SOLVOLYSIS OF BICYCLO[2,2,1]OCTAN-3-YL p-TOLUENESULPHONATES

by

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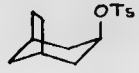
ABSTRACT

The solvolytic mechanisms for the pair of bicyclo[3, 2, 1]octan-3-yl tosylates (1 and 2) have been investigated in buffered acetic and formic acids, and in some aqueous alcoholic mixtures. The rate constants, and α- and β-d_4 kinetic isotope effects were measured, and the products were analysed.



(1)

(2)

The α-effects are fairly high (1.16-1.20) and not very solvent dependent, and are therefore compatible with a mechanism involving little solvent nucleophilic participation. The β-d_4 effects are very high (1.93-2.75) for both isomers, suggesting that participation by these neighbouring carbon-hydrogen bonds is involved in the ionization of these compounds. A non-chair transition state is proposed for the exo tosylate (2), in parallel with results for many other cyclic systems with (initially) equatorial leaving groups.[1,2]

The product analyses for both isomers show predominant inversion of configuration, and varying amounts of rearranged products. The similarity in the rearranged products, and in their relative proportions from both tosylates suggests that a common non-classical carbonium ion intervenes in the rearranged product forming steps from both diastereoisomers. This ion appears to be similar to that implicated in the solvolysis of trans-bicyclo[3, 2, 1]octan-2-yl derivatives.[3]

The hypothesis that nucleophilic participation by solvent or by neighbouring groups or bonds occurs in most solvolysis reactions is made, and allows a new interpretation of some recent literature results.

ACKNOWLEDGEMENTS

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CHAPTER I. INTRODUCTION

Solvolysis reactions cover a large area of organic chemistry, and yet understanding of their detailed mechanisms remains incomplete. Investigations in this field have been fruitful, and have led to the development of many new concepts which have application in many other areas of study, e.g. S_N1 and S_N2 terminology, carbonium ions, solvent parameters and non-classical ions.[4] Recently another experimental method has been more widely employed for the study of solvolysis reactions, the measurement of secondary deuterium kinetic isotope effects. The theory and application of these isotope effects in solvolysis have been the subject of reviews.[5,6,7] They have been shown to be very useful tools for evaluating solvent and neighbouring group participation.

In the present work, secondary deuterium isotope effects have been used in the study of the solvolysis of the isomeric bicyclo[3, 2, 1]-octan-3-yl tosylates. This system was chosen for study since it allows comparison of the characteristics involved in solvolysis of compounds with axial or equatorial leaving groups. It provides an important modification to the 4-t-butylcyclohexyl system which has been studied by Shiner,[1,8] and by Whiting.[9] They showed that β-hydrogen participation was important in the solvolysis of both the cis and trans isomers, with the trans derivative reacting through a twist conformation to obtain the optimum stereochemistry for participation.

In the bicyclic system the ethane bridge imposes a severe restriction on the cyclohexane ring, and models suggest that twist forms are precluded.

Therefore only the ground state of the endo tosylate (1) has a suitable arrangement of two of the β-hydrogens for participation. The exo tosylate (2) might be expected to react by a different solvolysis

(1)

(2)

mechanism, possibly one involving extensive nucleophilic participation. The products of acetolysis reported by Jefford and co-workers[10] were in agreement with this hypothesis. However no rearranged products were noted from acetolysis of either tosylate, whereas comparison with the 4-t-butylcyclohexyl system suggested that some rearrangement might occur for the endo tosylate. The results of Lebel and Maxwell[11] for acetolysis of exo - and endo - bicyclo[3, 2, 1]oct-6-en-3-yl tosylate showed many similarities with the 4-t-butylcyclohexyl system, and therefore the behaviour of the bicyclo[3, 2, 1]octan-3-yl derivatives appeared to be anomalous. It represents an important type of cyclic compounds, and therefore a detailed investigation of the kinetics and products of solvolysis was undertaken. It has been stressed that to describe a solvolysis mechanism, as many methods as possible should be used to study the reactions.[12] The solvolysis rates, the α- and β-d_1 kinetic isotope effects, and the products have been determined for a wide range of solvent systems.

The classification of solvolysis mechanisms, the experimental methods, including kinetic isotope effects, used in their determination, and important literature results for cyclic systems are discussed in Chapter 2.

The preparation of the bicyclic tosylates and their labelled derivatives, measurement of the deuterium incorporation, and the solvents used are outlined in Chapter 3. The kinetic procedure and results are described in Chapter 4, and are compared with relevant literature data. Chapter 5 presents the product analyses, and compares the results for acetolysis with those of Jefford and co-workers.[10] A reaction scheme is described for the solvolysis of these bicyclic tosylates. Participation by solvent and by neighbouring groups or bonds is discussed in Chapter 6, and a new interpretation of some literature results is suggested. The preparation of all compounds and solvents used, the various tests of stability to reaction conditions, calibration of the g.l.c. detector, and the analysis methods are described fully in Chapter 7. The rate constants, α- and β-d_4 isotope effects are all given in the first part of the appendix, while complete figures for the product analyses are tabulated in the second part of the appendix.

CHAPTER 2 SOLVOLYSIS MECHANISMS

2.1 Classification of mechanisms

During the 1930's, Hughes, Ingold and co-workers showed that nucleophilic substitution reactions could be characterised by two general mechanistic pathways.[4] In one of these, breaking of the bond to the leaving group occurred concurrently with formation of the bond to the attacking nucleophile.

$$N: + R\text{-}X \rightarrow \left[N\cdots R\cdots X \right]^{\neq} \rightarrow N\text{-}R + X^-$$

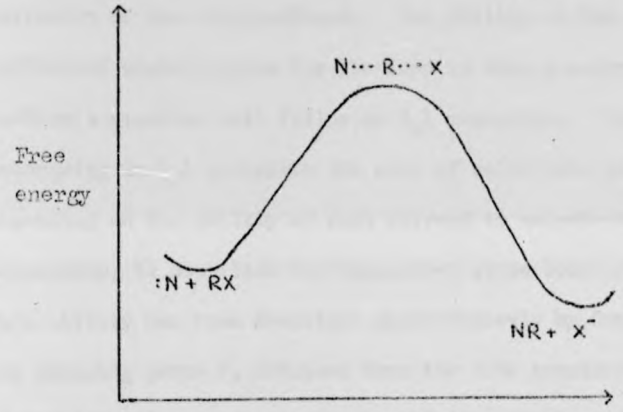
They termed this one-step reaction type S_N2 (substitution, nucleophilic, bimolecular). As the nucleophile has to approach the molecule from the rear, complete inversion of configuration occurs giving inverted substitution product. In the second type of mechanism, the bond to the leaving group is broken in a slow, rate-determing step, before the bond to the nucleophile is formed. The reaction therefore proceeds through an intermediate carbonium ion. The intermediate then reacts rapidly with the attacking nucleophile to give the product.

$$R\text{-}X \xrightarrow{\text{slow}} R^+ + X^-$$
$$R^+ + N \xrightarrow{\text{fast}} R\text{-}N$$

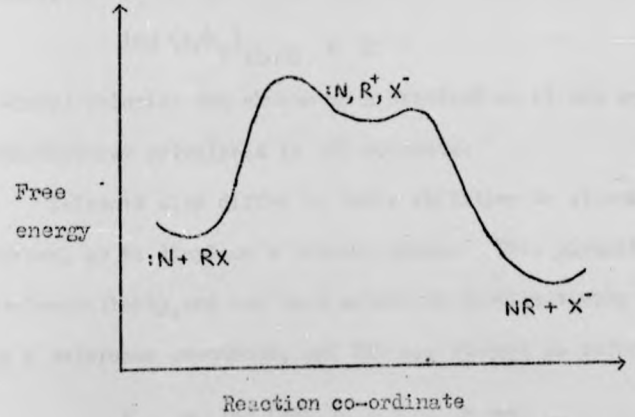
This pathway was described as S_N1 (substitution, nucleophilic, unimolecular), and was expected to yield both retained and inverted substitution products since the nucleophile could approach from either side of the planar intermediate. Free energy diagrams for these two mechanisms are shown in Figure 2.1.

Figure 2.1

Free energy diagrams for nucleophilic substitutions



(a) S_N2



(b) S_N1

The S_N1 mechanism at first encountered considerable opposition on the grounds that the heterolytic step would be highly endothermic. However it was argued that this would be compensated by the energy of solvation of the ions produced.[13] The ability of the solvent to provide sufficient stabilisation for the ions is thus a major factor in determining whether a reaction will follow an S_N1 mechanism. For a given substrate undergoing an S_N1 mechanism the rate of solvolysis will vary with solvent, depending on the ability of each solvent to solvate the ions, or more accurately, to stabilize the transition state leading to these ions. This ability has been described quantitatively by Grunwald and Winstein[14] as the ionising power Y, obtained from the rate constant of solvolysis, k, of t-butyl chloride in a solvent, relative to its rate constant of solvolysis, k_o, in 80% aq. ethanol (a reference solvent for which Y was chosen to be zero).

$$\log (k/k_o)_{tBuCl} = Y \qquad \text{Eq. 2.1}$$

t-Butyl chloride was chosen as a standard as it was expected to undergo unimolecular solvolysis in all solvents.

Solvents also differ in their abilities to attack electron-deficient carbon, or to displace a leaving group. This parameter is termed nucleophilicity, and has been expressed quantitatively using methyl tosylate as a reference substrate, and 80% aq. ethanol as reference solvent.[15]

$$N_{BS} = \log (k/k_o)_{MeOTs} - 0.30Y \qquad \text{Eq. 2.2}$$

The values of Y and N for a given solvent then provide a guide as to whether that solvent will favour bimolecular or unimolecular solvolysis for a given substrate.

The mechanism followed by a given substrate will also depend on the ability of that substrate to produce a relatively stable carbonium ion. Thus tertiary substrates generally react by S_N1 mechanisms, while primary compounds follow an S_N2 pathway. Equation 2.3 allows a parameter m to be assigned to a given substrate, reflecting its sensitivity to solvent ionising power.[14]

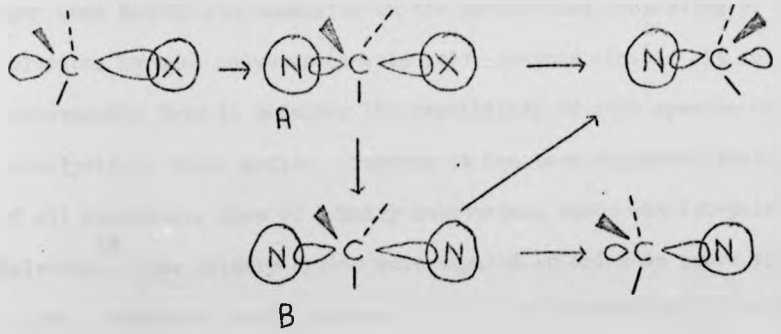
$$\log k/k_0 = mY \qquad \text{Eq. 2.3}$$

Tertiary substrates give m values that are close to unity, while lower values (~ 0.2) are obtained for primary compounds. The values obtained for secondary substrates often lie in between these two limits, showing that the dependence for such substrates on ionising power is not characteristic of that for a clear S_N1 or an S_N2 mechanism.

It has been suggested that S_N1 and S_N2 represent two mechanistic extremes, and that most compounds react by mechanisms that are intermediate to these limiting types.[16] Confusion can arise as to whether a substrate reacts by a single hybrid mechanism, or by a mixture of S_N1 and S_N2 mechanisms. The classification, introduced by Winstein and co-workers[17] describes reactions as being nucleophilic (N) if the activated complex in the rate-determining step has a covalent interaction between the incoming nucleophile and the substrate, and limiting (Lim) if there was no such interaction. The transition state is envisaged as a resonance hybrid of three canonical forms:

$$\underset{(1)}{N \quad R-X} \longleftrightarrow \underset{(2)}{N \overset{+}{R} \; X^-} \longleftrightarrow \underset{(3)}{N-R \quad X^-}$$

and varying contributions from these forms lead to a range of possible mechanisms. This classification thus includes the concept of a merged mechanism, unlike the earlier Hughes-Ingold system. The approach developed by Doering and Zeiss,[18] and by Streitwieser,[16] also suggests a range of mechanisms. This 'structural hypothesis' considers that two principal solvation sites are involved, one for the incoming nucleophile or solvent molecule, and one for the leaving group.



Formation of A is rate-determining; A can then lose X to give the product of inverted configuration, or X can be replaced to give B, which can lead to inverted or retained product. This approach allows a reaction which appears to follow an S_N1 pathway, to give incomplete racemisation.[13] This is often the case in borderline solvolyses.

It was suggested by Hammett that ion-pairs might be involved in the solvolyses of secondary substrates.[19] Intimate ion-pairs have been postulated to explain molecular rearrangements that occur in starting material,

concomitant with solvolysis, but at a faster rate than can be accounted for by return from free carbonium ions.[13] A second type, a solvent-separated ion-pair, which can be captured by added inert salts, has also been suggested.[20] A total ion-pair scheme involves three possible types of electron-deficient species occurring in solvolysis reactions, all of which can in principle undergo nucleophilic attack by solvent, return to starting material, elimination, or rearrangement.

The existence of ion-pairs in solvents of low dielectric constant has been used to explain anomalies in the conductance properties of dilute salt solutions in such solvents (acetic acid, acetone etc.).[21] It is not unreasonable then to consider the possibility of such species occurring in solvolysis in these media. However it has been suggested that solvolyses of all compounds, even of primary substrates, occur via ion-pairs in all solvents.[22] One primary system investigated in order to prove this hypothesis was the p-methoxybenzyl system. This is a very favourable choice, as it provides a carbonium ion of higher stability than is common for primary compounds. Primary compounds with no special stabilising influences probably react by nucleophilic mechanisms with considerable covalent interaction between the substrate and the attacking group. However for secondary and tertiary substrates, ion-pairs probably occur as intermediates in many cases.

2.2 Experimental determination of mechanism

In solvolysis reactions, the determination of the mechanism for a given substrate is complex. As the solvent is always present in large excess, the reaction always appears to follow first order kinetics, whether

the mechanism is unimolecular or bimolecular.

The Hughes-Ingold classification suggested that determination of the stereochemistry of the products would indicate whether bond-making and bond-breaking were concurrent. However complete inversion is common in reactions which in other respects appear to involve a two-step process.[12] This can be rationalised using the structural hypothesis approach, by considering that the mechanism is not totally limiting, by postulating ion-pair intermediates, or by one side of the intermediate being shielded by the continued presence of the leaving group. In some cases the amount of retained product (that formed with retention of configuration) is unusually large; this can be due to epimerisation of starting material,[23] or to participation by a neighbouring group.[24] Assignment of a mechanism solely by the stereochemistry of the products can therefore be erroneous.

In some cases the methods used to determine a mechanism may cause a change of mechanism to occur. This is possible when the effect of added nucleophiles or salts is studied. The results of Johnstam et al.[25] for the solvolysis of substituted benzyl chlorides illustrate that while in the absence of nucleophiles a unimolecular process occurs, as various nucleophiles are added, the bimolecular mechanism becomes important. Altering the ionic strength of the medium, by the addition of salts or nucleophiles, can also cause a variation in the mechanism.

In the 2-norbornyl system, the high *exo* to *endo* rate ratio was cited as evidence for neighbouring group participation in the solvolysis of the *exo* derivative.[26] However it has been suggested that the solvolysis rate of the *exo* derivative is normal, and that the *endo* isomer reacts very slowly because

of unusual steric factors.[27] Comparison with a 'standard' system can therefore be misleading. Similarly, varying a substituent may provide ambiguous information about a given substrate, since the mechanism may alter as a substituent is changed.

For substrates where neighbouring group participation is thought to enhance the solvolysis rates, the difficulty lies in deciding whether the experimental rates are faster than normal.[28,29] The Schleyer-Foote approach allows an estimate of the unassisted rate constant to be made. The model considers the effects of changes in bond-angle and torsional strain, non-bonded interactions, and polar effects on going from the ground state to the transition state. For compounds reacting with assistance to ionization from neighbouring groups, the calculated relative rate constant (relative to cyclohexyl tosylate) is smaller than the experimental value. This method is fairly successful, but should always be applied with care. An increase in solvolysis rate could be due to other factors which have not been considered, such as a decrease in ion-pair return.

Determination of a solvolysis mechanism is therefore a complex process, and the use of as many probes as possible is advisable. Generally then, a thorough study of the kinetics and a careful analysis of the products is necessary, as a single piece of information can be open to several interpretations.

2.3 Secondary deuterium isotope effects

Primary kinetic isotope effects are of limited usefulness in solvolysis reactions, as a result of the very small size of heavy-atom isotope effects.

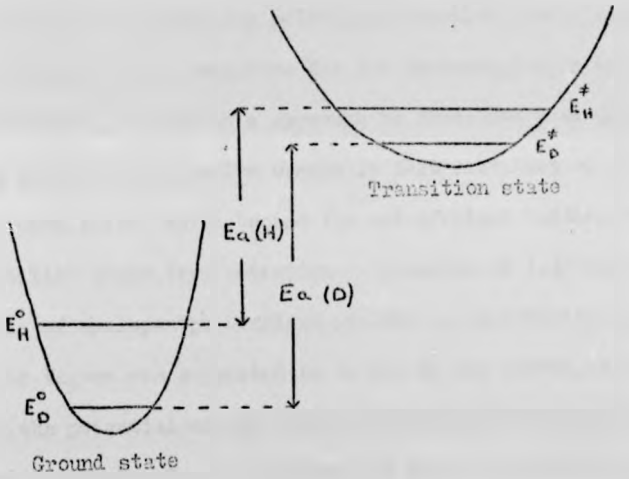
Thus ethanolysis of 1-phenyl-1-bromoethane ($C_6H_5CHBrCH_3$) gives an observed carbon isotope effect of $k_{12/13} = 1.0065$.[30] Secondary kinetic isotope effects are usually smaller than primary effects, as the bond to the isotope is only perturbed, not broken. However since isotope effects are related to isotopic mass ratios, they are largest when hydrogen isotopes are used. Secondary deuterium isotope effects therefore though small, are measurable, involving rate retardations of up to 30% per deuterium.[5] The effects are much smaller than when non-isotopic substituents are used, but are of great value since the potential energy surface for the reaction is not altered by isotopic substitution, whereas any other substituent changes the surface completely.

The theory used to formulate primary isotope effects, based on transition-state theory, has been applied to secondary isotope effects with some success.[31,32] However the difficulty in describing the geometry and the force constants for the transition state results in a very empirical approach being used, both in calculating the isotope effects, and in rationalising experimental results.

For hydrogen isotopes, the difference in zero-point energies between C-H and C-D vibrations largely determines the rate effects.[5] The origin of a normal ($k_H/k_D > 1$) isotope effect is illustrated in Figure 2.2. The same potential energy curves are involved for both isotopes, only the energy levels are different. If the force constant decreases on going from the ground state to the transition state, the potential energy curve becomes shallower, the energy levels become closer together and hence the

Figure 2.2

A representation of the zero-point energies responsible for a normal secondary deuterium isotope effect



The potential energy curves represent the C — H (or C — D) vibrations in the ground and transition states. The difference in energy levels has been exaggerated to show more clearly the difference in activation energies.

$$f^{o} > f^{\neq} \Rightarrow Ea(D) > Ea(H) \Rightarrow k_H/k_D > 1$$

where f is the force constant, Ea is the activation energy, and k is the rate constant.

activation energy for the deuterium-substituted compound exceeds that for the protium compound. Thus k_H is greater than k_D, and a positive, or normal isotope effect is observed.

Streitweiser attempted to calculate the α-deuterium kinetic isotope effect (α-kie) in a limiting solvolysis reaction, using an aldehyde as a model to estimate the parameters for the carbon-hydrogen bond in the transition state.[33] From this approach he concluded that the main cause of the isotope effect lay in the change in that vibration of the C - H bond in the ground state, which became the out-of-plane bending vibration in the transition state for ionization. An α-kie of 1.3[8] was obtained. Acetolysis of cyclopentyl tosylate yielded an experimental value of 1.15; this lower figure was suggested to be due to the effect of the leaving group on the potential energy curve at the transition state. A value of 1.00 for the bimolecular displacement of isopropyl bromide by sodium ethoxide[34] was then rationalised as being the result of restriction of the out-of-plane bending by both the leaving group and the incoming nucleophil, and hence little change in the force constant occurs.

The main weakness of Streitweiser's approach is his assumption that those modes of vibration other than those identified as carbon-hydrogen stretching or bending modes, are isotope-insensitive. In some cases vibrations are very strongly coupled, and hence deuterium substitution can affect other vibrational modes, which should therefore be considered when the isotope effect is calculated.

It has been suggested that secondary isotope effects are due to

differences in anharmonicity.[7] While this could produce an isotope effect, it is generally thought to be a minor factor, and that most results can be explained in terms of harmonic oscillations.[5]

Streitweiser's postulate that isotope effects close to unity would occur in bimolecular solvolyses and that higher effects would be observed in unimolecular solvolyses is in agreement with experimental results. Over the past 20 years the α-kies for many more systems have been measured. For primary systems such as methyl and ethyl tosylate the α-effects are very low, and even inverse ($k_H/k_D < 1$) in some cases.[35] Thus very little change in force constant occurs on going from ground state to transition state. This has been interpreted as involving a transition state which is as crowded as the ground state, following Streitweiser's approach, or as the result of only small changes in the hybridisation of the central carbon atom. Care must be taken in describing an isotope effect as being due to steric reasons, to distinguish between harmonic steric isotope effects (due to differences in steric factors between the ground state and the transition state) and anharmonic effects (a C - D bond which is slightly shorter on average than a C - H bond).[4]

As the stability of the carbonium ion which would be produced in solvolysis increases, the nucleophilic character of the mechanism decreases, and higher α-effects are observed (Table 2.1). The α-kie for the 2-adamantyl system has been suggested to be a maximum value for secondary arenesulphonates, and to be characteristic of a limiting mechanism.[12] (The α-effect is dependent on the leaving group, though no significant variation is observed between different arenesulphonates. However a leaving chloride

Table 2.1

Secondary ∝-deuterium isotope effects for some solvolysis reactions at 25°C[5]

Substrate	Solvent	k_H/k_D [a]
Methyl tosylate	H_2O	0.984
Ethyl tosylate	H_2O	1.018
Isopropyl tosylate	H_2O	1.134
2-butyl brosylate	70T	1.165
3-pentyl brosylate	70T	1.179
2-adamantyl tresylate	70T	1.225
Benzyl bromylate	80T	1.159

(a) per ∝-deuterium

70T is 70% 2, 2, 2-trifluoroethanol - 30% water

80T is 80% 2, 2, 2-trifluoroethanol - 20% water

group gives much smaller effects, and the maximum value for a limiting mechanism of a chloride is suggested to be 1.15.[36] Along the series methyl, ethyl, and benzyl arenesulphonates, the mechanism is expected to become less nucleophilic in character, and the α-effects increase. Similarly as the substituents in the benzene ring of benzyl brosylate are varied, the α-effects change, with an electron-withdrawing substituent giving a lower α-kie, in agreement with theory.[37] For a given substrate, as the solvent nucleophilicity is decreased, the α-kie increases, illustrating the change to a less nucleophilic mechanism. Thus for isopropyl tosylate,[38,39] as the solvent is varied from 90% aq. ethanol to trifluoroacetic acid, the α-kie increases from 1.083 to 1.22 (see Table 2.2). The α-kie therefore appears to be very sensitive to variations in the extent of solvent nucleophilic participation.

The α-effect also appears to be reduced if neighbouring group participation occurs. Solvolysis of 4-methoxy-1-pentyl brosylate proceeds with π-participation, and α-deuteration causes no rate retardation.[40] This is interpreted as being due to restriction of the bending vibration in the transition state by the neighbouring oxygen atom, in an analogous fashion to the reduction of the isotope effect by a solvent molecule in a nucleophilic solvolysis reaction.

Substitution of deuterium in a β-position can also significantly lower the rate of solvolysis. It is found that nucleophilic solvolyses give fairly small β-isotope effects but that as the mechanism approaches limiting character the effects increase.[5] For example in isopropyl solvolyses, the

Table 2.2

Secondary deuterium isotope effects in solvolysis of isopropyl compounds [38,39]

Leaving group	Solvent	$k_H/k_{\alpha D}$ (25°C)	$k_H/k_{\beta D_3}$
OTs	TFA	1.22	1.46 (25°C)
OBs	97T	1.16	1.256 (45°C)
OBs	70T	1.140	
OBs	50T	1.122	1.246 (45°C)
OBs	50E	1.114	1.189 (25°C)
OBs	80E	1.098	
OBs	90E	1.083	1.130 (25°C)

β-d_3 effects increase from 1.130 to 1.46 as the solvent is changed from 90% aq. ethanol to trifluoracetic acid (see Table 2.2). The β-effects are commonly ascribed to hyperconjugative stabilisation of the developing positive charge on the adjacent carbon atom. The need for hyperconjugation is greatest when the substrate reacts by a limiting mechanism and significant positive charge develops, and hence the β-isotope effects are largest for limiting solvolyses.

Hyperconjugation is most effective when the carbon-hydrogen bond is trans co-planar to the developing p-orbital, and hence β-effects are strongly dependent on conformation, and are maximal for a trans co-planar arrangement of the β-hydrogen and the leaving group.[41]

2.4 Solvolysis of some cyclohexyl derivatives

In cyclohexyl systems, substituents may be either axial or equatorial. In cyclohexane itself, these are rapidly interconverted by ring inversion and hence the properties associated with these two individual configurations cannot easily be compared. A t-butyl group has been used as a second substituent to raise the barrier to ring inversion for cyclohexyl tosylates. The 4-t-butylcyclohexyl tosylates provide an isomeric pair which it was thought would allow the different properties of axial and equatorial tosylates in solvolysis reactions to be investigated.

The rates of solvolysis were first measured by Winstein,[42] who found k_{cis}/k_{trans} ratios of between 3 and 5, depending on solvent. This very small difference he suggested precluded β-hydrogen assistance to cleavage of the carbon-tosylate bond, since a suitable orientation of the β-hydrogens

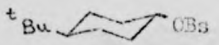
existed only for the cis tosylate. More recently Shiner and Jewett[1,6] investigated the effect of deuteration of the β-position on the rates of solvolysis in 50% aq. ethanol. They used a conductometric method of measuring the rates, that is claimed to have a precision of 0.1%. Their results are shown in Table 2.3. The α-effects are fairly high, showing that the solvolysis mechanism involves only slight solvent nucleophilic participation. For the cis brosylate, the effect of a single, axial β-deuterium on the rate is exceptionally large. The value of 1.436 is ten times larger than the 'steric isotope effect' predicted by Bartell.[4,3] For comparison the β-d_3 isotope effect in the solvolysis of isopropyl brosylate was only 1.189 (Table 2.2)[38]. The isotope effect when the β-deuterium is equatorial is much smaller, 1.096. The very large conformational isotope effect was ascribed to hydrogen participation. However the trans brosylate also gives a very high isotope effect which depends on orientation. This is incompatible with a transition state where the cyclohexane ring has a chair conformation. Only in a twist conformation can the tosylate group and the β-hydrogen (both formerly equatorial) adopt pseudo-axial orientations, and give rise to these isotope effects. The isotope effects have therefore shown that hydrogen participation is important for both isomers.

The products of acetolysis of these compounds were investigated in detail by Whiting and co-workers[9] (Table 2.4). Rearranged products compatible with β-hydrogen migration are observed for both isomers, showing that the product-forming steps are also similar for both isomers.

Table 2.3

Secondary deuterium isotope effects in the solvolysis of cis- and trans-4-t-butylcyclohexyl brosylates in 50% aq. ethanol at 35°C [1,8]

Position	k_H/k_D
α-D (e)	1.202
β-D (a)	1.436
β-D (e)	1.096
β-D_4	2.862

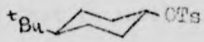
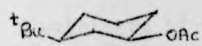
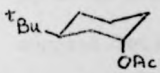
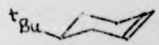
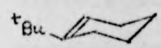


Position	k_H/k_D
α-D (a)	1.172
β-D (a)	1.127
β-D (e)	1.340
β-D_4	2.425

(a) and (e) denote axial and equatorial respectively

Table 2.4

The products of acetolysis [a] of cis- and trans-4-t-butylcyclohexyl tosylates at 100°C[9]

		
	7.3	0.4
	0.7	19.5
	0.3	1.5
	4.5	0.5
	84.0	73.6
	2.8	5.0
	0.2	0.6

(a) containing 0.05M sodium acetate

It might have been considered that the free energy difference between the chair form and the twist conformation would be so high that the total activation energy for solvolysis of the trans isomer would be much greater than for the cis tosylate. It is probably compensated by the twist conformation having a much lower solvolysis activation energy than that of the cis tosylate. Recent results suggest that in another system the twist conformation is extremely reactive.[44]

The t-butyl group therefore provides an insufficient restriction on the flexibility of the cyclohexane. The bicyclo[3, 2, 1]octane skeleton represents a more seriously constrained cyclohexyl system, in which models suggest twist forms are precluded. Product analyses for acetolysis and 80% aq. ethanolysis were published by Jefford[10] and Jackisch[45] respectively. The latter noted bicyclo[3, 2, 1]oct-2-ene and inverted, unrearranged alcohols and ethers as the only products; no rearranged products were reported, in contrast to Whiting's results for the 4-t-butylcyclohexyl tosylates.[9] Jefford's results for acetolysis of the bicyclic tosylates include an additional difference in that while the exo tosylate gave a sole substitution product, that of inverted configuration, the endo tosylate gave similar amounts of both inverted and retained substitution products. Again, no rearrangement was reported. These results suggested that the more severe restriction on the flexibility of the ring had led to very different solvolysis mechanisms for the exo and endo isomers. More recent results on the similar bicyclo[3, 2, 1]oct-6-en-3-yl system[11] showed strong resemblances with the results for the 4-t-butylcyclohexyl derivatives, and thus either the

bicyclo[3, 2, 1]octan-3-yl system was a special case, or the product analyses were incorrect. The next chapters describe a detailed study of the solvolysis of exo- and endo- bicyclo[3, 2, 1]octan-3-yl tosylates, with particular emphasis on the measurement of the secondary deuterium kinetic isotope effects, and analysis of the products.

Several solvent systems have been used to determine changes in mechanism as the ionising power and the nucleophilicity of the solvent are varied.

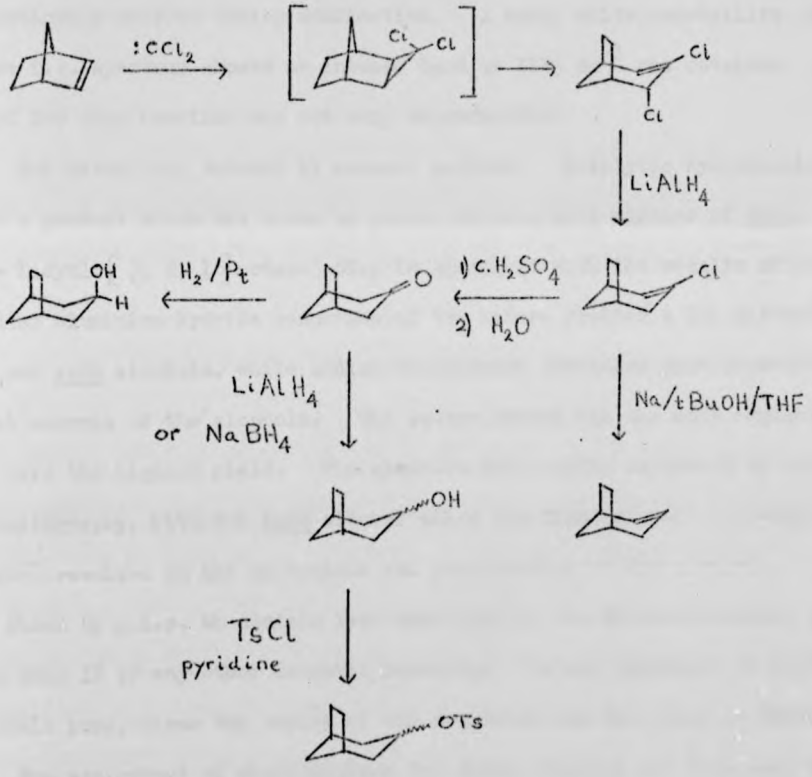
CHAPTER 3. PREPARATIVE METHODS

3.1 General preparative scheme

The basic procedure for the preparation of the isomeric bicyclo[3, 2, 1]octan-3-ols was developed by Jefford and co-workers,[46] and by Kraus.[47] The bicyclo[3, 2, 1]octan-3-yl skeleton was obtained by the addition of dichlorocarbene to norbornene followed by opening of the cyclopropane ring (Figure 3.1). Various methods of generating the carbene have been described in the literature;[48] in this work two of these were employed. The first, that used by Jefford and co-workers used ethyl trichloroacetate as the carbene precursor, sodium methoxide as the base, and pentane as the solvent. This method gave a rather low yield (ca. 20%) of exo- 3,4-dichlorobicyclo[3, 2, 1]oct-2-ene. A more convenient method is that described by Kraus, which makes use of a phase-transfer catalyst. Chloroform was used both as the carbene precursor and as the solvent, and 50% aqueous sodium hydroxide was used as the base. These two reagents were stirred at 0°C with norbornene and tridodecylmethylammonium bromide, and the product was extracted into chloroform. Fractional distillation under reduced pressure gave a 64% yield of the adduct, whose spectral characteristics agreed with literature values.[46] Reduction of an ethereal solution of the adduct with lithium aluminium hydride yielded 3-chlorobicyclo[3,2,1]oct-2-ene. This was hydrolysed to bicyclo[3, 2, 1]octan-3-one by stirring the vinylic chloride in ice-cold concentrated sulphuric acid, then cautiously pouring the mixture onto ice. This method caused considerable charring which was reduced when the chloride was added in an inert solvent, such as tetrahydrofuran. The

Figure 3.1

Preparative Scheme



product was extracted into ether, but it was difficult to isolate the ketone from the last traces of ether. A very concentrated, ethereal solution of the product therefore was placed in a sublimation apparatus, and was magnetically stirred during sublimation. A waxy, white, crystalline solid whose i.r. spectrum showed an intense band at 1715 cm^{-1} was obtained. The yield for this reaction was not very reproducible.

The ketone was reduced by several methods. Catalytic hydrogenation gave a product which was shown by g.l.c. to be a 40:1 mixture of *endo*- and *exo*- bicyclo[3, 2, 1]octan-3-ols, in agreement with the results of Kraus.[47] Lithium aluminium hydride reduction of the ketone yielded a 2:1 mixture of *exo* and *endo* alcohols, while sodium borohydride reduction gave approximately equal amounts of the alcohols. The latter method was the most convenient and gave the highest yield. The alcohols were easily separated by column chromatography, with the *endo* alcohol being the first eluted. A high recovery (> 90%) resulted on the separation and purification of the alcohols. Each was shown by g.l.c. to contain less than 0.1% of its diastereoisomer, and less than 1% of any other detected impurity. It was important to have the alcohols pure, since the purity of the tosylates was less easy to demonstrate.

The assignment of configuration for these alcohols has been made by several other workers,[10,45,47] and the physical and spectral properties of the alcohols prepared by the above methods allowed for easy identification of the *exo* and *endo* alcohols.

The tosylates were prepared from the alcohols and p-toluenesulphonyl chloride in the minimum quantity of pyridine at 0°C.[49] The tosylates were precipitated by the addition of water, and after being thoroughly dried, were

recrystallised at -70°C as described in Chapter 7. They were sharp-melting, odourless, white, crystalline solids whose i.r. spectra showed no bands characteristic of the parent alcohol. The compounds were stored in a desiccator at -15°C until required.

3.2 Preparation of deuterium-labelled derivatives

The α-deuterated alcohols were prepared by the reduction of bicyclo[3, 2, 1]octan-3-one with either sodium borodeuteride or lithium aluminium deuteride. The mixture of exo and endo alcohols were separated by column chromatography, the pure alcohols were sublimed, and converted to the tosylates following the same methods as for the non-deuterated compounds.

Bicyclo[3, 2, 1]octan-3-one - 2, 2, 4, 4 -d_4 was prepared by heating under reflux the non-deuterated ketone and weakly basic deuterium oxide, with a small amount of acetone-d_6 being added to increase the solubility of the ketone in the aqueous solution. A strictly anhydrous work-up procedure was used. The n.m.r. spectrum showed that the signal at τ = 7.7, which integrated for 4 protons in the non-deuterated ketone, was absent, indicating a very high incorporation of deuterium at positions 2 and 4. The deuterated ketone was immediately reduced with lithium aluminium hydride to give a 2:1 mixture of exo and endo tetradeuterated alcohols. These were separated by column chromatography, sublimed, and converted to the tosylates as usual.

3.3 Determination of the deuterium incorporation

Routine n.m.r. showed that a high percentage incorporation of deuterium

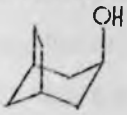
in the appropriate positions of the alcohols and tosylates had been achieved. However as the isotope effects which are to be measured are small, it was desirable to know the accurate percentage incorporation.

Samples of the monodeuterated alcohols, acetates and olefin, along with samples of the non-deuterated compounds were sent to the Physico-chemical measurements unit at Harwell for isotope-abundance measurements, using combined g.l.c. and mass spectrometry. For such measurements to be accurate, there must be no loss of deuterium in the instrument. The occurrence of an $(M-1)^+$ peak in the spectrum of the non-deuterated sample could be due to loss of a hydrogen atom which is replaced by deuterium in the labelled compound. If the rates of loss of protium and deuterium are different, then the mass spectra are not comparable. Therefore ideally a compound should give an intense parent-ion peak, and a negligible $(M-1)^+$ peak. Also, $(M+1)^+$ peaks, due to ion-molecule collisions often occur with polar molecules, and lead to inaccurate heavy-isotope incorporation measurements.

The alcohols were found to be unsuitable for accurate measurements since the intensity of the parent-ion peak was too low. Consequently they were converted to the corresponding trimethylsilyl ethers. These compounds gave a large $(M-1)^+$ peak, which suggests that loss of label in the spectrometer could be a complication. Calculations were carried out using the intense $(M-15)^+$ peak (loss of a methyl group), and indicated a deuterium incorporation varying from 88.6 - 89.8%, depending on the sample. This is surprisingly low, since there is no obvious process by which protium could be introduced to the α-position to this extent.

The tetradeuterated alcohols were also analysed as the trimethylsilyl

derivatives. The data for these are shown below:-



	% d_3	% d_4	% d_5	% d_6
	5	70	20	5
	8	90	2	-

The isomers were prepared simultaneously from the same precursor, and were subjected to a common work-up procedure. It is therefore difficult to explain the apparent difference in deuterium incorporation.

The results for both the mono- and tetradeuterated samples can be rationalised if the fragmentation patterns are different for deuterated and non-deuterated samples. The presence of an $(M-1)^+$ peak suggests that this is a possible explanation of the low values for the deuterium incorporation.

<u>endo</u>-Bicyclo[3, 2, 1]octan-3-yl acetate and its α-deuterated derivative gave spectra which were even less suitable for accurate analysis, and only a very approximate value of 88% deuterium incorporation at the α-position was obtained.

It was desirable to prepare a derivative that would give an intense parent-ion peak. <u>exo</u>-Bicyclo[3, 2, 1]octan-3-yl-3-$\underline{d}_1$ tosylate was heated in the acetolysis medium for at least 10 half-lives. The products were extracted into pentane, and the olefin fraction was separated from the acetates by column chromatography on alumina. The olefin in pentane was sent for mass-spectral analysis, and was found to give an intense parent-ion peak, and very small $(M-1)^+$ and $(M+1)^+$ peaks. A value of 99% deuterium incorporation at carbon-3 was obtained.

In order to check this value an n.m.r. spectrum of exo-bicyclo[3, 2, 1]octan-3-yl-3d_1 tosylate was run by Mr D. Dance of this department on a Perkin-Elmer R32 90MHz spectrometer. A protium incorporation at carbon-3 of 10% would have been easily observable, but it proved impossible to detect any resonance due to an α-proton. An upper limit of ca. 2% is placed on the protium content at carbon-3, and hence this corroborates the mass-spectral analysis of the olefin, and shows that of the trimethylsilyl derivatives to be incorrect.

Combined g.l.c. and mass spectrometry on the trimethylsilyl ethers of the α-deuterated 4-t-butylcyclohexanols gave a deuterium incorporation of 96-97%. In this case therefore the ethers give suitable mass spectra and it is concluded that the suitability of the fragmentation patterns of trimethylsilyl ethers for isotope-abundance measurements varies with alkyl structure.

3.4 Preparation of compounds for g.l.c. standards

Whiting's[9] results for the solvolyses of the 4-t-butylcyclohexyl arenesulphonates suggested that hydride-shift products could occur in the solvolyses of bicyclo[3, 2, 1]octan-3-yl tosylates. It was therefore necessary to prepare the two bicyclo[3, 2, 1] octan-2-ols. In addition Goering and his co-workers have shown that skeletal rearrangement from the trans-bicyclo[3, 2, 1]octan-2-yl system to bicyclo[2, 2, 2]octan-2-yl derivatives may occur.[3]

Catalytic hydrogenation of bicyclo[3, 2, 1]octan-2-one yielded approximately equal amounts of cis- and trans- bicyclo[3, 2, 1]octan-2-yl

acetates along with a small amount of bicyclo[2, 2, 2]octan-2-yl acetate. This is thought to be due to some bicyclo[2, 2, 2]octan-2-one present in the commercial ketone. The acetates were reduced by lithium aluminium hydride to the alcohols which were partly separated by column chromatography on alumina. Samples of trans-bicyclo[3, 2, 1]octan-2-ol containing 4% of the cis alcohol, and cis-bicyclo[3, 2, 1]octan-2-ol containing 1% of the trans alcohol were used to obtain i.r. and n.m.r. spectra, and approximate melting points, which allowed assignment of configuration by comparison with literature values.[50] Bicyclo[2, 2, 2]octan-2-ol and bicyclo[2, 2, 2]-oct-2-ene were kindly supplied by Dr. H. Maskill.

The acetates were prepared by heating under reflux the corresponding alcohols, acetic anhydride and pyridine. As they were only required for g.l.c. standards, these preparations were carried out on a small scale, and the products were stored as ether solutions until required.

The formates were prepared by mixing the alcohol and an excess of formic-acetic mixed anhydride. The solution was left to stand for about 1 week, then made alkaline, and extracted with ether. The formates prepared by this method contained up to 5% of the corresponding acetates, but this was not a complication since the acetates and formates were easily resolvable by g.l.c.

The ethyl ethers were prepared by heating under reflux the alcohols, silver oxide, and a large excess of ethyl iodide. The mixture was extracted

with ether, and percolated down a column of dry alumina. The product was eluted with diethyl ether, and stored in solution.

Bicyclo[3, 2, 1]oct-2-ene was prepared by sodium-induced dechlorination of 3-chlorobicyclo[3, 2, 1]oct-2-ene after the method of Gassman and Pape.[51] The product was extracted into pentane, and most of the solvent was removed by fractional distillation. The last traces of solvent proved very difficult to remove, as the olefin was very volatile. The residual solution was percolated down a column of silica gel impregnated with silver nitrate, with pentane being used to elute the olefin. This procedure removed some of the tetrahydrofuran and t-butanol, but preparative g.l.c. was necessary to isolate the olefin from the last traces of these impurities. Sublimation then yielded a waxy, white, crystalline solid whose melting point and spectra agreed with literature values.[47] Several other methods of preparation were attempted, including the Bamford-Stevens reaction of the tosyl hydrazone of the ketone with methyl lithium (60% yield by g.l.c.), lithium-induced dechlorination of 3-chlorobicyclo[3, 2, 1]oct-2-ene (ca.90% conversion of starting material to olefin by g.l.c.), and treatment of exo- 3, 4-dichlorobicyclo[3, 2, 1]oct-2-ene with sodium in liquid ammonia (better than 90% reaction of starting material). However in no case was it possible to isolate the olefin in reasonable yield without preparative g.l.c. being necessary.

3.5 Test of the stability of the products to the solvolysis media and the work-up procedure

Two of the acetates, trans-bicyclo[3, 2, 1]octan-2-yl acetate and

bicyclo[2, 2, 2]octan-2-yl acetate, and bicyclo[3, 2, 1]oct-2-ene were heated at 60°C in the acetolysis medium, and all five formates and bicyclo[3, 2, 1]oct-2-ene were treated with the formolysis medium at 25°C for 10 half-lives of exo-bicyclo[3, 2, 1]octan-3-yl tosylate. Within the limits of detection, no rearrangement was observed for any formate or acetate, and no addition to the olefin or rearrangement of the olefin occurred.

As the analysis of the alcohols by g.l.c. is much simpler than that of the acetates or formates, the products of acetolysis and formolysis were reduced by lithium aluminium hydride to convert the substitution products to alcohols. This process was shown to convert the acetates and formates cleanly to the corresponding alcohols, without any detectable rearrangement. Bicyclo[3, 2, 1]oct-2-ene was also shown to be unchanged by this procedure.

3.6 Calibration of the detector

The products were analysed by g.l.c. and were not isolated. It was therefore necessary to employ an internal, inert standard, and to calibrate the flame-ionisation detector to the products so that absolute percentage yields could be quoted. This ensures that all the major products have been observed. The molar response factors of the detector to bicyclo[3, 2, 1]-oct-2-ene and to two of the isomeric alcohols were determined by analysing standard solutions of the compound and a hydrocarbon standard. Because of the large difference in retention time between the olefins and the alcohols,

separate hydrocarbon standards were used.

A molar response factor was calculated for the ethyl ethers.

When the solvolyses for the product analyses were carried out, known amounts of both hydrocarbon standards were added when the solvolysis solutions were prepared, and were used to determine the percentage yield of each product.

3.7 Preparation of the 4-t-butylcyclohexyl p-toluenesulphonates

The α-kinetic isotope effects for the 4-t-butylcyclohexyl tosylates were required in 50% aqueous ethanol, as a check on the solvolytic procedure, and in buffered acetic acid for comparison with the bicyclo[3, 2, 1]octan-3-yl tosylates.

The commercial mixture of cis- and trans-4-t-butylcyclohexanols was separated by column chromatography on alumina, with the cis alcohol being eluted first. The alcohols were sublimed and converted to the corresponding tosylates as usual.

In order to prepare the labelled compounds, the commercial alcohol mixture was oxidised to 4-t-butylcyclohexanone by Mrs P.H. Maiden of this department. Sodium borodeuteride reduction of the ketone gave a 3:1 mixture of trans to cis α-deuterated alcohol which was separated by column chromatography. The alcohols were sublimed and converted to the tosylates as usual.

CHAPTER 4 KINETICS: PROCEDURE AND RESULTS

4.1 The choice of solvents

The solvents used covered a wide range of solvent parameters. The ionising power (Y) and nucleophilicity (N_{BS}) of each solvent are shown in Table 4.1. The use of acetic and formic acids, which have the same nucleophilicity, allows the effect of ionising power to be determined. Acetic acid and 98% aq. ethanol have very similar Y-values but very different nucleophilicities, and allow the effect of nucleophilicity to be studied. A range of aqueous ethanol mixtures, which are the most common solvent systems used in recent measurements of isotope effects, have been used. A less nucleophilic aqueous alcoholic mixture, 97% aq. 2, 2, 2-trifluoroethanol[52], was also used for comparison with recent results for other systems[12,53].

4.2 Procedure

Generally a stock solution of the solvent mixture was prepared, and a small amount was withdrawn to dissolve the tosylate required (2-5mg) for each run. A stock solution of the tosylate in the solvolysis medium was not prepared, because of the instability of the tosylates. The low solubility of the tosylates in 50% aq. ethanol required that a slightly different method be used. A stock solution of 50% aq. ethanol was not prepared; instead an appropriate amount of the tosylate was dissolved in a known volume of spectroscopic ethanol, and an equal volume of water (or aqueous borax) was added. Fresh solutions were prepared for each run as usual.

Table 4.1

Solvent parameters[a]

Solvent	Ionising Power (Y)[54,55]	Nucleophilicity (N_{BS})[15,52]
Formic Acid	2.05	-2.05
Acetic Acid	-1.64	-2.05
97% aq. Trifluoroethanol	1.15	-2.10
50% aq. Ethanol	1.66	-0.20
80% aq. Ethanol	0.00	0.00
98% aq. Ethanol	-1.68	~0.09

(a) The values are for the solvents in the absence of dissolved salts.

An adaptation of the spectrophotometric method of Swain and Morgan[54] was used to measure the rates of the reactions. A Unicam SP500 Series 2 with an SP50 programme controller, and a thermostatted cell compartment was used. The temperature of the cell compartment was controlled by a water bath fitted with a circulating pump and a Grant contact thermometer. The temperature variation during a run was shown to be less than 0.1°C.

Fresh solutions were made up for each run; protium and deuterium compounds were run concurrently to reduce the effects of small temperature variations between runs. Typically, three 1 cm matched silica cells fitted with P.T.F.E. stoppers were filled with solvent in the first cell, an approximately 0.00[illegible]M solution of the non-deuterated tosylate in the solvolysis medium in the second, and a similar solution with the deuterium-labelled tosylate in the third. These were placed in the thermostatted cell compartments, and allowed to come to thermal equilibrium (about 2 minutes). The wavelength chosen was usually 272 nm, at which value all the solvents had low absorbances, and the absorbance of the solvent-containing cell was then set at zero. The absorbances of all three cells were then recorded at this wavelength at chosen time intervals by use of the programme controller. By repeatedly timing a large number of cycles of measurements of absorbances, the maximum error in time was estimated at ± 0.5%. The maximum error in absorbance was about 1%.

The reactions were followed for not less than 5 half-lives. The first order rate constants were evaluated from about 40 points by a computer program using a non-linear minimisation routine written by Dr. R.L. Tranter of this department. The standard deviation of the

rate constant for an individual run was always less than ± 0.5% (with the exception of some runs involving tetra-deuterated tosylates, where it was about 1%, due to the large rate retardations involved) showing that good first order kinetics were followed. The runs were repeated about six times, and a rate ratio was quoted for each pair of protium and deuterium compounds. The mean rate ratio was calculated from the individual rate ratios, and the standard error was computed from the formula:

$$\delta_{\bar{x}} = \left[\frac{\sum_{i=1}^{n} x_i^2}{n(n-1)} - \frac{\overline{x^2}}{n-1} \right]$$

It was usually less than ± 1%.

(The standard error is defined to have 2/3 confidence limits) [57]

The isotope effects have not been corrected for the deuterium incorporation being slightly less than 100%.

4.3 Checks on the kinetic method

In order to check that the isotope effects measured were not being affected by any bias in the spectrophotometer, six runs were performed in 50% aq. ethanol with the non-deuterated tosylate in both cell positions. This gave a rate ratio of 1.00 ± 0.01, showing that within experimental error there is no bias in the procedure.

The α-kinetic isotope effects for the 4-t-butylcyclohexyl tosylates in 50% aq. ethanol were measured for comparison with those measured by Shiner and Jewett [18] for the corresponding brosylates by a very precise

conductometric method. (The use of tosylates instead of brosylates does not affect the α-deuterium isotope effect.[5]) For the cis tosylate a value of 1.200 ± 0.007 was obtained, which compares well with 1.202 ± 0.001 quoted by Shiner and Jewett, while for the trans tosylate 1.16 ± 0.01 was obtained in agreement with the literature value of 1.172 ± 0.001.

The α-kinetic isotope effects in some aqueous alcoholic mixtures were measured without the presence of a buffer. To determine whether this would influence the rate ratio, the results for exo-bicyclo[3, 2, 1]octan-3-yl tosylate in 50% aq. ethanol were determined both in the presence and absence of a borax buffer. Mean α-isotope effects of 1.198 ± 0.008 and 1.182 ± 0.006 respectively were obtained. Therefore within experimental error the lack of a buffer in aqueous ethanol does not affect the isotope effect.

Because of the difficulties in preparing the solvolysis solutions, the errors in 50% aq. ethanol are probably the largest for all the solvent systems used. Three independent mean values of the α-isotope effect were obtained for the endo tosylate. On the SP500 values of 1.214 ± 0.007 (mean of 7 runs) and 1.186 ± 0.005 (mean of 5 runs) were obtained, and a value of 1.204 ± 0.003 (mean of 5 runs) was obtained on a Gilford 2400 spectrophotometer. These isotope effects are in reasonable agreement, but suggest that the errors in this solvent system are slightly higher than the computed values.

These checks on the kinetic method have therefore shown that there is no bias in the procedure, that literature results can be reproduced, and

that the use of the standard error gives a good estimate of the error in the isotope effect.

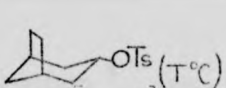
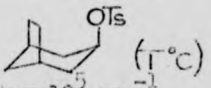
4.4 Rates of solvolysis

The rates of solvolysis of the bicyclo[3, 2, 1]octan-3-yl tosylates are shown in Table 4.2. The temperatures have been chosen to give conveniently measured rate constants.

The rates of acetolysis of both tosylates are slightly faster than those measured by Jefford[10], since in the present case a high concentration of buffer salt was used, increasing the ionic strength of the medium. The bicyclo[3, 2, 1]octan-3-yl tosylates react faster than both the cyclohexyl[2] and 4-t-butylcyclohexyl tosylates[42]. A quantitative comparison of the rates of acetolysis with that of cyclohexyl tosylate using the Schleyer-Foote equation[29,29] is shown in Table 4.3. Two values of the $\log_{10} k_{rel}$ (calcd) are shown; in column I the relative rate has been calculated from Foote's equation, and only takes into account the bond angle strain, while those in column II include a term for the relief of non-bonded strain. It can be seen that while the former method underestimates the rate constants, the latter provides overestimates. The calculations do not allow for possible flattening of the six-membered ring. Such an effect would decrease the non-bonded repulsions, but would require that a term be included for torsional strain, since the staggering of adjacent groups would become less perfect. If all three types of strain are taken into account, the calculated rates of acetolysis would be very close to the observed values, and hence the rates appear to be normal. The bicyclo[3, 2, 1]octan-3-yl tosylates react

Table 4.2

Rates of solvolysis of exo- and endo- bicyclo[3, 2, 1]octan-3-yl paratoluenesulphonates

Solvent	 k x 10^5 sec^{-1} (T°C)	 k x 10^5 sec^{-1} (T°C)
Formic acid [a]	10.6 ± 0.2 (24.8)	333 ± 2 (24.8)
Acetic acid [b]	14.4 ± 0.2 (70.6)	63.4 ± 0.6 (60.6)
97% aq. Trifluoroethanol	6.32 ± 0.06 (41.4)	119 ± 1 (41.4)
50% aq. Ethanol [c]	4.26 ± 0.08 (36.0)	48.3 ± 0.3 (24.8)
80% aq. Ethanol	5.12 ± 0.06 (55.0)	164 ± 2 (55.0)
90% aq. Ethanol	4.90 ± 0.05 (70.1)	35.4 ± 0.3 (60.4)

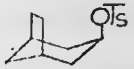
(a) containing 0.1% sodium formate

(b) containing 0.1% potassium acetate

(c) buffered with 0.003% borax for the exo isomer and 0.009% for the endo isomer.

Table 4.3

Calculation of acetolysis rates using the Schleyer-Foote equation

Tosylate	$\bar{\nu}_{CO}$ cm^{-1}	(OS-TS) strain [a] kcal/mole	$\log_{10} k_{rel}$ [b] obsd.	$\log_{10} k_{rel}$ calcd. I	II
	1714	1.8	1.11	0.66	1.45
	1714	3.8	2.15	0.66	2.92

(a) see ref. 58

(b) using Jefford's values for unbuffered acetolysis at 25°C, relative to acetolysis of cyclohexyl tosylate

faster than the 4-t-butylcyclohexyl tosylates presumably because of higher torsional strain, and of more serious non-bonded strain in the ground states of the bicyclic tosylates.

The solvolysis rates in different solvents vary with ionising power in a manner expected for a mechanism involving a more polar transition state than ground state. Thus the formolysis rates are considerably greater than the rates of acetolysis, and in the aqueous ethanol mixtures, the fastest rate is observed in 50% aq. ethanol, and the slowest in 98% aq. ethanol.

The endo tosylate reacts faster than the exo isomer by factors ranging from 14 in acetic acid at 70° to about 50 in 50% aq. ethanol at 25°C. Lebel[11] has shown that exo- bicyclo[3, 2, 1]oct-6-en-3-ol is more stable than the endo isomer by about 2 kcal/mol. The free energy difference is probably slightly higher for the saturated analogues where the six-membered ring will be more puckered. This difference would give rise to the rate ratios obtained, suggesting that these are predominantly ground state effects, as in the case of the 4-t-butylcyclohexyl derivatives.

Schleyer has suggested some criteria to test the sensitivity of a system to solvent nucleophilicity.[59] The Winstein-Grunwald m-value of a compound may be calculated, and is found to be between 0.2 and 0.4 for compounds reacting with considerable solvent nucleophilic participation, while it is close to unity for tertiary systems reacting by limiting

mechanisms. For endo- bicyclo [3, 2, 1] octan-3-yl tosylate an m-value of 0.54 at 60°C can be calculated from solvolysis rates in 80% and 90% aq. ethanol, while for the exo tosylate a value of 0.45 at 70° is obtained. These values will be higher at 25°, and thus indicate that these compounds lie on the borderline between nucleophilic and limiting mechanisms. A second probe is the ratio of the rate constants for a given compound in 98% aq. ethanol and acetic acid, where the ionising power is constant. If a compound reacts with solvent nucleophilic participation then this ratio will be greater than unity, since 98% aq. ethanol is more nucleophilic than acetic acid. Thus the ratio is 7.8 for isopropyl tosylate, and 4.3 for cyclohexyl tosylate, while it is reduced to 0.16 for the tertiary 1-adamantyl system. For exo- and endo- bicyclo[3, 2, 1]octan-3-yl tosylates the ratios are 0.46 and 1.09 respectively (using Jefford's rate constants for unbuffered acetolysis[10]). Both of these criteria therefore suggest that less solvent nucleophilic participation occurs in the solvolyses of these compounds than for cyclohexyl tosylate.

For 2-adamantyl tosylate, an m-value of 0.91, and a rate ratio in aqueous alcohol and acetic acid of 0.13 were obtained. Schleyer has suggested that this compound reacts without any solvent or neighbouring group participation, and hence can be used as a standard for secondary systems.[54] The variation with solvent of the ratio of the rate constant for a given substrate to that for 2-adamantyl tosylate then demonstrates the dependence of that substrate on solvent nucleophilicity. This test is most effective if the rate ratio in trifluoroacetic acid, often described as a limiting solvent, is known. Higher rate ratios in other solvents then suggest that nucleophilic

participation occurs in these solvents. As it is difficult to measure rates accurately in trifluoroacetic acid, formic acid has been used. The ratios are shown in Table 4.4 with the values for isopropyl tosylate for comparison. The 2-adamantyl system reacts the slowest of these four tosylates. For isopropyl tosylate the rate ratio increases by a factor of 40 when the solvent is changed from formic acid to 80% aq. ethanol. For the bicyclo[3, 2, 1]octan-3-yl tosylates the ratios increase by less than a factor of three. Therefore the dependence on solvent nucleophilicity is less for these compounds than for isopropyl tosylate.

All three criteria indicate that while some solvent nucleophilic participation occurs, it is less important than for simple secondary systems. The mechanisms for both tosylates appear to be very similar.

4.5 α-Kinetic isotope effects

The α-kinetic isotope effects for exo- and endo- bicyclo[3, 2, 1]octan-3-yl tosylates in various solvents are shown in Table 4.5. α-Isotope effects are known to be slightly temperature dependent, and decrease by about 0.01 for a 20° rise in temperature.[5] If allowance is made for temperature differences, then the values for the exo tosylate are all within 1% of 1.20 at 25°C. A change of solvent from the very weakly nucleophilic formic and acetic acids to the comparatively nucleophilic aqueous alcohol mixtures does not decrease the α-isotope effect. The results are very similar for the endo tosylate. If allowance is made for the temperature differences, an α-isotope effect of 1.19 ± 0.01 at 25°C is obtained, except in formic acid and 98% aq. ethanol. The error in formolysis is rather high, and hence the

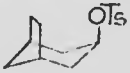
Table 4.4

Comparison of rate constants with 2-adamantyl tosylate at 25°C [59]

Solvent	$k_{iPr}/k_{2\text{-ada}}$	$k_{exo}/k_{2\text{-ada}}$	$k_{endo}/k_{2\text{-ada}}$
Formic Acid	3.16	9.14	287
Acetic Acid	12.6	30.6 (70°)	253 (70°)
50% aq. Ethanol	20.0	13.5	627
80% aq. Ethanol	126	17.8 (55°)	569 (55°)

Table 4.5

α-Kinetic isotope effects for exo- and endo- bicyclo[3, 2, 1]octan-3-yl tosylates

Solvent	 (T°C)	 (T°C)
Formic Acid [a]	1.20 ± 0.01 (24.8)	1.17 ± 0.01 (24.8)
Acetic Acid [b]	1.163 ± 0.008 (70.6)	1.169 ± 0.008 (60.6)
97% aq. Trifluoroethanol	1.203 ± 0.007 (41.4)	1.188 ± 0.006 (41.4)
50% aq. Ethanol [c]	1.198 ± 0.008 (36.0)	1.186 ± 0.005 (24.8)
80% aq. Ethanol	1.178 ± 0.007 (55.0)	1.177 ± 0.009 (55.0)
98% aq. Ethanol	1.183 ± 0.007 (70.1)	1.141 ± 0.002 (60.4)

(a) containing 0.15% sodium formate

(b) containing 0.15% potassium acetate

(c) buffered with 0.0035% borax for the exo isomer and 0.009% for the endo isomer

actual value could well lie in the range noted for the other solvents. However in 98% aq. ethanol the standard error is small, and the lower α-isotope effect is significant. As this solvent mixture has the highest nucleophilicity of all those studied, the lower α-effect is possibly due to increased solvent nucleophilic participation.

The results of Jefford for the acetolysis of these tosylates[10] could have been interpreted in terms of different solvolysis mechanisms for the exo and endo compounds, with the exo tosylate reacting by a more nucleophilic mechanism. The present results show that this is not the case since the α-effects for the exo tosylate are at least as high as for the endo tosylate, and show little variation with solvent. However the values are below 1.23 which was obtained for the solvolyses of 2-adamantyl tosylate, and was suggested to be the value for a limiting mechanism.[12,53] The lower effects can be rationalised in terms of some solvent nucleophilic participation, though this cannot be extensive, and as there is little variation of the effect with solvent, the extent of participation must be similar in all the solvent mixtures studied, with the possible exception of the endo tosylate in 98% aq. ethanol.

In Chapter 2, it was mentioned that participation by a neighbouring group could reduce the α-effect.[40] For the endo tosylate there are suitably oriented β-hydrogens which could participate, but there are too few literature examples to conclude whether such participation reduces the α-effect. To help to determine whether such participation occurs, the β-deuterium isotope effects were measured.

4.6 β-Kinetic isotope effects

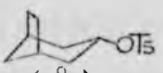
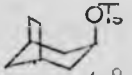
β-Hydrogen participation was shown by Shiner et. al. to occur during the solvolysis of both 4-t-butylcyclohexyl brosylates.[1,9] Exceptionally large rate retardations were observed when all four β-positions were substituted with deuterium. Measurement of individual β-isotope effects in these and in other systems showed that the magnitude of the β-effect depended significantly on the relative orientations of the β-deuterium and the leaving group, with a maximum effect being observed when a trans co-planar arrangement occurs.[41] For trans-4-t-butylcyclohexyl brosylate, the β-isotope effects suggested that a non-chair transition state intervened.[1]

For the bicyclo[3, 2, 1]octan-3-yl derivatives in chair conformations, the β-hydrogens are suitably oriented only for the endo tosylate. Models suggest that the ethane bridge reduces the flexibility of the ring, and hence the exo tosylate cannot adopt the twist arrangement which occurred for trans-4-t-butylcyclohexyl brosylate. Thus though β-hydrogen participation could be predicted to occur in the solvolysis of the endo tosylate, it appeared to be unfavourable for the exo tosylate in the ground state conformation. The results of replacing all four β-positions with deuterium are shown in Table 4.6

The temperature dependence of β-effects is complex.[5] In some cases, such as isopropyl tosylate, the effects appear to be temperature independent,[60] but usually the effects decrease slightly as the temperature is increased. As the temperature dependence of the effects for the bicyclo[3, 2, 1]octan-3-yl tosylates is not known, the values should only be compared when the temperature

Table 4.6

β-Deuterium isotope effects for exo- and endo- bicyclo[3,2,1]octan-3-yl tosylates [a]

Solvent	 (T°C)	 (T°C)
Formic Acid [b]	2.36 ± 0.02 (36.0)	2.75 ± 0.05 (28.3)
Acetic Acid [c]	2.14 ± 0.03 (70.5)	2.43 ± 0.03 (61.4)
50% aq. Ethanol [d]	2.19 ± 0.02 (46.6)	2.58 ± 0.02 (30.0)
98% aq. Ethanol	1.93 ± 0.03 (69.8)	2.23 ± 0.02 (60.0)

(a) for tetra-deuteration of the β-positions

(b) containing 0.15 M sodium formate

(c) containing 0.15 M potassium acetate

(d) containing 0.003 M borax

difference is fairly small. The values in formic acid can be compared with those in 90% aq. ethanol, and those in acetic acid with those in 98% aq. ethanol. The values for both tosylates are very high. For comparison, isopropyl tosylate gave a β-d_6 effect of 1.55 in hydrolysis[60] while t-butyl chloride gave a β-d_9 effect of 2.39 in 50% aq. ethanol.[61] The isotope effects in the poorly nucleophilic acid solvents are higher than those in the aqueous ethanol mixtures (comparing pairs at similar temperatures). Shiner has suggested that β-isotope effects are more indicative of slight changes in mechanism than the α-effects,[5] and in the present case the β-effects do suggest slight changes in mechanism as the nucleophilicity of the solvent varies. They therefore suggest that the α-effects are lower than 1.23 at least in part due to some solvent nucleophilic participation. However, the magnitude of the β-effects suggests that hydrogen participation also occurs. It is surprising that the β-effects for the exo tosylate are nearly as high as those for the endo isomer. The strong conformational dependence of hydrogen participation therefore is very strong evidence that the exo tosylate reacts through a transition state where the six-membered ring adopts a non-chair conformation, probably a rather flattened boat. Though the difference in free energy between the chair and boat conformations will probably be greater in this system than in cyclohexyl tosylate,[50] the barrier for ring flip from the chair to the boat will be lower for the bicyclic system, since the ethane bridge flattens the cyclohexane ring.[11]

Whiting[9] has pointed out that reactions through high-energy conformers

are not precluded by the Winstein-Holness equation:[42]

$$k = k_1 n_1 + k_2 n_2 + \ldots \qquad \text{Eq. 4.1}$$

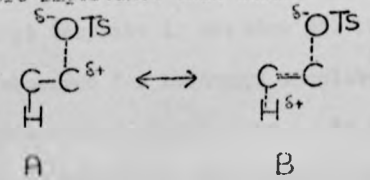
(where k is the overall rate constant, numbers 1, 2 etc. refer to different conformers of the same compound, k_1 is the rate constant for reaction through conformer 1, and n_1 is the mole fraction in conformation 1, etc.) since while n_1 may be very much greater than n_2, k_2 may be much higher than k_1. For the exo tosylate, the rate constant for reaction through the higher energy boat form should be much higher than from the chair, for two reasons. Firstly the departure of the leaving group will reduce steric strain in a similar way as for the endo tosylate (see section 4.4), and secondly two β-hydrogens and the tosylate group have a trans co-planar arrangement which allows the β-hydrogens to participate in the breaking of the carbon-tosylate bond. Therefore though $n_{boat} \ll n_{chair}$, $k_{boat} \gg k_{chair}$, and reaction through a boat conformation, flattened somewhat to reduce non-bonded strain, is feasible, and would account for the high $\beta\text{-}d_4$ isotope effects.

In conclusion some solvent nucleophilic participation probably occurs for both tosylates. The m-values are intermediate between those for nucleophilic and limiting mechanisms, the ratios $k_{HCOOH}/k_{90\%EtOH}$ are very low for secondary systems, and the variation of the ratios of the rate constants to 2-adamantyl tosylate over a range of solvents is slight. The α-isotope effects are high and show little dependence on solvent, though the $\beta\text{-}d_4$ isotope effects do decrease slightly as the nucleophilicity of the solvent is increased. The extent of such solvent participation

however cannot be very great, as all these probes do suggest a mechanism that is close to being limiting.

The similarity in the extent of solvent nucleophilic participation for both tosylates supports the conclusion from the β-d_4 isotope effects that the exo tosylate reacts through a transition state in which the cyclohexane ring adopts a boat conformation. Thus the approach of a solvent molecule is seriously hindered by the ethano bridge in the case of the exo tosylate if it reacts through a chair conformation. However in the boat conformation the approach becomes much easier, and more similar to that in the case of the endo tosylate.

The high β-d_4 isotope effects for both tosylates point to participation by the β-hydrogens in the breaking of the carbon-tosylate bond. Shiner et al. have shown that this is normally strongly dependent on the relative orientations of the β-hydrogens and the leaving group,[41] and hence the effects are unlikely to be cumulative in the present case. It is therefore probably incorrect to conclude that because the β-d_4 isotope effects are lower for the exo tosylate than for the endo, that less participation occurs for the former. The results do not provide any clear indication of what form such participation takes. It is possible that only delocalisation of the electrons occurs, and that the participation can be described by hyperconjugation in which the role of the resonance hybrid B is of more importance than usual.



A B

Some movement of the β-hydrogens to give a hydrogen-bridged ion, perhaps unsymmetrical, could however occur. Bridging by a hetero-atom reduces the α-isotope effect significantly[40], but it is controversial whether participation by a neighbouring carbon-hydrogen σ-bond could also contribute to the reduction of the α-effect.[5]

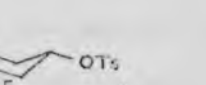
4.7 α-Kinetic isotope effects for cis- and trans -4-t-butylcyclohexyl tosylates

The α-effects for solvolyses of the brosylates had been measured very accurately in 50% aq. ethanol by Shiner and Jewett.[1,2] It was felt that it would be useful to determine the α-effects in at least one other solvent system to compare the variation with solvent with that for the bicyclo[3, 2, 1]octan-3-yl system. The solvent chosen was acetic acid, for which product analyses have been reported,[9] and which was also used in the study of the bicyclo[3, 2, 1]octan-3-yl tosylates. The measurements in 50% aq. ethanol were reinvestigated in the present work by the spectrophotometric method as a check on the procedure (see Section 4.3). The results are shown in Table 4.7, while Table 4.8 shows the rate ratios with respect to 2-adamantyl tosylate (the buffer concentration in the acetolysis of 2-adamantyl tosylate was not reported).[59]

If temperature differences are allowed for, then the α-isotope effects are seen to be similar in both solvents. The rate ratios relative to 2-adamantyl tosylate do not show the increase with solvent nucleophilicity that is observed for isopropyl tosylate,[59] though the temperature dependence of the rate ratios is not known. In these respects the tosylates behave in a similar fashion to the bicyclo[3, 2, 1]octan-3-yl derivatives.

Table 4.7

Rate constants and α-kinetic isotope effects for cis- and trans-4-t-butylcyclohexyl tosylates

Solvent	T°C	 $k_H \times 10^5$ (sec^{-1})	k_H/k_D	 $k_H \times 10^5$ (sec^{-1})	k_H/k_D
50% aq. Ethanol	44.8	20.6 ± 0.4	1.200 ± 0.007	4.55 ± 0.08	1.16 ± 0.01
Acetic Acid [a]	79.6	18.8 ± 2	1.172 ± 0.004	7.92 ± 0.3	1.13 ± 0.01

(a) containing 0.15M potassium acetate

Table 4.8

Comparison of the rates of solvolysis for cis- and trans-4-t-butylcyclohexyl tosylates with 2-adamantyl tosylate

Solvent	$k_{ih}/k_{2\text{-ada}}$ [a]	$k_{cis}/k_{2\text{-ada}}$	$k_{trans}/k_{2\text{-ada}}$
50% aq. Ethanol	20.0 (25°C)	15.4 (45°C)	3.40 (45°C)
Acetic Acid	12.6 (25°C)	16.1 (80°C)	6.77 (80°C)

(a) see ref. 59

However the two systems differ in that while the exo- and endo-bicyclo[3, 2, 1]octan-3-yl tosylates gave α-isotope effects which are very close, the trans tosylate in the 4-t-butylcyclohexyl system gives a significantly lower value than the cis tosylate in both solvents. This result is difficult to rationalise. Shiner has shown that the trans derivative reacts probably through a twist conformation in which steric effects are likely to be similar to those for the cis tosylate, and hence the α-effect cannot be lowered by severe steric factors. The extent of β-hydrogen participation is indicated by the β-isotope effects (see Table 1.3) to be less for the trans than for the cis tosylate, and hence the lower α-effect for the trans tosylate cannot be due to more hydrogen participation. It seems therefore that the solvolysis of the trans tosylate must involve more solvent nucleophilic participation. The product analysis showed that a higher ratio of inverted to retained product was obtained for the trans tosylate, 50 compared to 10, suggesting that the intermediate in this case is more susceptible to nucleophilic attack than that in the solvolysis of the cis tosylate. It is therefore possible that in the ionisation step, the transition states preceding such intermediates also differ in their susceptibility to solvent attack, possibly due to steric differences between the twist and chair conformers. Therefore probably a lower α-effect is observed since the mechanism is more nucleophilic.

CHAPTER 5 ANALYSIS OF PRODUCTS

5.1 Introduction

Four solvent systems in which the α- and β- isotope effects had been determined were used for analyses of the products. Acetic acid was chosen to allow comparisons to be made with the results of Jefford et al.[10] for the bicyclo[3, 2, 1]octan-3-yl tosylates, and with those of Lebel[11] and Whiting[9] for related systems. Formic acid and 98% aq. ethanol were used to allow the effects of ionising power and nucleophilicity respectively to be determined by comparison with acetic acid. 50% aq. ethanol was chosen as a second aqueous ethanol mixture, having a similar nucleophilicity to 98% aq. ethanol, but a much higher ionising power. It was also used by Whiting[9] for the 4-t-butylcyclohexyl derivatives. Trifluoroacetic acid has a very low nucleophilicity and a very high ionising power and would have been an interesting solvent for a product analysis, but it was not used since it has been reported that even with a high buffer concentration, considerable addition of the acid to olefins occurs.[62]

All the probable reaction products were prepared and shown to be stable to the solvolysis conditions and the work-up procedure. The acetates and formates were first reduced to the corresponding alcohols, while the hydrocarbons and ethers were analysed directly by g.l.c. Details of the tests of stability, and the g.l.c. conditions are given in chapter 7. Calibration of the flame-ionisation detector, and the use of internal, inert, hydrocarbon standards allowed absolute yields and hence a total recovery to

be quoted without isolation of the products.

5.2 Acetolysis

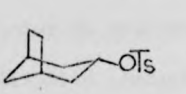
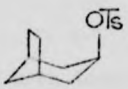
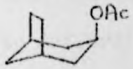
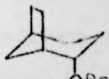
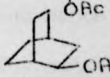
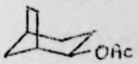
The products of the acetolysis of the exo and endo tosylates are shown in Table 5.1, with the results of Jefford et al.[10] shown in brackets for comparison.

There are many differences between the present results and those of Jefford. Firstly a much higher yield of bicyclo[3, 2, 1]oct-2-ene is observed, about 70% compared to around 40%. In the present analysis, the amount of olefin was determined directly after the extraction of the products, before the acetates were reduced to the alcohols. A separate hydrocarbon standard was used for the g.l.c. analysis of the olefin, and the total recovery of the products of acetolysis varied from 98-103%, while in Jefford's analysis no standards were used and a large amount of solvent was removed before g.l.c. analysis. It is therefore likely that a lower yield of olefin was obtained in his analysis due to loss of olefin during the evaporation of the solvent, and that this was not detected due to the absence of internal standards.

Secondly, in the present analysis the unrearranged substitution product from both tosylates is predominantly inverted, while Jefford reported a large amount (21.5%) of retained product from the acetolysis of the endo tosylate. Also, significant percentages of rearranged substitution products are observed from both tosylates, while Jefford reported no rearrangement in either case. These differences are probably

Table 5.1

The products of acetolysis[a] of exo- and endo- bicyclo[3, 2, 1]octan-3-yl p-toluenesulphonates[b]

Product		
	0	0
	69.0 (35.8)	68.8 (44.0)
	26.5 (64.2)	0.8 (21.5)
	0.3	16.6 (34.5)
	2.1	8.0
	1.9	5.2
	0.2	0.6
	0	0
Retention/Inversion	0.011	0.048
% Rearranged Product	4.2	13.8

(a) Containing 0.15M potassium acetate

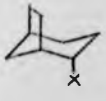
(b) Jefford's values shown in parentheses[10]

due to improved analytical methods in the present analysis, where 50' SE30T columns were used instead of the earlier short, packed columns. Also, the products were not analysed as the acetates, whose resolution is difficult, even on wall-coated capillary columns, but as the corresponding alcohols, which are much easier to resolve.

The unrearranged substitution product from both tosylates is predominantly inverted, with retention to inversion ratios of 0.011 and 0.048 being observed for the exo and endo tosylates respectively. Less than 1% of retained product is obtained from either tosylate, in contrast to Jefford's earlier results, but in accordance with the results of Whiting for the 4-t-butylcyclohexyl brosylates[9] (see Table 2.4), and of Lebel[11] for the bicyclo[3, 2, 1]oct-6-en-3-yl tosylates. These are all secondary systems which would not be expected to yield very stable carbonium ions, and hence the intermediates will be shielded on one side by the counter ions. The substitution products are therefore predominantly inverted.

Whiting's product analyses from the 4-t-butylcyclohexyl brosylates suggested that some rearrangement to the bicyclo[3, 2, 1]octan-2-yl system might be expected from the bicyclo[3, 2, 1]octan-3-yl tosylates. In addition, Goering[3] has shown that the interconversion of the trans-bicyclo[3, 2, 1]octan-2-yl and the bicyclo[2, 2, 2]octan-2-yl systems by a 1,2 carbon shift occurs in the solvolysis of these bicyclo-octan-2-yl tosylates. Therefore in the present work, rearrangement to the 2-position might be expected to lead to some skeletal rearrangement to the bicyclo-[2, 2, 2]octan-2-yl system.

The occurrence of rearranged products from the acetolysis of both tosylates was easily observed by g.l.c. From the endo tosylate a total of 14% rearranged product is observed, comprising nearly half of the total substitution product. This is partly a result of the low nucleophilicity of the solvent, which allows rearrangement to occur before collapse of the intermediate with a solvent molecule. A smaller amount, 4%, is obtained from the exo tosylate, suggesting that in this case rearrangement is less favourable relative to unrearranged substitution. The rearranged product from each tosylate is composed of the same three acetates in very similar relative amounts. Significant amounts of trans-bicyclo[3, 2, 1]-octan-2-yl acetate (1a) and bicyclo[2, 2, 2]octan-2-yl acetate (2a), but only traces of cis-bicyclo[3, 2, 1]octan-2-yl acetate (3a) are observed. These proportions are comparable to those obtained by Goering in solvolyses of the tosylates 1b and 2b, though in those systems more 2a and less 1a was reported.[3]



1a, x = OAc
b, x = OTs

2a, x = OAc
b, x = OTs

3a, x = OAc

In the solvolyses of the 4-t-butylcyclohexyl brosylates, Whiting[4] noted that the stereochemistry of the rearranged product depended on that of the starting tosylate. Thus cis-4-t-butylcyclohexyl brosylate (4a) gave trans-3-t-butylcyclohexyl acetate (5a) as the major rearranged substitution product, while the trans brosylate (4b) gave predominantly

the cis acetate (5b).

4 a, X = OTs, Y = H

b, X = H, Y = OTs

5 a, X = OAc, Y = H

b, X = H, Y = OAc

However, the rearranged substitution products from the acetolyses of the bicyclo[3. 2, 1]octan-3-yl tosylates do not show a similar stereochemical pattern. Thus the same products occur in the same relative amounts from both the exo and endo tosylates. Comparison with Whiting's results would have suggested that 3a should have been the major rearranged product from solvolysis of the exo tosylate, whereas the relative amount of 3a to 1a and 2a (1:20) is not significantly larger than from the endo tosylate (1:22).

The occurrence of similar products from two different routes has been explained in the literature by postulating that the same non-classical ion intervenes in both reactions.[a1] Goering has suggested[3] that the solvolyses of the bicyclo-octyl tosylates 1b and 2b lead to the same non-classical ion (6):

6

The present results are in accordance with rearrangement from both bicyclo-[3, 2, 1]octan-3-yl tosylates leading to cation 6, though it may not be the first-formed ion. Rearrangement could lead initially to classical cations, but the low yield of the acetate 3a requires that the lifetimes of such ions be short, and that rapid conversion to the non-classical ion must occur.

Further evidence for rearrangement leading to a non-classical ion is obtained from the elimination product. The olefin yield comprises nearly

70% of the solvolysis products from both tosylates, and is composed only of bicyclo[3, 2, 1]oct-2-ene; a limit of less than 0.3% can be placed on the occurrence of bicyclo[2, 2, 2]oct-2-ene. Thus the intermediate which gives bicyclo[2, 2, 2]octan-2-yl acetate shows an overwhelming preference for substitution as opposed to elimination. (Comparison with Goering's results suggests that a maximum of 2% bicyclo[3, 2, 1]oct-2-ene could be due to elimination from the rearranged carbonium ion.) In the literature, it is commonly found that solvolysis reactions involving non-classical ions give low yields of elimination products.[21] For example, Goering observed less than 15% elimination in the acetolyses of 1b and 2b, with the olefin being predominantly bicyclo[3, 2, 1]oct-2-ene. In addition, the exo-2-norbornyl derivatives, which are postulated to solvolyse through a non-classical ion, give low yields of olefin.[63]

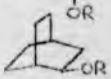
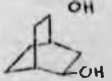
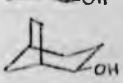
Therefore, in the present work the occurrence of the same rearranged products from both tosylates, the low yields of cis-bicyclo[3, 2, 1]octan-2-yl acetate, and the absence of bicyclo[2, 2, 2]oct-2-ene are strong evidence for rearrangement to the 2-position leading to a non-classical carbonium ion. This is in contrast with the results for the 4-t-butylcyclohexyl brosylates which could be interpreted in terms of classical cations.

5.3 The variation of the product analysis with solvent

Summaries of the product analyses for exo- and endo- bicyclo[3, 2, 1] octan-3-yl tosylates in all four solvent systems are shown in tables 5.2, 5.3 and 5.4. The products can be divided into three groups, the elimination product, the unrearranged substitution product, and the rearrangement products.

Table 5.2

Analysis of the products from endo- bicyclo[3, 2, 1]octan-3-yl p-toluenesulphonate

	Formic Acid [a] 25°C	Acetic Acid [b] 60°C	50% aq. Ethanol [c] 35°C	90% aq. Ethanol [d] 60°C
	46.1	68.8	63.4	56.5
	0.7	0.8	-	0.6
	15.9	16.6	5.6	36.5
	19.5	8.0	0.5	1.0
	16.7	5.2	0.5	0.6
	1.2	0.6	-	-
			0.4	0.1
			24.6	4.4
			3.1	0.3
			1.8	0.1
			0.2	-

(a) containing 0.15% sodium formate

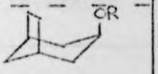
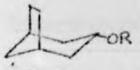
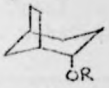
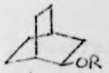
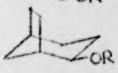
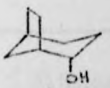
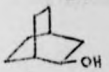
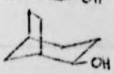
(b) containing 0.15% potassium acetate

(c) containing 0.017% borax

(d) containing 0.0% 1,4-diazabicyclo[2, 2, 2]octane

Table 5.3

Analysis of the products from exo- bicyclo[3, 2, 1]octan-3-yl p-toluenesulphonate

	Formic Acid [a] 25°C	Acetic Acid [b] 60°C	50% aq.Ethanol [c] 36°C	98% aq. Ethanol [d] 60°C
	52.6	69.0	40.4	39.6
	30.0	26.5	8.7	51.3
	0.5	0.3	-	0.8
	8.0	2.1	0.4	0.6
	8.4	1.9	0.5	0.7
	0.5	0.2	-	-
			45.7	6.7
			0.2	-
			2.0	0.2
			2.2	0.1
			-	-

(a) containing 0.15M sodium formate

(b) containing 0.15M potassium acetate

(c) containing 0.017M borax

(d) containing 0.05M 1,4-diazabicyclo[2, 2, 2]octane

Table 5.4

Summary of Product Analyses

		Formic Acid	Acetic Acid	50% aq.Ethanol	98% aq.Ethanol
Retention / Inversion	exo	0.017	0.011	0.007	0.015
	endo	0.044	0.048	0.014	0.016
Rearrangement / Total substitution	exo	0.36	0.14	0.08	0.027
	endo	0.69	0.44	0.17	0.044
% Rearrangement	exo	16.9	4.2	5.0	1.6
	endo	37.3	13.8	6.0	1.9
% Unrearranged Substitution	exo	30.5	26.8	54.6	58.8
	endo	16.8	17.4	30.6	41.6
% Elimination	exo	52.6	69.0	40.4	39.6
	endo	46.1	68.8	63.4	56.5

A limit of less than 0.3% can be placed on the yield of bicyclo[2, 2, 2]oct-2-one in all solvolyses.

The processes by which these products are formed compete with one another, and the relative amounts of each product vary with solvent.

In formolysis the yields of olefin from both tosylates are reduced by about 20% compared to those observed in acetolysis. This is a result of the greater polarity of formic acid, and of the lower temperature used, both of which tend to reduce elimination relative to substitution.[64]

The unrearranged substitution products in formolysis show very low ratios of retention to inversion, similar to those in acetolysis. Thus both the exo and endo tosylates give rise to predominantly inverted substitution products, and there is no preference for exo or endo attack in this system, in contrast to the strong preference for exo attack which is observed in the 2-norbornyl system.[26] It is a little surprising that the amount of retained product is not greater in formolysis than in acetolysis. The greater ionising power of formic acid should increase the lifetime of the carbonium ion intermediates, and this is generally thought to increase the ratio of retention to inversion.[13] The ratios of retention to inversion are probably similar because of the similar nucleophilicities of the two acids.

The longer lifetime of the intermediate in formic acid allows more rearrangement to occur relative to substitution without rearrangement. Thus for the exo tosylate the ratio of rearranged to total substitution product increases from 0.14 in acetolysis to 0.36 in formolysis. The percentage of rearrangement product increases from 4% to 17%. For the endo tosylate the ratio increases from 0.44 in acetolysis to 0.69 in formolysis, and the percentage of rearranged products increases from 14% to 37%. In

this case, rearrangement is almost as favourable a process as elimination. The high ionising power and low nucleophilicity of the solvent, which allow the intermediate to be relatively long-lived, are the main factors leading to the high percentages of rearranged products.

The rearranged products observed in formolysis are the same three that were obtained in acetolysis. It is interesting to note that though the importance of rearrangement increases markedly, still no rearranged olefin, bicyclo[2, 2, 2]oct-2-ene, is observed. The rearranged intermediate shows a very strong preference for substitution relative to elimination.

It has been reported that the acetolyses of exo- and endo-bicyclo[3, 2, 1]octan-6-yl tosylates gave high yields of the rearranged trans-bicyclo[3, 2, 1]octan-2-yl and bicyclo[2, 2, 2]octan-2-yl acetates.[65] It was postulated that ionisation led to the non-classical ion 7, which could be converted by hydride shift to the non-classical ion 6, which is the ion thought to be generated by rearrangement from the bicyclo[3, 2, 1]octan-3-yl tosylates.

7

6

There are no examples in the literature of ion 6 being converted back to ion 7, though the solvolysis of bicyclo[2, 2, 2]octan-2-yl brosylate was reported to give about 1% of an unidentified compound,[66] which could have been the result of such a rearrangement. There is no evidence for this process occurring in the solvolyses of exo- and endo- bicyclo[3, 2, 1]-octan-3-yl tosylates. In formolysis of the endo tosylate where a total of

37% rearranged products are produced, a limit of less than 2% can be placed on the yield of exo- or endo-bicyclo[3, 2, 1]octan-6-yl acetates. It is probable therefore that ion 6 is more stable than ion 7, and hence conversion of 6 to 7 is an unfavourable process.

In 98% aq. ethanol the amount of rearrangement is considerably reduced for both tosylates relative to the values in acetic and formic acid. The total percentage of rearranged substitution products is less than 2% for each tosylate, and the ratio of rearrangement to total substitution has been reduced to 0.027 for the exo tosylate, relative to 0.14 in acetolysis, and to 0.014 compared to 0.44 for the endo isomer. The percentage of unrearranged substitution has markedly increased, by 30% for the exo tosylate, and by 25% for the endo tosylate. The yield of bicyclo[3, 2, 1]oct-2-ene has been reduced for both isomers, by about 30% for the exo tosylate, and by 12% for the endo tosylate.

The ionising powers of acetic acid and 98% aq. ethanol are very similar, and the solvolyses were performed at similar temperatures. The major difference between the two solvent systems is in the higher nucleophilicity of the alcoholic medium. Thus, though the intermediates will be formed at similar rates in acetic acid and 98% aq. ethanol, their rates of reaction with solvent will be much greater in the more nucleophilic aqueous alcohol. Hence the lifetimes of the intermediates are reduced and less rearrangement occurs. It is interesting to note that in the aqueous alcoholic media both tosylates give similar amounts of rearranged products, whereas in the acidic solvents the endo tosylate gave a significantly higher percentage than the

exo isomer.

The higher nucleophilicity also favours substitution relative to elimination, and therefore since these processes compete with one another, the yield of olefin is significantly lower than in acetolysis.

The product analyses in 50% aq. ethanol are very similar to those in 98% aq. ethanol. These two solvents have similar nucleophilicities, but 50% aq. ethanol has a much higher ionising power. Hence in this solvent system the intermediates have more time to rearrange, and about 6% of the products are rearranged, compared to less than 2% in 98% aq. ethanol. However the ratios of rearrangement to total substitution in 50% aq. ethanol are lower than in either of the acidic solvolysis media due to the higher nucleophilicity of the alcoholic solvent.

It is found in both aqueous alcoholic mixtures that the ratio of alcohols to ethers formed is greater than might have been expected from the molar ratios of water to ethanol. Thus the molar ratio of water to ethanol is only 0.06 for 98% aq. ethanol, and yet both tosylates give 0.13 for the ratio of alcohols to ethers. The molar ratio of 50% aq. ethanol is 3.2, while the ratio of alcohols to ethers is 4.6 for the *endo* tosylate, and 5.3 for the *exo* tosylate. As ethanol is suggested to have a higher nucleophilicity than water, this is the opposite of what might have been expected. The explanation probably lies in the greater solvating power of water, and illustrates that such solvent mixtures are not homogeneous at the molecular level.

A possible reaction scheme for the *endo* tosylate which is suggested

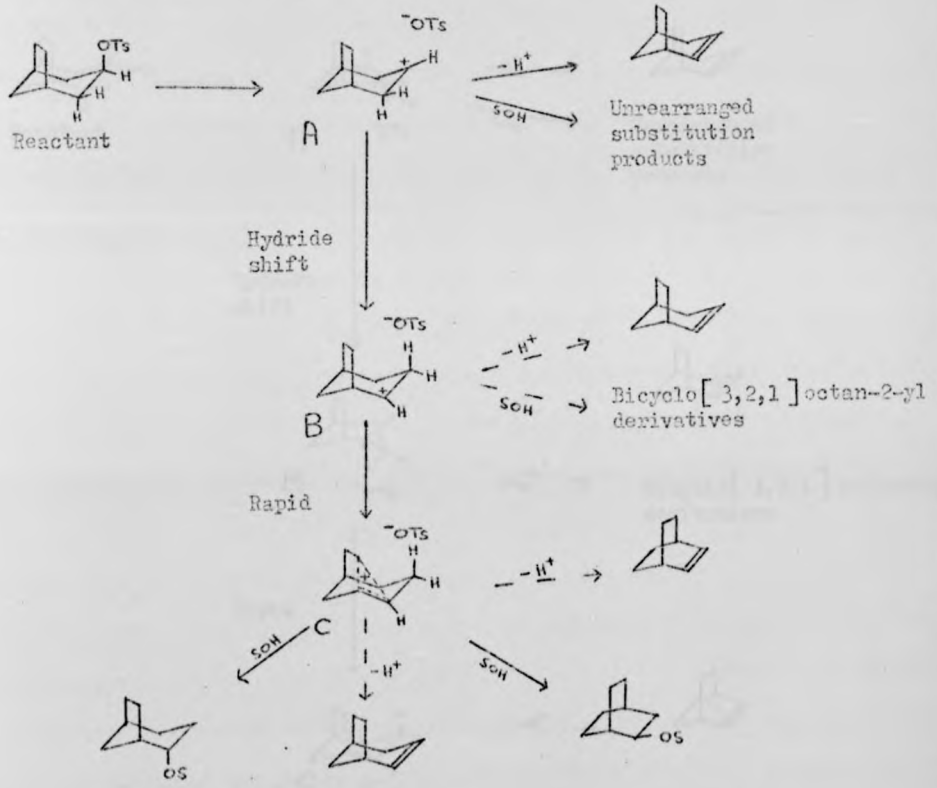
by the product analyses in the various solvents, is shown in Figure 5.1. The rate determining ionisation produces an intermediate A, which has been represented as an intimate ion-pair. There are three competing processes which A can then undergo. If a β-proton is lost, then bicyclo[3, 2, 1]oct-2-ene is formed, while if a solvent molecule is captured, substitution product results. Finally a β -proton may migrate from the 2-position, and this probably generates a short-lived classical ion, B. The existence of this ion is suggested by small amounts of cis-bicyclo[3, 2, 1]octan-2-yl derivatives in the product analyses, and from the percentages of the trans-bicyclo[3, 2, 1]octan-2-yl derivatives being greater than those of the bicyclo[2, 2, 2]octan-2-yl derivatives (the converse of Goering's results[3]). The classical ion rapidly rearranges to the non-classical ion C, which gives most of the rearranged products.

In the acidic solvents rearrangement from A through B to C is a favourable process relative to collapse of A with a solvent molecule. In the aqueous alcoholic media however, the higher nucleophilicities of these mixtures favour reaction of A with a solvent molecule, rather than rearrangement.

The reaction scheme suggested for the exo tosylate is as in Figure 5.2. It is very similar to that proposed for the endo tosylate, but there is one important difference in that the intermediate A is suggested to have the six-membered ring in a boat conformation. In Chapter 4 the isotope effects indicated that the transition state in the ionisation step was in a boat conformation, and therefore the possibility of this arrangement persisting in

Figure 5.1

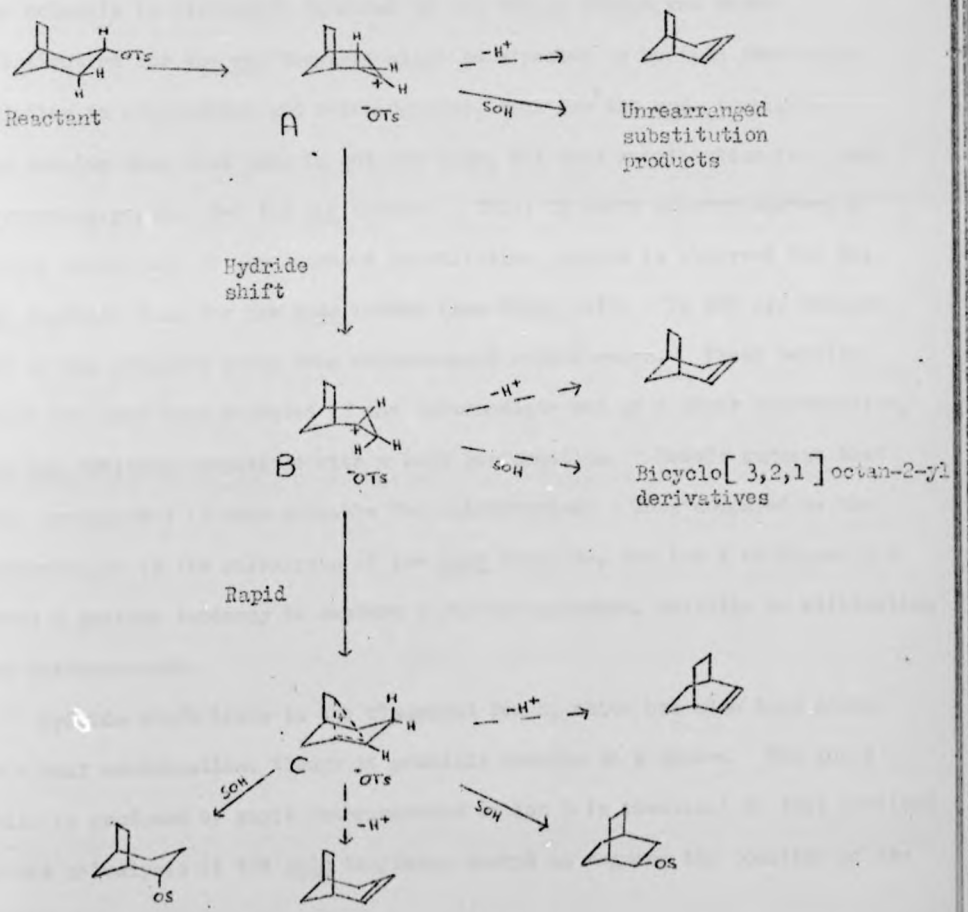
Possible reaction scheme for the solvolysis of endo-bicyclo-[3, 2, 1] octan-3-yl p-toluenesulphonate



A, B and C are ion-pair intermediates. Minor processes are shown in broken lines.

Figure 5.2

Possible reaction scheme for the solvolysis of exo-bicyclo-[3, 2, 1] octan-3-yl p-toluenesulphonate



the intermediate existed. It was mentioned earlier that no preference for exo or endo attack was exhibited in solvolysis of the bicyclo[3,2,1]-octan-3-yl derivatives, and that inversion predominated in the substitution process. However, approach of a solvent molecule from the endo side of the molecule is sterically hindered by the ethano bridge, and hence substitution for the exo tosylate might be expected to be less favourable, relative to elimination and rearrangement, than for the endo tosylate. The results show that this is not the case, but that substitution is a very favourable process for the exo isomer. Thus, in every solvent system, a higher percentage of unrearranged substitution product is observed for the exo tosylate than for the endo isomer (see Table 3.4). In 90% aq. ethanol 60% of the products arose from unrearranged substitution. These results would not have been expected if the intermediate was in a chair conformation, but are entirely compatible with a boat conformation. Models suggest that this arrangement is more suitable for substitution. Thus compared to the intermediate in the solvolysis of the endo tosylate, the ion A in Figure 3.2 shows a greater tendency to capture a solvent molecule, relative to elimination and rearrangement.

Hydride shift leads to the classical ion B, which has also been drawn in a boat conformation, though it possibly inverts to a chair. The ion C which is produced by rapid rearrangement of ion B is identical to that involved in the solvolysis of the endo tosylate, except as regards the position of the counterion.

The trends in the product analyses are therefore explicable in terms

of the common solvent parameters. The results suggest reaction schemes which are very similar for both tosylates. There are many similarities with literature results. Thus in common with the observations of Whiting[9] for the 4-t-butylcyclohexyl system and of Lebel[11] for the bicyclo[3,2,1]-oct-6-en-3-yl derivatives, the substitution product is predominantly inverted. Rearrangement also occurs, giving products that are due to hydride shift. In contrast with the 4-t-butylcyclohexyl system, hydride shift leads in this system to a non-classical ion, and thus the exo and endo isomers give the same rearranged products in similar relative amounts. This is in accordance with the suggestions of Lebel, and in contrast to the earlier results of Jefford.[10]

Less olefin is obtained in this system than from the 4-t-butylcyclohexyl brosylates (see Tables 5.4 and 2.4) The bicyclic olefin is highly strained, and hence the energy difference between the transition states for elimination and substitution from the intermediate, is larger than in the unbridged system. Elimination is therefore a less favourable process relative to substitution in the bicyclic system.

CHAPTER 6 PARTICIPATION IN SOLVOLYSIS REACTIONS

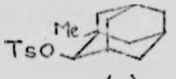
The Hughes-Ingold classification of mechanism suggested that S_N2 reactions would give complete inversion of configuration, since the bond to the incoming nucleophile was formed as the bond to the leaving group was broken. An S_N1 reaction could give retained and inverted product, as the product-forming step involved attack of the nucleophile on a planar carbonium-ion intermediate. However only systems which can provide very stable carbonium ions give equal amounts of retained and inverted substitution product. In general the continued presence of the leaving group, to provide stabilisation of an unstable intermediate, results in predominant inversion of configuration.[13] The classification scheme of Winstein[17] suggests that most solvolyses involve some solvent nucleophilic participation, and hence predominant inversion of configuration is common.

The bicyclo[3, 2, 1]octan-3-yl tosylates give high ratios of inversion to retention (Table 5.4), similar to those observed in solvolyses of cis- and trans-4-t-butylcyclohexyl arenesulphonates.[9] Predominant inversion of configuration will occur for most secondary systems, unless a relatively stable intermediate can be produced, as when an aryl group is adjacent to the reacting centre.[13] The 2-octyl system gave an unusual amount of retained product, but this was found to have arisen from racemisation of the starting material.[23]

Solvolysis of 2-adamantyl tosylate (1), however, gives net retention of configuration.[67] Schleyer and co-workers rationalised this result in terms of a limiting solvolysis mechanism.[12] The unusual cyclic structure hindered backside approach by solvent, eliminated solvent nucleophilic

participation and hence reduced the yield of inverted product. Whiting[67] reported that acetolysis gave 0.5% of a rearranged product, which was later shown to be exo-4-protoadamantyl acetate.[68] He pointed out that the 2-adamantyl system manifests two of the three results of neighbouring group participation, a decrease in the inversion to retention ratio and the observation of rearranged products. The 2-adamantyl system has a suitably oriented carbon-carbon σ-bond which could participate in the ionisation of the carbon-tosylate bond. He suggested that delocalisation of charge in the transition state for ionisation was not extensive, and therefore had little effect on the rate, though it could be more important in the product-forming step, and account for the product analysis. Recent papers by Schleyer and co-workers confirm that this type of participation is extensive in the 1-methyl-2-adamantyl system (2)[69]

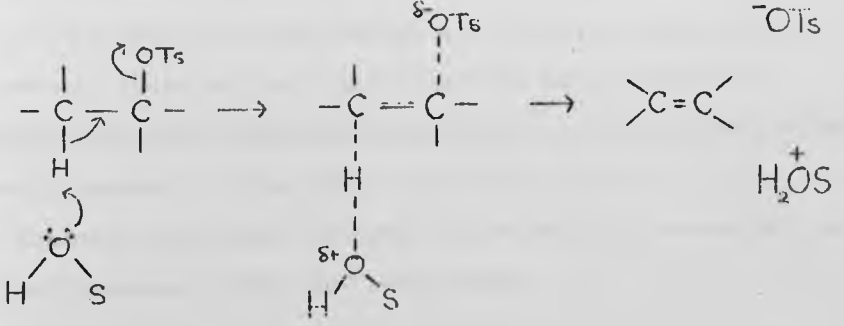
(1)



(2)

where considerable driving force is supplied by the conversion of a secondary to a tertiary carbonium ion. This driving force is absent in the 2-adamantyl case, but the similarity in the structures indicates that such participation can occur. In formic acid, 2-adamantyl tosylate solvolyses only three times slower than isopropyl tosylate where solvent nucleophilic participation and hyperconjugation can assist ionisation. If 2-adamantyl tosylate reacted without any type of assistance, a greater difference in the rates would probably be obtained.

The 4-t-butylcyclohexyl brosylates[1,8] and the bicyclo[3, 2, 1]octan-3-yl tosylates all gave unusually high β-d_1 isotope effects. These are interpreted as due to participation by the trans coplanar carbon-hydrogen bonds. The product analyses show that hydride shift from the β-position occurred in all cases, but that there was little retained product. The rates also appeared to be normal, and therefore evidence of hydrogen participation is only obtained from the high β-isotope effects. (The rearranged products could have been produced from hydrogen migration after the rate-determining step.) High β-isotope effects could also be the effect of a bimolecular elimination process, in which a solvent molecule attacked the β-hydrogen as the carbon-tosylate bond was broken.



This would be a primary isotope effect, which could be of the observed magnitude. This type of elimination is favoured by a non-polar solvent, and by a strongly basic nucleophile.[64] The solvolyses of the bicyclic tosylates did not involve strong nucleophiles; the most favourable circumstances were obtained in 96% aq. ethanol. In this solvent the β-d_1 effects were however the lowest, and the yields of olefin were also

low. In the solvolysis of cyclopentyl brosylate in 70% aq. ethanol, β-tetradeuteration reduced the rate by 47%, but only reduced the olefin fraction by 8%.[5] The correlation between high β-isotope effects and high olefin yields is not therefore a result of a rate-determining elimination process, but reflects that both hydrogen participation and elimination are facilitated by a trans co-planar arrangement of the β-hydrogen and the leaving group. This situation often exists in cyclic systems, or can be achieved by slight changes in conformation. Steric hindrance to an incoming solvent molecule leads to substitution being less favourable relative to elimination than for an acyclic compound.

It is probable that many compounds solvolyse with assistance from neighbouring groups, or from a suitably aligned bond, in addition to possibly some solvent nucleophilic participation. This hypothesis allows a new interpretation of some recent results to be made.

(1). Sunko and co-workers[70] reported that solvolysis of menthyl tosylate (3) gave predominant retention of configuration.

(3) (4)

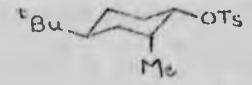
A very low β-d_3 isotope effect of 1.27 was measured in 97% aq. trifluoroethanol. These results are in contrast to those for trans-4-t-butylcyclohexyl brosylate(4) where solvolysis in 50% aq. ethanol gave predominant inversion of

configuration,[9] and a β-d_4 effect of 2.43.[1] Sunko rationalised those differences by suggesting that menthyl tosylate reacts through a chair transition state, whereas the t-butylcyclohexyl derivative has been shown to react through a twist transition state.[1] He concluded that retention of configuration arose from steric hindrance, as in the 2-adamantyl system.

Examination of models suggests that steric hindrance to solvent in the menthyl system is much less severe than for exo-bicyclo[3, 2, 1]octan-3-yl tosylate and for 2-adamantyl tosylate. Thus it is surprising that the solvolysis of menthyl tosylate gives the highest ratio of retention to inversion. The hypothesis that some form of nucleophilic participation occurs in most systems suggests that menthyl tosylate, in common with many cyclic systems with equatorial leaving groups,[1,2] reacts through a non-chair transition state. In a twist conformation the formerly equatorial isopropyl and tosylate groups could become trans co-planar, and therefore ionisation of the carbon-tosylate bond could be assisted by participation of the carbon-carbon σ-bond. Such participation would protect the rearside of the developing carbonium ion, and would lead to the predominant retention of configuration.

(2). Significant retention of configuration was also observed in the solvolysis of the 2-methyl-4-t-butylcyclohexyl tosylate, 5.[71]

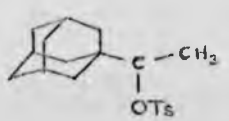
(5)



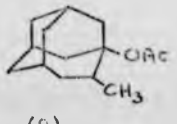
(6)

This compound probably also reacts through a twist transition state and involves participation by the β-carbon-carbon σ-bond. The isomeric compound 6, reacts through a twist conformation with β-hydrogen participation. The rate is 100 times faster than that of 5, and this may suggest that participation by carbon-hydrogen bonds produces more anchimeric assistance than that by carbon-carbon bonds.

(3). Acetolysis of optically active 1-adamantylmethylcarbinyl tosylate (7) gave an excess of retained product, and n.m.r. analysis after partial reaction suggested that up to 25% of the rearranged product, 8, was formed.[72]



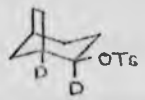
(7)



(8)

This system therefore probably also reacts with participation by the suitably aligned carbon-carbon σ-bond. The α-kinetic isotope effect in 97% aq. trifluoroethanol is only 1.11 ± 0.01, much lower than the limiting value of 1.23 observed for 2-adamantyl tosylate.[12] This suggests that the α-isotope effect may have been reduced by σ-participation, as was observed when π-participation occurred[40] (section 2.3). The α-isotope effect in the solvolysis of exo-2-norbornyl brosylate has been reported to be much lower than that for the endo isomer.[73,74] This is probably due in part to scrambling of the label,[5] but could also be the result of σ-participation. Recent results in this department for cis-bicyclo[3, 2, 1]octan-2-yl - 1,2-d_2

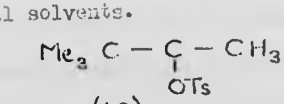
tosylate (9) show that σ-participation does lower the α-effect. A value of 1.12 was obtained in 80% aq. ethanol, which is considerably lower than



(9)

the α-effects observed for the bicyclo[3, 2, 1]octan-3-yl tosylates. The second deuterium eliminates reduction of the effect by scrambling, and hence the results are compatible with the reduction being due to σ-participation.

(4). The solvolysis of pinacolyl brosylate (10) gives an α-effect of 1.15 in several solvents.[75]



(10)

This is lower than the limiting value, and the β-d_3 effect of 1.19 is also rather low. Most of the products are rearranged and have arisen from migration of a β-methyl group. The γ-d_9 effect of 1.011 in 97% w. trifluoroethanol though small, is positive. γ-Deuterium effects are usually inverse,[5] and hence participation of the carbon-methyl bond probably occurs, and lowers the α-effect.

(5). Acetolysis of 3-methyl-2-butyl brosylate gives a β-d_3 effect of only 1.09, and a β-effect of 2.26 for single deuteration on carbon-3.[76] These suggest that the β-hydrogen on carbon-3 participates in ionisation, and the α-effect is found to be fairly low, 1.17, and solvent invariant. The α-effect appears to be reduced therefore by participation of the carbon-hydrogen bond.

CHAPTER 7. EXPERIMENTAL METHODS

The pentane and light petroleum were washed with concentrated sulphuric acid, then with aq. sodium hydroxide, and brine. It was then fractionally distilled from phosphorus pentoxide. The ethyl acetate used for column chromatography was redistilled, b.p. 77°C. The diethyl ether required for the product analyses was redistilled AnalaR ether, b.p. 34°C.

The 60Mhz nuclear magnetic resonance (n.m.r.) spectra were run on either a Perkin-Elmer R10 or R24 spectrometer using carbon tetrachloride as solvent and tetramethylsilane as an internal standard. The infra-red (i.r.) spectra were obtained on a Perkin-Elmer 457 grating spectrophotometer and routine ultra-violet (u.v.) spectra were obtained on a Unicam S.P. 8000.

Where possible melting points were determined on a Kofler block, but in some cases, including the alcohols which sublimed on a Kofler block, the melting points were determined in sealed capillaries in an oil bath. They are all uncorrected.

Routine analytical gas-liquid chromatography (g.l.c.) was performed on a Perkin-Elmer F11 with 2m by ¼" packed columns. Nitrogen was the carrier gas and a flame-ionization detector was used. A Varian 700 was used for preparative g.l.c. with a 10' by ⅜" column of Carbowax 20M on Chromosorb and a hot-wire detector.

Preparative Section

exo - 3, 4-Dichlorobicyclo [3,2,1] oct-2-ene

Method A. To a vigorously-stirred suspension of norbornene (50g, 0.53 mol) and freshly-prepared sodium methoxide (119g, 2.1 mol) in dry, redistilled pentane (300 ml) at - 15°C was added over 3 hours ethyl trichloroacetate, (268g, 1.4 mol; redistilled, b.p. 56°/8 mm) and the mixture was kept at -15° for a further 4 hours. Stirring was continued at room temperature for 48 hours, then water (400 ml) was added, the layers were separated, and the aqueous layer was extracted 3 times with light petroleum (b.p. 40-60°). The combined petrol layers were dried over magnesium sulphate, treated with activated charcoal, filtered and distilled down. The residue was fractionally distilled to give a colourless liquid (40g, 2[illegible]) b.p. 80-90°/0.1 mm. (lit. 72-73°/0.9mm.[4,6])

Method B. To a stirred solution of norbornene(75g, 0.8 mol) and tridodecylmethylammonium bromide (1.8g) in chloroform (475g, 4mol) at 0°C was added slowly a 50% aqueous solution of sodium hydroxide (325g of solid sodium hydroxide). After stirring the mixture at room temperature for three days, water (800 ml) was added and the mixture was extracted 3 times with chloroform. The combined chloroform layers were washed twice with water, dilute hydrochloric acid, and brine, and dried over magnesium sulphate. The solution was filtered, the solvent was removed by fractional distillation, and the brown residue was fractionally distilled under reduced pressure to give a colourless liquid (90g, 64%) b.p. 64-70°/0.1 mm;

i.r. (liquid film): $\bar{\nu}_{max.}$ = 3040(w), 1635, 1305, and 740 cm^{-1};

n.m.r. (CCl_4): τ = 3.87 (d, J≈7Hz; vinyl protons), 5.85 (d, J ≈ 3Hz; allyl protons), and 7.35 - 8.80 (mult., 8H);

g.l.c. (2m Carbowax 20M; 160°): Retention time = 12.3 min.

3 - Chlorobicyclo [3, 2, 1] oct-2-ene

Lithium aluminium hydride (3.04g, 0.08 mol) was added cautiously to anhydrous ether (100 ml) and the suspension was stirred at 0°C. exo - 3, 4 - Dichlorobicyclo [3, 2, 1] oct-2-ene (12g, 0.07 mol) was added slowly, and the mixture was heated under reflux for 40 hours. After cooling the reaction mixture in ice, wet ether then water were carefully added, and the mixture was poured onto ice. The mixture was acidified, and extracted 3 times with ether. The combined ether layers were washed with brine, and dried over magnesium sulphate. After being filtered, the solution was distilled down to remove the ether, then the residue was fractionally distilled under reduced pressure to give 7.6g (79%) of 3-chlorobicyclo [3, 2, 1] oct-2-ene as a colourless liquid b.p. 70 - 71 °/3mm. (lit.[46] 76 - 77 °/21 mm.);

i.r. (CCl_4): $\bar{\nu}_{max.}$ = 3060 (w), 1645 (m), 1042 (m), and 690 (m) cm^{-1};

n.m.r. (CCl_4) : τ = 4.01 (d, 1H, J≈7Hz), and 7.1 - 8.8 (mult. 10H);

g.l.c. (2m Carbowax 20M; 160°): Retention time = 2.2 min.

Bicyclo [3. 2. 1]octan-3-one

To concentrated sulphuric acid (80 ml) at 0°C was added dropwise and with stirring, a solution of 3-chlorobicyclo [3, 2, 1] oct-2-ene (8g, 0.056 mol) in dry tetrahydrofuran (15 ml). The solution was stirred at 0°C for 3 hours, allowed to come to room temperature overnight, then was poured onto 300g of

ice. The mixture was made alkaline by the addition of solid sodium carbonate and aq. sodium hydroxide, then was extracted 3 times with ether. The combined ether layers were washed with brine and dried over magnesium sulphate. The solution was filtered, the ether was removed by fractional distillation and the residue was sublimed at 80°C and 20 mm to give 4g (57%) of a white crystalline solid m.p. 127 - 130° (lit. 135 - 136°)[47];

i.r. (CCl_4): $\bar{\nu}_{max.}$ = 1715 (s) cm^{-1};

n.m.r. (CCl_4): τ = 7.45 (mult.,2H), 7.7 (mult., 4H), and 8.3 (mult., 6H);

g.l.c. (2m Carbowax 20M; 160°): Retention time = 4.7 min.

Reductions of Bicyclo[3, 2, 1]octan - 3 - one

Method A. Bicyclo[3, 2, 1]octan - 3 - one (2g, 0.016 mol) in acetic acid (50 ml) and concentrated hydrochloric acid (5 ml) was hydrogenated over platinum oxide (Adams' catalyst) at a pressure of 3 atmospheres for 18 hours. The solution was then made alkaline with aq. sodium hydroxide and extracted 3 times with ether. The combined ether layers were washed with brine, dried over magnesium sulphate, and the ether was removed by fractional distillation. The residual solution was added dropwise to a stirred suspension of lithium aluminium hydride (1.12 g, 0.03 mol) in ether (50 ml) at 0°C and the mixture was then heated under reflux for 1 hour. The suspension was cooled in ice, wet ether then water were added cautiously, and the mixture was poured onto ice, acidified, and extracted 3 times with ether. The combined ether layers were washed with brine, dried over magnesium sulphate and the ether was removed by fractional distillation. The product was shown by g.l.c. to be a 40:1 mixture of endo- and exo - bicyclo[3, 2, 1]octan - 3 - ols. The endo alcohol was isolated by column chromatography on alumina (100 g; 5% deactivated

with water; petrol, ethyl acetate and petrol mixtures) and sublimed at 80° and 4 mm to give 1.3 g (64%) m.p. 204-204.5° (lit. 206-206.5°)[47]; i.r. (CCl_4): $\bar{\nu}_{max.}$ = 3625 (m), 1100 (s), 1050 (s), 970 (m), and 920 (m) cm^{-1}; n.m.r. (CCl_4): τ = 6.0 (mult., 1H), and 7.8-8.7 (mult., 13H).

Method B. To a stirred suspension of lithium aluminium hydride (0.16 g, 0.004 mol) in ether (20 ml) at 0°C was added dropwise a solution of bicyclo-[3, 2, 1]octan-3-one (0.5 g, 0.004 mol) in ether (10 ml). The mixture was heated under reflux overnight, then was cooled in ice, and water was added cautiously. Dilute hydrochloric acid was added to bring the solution to pH4, and it was then extracted 3 times with ether. The combined ether layers were washed with brine, dried over magnesium sulphate, filtered and distilled down to give 0.36 g (72%) of a white crystalline solid. This was shown by g.l.c. on a 50 foot SCOT Carbowax 20M column (140°C) to be a 2:1 mixture of exo- and endo-bicyclo[3, 2, 1]octan-3-ols. The endo alcohol had the shorter retention time, 13.5 minutes; that of the exo alcohol was 16.6 minutes under identical conditions. The alcohols were separated by column chromatography on alumina (100 g; 5% deactivated with water; petrol, ethyl acetate and petrol mixtures) using g.l.c. to monitor the fractions. The endo alcohol was eluted first (0.15 g, 30%; m.p. 204-204.5°) followed by the exo alcohol (0.21 g, 41%; m.p. 113.5-114°, lit. 114-115°)[47].

Method C. To a stirred suspension of sodium borohydride (0.69 g, 0.018 mol) in ethanol (30 ml) was added dropwise a solution of bicyclo[3, 2, 1]octan-3-one (1.97 g, 0.016 mol) in ethanol (30 ml) at room temperature. The mixture was maintained at a reflux temperature overnight, then it was cooled and aq. sodium hydroxide (40 ml; 2%) was added. The solution was heated under

reflux for a further two hours, then water (20 ml) was added, and most of the ethanol was removed by fractional distillation. The resulting solution was extracted 3 times with pentane. The combined pentane layers were washed with brine, dried over magnesium sulphate, and fractionally distilled down to leave 1.9 g (98%) of a white crystalline solid. This was shown by g.l.c. to be a 1:1 mixture of the exo and endo alcohols. After column chromatography and sublimation as in method B, pure endo alcohol (0.9 g, 45%; m.p. 205-206) and exo alcohol (0.8 g, 40%; m.p. 114-115) were obtained. The following spectral data were obtained for exo-bicyclo[3, 2, 1]octan-3-ol:-

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 3620 (m), 1100 (m), 1060 (s), and 950 (m) cm^{-1};

n.m.r. (CCl_4): τ = 6.2 (mult., 1H), and 7.3-9.0 (mult., 13H).

exo-Bicyclo[3, 2, 1]octan-3-yl p-toluenesulphonate

To a solution of exo-bicyclo[3, 2, 1]octan-3-ol (0.2 g, 0.016 mol) in dry pyridine (1 ml) at 0°C was added slowly a solution of p-toluenesulphonyl chloride (0.37 g, 0.019 mol; recrystallised from petrol, b.p. 40-60°C) in pyridine (2 ml). The resulting yellow solution was kept at 0°C for 3 days, during which time the solution turned pink and needle-shaped crystals were formed. Water (30 ml) was added dropwise, and the white precipitate which then formed was filtered off, washed well with ice-cold water and dried thoroughly in a desiccator. Recrystallization from hot petrol (b.p. 40-60°) gave a white crystalline product (0.29 g, 65% yield) m.p. 80-81°C (lit. m.p. 76-77°);

i.r. (CCl_4) : $\overline{\nu}_{max.}$ = 1375 (s), 1190 (s), 1180 (s), 1100 (s) and 950 (s) cm^{-1} ;

n.m.r. (CCl_4): τ = 2.2-2.9 (quartet, 4H), 5.2-5.7 (mult., 1H) and 7.5-8.8 (mult., 15H);

u.v. (AcOH): λ = 273 nm (ϵ = 412), λ = 267 (ϵ = 455), and λ = 262 (ϵ = 47[illegible])

(EtOH): λ = 273 nm (ϵ = 482), λ = 267 (ϵ = 540), λ = 262 (ϵ = 604), and

λ = 257 (ϵ = 488).

endo-Bicyclo[3, 2, 1]octan-3-yl p-toluenesulphonate

The same method of preparation as for the exo tosylate was used, but with a different method of recrystallization. The crude tosylate (0.5 g) was dissolved in dry, redistilled petrol (b.p. 40-60°) at room temperature, and the solution was filtered into a pear-shaped flask. The flask was stoppered and placed in an acetone bath, the temperature of which was slowly reduced to - 20°C with solid carbon dioxide. The solution was then seeded and the temperature was gradually reduced to - 70°C. The petrol was then withdrawn using a pipette, the crystals were washed with more petrol, the temperature being kept at - 70°, and the washings were removed by pipette. The last traces of solvent were removed by pumping as the bath was slowly allowed to come to room temperature. endo-Bicyclo[3, 2, 1]octan-3-yl p-toluenesulphonate (0.38g, 76%) was obtained, m.p. 75-76°C (lit. 71-73°)[10]. The following spectral data were recorded:-

i.r. (CCl_4): $\bar{\nu}_{max.}$ = 1370 (m), 1190 (m), 1180 (s), and 910 (s) cm^{-1};

n.m.r. (CCl_4): τ = 2.2-2.8 (quartet, 4H), 5.2-5.4 (mult., 1H), and 7.6-8.7(mult., 15H);

u.v. (AcOH): λ = 273 nm (ϵ = 417), λ = 267 (ϵ = 463), and λ = 262 (ϵ = 481);

(EtOH): λ = 273 (ϵ = 488), λ = 267 (ϵ = 552), λ = 262 (ϵ = 615), and

λ = 257 (ϵ = 494).

exo- and endo-Bicyclo[3, 2, 1]octan-3-ol-3d_1

These alcohols were prepared using either sodium borodeuteride (minimum

deuterium incorporation = 98%) or lithium aluminium deuteride (deuterium incorporation > 99%) to reduce bicyclo[3, 2, 1]octan-3-one. The resulting mixture of exo and endo alcohols was separated by column chromatography as for the protium compounds, and the alcohols were finally sublimed. The following data were obtained for endo-bicyclo[3, 2, 1]octan-3-ol-3d_1:-

m.p.=203-204°C;

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 3625 (m), 1110 (s), 1050 (m), and 920 (m) cm^{-1};

n.m.r. (CCl_4): τ = 7.6-8.8 (mult.).

exo-Bicyclo[3, 2, 1]octan-3-ol-3d_1 gave the following data:-

m.p.=108.5-109°C;

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 3620 (m), 1170 (m), 1035 (s), and 955 (s) cm^{-1};

n.m.r. (CCl_4): τ = 6.5 (s, 1H), and 7.6-9.0 (mult., 12H).

exo- and endo- Bicyclo[3, 2, 1]octan-3-yl-3d_1 p-toluenesulphonates

The tosylates were prepared from the deuterated alcohols using the same procedure as for the non-deuterated species. For exo-bicyclo[3, 2, 1]octan-3-yl-3d_1 p-tosylate (m.p. 79.5-80.4°C) the spectral data were as follows:-

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 1375 (s), 1190 (s), 1180 (s), 1100 (m), and 940 (s) cm^{-1};

n.m.r. (CCl_4): τ = 2.2-2.9 (quartet, 4H), and 7.5-8.8 (mult., 15H);

and for the endo tosylate (m.p. 75-76°C) :-

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 1375 (s), 1190 (s), 1180 (s), 1100 (s), and 910 (s) cm^{-1},

n.m.r. (CCl_4): τ = 2.2-2.8 (quartet, 4H), and 7.6-8.6 (mult., 15H).

Bicyclo[3, 2, 1]octan-3-one-2, 2, 4, 4-d_4

Bicyclo[3, 2, 1]octan-3-one (1.52 g, 0.012 mol), anhydrous sodium carbonate (0.1 g), acetone-d_6 (1ml) and deuterium oxide (20 ml; 99.8% deuterium incorporation) were stirred at a reflux temperature for 40 hours.

The mixture was extracted 3 times with anhydrous ether, dried twice over anhydrous sodium sulphate, and filtered. The solvent was removed by fractional distillation, and the tetradeuterated ketone was sublimed at 90°/10 mm, (1.18g, 78%; m.p. 131-134°);

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 2220-2100 (w), and 1710 (s) cm^{-1};

n.m.r. (CCl_4) : τ = 7.5 (broad band, 2H), and 8.1-8.7 (mult., 6H);

the signal at τ = 7.7 which integrated for 4 protons in the non-deuterated species is absent in the n.m.r. spectrum for the deuterated ketone.

exo- and endo-Bicyclo[3, 2, 1]octan-3-ols-2, 2, 4, 4-d_4.

The tetradeuterated ketone (0.95g, 0.0077 mol) was reduced with lithium aluminium hydride (0.3g, 0.0078 mol) and worked up in the usual manner to give 0.8g (84%) of a 2:1 mixture of exo and endo alcohols respectively. These were separated on alumina as usual, and sublimed to give 0.25g (26%) of endo-d_4 alcohol (m.p. 202-202.5°), and 0.47g (49%) of exo-d_4 alcohol (m.p. 108-108.5°). The endo alcohol gave the following spectra:-

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 3625 (m), 2200(w), 2100 (w), and 1085 (s) cm^{-1};

n.m.r. (CCl_4): τ = 6.1 (broad s, 1H), and 7.7-9.0 (mult., 9H);

and for the exo-d_4 alcohol:-

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 3620 (m), 2200 (m), 2110 (m), 1130 (m), 1080 (m), and 940 (m) cm^{-1};

n.m.r. (CCl_4): τ = 6.25 (broad s, 1H), and 7.6-8.8 (mult., 9H).

exo - and endo - Bicyclo[3, 2, 1]octan -3-yl- 2, 2, 4, 4 - d_4 p-toluenesulphonates

These were prepared from the d_4 alcohols, p-toluenesulphonyl chloride,

and pyridine, following the same procedure as for the non-deuterated compounds.

The endo - d_1 tosylate (m.p. 74-75°) gave the following spectra:-

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 2200 (w), 2100 (w), 1360 (m), 1190 (s), 1180 (s), and 900 (s) cm^{-1};

n.m.r. (CCl_4): τ = 2.2-2.8 (quartet, 4H) 6.3 (broad s, 1H), and 7.5-8.8 (mult, 11H);

and the exo - d_1 tosylate (m.p. 79-80°):-

i.r. (CCl_4) : $\overline{\nu}_{max.}$ = 2200 (w), 2100 (w), 1370 (m), 1190 (s), 1180 (s) and 935 (s) cm^{-1};

n.m.r. (CCl_4): τ = 2.2-2.9 (quartet, 4H) 5.4 (broad s, 1H), and 7.4-8.8 (mult., 11H).

Bicyclo[3, 2, 1]oct-2-ene

To a stirred solution of anhydrous t-butanol (4.7g, 0.06 mol) in tetrahydrofuran (25 ml; redistilled from lithium aluminium hydride) under nitrogen was added sodium (2.9g, 0.12 mol) in small pieces, and the mixture was brought to a reflux. A solution of 3-chlorobicyclo[3, 2, 1]oct-2-ene (3g, 0.02 mol) in dry tetrahydrofuran (10 ml) was added dropwise by means of a pressure-equalising dropping funnel, and the mixture was maintained at a reflux temperature for 20 hours. A purple colour developed during this time. The solution was decanted from the excess of sodium, and methanol was added to destroy any further traces. The solution was then poured onto ice, and extracted 3 times with pentane. The combined pentane layers were washed with brine, dried over magnesium sulphate and filtered. Most of the solvent was removed by fractional distillation, and the residual solution was percolat

down a chromatography column of dry silica gel, impregnated with silver nitrate, with redistilled pentane being used to elute the olefin. The solution was concentrated by fractional distillation and the olefin was isolated by preparative g.l.c. using a column of 10% Carbowax 20M on Chromosorb with an oven temperature of 100°C. After sublimation at 40°/0 mm the olefin was obtained as a white crystalline solid (1g, 45%) m.p. 38-38.5 (lit.[47] 35-36). The following spectra were obtained:-

i.r. (CCl_4): $\bar{\nu}_{max.}$ = 3030 (s), 1640 (m), and 685 (s) cm^{-1};

n.m.r. (CCl_4): τ = 4-5 (mult., 2H), and 7.4-8.8 (mult., 10H);

in agreement with literature values.

Several other methods of preparation were attempted, but while these were shown by analytic g.l.c. to have produced olefin in good yield, in no case was it found possible to isolate the olefin without preparative g.l.c. being used. Isolation was complicated by the low melting point of the compound, its high volatility and its high solubility in organic solvents. Any small amounts of impurities made sublimation of the olefin very unsuccessful. Bicyclo[2, 2, 2]oct-2-ene, required for comparison was kindly supplied by Dr. H. Maskill.

cis- and trans - Bicyclo[3, 2, 1]octan-2-ol

Bicyclo[3, 2, 1]octan-2-one (0.5lg, 0.004 mol; supplied by Emanuel) in acetic acid (15 ml) and concentrated hydrochloric acid (1 ml) was hydrogenated over platinum oxide (Adams' catalyst) at a pressure of 3 atmospheres for 18 hours. The solution was then made alkaline with aq. sodium hydroxide and extracted 3 times with ether. The combined ether layers were washed with brine, dried over magnesium sulphate and filtered.

The solution was reduced in volume by fractional distillation, then was added dropwise to a stirred suspension of lithium aluminium hydride (0.24 g, 0.006 mol) in ether at 0°C. The mixture was maintained at a reflux temperature for 1½ hours, then was cooled in ice, and water was added carefully. The mixture was acidified and extracted 3 times with ether. The combined ether layers were washed with aq. sodium carbonate, brine, and dried over magnesium sulphate and filtered. Removal of the ether left a white crystalline solid (0.38g, 73%) which was shown by g.l.c. on a 50' SCOT DEGS (diethylene glycol succinate) column (100°) to be a mixture of three alcohols, 50% trans-bicyclo[3, 2, 1]octan-2-ol (retention time = 27.4 min), 14% bicyclo[2, 2, 2]octan-2-ol (retention time = 29.4 min), and 36% cis-bicyclo[3, 2, 1]octan-2-ol (retention time = 31.0 min). The alcohols were partially separated by chromatography on alumina to give:

trans-bicyclo[3, 2, 1]octan-2-ol (0.085g, 17%; containing about 4% bicyclo[2, 2, 2]octan-2-ol) m.p. 191-192° (lit.[3] 194.2-195.2°);
i.r. (CCl_4): $\bar{\nu}_{max.}$ = 1015 (s) cm^{-1};

cis bicyclo[3, 2, 1]octan-2-ol (0.077g, 15%; containing 1% of the trans alcohol; 0.033g, 6%; containing 4% trans alcohol)
m.p. 173-174° (lit.[3] 174.5-177°);
i.r. (CCl_4): $\bar{\nu}_{max.}$ = 1065 (s) cm^{-1};

and 0.12g (23%) of a mixture of alcohols. Bicyclo[2, 2, 2]octan-2-ol was kindly supplied by Dr. H. Laskill, and after sublimation had m.p. 216-216.5° (lit.[77] 216-217°).

cis- and trans-4-t-Butylcyclohexanol

The mixture of alcohols obtained commercially (Emanuel; a 2:1 mixture of trans to cis alcohols) was separated on alumina (130g of 5% deactivated alumina to 2g alcohol; petrol and ethyl acetate-petrol mixtures). The cis alcohol was eluted first, and after sublimation at 80°/4mm had m.p. 78-78.5° (lit. 81-82°)[42] and gave the following data:-

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 3620 (m), 1370 (s), 1030 (s), 1010 (s), and 955 (s) cm^{-1};

n.m.r. (CCl_4): τ = 6.0 (broad s, 1H), and 8.05-9.15 (mult., 19H);

g.l.c. (50' SCOT Carbowax 20%; 160°): Retention time = 8.2 min.

The trans alcohol had m.p. 76-77° (lit. 78-79°)[42];

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 3620 (m), 1365 (s), 1035 (s), 1040 (m), and 980 (m) cm^{-1};

n.m.r. (CCl_4): τ = 6.6 (broad band, 1H), and 7.6-9.15 (mult., 19H);

g.l.c. (50' SCOT Carbowax 20%; 160°): Retention time = 9.7 min.

It was shown by g.l.c. that each alcohol contained less than 0.7% of its diastereoisomer.

cis- and trans-4-t-Butylcyclohexyl p-toluenesulphonates

To a solution of cis-4-t-butylcyclohexanol (0.16g, 0.001 mol) in dry pyridine (1 ml) at 0°C, was added slowly a solution of p-toluenesulphonyl chloride (0.29g, 0.0015 mol) in pyridine (2 ml), and the solution was kept at 0° for three days. Water (30 ml) was added dropwise and the resulting white precipitate was filtered off and washed well with ice-cold water. The crude tosylate was dried in a desiccator to give 0.21g (66%). It was recrystallized at -70°C following the procedure already described to give 0.15g (50%) of a white crystalline solid,

m.p. 74.5-75°C (lit. 79-80°);[42]

i.r. (CCl_4): $\overline{\nu}_{max.}$ = 1370 (m), 1190 (s), 1175 (s), 910 (s), and 675 (m) cm^{-1};
n.m.r. (CCl_4): τ = 2.2-2.9 (quartet, 4H), 5.3 (mult., 1H) and 7.5-9.2 (mult., 21H).

For the trans tosylate a yield of 60% was obtained, m.p. 88-89°C (lit. 89.4-90°)[42];
i.r. (CCl_4): $\overline{\nu}_{max.}$ = 1370 (s), 1190 (s), 1180 (s), and 950 (s) cm^{-1};
n.m.r. (CCl_4): τ = 2.2-2.9 (quartet, 4H), and 7.6-9.2 (mult., 22H);
sharp singlets at τ = 7.6 and τ = 9.2 within the multiplet could be assigned to the methyl and t-butyl groups respectively.

4-t-Butylcyclohexanone

This was kindly prepared by Mrs P.H. McAdam from 4-t-butylcyclohexanol following the method of Brown and Garg.[78] It was recrystallized from pentane, and had m.p. 46-47° (lit. 47.5-48.5°)[42];
i.r. (CCl_4): $\overline{\nu}_{max.}$ = 1720 (s) cm^{-1}.

cis- and trans-4-t-Butylcyclohexanol-1-d_1

A solution of 4-t-butylcyclohexanone (9.8g, 0.065 mol) in ethanol (50ml) was added dropwise to a stirred suspension of sodium borodeuteride (0.98g, 0.02 mol; isotopic purity > 98%) in ethanol (80 ml). The mixture was heated under reflux for 48 hours, then cooled, and sodium hydroxide solution (2N; 100ml) was added. The mixture was heated under reflux for a further 3 hours, then most of the ethanol was removed by distillation. The remaining solution was saturated with solid sodium chloride, and extracted 3 times with pentane. The combined pentane layers were washed with brine, dried over magnesium sulphate, and filtered, and the solvent was removed

by fractional distillation to give 9.5g (95%) of a white crystalline solid. This was shown by g.l.c. to be a 3:1 mixture of trans to cis alcohol. The two alcohols were separated by column chromatography following the same method as for the non-deuterated species. The first eluted was the cis alcohol (2.3g, 23% overall) m.p. 78-78.5°;

i.r. (CCl_4): $\bar{\nu}_{max.}$ = 3620 (m), 2130 (w), 1365 (s), and 1190 (s) cm^{-1}.

The trans alcohol (7.1g, 71% overall) had m.p. 76-77°;

i.r. (CCl_4): $\bar{\nu}_{max.}$ = 3620 (m), 2100 (w), 1365 (s), 1120 (s), and 1080 (s) cm^{-1}.

cis and trans -4-t-Butylcyclohexyl-1-d_1 p-toluenesulphonates

The tosylates were prepared from the deuterated alcohols following the same method as for the non-deuterated compounds. The cis tosylate had m.p. 73.5-74.5°;

i.r. (CCl_4): $\bar{\nu}_{max.}$ = 1370 (s), 1190 (s), 1175 (s), 910 (s), and 675 (s) cm^{-1};

while the trans tosylate (m.p. 87-88°) gave:-

i.r. (CCl_4): $\bar{\nu}_{max.}$ = 1370 (s), 1190 (s), 1180 (s), and 920 (s) cm^{-1}.

Preparation of g.l.c. standards and solvolysis media

Preparation of acetates

Typically, the alcohol (0.2g) was dissolved in pyridine (3ml) and acetic anhydride (1.5ml), and the solution was maintained at a reflux temperature for 1 hour. Water (1 ml) was then added, and the mixture was heated for a further 15 min. The solution was then cooled in ice and extracted 3 times with ether. The combined ether layers were washed with dilute sulphuric acid, dilute sodium hydroxide and brine, and dried over magnesium sulphate. The solution was filtered and concentrated by fractional distillation. The acetates were never isolated, but in some cases some impurities were removed by column chromatography, prior to g.l.c. use.

Preparation of formic-acetic mixed anhydride

To acetic anhydride (51.7g, 0.5 mol) was added with stirring, anhydrous, redistilled formic acid (23.1g, 0.5 mol;) over about 15 minutes, with the temperature being kept around 10°C. The mixture was stirred at 45° for 1 hour, then stored in a refrigerator.

Preparation of formates

Typically, the alcohol (ca. 0.05g) and formic-acetic mixed anhydride (ca. 2ml) were mixed at room temperature. The solution was allowed to stand at room temperature for about 1 week, then was poured into a separating funnel, and was made alkaline with sodium carbonate solution. The product was extracted into ether, for direct g.l.c. use.

Preparation of ethers

A stirred suspension of the alcohol (ca 0.02g), silver oxide (ca 0.09g), and ethyl iodide (ca 0.5g; used in large excess to raise the reflux temperature) in ether (2ml) was heated under reflux for 48 hours. The mixture was cooled, filtered, and percolated down a column of dry alumina (ca 20g). The product was eluted with pentane, for direct g.l.c. use.

Purification of hydrocarbon standards

The hydrocarbons (supplied by BDH; purity by g.l.c. > 99%) were redistilled under reduced pressure. n-Undecane had b.p. 57°/2 mm while n-pentadecane had b.p. 100°/0.3 mm. They were both shown by g.l.c. to have no impurities which would co-chromatograph with any possible reaction products.

Preparation of solvolysis media

A. Acetolysis medium: To two litres of dry glacial acetic acid (AnalaR) was added anhydrous potassium acetate (29.41 g, 0.3 mol) and acetic anhydride (20 ml). This solution is then 1% in acetic anhydride and 0.15M in potassium acetate. For the kinetics, the tosylate concentration would be about 0.003M, while for the product analysis it would be about 0.03M.

B. Formolysis medium: Formic acid (1 litre; 98%; AnalaR) was dried over boric anhydride (80g) for three days.[26] It was filtered, and distilled under reduced pressure (b.p. 36°/100 mm) from a fresh batch of boric anhydride. It was then made 0.1M in sodium formate by dissolving anhydrous sodium formate

(3.36g, 0.049 mol) in the anhydrous acid (330 ml). The tosylate concentrations used were similar to those in acetolysis.

C. Aqueous ethanol mixtures: Commercial absolute spectroscopic ethanol was used. The water required was distilled from potassium permanganate. For the 80% and 98% mixtures, the required volume of water was pipetted into a 100 ml volumetric flask, and the solution was made up to the mark with ethanol. For the runs in 50% ethanol, it was necessary to make up the solutions individually; typically the tosylate (ca 0.002g) was dissolved in ethanol (2ml) then water (2ml) was added. For the buffered runs in 50% ethanol, instead of water, a solution of borax (Analar; 0.267g, 0.0007mol) in distilled water (100ml) was added. For the kinetics in buffered 50% ethanol, the tosylate concentration was about 0.001M, and the borax concentration was 0.003M, while in the product analysis the concentrations were about 0.007M, and 0.017M respectively.

D. Aqueous trifluoroethanol: 2, 2, 2-Trifluoroethanol (supplied by Koch-Light Laboratories; puro) was dried over phosphorus pentoxide, and fractionally distilled (b.p. 74°C). Distilled water was added to make the solution 96.7% trifluoroethanol - 3.3% water by weight. A tosylate concentration of about 0.003M was used.

Test of stability of reaction products

(a) of the acetates to the work-up procedure

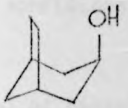
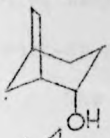
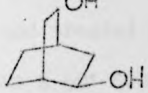
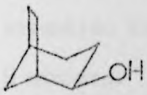
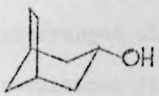
endo-Bicyclo[3, 2, 1]octan-3-ol was acetylated following the previously described method. The ethereal solution of the acetate was added to a suspension of lithium aluminium hydride in ether, and the mixture was heated under reflux for 1½ hours. It was then cooled, water was added dropwise, and the mixture was brought to pH4 using dilute hydrochloric acid. The product was extracted into ether, the ethereal solution was washed with aq. sodium hydroxide and brine, and dried over magnesium sulphate. The initial and final alcohols were analysed by g.l.c. on a 50' SCOT DEGS column (100°C). The retention times of the probable alcohol products are given in Table 7.1. It could therefore be shown that the conversion of endo-bicyclo[3, 2, 1]octan-3-yl acetate to the corresponding alcohol produced neither the exo alcohol nor rearranged alcohols, to a limit of 0.1%. The procedure was repeated with the exo alcohol, with the same result. A mixture of cis- and trans-bicyclo-[3, 2, 1]octan-2-ol, and bicyclo[2, 2, 2]octan-2-ol, containing approximately equal amounts of the three alcohols, was acetylated and reduced by lithium aluminium hydride. In this case, the initial and final mixtures were identical to within the precision of the method, about 2%.

(b) of the acetates to the acetolysis medium

trans - Bicyclo[3, 2, 1]octan-2-ol and bicyclo[2, 2, 2]octan 2-ol were acetylated and heated at 60° for 40 hours in the acetolysis medium. The initial and final acetates were tested by g.l.c. on a 100 metre wall-coated UCON capillary column (120°). Under these conditions the

Table 7.1

G.l.c. retention times on a 50' SCOT DEGS column (100°C)

Alcohol	Retention time (measured in minutes from the solvent peak)
	17.6
	22.3
	23.9
	25.3
	28.0

retention times were : trans-bicyclo[3, 2, 1]octan-2-yl acetate, 39.6 min.; bicyclo[2, 2, 2]octan-2-yl acetate, 40.3 min.; and cis-bicyclo[3, 2, 1]-octan-2-yl acetate, 41.0 min. It could therefore be shown that within the limit of precision, about 2%, the acetates were stable to the acetolysis conditions.

(c) of bicyclo[3, 2, 1]oct-2-ene to the acetolysis medium and to the work-up procedure.

The olefin was heated in the acetolysis medium at 60° for 40 hours and treated with lithium aluminium hydride following the work-up procedure. On a 50' SCOT Carbowax 20M column (60°) bicyclo[2, 2, 2]oct-2-ene had a retention time of 7 minutes while that of bicyclo[3, 2, 1]oct-2-ene was 8 minutes. It could therefore be shown by g.l.c. that less than 0.4% of rearranged olefin had been formed. Using previously described g.l.c. conditions it was shown that less than 1% of any alcohols had been formed in the acetolysis or the work-up.

(d) of the formates to the formolysis medium and to the work-up procedure. Pure samples of exo- and endo- bicyclo[3, 2, 1]octan-3-ol, and a mixture of trans-bicyclo[3, 2, 1]octan-2-ol and bicyclo[2, 2, 2]octan-2-ol were converted to the corresponding formates and treated with the formolysis medium for 18 hours at room temperature. They were then reduced back to the alcohols by lithium aluminium hydride and tested by g.l.c. For exo- and endo-bicyclo[3, 2, 1]octan-3-ol a limit of 0.2% could be placed on the

presence of any other alcohol, while for the mixture, the initial and final samples were identical to within 3%.

(e) of bicyclo[3, 2, 1]oct-2-ene to the formolysis medium

The olefin was treated with the formolysis medium for 18 hours at room temperature, and g.l.c. analysis showed that less than 1% of any formate had been formed.

Large-scale acetolysis of exo-bicyclo[3, 2, 1]octan-3-yl-3d$_1$ tosylate

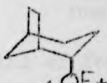
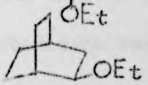
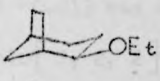
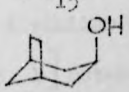
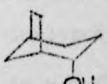
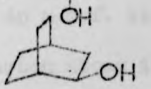
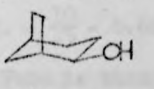
The tosylate (ca. 0.2g) was heated in the acetolysis medium (5ml) at 60° for at least 10 half-lives. The solution was made alkaline, and extracted twice with pentane. The pentane solution was percolated down a column of dry alumina and bicyclo[3, 2, 1]oct-2-ene was eluted with pentane. This solution was sent for mass-spectral analysis.

Analysis of the solvolysis products

The purification of the solvents and the hydrocarbon standards has been described. The alcohols used to prepare the tosylates were all shown to be at least 99% pure by g.l.c. The tosylates themselves were all sharp-melting, odourless, white, crystalline solids whose i.r. and n.m.r. spectra showed no bands characteristic of alcohols. All probable reaction products were synthesised as previously described, and it was shown that these were all resolvable by g.l.c. SCOT columns were used in preference to wall-coated capillary columns since the latter are more susceptible to over-loading. In the case of formolysis and acetolysis, the products were analysed as alcohols rather than as formates or acetates as their resolution is much easier. The retention times are shown in the following table (Table 72) for a 50 foot Perkin-Elmer SCOT Carbowax 20M column (120°). Because of the large difference in retention times of the olefins and alcohols, these were analysed seperately using n-undecane to calculate the yield of olefin, and n-pentadecane to calculate the yield of the alcohol fraction. Bicyclo[2, 2, 2]octan-2-ol and cis-bicyclo-[3, 2, 1]octan-2-ol were first estimated together as they co-chromatographed on Carbowax 20%, and then the relative amounts of each were determined using a SCOT DNGS column at 100° where the retention times were 23.9 and 25.3 minutes respectively, and were well resolved from other alcohols. The olefin fraction was analysed on the same column, at a lower temperature, 60°. Under these conditions bicyclo[2, 2, 2]oct-2-ene had a retention time of 7 minutes, that of bicyclo[3, 2, 1]oct-2-ene was 8 minutes, and that of n-undecane was 17 minutes.

Table 7.2

G.l.c. retention times on a 50' SCOT Carbowax 20M column (120°)

Compound	Retention Time (measured in minutes from the solvent peak)
	0.90
	0.95
n-C_{11}	1.40
	3.30
	3.95
	4.15
	4.55
	4.90
n-C_{15}	12.60
	17.10
	19.50
	20.90
	20.90
	22.00

Calibration of the detector

It is known that g.l.c. detectors have different response factors to different compounds. Calibration factors were determined using n-undecane as a standard for the olefin, and n-pentadecane as the standard for the alcohols. Typically about 30mg of each of the alcohol and the hydrocarbon standard were accurately weighed out and dissolved in redistilled pentane. This solution was then injected several times into the g.l.c. machine, and the areas of the peaks were measured using a precision disc planimeter. The molar response factor (m.r.f.) is then given by:-

$$\text{m.r.f.} = \frac{\text{area of the alcohol peak}}{\text{number of moles of alcohol}} \div \frac{\text{area of the hydrocarbon standard peak}}{\text{number of moles of hydrocarbon standard}}$$

A total of four standard solutions of exo-bicyclo[3, 2, 1]octan-3-ol and n-pentadecane were analysed in this way, and a mean molar response factor of 0.624 ± 0.013 was obtained. The procedure was repeated for one solution of bicyclo[2, 2, 2]octan-2-ol, and an m.r.f. of 0.609 ± 0.016 was obtained, in good agreement, showing that within experimental error the isomeric alcohols have the same molar response.

A similar procedure was used to calibrate the detector for bicyclo-[3, 2, 1]oct-2-ene, using n-undecane as the standard. Three solutions were analysed, and an m.r.f. of 0.701 ± 0.006 was obtained.

An m.r.f. was calculated for the others simply by dividing the number of carbon atoms in the ether molecule by the number in n-pentadecane i.e. m.r.f. $= \frac{10}{15} = 0.667$, according to a semi-quantitative method.

This is thought to be a reasonable estimate, since the m.r.f. calculated for the alcohols by this method is in good agreement with the experimentally

determined value (0.533 and 0.524 ± 0.016 respectively).

Acetolysis A standard solution was prepared by weighing accurate amounts (about 0.1g) of the two hydrocarbon standards into a 100ml volumetric flask, and adding buffered acetic acid (the solution described previously) up to the mark. Between 0.04 and 0.05g of tosylate were accurately weighed out into a 5ml volumetric flask, and the standard acetolysis mixture was added up to the mark. The molar ratio of tosylate to markers in this solution was therefore known, and allowed a total recovery of the products to be quoted. The solution was introduced into a thick-walled ampoule, which was then sealed and immersed in a water bath at about the same temperature as was used for the kinetics, for at least 10 half-lives. The ampoule was then cooled, opened, and the contents were added slowly to an ice-cold solution of tri-potassium orthophosphate (25ml; 3.5%) in a separating funnel. The solution was extracted twice with ether, and the ethereal layer was dried over magnesium sulphate. The ethereal solution was decanted and divided into two. One part (about 2 mls) was retained for analysis of the olefinic products, and the remainder (about 8 mls) was added to a suspension of lithium aluminium hydride (about 0.1g), and the mixture was refluxed for 2 hours. The solution was then cooled, and water was added. The solution was acidified and extracted twice with ether. The combined ether layers were washed with brine, and analysed by g.l.c. for the alcohol fraction. Each solution was analysed at least four times, and the determination of individual peak areas was repeated until concordant results were obtained. The percentage yield of the product that a peak area represents, is given by the formula:

$$\% \text{ yield} = \frac{\text{peak area for the product}}{\text{peak area for the hydrocarbon standard}} \times \frac{1}{\text{m.r.f.}}$$

$$\times \frac{\text{no. of moles hydrocarbon standard}}{\text{no. of moles tosylate}} \times 100$$

The percentage yields for all the products were summed to give the total recovery, which varied from 100-108%.

The yields of the individual products were then normalized by dividing them by the total recovery. The whole solvolysis procedure was then repeated, and mean normalized percentage yields were calculated for each product.

A blank solution was also analysed, i.e. 5 mls of the standard acetolysis mixture was added to the solution of tri-potassium orthophosphate, and the mixture was extracted with ether. This solution was tested by g.l.c., then treated with lithium aluminium hydride, worked up and retested. This procedure showed that three small peaks which appeared in the product chromatograms were due to traces of impurities in the buffer solution, and were thus not products of the tosylate solvolysis.

Formolysis The method had to be slightly adapted from that used in acetolysis because of the low solubility of the hydrocarbons in the formolysis medium. Into a 10 ml volumetric flask were accurately weighed 20-30mg each of the tosylate, and of the hydrocarbon markers. The formolysis solution (ca. 3.5ml) was added, the flask was tightly stoppered, shaken to dissolve the tosylate, and placed in a water bath at 25°C for 10 half-lives. It was then removed from the bath, cooled in ice, and ether was added to make the solution homogeneous. The solution was added slowly to an ice-cold

solution of tri-potassium orthophosphate, and the analysis was then performed as for acetolysis. The recovery varied from 105-109%.

50% aqueous ethanol In this solvent system too, the insolubility of the hydrocarbons required that they should be weighed out at the same time as the tosylate, as in formolysis. Again about 30mg of each was used. Spectroscopic ethanol (7ml) was added to dissolve the tosylate, then an aqueous solution of the borax buffer (7ml; 0.03M). The flask was stoppered and placed in a water bath at 36° for at least 10 half-lives. It was then cooled in ice, and ether was added. The solution was transferred to a separating funnel, saturated with sodium chloride, and extracted between sodium hydroxide and ether. The combined ether layers were then analysed by g.l.c. for olefins, ethers, and alcohols. The recovery varied between 107% and 113%.

98% ethanol A standard solution was prepared by weighing out accurate amounts of the hydrocarbon markers, and 1,4-diazabicyclo[2, 2, 2]octane (recrystallized from pentane; sublimed) as buffer into a volumetric flask, and making the solution up to the mark with 98% ethanol. About 40-50mg of tosylate were weighed into a 5ml volumetric flask, and the solution was made up to the mark with 98% ethanol containing the buffer and markers. This solution was about 0.04M in tosylate, and 0.03M in 1,4-diazabicyclo[2, 2, 2]-octane. It was transferred to a glass ampoule which was then sealed, and immersed in a water bath at the required temperature for at least 10 half-lives. The ampoule was withdrawn, cooled in ice, and opened, and ether was added to ensure homogeneity. The solution was then transferred to a separating funnel, and extracted between ether and brine. The combined ether layers were washed

with dilute hydrochloric acid and brine, then analysed by g.l.c. The recovery ranged from 106-110%.

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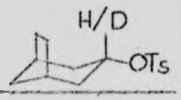
A P P E N D I X

I KINETIC RESULTS

All rate constants are x 10^{-5} sec^{-1}

A. ∝- Kinetic Isotope Effects

Acetolysis of 

(a) T = 60.6°C

k_H	k_D	k_H/k_D
4.690	3.873	1.2108
4.368	3.805	1.1481
4.302	3.863	1.1135
4.615	3.895	1.1848

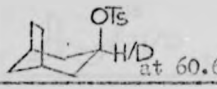
$\overline{k_H}$ = (4.46 ± 0.08) x 10^{-5} sec^{-1} $\overline{k_H/k_D}$ = 1.16 ± 0.02

These results were repeated at a higher temperature to give a more precise isotope effect which is quoted in the text.

(b) T = 70.6°C

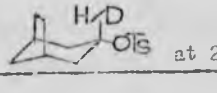
k_H	k_D	k_H/k_D
14.02	12.02	1.1663
14.51	12.80	1.1338
14.08	11.93	1.1798
14.25	12.29	1.1592
15.30	13.01	1.1756

$\overline{k_H}$ = (14.4 ± 0.2) x 10^{-5} sec^{-1} $\overline{k_H/k_D}$ = 1.163 ± 0.008

Acetolysis of  at 60.6°C

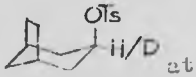
k_H	k_D	k_H/k_D
61.98	52.37	1.1839
61.83	53.60	1.1536
61.23	54.13	1.1314
63.23	54.87	1.1523
66.37	55.82	1.1889
65.48	55.87	1.1784
63.42	53.03	1.1945
63.46	54.18	1.1715

$\overline{k_H} = (63.4 \pm 0.6) \times 10^{-5}$ sec^{-1} $\overline{k_H/k_D} = 1.169 \pm 0.008$

Formolysis of  at 24.8°C

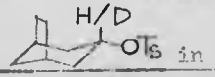
k_H	k_D	k_H/k_D
10.75	8.868	1.2272
11.26	9.177	1.2123
10.48	8.413	1.2460
9.923	8.302	1.1953
10.93	9.442	1.1576
10.26	8.728	1.1757
10.32	8.902	1.1592

$\overline{k_H} = (10.6 \pm 0.2) \times 10^{-5}$ sec^{-1} $\overline{k_H/k_D} = 1.20 \pm 0.01$

Formolysis of  at 24.8°C

k_H	k_D	k_H/k_D
340.4	281.2	1.2105
335.7	284.8	1.1787
325.7	285.7	1.1400
329.7	278.9	1.1821
338.8	296.5	1.1427
327.0	294.5	1.1104
333.5	284.8	1.1709
333.4	280.9	1.1868

$\bar{k}_H = (333 \pm 2.0) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.17 \pm 0.01$

Solvolysis of  in 50% aqueous ethanol

(a) Borax concentration = 3.5×10^{-3} M; T = 24.6°C

k_H	k_D	k_H/k_D
1.100	0.8617	1.2766
1.042	0.8450	1.2326
1.062	0.9083	1.1688
1.105	0.8867	1.2462
0.9267	0.7400	1.2630
0.9017	0.7117	1.3372
1.182	0.9817	1.2037

$\bar{k}_H = (1.04 \pm 0.03) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.24 \pm 0.02$

These results are imprecise, and have been repeated at a higher temperature.

(b) Borax concentration = 3.5×10^{-3} M; T = 36.0°C

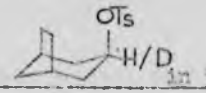
k_H	k_D	k_H/k_D
4.055	3.432	1.1846
4.095	3.315	1.2353
4.620	3.893	1.1866
4.248	3.585	1.1850
4.302	3.583	1.2005
4.238	3.548	1.1945

$\overline{k_H} = (4.26 \pm 0.08) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.198 \pm 0.008$

(c) No buffer; T = 36.0°C

k_H	k_D	k_H/k_D
3.860	3.220	1.1988
3.608	3.070	1.1754
3.723	3.148	1.1826
3.750	3.133	1.1968

$\overline{k_H} = (3.74 \pm 0.05) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.188 \pm 0.008$

Solvolysis of 

in 50% aqueous ethanol

(a) Borax concentration = 3.5×10^{-3} M; T = 24.8°C

k_H	k_D	k_H/k_D
47.18	38.97	1.2111
51.08	41.40	1.2340
49.22	39.88	1.2338
50.95	41.57	1.2256
48.02	40.03	1.2000
48.85	40.78	1.1979
48.63	40.80	1.1923

$\overline{k_H} = (49.1 \pm 0.6) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.213 \pm 0.007$

(b) Borax concentration = 8.9×10^{-3} M; T = 24.8

k_H	k_D	k_H/k_D
46.92	40.07	1.1709
48.75	40.73	1.1968
47.93	40.87	1.1727
48.78	40.67	1.1997
48.88	40.93	1.1941
48.23	40.83	1.1810

$\overline{k_H} = (48.3 \pm 0.3) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.186 \pm 0.005$

(c) Conditions as in (b) but using a Gilford 2400 spectrophotometer

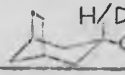
k_H	k_D	k_H/k_D
48.33	40.12	1.2050
48.23	39.87	1.2099
47.12	38.97	1.2092
48.87	40.73	1.1993
49.50	41.33	1.1976

$\overline{k_H} = (48.4 \pm 0.4) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.204 \pm 0.003$

(d) Conditions as in (b) using the protium compound in both cell positions

k_H (Posn. A)	k_H (Posn. B)	$\frac{k_H \text{ (Posn. A)}}{k_H \text{ (Posn. B)}}$
45.68	45.68	1.0000
46.32	43.95	1.0537
44.62	45.48	0.9811
47.70	47.33	1.0008
42.07	43.87	0.9589
46.02	46.20	0.9959

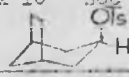
$\overline{\frac{k_H \text{ (Posn. A)}}{k_H \text{ (Posn. B)}}} = 1.00 \pm 0.01$

Solvolysis of 

in 80% aqueous ethanol at 55.0°C

k_H	k_D	k_H/k_D
5.175	4.363	1.1860
5.268	4.540	1.1604
5.068	4.285	1.1828
5.143	4.298	1.1966
4.922	4.230	1.1635

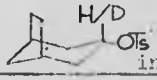
$\overline{k_H} = (5.12 \pm 0.06) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.178 \pm 0.007$

Solvolysis of 

in 80% aqueous ethanol at 55.0°C

k_H	k_D	k_H/k_D
160.4	140.4	1.1421
162.8	136.3	1.1949
157.3	138.7	1.1339
167.3	140.7	1.1894
160.3	134.2	1.1946
167.2	141.4	1.1818
168.3	140.3	1.1899
169.0	141.9	1.1910

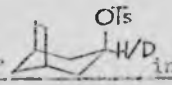
$\overline{k_H} = (16[illegible] \pm 2) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.177 \pm 0.0[illegible]$

Solvolysis of 

in 98% aqueous ethanol at 70.1°C

k_H	k_D	k_H/k_D
5.108	4.280	1.1935
4.900	4.170	1.1751
4.877	4.150	1.1751
4.872	4.143	1.1758
5.150	4.418	1.1656
4.995	4.110	1.2153

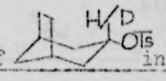
$\overline{k_H} = (4.98 \pm 0.05) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.183 \pm 0.007$

Solvolysis of 

in 98% aqueous ethanol at 60.4°C

k_H	k_D	k_H/k_D
35.28	31.03	1.1369
34.68	30.50	1.1372
35.40	30.85	1.1475
34.75	30.37	1.1443
36.60	32.18	1.1378

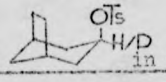
$\overline{k_H} = (35.4 \pm 0.3) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.141 \pm 0.002$

Solvolysis of 

in 97% aqueous trifluoroethanol at 41.4°C

k_H	k_D	k_H/k_D
6.253	5.208	1.2006
6.377	5.262	1.2119
6.117	4.998	1.2237
6.475	5.420	1.1947
6.388	5.405	1.1819

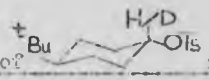
$\overline{k_H} = (6.32 \pm 0.06) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.203 \pm 0.007$

Solvolysis of 

in 97% aqueous trifluoroethanol at 41.4°C

k_H	k_D	k_H/k_D
118.9	100.4	1.1843
118.2	97.88	1.2072
118.6	100.3	1.1824
117.2	97.97	1.1961
118.0	100.8	1.1711

$\overline{k_H} = (118.8 \pm 0.3) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.188 \pm 0.006$

Acetolysis of  at 79.6°C

k_H	k_D	k_H/k_D
6.865	6.177	1.1114
8.848	8.057	1.0983
8.108	7.148	1.1343
8.528	7.165	1.1873
7.528	6.702	1.1232
7.647	6.747	1.1335

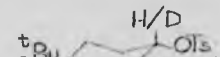
$\overline{k_H} = (7.92 \pm 0.3) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.13 \pm 0.01$

Acetolysis of  at 79.6°C

k_H	k_D	k_H/k_D
22.67	19.48	1.1630
21.98	18.52	1.1866
17.20	14.63	1.1761
18.74	16.04	1.1674
13.57	11.65	1.1648

$\overline{k_H} = (18.8 \pm 2) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.172 \pm 0.004$

The imprecision in the rate constant does not lead to a high error in the isotope effect, since the former is due to temperature variations between runs, which cancel out when the ratios are taken.

Solvolysis of  in 50% aqueous ethanol at 44.8°C

k_H	k_D	k_H/k_D
4.533	3.888	1.1672
4.637	4.023	1.1524
4.192	3.607	1.1622
4.613	4.135	1.1157
4.713	3.933	1.1983
4.583	3.983	1.1506

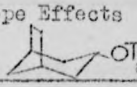
$\bar{k}_H = (4.55 \pm 0.08) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.16 \pm 0.01$

Solvolysis of  in 50% aqueous ethanol at 44.8°C

k_H	k_D	k_H/k_D
22.25	18.52	1.2015
20.50	16.62	1.2330
20.20	17.03	1.1853
21.03	17.77	1.1844
19.42	16.28	1.1930
20.15	16.73	1.2052

$\bar{k}_H = (20.6 \pm 0.4) \times 10^{-5}$ sec^{-1} $\qquad \overline{k_H/k_D} = 1.200 \pm 0.007$

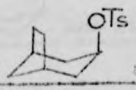
B. β-Deuterium Isotope Effects

Acetolysis of  and its tetradeuterated derivative

T = 70.5°C

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
16.67	8.060	2.0734
	8.060	2.0734
16.16	7.518	2.1490
	7.657	2.1101
15.98	7.183	2.2244
	7.275	2.1963

$\overline{k_H/k_{\beta D_4}} = 2.14 \pm 0.03$

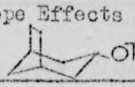
Acetolysis of  and its tetradeuterated derivative

T = 61.4°C

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
70.96	29.33	2.4194
	29.57	2.4000
72.53	29.20	2.4836
	29.15	2.4885
69.76	28.55	2.4435
	29.98	2.3268

$\overline{k_H/k_{\beta D_4}} = 2.43 \pm 0.03$

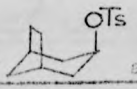
B. β-Deuterium Isotope Effects

Acetolysis of  and its tetradeuterated derivative

T = 70.5°C

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
16.67	8.060	2.0734
	8.060	2.0734
16.16	7.518	2.1490
	7.657	2.1101
15.98	7.183	2.2244
	7.275	2.1963

$\overline{k_H/k_{\beta D_4}} = 2.14 \pm 0.03$

Acetolysis of  and its tetradeuterated derivative

T = 61.4°C

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
70.96	29.33	2.4194
	29.57	2.4000
72.53	29.20	2.4836
	29.15	2.4885
69.76	28.55	2.4435
	29.98	2.3268

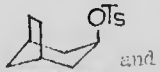
$\overline{k_H/k_{\beta D_4}} = 2.43 \pm 0.03$

Formolysis of  and its tetradeuterated derivative

T = 36.0°C ; Sodium formate concentration = 0.16M

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
45.97	18.96	2.4254
	19.43	2.3665
46.10	19.43	2.3725
	19.26	2.3934
45.73	19.92	2.2961
	19.85	2.3031

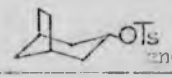
$\overline{k_H/k_{\beta D_4}}$ = 2.36 ± 0.02

Formolysis of  and its tetradeuterated derivative

T = 28.3°C

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
524.3	193.6	2.7079
	194.6	2.6940
495.1	189.2	2.6174
	186.9	2.6497
529.9	184.4	2.8737
	179.2	2.9567

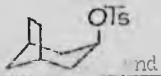
$\overline{k_H/k_{\beta D_4}}$ = 2.75 ± 0.06

Solvolysis of  and its tetradeuterated derivative in 50% aqueous ethanol

T = 46.6°C; Borax concentration = 1.9 x 10^{-3} M

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
17.37	7.915	2.1949
	7.975	2.1783
18.05	8.500	2.1233
	8.253	2.1870
18.36	8.189	2.2425
	8.193	2.2400

$\overline{k_H/k_{\beta D_4}}$ = 2.19 ± 0.02

Solvolysis of  and its tetradeuterated derivative in 50% aqueous ethanol

T = 30.0°C

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
89.98	34.36	2.6184
	33.90	2.6543
86.12	33.75	2.5517
	34.15	2.5218
89.41	34.87	2.5637
	35.13	2.5453

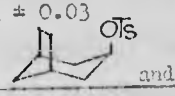
$\overline{k_H/k_{\beta D_4}}$ = 2.58 ± 0.02

Solvolysis of  and its tetradeuterated derivative in 90% aqueous ethanol

T = 69.8°C

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
6.544	3.241	2.0192
	3.359	1.9480
6.332	3.487	1.8159
	3.579	1.7690
6.506	3.370	1.9044
	3.360	1.9297
5.939	3.077	1.9472
	3.011	1.9892

$\overline{k_H/k_{\beta D_4}} = 1.93 \pm 0.03$

Solvolysis of  and its tetradeuterated derivative in 90% aqueous ethanol

T = 60.0°C

k_H	$k_{\beta D_4}$	$k_H/k_{\beta D_4}$
40.23	17.64	2.2799
	17.82	2.2573
41.47	18.71	2.2164
	19.18	2.1621
41.01	18.25	2.2476
	18.45	2.2231

$\overline{k_H/k_{\beta D_4}} = 2.23 \pm 0.02$

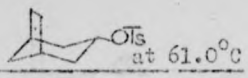
II ANALYSIS OF PRODUCTS

Abbreviations

fm = formate, OH = alcohol, OEt = ethyl ether

2-one	bicyclo[3, 2, 1] oct-2-one
endo-3-ac	endo-bicyclo[3, 2, 1] octan-3-yl acetate
t-2-ac	trans-bicyclo[3, 2, 1] octan-2-yl acetate
2-ac	bicyclo[2, 2, 2] octan-2-yl acetate
c-2-ac	cis-bicyclo[3, 2, 1] octan-2-yl acetate
exo-3-ac	exo-bicyclo[3, 2, 1] octan-3-yl acetate

For each compound, two runs were performed. For each run, 3-5 injections of the final solutions were made, and the area of every peak was measured at least twice by planimeter. The numbers listed under columns 1-5 correspond to the mean areas, converted to percentage yields for a single injection. The mean from all injections for a single run appears at the right-hand side of the page. The normalized values from each run and a final mean from both runs are shown in a separate table.

Acetolysis of  at 61.0°C

Run 1

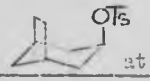
Products	1	2	3	4	Mean
2-ene	70.8	70.2	67.2	67.8	69.0
endo-3-ac	26.0	25.8	26.6	27.5	26.5
t-2-ac	1.8	2.2	2.1	2.3	2.1
2-ac	1.8	2.3	2.2	2.1	1.9
C-2-ac					0.2
exo-3-ac	0.3	0.3	0.3	0.3	0.3
Recovery					100.0

Run 2

Products	1	2	3	4	Mean
2-ene	70.6	73.1	71.3	68.7	70.9
endo-3-ac	27.5	27.5	26.8	26.6	27.1
t-2-ac	2.3	2.2	2.2	1.9	2.2
2-ac	2.2	2.3	2.2	2.0	2.0
C-2-ac					0.2
exo-3-ac	0.2	0.4	0.2	0.2	0.3
Recovery					102.7

Acetolysis of  at 61.0°C

Products	Normalised Mean Run (1)	Normalised Mean Run (2)	Mean
2-one	69.0	69.1	69.0
endo-3-ac	26.5	26.4	26.5
t-2-ac	2.1	2.1	2.1
2-ac	1.9	1.9	1.9
c-2-ac	0.2	0.2	0.2
exo-3-ac	0.3	0.3	0.3

Acetolysis of  at 61.0°C

Run 1

Products	1	2	3	4	Mean
2-one	68.3	65.4	72.7	69.5	69.0
endo-3-ac	0.8	0.9	0.8	0.5	0.8
t-2-ac	7.3	7.5	7.2	7.3	7.3
2-ac)	5.4	5.5	5.4	5.3	4.9
C-2-ac)					0.5
exo-3-ac	15.2	15.3	14.6	15.3	15.1
Recovery					97.6

Run 2

Products	1	2	3	4	Mean
2-one	68.8	76.6	72.6	70.8	72.2
endo-3-ac	0.9	0.6	0.8	0.9	0.8
t-2-ac	8.8	9.2	9.4	9.1	9.1
2-ac)	6.0	6.8	6.8	6.5	5.9
C-2-ac)					0.6
exo-3-ac	16.4	19.2	19.2	19.9	19.2
Recovery					107.8

Acetolysis of 

at 61.0°C

Products	Normalised Mean Run (1)	Normalised Mean Run (2)	Mean
2-ene	70.6	66.9	68.8
endo-3-ac	0.8	0.7	0.8
t-2-ac	7.5	8.4	8.0
2-ac	5.0	5.5	5.2
C-2-ac	0.6	0.6	0.6
exo-3-ac	15.5	17.9	16.6

The maximum possible amount of bicyclo[2,2,2]octene occurring in the acetolyses of the exo or endo tosylate is 0.3%

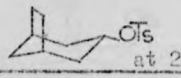
Formolysis of  at 25°C

Run 1

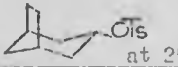
Products	1	2	3	4	5	Mean
2-ene	53.7	56.1	57.4	55.6	57.0	55.9
endo-3-fm	34.4	34.3	32.5	33.5	31.6	33.3
t-2-fm	9.2	9.4	9.2	8.7	8.8	9.0
2-fm)	10.6	10.4	9.7	9.7	9.5	9.3
C-2-fm)						0.7
exo-3-fm	0.6	0.5	0.7	0.7	0.7	0.7
Recovery						108.9

Run 2

Products	1	2	3	4	5	Mean
2-ene	56.9	59.5	57.7	57.6	57.1	57.5
endo-3-fm	31.5	33.4	30.3	32.0	30.0	31.5
t-2-fm	8.2	8.4	8.6	8.3	8.1	8.3
2-fm)	9.1	9.6	9.3	9.3	9.0	9.0
C-2-fm)						0.3
exo-3-fm	0.4	0.5	0.3	0.6	0.5	0.5
Recovery						107.1

Formolysis of  at 25.0°C

Products	Normalised Mean Run 1	Normalised Mean Run 2	Mean
2-ene	51.3	53.8	52.6
endo-3-fm	30.6	29.4	30.0
t-2-fm	8.3	7.8	8.0
2-fm	8.5	8.3	8.4
c-2-fm	0.7	0.3	0.5
exo-3-fm	0.6	0.4	0.5

Formolysis of  at 25.0°C

Products	Normalised Mean Run 1	Normalised Mean Run 2	Mean
2-ene	51.3	53.8	52.6
endo-3-fm	30.6	29.4	30.0
t-2-fm	8.3	7.8	8.0
2-fm	8.5	8.3	8.4
C-2-fm	0.7	0.3	0.5
exo-3-fm	0.6	0.4	0.5

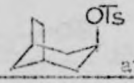
Formolysis of  at 25.0°C

Run 1

Products	1	2	3	4	5	Mean
2-ene	46.1	49.3	52.4	52.6	52.1	50.5
endo-3-fm	0.6	0.5	0.9	0.7	0.8	0.7
t-2-fm	20.3	19.2	21.1	21.1	23.0	21.0
2-fm	18.6	18.2	19.2	19.2	20.7	17.7
C-2-fm						1.5
exo-3-fm	16.9	15.7	17.6	18.3	18.0	17.3
Recovery						108.7

Run 2

Products	1	2	3	4	5	Mean
2-ene	48.1	48.1	48.8	46.7	49.1	48.2
endo-3-fm	0.9	0.8	0.8	0.9	0.6	0.8
t-2-fm	19.8	21.9	19.5	21.1	21.0	20.6
2-fm	18.1	19.9	13.5	19.0	19.1	17.9
C-2-fm						1.0
exo-3-fm	16.4	16.7	16.9	16.5	16.9	16.7
Recovery						105.2

Formolysis of  at 25.0°C

Products	Normalised Mean Run 1	Normalised Mean Run 2	Mean
2-ene	46.4	45.9	46.0
endo-3-fm	0.7	0.7	0.7
t-2-fm	19.3	19.6	19.5
2-fm	16.3	17.0	16.7
C-2-fm	1.4	0.9	1.2
exo-3-fm	15.9	15.8	15.9

The maximum possible amount of bicyclo[2, 2, 2]octene occurring in the formolyses of the exo or endo tosylate is 0.1%

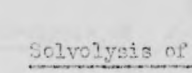
Solvolysis of  in 50% aqueous ethanol at 36.0°C

Run 1

Products	1	2	3	4	Mean
2-ene	46.0	46.9	50.7	43.4	46.8
endo-3-OH	49.7	52.2	50.6	49.8	50.6
t-2-OH	2.2	2.3	2.3	2.1	2.2
2-OH	2.3	2.9	2.1	2.8	2.5
exo-3-OH	0.4	0.4	0.3	0.3	0.4
endo-3-OEt	9.7	9.5	9.6	9.2	9.5
t-2-OEt	0.4	0.4	0.4	0.5	0.4
2-OEt	0.4	0.5	0.5	0.5	0.5
Recovery					112.9

Run 2

Products	1	2	3	4	Mean
2-ene	44.4	45.0	44.0	44.2	44.4
endo-3-OH	52.0	53.7	53.6	50.2	52.4
t-2-OH	2.2	2.3	2.3	2.2	2.3
2-OH	2.3	2.5	2.8	2.4	2.5
endo-3-OEt	9.9	10.3	10.4	10.0	10.2
t-2-OEt	0.4	0.3	0.5	0.5	0.4
2-OEt	0.7	0.4	0.6	0.7	0.6
Recovery					112.8

Solvolysis of  in 50% aqueous ethanol at 36.0°C

Products	Normalised Mean Run 1	Normalised Mean Run 2	Mean
2-ene	41.5	39.4	40.4
endo-3-OH	44.9	46.5	45.6
t-2-OH	1.9	2.0	2.0
2-OH	2.2	2.2	2.2
exo-3-OH	0.3	-	0.2
endo-3-OEt	8.4	9.0	8.7
t-2-OEt	0.4	0.4	0.4
2-OEt	0.4	0.5	0.5

The maximum amounts of other products were:

bicyclo[2, 2, 2]oct-2-ene	0.3%
C-2-OH	0.3%
exo-3-OEt	0.1%
C-2-OEt	0.1%

Solvolysis of 

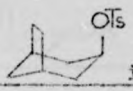
in 50% aqueous ethanol at 36.0°C

Run 1

Products	1	2	3	Mean
2-one	71.3	71.9	71.7	71.6
endo-3-OH	0.5	-	0.5	0.5
t-2-OH	3.3	3.5	4.0	3.6
2-OH	2.1	2.0	2.8	2.3
exo-3-OH	27.0	27.9	28.2	27.7
t-2-OEt	0.5	0.7	0.5	0.6
2-OEt	0.5	0.5	0.5	0.5
exo-3-OEt	6.0	6.1	6.6	6.3
Recovery				113.1

Run 2

Products	1	2	3	4	Mean
2-one	69.7	70.1	66.2	66.2	68.1
endo-3-OH	0.4	0.3	0.5	0.4	0.4
t-2-OH	2.8	3.4	3.2	3.2	3.1
2-OH	2.1	2.0	2.1	2.1	2.1
exo-3-OH	27.1	27.7	24.5	26.3	26.4
t-2-OEt	0.7	0.6	0.5	0.7	0.6
2-OEt	0.6	0.5	0.5	0.5	0.5
exo-3-OEt	6.2	6.2	6.2	6.1	6.2
Recovery					107.4

Solvolysis of 

in 50% aqueous ethanol at 36.0°C

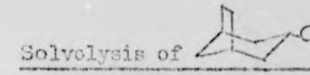
Products	Normalised Mean Run 1	Normalised Mean Run 2	Mean
2-ene	63.3	63.3	63.3
endo-3-OH	0.5	0.4	0.4
t-2-OH	3.2	2.9	3.1
2-OH	1.9	1.6	1.8
C-2-OH	0.2	0.3	0.2
exo-3-OH	24.5	24.6	24.6
t-2-OEt	0.5	0.6	0.5
2-OEt	0.4	0.5	0.5
exo-3-OEt	5.5	5.8	5.6

The maximum possible amounts of other products were:

bicyclo[2, 2, 2]oct-2-ene 0.3%

endo-3-OEt 0.2%

C-2-OEt 0.2%

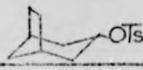
Solvolysis of  in 98% aqueous ethanol at 70.0°C

Run 1

Products	1	2	3	4	Mean
2-ene	40.4	42.7	43.2	41.9	42.0
endo-3-OH	7.1	7.5	7.4	8.0	7.5
t-2-OH	0.1	0.1	0.2	-	0.2
2-OH	0.1	0.1	0.1	-	0.1
exo-3-OH	0.1	0.1	0.1	-	0.1
endo-3-OEt	52.2	57.6	58.4	61.4	57.4
t-2-OEt	0.6	0.8	0.7	0.7	0.7
2-EOt	0.8	0.8	0.8	0.8	0.8
exo-3-OEt	0.9	0.9	0.7	1.1	0.9
Recovery					109.7

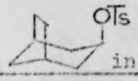
Run 2

Products	1	2	3	4	Mean
2-ene	42.9	42.8	43.5	43.9	43.3
endo-3-OH	6.9	6.6	6.7	7.1	6.8
t-2-OH	-	0.3	0.1	0.2	0.2
2-OH	-	0.3	0.1	0.1	0.1
endo-3-OEt	52.1	52.8	51.9	55.8	53.2
t-2-OEt	0.6	0.6	0.6	0.6	0.6
2-OEt	0.7	0.8	0.7	0.8	0.7
exo-3-OEt	0.7	0.8	0.7	0.7	0.7
Recovery					105.6

Solvolysis of  in 98% aqueous ethanol at 70.0°C

Products	Normalised Mean Run 1	Normalised Mean Run 2	Mean
2-ene	38.4	40.9	39.6
endo-3-OH	6.8	6.5	6.7
t-2-OH	0.1	0.2	0.2
2-OH	0.1	0.1	0.1
exo-3-OH	0.1	-	0.1
endo-3-OEt	52.4	50.3	51.2
t-2-OEt	0.6	0.6	0.6
2-OEt	0.7	0.7	0.7
exo-3-OEt	0.8	0.7	0.8

A limit of less than 0.1% can be placed on the presence of each of bicyclo[2, 2, 2]octene, cis-bicyclo[3, 2, 1]octan-2-ol and cis-bicyclo[3, 2, 1]octan-2-yl ethyl ether.

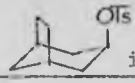
Solvolysis of  in 98% aqueous ethanol at 60.0°C

Run 1

Products	1	2	3	4	5	Mean
2-ene	59.9	60.0	60.7	-	-	60.2
endo-3-OH	0.1	-	0.1	0.1	0.1	0.1
t-2-OH	0.2	0.2	0.2	0.2	0.2	0.2
2-OH	0.1	0.1	0.1	0.1	0.1	0.1
exo-3-OH	4.9	4.5	4.7	4.7	4.7	4.7
endo-3-OEt	0.6	0.6	0.6	0.6	0.6	0.6
t-2-OEt	1.1	0.9	1.0	1.0	1.0	1.0
2-OEt	0.6	0.6	0.6	0.7	0.6	0.6
exo-3-OEt	40.0	38.7	40.1	39.0	39.2	39.5
Recovery						107.0

Run 2

Products	1	2	3	4	Mean
2-ene	63.0	60.8	60.0	63.2	61.7
endo-3-OH	-	0.1	0.1	0.1	0.1
t-2-OH	0.3	0.3	0.4	0.5	0.4
2-OH	0.1	0.1	0.2	0.1	0.1
exo-3-OH	5.1	4.8	4.8	4.7	4.9
endo-3-OEt	0.7	0.7	0.6	0.5	0.6
t-2-OEt	1.1	1.1	1.1	1.0	1.1
2-OEt	0.7	0.7	0.7	0.7	0.7
exo-3-OEt	41.4	38.2	40.1	37.3	39.3
Recovery					108.9

Solvolysis of 

in 98% aqueous ethanol at 60°C

Products	Normalised Mean Run 1	Normalised Mean Run 2	Mean
2-ene	56.2	56.7	56.3
endo-3-OH	0.1	0.1	0.1
t-2-OH	0.2	0.3	0.3
2-OH	0.1	0.1	0.1
exo-3-OH	4.4	4.5	4.5
endo-3-OEt	0.6	0.6	0.6
t-2-OEt	0.9	1.0	1.0
2-OEt	0.6	0.6	0.6
exo-3-OEt	36.9	36.1	36.5

A limit of less than 0.1% can be placed on the presence of each of bicyclo[2, 2, 2] octene, cis-bicyclo[3, 2, 1] octan-2-ol, and cis-bicyclo[3, 2, 1] octan-2-yl ethyl ether.