

SOLVOLYSIS OF DEUTERATED
NORBORNYL BROMIDES

by
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A Dissertation Submitted to the Faculty of the
DEPARTMENT OF CHEMISTRY
In Partial Fulfillment of the Requirements
For the Degree of
DOCTOR OF PHILOSOPHY
In the Graduate College
THE UNIVERSITY OF ARIZONA

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SIGNED:

Michael J. Dagani

To my wife.

ACKNOWLEDGMENT

The author wishes to thank Dr. John P. Schaefer for his aid throughout the course of this investigation.

The author also acknowledges the receipt of a National Science Foundation Graduate Traineeship (1965-1967).

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ABSTRACT

The β -deuterium isotope effect observed for the solvolysis of 3,3- d_2 -endo-2-norbornyl bromide in 50% aqueous ethanol was 1.6 per deuterium. The α -deuterium isotope effect for the solvolysis of 2- d_1 -endo-2-norbornyl bromide ($k_H/k_D = 1.28$ per deuterium) in 50% aqueous ethanol was calculated from the observed isotope effect of 2,3,3- d_3 -endo-2-norbornyl bromide and 3,3- d_2 -endo-2-norbornyl bromide in 50% aqueous ethanol.

Comparison of the β -deuterium isotope effect of 3,3- d_2 -endo-2-norbornyl bromide with the isotope effect of 3,3- d_2 -exo-2-norbornyl bromide ($k_H/k_D = 1.04$ per deuterium) in aqueous acetic acid-sodium acetate provides strong supporting evidence that the formation of the transition state in the solvolysis of exo-norbornyl derivatives is anchimerically assisted and proceeds via a nonclassical carbonium ion, but that the solvolysis of endo-norbornyl derivatives proceeds with unassisted solvolysis to a classical carbonium ion.

The deuterated endo-2-norbornyl bromides were prepared by the catalytic hydrogenation of the Diels-Alder adduct of cyclopentadiene and the appropriately deuterated vinyl bromides. The catalytic deuteration of 2-bromo-2-norbornene using platinum as the catalyst led to scrambling of the deuterium atoms in the endo-2-norbornyl bromide.

Direct displacement reactions of various exo-2-norbornyl derivatives by electronegative halogen were attempted but these reactions

did not proceed by the usual SN2 mechanism. The implication of these results is discussed.

INTRODUCTION

1. Theoretical Aspects of Isotope Effects

An isotope effect may be described as any change which occurs in the chemical or physical properties of a compound upon isotopic substitution. This subject has recently been reviewed by Melander¹ who summarizes the current status of the theory of isotope effects.

The majority of isotope effect studies have been concerned with establishing differences in rate constants for two isotopically different species of the same compound. The largest amount of work has been done with hydrogen versus deuterium since the kinetic isotope effects are usually large and easily measured.

Two main types of kinetic isotope effects have been studied and reported:

1. primary isotope effects, in which rate differences between two species which differ only in isotopic substitution are due to the breaking or formation of the isotopic bonds, and
2. secondary isotope effects, in which isotopically different chemical bonds are not broken or formed in the reaction.

The secondary isotope effect is further distinguished by α -deuterium and β -deuterium isotope effects. In the former, the deuterium atom is α to the reacting bond and in the latter, the deuterium atom is β to the reacting bond.

Molecules possess vibrational energy even in their lowest possible energy state. This can be seen from the equation for the

vibrational energy of a molecule

$$E = h(m + \frac{1}{2})\nu \quad (1)$$

in which only certain energy levels are allowed. The vibrational quantum number is symbolized by m and may be any integer; ν is the frequency of the vibration and h is Planck's constant. When m is equal to zero (the lowest possible energy state) the vibrational energy is equal to one-half the frequency times Planck's constant and is called the zero-point energy.

If a diatomic molecule, A-B, is taken as a model, the vibrational frequencies, ν_1 and ν_2 , can be calculated for the two isotopic species A-B₁ and A-B₂. The assumption that a molecule behaves as a simple harmonic oscillator gives the frequency of vibration as

$$\nu = \frac{1}{2\pi} \sqrt{\frac{k}{\mu}} \quad (2)$$

where k is the force constant (considered equal for two isotopic species) and μ is the reduced mass. Substituting μ_1 and μ_2 into equation 2 and taking the ratio of ν_1 and ν_2 leads to

$$\frac{\nu_1}{\nu_2} = \frac{m_{B2}(m_A + m_{B1})}{m_{B1}(m_A + m_{B2})} \quad (3)$$

from which it follows that ν_1 should be greater than ν_2 when m_{B2} is greater than m_{B1} .

When the A-B bond is broken, the rate process depends on the activation energy, which is the energy required to raise a molecule

from its ground state to the transition state. In the transition state the A-B bond has been stretched far enough so that there is no restoring force to pull the molecule back together and the vibrational energy levels of the two transition states become equivalent.

A calculation of the activation energy is difficult, but the difference in activation energies may be calculated easily

$$E_{A-B_1} - E_{A-B_2} = \frac{1}{2}h\nu \left(1 - \sqrt{\frac{m_{B1}(m_A + m_{B2})}{m_{B2}(m_A + m_{B1})}} \right) \quad (4)$$

and the molecule containing the A-B₁ bond (light isotope) has a larger zero-point energy than the one with the A-B₂ bond (heavy isotope) by the amount in equation 4. When the A-B bond is broken, the vibrational energy disappears, as do the isotopically caused differences in vibrational energies. The transition states for the cleavage of A-B₁ and A-B₂ bonds will therefore have identical energies, and the activation energy for the cleavage of A-B₂ will be greater than for A-B₁, since A-B₂ starts from a lower energy level in the ground state. Therefore, A-B₁ will cleave faster than A-B₂. Reference to a Morse potential energy diagram (Figure 1) illustrates these differences.

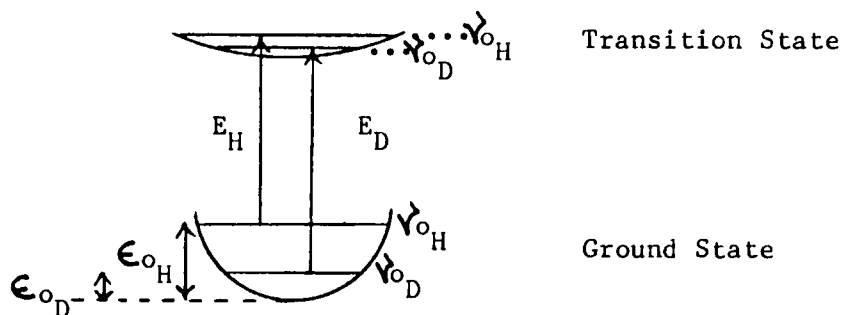
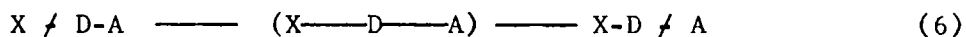
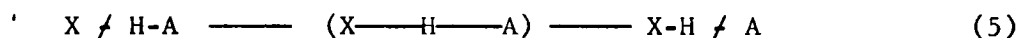


Figure 1. Diagram Showing the Effect of Deuterium Substitution on Reaction rates.

Figure 1 illustrates a case for which a bond has a smaller force constant in the transition state than in the reactant, and the zero-point energy difference in the ground state is larger than the zero-point energy difference in the transition state.

If the vibrational frequency is the same in the reactant and in the transition state, it does not contribute to the isotope effect. Thus for two isotopic species having frequencies ν_1 and ν_2 , the difference in zero-point energy for both the reactants and the transition states is $\frac{1}{2}h(\nu_1 - \nu_2)$. Since the activation energy is just this energy, all terms of this type are equivalent and will cancel. Because of these cancellations, it is often possible to approximate the isotope effect of polyatomic molecules using simpler models.^{2,3,4}

Consider the reactions



The zero-point energy for the reactants is obtained from the stretching frequencies of the H-A and D-A bonds, but the transition state is a linear triatomic molecule with four modes of vibration: asymmetric stretch, symmetric stretch, and two degenerate bending modes. The asymmetric stretch represents transfer of hydrogen and is called the motion along the reaction coordinate; to a first approximation it does not affect the zero-point energy.

In the symmetric stretch, H will remain stationary during the vibration and the frequencies for X - H - A and X - D - A will be identical. Thus the stretching contribution to the isotope effect will be

determined by the zero-point energy difference for the H-A and D-A stretching frequencies of the reactant. If the H-A bond is stronger than the X-H bond in the transition state, then the symmetric stretching frequency will be smaller for X - D - A than for X - H - A. This difference in zero-point energy will partially cancel the difference between H-A and D-A in the reactants and will give a smaller isotope effect. When the X-H bond is stronger than the H-A bond in the transition state, a smaller isotope effect will also be observed. Consequently, when the proton is half transferred in the transition state, a maximum deuterium isotope effect is to be expected, and a smaller isotope effect is to be expected when it is either more or less than half transferred. These considerations apply to symmetrical transition states; extension of these notions to non-ideal systems is readily accomplished.

The role of the two degenerate bending frequencies contributing to the isotope effect does not seem to be well known,¹ and further discussion will be deferred.

2. β -Secondary Deuterium Isotope Effects

A secondary isotope effect can be observed provided a bond to an isotopic atom is either strengthened or weakened in going from the reactant to the transition state. If a C-H bond is weaker in the transition state than in the reactant, the motions of the bond will be of lower frequency in the transition state and will contribute less to the zero-point energy. Thus the two isotopic transition states will be closer in zero-point energy than the two isotopic reactants, and the

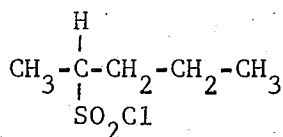
activation energy for the lighter species is lower, implying that the lighter species will react faster than the heavier species.

These secondary isotope effects are seldom greater than 40%, while primary isotope effects may be 600% or greater. Also, secondary isotope effects may be inverse; i.e., the deuterium compound reacts faster than the protium compound, if bonds to the deuterium atom become stronger in the transition state than in the reactant.

The remainder of this discussion will apply to secondary deuterium isotope effects in solvolytic reactions. These effects are believed to arise from the weakening of C-H or C-D bonds during the ionization of a suitable organic compound to a carbonium ion. The bond weakening reduces the contribution of vibrational modes involving these bonds to the zero-point energy of the transition state. Therefore, the difference between the deuterium compound and the protium compound will be narrower in the transition state than for the reactants (see Figure 1). Consequently, the deuterated compound will have a higher activation energy and will react slower than the protium compound.

The physical, chemical, and theoretical aspects of secondary isotope effects have been thoroughly reviewed by Halevi.⁵

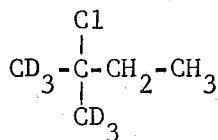
The first secondary deuterium isotope effect was reported by Lewis and Boozer.⁶ They found that the rate of decomposition of 2-pentyl chlorosulfite (1) in dioxane was retarded when the hydrogen atoms in the β -position were replaced by deuterium. The observed k_H/k_D ratio was about 1.4.



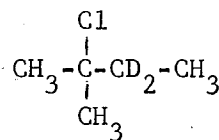
1

The products of the reaction were a mixture of 2-pentenes and 2-chloropentane, which probably were formed from the intermediate carbonium ion. The possibility that hyperconjugation might be responsible for the solvolytic β -deuterium isotope effect was also mentioned by Lewis and Boozer.⁶

Shiner⁷ studied the effect of β -deuterium substitution in *t*-amyl chloride solvolysis in 80% aqueous ethanol; the observed $k_{\text{H}}/k_{\text{D}}$ ratio for 2 and 3 was 1.78 and 1.41, respectively.



2

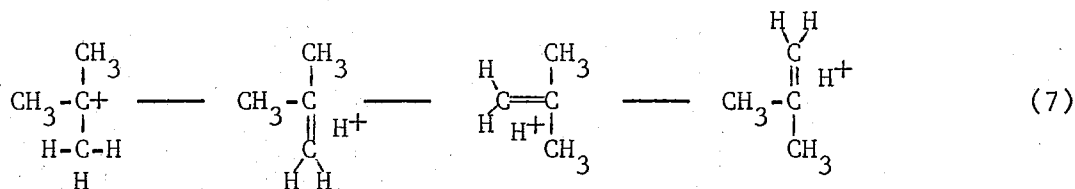


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These isotope effects were reported for tertiary chlorides and presumably refer to SN1 reactions. When the β -deuterium isotope effect for the SN2 reaction of 2-*d*-isopropyl bromide with sodium ethoxide in ethanol was studied, an isotope effect of unity was observed.⁸

These initial experiments led to the conclusion that secondary β -deuterium isotope effects are appreciable only for SN1 solvolyses. When the reaction mechanism involves a bimolecular displacement or if the reaction becomes borderline between SN2 and SN1, then much smaller or even inverse isotope effects can and do occur.

The effect of β -hydrogen atoms in stabilizing positive charge has long been known as hyperconjugation,⁹ and was originally introduced to account for the special properties of conjugated dienes. The greater stabilization of a carbonium ion derived from t-butyl chloride compared to methyl chloride was related to the contribution of the following structures for the t-butyl carbonium ion:



Contributions of these non-bonded structures weaken the bonds to the β -hydrogen atoms and therefore must reduce the corresponding C-H vibration frequencies, which will be less in the carbonium ion than in the reactant. The same factor applies to the transition state, but to a smaller extent, since the configuration of the transition state is intermediate between the reactant and the carbonium ion. Therefore, the vibrational energy of the C-H bonds (β -hydrogens) should be less in the transition state for SN1 solvolysis of t-butyl chloride than in the reactant (t-butyl chloride). The activation energy for solvolysis should be decreased by an amount equal to this vibrational energy. If the hydrogen atoms on the β -carbon are replaced by deuterium, the total vibrational energy decreases and so will the change in energy decrease when the chloride is solvolyzed. This should lead to a rate retardation of t-butyl-d₉ chloride solvolysis relative to t-butyl chloride.

The above discussion can be applied to the β -deuterium isotope effects of a series of compounds undergoing hydrolysis. The results of Leffek and co-workers¹⁰ are summarized in Table 1.

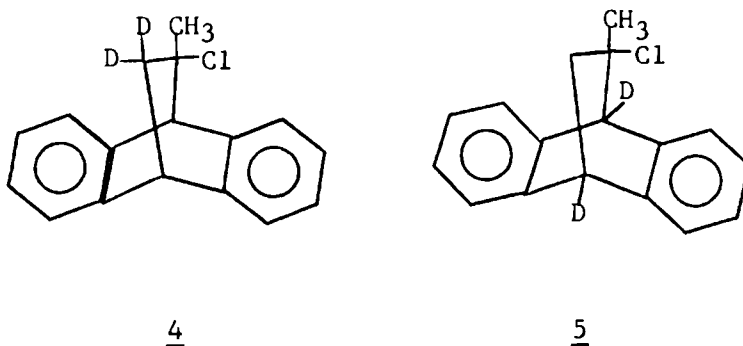
Table 1. Effect of β -Deuteration of Alkyl Derivatives in Hydrolysis.

Compound	Temperature (°C)	k_H/k_D
ethyl- \underline{d}_3 p-toluenesulphonate	60	1.01
ethyl- \underline{d}_3 methanesulphonate	60	1.02
ethyl- \underline{d}_3 bromide	80	1.03
ethyl- \underline{d}_3 iodide	80	1.03
isopropyl- \underline{d}_6 p-toluenesulphonate	30	1.55
isopropyl- \underline{d}_6 methanesulphonate	30	1.54
isopropyl- \underline{d}_6 bromide	60	1.33
isopropyl- \underline{d}_6 iodide	60	1.31
\underline{t} -butyl- \underline{d}_9 chloride	2	2.56

From the data of Table 1, it can be seen that the magnitude of the total isotope effect increases as the transition state becomes more ionic. A comparison of isopropyl sulphonates ($k_H/k_D = 1.55$) with isopropyl halides ($k_H/k_D = 1.33$) seems to indicate that the transition state for the sulphonate solvolysis is more ionic and involves greater electron withdrawal from neighboring bonds than the transition state for the isopropyl halides. Further consideration of the ethyl

derivatives seems to indicate that solvent participation is occurring; i.e., the reaction is no longer SN1. The distinction among SN1, SN2, and borderline solvolysis mechanisms has been used widely in secondary isotope effect studies.

One of the special properties exhibited by hyperconjugative interaction between a single bond and an adjacent p-orbital is that of angular dependence. Shiner¹¹ determined the β -deuterium isotope effect in the solvolysis of compounds 4 and 5 in 60% aqueous ethanol.



In these compounds the C-D bond axis is fixed in a direction perpendicular to the axis of the developing p-orbital. The observed isotope effects for 4 and 5 at 45° were 1.14 and 0.986, respectively. Compound 4 shows a typical isotope effect for carbonium ion solvolysis, but compound 5 exhibits an inverse isotope effect. These results support the idea that normal β -deuterium isotope effects are mainly due to hyperconjugation and that the inductive effect, as measured by the bridge-head deuterated compound (5), is small.

Shiner¹² has shown that there is a strong conformational dependence in β -deuterium isotope effects, and he predicted that rate retardations caused by successive replacements of the hydrogen atoms of a methyl group adjacent to a solvolyzing center would not be precisely cumulative. Consequently, Shiner and co-workers¹³ synthesized and measured the solvolysis rates of mono-, di-, tri-, hexa-, and nonadeuterated t-butyl chlorides in 60% aqueous ethanol. A summary of their results is given in Table 2.

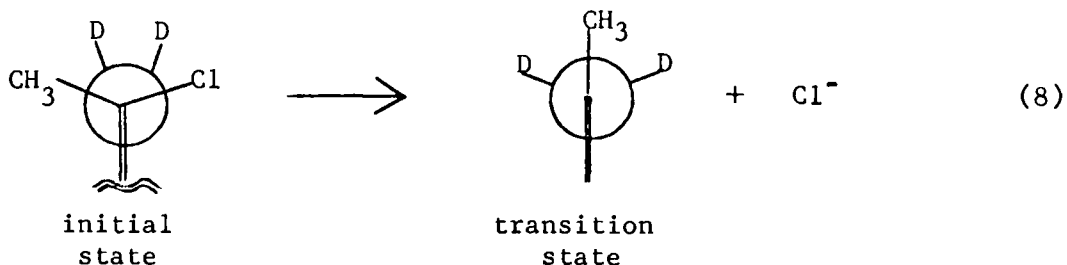
Table 2. Isotope Effects of Deuterated t-Butyl Chlorides in 60% Aqueous Ethanol at 25°.

Compound	k_H/k_D	k_H/k_D per D
$(CH_3)_2CClCH_2D$	1.092	1.092
$(CH_3)_2CClCHD_2$	1.202	1.096
$(CH_3)_2CClCD_3$	1.330	1.100
$(CD_3)_2CClCH_3$	1.710	1.102
$(CD_3)_3CCl$	2.327	1.103

The results show that the isotope effect per deuterium atom increases as the amount of methyl group deuteration increases. As the extent of deuteration of one, two, or three methyl groups increases, the isotope effect per deuterium atom is almost constant, and not quite cumulative. The rate retardations caused by complete deuteration of one, two, and three methyl groups are more nearly cumulative. Calculations by Shiner

and co-workers¹³ indicate that the results are consistent with a strong conformational dependence of the isotope effect and are readily explained if it is assumed that the isotope effect per deuterium substitution trans to the leaving group (chloride) in the transition state is about 1.31, while that for deuterium substitution in the gauche conformation is about 1.01.

Shiner and Humphrey¹⁴ calculated the relationship of the isotope effect as a function of the dihedral angle for compound 4. If the conformations of the initial state and the carbonium ion for compound 4 are represented as

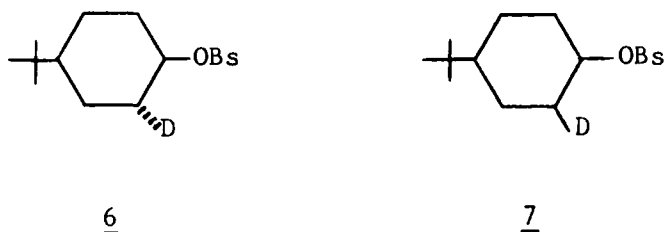


then the variation of k_H/k_D with conformation seems to be

Dihedral angle	30°	60°	90°	180°
k_H/k_D	1.07	1.01	0.99	1.31

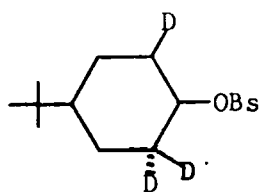
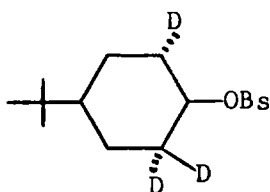
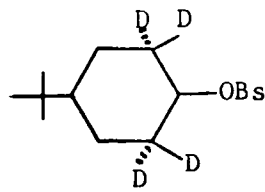
These results, which correlate well with hyperconjugation and the expected angular dependence, are not correlated by relief of non-bonded repulsions on activation, which Bartell¹⁵ suggested as the reason for β -deuterium isotope effects in carbonium ion reactions.

Further studies of conformational dependence were made by Shiner and Jewett,¹⁶ who reported the isotope effects for the solvolysis of compounds 6 and 7 in 50% aqueous ethanol.



The conformation of the initial and the transition state for 6 has a dihedral angle between the leaving group and the β -carbon-hydrogen bond axis of 180° and a dihedral angle of 60° for compound 7. The isotope effects were 1.096 and 1.436 for compounds 6 and 7, respectively, and the conformational dependence predicted by hyperconjugation was confirmed. The results cannot be explained in terms of the steric model proposed by Bartell.¹⁵ The isotope effect reported for compound 7 ($k_H/k_D = 1.436$) is the largest secondary isotope effect attributed to a single deuterium atom.

The suggestion that the large axial β -deuterium isotope effect of compound 7 might be due to neighboring hydrogen participation led Shiner and Jewett¹⁷ to study the isotope effect of a series of β -deuterated cis-4-t-butylcyclohexyl brosylates (compounds 8, 9, and 10) in 50% aqueous ethanol. The observed k_H/k_D rate ratios for 8, 9, and 10 are 2.565, 1.784, and 2.862, respectively. Successive β -deuterium substitution of conformationally equivalent sites does not lead to

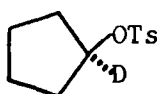
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cumulative isotope effects and this is in accord with neighboring hydrogen participation in the solvolytic transition state. This participation was viewed as a type of electronic interaction associated with hyperconjugation.

Karabatsos and co-workers¹⁸ recently reported that in ordinary systems capable of hyperconjugation, less than 10% (probably 2-5%) of the observed isotope effect is due to non-bonded interactions. This is further support that hyperconjugation is mainly responsible for β -deuterium isotope effects.

3. α -Secondary Deuterium Isotope Effects

The effect of α -deuterium in isotope effects is not related to hyperconjugation. Streitwieser and co-workers¹⁹ reported the first example of α -deuterium isotope effects in the acetolysis of cyclopentyl-1- d_1 tosylate (11).

11

Since deuterium substitution will change significantly only those vibrational frequencies which involve vibration of the substituted hydrogen in an important way, then the majority of the fundamental frequencies will hardly be altered by deuterium substitution. The vibrations most affected in going from cyclopentyl-1- \underline{d}_1 tosylate to cyclopentyl tosylate are the stretching and bending frequencies of the C_1 -H bond, which are of high enough frequency so that only the zero-point energy differences need to be considered.

The assignment of the C_1 -H stretching and bending frequencies to the reactant is accomplished readily, but the assignment of frequencies to the fundamental vibrations in the transition state is difficult. Streitwieser¹⁹ approximated the fundamental frequencies of the cyclopentyl cation as C-H stretching, C-H in-plane bending and C-H out-of-plane bending. Acetaldehyde was chosen as a model for a C-H bond in a carbonium ion, since the carbon is sp^2 hybridized in both the carbonium ion and the aldehyde. The change in stretching frequency was calculated to give a k_H/k_D ratio of 1.06, but there is essentially no change in the in-plane bending vibration. The out-of-plane bending vibration gave a calculated k_H/k_D ratio of 1.38. Consequently, it appeared that the most important factor involved in the α -deuterium isotope effect of compound 11 is the isotopic inhibition of the out-of-plane bending vibration of the cation, which is weaker than the corresponding vibration in the ground state.

Acetolysis of secondary alkyl tosylates is unassisted by backside solvent participation in the transition state; i.e., it

solvolyzes by a limiting mechanism.²⁰ Although the backside of the reacting carbon atom is free, the leaving group is still reasonably close to the forming carbonium ion and will probably impede the C-H wagging motion, thus lowering the k_H/k_D ratio. Therefore, the k_H/k_D ratio calculated for out-of-plane bending ($k_H/k_D = 1.38$) could be lowered to the observed isotope effect of compound 11 ($k_H/k_D = 1.15$) by hindrance of the C-H wagging motion by the leaving toluenesulphonate group.

In direct displacement reactions, Shiner⁸ and Johnson and Lewis²¹ found very small or inverse isotope effects. In these cases the transition state should contain both the entering and the leaving groups, and the C-H wagging motion would be impeded even more, resulting in a smaller isotope effect. Accordingly, it seems that a S_N1 mechanism must operate, just as in β -deuterium isotope effects, in order for the α -deuterium effect to be appreciable.

Johnson and Lewis²¹ found that the force constant for C-H bond bending in the transition state is quite sensitive to the proximity of the entering and leaving groups, and the effect of the α -deuterium on the rate is a measure of the hindrance to this motion. Therefore it seems that the α -deuterium isotope effect may provide a method for determining the degree of solvent participation or neighboring group assistance in the transition state of solvolytic displacement reactions.

The α -deuterium isotope effect observed in the solvolysis of primary alkyl derivatives is generally small or inverse, indicating solvent participation in the transition state (see Table 3). This is

Table 3. α -Deuterium Isotope Effects in Solvolysis.

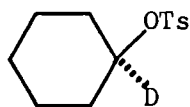
Compound	Solvent	Temperature	k_H/k_D per D	Reference
methyl- \underline{d}_3 brosylate	CH ₃ OH	40°	0.97	21
methyl- \underline{d}_3 tosylate	H ₂ O	70°	0.98	22
methyl- \underline{d}_3 chloride	"	90°	0.97	22
methyl- \underline{d}_3 bromide	"	80°	0.96	22
methyl- \underline{d}_3 iodide	"	70°	0.95	22
methyl- \underline{d}_3 mesylate	"	60°	0.98	22
ethyl-1,1- \underline{d}_2 brosylate	"	40°	1.02	24
ethyl-1,1- \underline{d}_2 tosylate	"	54°	1.02	23
ethyl-1,1- \underline{d}_2 bromide	"	80°	0.99	23
ethyl-1,1- \underline{d}_2 iodide	"	90°	0.99	23
ethyl-1,1- \underline{d}_2 mesylate	"	60°	1.02	23
1-propyl-1,1- \underline{d}_2 benzylate	"	54°	1.02	23
1-propyl-1,1- \underline{d}_2 mesylate	"	60°	1.02	23
1-propyl-1,1- \underline{d}_2 bromide	"	80°	0.99	23
1-propyl-1,1- \underline{d}_2 iodide	"	90°	1.00	23

in accord with the current theory of solvolytic displacement reactions.²⁰

From Table 3 it can be seen that sulphonates give larger isotope effects than halides, a result that is consistent with the concept that sulphonates are better leaving groups than halides,²⁰ and accordingly should require less solvent participation from the backside. Solvent

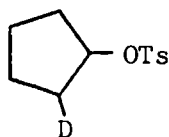
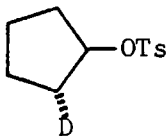
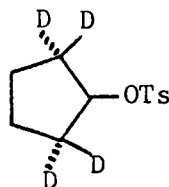
participation should require a transition resembling a direct displacement reaction, and the α -isotope effect should be less than a transition state without solvent participation.

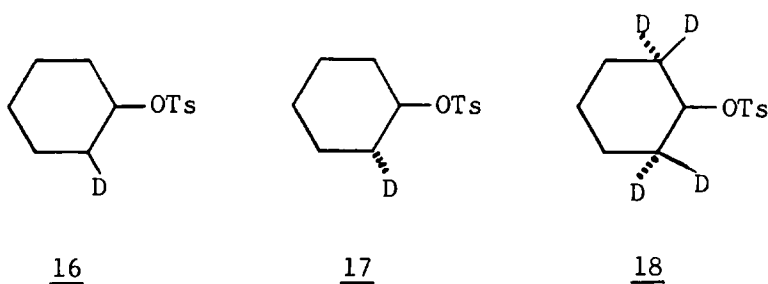
Saunders and Finley²⁵ studied the α -isotope effect in the acetolysis of cyclohexyl-1-d₁ tosylate (12) and found the observed k_H/k_D ratio to be 1.22 (compare compound 11; $k_H/k_D = 1.15$). This result

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suggests that the C-O bond is less stretched or that solvent can participate better in the cyclopentyl system than in the cyclohexyl system.

Streitwieser and co-workers¹⁹ also studied the β -deuterium isotope effect in the acetolysis of compounds 13, 14, and 15; Saunders and Finley²⁵ studied the acetolysis of the cyclohexyl analogs, 16, 17, and 18.

131415



The results are summarized in Table 4.

Table 4. β -Deuterium Isotope Effects of Cyclopentyl and Cyclohexyl Tosylates.

Compound	Observed k_H/k_D
<u>13</u>	1.22
<u>14</u>	1.16
<u>15</u>	2.06
<u>16</u>	1.25
<u>17</u>	1.30
<u>18</u>	2.34

The isotope effects are similar but larger in the cyclohexyl system. This would seem to indicate that there is little average difference in the dihedral angle between the C-O and C-D bonds for the cis and trans isomers in both systems. The alternative explanation, that the isotope effect is independent of the dihedral angle, seems unlikely due to the work of Shiner and Jewett.¹⁷ Consequently, the conventional picture of

the solvolysis of cyclohexyl derivatives via a chair conformation requires that the leaving group be equatorial,²⁶ which would predict similar dihedral angles for both isomers. A more likely explanation is that solvolysis of the more mobile cyclohexyl system proceeds via a transition state having a twist-boat conformation. Shiner and Jewett²⁷ have presented strong evidence for such a transition state in the solvolysis of deuterated trans-4-t-butylcyclohexyl brosylates. This twist-boat conformation should account for the similar isotope effects of compounds 16 and 17.

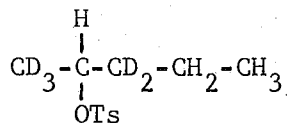
Leffek and co-workers²⁸ studied the effects of α , β , and γ -deuterium substitution of n-propyl tosylate, mesylate, bromide, and iodide during hydrolysis. The α - and β -substituted deuterium derivatives gave the expected rate retardation, but the γ -substituted deuterium compounds gave inverse isotope effects. This result was explained as being due to inhibition of vibrations involving the methyl hydrogen and methyl deuterium atoms stemming from increased intramolecular van der Waals forces in the transition state. The inhibition of vibrations involving the terminal methyl group are probably caused by the leaving group. Halevi³ has presented evidence for the greater electropositivity of deuterium compared to protium based on dipole moment results²⁹ and nmr chemical shifts of deuterated compounds.³⁰ Halevi and co-workers³¹ have studied the effect of deuterium substitution on the α -carbon of acetic and propionic acids and found that deuteration reduces the acid strength by about 6%. The effect for β -deuteration decreases the acid strength by about 2%. The carbon-deuterium bond thus shows signs of being electron repelling relative

to the carbon-hydrogen bond, presumably because of anharmonicity effects.³² Consequently, Halevi³ offers the following tentative hypothesis for γ -deuterium effects in solvolysis: the γ -position is the one closest to the reaction site from which the inductive effect of three deuterium atoms can operate unopposed by either an α - or β -effect. Therefore, the γ -effects are simply due to the greater electropositivity of deuterium compared to hydrogen.

Shiner³³ found that the isotope effect of 3- \underline{d}_1 -2,3-dimethyl-2-chlorobutane in aqueous ethanol decreases strongly with temperature, but Lewis and Boozer³⁴ found that the temperature dependence on the acetolysis and formolysis of tosylates was not as strong. Leffek and co-workers³⁵ observed a small temperature dependence on hydrolysis of β -deuterium substituted isopropyl sulphonates and bromides.

Recently Robertson and co-workers³⁶ determined the temperature dependence of the β -deuterium isotope effect of \underline{t} -butyl- \underline{d}_9 chloride in 50% aqueous ethanol and in water over a temperature range of 5-30° at 5 degree intervals. The isotope effect was essentially constant over the temperature range studied. Since zero-point energy differences are considered to be the dominant factor in secondary isotope effects, such temperature independence, as shown by Leffek and co-workers³¹ and Robertson and co-workers,³⁵ is in apparent conflict with the requirements of the zero-point hypothesis and the earlier work of Shiner³³ and of Lewis and Boozer.³⁴ The results were explained in terms of probable solvation differences and by a theoretical analysis of the temperature effects.

Lewis and Boozer⁶ studied the solvolysis of 2-pentyl-d₅ tosylate (19) in 80% aqueous ethanol, acetic acid and formic acid and found isotope effects of 1.40, 1.64, and 1.64, respectively. The results



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can be explained by the following argument: the greater the nucleophilicity of the solvent, the greater the demand for electrons can be fulfilled by orbital overlap with a solvent molecule and the less the necessity for the weakening of neighboring bonds. Consequently, the $k_{\text{H}}/k_{\text{D}}$ ratio will be less for more nucleophilic solvents.

Robertson and co-workers³⁶ found that the isotope effect of t-butyl-d₉ chloride solvolysis is essentially the same in water ($Y^{37} = 3.5$) and in 50% aqueous ethanol ($Y = 1.6$), but not in methanol ($Y = -1.1$). These results seem to support the suggestion of Robertson³⁸ that there is no specific interaction between the solvent and the developing carbonium ion, or that the interaction is the same in both water and in 50% aqueous ethanol. The different isotope effect in methanol is in the direction (increase) required by a greater degree of charge development and is incompatible with the suggestion that the reaction is less limiting in the poorer ionizing solvent.

Thornton and Frisone³⁹ determined the isotope effects for the solvolysis of t-butyl-d₉ chloride at 25° in six solvent mixtures having

the same Y values, but differing widely in nucleophilic and electrophilic properties. Their results are tabulated in Table 5.

Table 5. Solvolysis of t-Butyl-d₉ Chloride at Constant Ionizing Power.

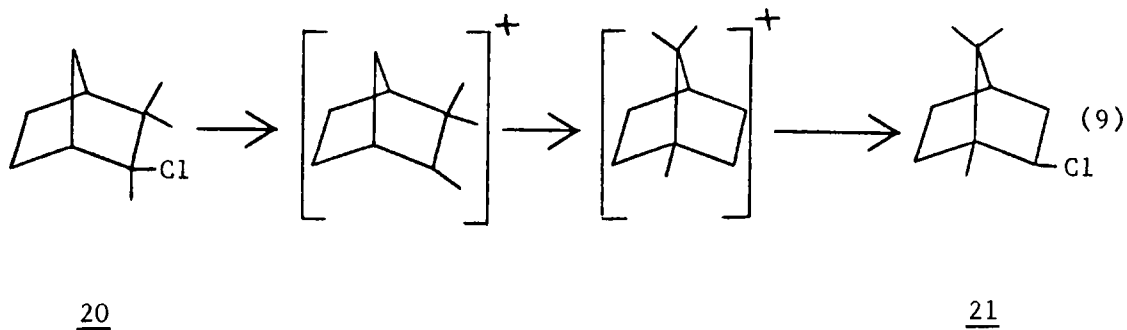
Solvent	k_H/k_D
ethanol-water (54:46)	2.35
acetone-water (49:51)	2.40
acetic acid-water (63:37)	2.41
pyridine-water (51:49)	2.46
isopropanol-water (48:52)	2.42
acetic acid-formic acid (29:71)	2.30

Since the isotope effects are hardly solvent dependent, the structural features of the transition state for t-butyl chloride solvolysis are insensitive to the presence of solvents of widely varying electrophilic and nucleophilic properties, and probably are similar.

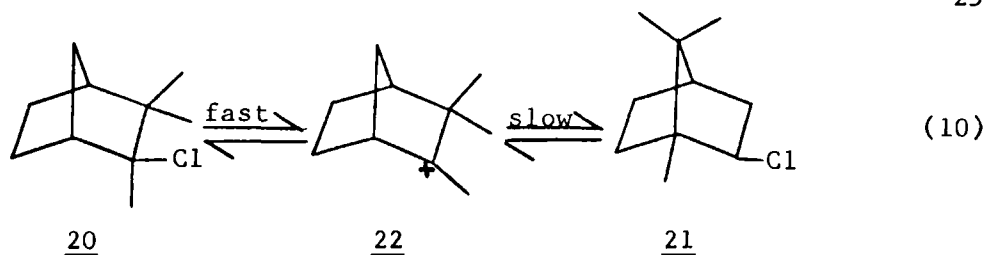
Thus it now seems to be established that hyperconjugation is the main source of secondary isotope effects. Other sources are responsible for α -substitution and inductive effects, though the latter are probably small.¹⁸ Steric effects also seem to play a part in these effects, but they are not well understood as are the effects of solvent and temperature. Nonetheless, secondary isotope effects provide a valuable method for the study of reaction mechanisms, especially for gaining an insight to the structure of the transition state.

4. Nonclassical Carbonium Ions

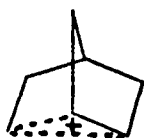
Bartlett and Pöckel⁴⁰ investigated the rearrangement of camphene hydrochloride (20) to isobornyl chloride (21). The postulated mechanism⁴¹



was criticized because it would be expected that the product of this conversion should be a mixture of bornyl and isobornyl chlorides, whereas only isobornyl chloride is produced. Bartlett and Pöckel suggested that the rearrangement occurs by the reaction of a molecule of hydrogen chloride with camphene hydrochloride so that free ions are not formed in the conversion. Wilson and co-workers⁴² reinvestigated this rearrangement using deuterium and radio-chloride to compare the rates of chlorine exchange and hydrogen exchange. They concluded that the rearrangement proceeds in two steps: the first step involves rapid ionization and the second step involves a relatively slow bimolecular reaction between the ion produced and hydrogen chloride.



They also suggested that the intermediate ion (22) might be mesomeric between the camphene and isobornyl structures (23) so that the stereochemical identity of the bridgehead carbon to which chloride is attached in isobornyl chloride is preserved.



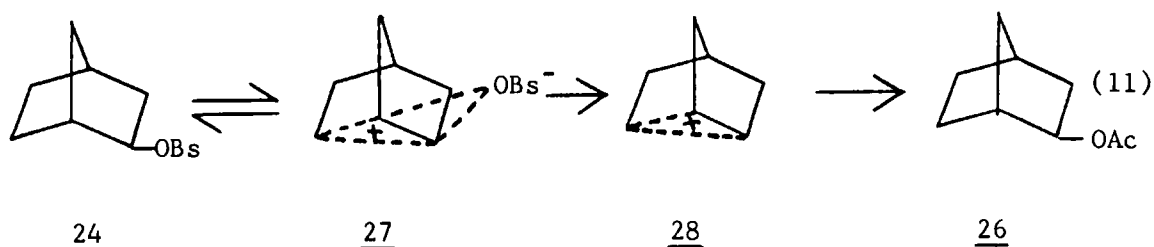
23

This intermediate (23) was the first postulated nonclassical (bridged) carbonium ion.

Nonclassical carbonium ions were placed on a firmer basis by Winstein and Trifan,⁴³ who studied the acetolysis of exo- and endo-2-norbornyl brosylate (24 and 25). It was found that the exo isomer solvolyzes 350 times faster than the endo isomer, and that the product was almost exclusively exo-2-norbornyl acetate (26). A recent investigation of this solvolysis reaction using modern techniques⁴⁴ revealed that some elimination accompanies the acetolysis of the exo brosylate to the extent of 4.5%, but the product is more than 99.7% exo acetate. When optically active exo brosylate was solvolyzed, the exo acetate was found to be completely racemic and the rate of racemization (k_r) exceeded the rate of solvolysis (k_t) by a factor of 3.5.

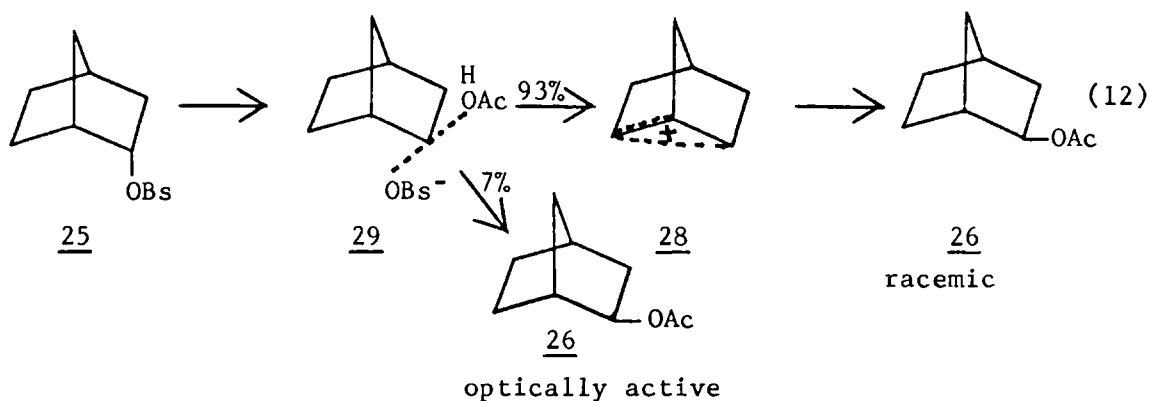
The large rate enhancement of the exo brosylate ($k_{\text{exo}}/k_{\text{endo}} = 350$) was explained in terms of an intramolecular displacement reaction by the C_6-C_1 bond on C_2 . Winstein and co-workers⁴⁵ had already presented evidence for the participation of neighboring groups as the driving force in Wagner-Meerwein rearrangements, and that stereoelectronic considerations require backside attack. Thus, the exo brosylate is ideally situated for this σ bond participation, whereas comparable participation in the endo brosylate is geometrically prohibited. Participation by the C_7-C_1 in the endo isomer is feasible, but this would involve a high degree of strain in the already strained carbon nucleus.

The difference between the polarimetric and titrimetric rate constants ($k_{\alpha}/k_t = 3.5$) led Winstein and Trifan⁴³ to postulate an intimate ion pair⁴⁶ (27) to be formed from the initial ionization of the brosylate. The ion pair is capable of collapsing to give racemic brosylate, or of reacting with solvent to form product. In order to explain the exclusive formation of exo product and the stereospecificity of internal return, a nonclassical bridged structure (31) was proposed since backside attack by solvent at either C_1 or C_2 would yield only exo product.



A classical ion could lead to racemization by a Wagner-Meerwein migration of C_6 from C_1 to C_2 , by a C_3 - C_2 hydride shift or by a C_6 - C_2 hydride shift, but these processes could not account for the high exo/endo solvolytic rate ratio.

Acetolysis of endo-2-norbornyl brosylate (25) also produced only the exo acetate, but optically active endo brosylate gave a product in which 7% of the optical activity was retained. The k_x/k_t ratio was essentially unity within experimental error. Winstein and Trifan⁴³ postulated that the endo brosylate solvolyzed with unassisted ionization to a classical norbornyl cation coordinated with solvent (29), which could react with coordinated solvent to give optically active exo acetate (7%) or which could rearrange to a nonclassical cation (28) to the extent of 93% to give racemic exo acetate.



Roberts and co-workers⁴⁷ studied the acetolysis of exo-2-norbornyl brosylate labelled with carbon-14 at C_2 and C_3 . If the intermediate is the bridged ion (28) postulated by Winstein and Trifan,⁴³ the product acetate should have carbon-14 at the C_1 , C_2 , C_3 , and C_7 positions. Carbon-14 was found to be present in all positions except C_4 and the percent activity is shown in Figure 2.

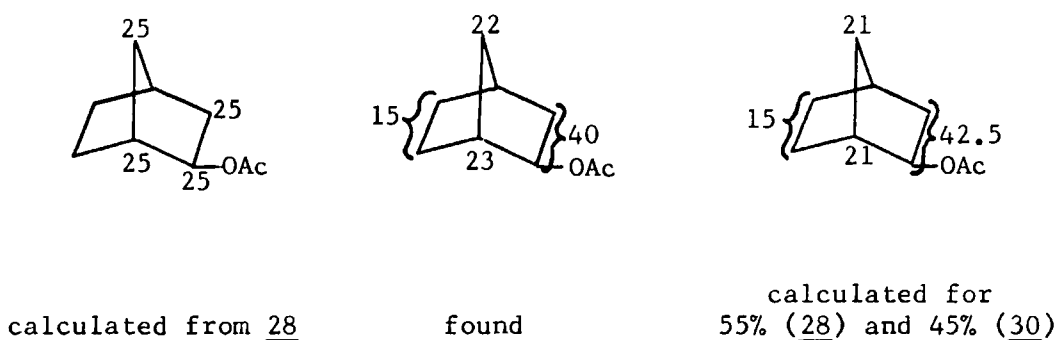
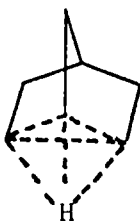


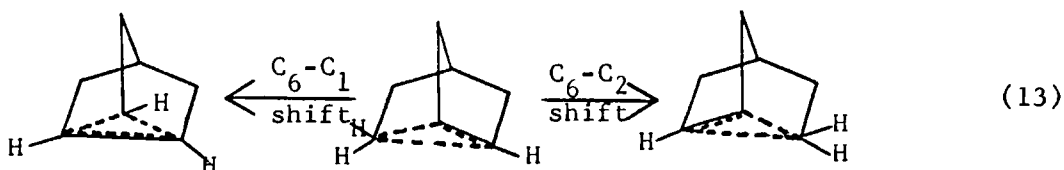
Figure 2. Distribution of C^{14} in the Acetolysis of 2,3- C_2^{14} -exo-2-Norbornyl Brosylate.

This result led Roberts⁴⁷ to suggest the intervention of the highly symmetrical nortricyclonium ion (30) to account for the C_6 - C_2 hydride shifts that occur during the reaction. The carbon-14 distribution can be accounted for if it is assumed that 45% of the reaction proceeds via 30 and 55% by 28.



30

The carbon-14 distribution could also arise by means of C_6 - C_2 and C_6 - C_1 hydride shifts as shown below.



An nmr study of the norbornyl cation, as its SbF_6^- salt,^{48,49} showed that the spectrum of the ion is temperature dependent. At -23° only one peak was observed, indicating that all of the protons are equivalent at this low temperature. This equivalence is possible if three processes are occurring simultaneously:

1. the formation of a bridged ion (28) or a Wagner-Meerwein rearrangement,
2. $\text{C}_6\text{-C}_2$ hydride shift,
3. $\text{C}_3\text{-C}_2$ hydride shift.

At -120° three peaks are observed at 5.3τ (4 protons), 3.1τ (1 proton) and 2.2τ (6 protons). This low temperature spectrum was postulated to arise as a result of the $\text{C}_3\text{-C}_2$ hydride shift becoming slow in comparison to the Wagner-Meerwein rearrangement and the $\text{C}_6\text{-C}_2$ hydride shift. The four proton peak at 5.3τ is due to the protons at C_1 , C_2 , and C_6 becoming equivalent; the single proton peak at 3.1τ is due to the proton at C_4 ; and the six proton peak at 2.2τ is due to the protons at C_3 , C_5 , and C_7 becoming equivalent. These results indicate

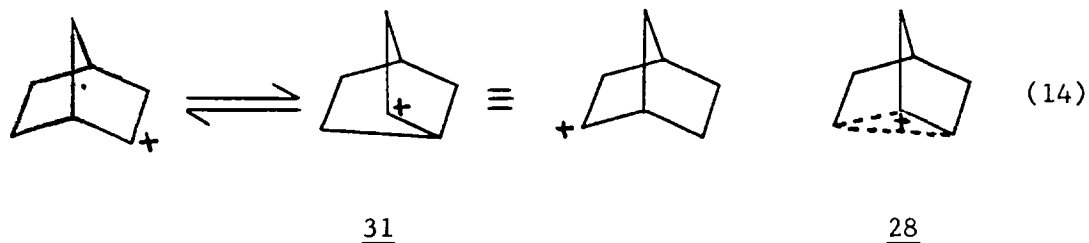
that there is a higher degree of equivalence among different protons than predicted by the nonclassical ion (28) and the nortricyclonium ion (30).

A qualitative relationship between the frequency of the carbonyl stretch of ketones and solvolysis rate was observed by Schleyer and Nicholas.⁵⁰ This result was not unexpected since both infrared carbonyl stretching frequencies and solvolysis rates are sensitive to bond angle and hybridization.⁵¹ Foote⁵² plotted the acetolysis rates of twenty arenesulphonates versus the carbonyl stretching frequencies of the corresponding ketones and found an excellent correlation, which allows solvolysis rates to be predicted. This correlation also allows the estimation of rate enhancements after the effects of angle strain have been removed from a model compound. When this correlation was attempted with arenesulphonates suspected of solvolyzing via nonclassical carbonium ions, e.g., exo-2-norbornyl brosylate, these compounds had rates faster than the rates predicted by the correlation.

Schleyer⁵³ modified this correlation by estimating effects for bond angle strain, torsional strain, and non-bonded interaction strain by using cyclohexyl arenesulphonate as a model free from these strains. This modification was sufficient to account quantitatively for the observed solvolysis rates within a factor of ten. After inductive effects have been corrected for, any excess of observed over calculated solvolysis rates must be due to anchimeric assistance. Schleyer⁵³ has stated that these enhanced reaction rates can serve to distinguish between a bridged ion and a rapidly equilibrating pair of classical ions.

Consequently, exo-2-norbornyl arenesulphonates, which gave $\log k_{\text{obs}}/k_{\text{calcd}}$ of 3.3, solvolyze with considerable anchimeric assistance; endo-2-norbornyl arenesulphonates, on the other hand, undergo non-assisted solvolysis. The anchimeric assistance of the exo isomer was considered as conclusive evidence for a bridged structure for the resulting carbonium ion.

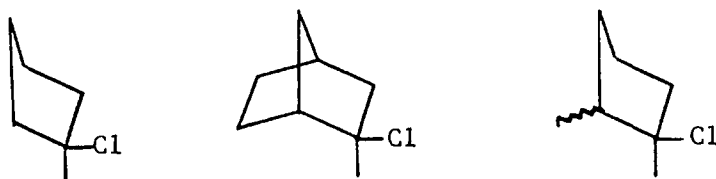
Brown⁵⁴ has argued that the nonclassical ion proposed by Winstein and Trifan⁴³ is not necessary; a rapidly equilibrating pair of classical carbonium ions could explain the high exo/endo rate ratio and the exclusive formation of exo products. Brown⁵⁴ argued that the rate of solvolysis of exo-2-norbornyl brosylate is normal, rather than enhanced; and the rate of solvolysis of endo-2-norbornyl brosylate is unusually slow, rather than being normal. In the endo isomer, the leaving brosyl group must pass unusually close to the endo hydrogens at C₅ and C₆, and steric hindrance to ionization could occur. The stereochemistry of the product was attributed to the fact that the rear side of the norbornyl cation is sterically protected. Brown⁵⁵ has stated the problem simply as: "In the rapid interconversion of two equilibrating classical norbornyl cations (31) the system must pass over the transition state (28). The problem is whether (28) is a high-energy transition state, or is a resonance-stabilized intermediate, so stable that we no longer need to consider the two individual classical intermediates (31)."



The three major foundations for proposing a nonclassical structure for the norbornyl cation are:⁵⁶

1. unusually fast rates of solvolysis for the exo derivatives,
2. high exo/endo solvolytic rate ratios,
3. predominant exo substitution in the cation.

In order to prove his arguments, Brown first compared the rates of exo-norbornyl derivatives with a suitable model, which was chosen on the basis that carbonyl stretching frequency provides a measure of angle strain and correlates solvolytic reactivity.^{52,53} The model chosen for this study was cyclopentane since cyclopentanone (ν_{CO} 1750) compares favorably with norcamphor (ν_{CO} 1751). Brown and Chloupek⁵⁷ found the following relative rates for norbornyl derivatives:

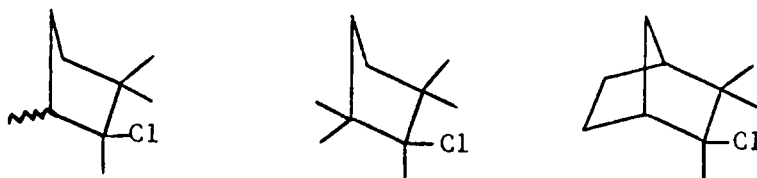


Relative rate:

1

5.4

2.3



Relative rate: 36

82

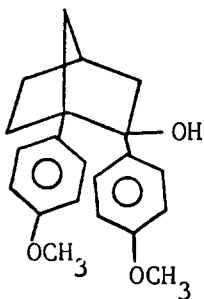
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The results are in accord with the postulated effect of steric strain increasing the rate of ionization,⁵⁸ and is not due to participation of the C_6-C_1 bonding electrons. It must be kept in mind that initial ionization to a classical tertiary cation does not preclude subsequent rearrangement to a nonclassical carbonium ion. The choice of the cyclopentyl system as a model has inherent difficulties since there are ten eclipsed interactions in planar cyclopentane, but only four such interactions in norbornane. The elimination of six of these interactions must be accomplished, at the expense of increased angle strain, by puckering. When the norbornane skeleton is hybridized to sp^2 , two of these eclipsing interactions are relieved; when cyclopentane undergoes the same rehybridization, four of these interactions are relieved. Consequently, when cyclopentane is bridged to form the norbornane skeleton, a decrease in the ease of solvolysis would be expected rather than an increase.

Brown^{54,55} argues that the high exo/endo rate ratios are due to steric hindrance to ionization of the endo isomer rather than participation in the exo isomer. For the endo isomer the leaving group must depart in close proximity to the endo hydrogens at C_5 and C_6 ; accordingly the transition state for ionization of endo-norbornyl derivatives

is sterically destabilized, which should result in a steric deceleration of the endo isomer compared to the exo isomer. A comparison of the relative rates of exo- and endo-norbornyl derivatives with C₅ and C₆ endo substituents is given in Table 6. Although the endo arenesulphonates have decelerated rates, it is clear that the exo isomers also undergo a deceleration in rate due to the endo substituents at C₅ and C₆. Consequently, the effect of increasing bulky substituents fails to account for the decrease in rate for the exo derivatives, which are clearly not sterically hindered by the departing leaving group.

Schleyer and co-workers⁶² investigated the nmr spectrum of the cation generated from alcohol 32



32

and found that the protons in the benzene rings were non-equivalent at low temperatures. If the ion is nonclassical the two anisyl groups should be identical; if the ion is classical the two anisyl groups should be distinct. Nonetheless, it was noted that the results do not preclude the possibility of nonclassical structures for non-aryl substituted norbornyl derivatives.⁷⁰

Table 6. Relative Rates of Acetolysis of Arensulphonates at 25°.

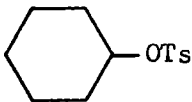
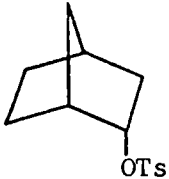
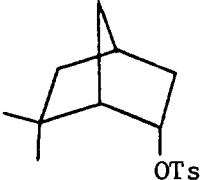
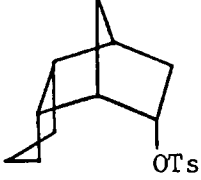
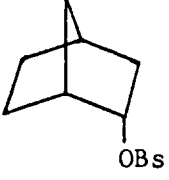
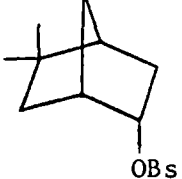
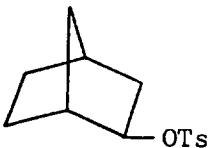
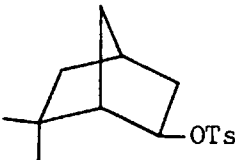
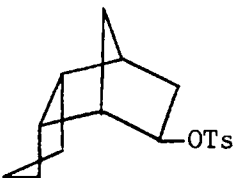
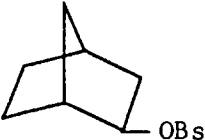
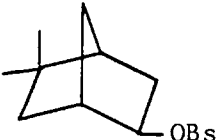
Compound	Relative Rate	$\frac{k_{\text{exo}}}{k_{\text{endo}}}$	Reference
	1.0		59
	1.8		59
	0.090		59
	0.062		60
	1.47 ^a		43
	1.05 ^a		61

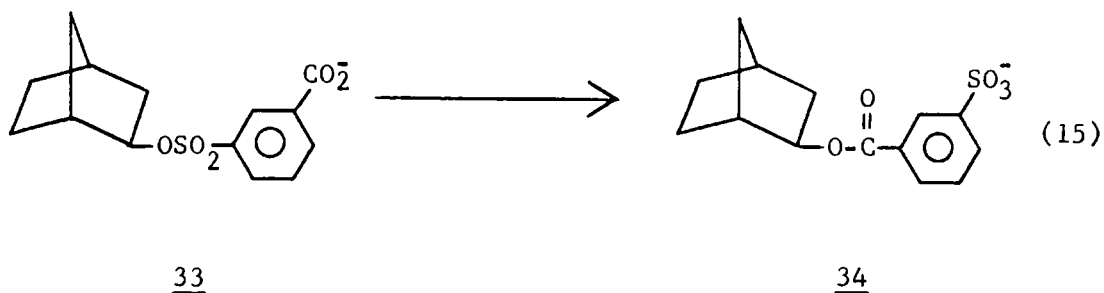
Table 6.--Continued.

Compound	Relative Rate	$\frac{k_{\text{exo}}}{k_{\text{endo}}}$	Reference
	505	280	59
	19.7	222	59
	9.52	153	60
	517 ^a	350	43
	153 ^a	145	61

a. Rate relative to cyclohexyl brosylate at 25°.

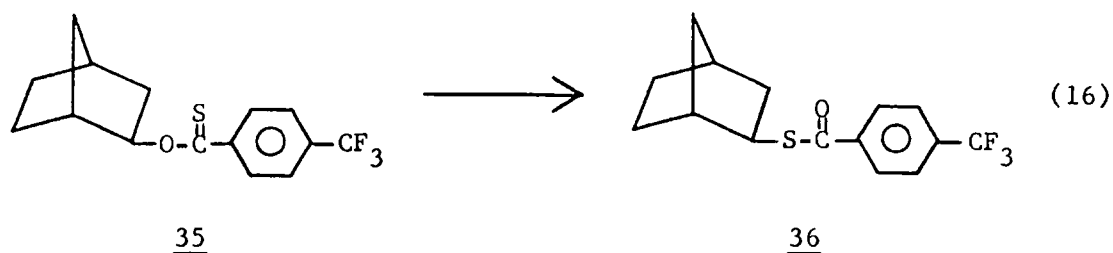
The extensive formation of exo products from the solvolysis of exo norbornyl derivatives has also been challenged by Brown.⁵⁵ Steric hindrance to substitution from the endo direction should lead to exclusive exo substitution. This argument is just the converse of that used by Brown to describe the steric deceleration of endo norbornyl derivatives by bulky substituents in the C₅ and C₆ endo positions. Brown's other argument is that rapidly equilibrating classical ions (31) result in a rapid movement of C₆ and its σ bond between C₁ and C₂, thus preventing the accumulation of solvent in the endo direction (windshield wiper effect).

Corey and co-workers⁶³ tested the windshield wiper effect by solvolyzing optically active exo-2-norbornyl m-carboxybenzenesulphonate (33). Their results showed that the carboxylic ester (34) produced was racemic.



If a pair of rapidly equilibrating classical ions formed as the intermediate, then collapse of these ions should give product with some net retention of optical activity. Corey concluded that the interconversion rate of classical ions must be so rapid that the ion may be considered to be bridged or nonclassical.

Smith and Petrovich⁶⁴ observed the same results in the acetolysis of optically active exo-2-norbornyl p-trifluoromethyl-thionbenzoate (35).



The products were 73% exo acetate and 16% thiobenzoate (36), which was racemic. Thus, the norbornyl cation must be symmetrical toward ion-pair return by sulfur.

Goering and Schewene⁶⁵ reported the rates of racemization, the rates of acetate exchange and the equilibration of the isomeric acetates for the acid-catalyzed (HClO_4) acetolysis of exo- and endo-2-norbornyl acetates. Their results are summarized in Figure 3. The lower transition state energy of the exo isomer compared to the endo isomer indicates that delocalization of the carbonium ion to a non-classical carbonium ion lowers the exo transition state energy by $\Delta E_a = 4.4$ kcal/mole, which probably represents the lower limit for the energy difference of the classical and nonclassical ions. According to Brown's arguments, the transition state for the exo acetate is normal, and the higher energy for the endo acetate is just that due to steric strain.

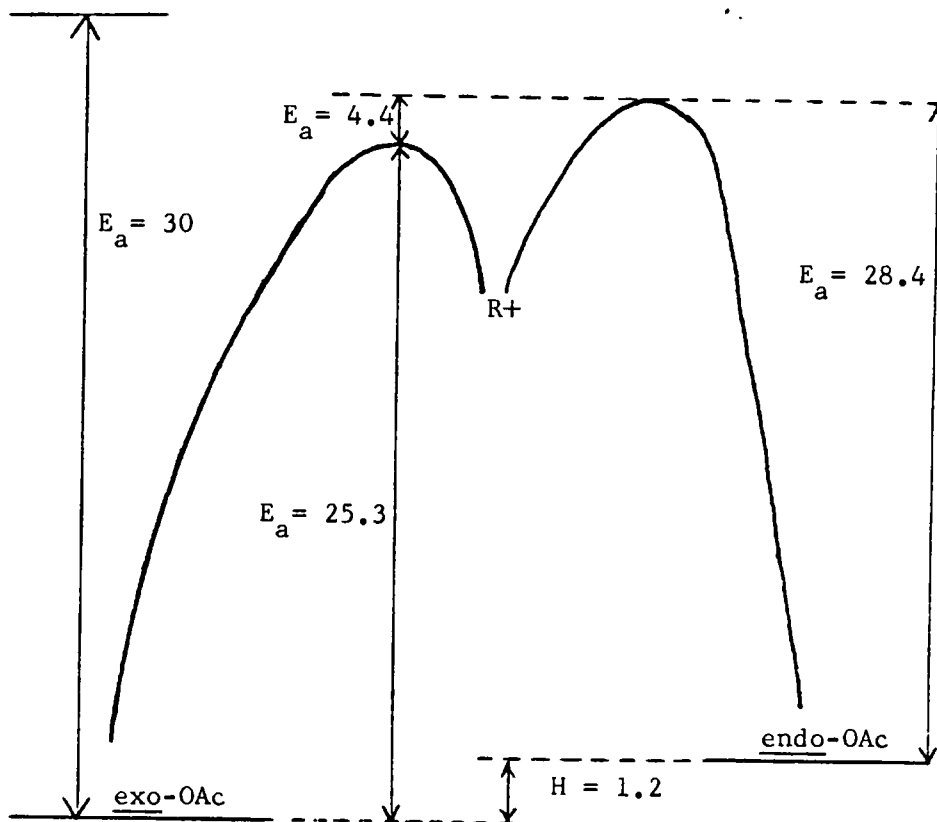


Figure 3. Activation Energies for the Acid Catalyzed Reactions of exo- and endo-2-Norbornyl Acetates.

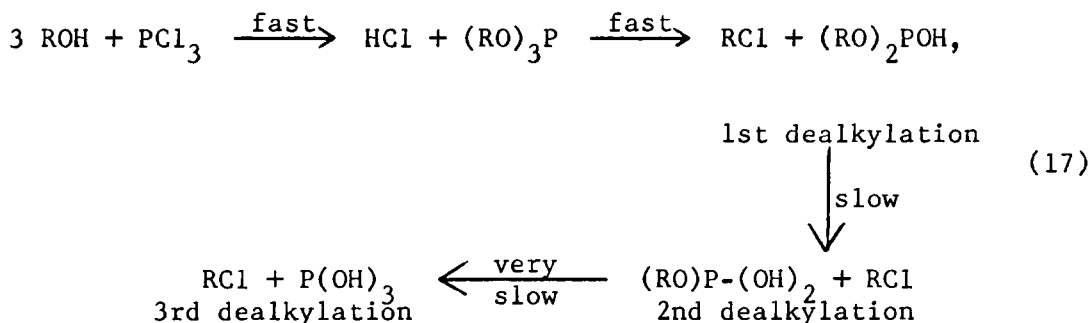
Berson and Remanick⁶⁶ studied the deamination of optically active exo- and endo-2-norbornyl amines in acetic acid, and set an upper limit of the exo/endo product ratio arising from nucleophilic attack by solvent on a classical norbornyl cation at about 9:1. This result, compared to the exo/endo product ratio resulting from the acetolysis of exo- and endo-2-norbornyl brosylates, conflicts with the argument that attack occurs on a classical carbonium ion.

The various aspects of the chemistry of classical and nonclassical carbonium ions are discussed in greater detail by several authors.⁶⁷⁻⁷⁰

EXPERIMENTAL RESULTS AND DISCUSSION

1. Synthesis of Norbornyl Bromides

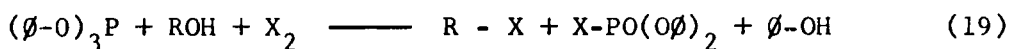
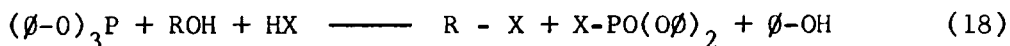
Gerrard and co-workers⁷¹ have shown that alcohols with typical reactivity react with phosphorous trihalides to form trialkyl phosphites rapidly and then undergo slow stepwise dealkylation to form alkyl halides.



The first and second dealkylations gave optically active halides, but the third dealkylation involved considerable loss of optical activity. Accordingly, the first two dealkylations involved direct displacement reactions while the third dealkylation has a change in mechanism. Therefore, if the first dealkylation could be quenched in the reaction of exo-2-norborneol with phosphorous trichloride, then a direct displacement reaction by chloride ion on the trinorbornyl phosphite should result in endo-2-norbornyl bromide. Analysis of the norbornyl chloride indicated that it was 83% exo and 17% endo. Since bromide ion is a stronger nucleophile than chloride ion, the dealkylations should be much more rapid and quenching at the first or second dealkylation step.

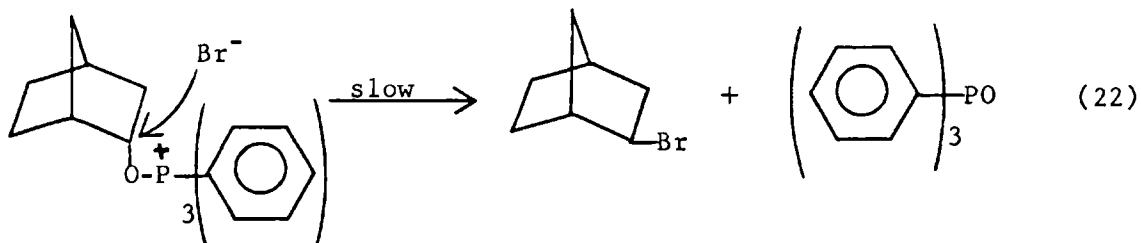
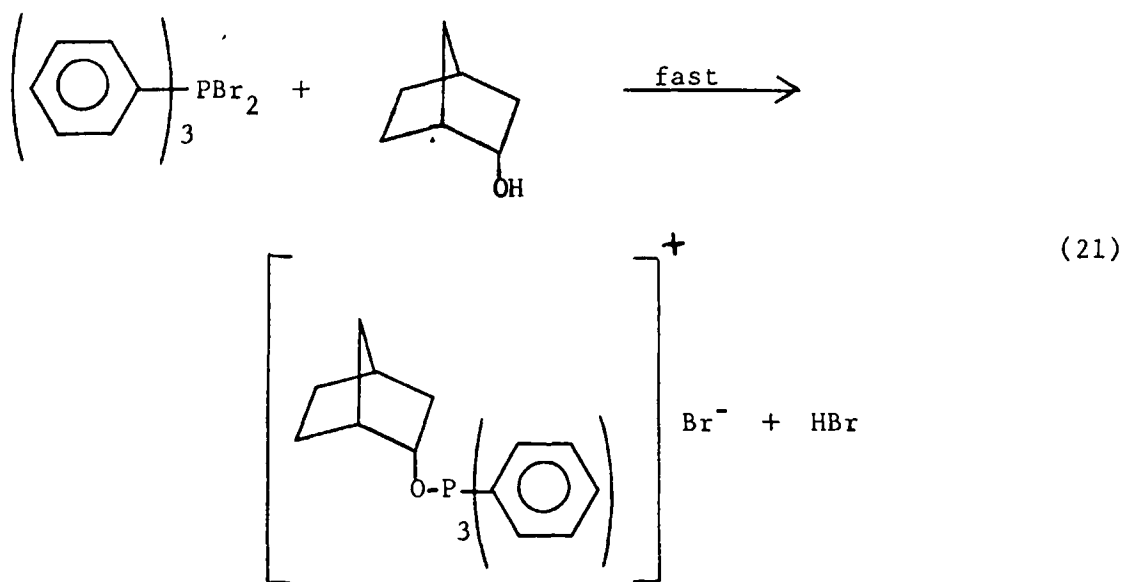
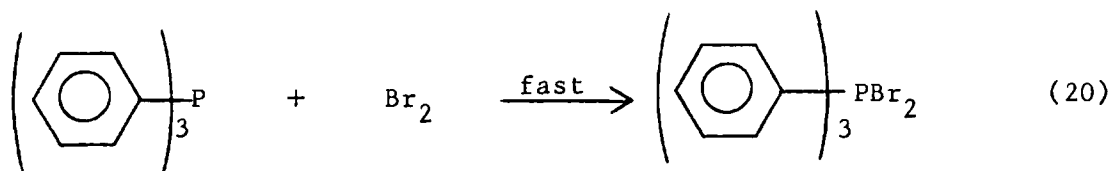
Therefore the reaction with phosphorous tribromide was not attempted.

Rydon and co-workers^{72,73} have shown that the following reactions occur:



These reactions were postulated to proceed by an SN2 mechanism. Consequently, the reaction of exo-2-norborneol with these reagents was expected to undergo direct displacement to give the endo halide. The product from the reaction of the exo alcohol with triphenyl phosphite and bromine was norbornyl bromide, which was a mixture of 90% exo isomer and 10% endo isomer. The direct displacement reaction was reduced considerably and the reaction was not investigated further since a lower exo/endo product ratio was required.

Wiley and co-workers⁷⁴ reported an excellent method for converting alcohols to alkyl halides by a highly concerted displacement process. Schaefer and Weinberg⁷⁵ employed this reaction to convert endo-2-norborneol to exo-2-norbornyl bromide. When optically active endo-2-norborneol was reacted with triphenylphosphine and bromine in triglyme, it was found that the exo-2-norbornyl bromide was optically active and no significant racemization occurred in this conversion. These results and other experiments led Schaefer and Weinberg to postulate the following mechanism for this reaction:



This reaction constitutes one of the few documented bimolecular displacement reactions in the norbornyl system. Smith and Petrovich⁶⁴ prepared the p-trifluoromethyl thiobenzoate of norborneol by a direct displacement reaction of the potassium salt of p-trifluoromethyl thiobenzoate on endo-2-norbornyl brosylate. Lee and Wong⁷⁶ synthesized 2-endo-d₁-exo-2-norbornyl acetate by the reaction of 2-exo-d₁-2-endo-norbornyl brosylate with tetramethylammonium acetate in acetone.

Schaefer and Weinberg⁷⁷ also reported the reaction of optically active exo-2-norborneol with triphenylphosphine and bromine in triglyme and N,N-dimethylformamide. The products consisted of a mixture of 12% endo-2-norbornyl bromide, 79% exo-2-norbornyl bromide and 9% nortricyclene if triglyme was the solvent; in N,N-dimethylformamide these values changed to 1%, 84%, and 15%, respectively. The exo bromide was racemic, but the endo bromide was optically active. It is probable that a change in mechanism occurred and that carbonium ion formation predominates over the displacement reaction. This conclusion is confirmed by the product distribution in the two solvents; i.e., in triglyme (higher dielectric constant than N,N-dimethylformamide) decomposition of the intermediate via a carbonium ion is highly favored as evidenced by the amount of direct displacement product formed.

The direct displacement reaction of the intermediate adduct of triphenylphosphine dibromide and exo-2-norborneol in various non-polar solvents was investigated. The results are summarized in Table 7. From the results it can be seen that direct displacement by bromide ion occurred to the extent of 6-22%. Apparently the C₆ endo hydrogen

Table 7. Reaction of exo-2-Norborneol With Triphenylphosphine Dibromide in Non-polar Solvents.

Solvent	Reaction Time (hr)	Temperature	Norbornyl % <u>exo</u>	Bromide % <u>endo</u>
benzene	18	reflux	89.5	10.5
benzene	0	--	91.7	8.3
benzene	23	reflux	90.5	9.5
benzene / Li ₂ CO ₃	3	reflux	93.6	6.4
xylene	10	reflux	92.0	8.0
xylene-biphenyl	0	--	85.2	14.8
toluene	20	reflux	91.0	9.0
toluene	2	reflux	84.0	16.0
toluene- ϕ_2 CH ₂	0	--	82.3	17.7
toluene- ϕ_2 CH ₂	1	reflux	78.0	22.0
diphenylmethane	0	--	89.0	11.0
diphenylmethane	1	25°	84.5	15.5
none	2	25°	no reaction	

sterically hinders attack of the bromide ion from the endo side of the carbon undergoing reaction, or triphenylphosphine oxide is such a good leaving group that the formation and subsequent collapse of tight ion pairs leads to predominant exo substitution. Since a lower exo/endo product ratio was required, this reaction was not used in the preparation of the deuterated endo-2-norbornyl bromides.

2. Synthesis of Deuterated Norbornyl Bromides

2,3,3- d_3 -2-Norborn-5-enyl bromide (37) was prepared by the Diels-Alder reaction of cyclopentadiene and vinyl bromide- d_3 . Subsequent catalytic hydrogenation of the 37, using palladium on charcoal as the catalyst, afforded the saturated norbornyl bromide- d_3 as a mixture of exo and endo isomers. Deuterium analysis indicated that there were 2.61 deuterium atoms present per molecule of 38.

Vinyl bromide- d_3 was prepared by the elimination of deuterium bromide from 1,2-dibromoethane- d_4 , which was commercially available. When the elimination reaction was attempted with 1,2-dibromoethane using potassium t-butoxide in t-butyl alcohol, only a 60% yield of vinyl bromide was obtained. Presumably another elimination of hydrogen bromide occurred to give acetylene. When a weaker base, potassium hydroxide in 95% ethanol, was employed, the yield of vinyl bromide was increased to 90%; consequently, the elimination reaction of 1,2-dibromoethane- d_4 was carried out with the weaker base.

3,3- d_2 -2-Norborn-5-enyl bromide (39), which was prepared by the Diels-Alder reaction of cyclopentadiene and 2,2- d_2 -vinyl bromide, was catalytically hydrogenated with palladium on charcoal to give 3,3- d_2 -2-norbornyl bromide (40) as a mixture of exo and endo isomers. Deuterium analysis indicated that 40 contained 1.44 deuterium atoms per molecule.

2,2- d_2 -Vinyl bromide was prepared by the following sequence of reactions. Malonic acid was exchanged three times with deuterium oxide and then decarboxylated to give acetic acid- d_4 . Nmr analysis indicated

that the acetic acid was about 86% deuterated. Reduction of acetic acid- d_4 with lithium aluminum hydride afforded 3,3,3- d_3 -ethanol (as the water azeotrope), which was subsequently oxidized to acetaldehyde- d_3 by potassium dichromate in aqueous acid. Nmr analysis showed that there were 2.5 and 2.3 deuterium atoms in the methyl groups of ethanol and acetaldehyde, respectively.

The reaction of phosphorous trichlorodibromide and acetaldehyde- d_3 resulted in a mixture of 2,2,2- d_3 -1,1-dibromoethane and deuterated crotonaldehyde. Since the next step in this sequence of reactions is the elimination of deuterium bromide from ethylidene bromide- d_3 in a basic medium, it was expected that crotonaldehyde would undergo a condensation reaction, and the condensed product should be sufficiently high boiling to permit the separation of the low boiling vinyl bromide. Accordingly, the ethylidene bromide- d_3 -crotonaldehyde mixture was not purified further.

The dehydrobromination of ethylidene bromide using potassium hydroxide in 95% ethanol, pyridine, potassium *t*-butoxide in *t*-butyl alcohol and potassium *t*-butoxide without solvent resulted in very low yields of vinyl bromide. A search of the literature revealed that ethylidene bromide was readily dehydrobrominated by sodium ethoxide in ethanol if the ethylidene bromide was added to the basic solution in one portion; if it was added dropwise, a very low yield of vinyl bromide is obtained.

Consequently, when ethylidene bromide- d_3 was reacted under these conditions, 2,2- d_2 -vinyl bromide was obtained; nmr analysis

indicated that 1.7 deuterium atoms were present at the C₂ carbon atom.

Bromination of acetylene afforded 1,1,2,2-tetrabromoethane, which was debrominated with zinc dust in ethanol to afford a mixture of cis- and trans-dibromoethylene. The Diels-Alder reaction of this mixture of dibromoethylenes and cyclopentadiene resulted in a mixture of cis-exo- and trans-5,6-dibromo-2-norbornene, which was hydrogenated as the mixture, to form a mixture of cis-exo- and trans-2,3-dibromonorbornane.

LeBel⁷⁸ has shown that cis dehydrohalogenation predominates over trans dehydrohalogenation in this system, and thus the reaction conditions used for dehydrobromination of the isomeric mixture of 2,3-dibromonorbornane were for the trans isomer, which undergoes elimination much more difficultly than the cis isomer. The elimination reaction was accomplished with potassium t-butoxide in t-butyl alcohol to produce 2-bromo-2-norbornene. Inadvertently, platinum was used as the catalyst for the deuteration of the unsaturated bromide with deuterium gas, and subsequent deuterium analysis indicated that the endo-norbornyl bromide (41) contained 2.77 deuterium atoms per molecule. Since it is known that deuteration of norbornene and its derivatives goes by exo-cis addition,^{79,80} it seems probable that the 3-endo hydrogen underwent exchange with deuterium to give 2,3,3-d₃-2-norbornyl bromide. The nmr spectrum is almost superimposable on the nmr spectrum of 38, but the infrared spectrum is different from that of 38. The isotope effect observed when 41 was solvolyzed is almost the same as the isotope effect for 38. All the syntheses are outlined in Figure 4.

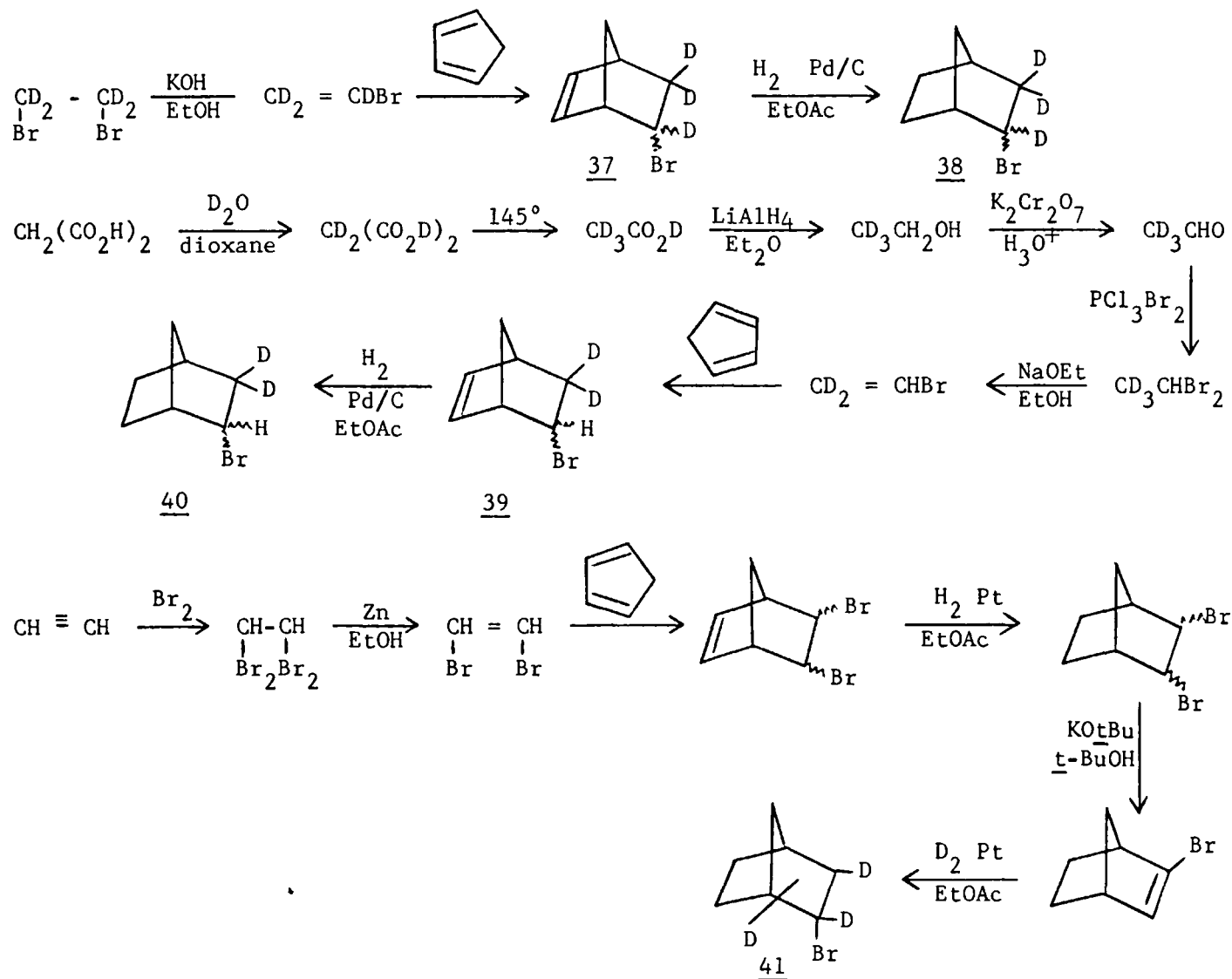
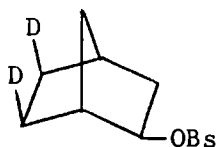
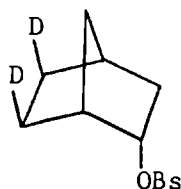


Figure 4. Synthesis of Deuterated Norbornyl Bromides.

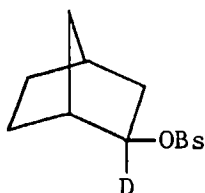
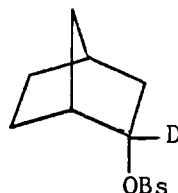
3. Isotope Effects of Deuterated Norbornyl Derivatives

Borcic^v and co-workers⁸¹ determined the isotope effects on the solvolysis of exo-5,6-d₂-exo-2-norbornyl brosylate (42) and the corresponding endo isomer (43).

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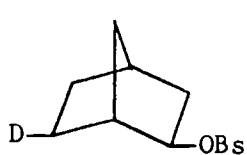
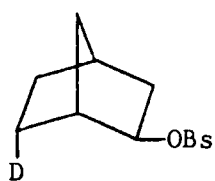
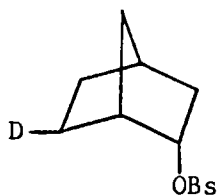
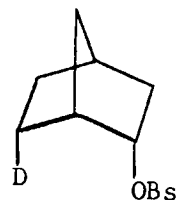
Acetolysis of the endo isomer (43) at 65° was unaffected by deuteration, but the more reactive exo isomer was retarded by 7%. This isotope effect supports the contention that solvolysis of the exo brosylate involves some neighboring group interaction with the C₆ carbon atom, but is not capable of distinguishing between the bridged nonclassical carbonium ion (28) or the nortricyclonium ion (30). In addition, internal return occurs in this system and the isotope effect is complicated by this phenomenon.

Lee and Wong⁷⁶ studied the acetolysis of exo- and endo-2-d₁-2-norbornyl brosylates (44 and 45) at various temperatures and found k_H/k_D ratios for 44 and 45 to be 1.07 and 1.20, respectively, at 50° (by extrapolation).

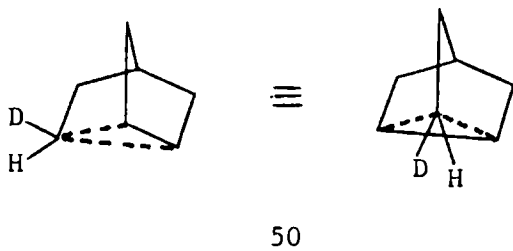
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The isotope effects were almost independent of temperature, in accord with the recent report of Robertson and co-workers.³⁶ Participation of a neighboring group in the rate determining step of a carbonium ion reaction should lead to a decrease in the magnitude of the α -deuterium isotope effect, and this result is found for the exo isomer (44). Consequently 44 seems to be solvolyzing via a nonclassical carbonium ion that is formed by participation of the C_6-C_1 bonding electrons on C_2 , just as Winstein and Trifan⁴³ postulated fifteen years ago. The isotope effect for the exo isomer is undoubtedly complicated by the possibility of internal return and may be larger than reported.

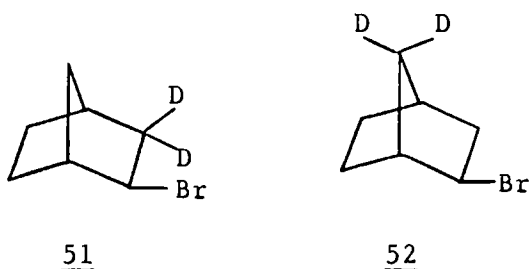
Recently the γ -deuterium isotope effects on the solvolysis of exo- and endo-2-norbornyl brosylates were reported.^{82,83} Solvolyses of compounds 46, 47, 48, and 49 in acetic acid-potassium acetate and in 80% ethanol-water were solvent independent and had isotope effects of 1.09, 1.11, 0.99, and 0.98, respectively.

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The γ -deuterium isotope effects for 48 and 49 are those expected of a transition state for ionization to a classical carbonium ion since other isotope effects of compounds solvolyzing via classical carbonium ions are slightly inverse. The large isotope effect observed for 46 and 47 are not expected to arise from ionization to a classical transition state, but probably resemble a bridged ion (28), in which the distinction between the exo and endo hydrogens (deuteriums) at C₆ is lost (50).



Schaefer and Weinberg⁸⁴ studied the acetolysis of optically active 3,3-d₂-exo-2-norbornyl bromide (51).



The polarimetric (k_{κ}) and titrimetric (k_t) rate constants gave the following (β -deuterium isotope effects: $(k_H/k_D)_{\kappa} = 1.09$ and $(k_H/k_D)_t = 1.04$. Shiner's¹¹ deuterated anthracene adduct (4) was chosen as a model

($k_H/k_D = 1.14$) since the stereochemical geometry of the halogen and the adjacent methylene groups is almost identical to that of C_2 and C_3 of 51. It was shown that the polarimetric isotope effect was about 44% less than the isotope effect for the model compound (4). This result was interpreted as further evidence that the transition state for the solvolysis of exo norbornyl derivatives is stabilized by delocalization of the C_6-C_1 bond.

An estimate of the polarimetric isotope effect for 7,7- d_2 -2-norbornyl bromide (52), the rearranged compound resulting from internal return, was made and was calculated to approach a value of unity. This value in addition to other considerations indicated that the geometry of the norbornyl skeleton had not changed significantly in the transition state.⁸⁴

4. Isotope Effects of Deuterated Norbornyl Bromides

The solvolysis of endo-2-norbornyl bromide, 2,3,3- d_3 -endo-2-norbornyl bromide and 3,3- d_2 -endo-2-norbornyl bromide in 50% aqueous ethanol (volume/volume) at 60.21° was followed by measuring the change in conductance with time. All of the samples underwent first order solvolysis. The rate constants were determined by a Guggenheim analysis⁸⁵ to minimize errors due to uncertainties in the determination of the infinity point, and were calculated by the linear least squares method.⁸⁶

The rate constants for the solvolysis of the endo-2-norbornyl bromides are summarized in Table 8 and the isotope effects are summarized in Table 9. All of the data are listed in Tables 10-25 and were

obtained from a plot of conductivity (micromhos) versus time (minutes) over a five half life period. The solvent was 50% aqueous ethanol ($\frac{V}{V}$) and the temperature was $60.21 \pm 0.01^\circ$ for all of the kinetic runs.

Table 8. Rate Constants for the Solvolysis of endo-2-Norbornyl Bromides in 50% Aqueous Ethanol at 60.21° .

Compound	$k \times 10^3$ (min. ⁻¹)	Average $k \times 10^3$ (min. ⁻¹)
<u>endo-2-norbornyl</u> bromide	1.03	1.05 ± 0.010
	1.05	
	1.05	
	1.06	
2,3,3- <u>d</u> ₃ - <u>endo-2-norbornyl</u> bromide (<u>38</u>)	0.653	0.653 ± 0.006
	0.664	
	0.658	
	0.646	
3,3- <u>d</u> ₂ - <u>endo-2-norbornyl</u> bromide (<u>40</u>)	0.847	0.850 ± 0.003
	0.856	
	0.847	
	0.850	
<u>endo-2-norbornyl</u> bromide- <u>d</u> ₃ (<u>41</u>)	0.684	0.700 ± 0.008
	0.705	
	0.702	
	0.709	

Table 9. Isotope Effects of Deuterated 2-Norbornyl Bromides.

Compound	Number of Deuterium Atoms per Molecule	k_H/k_D	k_H/k_D per D
2,3,3- d_3 -endo-2-norbornyl bromide (38)	2.61	1.61 ± 0.01	
3,3- d_2 -endo-2-norbornyl bromide (40)	1.44	1.24 ± 0.01	1.16^a
exo-2- d_1 -endo-2-norbornyl bromide			1.28^a
3,3- d_2 -exo-2-norbornyl bromide (51)	1.92	1.09 ± 0.01^b	1.04^a
endo-2-norbornyl bromide- d_3 (41)	2.77	1.50 ± 0.01	

a. See appendix for calculations

b. See reference 84

The rate constant for endo-2-norbornyl bromide- d_3 (41), prepared by deuteration of 2-bromo-2-norbornene, was $0.700 \times 10^{-4} \pm 0.008$ (average of 4 runs) and had an isotope effect of 1.50 ± 0.01 . Since this compound analyzed for 1.44 deuterium atoms per molecule, it seems probable that the deuterium atoms are located in the C_2 and exo and endo C_3 positions by comparing the deuterium isotope effect of 2,3,3- d_3 -endo-2-norbornyl bromide ($k_H/k_D = 1.61$ for 2.61 deuteriums), with compound 41.

Since internal return is unimportant in the solvolysis of endo norbornyl derivatives,⁴³ polarimetric rate constants need not be

measured to obtain accurate secondary deuterium isotope effects for the endo isomers. Comparison of the polarimetric β -deuterium isotope effect of 3,3- d_2 -exo-2-norbornyl bromide (51) in aqueous acetic acid at 51° with the endo analog (38) in 50% aqueous ethanol at 60° can be justified if the differences in solvent and temperature effects are slight. Since it has been shown that secondary isotope effects are independent of solvents with varying nucleophilic and electrophilic properties at constant Y values,³⁹ variation of Y over a range of 2-3 log units should cause less than a 1% variation of the isotope effect per deuterium. It has also been shown that the isotope effect is fairly temperature independent.³⁶ Consequently, the difference in solvent and temperature (9°) should not seriously affect the interpretation of these results. The small β -deuterium isotope effect observed for the exo bromide (51) indicates that charge delocalization is important in the transition state, but the large β -deuterium isotope effect for the endo bromide (38) indicates that there is considerable charge concentration at the C₂ position.

The solvolysis of α -(p-tolyl)ethyl- d_3 chloride in 80% aqueous acetone is probably close to limiting and a β -deuterium isotope effect of 1.05 per deuterium was observed.⁸⁷ In contrast with this value, the β -deuterium isotope effect for 3,3- d_2 -t-amyl chloride is 1.19 per deuterium.⁷ Although suitable data are scant, these results are in accord with what would be expected on the basis of delocalization of the positive charge at C₁ by the attached aromatic ring. Charge delocalization implies that the exo bromide solvolyzes via a nonclassical bridged ion

that results from participation of the C₆-C₁ σ bond. Charge concentration must be due to the endo bromide (38) proceeding with unassisted solvolysis to a classical carbonium ion in the transition state. These results are in agreement with the results of Winstein and Trifan,⁴³ but are in disagreement with Brown's proposal that the exo-norbornyl derivatives solvolyze via equilibrating classical ions, which should result in an isotope effect comparable to the endo-2-norbornyl bromide. Consequently, the nonclassical carbonium ion (28) seems to be a resonance-stabilized intermediate rather than a high-energy transition state.

Lee and Wong⁷⁶ found that the α -deuterium isotope effects for exo-d₁-endo-2- (45) and endo-d₁-exo-2-norbornyl brosylate (44) in acetic acid at 50° were 1.21 and 1.08 per deuterium, respectively. The α -deuterium isotope effect calculated for 2-exo-d₁-2-endo-norbornyl bromide in 50% aqueous ethanol ($k_H/k_D = 1.28$ per D) compares favorably with the endo-2-norbornyl brosylate analog. Since solvent and temperature effects can be assumed to be small, the only difference in these compounds is the nature of the leaving groups. According to the Hammond postulate,⁸⁸ the transition state for the brosylate should be more stable than the transition state for the bromide. Therefore, the transition state for the brosylate should be more like the reactant, i.e., more sp³ character, than the transition state for the bromide. Consequently, the carbon-oxygen bond is less stretched than the carbon-bromine bond in the transition state; and the out-of-plane bending vibration is more hindered for the brosylate than for the bromide. Accordingly, the α -deuterium isotope effect for the endo-2-norbornyl

brosylate should be less than that for the endo-2-norbornyl bromide.

The α -deuterium isotope effect of 1.28 is the largest effect of this kind recorded, and it appears that the degree of bond breaking which has occurred in the transition state for the endo-2-norbornyl bromide is very large. Since nucleophilic approach from the endo face of the molecule is unfavorable due to the shielding effect of the C₆ methylene group, this result is reasonable since the departure of a relatively large group like bromine should also be hindered and the transition state will not be reached until a larger than normal degree of bond breaking has occurred. The large β -secondary isotope effect for the endo bromide is also in accord with this conclusion.

These data provide strong supporting evidence that the formation of the transition state in the solvolysis of exo norbornyl derivatives is anchimerically assisted, but that solvolysis of endo norbornyl derivatives proceeds with unassisted solvolysis to a classical carbonium ion.

Table 10. Solvolysis of endo-2-Norbornyl Bromide - Run 1.

Time (min)	c_t	c_{t+1400}	$c_{t+1400} - c_t$	$\text{Log}(c_{t+1400} - c_t)$
800	720	901	181	2.2577
900	748	907	159	2.2014
1000	771	912	141	2.1492
1100	790	916	126	2.1004
1200	806	920	114	2.0569
1300	820	924	104	2.0170
1400	832	928	96	1.9823
1500	844	931	87	1.9395

Rate constant: $k = 1.03 \times 10^{-3} \text{ min}^{-1}$.

Table 11. Solvolysis of endo-2-Norbornyl Bromide - Run 2.

Time (min)	c_t	c_{t+1400}	$c_{t+1400} - c_t$	$\text{Log}(c_{t+1400} - c_t)$
800	654	822	168	2.2253
900	677	828	151	2.1790
1000	697	833	136	2.1335
1100	715	837	122	2.0864
1200	731	841	110	2.0414
1300	745	844	99	1.9956
1400	758	847	89	1.9494
1500	769	850	81	1.9085

Rate constant: $k = 1.05 \times 10^{-3} \text{ min}^{-1}$.

Table 12. Solvolysis of endo-2-Norbornyl Bromide - Run 3.

Time (min)	c_t	c_{t+1400}	$c_{t+1400} - c_t$	$\text{Log}(c_{t+1400} - c_t)$
800	595	746	151	2.1790
900	614	751	137	2.1367
1000	632	755	123	2.0899
1100	647	759	112	2.0492
1200	662	762	100	2.0000
1300	674	765	91	1.9590
1400	686	767	81	1.9085
1500	697	769	72	1.8573

Rate constant: $k = 1.05 \times 10^{-3} \text{ min}^{-1}$.

Table 13. Solvolysis of endo-2-Norbornyl Bromide - Run 4.

Time (min)	c_t	c_{t+1400}	$c_{t+1400} - c_t$	$\text{Log}(c_{t+1400} - c_t)$
800	687	870	183	2.2625
900	711	875	164	2.2148
1000	732	880	148	2.1703
1100	752	884	132	2.1206
1200	769	888	119	2.0755
1300	784	892	108	2.0334
1400	798	895	97	1.9868
1500	811	898	87	1.9395

Rate constant: $k = 1.06 \times 10^{-3} \text{ min}^{-1}$.

Table 14. Solvolysis of 2,3,3-d₃-endo-2-Norbornyl Bromide - Run 5.

Time (min)	c _t	c _{t+2000}	c _{t+2000} -c _t	Log(c _{t+2000} -c _t)
800	616	840	224	2.3502
900	638	846	208	2.3181
1000	654	850	196	2.2934
1100	671	855	184	2.2648
1200	687	859	172	2.2355
1300	702	863	161	2.2068
1400	715	866	151	2.1790
1500	728	869	142	2.1507

Rate constant: $k = 0.653 \times 10^{-3} \text{ min}^{-1}$.

Table 15: Solvolysis of 2,3,3-d₃-endo-2-Norbornyl Bromide - Run 6.

Time (min)	c_t	c_{t+2000}	$c_{t+2000} - c_t$	$\text{Log}(c_{t+2000} - c_t)$
800	551	748	197	2.2956
900	568	753	185	2.2672
1000	584	758	174	2.2405
1100	600	762	162	2.2095
1200	614	766	152	2.1804
1300	626	769	143	2.1538
1400	639	772	133	2.1239
1500	651	775	124	2.0934

Rate constant: $k = 0.664 \times 10^{-3} \text{ min}^{-1}$.

Table 16. Solvolysis of 2,3,3-d₃-endo-2-Norbornyl Bromide - Run 7.

Time (min)	c _t	c _{t+2000}	c _{t+2000} -c _t	Log(c _{t+2000} -c _t)
800	575	780	205	2.3118
900	593	785	192	2.2833
1000	610	789	179	2.2529
1100	626	793	167	2.2227
1200	640	797	157	2.1959
1300	654	801	147	2.1673
1400	667	804	137	2.1367
1500	678	808	130	2.1139

Rate constant: $k = 0.658 \times 10^{-3} \text{ min}^{-1}$.

Table 17. Solvolysis of 2,3,3-d₃-endo-2-Norbornyl Bromide - Run 8.

Time (min)	c _t	c _{t+2000}	c _{t+2000} -c _t	Log(c _{t+2000} -c _t)
800	487	660	173	2.2380
900	502	664	162	2.2095
1000	516	668	152	2.1818
1100	529	671	142	2.1523
1200	542	674	132	2.1206
1300	553	677	124	2.0934
1400	564	680	116	2.0645
1500	574	682	108	2.0334

Rate constant: $k = 0.646 \times 10^{-3} \text{ min}^{-1}$.

Table 18. Solvolysis of 3,3-d₂-endo-2-Norbornyl Bromide - Run 9.

Time (min)	c _t	c _{t+1600}	c _{t+1600} - c _t	Log(c _{t+1600} - c _t)
800	646	856	210	2.3222
900	668	862	194	2.2878
1000	689	868	179	2.2529
1100	709	873	164	2.2148
1200	728	878	150	2.1761
1300	744	882	138	2.1399
1400	759	886	127	2.1038
1500	773	890	117	2.0682

Rate constant: $k = 0.847 \times 10^{-3} \text{ min}^{-1}$.

Table 19. Solvolysis of 3,3-d₂-endo-2-Norbornyl Bromide - Run 10.

Time (min)	c _t	c _{t+1600}	c _{t+1600} - c _t	Log(c _{t+1600} - c _t)
800	544	702	158	2.1987
900	560	706	146	2.1659
1000	576	710	134	2.1255
1200	605	718	113	2.0531
1300	618	722	104	2.0149
1400	629	724	95	1.9777
1500	640	727	87	1.9395

Rate constant: $k = 0.856 \times 10^{-3} \text{ min}^{-1}$.

Table 20. Solvolysis of 3,3-d₂-endo-2-Norbornyl Bromide - Run 11.

Time (min)	c_t	c_{t+1600}	$c_{t+1600} - c_t$	$\text{Log}(c_{t+1600} - c_t)$
800	592	763	171	2.2330
900	610	768	158	2.1987
1000	627	772	145	2.1614
1100	643	776	133	2.1239
1200	658	780	122	2.0864
1300	672	784	112	2.0511
1400	684	788	104	2.0149
1500	696	791	95	1.9754

Rate constant: $k = 0.847 \times 10^{-3} \text{ min}^{-1}$.

Table 21. Solvolysis of 3,3-d₂-endo-2-Norbornyl Bromide - Run 12.

Time (min)	c _t	c _{t+1600}	c _{t+1600} -c _t	Log(c _{t+1600} -c _t)
800	658	857	199	2.2989
900	680	862	182	2.2589
1000	702	867	165	2.2175
1100	722	871	149	2.1732
1200	740	875	135	2.1303
1300	757	878	121	2.0828
1400	772	881	109	2.0395
1500	784	884	100	2.0000

Rate constant: $k = 0.850 \times 10^{-3} \text{ min}^{-1}$.

Table 22. Solvolysis of endo-2-Norbornyl Bromide-d₃ - Run 13.

Time (min)	c_t	c_{t+2000}	$c_{t+2000} - c_t$	$\text{Log}(c_{t+2000} - c_t)$
800	354	521	167	2.2227
900	368	525	157	2.1959
1000	382	528	146	2.1659
1100	395	532	137	2.1367
1200	407	535	128	2.1072
1300	419	538	119	2.0755
1400	430	541	111	2.0453
1500	440	544	104	2.0170

Rate constant: $k = 0.684 \times 10^{-4} \text{ min}^{-1}$.

Table 23. Solvolysis of endo-2-Norbornyl Bromide-d₃ - Run 14.

Time (min)	c_t	c_{t+2000}	$c_{t+2000} - c_t$	$\text{Log}(c_{t+2000} - c_t)$
800	429	639	210	2.3222
900	448	643	195	2.2900
1000	466	647	181	2.2577
1100	482	651	169	2.2279
1200	497	655	158	2.1987
1300	511	658	147	2.1673
1400	525	662	137	2.1367
1500	537	665	128	2.1072

Rate constant: $k = 0.705 \times 10^{-3} \text{ min}^{-1}$.

Table 24. Solvolysis of endo-2-Norbornyl Bromide-d₃ - Run 15.

Time (min)	c_t	c_{t+2000}	$c_{t+2000} - c_t$	$\text{Log}(c_{t+2000} - c_t)$
800	354	524	170	2.2304
900	369	528	159	2.2014
1000	383	531	148	2.1703
1100	396	535	139	2.1430
1200	409	538	129	2.1106
1300	421	541	120	2.0792
1400	432	544	112	2.0492
1500	442	546	104	2.0170

Rate constant: $k = 0.702 \times 10^{-3} \text{ min}^{-1}$.

Table 25. Solvolysis of endo-2-Norbornyl Bromide-d₃ - Run 16.

Time (min)	c_t	c_{t+2000}	$c_{t+2000} - c_t$	$\text{Log}(c_{t+2000} - c_t)$
800	418	616	198	2.2967
900	435	620	185	2.2684
1000	451	625	174	2.2405
1100	466	628	162	2.2081
1200	481	631	150	2.1761
1300	494	634	140	2.1461
1400	506	636	130	2.1139
1500	517	638	121	2.0828

Rate constant: $k = 0.709 \times 10^{-3} \text{ min}^{-1}$.

EXPERIMENTAL

1. General

All boiling points and melting points are uncorrected.

Vapor-phase chromatography (vpc) was performed either on a Wilkens Instrument and Research, Inc., Aerograph gas chromatographic instrument or on an F and M Scientific Corporation Model 609 Flame Ionization gas chromatograph.

Infrared spectra were obtained on Perkin-Elmer spectrometers, Models 137 and 337.

Nuclear magnetic resonance (nmr) spectra were taken on a Varian Associates Model A-60 spectrometer.

Conductivity measurements were performed on an Industrial Instruments, Inc., Model RC 1682 Conductivity Bridge with a Heathkit Model IN-21 Decade Condenser used for phase balance of the bridge circuit.

Deuterium analyses were performed by Mr. Josef Nemeth of Urbana, Illinois.

2. Norbornene

Norbornene was obtained from Aldrich Chemical Company and purified by distillation through a 50-cm Vigreux column, bp 91-93°/700 mm (lit.⁸⁹ bp 94-97°).

3. exo-2-Norbornyl Bromide

The exo halide was prepared by hydrobromination of norbornene according to the method of Roberts and co-workers.⁹⁰ Distillation through a 50-cm Vigreux column gave a clear, colorless liquid, bp 39°/2 mm (lit.⁹⁰ bp 82°/29 mm), n_D^{23} 1.5141 (lit.⁹⁰ n_D^{25} 1.5126).

4. Cyclopentadiene

Cyclopentadiene was obtained by cracking dicyclopentadiene⁹¹ and was always freshly prepared before use.

5. endo-2-Norbornyl Bromide

endo-2-Dehydronorbornyl bromide was prepared by the Diels-Alder reaction of cyclopentadiene and vinyl bromide. Subsequent catalytic hydrogenation in ethyl acetate with platinum oxide according to the method described by Roberts and co-workers^{90,92} and distillation through a 50-cm Vigreux column gave the saturated bromide, bp 61°/9 mm (lit.⁹⁰ bp 69-70°/15.5 mm). Vpc examination of the dehydronorbornyl bromide on a Bentone 34 (10% on Chromosorb W, 60/80 mesh) $\frac{1}{2}$ " x 8' copper column at 68° showed 18.8% of the Diels-Alder product to be the exo isomer and 81.1% the endo isomer.

Selective solvolysis of the exo/endo mixture of 2-norbornyl bromides⁹² at 55° in 80% aqueous ethanol for 18 hrs. permitted the isolation of pure endo-2-norbornyl bromide.

6. exo-2-Norbornyl Formate

Formylation of norbornene according to the procedure in Organic Synthesis⁹³ gave the exo formate, bp 81-82°/20 mm (lit.⁹³ bp 170-173°).

7. exo-2-Norborneol

Saponification of 93.0 g (0.99 mole) of exo-2-norbornyl formate with 95.0 g (1.70 mole) of potassium hydroxide in 250 ml of 95% ethanol for 10 hr, at reflux temperature gave a dark brown solution which was steam distilled. The steam distillate was extracted with pentane, and the pentane solution was dried over anhydrous potassium carbonate before removal of the pentane with a rotary evaporator. The yield of exo alcohol, mp 123-125° (lit.⁴³ mp 127.8-128.5°), was 70.1 g (73%).

8. 2-Norbornanone

Oxidation of exo-2-norbornyl formate with chromium trioxide according to the procedure of Kleinfelter and Schleyer⁹³ gave, after distillation, the ketone, mp 90-92° (lit.⁹³ mp 90-91°), bp 167-171° (lit.⁹³ bp 170-173°).

9. endo-2-Norborneol

Reduction of 2-norbornanone with excess lithium aluminum hydride in anhydrous ether afforded the endo alcohol, mp 147-149° (lit.⁴³ mp 152-153°), in 92% yield.

10. Reaction of exo-2-Norborneol With Triphenylphosphine and Bromine in Various Non-polar Solvents

The general procedure is described below.

Triphenylphosphine (12.0 g, 0.045 mole) in 50 ml of solvent was placed in a three-necked, round-bottomed flask fitted with a condenser, dropping funnel, and mechanical stirrer. Bromine (7.15 g, 0.045 mole) was added dropwise to the cooled solution (ice-water) over a 20 minute

period; then the exo alcohol, in 50 ml of solvent, was added at a fairly rapid rate to the solution with stirring.

The reaction mixture was heated at reflux temperature for varying periods of time while a slow stream of nitrogen gas was admitted to remove hydrogen bromide gas. After the required time of reaction, a short Vigreux column was attached to the reaction flask and the solvent and norbornyl bromide were distilled under reduced pressure. The distillate was diluted with pentane and the pentane solution was washed quickly with ice water, aqueous sodium bicarbonate and again with ice water. After filtration of the dried pentane solution, distillation afforded 2-norbornyl bromide in 50-73% yields.

The ratio of exo/endo isomers was determined by solvolysis in 40% aqueous ethanol at 69°. Conductometric differential kinetic analysis according to the method of Brown and Fletcher⁵⁸ gave the results summarized in Table 7.

11. Reaction of exo-2-Norborneol With Triphenyl Phosphite and Bromine

The procedure described by Rydon and co-workers^{72,73} was followed. Bromine (7.2 g, 0.045 mole) was added to a solution of 14.0 g (0.045 mole) of triphenyl phosphite and 5.0 g (0.045 mole) of the exo alcohol with stirring and cooling (ice-water) in a nitrogen atmosphere. The reaction was stirred at room temperature for one hour, during which time vigorous evolution of hydrogen bromide gas occurred. The light yellow solution was distilled at 5 mm pressure until no more material distilled. The distillate was poured into 150 ml of ether: the ether solution was washed with three 20-ml portions of water and dried with

anhydrous calcium sulfate. After filtration, the ether solution was concentrated, and an aliquot was withdrawn and tested with ferric chloride solution to determine if phenol was present. A positive test was obtained and the product was diluted with ether; the ether solution was washed twice with 10% aqueous sodium hydroxide and once with water. After drying and concentration of the ether solution, distillation afforded 2-norbornyl bromide, bp 65°/10 mm (lit.⁹⁰ bp 69-70°/15.5°).

Differential kinetic analysis⁵⁸ showed the product to be a mixture of 90% exo isomer and 10% endo isomer.

12. Reaction of exo-2-Norborneol With Phosphorous Trichloride

Reaction of the exo alcohol with phosphorous trichloride according to the procedure of Gerrard and co-workers⁷¹ produced 2-norbornyl chloride, bp 67-69°/28 mm (lit.⁹⁴ bp 52°/11 mm).

Conductometric solvolysis in 40% aqueous ethanol and differential kinetic analysis⁵⁸ demonstrated that 83.5% of the product is the exo isomer and 16.5% of the product is the endo isomer.

13. Vinyl Bromide-d₃

1,2-Dibromoethane-d₄ (Isomet Corporation, 99 atom percent pure, 21.0 g, 0.019 mole) was placed in a three-necked flask fitted with a magnetic stirrer, dropping funnel, and a condenser with a distilling head attached. Potassium hydroxide (11.2 g, 0.20 mole) in 50 ml of 95% ethanol was added dropwise with stirring; potassium bromide precipitated almost immediately. The reaction mixture was heated to reflux until no more vinyl bromide distilled (about 3 hrs.). The product,

bp 16-20° (lit.⁹⁵ bp 16°), weighed 10.6 g (89% yield) and was used without further purification.

14. 2,3,3-d₃-endo-2-Norborn-5-enyl Bromide

Vinyl bromide-d₃ (10.6 g, 0.096 mole) and 6.4 g (0.096 mole) of cyclopentadiene were placed in a sealed tube and heated at 165° for 24 hrs. The dark colored product was distilled through a 30-cm Vigreux column to give 6.0 g (35% yield) of a colorless liquid, bp 58-59°/11 mm (lit.⁹⁰ bp 63-65.5°/15.5 mm). Vpc analysis on a Bentone 34 (10% on Chromosorb W, 60/80 mesh) ½" x 8' copper column at 68° showed that the product was a mixture of exo and endo isomers (18.7% exo and 81.3% endo).

Preparative vpc on a Bentone 34 column at 78° and subsequent deuterium analysis of the endo isomer gave the following results:

Anal. Calcd. for C₇H₆D₃Br: 33.33 atom percent excess deuterium. Found: 31.70 atom percent excess deuterium (2.85 deuterium atoms per molecule).

15. 2,3,3-d₃-2-Norbornyl Bromide

Dehydronorbornyl bromide-d₃ (2.0 g, 0.011 mole) was catalytically hydrogenated in ethyl acetate with 10% palladium on charcoal at atmospheric pressure. After filtration, distillation afforded 1.2 g of 2,3,3-d₃-norbornyl bromide, bp 66-67°/10 mm (lit.⁹⁰ 69-70°/15.5 mm).

Preparative vpc on a Bentone 34 column at 90° gave a mixture of exo and endo isomers, which could not be separated by any vpc columns

available in this laboratory. Deuterium analysis of this mixture of isomers gave the following results:

Anal. Calcd. for $C_7H_8D_3Br$: 27.27 atom percent excess deuterium. Found: 23.70 atom percent excess deuterium (2.61 deuterium atoms per molecule).

16. Acetic Acid-d₄

Malonic acid was exchanged three times with deuterium oxide in dioxane according to the method of Truce and co-workers.⁹⁶ Nmr analysis of the exchanged malonic acid indicated that the acid was about 90% deuterated.

Decarboxylation of the deuterated malonic acid at 145° and subsequent nmr analysis showed that the acetic acid was about 86% deuterated (85% yield).

17. 2,2,2-d₃-Ethanol

Reduction of acetic acid-d₄ with lithium aluminum hydride in ether⁹⁶ afforded 95% ethanol-d₃ in 85% yield. Nmr analysis indicated that the C₂ carbon atom contained 2.5 deuterium atoms per molecule.

18. 2,2,2-d₃-Acetaldehyde

Ethanol-d₃ (5% water) was oxidized with potassium dichromate in aqueous sulfuric acid by the same procedure used to oxidize *n*-propanol.⁹⁷ Distillation through a Widmer column afforded acetaldehyde-d₃, bp 21-25° (lit.⁹⁸ bp 20°), in 40% yield. About 12% of the alcohol was recovered and used in subsequent oxidations. The yield of aldehyde is greatest when 25 g of alcohol is used.⁹⁸

Nmr analysis indicated that the C₂ carbon atom contained about 2.3 deuterium atoms per molecule.

19. 2,2,2-d₃-1,1-Dibromoethane

The procedure which was employed has been described by Wibaut⁹⁹ and Burkhardt and Cocker.¹⁰⁰ Phosphorous trichloride (43.5 ml, 0.50 mole) was placed in a round-bottomed flask and cooled in an ice bath. Bromine (27.2 ml, 0.50 mole) was added slowly with occasional shaking. The reaction mixture was allowed to stand overnight at room temperature. Acetaldehyde-d₃ (16.5 g, 0.37 mole) in a dropping funnel cooled with circulating ice-water was added dropwise through a condenser cooled with ice-water at a slow rate. The reaction was violent and the addition was thus done slowly with efficient cooling of the reaction flask. After standing for one hour at 0°, the excess phosphorous pentahalide was decomposed by the slow addition of ice-water to the well-cooled reaction mixture. The dense ethylidene bromide was separated from the aqueous layer, which was extracted three times with 100-ml portions of ether. The bromide and the ether solutions were combined and washed several times with water and aqueous sodium bisulfite. After drying with anhydrous magnesium sulfate, the ether solution was concentrated with a rotary evaporator to give 17.5 g (27% yield) of a slightly yellow liquid.

Vpc analysis on a Reoplex 400 (10% on firebrick, 60/80 mesh) ½" x 5' copper column at 70° revealed that 5-10% crotonaldehyde was present. The deuterated bromide was not purified further. Nmr

analysis of the product mixture showed that about 2.4 deuterium atoms were present on the C₂ carbon atom.

20. 2,2-d₂-Vinyl Bromide

Vinyl bromide-d₂ was prepared according to the procedure of Loevenich and co-workers.¹⁰¹ Sodium (3.3 g, 0.14 g-atom) was added to 110 ml of absolute ethanol in a round-bottomed flask fitted with a condenser and a magnetic stirrer. After the sodium reacted with the ethanol, ethylidene bromide-d₃ was added in one portion to the basic solution. A distilling head was placed on top of the condenser and the reaction mixture was heated to 85° for 2.5 hrs. Vinyl bromide-d₂, 9.4 g (60% yield), bp 17-21° (lit.⁹⁵ bp 16°), was collected in a receiver cooled in Dry-Ice acetone.

Nmr analysis revealed that 1.7 deuterium atoms per molecule were present in the C₂ position.

21. 3,3-d₂-endo-2-Norborn-5-enyl Bromide

Vinyl bromide-d₂ (9.4 g, 0.086 mole) and cyclopentadiene (5.5 g, 0.083 mole) were heated in a sealed tube at 165° according to the procedure of Roberts and co-workers.⁹⁰ After distillation, 4.7 g (32.5% yield) of a colorless liquid, bp 55-57°/10 mm (lit.⁹⁰ bp 63-65.5°/15.5 mm), was obtained. Preparative vpc on a Bentone 34 column at 90° resulted in pure 3,3-d₂-endo-2-dehydronorbornyl bromide.

Anal. Calcd. for C₇H₇D₂Br: 22.22 atom percent excess deuterium. Found: 16.35 atom percent excess deuterium (1.47 deuterium atoms per molecule).

22. 3,3-d₂-2-Norbornyl Bromide

Catalytic hydrogenation of 3,3-d₂-2-norborn-5-enyl bromide (mixture of exo and endo isomers) with 10% palladium on charcoal in ethyl acetate gave a mixture of exo and endo-2-norbornyl bromide which was collected by preparative vpc on a Bentone 34 column at 90° as the mixture of exo and endo isomers.

Anal. Calcd. for C₇H₉D₂Br: 22.22 atom percent excess deuterium. Found: 13.10 atom percent excess deuterium (1.44 deuterium atoms per molecule).

23. 1,1,2,2-Tetrabromoethane

Acetylene was bubbled through bromine according to the procedure of O'Meara and Clemmer.¹⁰² Distillation through a Widmer column afforded a 63% yield of the tetrabromoethane, bp 64°/1 mm (lit.¹⁰³ bp 124°/19 mm).

24. 1,2-Dibromoethylene

Debromination of tetrabromoethane with zinc dust in ethanol according to the procedure of Lee and Miller¹⁰⁴ resulted in a 60% yield of dibromoethylene, as a mixture of cis and trans isomers. Vpc analysis on a 20M Carbowax (20% on Chromosorb W, 60/80 mesh) ¼" x 6' copper column at 130° showed that the ratio of cis to trans isomers was 1.32. Nmr analysis revealed a ratio of 1.25.

25. 5,6-Dibromo-2-Norbornene

5,6-Dibromo-2-norbornene was prepared according to the procedure of LeBel.¹⁰⁵ Cyclopentadiene (17.9 g, 0.27 mole) and a mixture of

cis and trans-dibromoethylene were placed in a sealed tube, which was flushed with nitrogen, and heated at 190° for 4 hrs. The dark-colored product was distilled, bp 103-135°/5-8 mm (lit.¹⁰⁵ bp 40-90°/1 mm) to give 26.0 g (38% yield) of a mixture of exo-cis- and trans-5,6-dibromo-2-norbornene, which was used without further purification.

26. 2,3-Dibromonorbornane

Catalytic hydrogenation of the isomeric mixture of 5,6-dibromo-2-norbornene with platinum in ethyl acetate resulted in a 91% yield of 2,3-dibromonorbornane (mixture of exo-cis and trans isomers).

27. 2-Bromo-2-Norbornene

Elimination of hydrogen bromide from 2,3-dibromonorbornane with potassium t-butoxide in t-butyl alcohol according to a modification of the procedure of Kwart and Kaplan^{105,106} gave the unsaturated bromide, bp 44-45°/9 mm (lit.¹⁰⁶ bp 61-63°/16 mm), n_D^{20} 1.5219 (lit.¹⁰⁵ n_D^{25} 1.5177).

28. Deuteration of 2-Bromo-2-Norbornene

2-Bromo-2-norbornene was deuterated catalytically with deuterium gas (Matheson) using platinum oxide in ethyl acetate. The deuterated norbornyl bromide was collected by preparative vpc on a Bentone 34 column at 90°.

Anal. Calcd. for $C_7H_9D_3Br$: 27.27 atom percent excess deuterium. Found: 25.20 atom percent excess deuterium (2.77 deuterium atoms per molecule).

29. Kinetic Measurements

A constant temperature bath was regulated to $\pm 0.01^\circ$ by a commercial thermostat; the temperature (60.21°) was determined with a National Bureau of Standards thermometer.

The solvent used in all of the kinetic measurements was aqueous ethanol (50 volume percent). Commercially available conductance cells were filled to the top in order to prevent condensation of the solvent on the walls of the cell.

Preparative vpc insured that the norbornyl bromides were pure. The norbornyl bromides used in all of the kinetic measurements were mixtures of exo and endo isomers. Separation of the isomers was not necessary since the exo isomer solvolyzes about fifty times faster than the endo isomer under the conditions used to measure the rate constants. Consequently, the first conductance measurements for the endo isomer were made after the exo isomer had solvolyzed for ten half life periods.

The sample size was 4 microliters and was introduced into the conductivity cell by a 25 microliter syringe. After ten solvolysis half life periods for the exo isomer (about 700 minutes), conductivity measurements for the endo isomer were started. Measurements were taken at appropriate time intervals over a five half life period for the endo isomer.

A plot of conductivity (micromhos) versus time (minutes) resulted in a curve that measures the production of hydrogen bromide as a function of time. Since conductivity, c , is directly proportional to

concentration, the usual first order rate expression can be written as

$$c = c_0 e^{-kt}$$

If times t_1, t_2, \dots, t_i and times $t_1 + Z, t_2 + Z, \dots, t_i + Z$ are chosen (Z is a constant increment of time), then values of c_i and c'_i , which are measurements of conductivity at t_i and $t_i + Z$, respectively, can be obtained from the curve. From these considerations the following equations can be derived:

$$(c_i - c_\infty) = (c_0 - c_\infty) e^{-kt_i}$$

$$(c'_i - c_\infty) = (c_0 - c_\infty) e^{-k(t_i + Z)}$$

Subtraction of the second equation from the first gives

$$(c_i - c'_i) = (c_0 - c_\infty) e^{-kt_i} (1 - e^{-kZ})$$

or
$$\ln(c_i - c'_i) = \ln(c_0 - c_\infty) (1 - e^{-kZ}) - kt_i$$

Accordingly, a plot of $\ln(c_i - c'_i)$ versus time allows the rate constant (k) to be calculated.

The increment of time (Z) should be at least twice the half life period to insure accuracy by this Guggenheim analysis.⁸⁵

APPENDIX

CALCULATION OF k_H/k_D PER D FOR DEUTERATED NORBORNYL BROMIDES

The exo and endo deuterium atoms at C_3 were assumed to be equivalent for 3,3- d_2 -endo-2-norbornyl bromide (40), 2,3,3- d_3 -endo-2-norbornyl bromide (38) and 3,3- d_2 -exo-2-norbornyl bromide (51), since the geometry of the norbornyl system is similar to the cyclopentyl system for which there is only a small conformational dependence for the secondary isotope effect.¹⁹ Deuterium analysis indicated that 40 had 1.44 deuterium atoms per molecule, and kinetic measurements showed that the β -deuterium isotope effect was 1.24. Consequently,

$$(k_H/k_D) = (1.24)^{1/1.44} = 1.16 \text{ per D for } \underline{40}.$$

Compound 38 had 2.61 deuterium atoms per molecule and had a combined α - and β -deuterium isotope effect of 1.61. Now, if the distribution of deuterium atoms in the C_2 , exo C_3 and endo C_3 positions is assumed to be statistical, i.e., 0.87 deuterium atoms at each of these three positions, then $k_H/k_D = (1.16)^{1.74} = 1.30$ for the β -deuterium isotope effect for 38. Therefore,

$$(k_H/k_D)_{\alpha} (k_H/k_D)_{\beta} = 1.61 \text{ for } \underline{38}, \text{ and}$$

$$(k_H/k_D)_{\alpha} = (1.61) (1.30) = 1.24 \text{ per } 0.87 \text{ D, and}$$

$$(k_H/k_D)_{\alpha} = (1.24)^{1/0.87} = 1.28 \text{ per D.}$$

Consequently, the α -deuterium isotope effect is 1.28 per D for exo-2-d₁-endo-2-norbornyl bromide and the β -deuterium isotope effect is 1.16 per D for endo-2-norbornyl bromide.

Compound 51 had 1.92 deuterium atoms per molecule and had a β -deuterium isotope effect of 1.09. Accordingly, $k_H/k_D = (1.09)^{1/1.92} = 1.04$ per D.

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