parameter are subject to systematic errors from two sources (p_0, p_∞). This is partly overcome by repeating each kinetic experiment and duplicating the "zero" and "infinity" readings. Equations 3.2.3a,b, with two disposable parameters, are subject to a systematic error from p_∞ only and this can be minimised as mentioned above. Equation 3.2.4b (no "log equivalent") has no systematic errors, but three disposable parameters. There is also an equation due to Guggenheim,[54] which has no systematic errors, but this is not applicable with the present kinetic data.

Final mean rate constants can be calculated from all the forms of the rate equation by the method of least squares (non-linear least squares for the exponential forms 3.2.1b - 3.2.4b) assuming, as is usually the case, that values of t_i are much more accurate than the corresponding ones for y_i (details in Appendix 3). Accurate measurements should lead to the same rate constant, within the limits of the experimental error, irrespective of the

Table 3.1

Forms of the general first-order rate equation (3.2)

Logarithmic forms			Exponential forms			
Equation	y_i	f_i	Equation	y_i	f_i	Notes
3.2.1a	$\frac{1}{t_i} \ln \frac{p_\infty - p_o}{p_\infty - p_i}$	k	3.2.1b	$\frac{p_\infty - p_i}{p_\infty - p_o}$	e^{-kt_i}	$i = 1, 2 \ldots\ldots (n-1)$
3.2.2a	$\ln \frac{p_\infty - p_o}{p_\infty - p_i}$	kt_i	-	-	-	$i = 1, 2 \ldots\ldots (n-1)$
3.2.3a	$-\ln(p_\infty - p_i)$	$A + kt_i$	3.2.3b	$p_\infty - p_i$	Ae^{-kt_i}	$i = 0, 1 \ldots\ldots (n-1)$
-	-	-	3.2.4b	p_i	$B-Ae^{-kt_i}$	$i = 0, 1 \ldots\ldots (n-1)$

General notes: a) $t_o = 0$, throughout

b) A and B are disposable parameters

rate equation used, although this does not apply to the standard error of k (σ_k), the generally accepted measure of reliability. By the nature of the least squares procedure, σ_k increases as the number of disposable parameters rises, and the crucial question is whether or not appreciable systematic errors can be tolerated when these are offset by a reduced σ_k from an equation with few disposable parameters. Values of σ_k are also calculated by the least squares procedure (see Appendix 3).

3.3 Weighting Schemes

Unlike k, σ_k can depend markedly on the statistical weight assigned to each experimental term y_i in equation 3.2, although the same weight factors (w_i=1) are usually used throughout. This weighting scheme, the simplest possible, has been shown to be most unsatisfactory e.g., a given error in a value of p_i used in equation 3.2.3, has a very much greater effect on the final mean k when $p_i = 0{\cdot}95p_\infty$ than when $p_i = 0{\cdot}5p_\infty$. This difficulty can be overcome by using a suitable weighting scheme, although the choice of an appropriate one has been thought difficult.[53]

Kohnstam[12] has suggested that since the distribution of errors in each experimental determination is normal (Gaussian), a suitable weight factor to be assigned to each experimental term is one which is proportional to the reciprocal of the variance (v_y) of that term (i.e. w_i=g_i; details are given later). This weighting scheme is not perfect, but is the best approximation available.

For a normal distribution of errors, the square of the residual (observed value-correct value) of any reading is less than 9 times the variance of the reading, but the weight could still be wrong by a factor of up to 9, as there is no guarantee that each reading has a square of the residual exactly equal to v_y. Nevertheless, over the whole range of a kinetic experiment, the weighting scheme with $w_i=g_i$ is a much better approximation than that with $w_i=1$. For example, there is a 100-fold variation of g_i for experimental points between 0 and 90 per cent reaction (equation 3.2.3a; see Fig.3.1). Such a variation in g_i is not allowed for when $w_i=1$. The weight factors to be assigned are calculated as discussed below.

A small random error in y_i ($y_i=f_i$; equation 3.2) resulting from a small random error in p_i (p_∞, p_0 assumed accurate) is given by

$$(\delta y_i)^2 = \left(\frac{\partial y_i}{\partial p_i}\right)^2 \cdot (\delta p_i)^2$$

If $\delta p_i = \sigma(p_i)$, the standard deviation of p_i about its correct value, $(\delta y_i)^2$ is the variance of y_i about its correct value and the weight factor to be assigned to each experimental term, y_i, on the assumption of a normal distribution of errors, is

$$w_i = g_i \propto \frac{1}{(\delta y_i)^2} \quad \text{i.e.} \quad w_i = g_i \propto \frac{1}{\left(\frac{\partial y_i}{\partial p_i}\right)^2 \cdot \sigma(p_i)^2} \qquad 3.3$$

This weighting procedure assumes that each p_i is in error by one standard deviation, $\sigma(p_i)$, although $\sigma(p_i)$ can only be obtained if many determinations of p_i are carried out. In practice, any one p_i may differ by more or less than $\sigma(p_i)$ from its correct value, but the approximation for w_i is the best that can be made, and probably does not give rise to much error, as there is a 99•7 per cent probability that each p_i is within $\pm$ $3\sigma(p_i)$ of its correct value. The use of the weighting scheme $w_i=g_i$ is therefore an advantage over $w_i=1$, if g_i varies by more than a factor of 9 over the course of a kinetic run, and it does so for many of the rate equations.

In order that g_i can be calculated, an expression for $\sigma(p_i)$ is needed. Two independent random errors contribute to the error in each p_i:

1. The measurement error in each titration value, due to burette reading and indicator errors, which is independent of the size of the titre (p_i).

$$\text{i.e.} \quad \sigma^M(p_i) = \text{constant} = \sigma^M(p_\infty)$$

where $\sigma^M(p_i)$ is the standard deviation of p_i resulting from the measurement error.

2. The sample error arises from an error $\sigma(V)$ in the sample volume, V, which is used. The resulting error in p_i is

$$\sigma^V(p_i) = p_i \cdot \frac{\sigma(V)}{V} = \frac{p_i}{p_\infty} \cdot \sigma^V(p_\infty)$$

where $\sigma^V(p_\infty)$ is the sample error (standard deviation) when $p_i = p_\infty$. The standard deviation of p_i about its correct value is therefore given by

$$\sigma(p_i)^2 = \sigma^M(p_i)^2 + \sigma^V(p_i)^2$$

$$= \sigma^M(p_\infty)^2 \left[1 + \left(\frac{p_i}{p_\infty}\right)^2 \cdot \left(\frac{\sigma^V(p_\infty)}{\sigma^M(p_\infty)}\right)^2\right]$$

It has been shown that $\sigma^V(p_\infty) \simeq \sigma^M(p_\infty)$ so that for the present experiments,

$$\sigma(p_i)^2 = \sigma^M(p_\infty)^2 \left[1 + \left(\frac{p_i}{p_\infty}\right)^2\right]$$

Substitution in equation 3.3 and omission of the constant term $\sigma^M(p_\infty)^2$ then gives

$$w_i = g_i = \left[\left(\frac{\partial y_i}{\partial p_i}\right)^2 \left\{1 + \left(\frac{p_i}{p_\infty}\right)^2\right\}\right]^{-1}$$

The expressions for $(\partial y_i/\partial p_i)^2$ appropriate to the various rate equations 3.2.1-3.2.4, are included in Table 3.2.

Table 3.2

Expressions for $(\partial y_i/\partial p_i)^2$ appropriate to equations 3.2.1-3.2.4

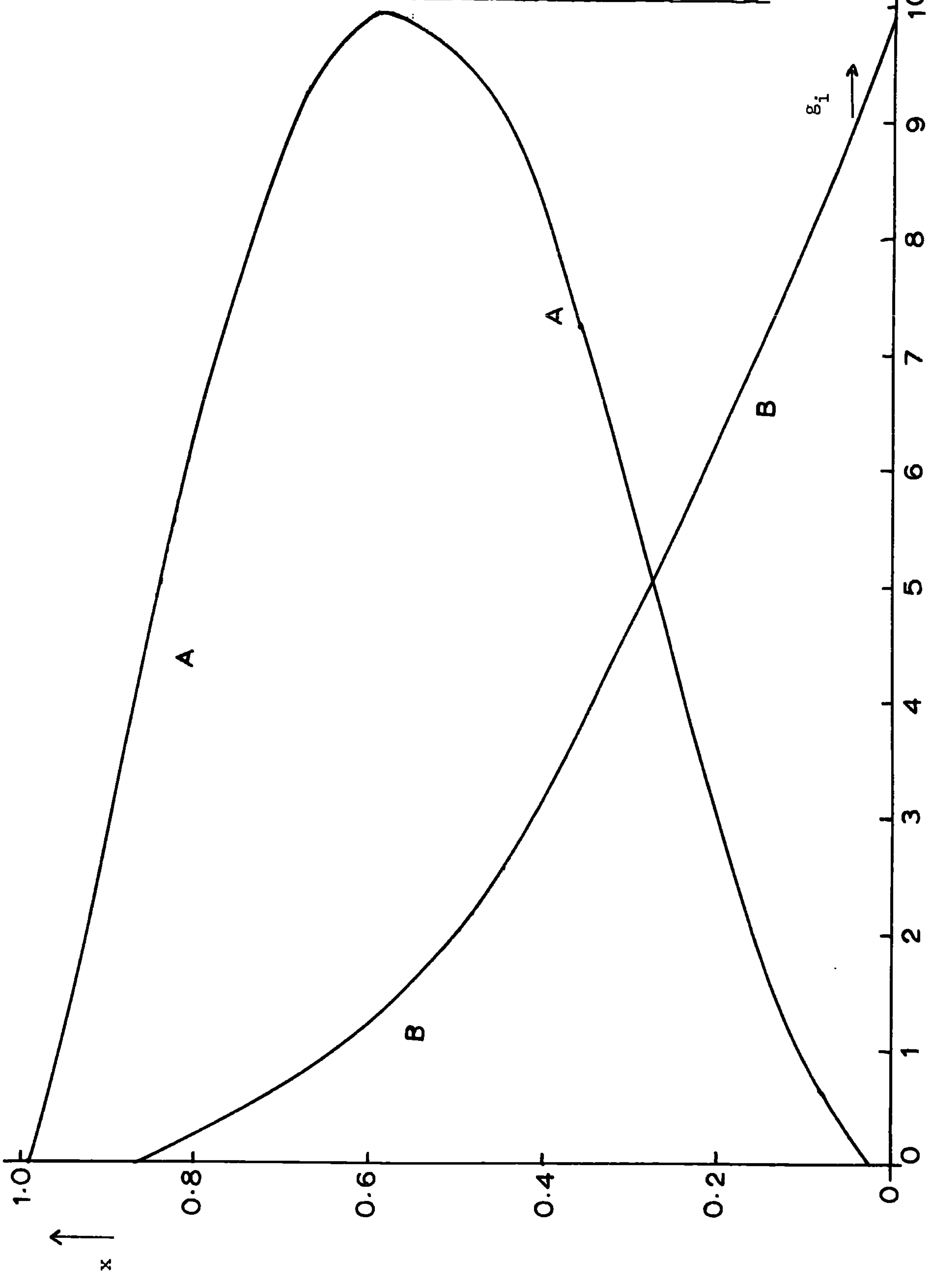
Equation	$\left(\frac{\partial y_i}{\partial p_i}\right)^2$	Equation	$\left(\frac{\partial y_i}{\partial p_i}\right)^2$
3.2.1a	$\frac{1}{t_i^2} \cdot \frac{1}{(p_\infty - p_i)^2}$	3.2.1b	1
3.2.2a	$\frac{1}{(p_\infty - p_i)^2}$	-	-
3.2.3a	$\frac{1}{(p_\infty - p_i)^2}$	3.2.3b	1
-	-	3.2.4b	1

The difference between equations 3.2.1 and 3.2.2 lies only in the weighting scheme used, as 3.2.2 with $w_i=1$ is equivalent to 3.2.1 with $w_i=1/t^2$.

Fig.3.1 is a plot of the extent of reaction against the weight factors for equations 3.2.1a, 3.2.2a, 3.2.3a. It can be seen that for equation 3.2.1a, g_i is almost constant (changes by a factor of ca.5) in the range 15-85 per cent reaction, and under these conditions, the assumption and use of $w_i=1$ makes little difference to the results obtained. However, for equations 3.2.2a and 3.2.3a, there is a relatively large variation in g_i, which changes by a factor of ca.100 in the range 15-85 per cent reaction, and in these cases it is futile to use $w_i=1$.

Fig. 3.1

A plot of fraction of reaction (x) ⟶ weight factors (g_i) for equations 3.2.1a (A), 3.2.2a, 3.2.3a (B). (The scales are arbitrary).



3.4 The Calculation of Rate Constants

The standard error of k, (σ_k), also depends on the experimental range studied. Kohnstam[12] has shown that for the experimental method employed in this work (that of sampling and then titrating for one of the products), the smallest σ_k for readings in the range 15-85 per cent reaction arises when $g_i \simeq 1$ in equation 3.2.1a (see Fig.3.1).

Occasionally, one of the measurements in the series has a relatively large error, due to adventitious factors, and this must be rejected during the calculation procedure. In a normal distribution of errors, all the experimental points, y_i, are such that there is a ca. 98 per cent chance that

$$w_i d_i^2 \leqslant 6{\cdot}25\, v_y^{est}$$

where $d_i = (y_i)_{obs} - (y_i)_{calc}$ and v_y^{est} is the estimated variance of y.

All the kinetic runs were carried out in duplicate or triplicate (see Appendix 8) with several determinations for p_∞ and p_0, to reduce systematic errors. Initially, a mean k was calculated from each run, but then a final mean k from all the points for all replicates was determined, and this value reported (see Appendix 5).

The importance of the choice of rate equation is illustrated in Table 3.3.

The results in Table 3.3 are representative of similar results (not shown) for many other kinetic runs and are fully in accord with the predictions of the general treatment. It can be seen that all the equations lead to the same k, within $\pm$ 2•5 σ_k, and that the difference in k from the logarithmic and exponential expressions is negligible when $w_i = g_i$, suggesting a normal distribution of errors. However, there is a small difference when $w_i = 1$ and this is to be expected when unsuitable weighting

Table 3.3

Kinetic data for the reaction of Ph_3CCH_2OTs with 85% aqueous acetone at 75^o. Expt. 42 (second run)

Equation	10^6k (sec^{-1})	$10^3\sigma_k/k$
3.2.1a, $w_i=1$	71•389	2•03
3.2.1b, $w_i=1$	71•516	1•62
3.2.1a, $w_i=g_i$	71•475	1•77
3.2.1b, $w_i=g_i$	71•477	1•75
3.2.2a	71•709	1•20
3.2.3a, $w_i=1$	71•937	1•48
3.2.3b, $w_i=1$	71•726	2•12
3.2.3a, $w_i=g_i$	71•684	2•25
3.2.3b, $w_i=g_i$	71•685	2•24
3.2.4b, $w_i=1$	70•969	6•98
3.2.4b, $w_i=g_i$	70•880	7•26

schemes are used. With equations 3.2.1a,b, the difference in σ_k for $w_i=1$ and g_i is a small one, due to the fact that $g_i \simeq 1$. The standard errors obtained from 3.2.2a and 3.2.3a ($w_i=1$) are almost too small, although this is probably fortuitous. When $w_i=g_i$, σ_k increases in the order 3.2.1 < 3.2.3 < 3.2.4, as the number of disposable parameters increases, and although σ_k is reasonable for 3.2.1, 3.2.3, it is relatively very large for 3.2.4.

An analysis of the results obtained from many sets of data, and using all the forms of the first-order rate equation, enabled conclusions to be drawn concerning the expression most suited to the present work. Equation

3.2.4 can be immediately discounted because of the large σ_k, in spite of the absence of systematic errors. Equation 3.2.1 gives a small σ_k, but systematic errors arise from p_o and p_∞. These can be reduced considerably by making several determinations of p_o and p_∞, although by the nature of the experimental method (see section 7.2.3) it is not always possible to make more than two measurements of p_o. Equation 3.2.3 is probably the "best" form of the rate expression to use and this gives a small σ_k, has a systematic error from one source only (p_∞), and two disposable parameters. The weighting scheme $w_i=g_i$ is more suitable than $w_i=1$, as suggested by the variation of g_i with the extent of reaction (see Fig.3.1).

Originally, all the rates were calculated by 3.2.1a ($w_i=1$), but for the compounds discussed in Chapters 4 and 6, recalculations were performed using 3.2.3a ($w_i=g_i$) and the rates obtained are those which are reported (see Appendix 5).

3.5 The Calculation of Activation Parameters

The absolute rate equation, discussed in Chapter 2, can be written

$$\ln k = \ln \frac{\bar{k}}{h} + \ln T + \frac{\Delta S^\ddagger}{R} - \frac{\Delta H^\ddagger}{RT} \qquad 3.4$$

Now $\frac{\partial \Delta H^\ddagger}{\partial T} = T\frac{\partial \Delta S^\ddagger}{\partial T} = \Delta C_p^\ddagger$, and for generality's sake it can be assumed that

$$\Delta C_p^\ddagger = c + dT \qquad 3.5$$

Also,

$$\Delta H^\ddagger = \int \Delta C_p^\ddagger \, dT + \text{constant}$$

$$= a + cT + \frac{1}{2} dT^2 \qquad 3.6$$

and

$$\Delta S^\ddagger = \int \frac{\Delta C_p^\ddagger}{T} dT + \text{constant}$$

$$= b + c\ln T + dT \qquad 3.7$$

The activation energy, E, is defined as

$$E = RT^2 \frac{d\ln k}{dT} = \Delta H^{\ddagger} + RT$$

$$= a + (c + R)T + \frac{1}{2} dT^2 \qquad 3.8$$

From equations 3.4-3.7

$$\ln k = [\frac{A}{T} + B + C\ln T + DT] \qquad 3.9$$

where $A = \left(- \frac{a}{R} \right)$, $B = \left(\ln \frac{\bar{k}}{h} + \frac{b}{R} - \frac{c}{R} \right)$, $C = \left(\frac{c}{R} + 1 \right)$, $D = \left(\frac{1}{2} \frac{d}{R} \right)$

A-D are calculated using the least squares procedure, with the same weight (w_i=1) for each point.

Then, at any temperature T, from equations 3.5-3.7,

$$E = (-AR + CRT + DRT^2)$$

$$\Delta S^{\ddagger} = (-R\ln \frac{\bar{k}}{h} + BR + (CR-R)(\ln T + 1) + 2DRT)$$

and $$\Delta C_p^{\ddagger} = (CR-R) + 2DRT$$

The errors in the activation parameters depend upon the errors of A-D, but as these are not independent parameters, covariances are also required (see Appendix 3).

Thus, at any temperature T,

$$v(E) = v(A)R^2 + v(C)R^2T^2 + v(D)R^2T^4 + 2cov(A,C)R^2T$$
$$+ 2cov(A,D)R^2T^2 + 2cov(C,D)R^2T^3$$

and $$v(\Delta C_p^{\ddagger}) = v(C)R^2 + 4v(D)R^2T^2 + 4cov(C,D)R^2T$$

where v(x) and cov(x,y) are the variances and covariances, respectively, of the different quantities. It can also be shown to a very good approximation that

$$\sigma(\Delta S^{\ddagger}) = \frac{\sigma(E)}{T}$$

The four parameter equation, 3.9, implies that $\Delta C_p^\ddagger$ is temperature dependent, but the experimental accuracy ($\sigma_k/k \leqslant 2 \times 10^{-3}$; see Appendix 5) is not sufficient to indicate that $\partial\Delta C_p^\ddagger/\partial T$ is significantly different from zero. This is illustrated in Table 3.4 for a typical series of experiments. It can be seen that $\sigma[(\partial\Delta C_p^\ddagger/\partial T)_{calc}] > 2(\partial\Delta C_p^\ddagger/\partial T)_{calc}$, and therefore too large to allow a value of $\partial\Delta C_p^\ddagger/\partial T$ other than zero to be meaningful.

The activation parameters which resulted from equation 3.9 when only three of the parameters (A,B,C) were used, were found to be considerably more reliable than those calculated from the four-parameter equation. This was due to the large uncertainty in the value of the parameter D, and hence in $(\partial\Delta C_p^\ddagger/\partial T)_{calc}$ (see Table 3.4). Table 3.5 shows the larger errors associated with the activation parameters when the four-parameter equation is used, particularly when a comparison is made at temperatures other than the mean temperature of the experimental range.

The activation parameters and their errors calculated from the rate constants for the various rate equations are shown, for one compound in Table 3.6 (part of Appendix 6). Equation 3.9 with D=0 has been used.

All the E, $\Delta S^\ddagger$, $\Delta C_p^\ddagger$ values are the same within the limits of error, as expected, and it therefore does not matter which form of the rate equation is used. The quoted activation parameters are those calculated from mean rate constants obtained from equation 3.2.3a ($w_i=g_i$). A summary of the activation parameters for the compounds studied, (from 3.9 with D = 0), is given in Appendix 6.

All the calculations mentioned in this chapter were performed using the Northumbrian Universities I.B.M. 360/67 computer. The programmes were written by Dr. G. Kohnstam.

Table 3.4

Rate data and activation parameters for $HO(CH_2)_4Cl$, calculated using equations 3.2.3a ($w_i=g_i$) and 3.5-3.9 (with 4 parameters, A-D)

Temp (^{o}C)	10^6k (sec^{-1})	$10^3\sigma_k/k$
94•82	468•46	0•97
85•11	214•56	1•37
74•80	88•026	1•38
65•00	35•542	1•16
54•96	13•179	0•77
45•18	4•6429	0•80
35•20	1•4782	1•39

Activation parameters at 65•01^{o}C (mean temp. of experiments)

E = (21726 ± 20) cal

$\Delta S^{\ddagger}$ = (-16•88 ± 0•06) cal deg^{-1} $mole^{-1}$

$\Delta C_p^{\ddagger}$ = (-26•99 ± 0•90) cal deg^{-1} $mole^{-1}$

$(\partial\Delta C_p^{\ddagger}/\partial T)_{calc}$ = (0•06 ± 0•16) cal deg^{-2} $mole^{-1}$

Note: The activation parameters for $HO(CH_2)_4Cl$ calculated using 3 parameters in equation 3.9, are given in Appendix 6.

Table 3.5

Activation parameters and their errors for $HO(CH_2)_4Cl$,

calculated using equations 3.2.3a ($w_i=g_i$) and 3.9 with 3 and 4 parameters

	3 parameter equation		4 parameter equation	
Temp. (°C)	E(cal)	$\Delta C_p^{\ddagger}$ (cal deg^{-1} $mole^{-1}$)	E(cal)	$\Delta C_p^{\ddagger}$ (cal deg^{-1} $mole^{-1}$)
65•01 §	21733 ± 6	-27•06 ± 0•77	21726 ± 20	-26•99 ± 0•90
50•00	22109 ± 14	-27•06 ± 0•77	22108 ± 16	-27•97 ± 2•47
25•00	22736 ± 32	-27•06 ± 0•77	22778 ± 113	-29•60 ± 6•46

§ Mean temperature of the experimental range.

Table 3.6

Summary of activation parameters for $HO(CH_2)_4Cl$ at 65•01° (mean temp. of experiments: E in cal, $\Delta S^\ddagger$ and $\Delta C_p^\ddagger$ in cal $deg^{-1}mole^{-1}$)

Equation	E	$-\Delta S^\ddagger$	$-\Delta C_p^\ddagger$
3.2.1a, $w_i=1$	21723 ± 7	16•88 ± 0•02	26•08 ± 0•72
3.2.1a, $w_i=g_i$	21725 ± 6	16•88 ± 0•02	26•81 ± 0•71
3.2.2	21736 ± 6	16•85 ± 0•02	25•55 ± 0•67
3.2.3a, $w_i=1$	21745 ± 10	16•83 ± 0•03	24•87 ± 1•03
3.2.3a, $w_i=g_i$	21733 ± 6	16•85 ± 0•02	27•06 ± 0•77

CHAPTER 4

NEIGHBOURING HYDROXYL PARTICIPATION

4.1 Results. Rate and Product Data

Five structurally similar members of a group of polymethylene chlorohydrins (I; n = 1-5) were hydrolysed in 50 per cent aqueous acetone and the rate coefficients determined.

$$HO(CH_2)_nCH_2Cl \qquad (I)$$

The rate coefficients for reaction at 100^o, interpolated from measurements at other temperatures with the appropriate allowance for the variation of the activation energy with temperature, are shown in Table 4.1. Also included are results for three of the corresponding n-alkyl chlorides (II; n = 1-3)

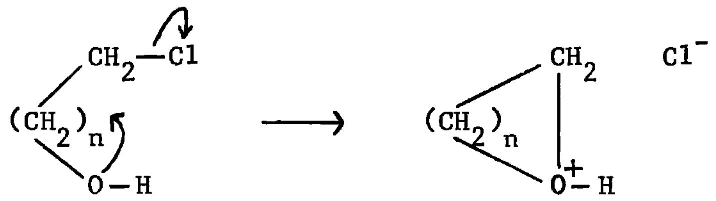
Table 4.1

Rate coefficients (10^6k in sec^{-1}) for reaction with 50 per cent aqueous acetone at 100^o

n	$HO(CH_2)_nCH_2Cl$ (I)	$H(CH_2)_nCH_2Cl$ (II) §
1	0•97	8•80
2	2•81	3•84
3	687•8	3•24
4	25•44	-
5	3•95	-

§ From results for the bromides[55] on the assumption that the corresponding chlorides react 18•7 times less rapidly. This factor applies (within ± 4 per cent) to the solvolysis of the benzyl halides and the ethylene halohydrins.[44]

which undergo bimolecular (S_N2) solvolysis in hydroxylic solvents. An increase in chain length in the alkyl chlorides slightly retards the reaction, the change being greatest for the first two compounds. The same structural alteration in the chlorohydrins results at first in an acceleration of the solvolysis and the rate coefficients pass through a substantial maximum when n= 3. This pattern of behaviour is in full agreement with the earlier findings[16,19] for the reactions in water of I (n = 1-4) which are summarised in Table 1.1. It was concluded that the lower members of the series (n = 1,2) undergo bimolecular solvolysis, but that when n = 3,4 the ω-hydroxyl group can act as an internal nucleophile and facilitate reaction via the cyclic intermediate, III. The product of proton loss by III (n = 3),



(III)

tetrahydrofuran, has been isolated from the reaction products of the hydrolysis of I (n = 3) in water.[56]

In the present study an examination of the reaction mixture by gas liquid chromatography, after complete solvolysis, revealed the quantitative formation of tetrahydrofuran from I (n = 3) and tetrahydropyran from I (n = 4), within the limits of the experimental error (ca. ± 5%). These two compounds could easily be produced by proton loss from the cyclic intermediates III (n = 3,4). Check experiments showed that the products (IV) expected from S_N2 solvolysis did not form the cyclic compounds under the

$$HO(CH_2)_nCH_2OH \qquad (IV)$$

conditions of the experiments. Trimethylene oxide, the possible product of solvolysis of I (n = 2) was found to undergo an acid-catalysed ring-opening under the experimental conditions and formation of a cyclic intermediate from I (n = 2) is therefore not entirely excluded by the observations. However, the activation parameters argue against such a conclusion and recent work on HO-n participation[57] (n = 4-9) has shown that although five- and six-membered rings containing oxygen are readily formed following neighbouring hydroxyl participation, the formation of a four-membered ring by this process does not occur. From the rate and product data it therefore seems certain that only the tetra- and pentamethylene chlorohydrins are subject to neighbouring group participation in their hydrolyses. The difference in the rates of reaction of these two compounds suggests that the formation of a five-membered cyclic intermediate is the energetically more favourable process. This conclusion is consistent with other information concerning the ease of closure of ring systems containing an oxygen atom.[16]

It is worth noting that the small reactivity of ethylene chlorohydrin (I; n = 1) relative to ethyl chloride (II; n = 1) is probably due to the proximity of the strongly electron-attracting hydroxyl group to the reaction centre.

4.2 Activation Parameters

The energies and entropies of activation for the hydrolysis of the chlorohydrins and alkyl chlorides at 100° are shown in Table 4.2.

Heat capacities of activation were not determined for compounds I (n = 1,2,5) and in each case, a value of (-21 ± 4) cal $\deg^{-1}$, appropriate for reaction by mechanism S_N2,[37] was used in the calculations of the activation parameters at 100°. This temperature is close to the mean

Table 4.2

Activation parameters for reaction with 50 per cent aqueous acetone at 100^{o} (E in kcal, $\Delta S^\ddagger$ in cal deg^{-1})

n	$HO(CH_2)_nCH_2Cl$ (I)		$H(CH_2)_nCH_2Cl$ (II) §	
	E φ	$-\Delta S^\ddagger$ φ	E	$-\Delta S^\ddagger$
1	25·28 ± 0·07	20·75 ± 0·19	22·53	23·71
2	23·74 ± 0·08	22·76 ± 0·20	22·39	25·74
3	20·86 ± 0·03	19·50 ± 0·10	22·27	26·41
4	22·78 ± 0·04	20·94 ± 0·11	-	-
5	22·77 ± 0·03	24·67 ± 0·08	-	-

§ From results for the bromides,[55] assuming E(RCl)-E(RBr) = 1·612 kcal and $\Delta S^\ddagger$(RCl)-$\Delta S^\ddagger$(RBr) = -1·5 cal deg^{-1}.[44]

φ The errors quoted are standard errors.

experimental temperature for these three compounds and was chosen so that the errors resulting from the use of assumed $\Delta C_p^\ddagger$ values are small. The heat capacities of activation for I (n = 3,4) are discussed in the following section.

The activation parameters for I (n = 3) were determined from the mean rate constants calculated in five different ways, as discussed in Chapter 3. However, the study of the chlorohydrins was completed before the development of the computer techniques for dealing with experimental data, and the parameters for I (n = 1,2,4,5) were determined from mean rate constants calculated from the "simple form" of the rate equation (3.2.1a with unit weight factors: see Chapter 3). It was shown in Chapter 3 that the different methods of calculation give activation parameters which are in close agreement, and any small differences in the data of Table 4.2 arising from the calculation procedure are within the experimental errors for each value. No errors are given for the alkyl chlorides but they are expected to be a little larger than those for the chlorohydrins, since the parameters have been calculated from data for the corresponding alkyl bromides.

It can be seen from Table 4.2 that when the reaction involves neighbouring hydroxyl participation (I; n = 3,4) $\Delta S^{\ddagger}$ is more positive than is the case when the bimolecular mechanism is operating (I; n = 2,5). Ethylene chlorohydrin (I; n = 1) has an anomalous $\Delta S^{\ddagger}$ relative to the other members of the series, but the <u>ca</u>. 2 cal deg^{-1} decrease in $\Delta S^{\ddagger}$ on passing to I (n = 2) is also found for the hydrolysis of the alkyl chlorides and the corresponding bromohydrins and alkyl bromides solvolysing in water at 100°.[38] This difference probably arises from the alteration in the size of the substrate and not from a change in the reaction mechanism.[38]

The activation energy for I (n = 3) is much lower than the values which apply to the S_N2 mechanism. The difference is expected for a solvolysis in which the participation of a neighbouring group provides a reaction path which is energetically more favourable than that for the S_N2 process. The activation energies for I (n = 4,5) are almost identical, and it is interesting that changes in the entropy of activation are entirely responsible for the different mechanisms in the hydrolysis of these two compounds.

Table 4.2 shows that $\Delta S^{\ddagger}$ for the S_N2 hydrolysis of the chlorohydrins is about 3 cal deg^{-1} greater than for the reaction of the corresponding alkyl chloride by the same mechanism. Robertson[38] has found a similar difference for the hydrolysis of the bromides in water. Also, $\Delta S^{\ddagger}$ for

I (n = 5) is less negative than expected for an alkyl chloride of similar chain length. The hydroxyl group is probably capable of non-bonding interactions with the reaction centre or the nucleophile in the transition state which replace the similar interactions occurring with the solvent when the substrate is an alkyl halide. The hydroxyl group interactions are therefore expected to result in a positive contribution to $\Delta S^{\ddagger}$, which would qualitatively explain the different observed values of this parameter.

4.3 The Entropies and Heat Capacities of Activation Associated with the $S_N i$ Mechanism

4.3.1 Introduction

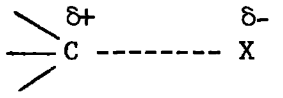
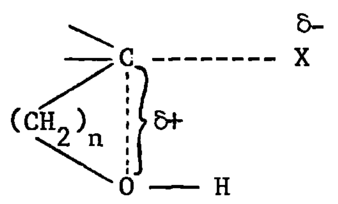
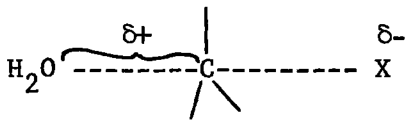
The activation parameters for the hydrolysis of tetra- and penta-methylene chlorohydrin are now discussed in more detail and compared with the results obtained for the solvolysis of these compounds in water. The intramolecular mechanism, $S_N i$, can be regarded as intermediate between the usual forms of the bimolecular and unimolecular mechanisms, and the transition states for the three reaction paths are shown in Table 4.3. Partial fission of the carbon-halogen bond is a feature of all three transition states. Mechanisms $S_N i$ and $S_N 2$ involve the partial formation of a new covalent bond, and a water molecule is removed from the solvent during the formation of the transition state for an $S_N 2$ hydrolysis. These simple considerations neglect changes in the solvent-solvent and non-bonding solute-solvent interactions during the activation process, but can be used as the basis of a useful working hypothesis.[44]

4.3.2 Entropies of Activation

The reactions of tetra- and penta-methylene chlorohydrin occur at the group $-CH_2Cl$, and as there is evidence that entropies of activation for

Table 4.3

Transition states for the hydrolysis of alkyl halides and their derivatives

Mechanism	Transition State
S_N1	
S_Ni	
S_N2	

solvolysis are affected by the structure of the substrate in the vicinity of the reaction centre, the values of $\Delta S^{\ddagger}$ for the hydrolysis of benzyl chlorides are suitable for the purposes of comparison. Benzyl chloride itself undergoes S_N2 reaction while the 4-phenoxy derivative with an electron-donating substituent far from the site of reaction solvolyses by mechanism S_N1. Table 4.4 shows the effect of changes in the mechanism on the entropy of activation and includes a value for the hydrolysis of tetramethylene chlorohydrin in water.[38] In the absence of data for the S_N1 reaction of a substituted benzyl chloride in water, the $\Delta S^{\ddagger}$ value of t-butyl chloride had to be used. The error caused by this is probably not large as the values of $\Delta S^{\ddagger}$ for the hydrolysis of this compound and of 4-phenoxybenzyl chloride in aqueous acetone are similar.[58,59]

Table 4.4

Entropies of activation (cal deg^{-1}) for

S_N reactions at 100°

Mechanism	Substrate	Solvent	
		50% aq. acetone	Water[38]
S_N1	$4\text{-}PhOC_6H_4CH_2Cl$	-15•17 ± 0•94 [58]	-
	t-BuCl	-14•16 ± 0•39 [59]	-8•5
S_Ni	$HO(CH_2)_4Cl$	-19•50 ± 0•10	-12•0
	$HO(CH_2)_5Cl$	-20•94 ± 0•11	-
S_N2	$PhCH_2Cl$	-25•46 ± 0•73 [55]	-17•8

The results in Table 4.4 show that at 100° decreases in the entropy of activation of 4-5•5 cal deg^{-1} and 4•5-6 cal deg^{-1} are associated with the changes in mechanism $S_N1 \longrightarrow S_Ni$ and $S_Ni \longrightarrow S_N2$, respectively. It is concluded from these figures that the loss of internal rotation in the chlorohydrins accompanying the activation process of an S_Ni reaction lowers the entropy by about 5 cal deg^{-1} but that the loss of translational and rotational motion by the water molecule during the activation step of an S_N2 hydrolysis decreases the entropy by approximately twice this amount. Although the assumptions that the changes in the solvent-solvent and solvent-solute interactions during reaction do not depend on mechanism are probably not justified[37,38,50] it is safe to conclude that the formation of a partial covalent bond by a neighbouring group results in a smaller entropy decrease than when the nucleophile is a solvent molecule in the initial state of reaction.

The results can also be explained on the basis of the fact that the volume of activation ($\Delta V^{\ddagger}$) for the S_Ni hydrolysis of tetramethylene chlorohydrin is appreciably less negative than for the S_N1 and S_N2 reactions of other chlorides.[60] The exclusion of molecules of solvent from the interior of the ring on cyclisation has been thought to be responsible for this observation.[61] The increase in the size of the substrate during cyclisation in the S_Ni reaction is expected to further disturb the solvent structure, and Robertson[62] has argued that a negative contribution to $\Delta S^{\ddagger}$ should result from this effect. However, it must be pointed out that the explanation ignores the contribution to $\Delta S^{\ddagger}$ from the formation of the partial covalent bond in the transition state of the S_Ni reaction.

4.3.3 Heat Capacities of Activation

Table 4.5 compares the heat capacities of activation for hydrolysis by the three mechanisms. All the values for aqueous acetone are similar and it is therefore not possible to establish any clear connection between $\Delta C_p^{\ddagger}$ and the mechanism for reaction in this solvent, especially as the values for the two compounds which undergo S_Ni solvolysis differ by a relatively large amount. It can be concluded, however, that as the magnitude of $\Delta C_p^{\ddagger}$ reflects the increase in solvation associated with the formation of the transition state,[37,50] the activation process in the present S_Ni reactions is not accompanied by a particularly large solvation increase.

In water, the heat capacities of activation for solvolysis by mechanisms S_N1 and S_N2 are markedly different, but for the S_Ni reaction of $HO(CH_2)_4Cl$ the parameter has a value which is very close to that for an S_N2 hydrolysis. At first sight, this result is rather unexpected, since the entropies of activation are significantly different for all three mechanisms. However,

Table 4.5

Heat capacities of activation (cal deg^{-1}) for S_N reactions

Mechanism	Substrate	Solvent	
		50% aq. acetone	water
S_N1	$4\text{-}PhOC_6H_4CH_2Cl$	-28•2 ± 4•5 [58]	-
	t-BuCl	-27•0 ± 2•1 [59]	-83 [38]
S_Ni	$HO(CH_2)_4Cl$	-27•06 ± 0•77	-41 [56]
	$HO(CH_2)_5Cl$	-16•76 ± 1•12	-
S_N2	$PhCH_2Cl$	-21•2 ± 3•6 [55]	-39 [38]

the numerically small $\Delta C_p^{\ddagger}$ value of $HO(CH_2)_4Cl$ (-41 cal deg^{-1}) relative to that for an S_N1 process (ca. 80 cal deg^{-1}) could be due to substantial hydrogen-bonding between the hydroxyl group and the solvent in the initial state.[44] This effect is thought to reduce the solvent-solvent interactions, resulting in an increase in $\Delta C_p^{\ddagger}$, and the value of the parameter for the S_Ni hydrolysis of the structurally similar $MeO(CH_2)_4Br$(-46 cal deg^{-1})[38] is in agreement with this interpretation.

An alternative explanation of the particular $\Delta C_p^{\ddagger}$ value for the solvolysis of $HO(CH_2)_4Cl$ in water is that reaction by two different concurrent mechanisms is occurring, resulting in a positive contribution to the observed heat capacity of activation if the two rate-determining steps have significantly different activation energies, but occur at approximately the same speed.[50] However, it is not possible to envisage a second process for the hydrolysis of tetramethylene chlorohydrin which would have a rate comparable with that of mechanism S_Ni. The numerically relatively small observed $\Delta C_p^{\ddagger}$ for the solvolysis of $HO(CH_2)_5Cl$ in aqueous acetone might be explainable in terms of two concurrent mechanisms, especially as in this case the observed and probable S_N2 rates are not very different (k_{obs} = ca. $7k_{S_N2}$; see Table 4.1), were it not for the fact that the reaction in this solvent yields exclusively the cyclic product.

The results of Table 4.5 provide clear evidence for different solvolytic behaviour in the two media under discussion, although the present work, whilst excluding certain possibilities, does not allow any firm mechanistic predictions to be made.

CHAPTER 5

NEIGHBOURING METHOXYL PARTICIPATION

5.1 Introduction

A study by Winstein and his co-workers[30] of neighbouring methoxyl participation in the solvolyses of a series of ω-methoxy-1-alkyl bromobenzenesulphonates in ethanol, acetic acid and formic acid, showed that the reactions of the 4-methoxy-1-butyl and 5-methoxy-1-pentyl esters were rapid compared with the other members of the series. It was concluded that MeO-5 and MeO-6 participation was important, especially as the kinetic results were qualitatively similar to those obtained for a series of chlorohydrins in water.[19]

In the present work, the series of compounds I (n = 1-5) was hydrolysed in 50 per cent aqueous acetone and it was hoped to obtain accurate activation

$$MeO(CH_2)_nCH_2Br \qquad (I)$$

parameters for each member, so that a direct comparison with the results of the structurally similar chlorohydrins could be made. In the event, however, although compounds I (n = 1,2,5) gave good first-order kinetics, a more complicated rate law in the reactions of I (n = 3,4) prevented the determination of accurate activation parameters for these substrates.

The results of product studies with I (n = 3,4) proved to be interesting and a reaction scheme involving concurrent S_N2 and S_Ni processes for the hydrolysis of I (n = 4) was postulated on the basis of product and kinetic data. More recently, work by Winstein[63] on MeO-5 and MeO-6 participation and involving accurate product analyses has been published and is discussed with the present results in the following sections.

5.2 Results

The rate coefficients for the reactions of I (n = 1-5) with 50 per cent aqueous acetone at 65° are shown in Table 5.1, and compared with the rates for the corresponding n-alkyl bromides.[55]

Table 5.1

Rate coefficients for reaction with 50% aqueous acetone at 65•13° (10^7k in sec^{-1})

n	$MeO(CH_2)_nCH_2Br$ (I)	$H(CH_2)_nCH_2Br$ [55] (II)
1	3•7	86
2	20	40
3	2575 §	35
4	180 §	-
5	38	-

§ These 2 values are from "initial rate" determinations.

For I (n = 3,4) the rate coefficients decreased as the reactions proceeded (see Appendix 8, experiments 19, 22). The kinetic data obtained are summarised in Table 5.2. Runs with added bromide ion were done to study mass-law and more complicated kinetic effects in the hydrolyses of the two compounds. The "initial" k values were determined from plots of k against time, using the results of experiments 19-21 (n = 3) and 23,25,27, 29 (n = 4). Mention is also made of the decrease or increase in the rate coefficients during the course of a kinetic run.

Table 5.2

Summary of kinetic data for I (n = 3,4) at 65°

n	concentration of added NaBr	"initial" k value (sec^{-1}), $(k_{obs})_{t=0}$
3	0	$2{\cdot}57 \times 10^{-4}$, decreasing
3	0•021M	$1{\cdot}50 \times 10^{-4}$, decreasing
3	0•052M	$1{\cdot}01 \times 10^{-4}$, decreasing
4 §	0	$1{\cdot}80 \times 10^{-5}$, decreasing
4 §	0•021M	$0{\cdot}76 \times 10^{-5}$, increasing
4 §	0•051M	$0{\cdot}62 \times 10^{-5}$, increasing
4 §	0•097M	$0{\cdot}53 \times 10^{-5}$, increasing

§ From kinetic runs with experimental points limited to the first 15-20% of reaction.

Product studies indicated the formation of small amounts of tetrahydrofuran in the hydrolysis of I (n = 3). The yields of the cyclic compound were ca. 1-2 per cent (solutions without added NaBr) and ca. 5-10 per cent (0•05M in NaBr). Solvolysis of I (n = 4) resulted in yields of ca. 63 per cent tetrahydropyran (no added NaBr) and ca. 77 per cent tetrahydropyran (0•5M NaBr).

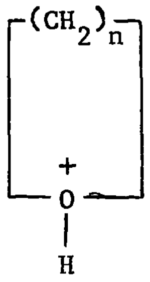
5.3 Introductory Discussion

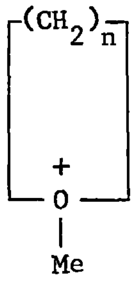
The results of Table 5.1 show, not surprisingly, striking similarities with those obtained for reactions of the corresponding p-bromobenzenesulphonates in acetic acid[30] and for the solvolysis of the structurally similar chlorohydrins in 50 per cent aqueous acetone (see Table 4.1).

A comparison of the rates for I (n = 1,2,5) with those for the corresponding n-alkyl bromides indicates that reaction of the former compounds occurs solely by mechanism S_N2. The small reactivity of I (n = 1) relative to ethyl bromide (II; n = 1) is presumed to arise from the proximity of the electron-attracting methoxyl group in I to the reaction centre.

Substrates I (n = 3,4) undergo rapid reaction relative to the other members of the series due to anchimeric assistance by the neighbouring methoxyl group. The essential difference between the hydroxyl and methoxyl containing compounds with regard to neighbouring group participation is that whereas the chlorohydrins exhibit normal first-order kinetic behaviour, the solvolyses of I (n = 3,4) show kinetic complications. The intermediates involved in the anchimerically assisted reactions of the two series are III and IV and the difference in behaviour is probably due to the fact that ion IV is much more stable than III. Ion III can easily undergo proton loss to

(III)





(IV)

(n = 3,4)

give a stable ring compound, and if this step is more rapid than the attack on the ion by nucleophiles (water molecules and bromide anions), the reaction will show first-order kinetics. Ion IV, however, can not readily lose its methyl group in a similar manner and attack by nucleophiles can be expected to involve a mass-law effect.

Further complicating kinetic features may also arise because of the possibility of anion attack both at the methyl group and at the C-O carbon atoms of the ring.

The results obtained for I (n = 3,4) are discussed in detail in the following two sections.

5.4 The Solvolysis of 4-methoxy-1-bromobutane (I; n = 3)

The results summarised in Table 5.2 show that the rate coefficients decrease steadily throughout a kinetic run and that the addition of sodium bromide, a "common-ion" salt, depresses the rate of reaction. The operation of a mass-law effect is suggested.

The reaction scheme for an S_N1 hydrolysis involving a mass-law effect is

$$\mathrm{RBr} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{R}^+ + \mathrm{Br}^- \xrightarrow[k_3]{\mathrm{H_2O}} \mathrm{ROH} + \mathrm{H}^+$$

The rate law can be written

$$\frac{dx}{dt} = \frac{k_1(a - x)}{1 + \alpha(c + x)} \qquad 5.1$$

where $\underline{a}$ and $(a - x)$ are the concentrations of RBr at zero time and time $\underline{t}$, respectively, $\underline{c}$ is the concentration of bromide ion at zero time and α is k_2/k_3.

If the effect of increasing ionic strength on k_1 and α is neglected, integration of equation 5.1 gives

$$k_1^{o} = k_{obs} + \alpha^{o}[k_{obs}\,(a + c) - x/t] \qquad 5.2$$

where the superscript $\underline{o}$ denotes zero ionic strength and k_{obs} is the observed rate constant. Equation 5.2 can be rewritten as

$$k_{obs} = \frac{k_1^{\,o}}{(1 + \alpha^o(a + c))} + \frac{\alpha^o}{(1 + \alpha^o(a + c))} \cdot \frac{x}{t} \qquad 5.3$$

Equation 5.3 predicts that a plot of k_{obs} against x/t should be linear, and such a relationship was observed for the three kinetic experiments. Fig.5.1 shows the k_{obs} against x/t plot for the run without added NaBr. From the slope (29•7 mole^{-1}ℓ) the calculated value of α^o is 51•7.

The observed initial rate constant, $(k_{obs})_{t=o}$, the initial ionisation rate, $k_1^{\,o}$, and the mass-law constant, α^o, are related in the equation

$$(k_{obs})_{t=o} = \frac{k_1^{\,o}}{1 + \alpha^o Br^-} \qquad 5.4$$

where Br^- is the concentration of added NaBr. Rearrangement and the inclusion of the relevant activity coefficients f_1 and f_3 (See Appendix 1) for the reacting species gives

$$\alpha^o = \frac{k_1^{\,o} f_1 - (k_{obs})_{t=o}}{(k_{obs})_{t=o} \cdot f_3 \cdot Br^-} \qquad 5.5$$

Equation 5.5 was used to calculate α^o from the data of the two runs with added NaBr and the results are summarised in Table 5.3. The determination of the activity coefficients is discussed in Appendix 1.

The values of α^o in Table 5.3 and that determined graphically from Fig.5.1 are in close agreement, and it can be concluded from this simple approach that the kinetic data obtained for I (n = 3) are consistent with the operation of a mass-law effect. However, the observation of a small amount of tetrahydrofuran in the hydrolysis product (1-10 per cent, depending on the concentration of added NaBr; see section 7.3.4), indicates that a little of the substrate reacts via a more complicated mechanism.

Fig.5.1

Plot of k_{obs} $\longrightarrow$ x/t for run of $MeO(CH_2)_4Br$, in the absence of added salt.

(Run 19)

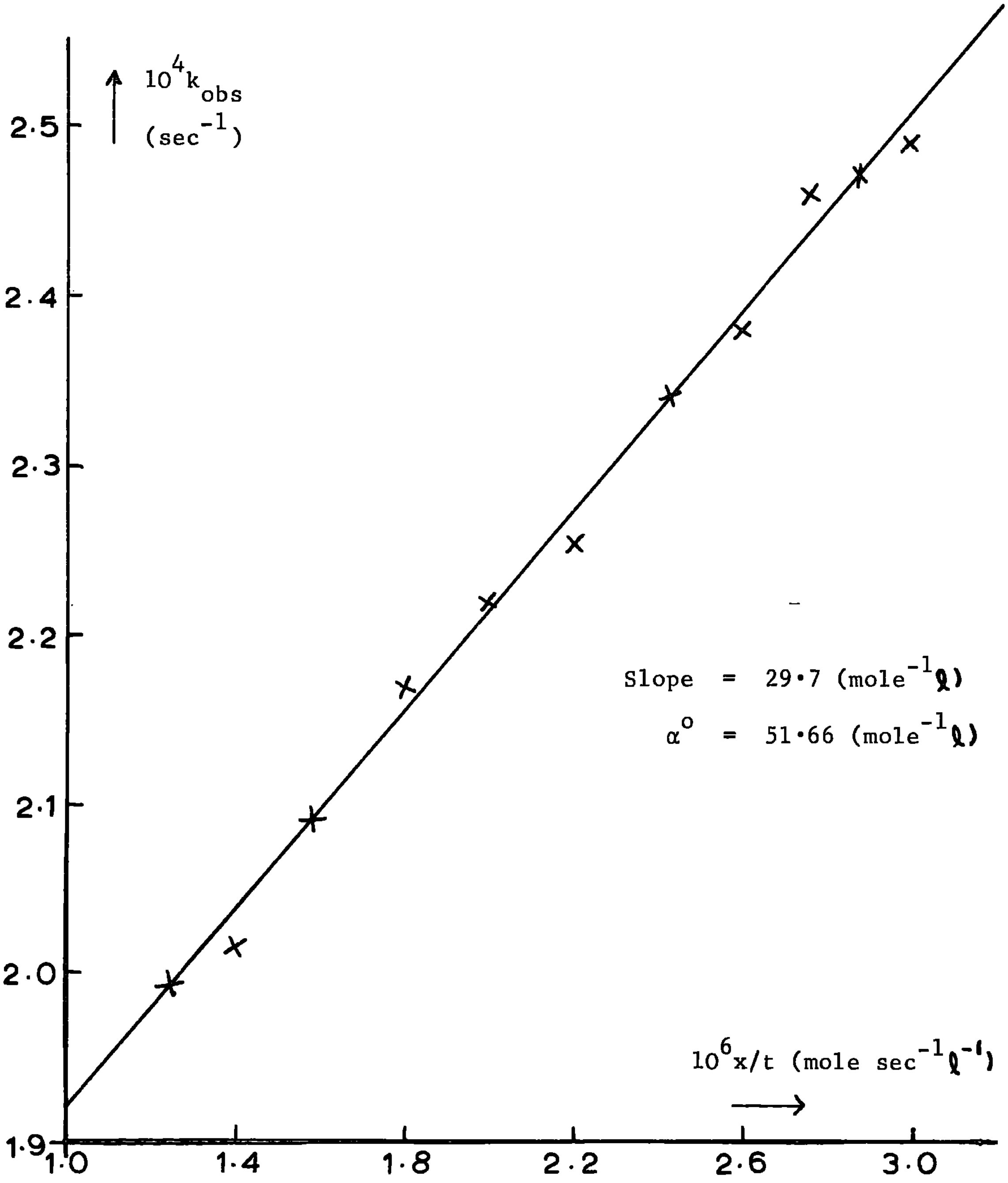


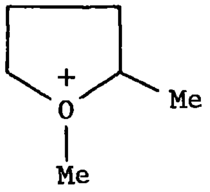
Table 5.3

Calculation of mass-law constants (α^o) for I (n = 3)

concentration of added NaBr	$(k_{obs})_{t=o}$	k_1^o §	f_1	f_3	α^o
0•021M	$1{\cdot}50 \times 10^{-4}$	$2{\cdot}57 \times 10^{-4}$	1•04	0•725	51•8
0•052M	$1{\cdot}01 \times 10^{-4}$	$2{\cdot}57 \times 10^{-4}$	1•10	0•649	53•5

§ $k_1^o = (k_{obs})_{t=o}$ when no added NaBr is present.

Allred and Winstein[63a] have studied MeO-5 participation in the solvolyses of 4-methoxy-1-pentyl and 5-methoxy-2-pentyl p-bromobenzenesulphonates in acetic acid and ethanol. Both substrates were found to give identical ratios of $CH_3OCH(CH_3)(CH_2)_2CH_2OS$ and $CH_3OCH_2(CH_2)_2CH(CH_3)OS$ as solvolysis products (60:40 for ethanol and 40:60 for acetic acid), indicating an intermediate common to both reactions. The presumed structure is the O-methyl-2-methyl-tetrahydrofuranium ion,V, the presence of which was confirmed by the observation that the two isomers afforded a small yield,(ca. 1•5 per cent) of 2-methyl-tetrahydrofuran on ethanolysis. This last result is in close



(V)

agreement with that obtained in the present study. The work in acetic acid and ethanol suggests that V is quite stable and survives long enough for attack to occur at the methyl and the primary and secondary C-O carbon atoms collectively. Two varieties of O-methyl-2-methyltetrahydrofuranium ion-pairs, as well as the dissociated ion have been identified in the acetolyses.[63b]

5.5 The Solvolysis of 5-methoxy-1-bromopentane (I; n = 4)

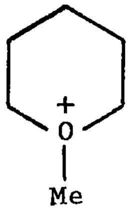
The unusual and interesting kinetic feature of the reactions of I (n = 4) in aqueous acetone is that although the rate coefficients decrease steadily throughout a run in the absence of NaBr, they increase in the presence of NaBr. Further, an experiment with the substrate at three times the normal concentration (0·045M) gave rate coefficients which passed through a minimum. These results are shown diagramatically in Fig.5.2.

The initial rates are depressed on the addition of common-ion and a mass-law effect is probably operating even though a plot of k against x/t is not linear (Fig.5.3). In addition to a mass-law effect, there are further complications, as clearly indicated in Fig.5.2.

In this section a reaction scheme is proposed and the kinetic data analysed.

5.5.1 Reaction scheme

In the absence of complicating kinetic features, substrate I (n = 4) is expected to solvolyse by mechanism S_Ni via the cyclic intermediate ion VI. Rapid attack by water on this ion would then give the corresponding alcohol

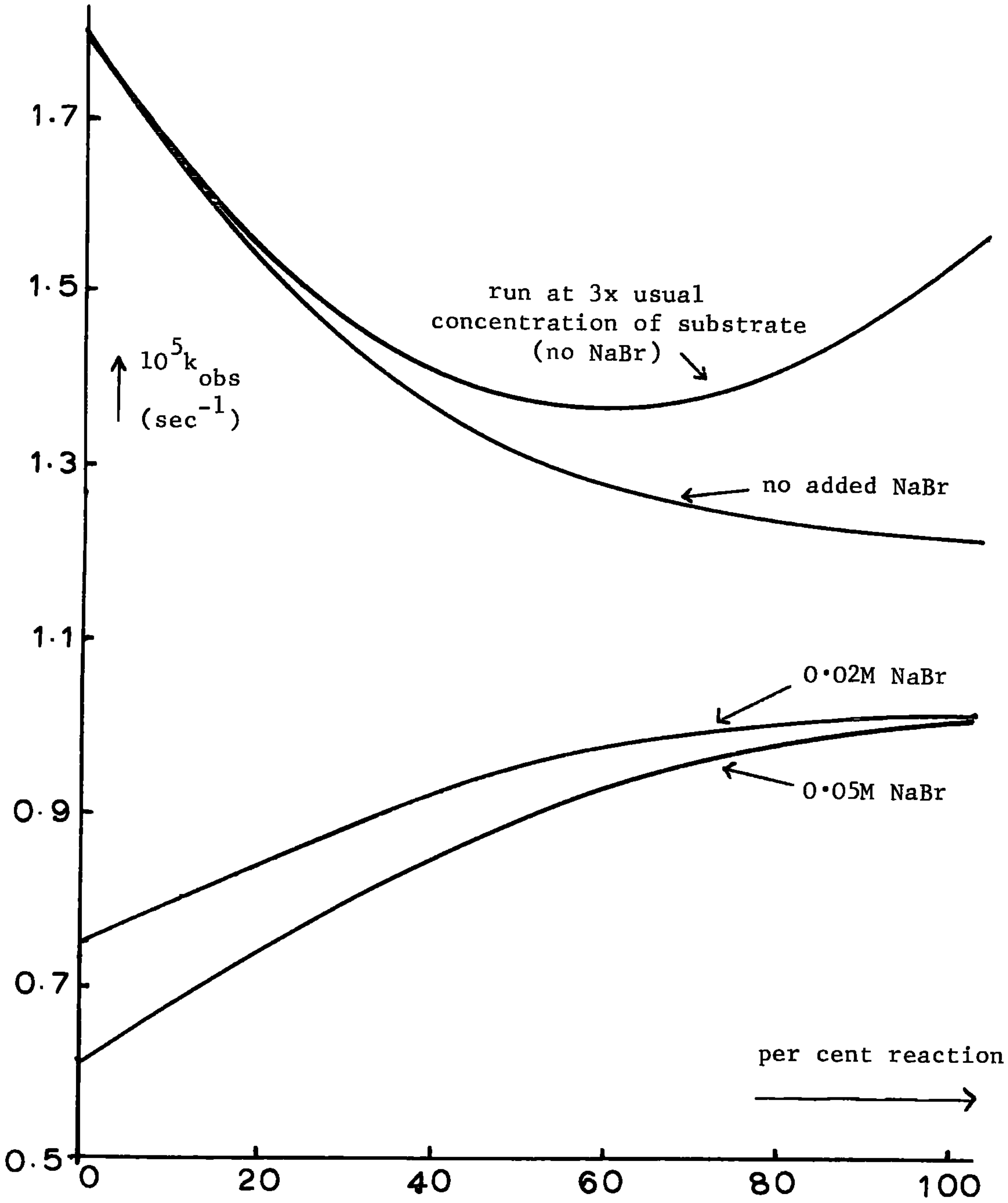


(VI)

as the only product.

Fig.5.2.

The variation of k_{obs} with percentage reaction for runs of I(n = 4) with varying amounts of added sodium bromide



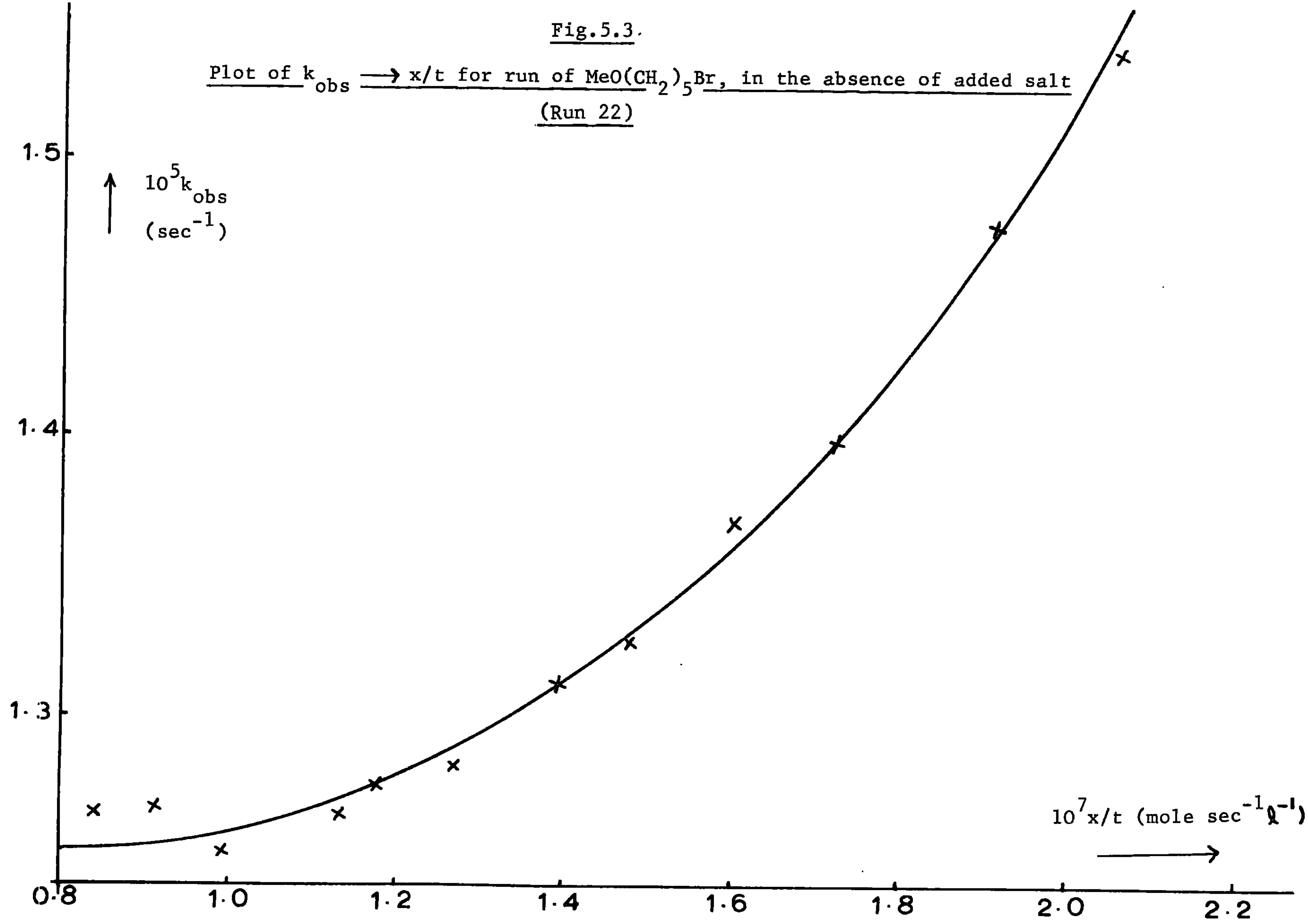


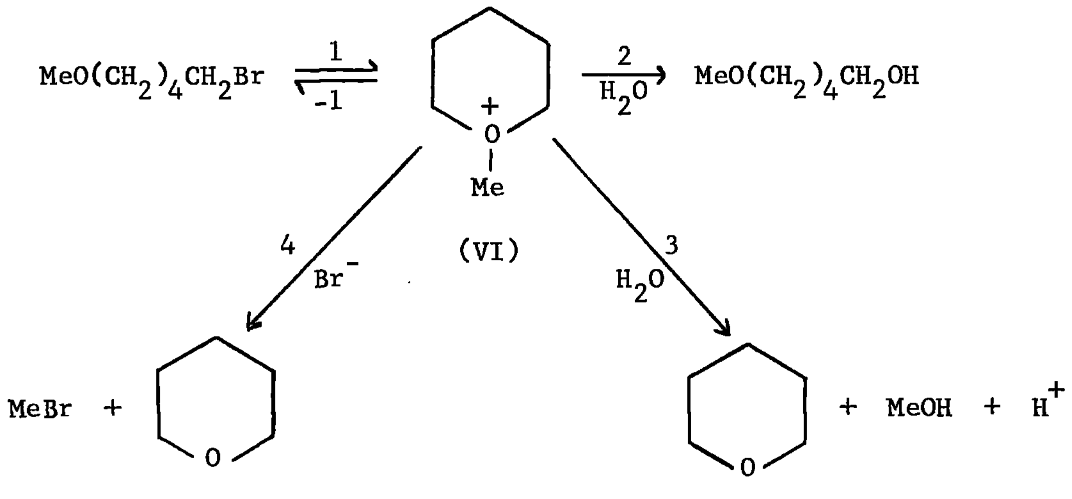
Fig.5.3.

Plot of k_{obs} ⟶ x/t for run of $MeO(CH_2)_5Br$, in the absence of added salt

(Run 22)

However, a study of the reaction products showed a substantial yield of tetrahydropyran (see section 5.2). This stable cyclic compound was also recovered by Winstein and his co-workers as one of the main products of the acetolysis of 5-methoxy-1-pentyl p-bromobenzenesulphonate.[63c] The tetrahydropyran probably arises from nucleophilic attack at the methyl group of ion VI. In the present work, attack by both water and bromide ion may well be possible and it is interesting to note that methyl bromide, one of the products of bromide ion attack on VI has been recovered after the acetolysis of 5-methoxy-1-pentyl p-bromobenzenesulphonate.[63c] In the present solvent, any methyl bromide formed as a result of bromide ion attack on VI will itself be hydrolysed to methanol. In addition, it is possible that a certain fraction of the substrate will be subject to direct S_N2 attack by water. The product work suggests this possibility, as indicated below.

As a result of these preliminary considerations, the following reaction scheme was suggested to account for the results of the kinetic and product work.



$$\mathrm{MeBr} \xrightarrow[H_2O]{5} \mathrm{MeOH} + H^+$$

$$\mathrm{MeO(CH_2)_4CH_2Br} \xrightarrow[H_2O]{6} \mathrm{MeO(CH_2)_4CH_2OH} \qquad (S_N2)$$

The intermediate carbonium ion, VI, is considered to undergo attack at both the methyl and the C-O carbon atoms in the ring. Attack by water (steps 3 and 2) and bromide ion (steps 4 and -1) can both occur. On this view the observed kinetics are further complicated by the fact that methyl bromide hydrolyses at a rate similar to that of I (n = 4) - the reactions were followed by noting the development of acidity. Direct bimolecular reaction between the substrate and the solvent (step 6) is included and this interpretation is supported by the observation that even in the presence of a large excess of bromide ion (0•5M), to promote reaction via step 4, not more than ca. 77 per cent of tetrahydropyran is produced.

A quantitative discussion of the implications of this reaction scheme is given below. The kinetic data are presented in outline, but full details are given in Appendix 4.

The following section introduces the expressions for the acidity, $([H^+]-[H_o^+])_{calc}$, to be expected at various stages of the reactions. These expressions contain a number of disposable parameters and the scheme can be considered to be valid if reasonable values for these parameters give values of acidity in close agreement with those observed.

5.5.2 Stoichiometry and Rate Equations

An application of the "steady state treatment" for $[I^+]$ gives

$$\frac{d[I^+]}{dt} = 0 = k_1[RBr] - k_{-1}[I^+][Br^-] - k_2[I^+] - k_3[I^+] - k_4[I^+][Br^-]$$

where $[I^+]$ is the concentration of the intermediate (VI), and [RBr] that of the substrate.

$$\therefore \quad [I^+] = \frac{k_1[RBr]}{[Br^-](k_{-1} + k_4) + (k_2 + k_3)}$$

Now $$\frac{-d[RBr]}{dt} = k_1[RBr].\frac{1+\gamma[Br^-]}{1+\alpha[Br^-]} + k_6[RBr]$$

where $$\alpha = \frac{k_4 + k_{-1}}{k_2 + k_3}, \quad \gamma = \frac{k_4}{k_2 + k_3}$$

$$\therefore \quad \ln\frac{[RBr_o]}{[RBr]} = k^o \int \left\{ r^o f_1 . \frac{1+\gamma^o f_3}{1+\alpha^o f_3} + (1-r^o)f_2 \right\} dt$$

where $$k^o = (k_1^o + k_6^o) \quad \text{and} \quad r^o = k_1^o/(k_1^o + k_6^o)$$

The superscript $\underline{o}$ denotes zero ionic strength. $[RBr_o]$ is the initial concentration of substrate and f_1, f_2, f_3 are activity coefficients (f_1, f_2 f_3 are discussed in Appendix 1).

The integral above can be designated G, so that

$$\ln\frac{[RBr_o]}{[RBr]} = k^o G \qquad 5.6$$

G, written $G = \int F\,dt$, can not be determined analytically, but is conveniently dealt with by expressing the function F as a power series in $\underline{t}$;

i.e. $$F = (a_1 + a_2t + a_3t^2 \;\ldots\ldots)$$

when $$G = (a_1t + \frac{a_2t^2}{2} + \frac{a_3t^3}{3} + \ldots.)$$

and determining the constants a_1, a_2 etc. via a curve-fitting procedure.

Also, for the proposed reaction scheme,

$$\frac{d[MeBr]}{dt} = \frac{\gamma[Br^-].k_1[RBr]}{1+\alpha[Br^-]} - k_5[MeBr]$$

$$\therefore \quad [\mathrm{MeBr}]e^{k_5 t} = r^o k^o [\mathrm{RBr}_o] \int \left\{ f_1 e^{-k^o G} \cdot \frac{\gamma^o f_3}{1 + \alpha^o f_3} \cdot e^{f_2 k_5^o t} \, dt \right\}$$

$$\therefore \quad [\mathrm{MeBr}] = k^o r^o [\mathrm{RBr}_o] e^{-f_2 k_5^o t} \, I \qquad 5.7$$

$$\text{If} \quad I = \int H dt$$

$$\text{and} \quad H = (a_1' + a_2' t + \ldots\ldots\ldots\ldots)$$

$$\text{then} \quad I = (a_1' t + \frac{a_2'}{2} t^2 + \ldots\ldots\ldots)$$

and can be determined as above for G.

The concentration of acid at any time can be written

$$([H^+]-[H^+_o]) = [\mathrm{RBr}_o] - [\mathrm{RBr}] - [\mathrm{MeBr}] \qquad 5.8$$

where $[H^+_o]$ and $[\mathrm{RBr}_o]$ are the concentrations of acid and substrate at zero time.

From equations 5.6-5.8,

$$([H^+]-[H^+_o])_{calc} = [\mathrm{RBr}_o](1 - e^{-k^o G}) - [\mathrm{RBr}_o] r^o k^o \, I e^{-f_2 k_5^o t} \qquad 5.9$$

and this equation can be used to determine sets of calculated acidities.

However, a knowledge of the values of several rate constants and other quantities is required before equation 5.9 can be used for the calculation of acidities.

Approximate values of α^o, k_1^o, k_6^o are obtainable from the data of the "initial rate" runs summarised in Table 5.2.

For reaction by the proposed mechanism

$$(k_{obs})_{t=o} = \frac{k_1}{1 + \alpha[\mathrm{Br}^-_o]} + k_6$$

where $[Br_o^-]$ is the concentration of bromide ion at zero time. Inclusion of activity coefficients f_1, f_2, f_3, and rearrangement gives

$$\frac{(k_{obs})_{t=o} - k_6^o f_2}{f_1} = k_1^o - \alpha^o [Br_o^-] f_3 \left\{ \frac{(k_{obs})_{t=o} - k_6^o f_2}{f_1} \right\} \qquad 5.10$$

With known values of f_1, f_2, f_3 (calculated as shown in Appendix 1), $(k_{obs})_{t=o}$, $[Br_o^-]$ and several trial values of k_6^o, plots of

$$\frac{(k_{obs})_{t=o} - k_6^o f_2}{f_1} \quad \text{against} \quad [Br_o^-] f_3 \left\{ \frac{(k_{obs})_{t=o} - k_6^o f_2}{f_1} \right\}$$

were constructed for each $[Br_o^-]$ concentration and approximate values of α^o obtained from the slopes. Also, approximate trial values of k_6^o and α^o were used in equation 5.10 to give some idea of the values of the constants which might lead to agreement with the observed data.

5.5.3 Calculation of Acidities

For each of the four kinetic runs (22, 24, 26, 28) sets of acidities were calculated using equation 5.9, and compared with the observed titres. Different values for several of the unknown constants and parameters were tried in an attempt to find a set of data which gave, for each kinetic run, a good agreement between calculated and observed results.

The integrals G and I in equation 5.9 were evaluated by fitting the data to a four parameter equation of the form shown in section 5.5.2

For the calculations, values were required for $[RBr_o]$, t, k_5^o, f_1, f_2 f_3, α^o, γ^o, k^o, r^o. These quantities are listed below.

$[RBr_o]$	(Infinity titre - zero titre). A value for each run.
t	Times of sampling.
k_5^o	Rate constant for the hydrolysis of methyl bromide, determined experimentally. $k_5^o = 1{\cdot}4 \times 10^{-5}$ sec^{-1} at $65{\cdot}13^o$ (Experiment 32).
f_1, f_2, f_3	Activity coefficients calculated for each sampling time using experimental bromide concentrations. Debye-Hückel and Davies coefficients are possible for f_3 (see Appendix 1 for discussion and determination).
α^o, γ^o	Ratios of rate constants. Ranges of values were tried.
k^o	$k^o = (k_1^o + k_6^o) = (k_{obs})_{t=o}$ for run in the absence of NaBr. $k^o = 1{\cdot}8 \times 10^{-5}$ sec^{-1}, initially (see below).
r^o	$r^o = k_1^o/k^o$

For each of the four runs the experimental data and k_5^o and k^o were considered, together with a trial k_1^o, several α^o and one or more γ^o for each α^o. When all the combinations of α^o, γ^o for a particular k_1^o had been calculated, another k_1^o was considered with a different set of α^o, γ^o. For each combination of k_1^o, α^o, γ^o, a set of calculated and observed acidities was printed, together with the appropriate "std. dev." (see footnote to Table 5.4).

The construction of the program allowed values of k^o other than the approximate $1{\cdot}8 \times 10^{-5}$ to be considered, and each complete set of results was accompanied by a summary of the "std. devs." for $k^o = 1{\cdot}76$, $1{\cdot}78$, $1{\cdot}82$, $1{\cdot}84 \times 10^{-5}$ (values within the experimental error of k^o). Calculations were made with both Debye-Hückel and Davies activity coefficients for f_3. The results of a typical set of calculations are shown in Table 5.4 (Not a particularly good set of results).

Table 5.4

Sample of computer output for one set of k_1^o, α^o, γ^o

Initial [Br^-] = $9 \cdot 754 \times 10^{-2}$M; $k_1^o = 1 \cdot 50$; $\alpha^o = 130$; $\gamma^o = 130$

Acidity (Titre in ml.)	
Observed	(Observed-calculated)
1•68	0•027
2•23	0•015
2•91	0•004
3•52	0•054
4•23	0•061
4•81	0•061
5•43	0•061
6•13	0•083
6•83	0•070
7•34	0•037
7•82	0•050
8•21	0•038

Mean Error = 0•043; $k^o = 1 \cdot 80 \times 10^{-5}$; Standard Deviation (std. dev.)§ = 0•050

§ std. dev. = $$\left\{ \frac{\sum (\text{calculated acidity-observed acidity})^2}{n} \right\}^{\frac{1}{2}}$$

where n is the number of experimental points in the kinetic run.

5.5.4 Conclusions from the Kinetic Study

Table 5.5 gives a summary of the results obtained for one kinetic run (Debye-Hückel activity coefficients for f_3). The data for the other runs are included in Appendix 4. An overall summary of the results for the four experiments is included in Tables 5.6 and 5.7. The comments below refer to the results as a whole.

From Table 5.6 it can be seen that there is no unique set of parameters or small range of k_1^o, α^o, γ^o which leads to good agreement with the observed data of all four runs. For experiments 22 and 24 low std. devs. between 0•015 and 0•02, indicating good agreement, are given by particular values of the parameters, but the same combinations of k_1^o and α^o result in much poorer agreement (std. dev. = ca. 0•05) with the data of experiments 26 and 28. For these two experiments no set of parameters leads to a std. dev. lower than 0•041 (see Table 5.6). It was hoped that std. devs. of 0•02 or better could be obtained for all four runs, but for solutions with considerable amounts of added salt (up to 0•1M) the simple salt - effect expressions used probably don't apply. It is worth noting here that for any combination of k_1^o and α^o, the value of γ^o which gives the lowest std. dev. is $\gamma^o = \alpha^o$ (i.e. there is a negligible mass-law effect), and this was used throughout the calculations.

The use of Davies activity coefficients in place of Debye-Hückel coefficients for f_3 results in small std. devs. at different values of k_1^o, α^o (see Table 5.6), but the trends are the same as those mentioned above.

The conclusions from the quantitative work are given in Table 5.7. Although the agreement between calculated and observed acidities was not as good as was hoped, approximate values of the rate constants for some of the steps in the reaction scheme were obtained. It can be seen that the use of Debye-Hückel or Davies activity coefficients for f_3 makes little difference in the final analysis.

The rate constants k_1^o (S_Ni reaction) and k_6^o (S_N2 reaction) are (1•32-1•50) x $10^{-5}sec^{-1}$ and (0•30-0•48) x $10^{-5}sec^{-1}$, respectively, and 17-27 per cent of the substrate reacts via the S_N2 step. The α^o values indicate that attack by Br^- ions on the intermediate (VI) occurs 130-200 times more rapidly than attack by water.

The proposed reaction scheme is clearly very feasible, although it is possible that a slightly different scheme might also explain the observed results.

Table 5.5 §

Summary of comparison between observed and calculated acidities

Experiment 28 Debye-Hückel values for parameter f_3

$10^5 k_1^o$	$\alpha^o (= \gamma^o)$	$10^5 k^o$ value giving lowest std. dev.	std. dev.$^{\phi}$
1•50	120	1•76	0•036
	130	1•76	0•017
	140	1•78	0•020
1•47	130	1•76	0•041
	140	1•76	0•020
	150	1•76	0•020
	160	1•78	0•022
1•44	140	1•76	0•052
	150	1•76	0•031
	160	1•76	0•017
	170	1•76	0•019
1•41	150	1•76	0•066
	160	1•76	0•047
	170	1•76	0•031
	180	1•76	0•018
1•38	160	1•76	0•084

ϕ See footnote to Table 5.4

§ Part of Appendix 4

Table 5.6

The sets of parameters§ which result in the lowest values of "std. dev." for the four experiments (22, 24, 26 and 28)

Experiment	Concentration of added bromide ion (M)	Activity Coefficient for f_3	$10^5 k_1{}^o (\text{sec}^{-1})$	$\alpha^o (= \gamma^o)$	$10^5 k^o (\text{sec}^{-1})$	std.dev.
22	0	Debye-Hückel	1•50	130	1•76	0•017
		"	1•44	160	1•76	0•017
		Davies	1•38	180	1•76	0•014
24	0•0210	Debye-Hückel	1•47	150	1•84	0•018
		"	1•44	160	1•82	0•018
		Davies	1•41	160	1•82	0•019
		"	1•38	180	1•82	0•019
26	0•0508	Debye-Hückel	1•47	150	1•84	0•047
		"	1•44	160	1•84	0•047
		Davies	1•38	180	1•84	0•045
		"	1•35	200	1•84	0•045
28	0•0975	Debye-Hückel	1•38	150	1•76	0•041
		Davies	1•32	170	1•78	0•041

§ The ranges of the parameters used are given in Appendix 4.

Table 5.7

The ranges of k_1^o and α^o which give the lowest std. devs.,§ and the corresponding values for k_6^o and the percentage of reaction by mechanism S_N2

	Debye-Hückel coefficient for f_3				Davies coefficient for f_3			
Experiment	α^o	$10^5k_1^o(sec^{-1})$	$10^5k_6^o(sec^{-1})$	% S_N2	α^o	$10^5k_1^o(sec^{-1})$	$10^5k_6^o(sec^{-1})$	% S_N2
22	140-180	1·44-1·50	0·30-0·36	17-20	150-200	1·38-1·44	0·36-0·42	20-23
24	130-170	1·41-1·50	0·30-0·39	17-22	150-190	1·35-1·41	0·39-0·45	22-25
26	140-160	1·41-1·47	0·33-0·39	18-22	160-180	1·35-1·41	0·39-0·45	22-25
28	140-170	1·38-1·50	0·30-0·42	17-23	150-180	1·32-1·44	0·36-0·48	20-27
Values for all 4 expts.	130-180	1·38-1·50	0·30-0·42	17-23	150-200	1·32-1·44	0·36-0·48	20-27

§ $k^o = 1{\cdot}8 \times 10^{-5}\ sec^{-1}$.

5.5.5 MeO-6 Participation in Acetic Acid

Very similar results have been obtained by Allred and Winstein,[63c] who studied the solvolysis of 5-methoxy-1-pentyl p-bromobenzenesulphonate in acetic acid, ethanol and formic acid. For ethanol and formic acid, the rate constants were first-order, but in acetic acid, reaction proceeded to *ca.*50 per cent completion and then acid formed at a very much reduced rate. The products of total acetolysis were examined and in addition to 5-methoxy-1-pentyl acetate (17%), the "normal" product, substantial yields of methyl p-bromobenzenesulphonate (54%), methyl acetate (67%) and tetrahydropyran (77%) were discovered. The authors rationalised these product data in terms of a reaction scheme which is very similar to that proposed in the present study. It is interesting to note that large yields of tetrahydropyran were found for reaction in both acetic acid and aqueous acetone.

The scheme for acetolysis includes a solvent-separated and two intimate ion-pairs, but as was mentioned in section 1.3, the intervention of ion-pairs is unlikely in aqueous acetone solvents. The mechanisms for the two solvents can thus be considered as almost identical, and the accurate product work of Allred and Winstein reinforces the evidence in favour of the scheme proposed for reaction in aqueous acetone.

5.6 Conclusion

The main difference in kinetic behaviour between hydroxyl and methoxyl assisted solvolyses has been mentioned in section 5.3 and attributed to the differing stabilities of the intermediate ions. However, the discussion in this chapter reveals a significant kinetic difference between MeO-5 and MeO-6 assisted hydrolyses. An explanation in terms of ring strain and steric hindrance has been proposed by Winstein.[63c] The furanium ion cannot adopt a conformation entirely free from H-H interaction and torsional strain, but the pyranium ion can readily assume a strain-free chair form, with the adjacent $-CH_2$ groups rotated 60^{o} with respect to each other. The O-methylene carbon atoms of the furanium ion are open to nucleophilic attack, while the corresponding carbons of the pyranium ion have hydrogen atoms partly in the line of nucleophile approach. This difference may well account for the substantial attack at the methyl group during MeO-6 assisted solvolysis.

CHAPTER 6

NEIGHBOURING PHENYL PARTICIPATION

6.1 Introduction

The rates at which ring closures of acyclic compounds take place through intramolecular nucleophilic displacements depend markedly on the size of the ring that is formed and also on the degree of alkyl substitution of the chain.[16,64] It has been found that reactions of this type may result in the rapid formation of three-, five- or six-membered rings. The ring-closure reactions discussed in Chapters 4 and 5 resulted in the rapid formation of five-membered rings by neighbouring hydroxyl and methoxyl participation, although cyclisation to a six-membered ring also occurred at an enhanced rate relative to that expected for unassisted hydrolysis. In the case of phenyl participation, a three-membered ring is most readily formed[16] and many halides and sulphonates containing one, two and three β-phenyl groups have been used in studies of neighbouring phenyl participation.

2,2,2-triphenylethyl chloride was found by Charlton and his co-workers[65] to exhibit marked steric hindrance in S_N2 replacements but to undergo a facile reaction in hydroxylic solvents, giving triphenylethylene as a result of the migration of one of the phenyl groups to the α carbon atom. The effect of β-phenyl substituents on the rate of acetolysis of ethyl p-toluenesulphonate was shown in Table 1.7, where it was seen that the trisubstituted compound solvolyses more than a thousand times faster than the monosubstituted substrate. In the present work both triphenylethyl p-toluenesulphonate and chloride were studied to obtain activation parameters characteristic of neighbouring phenyl participation, and the differences in the results for the two compounds are attributed to effects involving the two dissimilar leaving groups. For comparison purposes, 2-phenylethyl bromide, expected to hydrolyse by the S_N2 mechanism in aqueous organic solvents, was also studied.

The three compounds were all hydrolysed in different aqueous acetone solvents, a situation made necessary by the large solubility and reactivity differences within the group of reactants.

6.2 Results

The rates and activation parameters for the three substrates are recorded in Tables 6.1-6.3. It is immediately evident from an initial inspection of the data that the differences in the parameters are unexpectedly large. The use of three solvents may be partly responsible for this, and in the following section the experimental results obtained in a particular solvent are compared with data for S_N1 and S_N2 reactions in the same solvents.

Product work by gas liquid chromatography showed that both 2,2,2-triphenylethyl p-toluenesulphonate and chloride gave substantial amounts of triphenylethylene on hydrolysis. The precise quantitative results, obtained as described in section 7.3.5, are probably not of particular significance for comparison purposes as the composition of the products of hydrolysis is expected to alter with solvent composition and the temperature of the experiment.

6.3 Discussion

6.3.1 2-phenylethyl bromide(I)

The activation parameters for this compound are almost identical with those for the S_N2 hydrolysis of benzyl bromide in the same solvent,[37] but are quite unlike the values expected for S_N1 reaction. It therefore seems probable that in 50% aqueous acetone compound (I) hydrolyses solely by the S_N2 mechanism. Benzyl bromide reacts about 300 times more quickly, and the relatively large difference in the energy of activation for the two compounds is no doubt due to the accelerating effect of the phenyl group

Table 6.1

Rate constants and errors for the hydrolysis of 2-phenylethyl bromide in 50 per cent aqueous acetone

Temp (^{o}C)	10^{6}k(sec^{-1})	$10^{3}\sigma_{k}$/k
100•52	25•906	1•41
90•12	11•073	0•62
80•09	4•6322	1•64
71•02	1•9938	1•34
60•38	0•69363	0•84

Activation parameters:

At 50^{o}C, E = 22•972 $\pm$ 0•075 kcal mole^{-1}; $\Delta S^{\ddagger}$ = -19•97 $\pm$ 0•23 cal deg^{-1} mole^{-1}; $\Delta C_{p}^{\ddagger}$ = -23•52 $\pm$ 2•68 cal deg^{-1} mole^{-1}

Table 6.2

Rate constants and errors for the hydrolysis of 2,2,2-triphenylethyl p-toluenesulphonate in 85 per cent aqueous acetone

Temp (^{o}C)	10^{6}k(sec^{-1})	$10^{3}\sigma_{k}$/k
84•92	197•04	0•77
75•08	71•473	1•68
65•15	24•083	1•91
55•08	7•4710	1•28
45•13	2•1940	0•83

Activation parameters:

At 50^{o}C, E = 25•615 $\pm$ 0•039 kcal mole^{-1}; $\Delta S^{\ddagger}$ = -6•10 $\pm$ 0•12 cal deg^{-1} mole^{-1}; $\Delta C_{p}^{\ddagger}$ = -2•44 $\pm$ 2•53 cal deg^{-1} mole^{-1}

Table 6.3

Rate constants and errors for the hydrolysis of 2,2,2-triphenylethyl chloride in 70 per cent aqueous acetone

Temp (^oC)	$10^6k(sec^{-1})$	$10^3\sigma_k/k$
100•26	25•479	1•80
90•16	9•3045	1•89
80•05	3•1882	1•20
70•11	1•0441	1•80
60•39	0•32541	1•18

Activation parameters:

At 50^oC, $E = 27{\bullet}423 \pm 0{\bullet}090$ kcal $mole^{-1}$;

$\Delta S^{\ddagger} = -8{\bullet}14 \pm 0{\bullet}28$ cal deg^{-1} $mole^{-1}$;

$\Delta C_p^{\ddagger} = -14{\bullet}18 \pm 3{\bullet}15$ cal deg^{-1} $mole^{-1}$

when attached to the reaction centre in benzyl bromide. The present substrate, as mentioned in section 1.5 has recently been shown to solvolyse in part via neighbouring phenyl participation in solvents of high ionising power but low nucleophilicity. In these conditions the adjacent phenyl group can compete successfully with the solvent as a nucleophile at the reaction centre. Internal nucleophilic substitution is, however, very unlikely in highly nucleophilic aqueous acetone solvents.

6.3.2 2,2,2-triphenylethyl p-toluenesulphonate (II) and chloride (III)

In Table 6.4 the activation parameters at 50^o for these two compounds are compared with appropriate data for hydrolysis by the S_N1 and S_N2 mechanisms in the same solvents.[37] The results in Table 6.4 have been used to construct Tables 6.5 and 6.6. which are also useful in a comparison of different mechanisms.

Table 6.4

Rates and activation parameters for the hydrolysis at 50° of ROTs in 85% and RCl in 70% aqueous acetone.[37]

R	RCl			ROTs		
	log k	$\Delta S^{\ddagger}$	$\Delta C_p^{\ddagger}$	log k	$\Delta S^{\ddagger}$	$\Delta C_p^{\ddagger}$
$NO_2C_6H_4CHPh$- (S_N1)	-4·988	-9·96	-39·8	-1·804	-8·12	-24·5
$PhOC_6H_4CH_2$- (S_N1)	-4·170	-11·98	-43·1	-1·143	-10·47	-29·3
$MeOC_6H_4CH_2$- (S_N1)	-2·180	-11·99	-45·9	0·602	-10·29	-29·6
$PhCH_2$- (S_N2)	-6·380	-23·96	-21·7	-4·051	-19·62	-26·6
Ph_3CCH_2-	-7·073	-8·14	-14·2	-5·394	-6·10	-2·4

(k in sec^{-1}; $\Delta S^{\ddagger}$, $\Delta C_p^{\ddagger}$ in cal deg^{-1} $mole^{-1}$)

The results for compounds II and III are completely unlike those which apply both to the S_N1 and S_N2 mechanisms. Reactant III has been found to exhibit considerable steric hindrance in S_N2 replacements[65] and the possibility of the operation of this mechanism can be discounted.

Tables 6.5 and 6.6 show that the differences in the entropies and heat capacities of activation for compounds II and III are quite similar to the p-toluenesulphonate/chloride differences in these parameters which are characteristic of S_N1 reactions. This factor suggests that in both groups of substrates the leaving group has a similar effect on the value of $\Delta S^{\ddagger}$ and $\Delta C_p^{\ddagger}$.

Table 6.5

Differences at 50° between the rates and activation parameters of ROTs in 85% and RCl in 70% aqueous acetone

R	$[\log k_{OTs} - \log k_{Cl}]$	$[(\Delta S^{\ddagger})_{OTs} - (\Delta S^{\ddagger})_{Cl}]$	$[(\Delta C_p^{\ddagger})_{OTs} - (\Delta C_p^{\ddagger})_{Cl}]$
$NO_2C_6H_4CHPh$- (S_N1)	3·184	1·84	15·3
$PhOC_6H_4CH_2$- (S_N1)	3·027	1·51	13·8
$MeOC_6H_4CH_2$- (S_N1)	2·782	1·70	16·3
$PhCH_2$- (S_N2)	2·329	4·34	-4·9
Ph_3CCH_2-	1·679	2·04	11·8

Table 6.6

Differences at 50° between the activation parameters of RX and $(C_6H_5)_3CCH_2X$

R	X	$[(\Delta S^{\ddagger})_{RX} - (\Delta S^{\ddagger})_{Ph_3CCH_2X}]$	$[(\Delta C_p^{\ddagger})_{RX} - (\Delta C_p^{\ddagger})_{Ph_3CCH_2X}]$
MeO- or $PhOC_6H_4CH_2$-(S_N1)	-Cl	-3·84	-30·3
	-OTs	-4·28	-27·1
$PhCH_2$-(S_N2)	-Cl	-15·82	-7·5
	-OTs	-13·52	-24·2

However, there is no simple correlation when values of log k are compared in Table 6.5. The p-toluenesulphonate/chloride rate difference in S_N1 reactions is in the approximate range 500-2000, but the compounds II and III show a factor of only ca.50. In a true S_N1 process, the activation energy is largely determined by the energy required to break the bond between the leaving group and the incipient carbonium ion and the large rate difference between the p-toluenesulphonate and the chloride points to a considerable difference in the ease of bond-breaking for the two leaving groups. The relatively small factor for the present compounds must arise from the operation of another effect, in addition to bond-breaking, which makes a significant contribution to the activation process and leads to a reduction in the discrepancy between the rates. In view of the observation that a considerable fraction of the product of hydrolysis of II and III is triphenylethylene, formed by the 1,2-migration of one phenyl group at some stage of reaction, it seems that an important part of the activation process might be the partial formation of a bond between the reaction centre and a neighbouring phenyl group on the adjacent carbon atom.

Solvolysis entirely by the S_Ni mechanism is suggested by the results and the values of $\Delta S^\ddagger$ and $\Delta C_p^\ddagger$ for the two compounds can be rationalised on this basis. It must be pointed out, however, that the following approach is a simple one, but a more detailed explanation is not possible using the present experimental data.

The entropies and heat capacities of activation are both considerably more positive than for the S_N1 and S_N2 mechanisms. The $\Delta S^\ddagger$ values may be due to a "loosening" of the set of three phenyl groups when migration occurs in the activation step. However, a three-membered ring is presumably formed in the transition state and this will result in a negative contribution to $\Delta S^\ddagger$. The "solvation model" approach[37] has been used for several years to explain solvolysis processes in aqueous organic solvents and the values of $\Delta S^{\ddagger}$ and $\Delta C_p^{\ddagger}$ are considered to result entirely from the increased solvation of the transition state relative to the initial state. The heat capacity of activation for II is close to zero, a somewhat surprising result in view of the fact that solvation around the positive charge of the incipient carbonium ion is expected in the transition state for an S_Ni process. The near-zero $\Delta C_p^{\ddagger}$ value is consistent with the solvation model if the much reduced solvation of the transition state is due in part to a delocalisation of the positive charge over the α and β carbon atoms and the bridging phenyl group of the carbonium ion. A second factor may be steric hindrance to solvation, the positive charge being effectively shielded from the solvent by the closed bridged structure and the three bulky phenyl groups. The value of $\Delta S^{\ddagger}$ for II, in the absence of significant solvation of the transition state, should be almost wholly due to the loss of entropy associated with formation of a three-membered ring by neighbouring phenyl participation. It is therefore interesting to note that the $\Delta S^{\ddagger}$ value of <u>ca.</u> -6 cal deg^{-1} for the hydrolysis agrees quite well with the difference of <u>ca.</u>7·5 cal deg^{-1} between the calculated entropies at 298°K of n-propane[66] and cyclopropane.[67]

The chloride, (III), has $\Delta S^{\ddagger}$ and $\Delta C_p^{\ddagger}$ values which are more negative than those discussed above for the p-toluenesulphonate. This is not unexpected, and similar differences are found in S_N1 reactions, as shown in Table 6.5. The p-toluenesulphonate group is thought to be "pre-solvated" in the initial state as a result of hydrogen-bonded interactions with the water of the solvent.[37,50] Similar interactions do not occur in the initial state for a chloride[50] and the solvolysis requires greater solvation of the incipient anion during the activation process to stabilise the transition state. Thus, the more negative values of $\Delta S^{\ddagger}$ and $\Delta C_p^{\ddagger}$ for III are a reflection of the increased solvation on activation relative to the p-toluenesulphonate.

On the basis of the above discussion, the similarities between the present reactions and S_N1 processes, shown in Tables 6.5 and 6.6, are expected, since both mechanisms involve the separation of carbonium ion and leaving group in the rate-determining step.

6.3.3 The Nature of the Transition State and Intermediate in Reactions which proceed via Neighbouring Phenyl Participation

In recent years, there has been considerable controversy concerning the nature of the intermediate which is formed during reactions which involve nucleophilic participation by a neighbouring phenyl group. It must be stressed that the present kinetic work only provides information about the activation process and the transition state of the rate-determining step, and it seems clear that in reactions where migration of an internal nucleophile occurs, the transition state has a structure in which the neighbouring phenyl group is bonded or partially bonded to two carbon atoms. No mass-law effects were observed in the solvolyses, suggesting that the intermediate carbonium ions are not particularly stable. Further deductions could not be made.

Cram considers the intermediate in this type of reaction to be a "phenonium" ion, defined as a phenyl-bridged species containing a three-membered carbocyclic ring.[21] This ion is one of a large number of "non-classical" carbonium ions, species which were placed on a firm experimental foundation by the work of Winstein and Trifan[68] on the solvolysis of exo- and endo-2-norbornyl p-bromobenzenesulphonate. The phenonium ion is usually represented as shown in Fig.6.1.

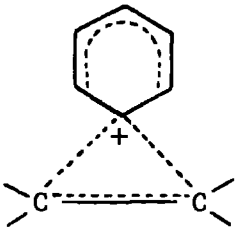


Fig.6.1

Brown disagrees with Cram's interpretation and has suggested that the results are most simply explained in terms of a rapidly equilibrating set of carbonium ions, classical in structure.[22] The cations, shown in Fig.6.2

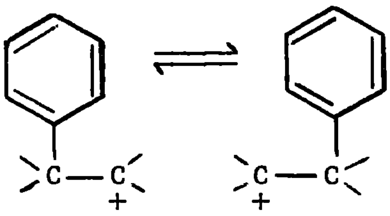


Fig.6.2

are identical isomeric species and are assumed to undergo equilibration at a rate that is fast compared to the rate of reaction of the system with solvent or other nucleophiles.[69]

Cram[70] and Brown,[22,69,71] respectively, have both put forward a great deal of kinetic and stereochemical evidence in support of either the "phenonium ion" or the "equilibrating cation" theory. A detailed review of the arguments surrounding this problem cannot be conveniently dealt with here.

6.3.4 The Possibility of Concurrent Processes in the Solvolyses of II and III

In section 6.3.2, the results for compounds II and III were discussed in terms of the solvation model, on the basis that hydrolysis occurs only by mechanism S_Ni. However, mechanisms S_Ni and S_N1 may be operating concurrently and this possibility has been investigated, since it was realised that hydrolysis by two processes would result in a positive contribution to the observed heat capacity of activation,[52] and might explain the relatively positive values of $\Delta C_p^{\ddagger}$ found for these two substrates. The mathematical equations involved are presented in Appendix 2, but a qualitative description of the method used for dealing with the problem is necessary in this section. The calculations were performed by computer and the following procedure has been applied to the results for both compounds.

Values of E, $\Delta S^{\ddagger}$, $\Delta C_p^{\ddagger}$ at the mean temperature of the kinetic experiments were known. $\Delta S_1^{\ddagger}$ values at 50° for the S_N1 hydrolysis of $MeOC_6H_4CH_2X$ (X = -Cl or -OTs) were assumed to apply to an S_N1 process in the present compounds, and $\Delta C_{p1}^{\ddagger}$ and E_1 calculated for the S_N1 process. E_1 applied to the mean experimental temperature and was obtained for values of $\underline{x}$ between 0·1 and 0·9, $\underline{x}$ being the fraction of the hydrolysis which proceeded by an S_N1 process. Corresponding E_2, $\Delta S_2^{\ddagger}$ and $\Delta C_{p2}^{\ddagger}$ for the S_Ni reaction were calculated. Parameters E_1, $\Delta S_1^{\ddagger}$, E_2, $\Delta S_2^{\ddagger}$ at the top and bottom temperatures of the experimental range were obtained, and the calculated and observed values of $\underline{k}$ and E compared at these temperatures. For both compounds, good agreement was obtained at the upper and lower temperatures between the calculated and observed k's (within ± 0·5%) and E's (within ± 70 cal.) for $\underline{x}$ values up to 0·7. The above procedure was repeated using $\Delta S_1^{\ddagger} \pm 2$ and $\Delta C_p^{\ddagger} \pm 2$. Table 6.7 shows one set of $\underline{x}$, k_1 (50°) and $\Delta S_2^{\ddagger}$ (50°) values for each of the compounds.

Table 6.7

k_1 (50°) and $\Delta S_2^{\ddagger}$ (50°) for compounds II and III, assuming a fraction $\underline{x}$ of the hydrolysis to proceed via the S_N1 mechanism

Compound II $\Delta S_1^{\ddagger}$ (50°) = -10•38;[37] $\Delta C_p^{\ddagger}$ = -2•4

$\underline{x}$	0•1	0•2	0•3	0•4	0•5	0•6	0•7
$10^8 k_1$ (50°)	40•6	83•8	128	173	219	265	311
$\Delta S_2^{\ddagger}$ (50°)	-6•34	-6•24	-5•87	-5•13	-3•80	-1•30	3•93

Compound III $\Delta S_1^{\ddagger}$ (50°) = -11•99;[37] $\Delta C_p^{\ddagger}$ = -14•2

$\underline{x}$	0•1	0•2	0•3	0•4	0•5	0•6	0•7
$10^8 k_1$ (50°)	0•89	1•89	2•95	4•04	5•15	6•29	7•44
$\Delta S_2^{\ddagger}$ (50°)	-8•41	-8•28	-7•78	-6•74	-4•75	-0•76	8•25

k_1 in sec^{-1}; $\Delta S^{\ddagger}$, $\Delta C_p^{\ddagger}$ in cal deg^{-1} $mole^{-1}$.

$\underline{x}$ refers to mean experimental temperature.

Despite the agreement between the observed and calculated parameters over a large range of x, other conditions must be met which drastically limit the chances of a concurrence of mechanisms. The first of these is that the p-toluenesulphonate : chloride rate ratio for S_N1 reactions in 85 per cent and 70 per cent aqueous acetone, respectively, is at least 500 : 1 as mentioned in section 6.3.2. Secondly, the $\Delta S^\ddagger$ difference between the p-toluenesulphonate and the chloride for the S_Ni mechanism is expected to be close to that which applies to the similar S_N1 process, i.e. about 2 cal deg^{-1}. From Table 6.7 it can be seen that the above conditions only apply when x is ca. 0•02 at the mean temperature for III, and at the same time x is between 0•1 and 0•2 for II. Thus, hydrolysis of both compounds by concurrent S_N1 and S_Ni mechanisms is consistent with the experimental results if the fractions of reaction via the S_N1 process are as quoted.

6.3.5 Conclusion

In section 6.3.2 the results for compounds II and III were discussed in terms of complete hydrolysis by the S_Ni mechanism, although as was shown in the previous section, reaction by concurrent processes is theoretically possible if ca. 2 per cent of the chloride and ca. 10-20 per cent of the p-toluenesulphonate hydrolyse by the S_N1 mechanism.

Thus, neighbouring phenyl participation predominates in the reactions of 2,2,2-triphenylethyl derivatives in aqueous acetone, and very little, if any hydrolysis proceeds by the S_N1 mechanism.

CHAPTER 7

EXPERIMENTAL

7.1 Preparation and Purification of Compounds

7.1.1 Chlorohydrins

The pure samples of the five chlorohydrins required for the kinetic study were all obtained from commercial samples by distillation, although in two cases a separation procedure to remove substantial amounts of the dichloride was necessary. Estimations of the purity, based on the hydrolysable chloride content of the samples,gave low values for compounds a), b) and e), for reasons discussed in section 7.2.5.

a) 2-chloroethanol. A commercial sample of this compound was distilled and a fraction collected with B.pt. 42°/20 mm. η^{25} = 1•4416 (Lit.[72] 1•4412).

b) 3-chloropropanol. A commercial sample was distilled and a fraction collected with B.pt. 42°/4 mm. η^{20} = 1•4467 (Lit.[73] 1•4469).

c) 4-chlorobutanol. Distillation of a commercial sample gave a fraction with B.pt. 33-35°/0•1 mm. η^{20} = 1•4514 (Lit.[74] 1•4518). The hydrolysable chloride content was 100•3 per cent of the theoretical amount.

d) 5-chloropentanol. A commercial sample (10 g.) was distilled and a fraction collected with B.pt. 75°/4-5 mm. However, the hydrolysable chloride content for this fraction was found to be 109•6 per cent of the theoretical amount, and a trial run gave rate constants which decreased steadily during the first 50 per cent of reaction. The results suggested that a considerable amount of 1,5-dichloropentane was present as impurity. Repeated distillations produced a purer sample, but all the dichloropentane could not be removed by this method.

A separation procedure was developed based on the fact that the dichloride is far less soluble in water than the chlorohydrin. An organic solvent, immiscible with water, and in which the compound is not very soluble, was required. Pentane proved to be satisfactory and preliminary experiments showed that after shaking 1 g. of the compound with a mixture of 50 ml. pentane and 50 ml. water, about 85 per cent remained in the water layer. Extraction from the water layer with 3 portions of pentane was expected to remove all the dichloride and leave pure chlorohydrin in the water.

On a preparative scale, the commercial sample (10 g.), pentane (500 ml.) and water (500 ml.) were used. After vigorous shaking, the pentane layer was removed and the water layer shaken with 3 further portions (500 ml.) of pentane. 3 portions of freshly distilled ether, totalling 650 ml., were used to remove the chlorohydrin from the water. The ether solution was dried with magnesium sulphate and the solvent removed. Distillation of the chlorohydrin gave 2•5 g. of product with B.pt. 65°/0•3 mm. η^{25} = 1•4515 (Lit.[75] 1•4512). The hydrolysable chloride content was 100•1 per cent of the theoretical amount.

e) <u>6-chlorohexanol</u>. The separation procedure which proved successful for the purification of 5-chloropentanol was used, after preliminary experiments to determine the relative amounts of water and pentane required. The commercial sample (10 g.), pentane (150 ml.) and water (1000 ml.) were vigorously shaken and the mixture treated as above for d). Distillation of the chlorohydrin gave 2 g. of product with B.pt. 72°/0•3 mm. η^{25} = 1•4533 (Lit.[75] 1•4531).

7.1.2 Methoxy-bromides

The compounds $MeO(CH_2)_nBr$, (n = 3-6), were all prepared by the reaction of sodium methoxide with the dibromide, using methanol as solvent.[76] The ratio of the reactants used was approximately 1•5 moles of dibromide to

1 mole of sodium methoxide. This method gave satisfactory yields for $MeO(CH_2)_nBr$, (n = 4,5,6), but a poor yield in the case of $MeO(CH_2)_3Br$. $MeO(CH_2)_2Br$ was prepared in a different way.

All the compounds were separated in a high state of purity from the reaction mixtures using a Pye 104 preparative gas liquid chromatography machine. A 30 ft. column was used with a stationary phase of 25 per cent methylsilicone gum on 60-72 mesh, acid-washed, siliconised celite. After isolation, the purity of each compound was checked by g.l.c., and no impurities were detected.

f) 3-methoxy-1-bromopropane. Sodium (1•9 g.) in dry methanol (100 ml.) was added dropwise over a period of 6 hours to a refluxing solution of 1,3-dibromopropane (25 g.) in dry methanol (25 ml.). After the addition, the solution was heated for a further 2 hours and the methanol then removed by distillation. A little water was added to the flask to dissolve sodium bromide, the organic material being extracted into 3 portions of ether, totalling 250 ml. After drying overnight with magnesium sulphate the ether was removed, and the required compound separated from unused starting material and dimethoxypropane by preparative scale g.l.c. at 125°.

Only a small amount (0•43 g.) of product was collected and the above procedure was repeated, the solution being refluxed for 22 hours after the addition of the sodium methoxide. However, the yield of the compound (0•45 g.) did not show an increase.

g) 4-methoxy-1-bromobutane; h) 5-methoxy-1-bromopentane;

i) 6-methoxy-1-bromohexane. These three compounds were all prepared by the method described above, using the dibromide (20 g.) and the corresponding amount of sodium. Separation by preparative scale g.l.c. gave g) (1•90 g. at

130°); h) (3•73 g. at 150°); and i) (3•32 g. at 150°). A second preparation of g) using 40 g. of dibromide, produced 4•69 g.

j) 2-methoxy-1-bromoethane. The reaction between phosphorus tribromide and 2-methoxy-ethanol[77] was used for the preparation.

Phosphorus tribromide (36 g.) in pyridine (5 ml.) was added dropwise for 1 hour to a flask containing 2-methoxyethanol (25 g.) in pyridine (2 ml.). During the addition, the flask was cooled to -10°. After the reaction, the content of the flask was distilled out at $108-113^\circ$, and 2-methoxy-1-bromoethane (3•09 g.) separated from the impure mixture by preparative scale g.l.c. at 80°.

7.1.3 Compounds containing Phenyl Groups

k) 2,2,2-triphenylethyl chloride was prepared by the method of Charlton and his co-workers.[65] The reaction steps were as follows:

1. $Ph_3COH + CH_3COCl \longrightarrow Ph_3CCl + CH_3COOH$
2. $Ph_3CCl + 2Na \longrightarrow Ph_3CNa + NaCl$
3. $Ph_3CNa + CH_2Cl_2 \longrightarrow Ph_3CCH_2Cl + NaCl$

Experimental details for the individual stages are given below:

Stage 1. Acetyl chloride was added in several small portions to a heated solution of triphenylmethanol in dry benzene. The mixture was refluxed for an hour and protected from atmospheric moisture by a calcium chloride tube. On cooling and adding excess petroleum ether, off-white crystals of triphenylmethyl chloride separated. After cooling the flask in an ice-bath for 2 hours, the product was rapidly filtered, washed and recrystallised from dry petroleum ether. M.pt.111° (Lit.[78] $111-112^\circ$).

Stage 2. Triphenylmethylsodium was prepared in ether solution by the reaction of triphenylmethyl chloride with sodium amalgam.[79] A 1 per cent sodium amalgam containing mercury (920 g.) and sodium (9•2 g.) was added to a solution of triphenylmethyl chloride (48 g.) in dry ether (1200 ml.). The passage of dry nitrogen over the solution minimised reaction with atmospheric oxygen during six hours of vigorous stirring. The solution became deep-red after ca. 1 hour due to the presence of triphenylmethylsodium. After the reaction, the triphenylmethylsodium was used immediately in stage 3.

Stage 3. Methylene chloride (16 g.) in dry ether (100 ml.) was added dropwise to the well-stirred ether solution of triphenylmethylsodium. The stirring was continued for an hour after the addition and the reaction mixture filtered to remove salt. After concentration of the ether solution and the addition of petroleum ether, orange crystals separated. The crude product was recrystallised from petroleum ether. From a sublimation at $80^{o}/10^{-2}$ mm., 2,2,2-triphenylethyl chloride (6•6 g.) was collected. M.pt. 102^{o} (Lit.[65] $101{\cdot}5^{o}$). (Found: C,81•6; H,5•1; Cl,11•93; Ph_3CCH_2Cl requires C,81•9; H,5•8; Cl,12•12%). The hydrolysable chloride content was 99•2% of the theoretical amount.

1) 2,2,2-triphenylethyl p-toluenesulphonate was prepared by the method employed by Winstein and his co-workers,[36] and shown in the following reaction steps. (-Ts ≡ $p\text{-}CH_3C_6H_4OSO_2\text{-}$)

1. $Ph_3COH + CH_3COCl \longrightarrow Ph_3CCl + CH_3COOH$
2. $Ph_3CCl + 2Na \longrightarrow Ph_3CNa + NaCl$
3. $Ph_3CNa + HCHO \longrightarrow Ph_3CCH_2OH$
4. $Ph_3CCH_2OH + TsCl \longrightarrow Ph_3CCH_2OTs + HCl$

Stages 1 and 2 were performed as described above for the chloride.

Stage 3. 2,2,2-triphenylethanol was formed by passing formaldehyde through an ether solution of triphenylsodium.[80] A three-fold excess of paraformaldehyde (50 g.), previously dried for two days over phosphorus pentoxide, was heated and the formaldehyde passed into the reaction flask by a slow stream of dry nitrogen. The entry tube, wide enough to reduce clogging, terminated about 1 cm. above the surface of the well-stirred ether solution of triphenylmethylsodium. Despite this, repolymerisation took place at the mouth of the tube, which was cleared from time to time. Formaldehyde was passed for 4 hours, the colour of the solution changing from red to light yellow in about half an hour. After filtration, the ether was removed completely and methanol added to the remaining thick orange oil. Two crops of crystals were separated from the methanol solution. The first of these (i) separated almost immediately, and the second (ii) after the solution had been stored overnight at 0°. The N.M.R. and I.R. spectra of (i) and (ii) showed that two different compounds had been formed. In the I.R. spectrum, sample (ii) showed a strong peak due to an -OH stretching vibration, but this peak was absent from the spectrum of sample (i). The melting points were 125-130° (i) and 102° (ii). The melting point for 2,2,2-triphenylethanol has been reported as 104-105°.[36] Compound (ii), the required alcohol was recrystallised from methanol.

Stage 4. The method of Tipson[81] was used for the conversion of the alcohol to the p-toluenesulphonate.

p-toluenesulphonyl chloride (9 g.) was added in one portion to a solution of triphenylethanol (7·2 g.) in dry pyridine (80 ml.) at -5°, and the stoppered flask swirled until all had dissolved. The mixture was maintained at 0-5° for 30 hours and at 20° for 36 hours. Water (2 ml.) was added in 5 small portions at 5 minute intervals, the flask being swirled and cooled to keep the temperature below 5°. The solution was diluted with water (25 ml.) and crystals of the product separated. These were filtered, washed with water and dried over phosphorus pentoxide. The sample was recrystallised twice from petroleum ether (B.pt.40-60°). M.Pt.108° (Lit.[36] 106°). (Found: C,74•7; H,5•19; Ph_3CCH_2OTs requires C,75•5; H,5•6%). The hydrolysable chloride content was 99•7% of the theoretical amount.

m) 2-phenylethyl bromide. A commercial sample of this compound was distilled and a fraction collected with B.pt. 66-68°/4 mm. The hydrolysable chloride content was 99•1% of the theoretical amount.

7.2 Rate Measurements

7.2.1 Thermostats

The thermostats were of a conventional type and the temperature of each was controlled to *ca.* ± 0•01°C using a contact thermometer and an intermittent heater in conjunction with a relay. Immersion heaters provided constant heating and 60 watt electric light bulbs were used as intermittent heaters.

The temperatures quoted in this thesis were measured with thermometers reading to 0•01°C, which had previously been standardised by the National Physical Laboratory.

In general, the thermostats contained water, and a layer of oil on the liquid surface reduced evaporation and heat loss. For temperatures above 70°, ucepal, a high molecular weight soap was used as the thermostat liquid.

7.2.2 Solvents

A.R. grade acetone was refluxed with sodium hydroxide and potassium permanganate for two hours and then distilled. The distillate, containing a little hydroquinone, was fractionated, generous head and tail fractions being discarded.

Solvents were made up by volume. To prepare an X per cent solvent, X ml. of solvent acetone were added to (100-X) ml. of demineralised water.

7.2.3 The Measurement of First-order Rates

The reactions of the compounds studied always went to completion and were followed by measuring the concentration of acid present in the reaction mixture at various times. The sealed ampoule method was used throughout this work and the techniques involved are fully described elsewhere.[82]

First-order integrated rate coefficients were calculated from equation 7.1, where t is the time in seconds, and T_∞, T_t and T_o are the titres at

$$k_1 = \frac{2{\cdot}303}{t} \log_{10} \frac{T_\infty - T_o}{T_\infty - T} \qquad 7.1$$

times t = infinity, t = t and t = 0, respectively. The calculations of mean rate constants from individual k values are described in Chapter 3.

7.2.4 The Potentiometric Determination of Chloride Ion

As mentioned in section 7.2.5 several titrations had to be done using samples containing triethylamine, and in these cases chloride ion concentrations were determined potentiometrically.

The sealed ampoules were broken in a jar under "quenching" acetone (commercial acetone distilled over sodium hydroxide and potassium permanganate) and the contents of the jar and two rinsing portions of acetone poured into a 600 ml. beaker. A glass electrode as reference and a silver wire electrode were used in the beaker and connected to a pH meter. Before titration, a few drops of analar nitric acid were added to the solution, and a cloth was wrapped round the beaker to keep out as much light as possible. The solution was well stirred throughout and the chloride ions titrated against an approximately 0·01M standard solution of silver nitrate. Near the end-point 0•1 ml. aliquots of silver nitrate solution were added and the relative sizes of swing of the pH meter needle on either side of that in which the end-point occurred, enabled the exact position of the end-point to be established.

7.2.5 Reversible Reactions in the Solvolysis of Chlorohydrins

The purity of the distilled sample of 6-chlorohexanol, based on its total hydrolysable chloride content was found to be only about 98 per cent, and a trial run gave rate constants which rose steadily by 3 per cent in the first 80 per cent of reaction. In view of the fact that contamination of a chlorohydrin by dichloride resulted in a purity greater than 100 per cent and first-order $\underline{k}$ values which decreased during a run, it was thought that the results for 6-chlorohexanol were due to an incorrect reduced infinity titre. A possible explanation is that at the high temperature of the purity determination some of the HCl formed on solvolysis recombines with the glycol also present to produce the chlorohydrin in a reversible reaction.

To test this suggestion, 10 ampoules, each containing a known volume of 50 per cent aqueous acetone solvent which was 0•015M with respect to HCl and hexamethylene glycol, (the concentration of the products after a kinetic experiment) were heated at 125^{o} for different times. Table 7.1 shows the times of heating and the corresponding titres.

It can be seen that the concentration of HCl in the solution falls a little with time before reaching a steady value. On the basis of the above data, infinity titres obtained using the same conditions are expected to be as much as 1 per cent too low.

A second test experiment was made to ascertain whether or not the addition of a little triethylamine to each ampoule before sealing, to form a complex with the HCl, would enable a higher "true" infinity to be measured

Table 7.1

Times of heating and titres for a solution of HCl and $HO(CH_2)_6OH$ in 50 per cent aqueous acetone

Time (hr.)	Titre (ml.)
0	10•25
5	10•20
16	10•19
23	10•18
29	10•16
40	10•16
48	10•16

by potentiometric titration. 7 ampoules were filled in the normal way, and triethylamine (3 drops) was added to 4 of them. All were heated at 125° for 40 hours. The ampoules with triethylamine were titrated potentiometrically against standard silver nitrate, and these gave infinity values which were about 1 per cent higher than those for the samples without added amine.

As a result of these experiments the kinetic runs with 6-chlorohexanol were carried out in the normal way, but the ampoules involved in the infinity titre measurements contained triethylamine. Good first-order rate coefficients resulted from this technique which was also applied to 2-chloroethanol and 3-chloropropanol, compounds solvolysing at about the same rate as 6-chlorohexanol.

7.3 Identification and Estimation of the Products of Solvolysis

7.3.1 The Products of Solvolysis of 4-chlorobutanol and 5-chloropentanol

These experiments were devised to determine as accurately as possible the percentage of tetrahydrofuran (THF) and tetrahydropyran (THP) formed on the complete solvolysis of 4-chlorobutanol and 5-chloropentanol, respectively.

Gas liquid chromatography was chosen as the technique most likely to provide the quantitative results required.

Initial experiments with test solutions of THF and THP in 50% aqueous acetone at 10 times the normal concentration for a run showed that the use of a 10 ft. APL column at 60-70°, with a detector of the flame-ionisation type, gave convenient and different retention times for acetone, THF and THP. The reference compounds or "markers", essential in a quantitative comparison of peak areas, were THP for the hydrolysis of 4-chlorobutanol and THF for 5-chloropentanol.

In the absence of neighbouring group participation the products of hydrolysis of these 2 chlorohydrins would be the 1,4- and 1,5-diols, and a preliminary experiment was conducted to see if either of these compounds reacted to form THF and THP under the prevailing conditions. Samples of solutions containing either $HO(CH_2)_4OH$ (0·02M) and HCl (0·02M), or $HO(CH_2)_5OH$ (0·02M) and HCl (0·02M), were heated for several different times and the chromatograms inspected for the presence of THF or THP. The $HO(CH_2)_4OH$ solutions were heated at 95° for times which corresponded approximately to 3,6,10,13 half-lives of 4-chlorobutanol. No THF could be detected for any sample. The $HO(CH_2)_5OH$ solutions were heated at 110° for 12,24 and 36 hours. All the samples showed the presence of THP, but after 12 hours, the amount was at most only 5 per cent of the total possible from complete ring closure of the glycol. 12 hours at 110° corresponded to *ca*. 92% of reaction for 5-chloropentanol.

A calibration, using different solutions containing known amounts of THF and THP, was necessary before comparisons of the peak areas for these 2 compounds in a mixture could be made. Three standard solutions were accurately prepared, each containing both THF and THP, but in different relative amounts. Several injections of each solution were made. The peak areas were measured directly using a Kent chromalog integrator connected to the g.l.c. machine, and the mean THF:THP area ratio calculated for each mixture. The results of the calibration are summarised in Table 7.2.

Two standard solutions of substrates at run concentrations in 50 per cent aqueous acetone were prepared. The first of these contained 4-chloro butanol (0•0219M) and THP (0•0204M) and had a calculated THF:THP mole ratio, assuming complete conversion of chlorohydrin to THF, of 1•07 [m(calc.)]. Heating at 95° for 3 hours 40 minutes gave complete hydrolysis. Several injections of the solution were made under the same conditions as described earlier. The mean THF:THP area ratio was 0•756, which from the calibration corresponded to a THF:THP mole ratio of 0•99 [m(obs.)]. The values for [m(obs.)] and [m(calc.)] pointed to a 92 per cent conversion of 4-chloro-butanol to THF.

Table 7.2

g.l.c. calibration of THF:THP peak area ratios

THF:THP mole ratio	THF:THP peak area ratio
0•9663	0•7478
1•9326	1•4552
0•4835	0•3767

The second solution contained 5-chloropentanol (0•0230M) and THF (0•0206M) and had a calculated THF:THP mole ratio of 0•896 [m(calc.)]. In this case, the samples were heated at 110° for 12 hours, after which time *ca.* 92 per cent of reaction had taken place. The mean THF:THP area ratio, based on several injections, and corrected so as to apply for a complete solvolysis, was 0•708, and corresponded to a THF:THP mole ratio of 0•93 [m(obs.)]. The results showed that in the solvolysis of 5-chloropentanol there is a 97 per cent conversion of substrate to THP.

The final results of this product estimation are each subject to an error of a few per cent, but one can conclude that in the solvolyses of 4-chlorobutanol and 5-chloropentanol in 50 per cent aqueous acetone, tetrahydrofuran and tetrahydropyran, respectively, account for at least 90 per cent and possibly 100 per cent of the product. If the formation of glycols occurs, only small amounts are involved.

7.3.2 Possible Ring Formation in the Solvolysis of 3-chloropropanol

The ring compound, trimethylene oxide, is a possible product of the solvolysis of 3-chloropropanol and preliminary experiments were carried out to see if this cyclic ether is stable in the acid conditions which apply in a kinetic run. Two solutions were prepared, each containing trimethylene oxide (0•25M) and 1,3-propane-diol (0•25M). One solution was slightly acidic (0•01M HCl) and the other neutral. Samples of both were heated for 1,2,4 and 17 hours. An examination by g.l.c. showed that in the neutral solutions the concentrations of trimethylene oxide and glycol did not alter noticeably with the time of heating. However, in the presence of a low concentration of acid the cyclic ether was undetectable after 2 hours of heating and present in a greatly reduced amount after only 1 hour. As expected, the concentration of glycol in the acid solutions approximately doubled during the experiment.

The experiment showed that if neighbouring hydroxyl participation occurred in the solvolysis of 3-chloropropanol to form trimethylene oxide, the presence of this cyclic compound could not be detected by g.l.c. analysis due to rapid ring opening to form the glycol. As mentioned in Chapter 4, however, the activation parameters for the hydrolysis of 3-chloropropanol in 50 per cent aqueous acetone argue strongly against the intervention of neighbouring group participation in this reaction.

7.3.3 The Products of the Hydrolysis of 5-methoxy-1-bromopentane

The complicated kinetics which apply to the solvolysis of 5-methoxy-1-bromopentane are fully discussed in Chapter 5. Winstein[63c] found a substantial amount of tetrahydropyran (THP) in the product of the acetolysis of the corresponding p-bromobenzenesulphonate. The present work on the products of hydrolysis in 50 per cent aqueous acetone was carried out to determine as accurately as possible the percentage of the substrate converted to THP in solutions containing (a) no added bromide, (b) added sodium bromide (0•5M).

The experimental details of the chromatographic procedure are almost identical with those described above for the chlorohydrins.

n-butanol was used as a "marker" in preference to THF, as preliminary experiments had shown that the peak for the latter compound was slightly too close to the large acetone peak for accurate measurements to be made.

The results of the calibration are shown in Table 7.3.

Two solutions, (a) and (b), were prepared, each containing 5-methoxy-1-bromopentane (0•0209M) and butanol (0•0230M) and having a calculated butanol:THP mole ratio, assuming complete conversion of the reactant to THP, of 1•098 [m(calc.)].

Table 7.3

g.l.c. calibration of butanol:THP peak area ratios

butanol:THP mole ratio	butanol:THP area ratio
1•0093	0•930
0•5046	0•514
2•0186	1•547

Solution (b) contained added sodium bromide (ca.0•5M; 2•798 g. in 50 ml.). No salt was present in solution (a). Both solutions were completely hydrolysed and several injections of each made. The mean butanol:THP area ratios were 1•388 (a) and 1•206 (b), corresponding to mole ratios of 1•74 (a) and 1•44 (b) [m(obs.)].

The values for [m(obs.)] and [m(calc.)] showed that in the absence of added sodium bromide ca. 63 per cent of the substrate was converted to THP, but for a 0•5M sodium bromide solution ca. 77 per cent of the reactant solvolysed to THP.

7.3.4 The Products of the Hydrolysis of 4-methoxy-1-bromobutane

Preliminary experiments showed that small amounts of tetrahydrofuran (THF) were formed during the hydrolysis of 4-methoxy-1-bromobutane. Approximate determinations of the yield of cyclic product were made using a simplified version of the chromatographic procedure described above.

Three solutions containing substrate (0•02M) and (a) no added NaBr, (b) added NaBr (0•02M), (c) added NaBr (0•05M), were completely hydrolysed. The small THF peak in the chromatogram of each sample (peak in (c) > (b) > (a)) was compared with that given by a solution containing a known concentration of THF, injected under identical conditions. An approximate comparison of the peak areas in the different chromatograms gave the following estimated yields of THF:

Solution (a)	1-2 per cent,
Solution (b)	ca.5 per cent,
Solution (c)	5-10 per cent.

7.3.5 Hydrolysis Products of 2,2,2-triphenylethyl p-toluenesulphonate and chloride

Winstein[36] has reported that several ethyl arenesulphonates and related compounds give rearranged unsaturated products on acetolysis. In particular, triphenylethylene is formed from 2,2,2-triphenylethyl p-toluenesulphonate. The present experiments were devised in an attempt to identify triphenylethylene as a product of the solvolysis of 2,2,2-triphenylethyl p-toluenesulphonate and chloride in aqueous acetone solvents, and if possible to determine its concentration in solution after complete hydrolysis.

In preliminary experiments, triphenylethylene was shown to have a characteristic absorption at ca. 300 mμ in the ultraviolet spectrum and an extinction coefficient of ca.20000 at this wavelength. All quantitative measurements were made at 300 mμ using a Unicam SP 500 spectrophotometer and cyclohexane as solvent.

A standard solution of triphenylethylene contained 0•0145 g. in cyclohexane (100 ml.). 5 ml. of this solution was diluted to 100 ml. to give a sample with an optical density of 0•568.

Portions of a standard solution of the p-toluenesulphonate in 85 per cent aqueous acetone (0•2378 g. in 50 ml.) were heated in sealed ampoules at 85° for 13 hours to ensure complete hydrolysis. A 5 ml. sample was taken by pipette, the solvent removed completely by pumping, and the remaining product diluted with cyclohexane. The observed optical density was 0•335, compared with a value of 0•555, calculated for a 100 per cent conversion of substrate to triphenylethylene. The significant optical density at 300 mμ indicated the presence of triphenylethylene, formed in ca.60 per cent yield during the hydrolysis in 85 per cent aqueous acetone at 85°.

An identical procedure was employed for the chloride. Portions of a standard solution in 70 per cent aqueous acetone (0•1641 g. in 100 ml.) were heated in sealed ampoules at 120° for 13 hours to ensure complete hydrolysis. The observed optical density of a cyclohexane solution, prepared as described above, was 0•496, compared with a value of 0•562 calculated for a 100 per cent conversion of the substrate to triphenylethylene. This points to the formation of the rearranged olefin in ca. 88 per cent yield for the solvolysis of the chloride in 70 per cent aqueous acetone at 120°.

Additional experiments showed that triphenylethylene was stable in acid solution under the experimental conditions used.

A comparison of the results for the p-toluenesulphonate and the chloride shows considerable differences in the composition of the products of hydrolysis. However, these experiments were carried out using quite different solvents and temperatures and it is well known that when substitution and elimination compete, the elimination process, which usually has the higher activation energy, becomes more important as the temperature is increased.[83] One can therefore only conclude that the hydrolysis of the p-toluenesulphonate and chloride in 85 per cent and 70 per cent aqueous acetone, respectively, leads in the main to the formation of triphenylethylene in an elimination step.

7.4 Calculations of Rate Coefficients and Activation Parameters

The kinetic work with the series of chlorohydrins was completed before the development by Kohnstam[12] of the several methods for calculating first-order rate coefficients which are briefly discussed in Chapter 3.

The simplest form of the first-order rate equation (3.2.1a, with unit weight factors) was applied to the experimental rate data for the chlorohydrins, and the activation parameters were determined by the well-known methods which have been discussed elsewhere.[84] A summary of the results is given in Appendix 7. However, the rate coefficients and activation parameters for 4-chlorobutanol were more recently determined by the additional methods, and the results for this compound are shown in Appendices 5, 6.

Rate coefficients for 4-chlorobutanol and the three compounds involved in the study of neighbouring phenyl participation were calculated by the several different forms of the rate equation and are summarised in Appendix 5. Five slightly different sets of parameters were obtained from rate coefficients calculated from rate equations 3.2.1a (with unit and Gaussian weight factors), 3.2.2a and 3.2.3a (with unit and Gaussian weight factors). A summary of the activation parameters for the four compounds is given in Appendix 6.

APPENDIX 1

ACTIVITY COEFFICIENTS USED IN CHAPTER 5

In equations 5.6 and 5.7 for calculating the concentrations [RBr] and [MeBr] in aqueous acetone solutions, activity coefficients f_1, f_2 and f_3 allow for variations in k_1^o, k_5^o, k_6^o, α^o and γ^o due to changing ionic strength.

The activity coefficient, f, of a neutral molecule in solution is related to the ionic strength, μ, of the solution by the equation

$$f = \exp(a\mu) \qquad 1.$$

where <u>a</u> is a constant.

Experiments 22 and 31 showed that in the presence of sodium perchlorate (0•05M solution) the reaction of $MeO(CH_2)_5Br$ was accelerated by <u>ca</u>.10 per cent.

From equation 1,

$$a_1 \, . \, 0{\cdot}05 = \ln f_1 = \ln 1{\cdot}1; \quad a_1 = 1{\cdot}906$$

Experiments 34 and 35 showed that the presence of 0•05M NaBr resulted in a <u>ca</u>. 2 per cent retardation in the S_N2 reaction of $MeO(CH_2)_6Br$.

From equation 1,

$$a_2 \, . \, 0{\cdot}05 = \ln f_2 = \ln 0{\cdot}98; \quad a_2 = -0{\cdot}404$$

Thus, the rate constant k_1^o is associated with an activity coefficient f_1, where

$$f_1 = \exp(a_1[Br^-]); \quad a_1 = 1{\cdot}906$$

and rate constants k_5^o and k_6^o (for S_N2 processes) are used with f_2, where

$$f_2 = \exp(a_2[Br^-]); \quad a_2 = -0{\cdot}404$$

α^o and γ^o are ratios of the rate constants which apply to the reactions of the intermediate carbonium ion (I^+) with water and bromide ion.

Now $$k_{H_2O} = k^o_{H_2O} \cdot \frac{f_{I^+}}{f_T[H_2O]}$$

and $$k_{Br^-} = k^o_{Br^-} \cdot \frac{f_{I^+} \cdot f_{Br^-}}{f_T[Br^-]}$$

where f_{I^+}, f_{Br^-} and f_T are the activity coefficients for I^+, bromide ion and the transition states. The activity coefficient for α^o and γ^o is therefore of the form

$$\frac{f_{I^+} \cdot f_{Br^-}}{f_T[Br^-]} \cdot \frac{f_T[H_2O]}{f_{I^+}} \simeq f_{Br^-}$$

and can be expressed by the Debye-Hückel limiting law equation:[85]

$$f_3 = \exp(a_3 \sqrt{[Br^-]}); \quad a_3 = -2{\cdot}3820 \text{ for reactions at}$$

65•13° in 50 percent aqueous acetone.

Activity coefficient f_3 can also be evaluated using the Davies equation,[86] which is an empirical extension of the Debye-Hückel limiting law equation.

i.e. $$f_3 = \exp\left(\frac{a_3\sqrt{[Br^-]}}{1 + \sqrt{[Br^-]}}\right) \cdot \exp(b[Br^-]); \quad a_3 = -2{\cdot}3820,$$
$$b = 0{\cdot}2$$

The Davies form is probably the more reliable of the two equations for the present work in solutions which are up to 0•1M in NaBr.

APPENDIX 2

MATHEMATICAL TREATMENT OF CONCURRENT MECHANISMS

When a solvolysis occurs via two concurrent mechanisms associated with rate constants k_1 and k_2, the observed rate constant, $\underline{k}$, can be written

$$k = k_1 + k_2 \qquad 1.$$

If E_1, E_2 are the activation energies, $\Delta S_1^\ddagger$, $\Delta S_2^\ddagger$ the entropies of activation and $\Delta C_{p1}^\ddagger$, $\Delta C_{p2}^\ddagger$ the heat capacities of activation for the two mechanisms, the following equations are applicable:

$$E = RT^2 \frac{d\ln k}{dT} = xE_1 + (1 - x)E_2 \qquad 2.$$

$$\Delta C_p^\ddagger = \frac{dE}{dT} - R = \frac{x(1 - x)(E_1 - E_2)^2}{RT^2} + x\Delta C_{p1}^\ddagger + (1 - x)\Delta C_{p2}^\ddagger \qquad 3.$$

$$\ln x = \frac{(\Delta S_1^\ddagger - \Delta S^\ddagger)}{R} - \frac{(E_1 - E)}{RT} \qquad 4.$$

$$\ln(1 - x) = \frac{(\Delta S_2^\ddagger - \Delta S^\ddagger)}{R} - \frac{(E_2 - E)}{RT} \qquad 5.$$

where $x = k_1/k$ and E, $\Delta S^\ddagger$ and $\Delta C_p^\ddagger$ are the observed activation parameters which apply at the mean temperature of the kinetic experiment.

A value of $\Delta S_1^\ddagger$ for a particular temperature (e.g. 50°) is assumed for a reaction taking place in the prevailing conditions by a single mechanism (S_N1). $\Delta C_{p1}^\ddagger$ is determined from known values of the ratio $\Delta C_{p1}^\ddagger/\Delta S_1^\ddagger$. E_1, E_2 and $\Delta S_2^\ddagger$ at the mean temperature of the kinetic experiments, and $\Delta C_{p2}^\ddagger$, can then be calculated using equations 4, 2, 5 and 3, respectively.

The energies and entropies of activation are obtained at the top(Ta) and the bottom (Tb) temperatures of the range, using the equations

$$(E_1)_{Ta} = (E_1)_{Tm} + (\Delta C^{\ddagger}_{p1} + R)(Ta - Tm) \qquad 6.$$

$$(\Delta S^{\ddagger}_1)_{Ta} = (\Delta S^{\ddagger}_1)_{Tm} + \Delta C^{\ddagger}_{p1} \ln(Ta/Tm) \qquad 7.$$

These activation parameters allow calculated values of E and $\underline{k}$ to be determined at the two temperatures, and a comparison with the observed data can be made.

APPENDIX 3[12]

MATHEMATICS OF THE LEAST SQUARES PROCEDURE

The method of least squares involves the fitting of n experimental terms, y_i and x_i, to the relation $y_i = f(x_i)$. The assumption is made that the x_i values are much more accurate than those of y_i. The least squares procedure can be either "linear" or "non-linear".

Linear least squares. The "best" values of np disposable parameters, i.e. $a_1 \ldots\ldots a_{np}$, do not give a perfect fit for each experimental point, but such that:

$$y_i = a_1x_{1,i} + a_2x_{2,i} + \ldots\ldots a_{np}X_{np,i} + d_i \qquad 1.$$

$$\text{i.e.} \qquad y_i = \sum_{j=1}^{np} a_jx_{j,i} + d_i$$

where d_i is the residual of $y_i = y_i - \sum_{j=1}^{np} a_jx_{j,i}$ 2.

The principle of least squares is that the "best" values of $a_1 \ldots\ldots a_{np}$ are those which satisfy the condition:

$$\sum_{i} w_id_i^{\,2} \quad \text{is a minimum} \qquad 3.$$

where w_i is the statistical weight assigned to each experimental point, y_i. The minimisation condition applies to each of np independent a_j values, and np equations are obtained.

$$\text{i.e.} \qquad \sum_{j=1}^{np} a_jX_{jk} = Y_k \qquad (k = 1 \ldots\ldots np)$$

$$\text{where } X_{jk} = \sum_i w_i x_{j,i} x_{k,i} \quad \text{and } Y_k = \sum_i w_i y_i x_{k,i}$$

$$\text{and } a_j = \sum_k Y_k X_{jk}^{-1} \qquad (k = 1 \ldots\ldots\ np)$$

where X_{jk}^{-1} is the typical element of the inverse of the matrix of typical element X_{jk}.

Non-linear least squares. This procedure involves a relationship of the type:

$$f(x_i) = A_1 e^{-A_2 x_i} + \ldots\ldots$$

Approximate values of the disposable parameters are chosen; A_1', A_2' .... The Taylor expansion to the first term only, then gives:

$$f(x_i) = f'(x_i) + a_1 \frac{\partial f'}{\partial A_1'} + a_2 \frac{\partial f'}{\partial A_2'} + \ldots\ldots$$

$$\therefore \qquad Y = y_i - f'(x_i) = a_1 \frac{\partial f'}{\partial A_1'} + \ldots\ldots \text{ and this is a}$$

linear equation. The "best" values of a_1, ... are calculated by the linear least squares method (see above) and are such that $A_1' + a_1$, ... are better approximations to A_1 ...... than A_1' ...... This procedure is repeated, starting with the new values $A_1' + a_1$ ...... etc., until the standard error of a_1 ($\equiv$ standard error of A_1) $> 10a_1$. In practice, only about three iterations are needed.

The estimated variance of the experimental y terms is given by:

$$vy^{est} = \frac{\sum_i w_i d_i^2}{n-np}$$

If any residual, d_i, is such that:

$$w_i d_i^2 > 6{\cdot}25\ vy^{est},$$

the point is discordant and is discarded. A new set of parameters is then recalculated.

The above procedure is only valid if the weighting scheme is justified, as only then is $w_i d_i^2$ virtually constant (within a factor of 9). If an incorrect weighting scheme is used (i.e. $w_i = 1$), $w_i d_i^2$ may not be constant, and there is no justification for a discarding method of this type.

Errors in the parameters obtained from the least squares procedure

For an assumed relation of the type

$$y_i = a_1 x_{1,i} + a_2 x_{2,i} + \dots\dots\ a_{np} x_{np,i}$$

the "best" values of the coefficients are given by:

$$a_j = \sum_k Y_k X_{jk}^{-1} \qquad (j,k = 1, \dots\dots\ np)$$

where $Y_k = \sum_i w_i y_i x_{k,i}$ and X_{jk}^{-1} is the typical element of the inverse of the matrix with typical element X_{jk} $(= \sum_i w_i x_{j,i} x_{k,i})$. Now, an error δy_i $(= d_i)$ in y_i leads to an error

$$(\delta a_j)_i = \frac{\partial a_j}{\partial y_i} \cdot d_i \quad \text{in each } a_j \text{, and}$$

$$(\delta a_j)_i = \sum_k X_{jk}^{-1} \frac{\partial Y_k}{\partial y_i} \cdot d_i$$

i.e. $$(\delta a_j)_i = \sum_k X_{jk}^{-1} w_i d_i x_{k,i}$$

$$\therefore \quad (\delta a_j)_i^2 = w_i d_i^2 \sum_l X_{jl}^{-1} \left\{ \sum_k w_i x_{l,i} x_{k,i} X_{jk}^{-1} \right\}$$

$$(k,l = 1 \ldots\ldots np) \qquad 4.$$

If w_i is chosen so that $w_i d_i^2$ is approximately constant (within a factor of 9 for correct weighting) and

$$\simeq \frac{\sum_i w_i d_i^2}{n}$$

then $$v(a_j) = \frac{n}{n-np} \sum_i (\delta a_j)_i^2$$

i.e. $$v(a_j) = \frac{n}{n-np} \frac{\sum_i w_i d_i^2}{n} \sum_l X_{jl}^{-1} \left\{ \sum_k X_{jk}^{-1} \left(\sum_i w_i x_{l,i} x_{k,i} \right) \right\} \qquad 5.$$

Now $\sum' w_i x_{1,i} x_{k,i} = X_{1,k}$, an element of the original matrix. Also, the properties of matrices are such that the product of two matrices, with typical elements A_{jk}, B_{jk}, is a matrix with typical element C_{jk} such that:

$$C_{jk} = \sum_k A_{jk} B_{jk}$$

If $B_{jk} = A_{jk}^{-1}$, the inverse of A_{jk}, then $C_{jk} = 0$ if $j \neq k$ and $C_{jk} = 1$ if $j = k$. 6.

Equation 5 can be written in the form:

$$v(a_j) = vy^{est} \sum_1 X_{j1}^{-1} \left\{ \sum_k X_{1k} X_{jk}^{-1} \right\} \qquad 7.$$

From equation 6 it is obvious that $\sum_k X_{1k} X_{jk}^{-1} = 0$ when $1 \neq j$, and equals unity when $1 = j$.

$$\therefore \quad v(a_j) = vy^{est} X_{jj}^{-1} \qquad 8.$$

Completely analogous arguments hold for the co-variance,

$$cov(a_j, a_k) = vy^{est} X_{jk}^{-1} \qquad 9.$$

Equations 8 and 9 only apply when the approximation

$$w_i d_i^2 = \frac{\sum w_i d_i^2}{n}$$

causes little error. When this does not apply, no simplification in the sum of equation 5 is possible, and

$$v(a_j) = \frac{n}{n-np} \sum_{l} X_{jl}^{-1} \left\{ \sum_{k} X_{jk}^{-1} \left(\sum_{i} w_i^2 d_i^2 x_{l,i} x_{k,i} \right) \right\}$$

APPENDIX 4

SUMMARY OF KINETIC DATA FOR $MeO(CH_2)_5Br$

A summary of the comparisons between observed and calculated acidities for four kinetic runs with 5-methoxy-1-bromopentane. Debye-Hückel and Davies values for the activity coefficient f_3 are included. For each combination of k_1^o and α^o the lowest "std. dev."§ which is associated with a k^o value between 1•76 and 1•84 x 10^{-5} $\sec^{-1}$, is shown (see section 5.5).

The experiment numbers given are those used in Appendix 8, where the relevant reaction conditions are recorded.

§ std. dev. $= \left\{ \frac{\sum (\text{calculated acidity} - \text{observed acidity})^2}{n} \right\}^{\frac{1}{2}}$

where n is the number of experimental points in the kinetic run.

Summary of comparison between observed and calculated acidities

Experiment 22 Debye-Hückel values for parameter f_3

$10^5 k_1^o$	$\alpha^o (= \gamma^o)$	$10^5 k^o$ value giving lowest std. dev.	std. dev.
1•53	110	1•76	0•090
	120	1•76	0•056
	130	1•76	0•051
1•50	120	1•76	0•065
	130	1•76	0•047
	140	1•78	0•050
	150	1•82	0•054
1•47	130	1•76	0•049
	140	1•78	0•048
	150	1•80	0•049
	160	1•82	0•051
	170	1•84	0•054
1•44	140	1•76	0•044
	150	1•78	0•047
	160	1•80	0•050
	170	1•84	0•051
	180	1•84	0•057
1•41	140	1•76	0•045
	150	1•78	0•045
	160	1•80	0•046
	170	1•82	0•047
	180	1•84	0•049
1•38	150	1•76	0•041
	160	1•78	0•043
	170	1•80	0•045

Summary of comparison between observed and calculated acidities

Experiment 22 Davies values for parameter f_3

$10^5 k_1^o$	$\alpha^o (= \gamma^o)$	$10^5 k^o$ value giving lowest std. dev.	std. dev.
1•44	130	1•76	0•054
	140	1•76	0•047
	150	1•80	0•050
1•41	140	1•76	0•045
	150	1•78	0•046
	160	1•80	0•048
	170	1•82	0•050
	180	1•84	0•052
1•38	150	1•76	0•044
	160	1•78	0•046
	170	1•82	0•049
	180	1•84	0•050
1•35	160	1•78	0•043
	170	1•80	0•044
	180	1•82	0•045
	190	1•84	0•046
	200	1•84	0•053
1•32	170	1•78	0•041
	180	1•80	0•042
	190	1•82	0•043

Summary of comparison between observed and calculated acidities

Experiment 24 Debye-Hückel values for parameter f_3

$10^5 k_1^{\,o}$	$\alpha^o (= \gamma^o)$	$10^5 k^o$ value giving lowest std. dev.	std. dev.
1•50	120	1•76	0•064
	130	1•80	0•056
1•47	120	1•76	0•079
	130	1•76	0•062
	140	1•80	0•054
	150	1•84	0•047
1•44	130	1•76	0•071
	140	1•78	0•059
	150	1•80	0•053
	160	1•84	0•047
1•41	140	1•76	0•067
	150	1•78	0•058
	160	1•80	0•053
	170	1•84	0•048
1•38	150	1•76	0•066
	160	1•78	0•058

Summary of comparison between observed and calculated acidities

Experiment 24 Davies values for parameter f_3

$10^5k_1^o$	$\alpha^o(=\gamma^o)$	10^5k^o value giving lowest std. dev.	std. dev.
1•44	130	1•76	0•063
	140	1•80	0•056
1•41	140	1•78	0•062
	150	1•80	0•055
	160	1•82	0•050
	170	1•84	0•048
1•38	150	1•78	0•062
	160	1•80	0•055
	170	1•82	0•050
	180	1•84	0•045
1•35	170	1•78	0•057
	180	1•82	0•052
	190	1•84	0•047
	200	1•84	0•045
1•32	180	1•78	0•056
	190	1•80	0•052

Summary of comparison between observed and calculated acidities

Experiment 26 Debye-Hückel values for parameter f_3

$10^5 k_1^o$	$\alpha^o (= \gamma^o)$	$10^5 k^o$ value giving lowest std. dev.	std. dev.
1•50	120	1•78	0•023
	130	1•82	0•020
1•47	120	1•76	0•032
	130	1•78	0•024
	140	1•80	0•022
	150	1•84	0•018
1•44	130	1•76	0•033
	140	1•78	0•025
	150	1•80	0•021
	160	1•82	0•018
1•41	140	1•76	0•037
	150	1•76	0•028
	160	1•78	0•025
	170	1•80	0•022
1•38	150	1•76	0•045
	160	1•76	0•030

Summary of comparison between observed and calculated acidities

Experiment 26   Davies values for parameter f_3

$10^5k_1^o$	$\alpha^o(=\gamma^o)$	10^5k^o value giving lowest std. dev.	std. dev.
1·44	130	1·80	0·026
	140	1·80	0·027
1·41	140	1·78	0·025
	150	1·80	0·022
	160	1·82	0·019
	170	1·82	0·031
1·38	150	1·78	0·029
	160	1·78	0·026
	170	1·80	0·022
	180	1·82	0·019
1·35	170	1·78	0·029
	180	1·78	0·026
	190	1·80	0·022
	200	1·82	0·021
1·32	180	1·76	0·032
	190	1·76	0·029

Summary of comparison between observed and calculated acidities

Experiment 28 Debye-Hückel values for parameter f_3

$10^5 k_1^o$	$\alpha^o (= \gamma^o)$	$10^5 k^o$ value giving lowest std. dev.	std. dev.
1•50	120	1•76	0•036
	130	1•76	0•017
	140	1•78	0•020
1•47	130	1•76	0•041
	140	1•76	0•020
	150	1•76	0•020
	160	1•78	0•022
1•44	140	1•76	0•052
	150	1•76	0•031
	160	1•76	0•017
	170	1•76	0•019
1•41	150	1•76	0•066
	160	1•76	0•047
	170	1•76	0•031
	180	1•76	0•018
1•38	160	1•76	0•084

Summary of comparison between observed and calculated acidities

Experiment 28 Davies values for parameter f_3

$10^5 k_1^o$	$\alpha^o (= \gamma^o)$	$10^5 k^o$ value giving lowest std. dev.	std. dev.
1•44	130	1•76	0•017
	140	1•78	0•019
	150	1•78	0•021
1•41	150	1•76	0•016
	160	1•76	0•019
	170	1•78	0•018
	180	1•80	0•020
1•38	170	1•76	0•019
	180	1•76	0•014
	190	1•78	0•019
	200	1•78	0•016
1•35	190	1•76	0•032
	200	1•76	0•023
	210	1•76	0•016
1•32	200	1•76	0•060
	210	1•76	0•051

APPENDIX 5

SUMMARY OF RATES AND ERRORS FOR THE SOLVOLYSES OF FOUR COMPOUNDS IN AQUEOUS ACETONE

The forms of the first-order rate equation used in the calculations are numbered as in Chapter 3. The weighting schemes used are either $w_i = 1$ or $w_i = g_i$.

Errors are expressed as $10^3 \sigma_k/k$, where σ_k is the standard error of $\underline{k}$.

4-CHLOROBUTANOL IN 50% AQUEOUS ACETONE

Rates ($10^6 k$ sec^{-1})

Equation	3.2.1a, $w_i=1$	3.2.1a, $w_i=g_i$	3.2.2a	3.2.3a, $w_i=1$	3.2.3a, $w_i=g_i$
94·82°	468·87	468·37	469·81	471·11	468·46
85·11°	213·94	214·23	213·87	213·31	214·56
74·80°	88·058	88·060	87·957	87·967	88·026
65·00°	35·553	35·557	35·481	35·434	35·542
54·96°	13·180	13·183	13·173	13·170	13·179
45·18°	4·6441	4·6446	4·6402	4·6327	4·6429
35·20°	1·4834	1·4812	1·4794	1·4775	1·4782

Errors($10^3 \sigma_k / k$)

Equation	3.2.1a, $w_i=1$	3.2.1a, $w_i=g_i$	3.2.2a	3.2.3a, $w_i=1$	3.2.3a, $w_i=g_i$
94·82°	1·17	1·28	1·32	2·09	0·97
85·11°	1·12	1·02	1·20	1·68	1·37
74·80°	1·04	0·85	0·68	1·59	1·38
65·00°	0·82	0·99	0·73	1·02	1·16
54·96°	0·84	0·77	0·63	0·47	0·77
45·18°	0·90	0·80	0·65	0·72	0·80
35·20°	1·28	1·07	1·05	1·54	1·39

2,2,2-TRIPHENYLETHYL CHLORIDE IN 70% AQUEOUS ACETONE

Equation	Rates (10^6k sec^{-1})				
	100•26°	90•16°	80•05°	70•11°	60•39°
3.2.1a, $w_i=1$	25•371	9•2777	3•1797	1•0410	0•32536
3.2.1a, $w_i=g_i$	25•413	9•2883	3•1830	1•0417	0•32536
3.2.2a	25•504	9•3072	3•1920	1•0427	0•32529
3.2.3a, $w_i=1$	25•554	9•3158	3•1972	1•0416	0•32498
3.2.3a, $w_i=g_i$	25•479	9•3045	3•1882	1•0441	0•32541
	Errors ($10^3\sigma_k/k$)				
3.2.1a, $w_i=1$	1•50	1•60	1•46	1•31	0•75
3.2.1a, $w_i=g_i$	1•25	1•55	1•21	1•18	0•84
3.2.2a	0•86	1•51	1•53	1•20	1•00
3.2.3a, $w_i=1$	0•58	2•65	1•33	2•27	1•92
3.2.3a, $w_i=g_i$	1•80	1•89	1•20	1•80	1•18

2,2,2-TRIPHENYLETHYL P-TOLUENESULPHONATE IN 85% AQUEOUS ACETONE

Equation	Rates ($10^6 k$ sec^{-1})				
	84·92°	75·08°	65·14°	55·08°	45·13°
3.2.1a, $w_i=1$	197·26	71·318	24·041	7·4605	2·1880
3.2.1a, $w_i=g_i$	197·18	71·361	24·056	7·4657	2·1910
3.2.2a	197·33	71·537	24·097	7·4695	2·1953
3.2.3a, $w_i=1$	197·20	71·747	24·109	7·4766	2·1987
3.2.3a, $w_i=g_i$	197·04	71·473	24·083	7·4710	2·1940
	Errors ($10^3\sigma_k/k$)				
3.2.1a, $w_i=1$	0·95	1·34	1·39	1·26	1·26
3.2.1a, $w_i=g_i$	0·94	1·28	1·52	1·14	0·89
3.2.2a	0·67	1·20	2·40	0·94	0·46
3.2.3a, $w_i=1$	1·39	1·33	2·66	1·73	0·56
3.2.3a, $w_i=g_i$	0·77	1·68	1·91	1·28	0·83

2-PHENYLETHYL BROMIDE IN 50% AQUEOUS ACETONE

Equation	Rates ($10^6 k$ sec^{-1})				
	100·52°	90·12°	80·09°	71·02°	60·38°
3.2.1a, $w_i=1$	25·904	11·068	4·6105	1·9934	0·69509
3.2.1a, $w_i=g_i$	25·906	11·073	4·6154	1·9938	0·69460
3.2.2a	25·936	11·057	4·6304	1·9935	0·69415
3.2.3a, $w_i=1$	25·885	11·057	4·6335	1·9948	0·69310
3.2.3a, $w_i=g_i$	25·906	11·073	4·6322	1·9938	0·69363
	Errors ($10^3 \sigma_k/k$)				
3.2.1a, $w_i=1$	1·09	0·91	1·83	0·80	0·96
3.2.1a, $w_i=g_i$	1·14	0·96	1·82	0·86	0·69
3.2.2a	1·48	0·77	1·02	0·95	0·51
3.2.3a, $w_i=1$	1·77	0·72	1·11	1·33	0·95
3.2.3a, $w_i=g_i$	1·41	0·62	1·64	1·34	0·84

APPENDIX 6

ACTIVATION PARAMETERS FOR THE SOLVOLYSES OF FOUR COMPOUNDS IN AQUEOUS ACETONE

Activation parameters were determined from sets of rate data calculated using five forms of the first-order rate equation. These equations are numbered as in Chapter 3. The weighting schemes used are either $w_i = 1$ or $w_i = g_i$.

Equation	E (cal)	$-\Delta S^{\ddagger}$ (cal deg^{-1} mole^{-1})	$-\Delta C_p^{\ddagger}$ (cal deg^{-1} mole^{-1})
4-CHLOROBUTANOL IN 50% AQUEOUS ACETONE AT 65•01°			
3.2.1a, $w_i=1$	21723 ± 7	16•88 ± 0•02	26•08 ± 0•72
3.2.1a, $w_i=g_i$	21725 ± 6	16•88 ± 0•02	26•81 ± 0•71
3.2.2a	21736 ± 6	16•85 ± 0•02	25•55 ± 0•67
3.2.3a, $w_i=1$	21745 ± 10	16•83 ± 0•03	24•87 ± 1•03
3.2.3a, $w_i=g_i$	21733 ± 6	16•85 ± 0•02	27•06 ± 0•77
2,2,2-TRIPHENYLETHYL P-TOLUENESULPHONATE IN 85% AQUEOUS ACETONE AT 65•07°			
3.2.1a, $w_i=1$	25624 ± 13	6•16 ± 0•04	1•18 ± 2•37
3.2.1a, $w_i=g_i$	25616 ± 11	6•19 ± 0•03	1•41 ± 2•21
3.2.2a	25615 ± 8	6•19 ± 0•02	1•64 ± 2•74
3.2.3a, $w_i=1$	25609 ± 14	6•20 ± 0•04	2•58 ± 3•39
3.2.3a, $w_i=g_i$	25608 ± 11	6•21 ± 0•03	2•44 ± 2•53
2,2,2-TRIPHENYLETHYL CHLORIDE IN 70% AQUEOUS ACETONE AT 80•19°			
3.2.1a, $w_i=1$	27035 ± 16	9•47 ± 0•05	13•37 ± 2•77
3.2.1a, $w_i=g_i$	27044 ± 14	9•44 ± 0•04	13•55 ± 2•44
3.2.2a	27065 ± 13	9•38 ± 0•04	14•16 ± 2•52
3.2.3a, $w_i=1$	27084 ± 20	9•32 ± 0•06	14•47 ± 3•32
3.2.3a, $w_i=g_i$	27054 ± 20	9•41 ± 0•06	14•18 ± 3•15
2-PHENYLETHYL BROMIDE IN 50% AQUEOUS ACETONE AT 80•43°			
3.2.1a, $w_i=1$	22308 ± 13	22•12 ± 0•04	18•76 ± 2•61
3.2.1a, $w_i=g_i$	22312 ± 12	22•11 ± 0•03	20•13 ± 2•54
3.2.2a	22317 ± 14	22•09 ± 0•04	21•42 ± 2•17
3.2.3a, $w_i=1$	22311 ± 18	22•11 ± 0•05	24•56 ± 2•68
3.2.3a, $w_i=g_i$	22317 ± 15	22•09 ± 0•04	23•52 ± 2•68

APPENDIX 7

RATES AND ACTIVATION PARAMETERS FOR THE SOLVOLYSES OF CHLOROHYDRINS IN 50% AQUEOUS ACETONE

	T (^{o}C)	$10^{6}k$ (sec^{-1})	E(cal)	$-\Delta S^{\ddagger}$(cal deg^{-1} mole^{-1})
2-chloroethanol	118•00	4•5845 ± 0•0071	25110 ± 36	21•24 ± 0•09
	99•45	0•91812 ± 0•00161		
3-chloropropanol	118•11	12•211 ± 0•028	23572 ± 43	23•25 ± 0•11
	99•48	2•6817 ± 0•0043		
6-chlorohexanol	113•90	11•833 ± 0•018	22695 ± 27	24•89 ± 0•07
	94•06	2•4023 ± 0•0027		
5-chloropentanol	100•02	25•493 ± 0•031	22923 ± 20	20•52 ± 0•05
	80•85	4•7813 ± 0•0037	23218 ± 10	19•57 ± 0•03
	60•24	0•62156 ± 0•00030		

$$\Delta C_p^{\ddagger} = -16{\cdot}76 \pm 1{\cdot}12 \text{ cal deg}^{-1}\text{ mole}^{-1}$$

4-chlorobutanol The results for this compound are summarised in Appendices 5,6.

APPENDIX 8

DETAILS OF INDIVIDUAL RUNS

First-order rate coefficients were calculated from the equation:

$$k = \frac{2{\cdot}303}{60t} \log \frac{a}{(a - x)}$$

where _k_ is the integrated rate coefficient in sec^{-1}, _t_ is the time in minutes, _a_ is the concentration of substrate at zero time and (a - x) is its concentration at time _t_. Titres are expressed in ml. of NaOH.

In each case, details of one run are given and the mean rate coefficients k', k" of duplicate runs are quoted. In addition, an overall mean rate coefficient, k (mean), and its standard error, are noted.

Experiment 1

2-chloroethanol in 50% aqueous acetone at 118•00°

Time	Titre	10^6k
0	0•00	-
1034	2•61	4•576
1276	3•12	4•574
1502	3•55	4•547
1807	4•15	4•604
2095	4•62	4•577
2383	5•12	4•639
2736	5•59	4•591
3172	6•14	4•576
3659	6•72	4•608
4130	7•20	4•621
4619	7•56	4•541
5047	7•92	4•578
∞	10•56	-

10^6k = 4•586 (12 readings)

$10^6k'$ = 4•583 (12 readings)

10^6k(mean) = (4•584 ± 0•007)

Experiment 2

2-chloroethanol in 50% aqueous acetone at 99•45°

Time	Titre	10^7k
0	0•00	-
2838	1•46	(8•829)
3824	1•96	9•043
5265	2•63	9•167
6747	3•26	9•226
8139	3•83	9•337
9565	4•30	9•226
11001	4•77	9•224
12855	5•34	9•262
15344	5•94	9•114
18210	6•63	9•195
21089	7•16	9•117
23959	7•65	9•143
∞	10•46	-

10^7k = 9•187 (11 readings)

$10^7k'$ = 9•176 (11 readings)

10^7k(mean) = (9•181 ± 0•016)

Experiment 3

3-chloropropanol in 50% aqueous acetone at 118•11°

Time	Titre		10^5k
0	0•02	0•00	-
204		1•47	1•230
319		2•21	1•232
431		2•86	1•227
549		3•52	1•237
674		4•14	1•237
786	4•54		1•194
965	5•34		1•220
1214	6•23		1•229
1501	7•03		1•223
1806		7•68	1•208
2229	8•44		1•211
2712	9•07		1•217
∞		10•52	-

10^5k = 1•222 (12 readings)

$10^5k'$ = 1•220 (11 readings)

10^5k(mean) = (1•221 ± 0•003)

Experiment 4

3-chloropropanol in 50% aqueous acetone at 99•48°

Time	Titre	10^6k
0	0•00	-
1048	1•65	2•645
1699	2•56	2•663
2398	3•44	2•674
3104	4•26	2•703
3863	5•01	2•700
4486	5•58	2•712
5385	6•26	2•694
6411	6•95	2•695
7658	7•63	2•682
8892	8•17	2•664
10058	8•60	2•655
11571	9•07	2•659
∞	10•77	-

10^6k = 2•679 (12 readings)

$10^6k'$ = 2•684 (12 readings)

10^6k(mean) = (2•682 ± 0•004)

Experiment 5

4-chlorobutanol in 50% aqueous acetone at 94•82°

Time	Titre		10^4k
0	0•485	0•535	-
9	2•57		4•630
13	3•37		4•685
17	4•06		4•676
21	4•71		4•720
25	5•24		4•681
31		5•99	4•688
37		6•58	4•662
43		7•11	4•684
51		7•67	4•678
60		8•17	4•678
70		8•61	4•704
∞	9•91		-

10^4k = 4•681 (11 readings)

$10^4k'$ = 4•697 (10 readings)

10^4k(mean) = (4•689 ± 0•005)

Experiment 6

4-chlorobutanol in 50% aqueous acetone at 85•11°

Time	Titre	10^4k
0	0•62	-
11	1•94	2•124
19	2•81	2•146
28	3•69	2•159
37	4•45	2•150
47	5•21	2•152
57	5•88	2•154
69	6•58	2•158
84	7•32	2•164
99	7•90	2•152
117	8•48	2•150
137	8•96	2•131
151	9•26	2•141
∞	10•71	-

10^4k = 2•148 (12 readings)

$10^4k'$ = 2•133 (11 readings)

$10^4k''$ = 2•136 (12 readings)

10^4k(mean) = (2•139 ± 0•002)

Experiment 7

4-chlorobutanol in 50% aqueous acetone at 74•80°

Time	Titre	10^5k
0	0•40	-
30	1•90	8•707
55	3•00	8•776
74	3•74	8•786
95	4•47	8•776
117	5•19	8•864
139	5•77	8•784
174	6•62	8•814
211	7•34	8•785
252	8•03	8•856
300	8•61	8•777
348	9•10	8•819
365	9•23	8•785
∞	10•74	-

10^5k = 8•794 (12 readings)

$10^5k'$ = 8•818 (11 readings)

10^5k(mean) = (8•806 ± 0•009)

Experiment 8

4-chlorobutanol in 50% aqueous acetone at 65•00°

Time	Titre	10^5k
0	0•34	-
70	1•79	3•546
114	2•60	3•551
164	3•42	3•536
214	4•18	3•554
259	4•80	3•567
309	5•50	(3•657)
384	6•22	3•574
465	6•94	3•561
547	7•56	3•558
662	8•25	3•539
787	8•86	3•550
864	9•15	3•543
∞	10•82	-

10^5k = 3•553 (11 readings)

$10^5k'$ = 3•554 (10 readings)

10^5k(mean) = (3•553 ± 0•003)

Experiment 9

4-chlorobutanol in 50% aqueous acetone at 54•96°

Time	Titre		10^5k
0	0•20	0•21	-
227	1•64		1•328
372	2•42		1•320
518	3•14		1•327
686	3•84		1•317
893		4•62	1•322
1068		5•18	1•324
1273		5•72	1•316
1553	6•36		1•321
1791	6•79		1•318
2051	7•17		1•312
2285		7•45	1•306
2579		7•77	1•318
∞	8•90		-

10^5k = 1•319 (12 readings)

$10^5k'$ = 1•317 (12 readings)

10^5k(mean) = (1•318 ± 0•001)

Experiment 10

4-chlorobutanol in 50% aqueous acetone at 45•18°

Time	Titre		10^6k
0	0•235	0•255	-
482	1•45		4•666
854		2•27	4•595
1214		3•02	4•661
1557	3•64		4•673
1920	4•23		4•655
2401		4•93	4•630
2989	5•68		4•651
3649		6•39	4•650
4335	6•99		4•652
5111		7•52	4•605
6034	8•06		4•631
7042		8•52	4•662
∞	9•86		-

10^6k = 4•644 (12 readings)

$10^6k'$ = 4•644 (11 readings)

10^6k(mean) = (4•644 ± 0•004)

Experiment 11

4-chlorobutanol in 50% aqueous acetone at 35•20°

Time	Titre	10^6k
0	0•25	-
1598	1•70	1•507
2884	2•70	1•490
4193	3•61	1•485
5535	4•42	1•473
6930	5•22	1•487
8351	5•89	1•478
9732	6•47	1•473
11428	7•14	1•486
12905	7•61	1•483
15455	8•27	1•469
18346	8•93	1•486
21747	9•46	1•477
∞	11•03	-

10^6k = 1•483 (12 readings)

$10^6k'$ = 1•484 (12 readings)

10^6k(mean) = (1•483 ± 0•002)

Experiment 12

5-chloropentanol in 50% aqueous acetone at $100{\cdot}02^{\circ}$

Time	Titre		10^5k
0	0•01	0•02	-
131	1•92		2•546
174	2•45		2•525
230	3•11		2•527
284	3•72		2•549
362	4•50		2•559
421	5•03		2•564
506	5•69		2•553
625	6•49		2•548
761		7•26	2•552
905		7•93	2•567
1038		8•41	2•565
1174		8•82	2•571
∞	10•54		-

10^5k = 2•552 (12 readings)

$10^5k'$ = 2•546 (12 readings)

10^5k(mean) = (2•549 ± 0•003)

Experiment 13

5-chloropentanol in 50% aqueous acetone at 80•85°

Time	Titre	10^6k
0	0•00	-
572	1•59	4•789
864	2•31	4•798
1164	2•96	4•747
1552	3•76	4•766
1878	4•35	4•753
2232	4•97	4•794
2729	5•70	4•787
3303	6•42	4•777
3928	7•11	4•805
4706	7•78	4•793
5656	8•43	4•796
6563	8•89	4•775
∞	10•49	-

10^6k = 4•782 (12 readings)

$10^6k'$ = 4•781 (12 readings)

10^6k(mean) = (4•781 ± 0•004)

Experiment 14

5-chloropentanol in 50% aqueous acetone at 60•24°

Time	Titre	10^7k
0	0•00	-
3469	1•26	(6•129)
5597	1•98	6•209
7643	2•61	6•218
9916	3•26	6•234
11831	3•73	(6•168)
14223	4•33	6•215
17173	4•98	6•224
21579	5•81	6•207
27172	6•71	6•230
32950	7•45	6•230
40158	8•16	6•203
47681	8•74	6•210
∞	10•52	-

10^7k = 6•218 (10 readings)

$10^7k'$ = 6•214 (11 readings)

10^7k(mean) = (6•216 ± 0•003)

Experiment 15

6-chlorohexanol in 50% aqueous acetone at 113•90°

Time	Titre	10^5k
0	0•00	-
254	1•44	1•174
366	2•01	1•182
486	2•53	1•164
607	3•09	1•189
798	3•79	1•178
967	4•33	1•169
1200	5•05	1•187
1442	5•64	1•186
1680	6•12	1•182
1986	6•63	1•178
2346	7•11	1•176
2717	7•49	1•172
∞	8•79	-

10^5k = 1•178 (12 readings)

$10^5k'$ = 1•189 (11 readings)

10^5k(mean) = (1•183 ± 0•002)

Experiment 16

6-chlorohexanol in 50% aqueous acetone at 94•06°

Time	Titre	10^6k
0	0•00	-
1179	1•63	2•402
1627	2•18	2•402
2219	2•86	2•407
2910	3•55	2•383
3690	4•32	2•415
4432	4•94	2•413
5190	5•51	2•413
5922	6•01	2•416
7031	6•68	2•425
8161	7•23	2•413
9947	7•95	2•407
12357	8•66	2•392
∞	10•43	-

10^6k = 2•407 (12 readings)

$10^6k'$ = 2•397 (11 readings)

10^6k(mean) = (2•402 ± 0•003)

Experiment 17

2-methoxy-1-bromoethane in 50% aqueous acetone at 65•13°

Time	Titre	10^7k
0	0•00	-
5416	1•01	3•713
8551	1•53	3•685
11213	1•94	3•662
14014	2•36	3•675
16964	2•78	3•690
19774	3•15	3•691
22660	3•51	3•699
25561	3•86	3•718
28576	4•17	3•699
31321	4•46	3•713
34185	4•73	3•709
∞	8•88	-

10^6k = 3•696 (11 readings)

$10^6k'$ = 3•691 (11 readings)

10^6k(mean) = (3•693 ± 0•003)

Experiment 18

3-methoxy-1-bromopropane in 50% aqueous acetone at 65•13°

Time	Titre	10^6k
0	0•03	-
1426	1•50	2•026
2136	2•14	2•023
2861	2•76	2•040
3607	3•33	2•042
4323	3•84	2•050
5036	4•22	2•000
6023	4•85	2•041
7189	5•44	2•042
8593	6•03	2•033
10029	6•53	2•020
11901	7•10	2•029
14446	7•68	2•030
∞	9•27	-

10^6k = 2•031 (12 readings)

$10^6k'$ = 2•034 (12 readings)

10^6k(mean) = (2•033 ± 0•003)

Experiment 19

4-methoxy-1-bromobutane in 50% aqueous acetone at 65•13°

(No NaBr added)

Time	Titre	10^4k
0	0•73	-
13	2•32	2•492
18	2•84	2•473
23	3•32	2•458
28	3•70	2•383
36	4•30	2•339
48	5•03	2•255
63	5•84	2•219
78	6•47	2•170
99	7•13	2•090
122	7•67	2•014
148	8•19	1•988
∞	9•73	-

A plot of k against time showed the initial rate $[(k_{obs})_{t=0}]$ to be $2{\cdot}57 \times 10^{-4}$ sec^{-1}

Experiment 20

4-methoxy-1-bromobutane in 50% aqueous acetone at 65•13^{o}

(0•021 M in added NaBr)

Time	Titre	10^4k
0	0•37	-
25	2•14	1•432
35	2•75	1•433
45	3•28	1•416
55	3•74	1•390
71	4•46	1•389
91	5•06	1•314
121	5•96	1•298
151	6•65	1•277
191	7•34	1•249
231	7•87	1•232
269	8•26	1•224
∞	9•53	-

A plot of k against time showed the initial rate $[(k_{obs})_{t=0}]$ to be 1•50 x 10^{-4} sec^{-1}

Experiment 21

4-methoxy-1-bromobutane in 50% aqueous acetone at 65•13°

(0•052 M in added NaBr)

Time	Titre	10^5k
0	0•25	-
35	2•03	9•868
50	2•69	9•886
65	3•26	9•760
80	3•79	9•700
100	4•42	9•621
120	4•93	9•412
150	5•67	9•377
185	6•30	9•109
231	6•97	8•848
283	7•61	8•752
335	7•97	8•309
∞	9•76	-

A plot of k against time showed the initial rate $[(k_{obs})_{t=0}]$ to be $1{\cdot}01 \times 10^{-4}$ sec^{-1}

Experiment 22

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13°

(No NaBr added)

Time	Titre		10^5k
0	0•08	0•06	-
228	2•01		1•538
307	2•50		1•475
455	3•31		1•399
600	4•04		1•370
756	4•68		1•327
907		5•26	1•312
1134		5•99	1•282
1349		6•62	1•275
1559		7•13	1•265
1874	7•76		1•251
2202		8•34	1•267
2507		8•73	1•265
∞	10•25		-

Experiment 23

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13°

(INITIAL RATE determination; no NaBr added)

Time	Titre	10^5k
0	0•105	-
15	0•37	1•725
25	0•55	1•748
35	0•72	1•734
45	0•89	1•731
55	1•03	1•676
65	1•20	1•687
75	1•34	1•656
85	1•50	1•659
95	1•65	1•652
105	1•81	1•658
∞	17•30	-

A plot of k against time showed the initial rate $[(k_{obs})_{t=0}]$ to be $1{\cdot}80 \times 10^{-5}$ sec^{-1}

Experiment 24

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13°

(0•0210 M in added NaBr)

Time	Titre		10^6k
0	0•04	0•03	-
346	1•69		8•230
496	2•39		8•503
639	3•04		8•768
800		3•73	9•028
944		4•33	9•277
1127		4•98	9•402
1306		5•61	9•647
1480		6•15	9•815
1696	6•74		9•972
1943	7•38		10•281
2206	7•93		10•495
2723		8•75	10•800
∞	10•55		-

Experiment 25

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13°

(INITIAL RATE determination; 0•0210M in added NaBr)

Time	Titre	10^6k
0	0•02	-
15	0•15	7•883
41	0•36	7•591
71	0•61	7•658
96	0•82	7•727
116	1•01	7•955
132	1•13	7•865
142	1•24	8•062
154	1•33	8•002
169	1•47	8•105
191	1•63	7•999
∞	18•40	-

A plot of k against time showed the initial rate $[(k_{obs})_{t=0}]$ to be 0•76 x 10^{-5} sec^{-1}

Experiment 26

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13°

(0•0508M in added NaBr)

Time	Titre	10^6k
0	0•04	-
387	1•58	7•219
569	2•33	7•635
752	3•04	7•920
938	3•75	8•256
1110	4•38	8•567
1286	4•98	8•854
1486	5•57	9•057
1776	6•34	9•363
2067	7•03	9•718
2313	7•47	9•832
2588	7•94	10•098
2850	8•26	10•148
∞	10•02	-

Experiment 27

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13°

(INITIAL RATE determination; 0•0508M in added NaBr)

Time	Titre	10^6k
0	0•05	-
30	0•26	6•737
60	0•45	6•450
80	0•57	6•310
100	0•72	6•534
120	0•87	6•693
140	1•01	6•745
160	1•12	6•599
180	1•26	6•662
200	1•41	6•770
220	1•56	6•865
∞	17•48	-

A plot of k against time showed the initial rate $[(k_{obs})_{t=0}]$ to be $0{\cdot}62 \times 10^{-5}$ sec^{-1}.

Experiment 28

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13°

(0•0975M in added NaBr)

Time	Titre		10^6k
0	0•03	0•02	-
455	1•71		6•722
590	2•26		7•116
760	2•94		7•524
934		3•55	7•741
1134		4•26	8•075
1308		4•84	8•347
1510		5•46	8•628
1774	6•16		8•891
2067	6•86		9•229
2305		7•37	9•543
2595		7•85	9•744
2862	8•24		9•966
∞	10•05		-

Experiment 29

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13^{o}

(INITIAL RATE determination; 0•0975M in added NaBr)

Time	Titre	10^6k
0	0•04	-
40	0•27	5•550
70	0•44	5•545
100	0•64	5•856
125	0•79	5•882
145	0•91	5•903
165	1•04	5•986
185	1•17	6•057
205	1•30	6•118
226	1•45	6•240
245	1•57	6•269
∞	17•42	-

A plot of k against time showed the initial rate $[(k_{obs})_{t=0}]$ to be $0{\bullet}53 \times 10^{-5}$ sec^{-1}

Experiment 30

5-methoxy-1-bromopentane in 50% aqueous acetone at 95•59°

(Run at *ca.* 3x the usual concentration of substrate)

Time	Titre	10^5k
0	0•36	-
14	1•46	1•576
23	2•02	1•503
38	2•84	1•440
53	3•54	1•398
73	4•36	1•371
98	5•26	1•369
123	6•03	1•384
153	6•75	1•391
193	7•52	1•426
264	8•36	1•472
∞	9•22	-

Experiment 31

5-methoxy-1-bromopentane in 50% aqueous acetone at 65•13°

(0•05M in added $NaClO_4$)

Time	Titre		10^5k
0	0•08	0•07	-
248	2•33		1•674
350	3•00		1•605
545	4•07		1•516
703	4•83		1•484
990		5•92	1•430
1250		6•70	1•395
1546		7•44	1•377
1858	8•05		1•361
2250		8•65	1•355
∞	10•29		-

Experiment 32

Methyl bromide in 50% aqueous acetone at 65•13°

Time	Titre		10^5k
0	0•18	0•10	-
161	2•04		1•454
267	2•73		1•236
359	3•62		1•288
455	4•65		1•385
575	5•56		1•380
679	6•37		1•406
776		7•26	1•495
977		8•21	1•432
1216		9•09	1•361
1448		10•30	1•442
1654	10•95		1•432
2032	11•85		1•415
∞	14•38		-

10^5k(mean) = (1•394 ± 0•020) §

§ The relatively large standard error results from inaccuracies due to the high volatility of MeBr (B.pt. = 4°), despite the fact that the ampoules were filled with a solution cooled to *ca.* 0°.

Experiment 33

6-methoxy-1-bromohexane in 50% aqueous acetone at 65•13°

Time	Titre		10^6k
0	0•00	0•01	-
727	1•54		3•753
1018		2•10	3•762
1383		2•74	3•760
1826	3•44		3•758
2273		4•11	3•779
2915		4•93	3•775
3658	5•74		3•774
4334		6•39	3•789
5075	6•96		3•773
5905	7•53		3•790
6598		7•93	3•802
7747	8•44		3•790
∞	10•19		-

10^6k = 3•775 (12 readings)

$10^6k'$ = 3•787 (12 readings)

10^6k(mean) = (3•781 ± 0•003)

Experiment 34

6-methoxy-1-bromohexane in 50% aqueous acetone at 95•55°

Time	Titre		10^5k
0	0•12	0•09	-
45	1•46		5•100
77	2•29		5•054
108	3•03		5•057
140	3•71		5•030
177	4•45		5•058
223	5•24		5•053
283	6•14		5•077
357	7•05		5•107
438	7•82		5•111
567	8•70		5•097
734		9•45	5•133
∞	10•54		-

10^5k(mean) = (5•080 ± 0•009)

Experiment 35

6-methoxy-1-bromohexane in 50% aqueous acetone at 95•55°

(0•05M in added NaBr)

Time	Titre	10^5k
0	0•11	-
49	1•43	5•020
78	2•11	4•984
108	2•75	4•957
140	3•39	4•970
177	4•02	4•917
223	4•78	4•974
283	5•60	4•988
357	6•41	4•976
438	7•13	4•989
567	7•93	4•940
∞	9•72	-

10^5k(mean) = (4•971 ± 0•009)

Experiment 36

2,2,2-triphenylethyl chloride in 70% aqueous acetone at 100•26°

Time	Titre		10^5k
0	0•04	0•07	-
116		1•58	2•510
161		2•09	2•498
214		2•67	2•515
267		3•21	2•531
321		3•70	2•527
396		4•35	2•550
471		4•89	2•536
565		5•54	2•564
650		6•02	2•561
750	6•50		2•557
900	7•11		2•553
1084	7•70		2•558
∞	9•49		-

10^5k = 2•539 (12 readings)

$10^5k'$ = 2•536 (11 readings)

10^5k(mean) = (2•537 ± 0•004)

Experiment 37

2,2,2-triphenylethyl chloride in 70% aqueous acetone at 90•16°

Time	Titre	10^6k
0	0•05	-
301	1•49	9•165
421	2•01	9•213
607	2•74	9•210
783	3•37	9•225
963	3•97	9•287
1149	4•53	9•335
1393	5•11	9•188
1558	5•55	9•347
1877	6•21	9•386
2227	6•76	9•285
2582	7•23	9•228
2989	7•72	9•334
∞	9•49	-

10^6k = 9•267 (12 readings)

$10^6k'$ = 9•289 (11 readings)

10^6k(mean) = (9•278 ± 0•015)

Experiment 38

2,2,2-triphenylethyl chloride in 70% aqueous acetone at 80•05°

Time	Titre		10^6k
0	0•04	0•02	-
943	1•60		3•189
1445	2•29		3•136
1877		2•86	3•166
2346	3•45		3•180
2821	3•96		3•166
3452		4•60	3•191
4054	5•15		3•199
4626		5•59	3•196
5339	6•10		3•200
6162		6•56	3•173
7175	7•10		3•193
8754		7•73	3•204
∞	9•49		-

10^6k = 3•183 (12 readings)

$10^6k'$ = 3•177 (12 readings)

10^6k(mean) = (3•180 ± 0•005)

Experiment 39

2,2,2-triphenylethyl chloride in 70% aqueous acetone at 70•11°

Time	Titre	10^6k
0	0•03	-
2922	1•58	(1•021)
4154	2•17	1•029
5611	2•83	1•042
7013	3•39	1•043
8536	3•96	1•048
9964	4•43	1•047
11472	4•88	1•044
13214	5•37	1•048
15154	5•82	1•041
17927	6•42	1•046
21544	7•01	1•036
25753	7•60	1•042
∞	9•49	-

10^6k = 1•042 (11 readings)

$10^6k'$ = 1•039 (12 readings)

10^6k(mean) = (1•041 ± 0•001)

Experiment 40

2,2,2-triphenylethyl chloride in 70% aqueous acetone at 60•39°

Time	Titre	10^7k
0	0•01	-
9985	1•69	3•256
13213	2•16	3•244
16310	2•59	3•246
19194	2•99	3•277
21993	3•36	(3•304)
24986	3•68	3•266
27930	3•99	3•249
30170	4•23	3•254
32960	4•51	3•255
35870	4•79	3•260
38820	5•06	3•266
42000	5•30	3•240
∞	9•49	-

10^7k = 3•256 (11 readings)

$10^7k'$ = 3•252 (11 readings)

10^7k(mean) = (3•254 ± 0•002)

Experiment 41

2,2,2-triphenylethyl p-toluenesulphonate in 85% aqueous acetone at 84•92°

Time	Titre		10^4k
0	0•555	0•615	-
16	2•06		1•982
23	2•63		1•978
30	3•14		1•963
38	3•70		1•972
47	4•26		1•972
58	4•86		1•967
77		5•72	(1•940)
93		6•37	1•972
108		6•86	1•987
123		7•24	1•980
143		7•65	1•971
163		8•01	1•991
∞	9•24		-

10^4k = 1•976 (11 readings)

$10^4k'$ = 1•969 (10 readings)

10^4k(mean) = (1•973 ± 0•002)

Experiment 42

2,2,2-triphenylethyl p-toluenesulphonate in 85% aqueous acetone at 75•08°

Time	Titre	10^5k
0	0•25	-
40	1•59	7•148
60	2•15	7•028
81	2•74	7•132
100	3•22	7•165
125	3•78	7•155
150	4•25	7•066
180	4•82	7•143
215	5•34	7•080
265	6•01	7•120
310	6•51	7•170
355	6•90	7•159
415	7•31	7•130
∞	8•75	-

10^5k = 7•124 (12 readings)

$10^5k'$ = 7•139 (12 readings)

10^5k(mean) = (7•132 ± 0•010)

Experiment 43a §

2,2,2-triphenylethyl p-toluenesulphonate in 85% aqueous acetone at 65•15°

Time	Titre		10^5k
0	0•17	0•15	-
121		1•59	2•425
174		2•15	2•432
235		2•72	2•410
299		3•29	2•419
385		3•97	2•420
481		4•64	2•425
593		5•32	2•435
709		5•87	2•410
850	6•51		2•433
954	6•83		2•410
1095	7•25		2•416
1249	7•64		2•440
∞	9•07		-

10^5k(mean) = (2•424 ± 0•003)

§ Experiment 43 was designed to obtain rate data at ca. 65°. However, the solvent used had a slightly different composition from that of experiments 41,42,44,45. Because of this, an additional run at 75•08° (43b) was also done in the second solvent, and the results used in conjunction with those of experiment 42 to apply the necessary correction factor to the data from 43a.

Experiment 43b §

2,2,2-triphenylethyl p-toluenesulphonate in 85% aqueous acetone at 75•08°

Time	Titre	10^5k
0	0•25	-
40	1•54	7•103
60	2•13	7•204
80	2•67	7•254
102	3•19	7•222
127	3•73	7•213
155	4•23	7•106
183	4•74	7•183
211	5•14	7•123
276	6•01	7•268
319	6•39	7•161
361	6•76	7•227
416	7•12	7•213
∞	8•48	-

10^5k(mean) = (7•190 ± 0•016)

§ See footnote to Experiment 43a.

Experiment 44

2,2,2-triphenylethyl p-toluenesulphonate in 85% aqueous acetone at 55•08°

Time	Titre	10^5k
0	0•14	-
385	1•48	7•436
572	2•05	7•426
748	2•55	7•439
925	3•04	7•530
1116	3•48	7•465
1375	4•04	7•455
1760	4•77	7•464
2170	5•41	7•446
2767	6•17	7•461
3275	6•71	7•565
3932	7•18	7•491
∞	8•63	-

10^5k = 7•471 (11 readings)

$10^5k'$ = 7•451 (11 readings)

10^5k(mean) = (7•460 ± 0•009)

Experiment 45

2,2,2-triphenylethyl p-toluenesulphonate in 85% aqueous acetone at 45•13°

Time	Titre		10^6k
0	0•15	0•12	-
1508		1•65	2•157
2117		2•20	2•171
2855	2•82		2•170
3489		3•29	2•187
4270	3•84		2•188
5027	4•30		2•184
5763	4•72		2•192
7143		5•38	2•194
8599		5•97	2•196
10100		6•47	2•196
11602		6•88	2•197
12867	7•17		2•195
∞	8•75		-

10^6k = 2•186 (12 readings)

$10^6k'$ = 2•191 (12 readings)

10^6k(mean) = (2•188 ± 0•003)

Experiment 46

2-phenylethyl bromide in 50% aqueous acetone at 100•52°

Time	Titre		10^5k
0	0•155	0•19	-
130		1•99	2•602
180		2•56	2•563
231		3•15	2•594
283		3•70	2•611
340		4•23	2•605
406		4•78	2•594
475		5•29	2•578
562		5•93	2•613
665		6•50	2•588
835	7•32		2•602
949	7•74		2•590
1079	8•14		2•581
∞	9•99		-

10^5k = 2•593 (12 readings)

$10^5k'$ = 2•587 (12 readings)

10^5k(mean) = (2•590 ± 0•003)

Experiment 47

2-phenylethyl bromide in 50% aqueous acetone at 90•12°

Time	Titre		10^5k
0	0•21	0•19	-
308	1•98		1•104
420	2•54		1•104
559	3•20		1•114
674	3•69		1•115
794		4•14	1•111
965		4•74	1•108
1151		5•33	1•108
1389		5•98	1•107
1616	6•53		1•110
1853	6•98		1•101
2103	7•42		1•104
2520		8•00	1•108
∞	9•80		-

10^5k = 1•108 (12 readings)

$10^5k'$ = 1•106 (11 readings)

10^5k(mean) = (1•107 ± 0•001)

Experiment 48

2-phenylethyl bromide in 50% aqueous acetone at 80•09°

Time	Titre		10^6k
0	0•11	0•12	-
705		1•87	4•614
905	2•27		4•543
1226	2•90		4•511
1547		3•59	4•667
1985		4•29	4•610
2377	4•85		4•582
2875	5•57		4•663
3450		6•23	4•662
4016	6•69		4•551
4675		7•29	4•621
5262	7•71		4•644
5909		8•08	4•632
∞	9•99		-

10^6k = 4•609 (12 readings)

$10^6k'$ = 4•612 (12 readings)

10^6k(mean) = (4•610 ± 0•008)

Experiment 49

2-phenylethyl bromide in 50% aqueous acetone at 71•02°

Time	Titre	10^6k
0	0•115	-
1759	1•95	1•990
2580	2•67	1•978
3148	3•15	1•990
4012	3•80	1•989
4661	4•26	1•997
5436	4•75	1•996
6031	5•08	1•986
7093	5•67	2•003
8307	6•21	1•991
9746	6•80	2•004
11238	7•26	1•985
13233	7•80	1•987
∞	9•80	-

10^6k = 1•993 (12 readings)

$10^6k'$ = 1•996 (10 readings)

10^6k(mean) = (1•993 ± 0•002)

Experiment 50

2-phenylethyl bromide in 50% aqueous acetone at 60•38°

Time	Titre	10^7k
0	0•11	-
4557	1•83	6•995
5965	2•28	6•929
7478	2•77	6•991
8846	3•15	6•928
10313	3•55	6•917
11767	3•93	6•923
13297	4•32	6•960
15533	4•82	6•949
17505	5•22	6•933
19788	5•66	6•948
22602	6•13	6•930
∞	9•99	-

10^7k = 6•946 (11 readings)

$10^7k'$ = 6•956 (11 readings)

10^7k(mean) = (6•951 ± 0•007)

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