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DEUTERIUM ISOTOPE EFFECTS ON THE SOLVOLYSIS RATES
OF CYCLOPENTYL BROSYLATES AND TOSYLATES

by

JIMMIE DUANE CHRISTEN, 1942

A DISSERTATION 541

Presented to the Faculty of the Graduate School of the
UNIVERSITY OF MISSOURI - ROLLA

In Partial Fulfillment of the Requirements for the Degree

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This dissertation is dedicated to
my wife, Janet

ABSTRACT

The brosylates and tosylates of cyclopentanol and its 1-d₁, cis-2-d₁, trans-2-d₁, and 2,2,5,5-d₄ analogs have been synthesized and their solvolysis rates measured at 25° in 70% vol. ethanol-water. The solvolysis reactions were monitored by a conductance method. The isotope effects, k_H/k_D , observed for the brosylates and tosylates of each of the isotopically substituted cyclopentyl alcohols are as follows: 1-d₁-brosylate (1.1869) and 1-d₁-tosylate (1.1836); cis-2-d₁-brosylate (1.1533) and cis-2-d₁-tosylate (1.1577); trans-2-d₁-brosylate (1.1803) and trans-2-d₁-tosylate (1.1765); 2,2,5,5-d₄-brosylate (1.8881) and 2,2,5,5-d₄-tosylate (1.8863).

The closeness in magnitude of the isotope effects for the cis- and trans-isomers is important in that it shows the cyclopentyl system to be very nearly planar. If they had been greatly different it would have indicated that the ring was quite puckered. More important, however, is the fact that the trans-isotope effect is greater than the cis-isotope effect. This means that specific solvation of the β -hydrogens, leading to an elimination driving force, is a possible explanation of secondary deuterium isotope effects.

The isotope effects for the d₄-compounds were calculated by taking the product of the squares of the cis- and trans-isotope effects. The calculated isotope effect was 1.8530 for the d₄-brosylate and 1.8552 for the d₄-tosylate. These values are very near the observed values of 1.8881 and 1.8863 for the brosylate and tosylate, respectively. Because of the great precision (~0.1-0.2%) of the technique used in obtaining these results, the difference between the calculated and the observed isotope effects for

both the brosylate and tosylate is considered to be a true difference. However, the closeness of the calculated and observed values does indicate an almost cumulative isotope effect which supports the hyperconjugation postulate as a possible explanation of secondary deuterium isotope rate effects.

There is very close agreement between the isotope effects for the brosylate and tosylate of any one given isotopically substituted cyclopentyl alcohol, e.g., the greatest difference exhibited was that of 0.38% for the cis-compounds. This close agreement tends to indicate that when changing from one leaving group to another structurally similar leaving group there is a negligible influence on the isotope effect.

Attempts were made to synthesize 2,2-d₂-cyclopentyl alcohol and cis-2-d₁-5,5-d₂-cyclopentyl alcohol and the procedures are described in the Experimental section. Unfortunately, these synthetic procedures were unsuccessful.

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INTRODUCTION

A considerable controversy in recent years over the nature and causes of secondary isotope effects prompted a study of isotope effects in cyclic systems. Several investigations made with six-membered ring compounds yielded consistent results but were not in agreement with the single investigation made with five-membered ring compounds. Due to the similarity in structure of cyclopentyl and cyclohexyl systems, similar data would be expected. In an attempt to resolve the discrepancy a reinvestigation of the cyclopentyl system was undertaken. The compounds chosen for this study were the α - and β -deuterated cyclopentyl tosylates studied in the original investigation, as well as the corresponding brosylates. In order to accurately determine the isotope effects it was planned to follow the solvolysis reactions by a precise conductometric method.

REVIEW OF LITERATURE

Introduction

The isotopes of any element, e.g., hydrogen, deuterium and tritium, differ only by the number of neutrons in their nuclei (zero, one and two neutrons, respectively); and the presence of additional neutrons in a particular nucleus has little effect on the electrons of an atom or molecule. Therefore, if one isotope is substituted for another, e.g., deuterium for hydrogen, it does not appreciably affect the electronic structure of the molecule although it does affect the mass of the isotopically substituted molecule. Isotopic substitutions of this sort do affect the rates of many chemical reactions since a change in atomic mass alters the translational,¹ rotational² and vibrational³ behavior of a molecule. These rate changes provide a useful means of obtaining information about the mechanism of these reactions.

The isotope effect is essentially a quantum-mechanical phenomenon due to the fact that the translational, rotational and vibrational energies of a molecule can have only certain discrete values.⁴ The effect of isotopic substitution is ordinarily larger on the vibrational energy levels than on the translational or rotational energy levels,⁵ so for qualitative discussions the effect on the vibrational energy levels is the only one that need be considered.

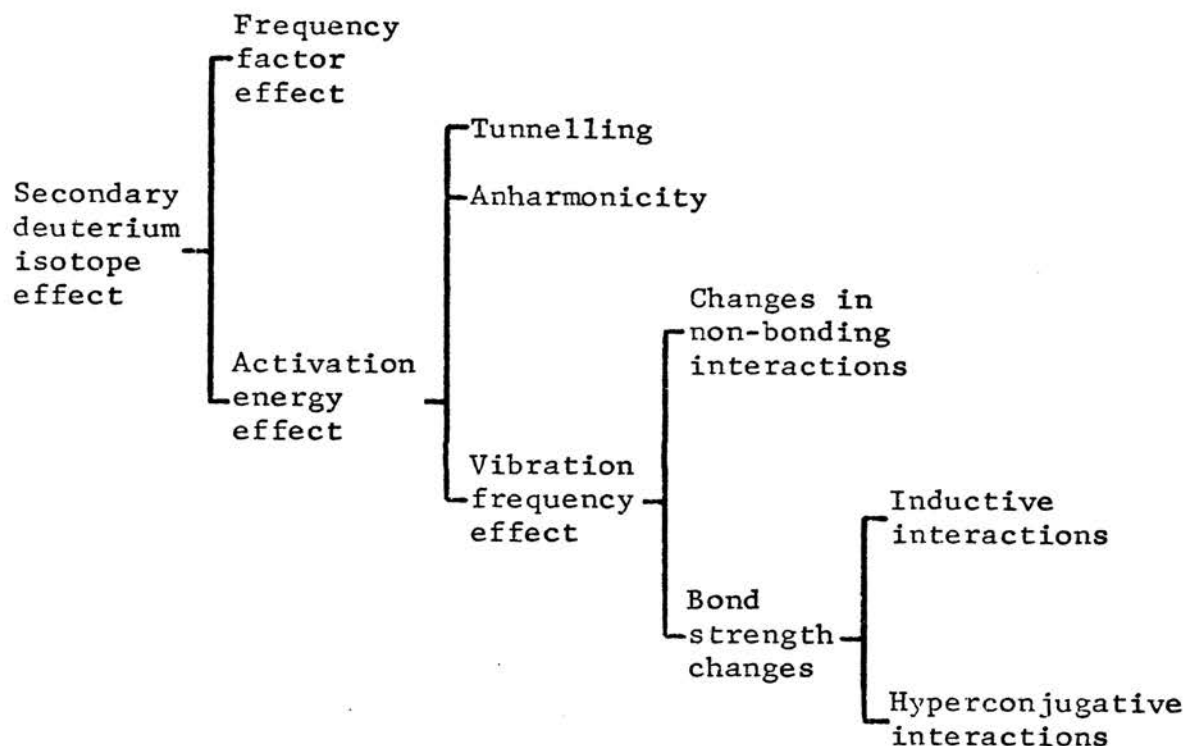
The deuterium isotope rate effect was first predicted by Cremer and Polyani⁶ and shortly thereafter by Sherman and Eyring.⁷ The phenomenon known as the primary isotope effect, which deals with reactions in which the isotopic atom is involved in a bond that is formed or broken during reaction, has been reviewed by Wiberg⁸ and it is not discussed here since it is not the subject of this dissertation. Rather, the

subject is secondary deuterium isotope rate effects, specifically those of the S_N1 type (substitution nucleophilic unimolecular). As opposed to primary isotope rate effects, secondary isotope rate effects are not caused by the formation or cleavage of bonds to isotopic atoms. A quotation from one of Shiner's publications states those phenomena most often considered as causes of secondary isotope effects:

There now exists ample published evidence which indicates that reactions with rate-determining steps which involve carbonium ion or partial carbonium ion formation are slowed by the substitution of a deuterium atom for a hydrogen atom in a hyperconjugating position. In each of the several cases where data are available it seems that the isotope rate effect is paralleled by an isotope activation energy effect although entropy factors also contribute. It seems fairly clear from theory that the isotope activation energy effects can only arise from (a) changes in vibration frequency of the hydrogen and deuterium atoms on activation, (b) tunnelling of the hydrogen atom or (c) anharmonicity effects. The second effect must be unimportant in these reactions although it might be a major factor in reactions where hydrogen bonds are directly broken. Several lines of evidence indicate that anharmonicity effects although small are present and may confuse the quantitative interpretation of the isotope rate effects. Thus the interpretation of secondary isotope rate effects is complicated but the application of the time-honored classical organic chemical method of comparing the effects in a large number of different compounds indicates that hyperconjugation is the predominant cause of these secondary isotope rate effects. If we further assume that the variations in these effects in closely related compounds are due to variations in hyperconjugation, the following conclusions are tentatively indicated: (1) There are steric effects on hyperconjugation. (2) There are substituent effects on hyperconjugation; conjugating and hyperconjugating substituents increase the extent of hyperconjugation of a single C-H bond. (3) There are solvent effects on hyperconjugation.⁹

Shiner has shown in chart form those factors which are presently believed to contribute to the secondary deuterium isotope effect.⁹ This chart is shown in order that the following discussion concerning the secondary deuterium isotope effect might be more easily visualized.

Chart I
Contributions to Secondary Isotope Effects



The following quotation shows what Brown¹⁰ feels are the major causes of secondary deuterium isotope effects. The similarity with and differences from Shiner's⁹ views should be noted.

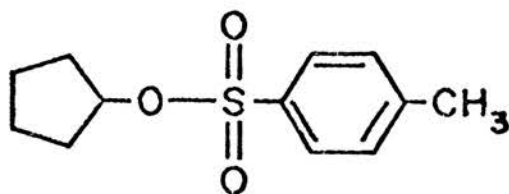
At the present time secondary isotope effects are commonly discussed and analyzed in terms of these three classical effects: hyperconjugative, inductive, and steric. It is unfortunate that no really satisfactory quantitative treatment for any of these effects is yet available. Qualitative predictions based on any one of these effects frequently lead to conflicting answers. Consequently, it is always possible to account for an observed result, but it is not possible to make predictions with any confidence. Nevertheless, wide use has been made of secondary isotope effects in exploring reaction mechanisms. One must admire the courage of those who have relied upon such evidence.¹⁰

Shiner¹¹ determined the rates of solvolysis of some deuterated tertiary-amyl chlorides in 80% vol. ethanol-water at 25°, and based on this study he was able to conclude that reaction rates of the S_N1 type are retarded by the substitution of deuterium for hydrogen either at the carbon atom bearing the leaving group (α -deuterium isotope rate

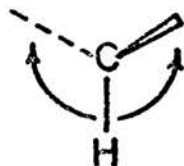
effect) or at the carbon adjacent to that bearing the leaving group (β -deuterium isotope rate effect).

As stated by Melander, one of the most commonly used methods of reporting an isotope effect is "...to make relative measurements, and to study the influence of certain internal or external conditions on the relative rate. Many unknown or poorly known magnitudes will be cancelled in the ratio of rates."¹² This technique is applied by taking the ratio of the rate constants, e.g., of the hydrogen compound to the deuterium compound (k_H/k_D), and by assuming that the difference in rate is caused solely by the isotopic substitution. This method of reporting isotope effects will be used throughout the following discussion.

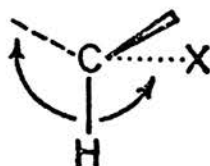
Streitwieser and Fahey¹³ observed the α -isotope effect in the acetolysis of cyclopentyl tosylate, the *p*-toluene-sulfonic acid ester. Streitwieser, Jagow, Fahey, and Suzuki⁵ suggested that the α -deuterium isotope effect is due predominantly to the change of a tetrahedral carbon-hydrogen bending vibration to an out-of-plane deformation in the transition state. They observed an isotope effect, k_H/k_D , of 1.15 for the acetolysis of cyclopentyl-1-d₁ tosylate (I-a), whereas their calculated isotope effect, k_H/k_D , for this compound was 1.38. The calculated value was obtained by assigning the appropriate vibrational frequencies (via infrared) to the molecules in their ground state, assuming corresponding vibrational frequencies for the transition state, and making use of the Bigeleisen equation¹⁴ which is described in detail in the following section. Using the following figures they explained this difference between the observed and calculated values.



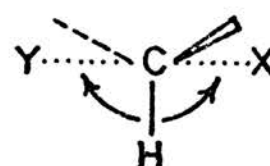
I-a



I-b



I-c



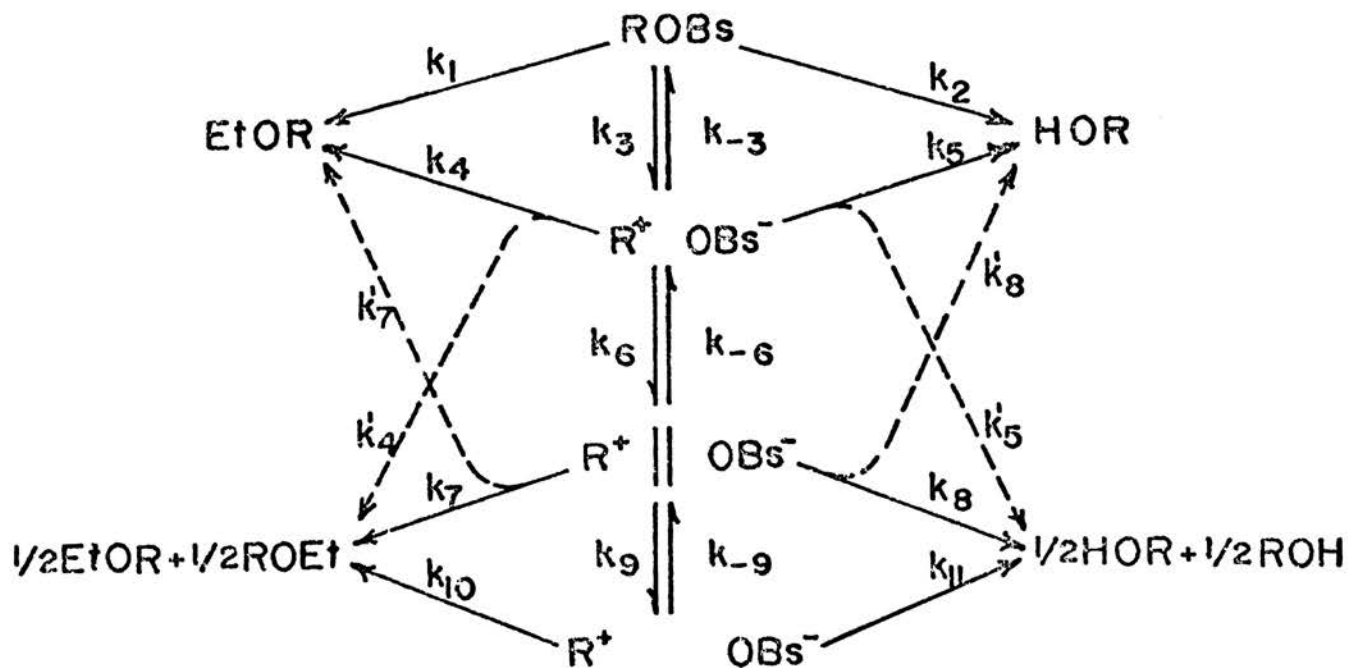
I-d

It appeared to them that the most important factor involved in the α -deuterium effect 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 (I-b). Solvolysis of secondary alkyl tosylates is unassisted by backside solvent participation in the transition state.¹⁵ This was demonstrated by solvolyzing several optically active secondary alkyl tosylates in various solvent systems, e.g., acetic acid, ethanol, and butanol, and observing that the products formed were almost completely racemized. However, although the backside of the reacting carbon is clear, the tosyl group (represented by X) is still reasonably close to the forming carbonium ion and its presence probably impedes the carbon-hydrogen wagging motion (I-c). The transition state would contain an entering group (represented by Y) and leaving group (represented by X) and the wagging motion would be impeded even more (I-d), probably about the same as a tetrahedral carbon-hydrogen bending vibration. In this connection, it is pertinent that in the direct displacement of isopropyl bromide by sodium ethoxide,

Shiner¹⁶ found an isotope effect, k_H/k_D , of 1.00 for the α -deutero compound. Streitwieser, Jagow, Fahey, and Suzuki⁵ concluded that if this idea of isotopic inhibition of the out-of-plane bending vibration should be substantiated by further work, the α -deuterium isotope effect might provide a new tool for determining the structural degree of solvent or neighboring group assistance provided at the transition state of solvolytic displacement reactions.

Several general solvolysis mechanism schemes have been proposed in the literature. The following mechanism, proposed by Shiner,¹⁷ gives a more detailed picture of the possible intermediates for this class of reactions. In proposing this scheme, Shiner assumed (a) that no nucleophiles other than the solvent molecules are added, (b) that only substitution reactions of ROBs (alkyl brosylate, *i.e.*, alkyl *p*-bromobenzene sulfonic acid ester) are taking place although olefins are formed in most of the solvolysis reactions which have been studied to date, and (c) that the R group is not undergoing any rearrangement.

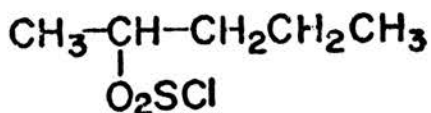
Scheme I
General Aqueous Ethanol Solvolysis Mechanism



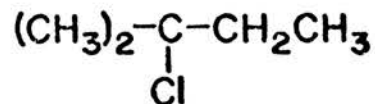
In Scheme I, substitution by ethanol is indicated on the left and substitution by water on the right. Both EtOR and HOR represent products of inverted configuration while ROEt and ROH represent products with retained configuration. The intermediates which are listed down the center are: $R^+ \text{ O}^-\text{S}$ the intimate ion pair, $R^+ \parallel \text{O}^-\text{S}$ the solvent-separated ion pair, and $R^+ \quad \text{O}^-\text{S}$ the free carbonium ion and free brosylate anion respectively. From Shiner's observations, external return from the solvent-separated ion pair (k_{-6}) was not very important. Shiner assumed that substitution in the intimate ion pair always led to inverted products; however, he also recognized the possibility of some racemized products being formed (k'_4 and k'_5). Substitution on the solvent-separated ion pair may give some net inversion (k'_7 and k'_8) and most definitely some racemization (k_7 and k_8).

Shiner's¹⁷ observations tended to indicate that the rate-determining step for limiting solvolyses (S_N1) was k_3 and that the products were derived mainly from the solvent-separated ion pair, and therefore, were mainly racemized (k_7 and k_8). Shiner's views are all quite compatible with the observations made by Weiner and Snee^{18,19} on the mechanism of solvolyses of 2-octyl sulfonates.

Lewis and Boozer²⁰ observed a β -isotope effect, k_H/k_D per D = 1.05, in the decomposition of 2-pentyl chlorosulfite (II), and at about the same time Shiner¹¹ measured the reduction in the rate of solvolysis, in 80% vol. ethanol-water, of β -amyl chloride (III), k_H/k_D per D = 1.05, caused by β -deuterium substitution. Shiner as well as Lewis and Boozer



II



III

suggested that the source of the β -isotope effect is a weakening of the β -hydrogen bonds by increased hyperconjugation in the transition state.

Shiner²¹ and Lewis and Coppinger²² have studied the isotope effect as a function of temperature. Both groups concluded that the rate effect was caused by a change in activation energy. Leffek, Robertson and Sugamori²³ felt that the isotope rate effect could be caused by activation entropy differences; however, nothing conclusive can be drawn from their work as the entropy effects were found to be quite small.

General Theory of the Deuterium Isotope Rate Effect

Both Bigeleisen¹⁴ and Melander²⁴ have investigated the theoretical aspects of isotopic substitution on the rates of chemical reactions. The Bigeleisen equation, Equation 1, which was derived from the absolute rate theory and statistical mechanics, shows that the isotope rate effect for the substitution of deuterium for hydrogen may be obtained by a knowledge of the molecular vibrational frequencies of the initial states and the transition states for the hydrogen and deuterium compounds.¹⁴ A vibrational analysis of this sort for the initial state is usually difficult and cannot be done at all for the transition state since much information is still lacking concerning the structure of the transition state for most chemical reactions. Melander²⁴ has suggested that the most important uses of isotope effects are as a check of a tentative transition state and as a tool for selecting the true one from the few which seem most likely. This approach has been used by several authors, a few of whom are Shiner,⁶ Halevi²⁵ and Miller.²⁶

$$\frac{k_H}{k_D} = \frac{\nu_{L(H)^\ddagger}}{\nu_{L(D)^\ddagger}} \prod_i^{3n^\ddagger-7} \left(\frac{u_i(H)^\ddagger}{u_i(D)^\ddagger} \cdot \frac{e^{-1/2 u_i(H)^\ddagger}}{e^{-1/2 u_i(D)^\ddagger}} \cdot \frac{1 - e^{-u_i(D)^\ddagger}}{1 - e^{-u_i(H)^\ddagger}} \right) \cdot \prod_i^{3n-6} \left(\frac{u_i(D)}{u_i(H)} \cdot \frac{e^{-1/2 u_i(D)}}{e^{-1/2 u_i(H)}} \cdot \frac{1 - e^{-u_i(H)}}{1 - e^{-u_i(D)}} \right) \quad (1)$$

In Equation 1, k_H and k_D are the rate constants for molecules containing hydrogen and deuterium, respectively; $\nu_{L(H)^\ddagger}/\nu_{L(D)^\ddagger}$ is the temperature-independent factor, which takes into account the effect of motion along the reaction coordinate; n is the number of vibrational degrees of freedom; and u contains the stretching frequency in the form of $h\nu/kT$, where h is Planck's constant, k is Boltzmann's constant, and T is the absolute temperature. The important terms in the expression are the ones which have the form $e^{-1/2 u_i(D)}/e^{-1/2 u_i(H)}$ since they describe the zero-point energies of the system.

It has been generally conceded that the most important contributing factor to the isotope effect arises from zero-point energy differences in the fundamental vibrations of the isotopes in question, hydrogen and deuterium.¹³ For the case in which hydrogen is attached to a fairly heavy organic residue and this carbon-hydrogen bond is weakened in the transition state, the vibration of this hydrogen is a function of the reduced mass of the system which is approximately the mass of hydrogen in a heavy molecule. The vibration of a diatomic molecule resembles the vibration of a pair of point masses (the atoms) connected

by a spring (the bond between them), with the vibrational frequency $\nu = (1/2\pi)(k/\mu)^{\frac{1}{2}}$. This equation which describes the vibrational frequency is arrived at using the harmonic oscillator system, which is the accepted quantum-mechanical model for the vibrational motion of diatomic molecules. Here k is a force constant which specifies the stiffness of the bond, and μ , the reduced mass, is given by $\mu = m_R m_H / (m_R + m_H)$ where m_R is the mass of the organic residue and m_H is the atomic mass of hydrogen. Since the organic residue is considerably heavier than hydrogen, m_R will not be appreciably different from $m_R + m_H$. Therefore, the above equations will reduce to $\mu \cong m_H$ and $\nu \cong (1/2\pi)(k/m_H)^{\frac{1}{2}}$.

The isotope rate effect, k_H/k_D , is given approximately by Equation 2, which is arrived at by reducing the Bigeleisen equation (Equation 1) to a simple dependence on the zero-point energies.

$$k_H/k_D = \text{EXP}(hc/2kT) (\Delta\nu_H - \Delta\nu_D) \quad (2)$$

This is a fairly good approximation if all the frequencies, ν , are high relative to kT/h . In this equation $\Delta\nu_H$ and $\Delta\nu_D$ are the changes in the frequencies of the carbon-hydrogen and carbon-deuterium oscillators, respectively, in going from the initial state to the transition state. Since the carbon-hydrogen and carbon-deuterium bonds have essentially the same force constants²⁵ but deuterium has a greater reduced mass than hydrogen ($\mu \cong m_D \cong 2m_H$), the carbon-deuterium oscillator will have a lower zero-point energy in the initial state. The carbon-hydrogen and carbon-deuterium bonds are weakened to about the same extent in the transition state, which results in approximately the same change in force constants of the two bonds. Since the carbon-hydrogen oscillator has a smaller reduced mass than the

carbon-deuterium oscillator it will have a greater change in frequency in going from the initial state to the transition state, making $\Delta\nu_H > \Delta\nu_D$, and hence $k_H/k_D > 1$. From Figure 1 it can be seen that the activation energy for the hydrogen compound (E_a^H) is less than that for the deuterium compound (E_a^D); hence the hydrogen compound will react faster.

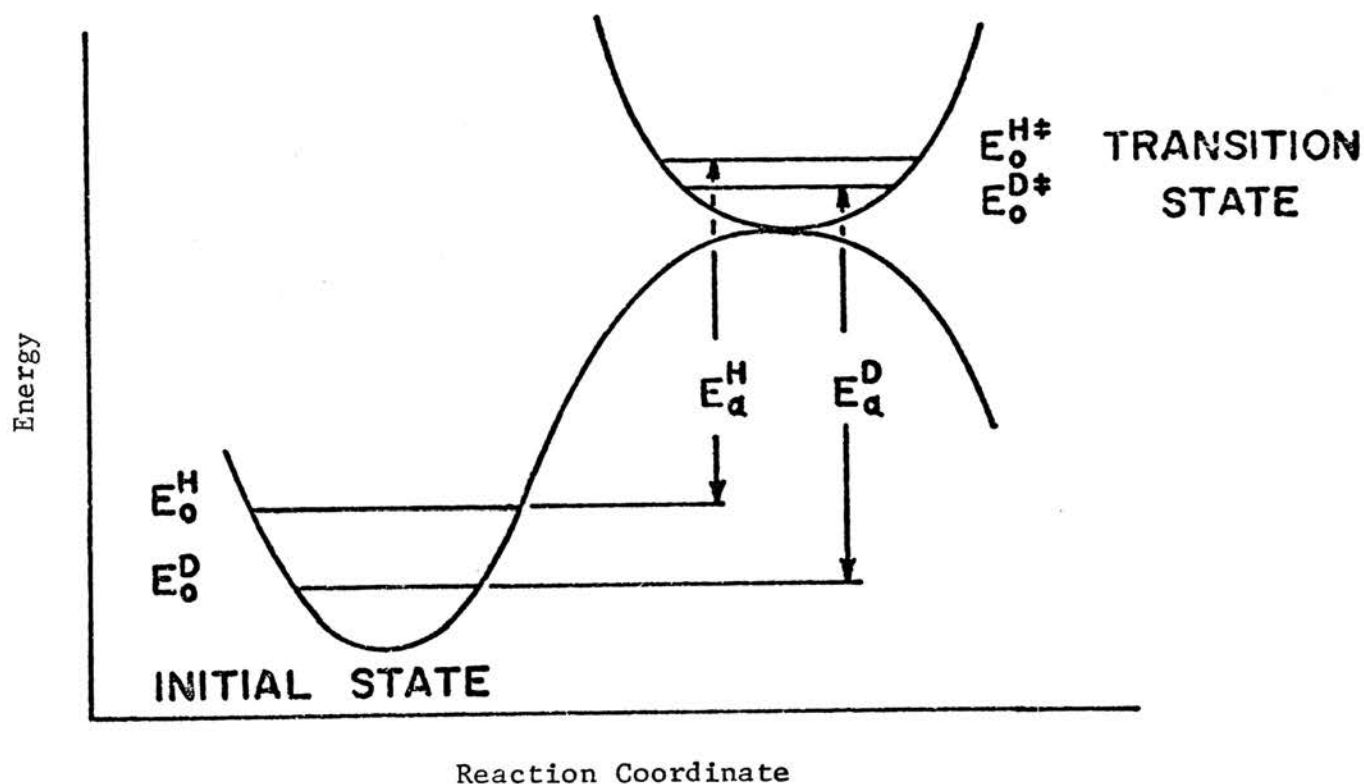
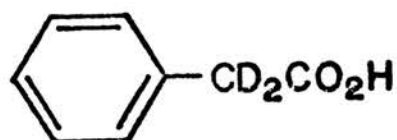


Figure 1: Potential Energy Profile

Halevi²⁷ observed an isotope effect, $k_H/k_D = 1.12$, for α -dideuterio-phenylacetic acid (IV), and he postulated that this isotope effect was



caused by differences in inductive effects of hydrogen and deuterium due to anharmonicity effects. He therefore questioned the Bigeleisen-Melander treatment because it does not take anharmonicity effects into account.

Anharmonicity is the deviation of the potential curve (e.g., of a carbon-hydrogen bond) from parabolic shape (Figure 2). The mean length

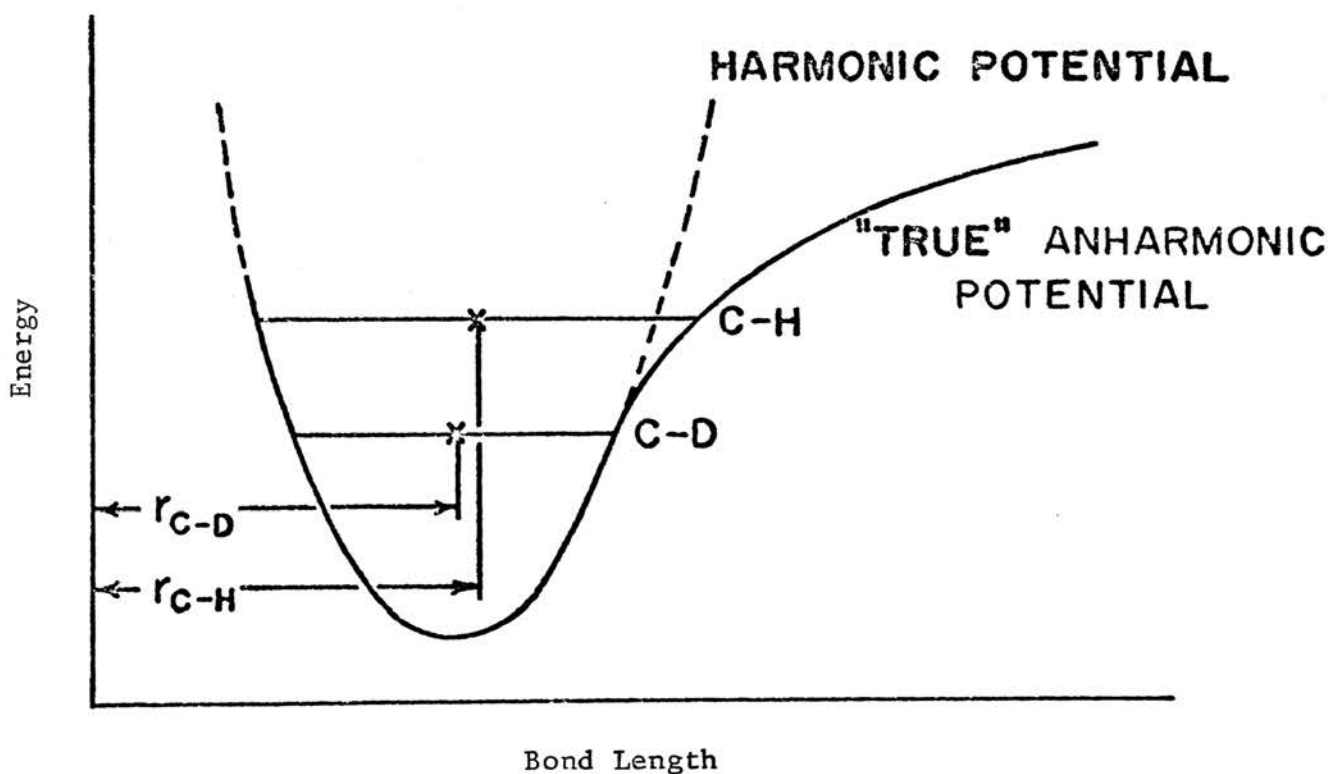


Figure II: Potential Energy Profile

of a carbon-hydrogen bond, averaged over a vibration, will be greater than that of a carbon-deuterium bond. Therefore, the electrons in a carbon-deuterium bond will, on the average, be closer to the carbon than will the electrons in a carbon-hydrogen bond, and deuterium will appear to be electron-donating relative to hydrogen even though there is no difference in the electron-attracting power of the two nuclei which differ only by one neutron.

More convincing evidence of the role of anharmonicity on the relative ground state electron-releasing abilities of carbon-hydrogen and carbon-deuterium bonds has been given by Tiers.²⁸ After comparison of the fluorine nuclear spin resonance spectrum of $n\text{-C}_3\text{F}_7\text{D}$ with that of $n\text{-C}_3\text{F}_7\text{H}$ he found that the fluorine nuclei in the $-\text{CF}_2\text{D}$ group are 0.60 ± 0.05 p.p.m. more shielded than those in the $-\text{CF}_2\text{H}$ group. He stated that this difference in shielding value ("chemical shift") should be of theoretical interest inasmuch as the molecular wave function is not substantially altered since both molecules have the same electronic structure. Qualitatively it may be seen that the direction of the shift indicates a greater electron-donating power for deuterium than for hydrogen. The atomic volume of deuterium in covalent compounds is known to be smaller than that of hydrogen,^{29,50} a fact which, by elementary particle-in-a-box considerations, requires a greater escaping tendency for the electrons. Streitwieser³¹ has observed a slight degree of optical activity ($\alpha_{\text{D}} = 3\text{-}4^\circ$) due solely to differences between hydrogen and deuterium atoms located at the asymmetric center, and has concluded that this must be due to anharmonicity effects. It is, however, difficult to extrapolate from Tiers and Streitwieser's observations and predict what kinetic or equilibrium constant effects should result from such anharmonicity influences.

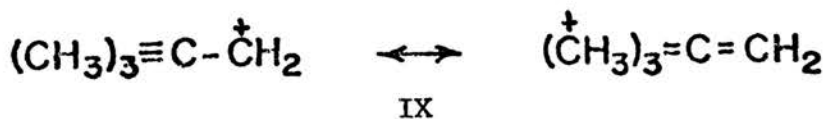
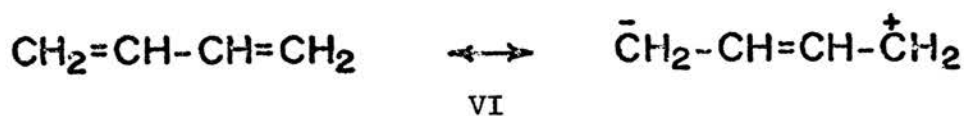
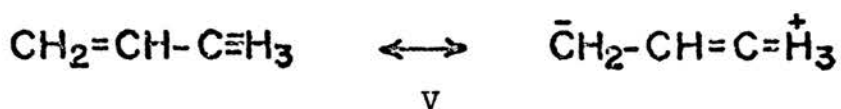
It is generally agreed that frequency changes involved in the activation process are responsible for the secondary deuterium isotope effect; however, there are differences of opinion concerning the relative importance of each of the possible causes of these frequency changes.⁶⁶ The causes suggested are: induction;^{25,27-30} conjugation, specifically hyperconjugation;^{5,9,11,30-36} hybridization;^{5,23,25,37,38} and steric interactions.^{5,9,29,30,32,38-44}

In the course of many chemical reactions there is a change in the charge distribution of the molecule as it goes from the initial state to the transition state. If there were a difference in inductive effect between deuterium and hydrogen an isotope effect should be observed. It has been observed that deuterium bonded to carbon appears to be more electropositive,⁴⁵⁻⁴⁹ but less polarizable,^{27,50} than hydrogen. Therefore, because deuterium appears to possess a greater electron donating ability than hydrogen, it should be more effective in stabilizing the positive charge which develops in the transition state of most solvolytic reactions. This would cause the deuterium compound to react faster than the hydrogen compound, and a $k_H/k_D < 1$ should be observed. However, most isotope effects are greater than one,^{25,51} so in those cases the inductive effect is of little importance.

Theory of Secondary Deuterium Isotope Effects

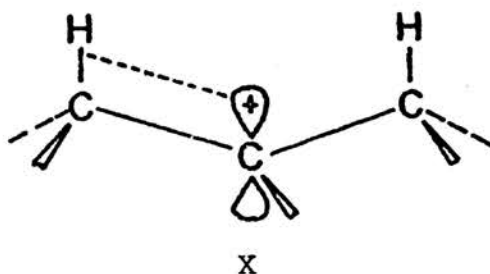
Lewis and Boozer²⁰ and Shiner¹¹ made the first observations of secondary deuterium isotope effects at about the same time. Both groups explained their observations by invoking the principle of hyperconjugation. The term hyperconjugation was first proposed by Mulliken, Rieke, and Brown⁵² as a quantum-mechanical description of carbon-hydrogen delocalization. Baker and Nathan⁵³ made some experimental observations prior to Mulliken, Rieke, and Brown's work and found substituent groups to be placed in order of decreasing electron-releasing strength as follows: $\text{Me} > \text{Et} > \text{i-Pr} > \text{t-Bu}$. Baker and Nathan explained their results by suggesting the possibility of carbon-hydrogen electron delocalization which has since become known as hyperconjugation.

The hyperconjugation theory as proposed by Mulliken, Rieke, and Brown suggests that the electrons of a carbon-hydrogen bond are less localized than the electrons of a carbon-carbon bond and, therefore, are able to conjugate with an unsaturated system.^{52,54} This mechanism of electron release depends on the number of suitably situated carbon-hydrogen bonds, and its magnitude decreases in the order Me > Et > *i*-Pr > *t*-Bu as observed by Baker and Nathan. In propylene (V), for example, the three carbon-hydrogen bonds of the methyl group can have hyperconjugative interactions with the π -orbital of the carbon-carbon double bond leading to stabilization, which is quite similar to the conjugative stabilization of butadiene (VI). The same type of



argument can be made for ionic species, which is more pertinent to the subject of this dissertation, in that the ethyl cation (VII) should be stabilized by hyperconjugation just as the allyl cation (VIII) is by conjugation. A methyl group has three hydrogens; the tertiary carbon of a *t*-butyl group, none. Therefore, the methyl group should give the greater hyperconjugative stabilization to an unsaturated system. Ingold⁵⁵ explained this unusual role of hydrogen by proposing that carbon-carbon electron delocalization (IX) is less likely than carbon-hydrogen electron delocalization (V and VII) based on directed polarizability studies. Hyperconjugation has not been universally accepted as an explanation for the Baker-Nathan effect for various reasons such as smallness of the effect⁵⁶ and cases of reactions which show either the Baker-Nathan order of reactivity ($\text{Me} > \text{Et} > \text{i-Pr} > \text{t-Bu}$) or the normal inductive order ($\text{t-Bu} > \text{i-Pr} > \text{Et} > \text{Me}$).⁵⁷

Kreevoy and Eyring³³ have determined by molecular orbital calculations that there is added stabilization of unsaturated systems by hydrogen atoms located in the 1- and 3-positions relative to the unsaturated center. This stabilization, which they termed α -hydrogen bonding, results from the overlap of the 1s-orbital of hydrogen and the p-orbital of the developing carbonium ion center (X). α -Hydrogen



bonding is very similar to the neighboring hydrogen participation theory which was described earlier by Simonetta and Winstein³⁴ and

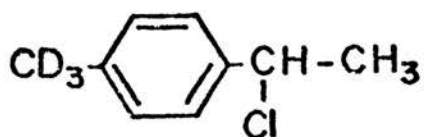
based on similar molecular orbital calculations. In summation, carbon-hydrogen electron delocalization (hyperconjugation), α -hydrogen bonding, and neighboring hydrogen participation have all been proposed as reasons for the unusual role of hydrogen in the Baker-Nathan effect. The secondary deuterium isotope rate effect can be rationalized in terms of these three theories in the following way. Based on the fact that the carbon-deuterium bond is shorter, the carbon-hydrogen bond will be looser than the carbon-deuterium bond and will enable the hydrogen to share its electrons (by hyperconjugation, α -hydrogen bonding, or neighboring hydrogen participation) more easily than will deuterium, thereby stabilizing the developing carbonium ion more, which in turn will allow the hydrogen compound to react faster than the deuterium compound. This will lead to an isotope effect of the usual type, $k_H/k_D > 1$.^{25,51}

Streitwieser, Jagow, Fahey, and Suzuki⁵ have observed the β -isotope effect in the acetolysis of cyclopentyl tosylate (I-a), as mentioned previously. They have suggested that β -isotope effects are caused by a bond-weakening in the transition state, which in turn is caused by hyperconjugation. Overlap of the carbon-hydrogen bond orbital with the electron-deficient p -orbital of the developing carbonium ion causes a weakening of the bond and a lowering of the bond frequencies. Streitwieser, Jagow, Fahey, and Suzuki made the following statement concerning the reasons for the lowering of the bond frequencies:

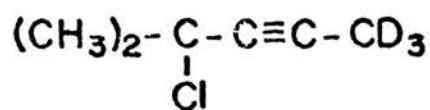
...The magnitude of the bond weakening should depend on the amount of positive charge to be distributed and on the extent of the orbital overlap. Overlap is greatest when the C-H bond is parallel to the direction of the carbonium p -orbital and least when the C-H bond is in the nodal plane of the carbonium ion. The recent results of Shiner⁵⁸ and of Saunders⁵⁹ provide important evidence for the dependence of the isotope effect on the angular relation between the C-H bond and the developing carbonium ion.⁵

Bartell³⁸ has proposed a theory of secondary deuterium isotope effects which explains the rate differences between hydrogen and deuterium compounds based on non-bonded repulsions or interactions. These repulsions, when averaged over all of the stretching and bending vibrations, are smaller for deuterium than for hydrogen. This is understandable since the carbon-hydrogen bond has a greater amplitude of vibration than the carbon-deuterium bond (Figure 2). The greater crowding about the reacting carbon when it is in its ground-state (tetrahedral configuration) causes the non-bonded interactions of β -hydrogens to be more strongly felt than those of β -deuteriums, thus causing the hydrogen compound to be more strained. In going to the transition state (trigonal configuration) this strain is relieved more for the hydrogen compound than for the deuterium compound. Therefore, the hydrogen compound will react faster than the deuterium compound.

The following two compounds that have appeared in the literature are examples of the exceptions to the Bartell model. Bartell has been able to obtain relatively good agreement between his calculated values and selected experimental values. However, the observed isotope effects in molecules such as XI⁶⁰ and XII,⁶¹ where steric differences between



XI



XII

hydrogen and deuterium should be relatively unimportant due to the remoteness of the deuterium from the reaction center, suggest that his

calculations overemphasize the contribution of non-bonded repulsions to secondary isotope effects. Shiner and Humphrey⁶² have proposed that Bartell's calculated isotope effects³⁸ would be smaller if carbonium ion-like structures were not used as models for the transition states.

Survey of Secondary Deuterium Isotope Effects

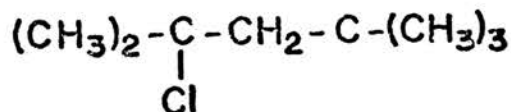
Shiner investigated the influence of various alkyl substituents on β -deuterium isotope effects, and the results are summarized in Table I.¹¹

Table I

Isotope Effects in the Solvolysis of
Tertiary Alkyl Chloride in 80% Vol. Ethanol-Water at 25°

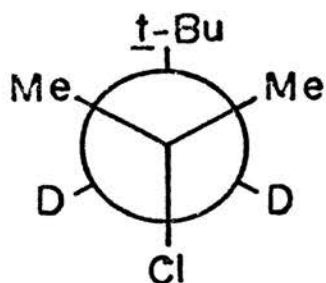
R	$\text{RCH}_2\text{C}(\text{Cl})(\text{CD}_3)(\text{CH}_3)$ $k_{\text{H}}/k_{\text{D}}$	$\text{RCD}_2\text{C}(\text{Cl})(\text{CH}_3)_2$ $k_{\text{H}}/k_{\text{D}}$
Me	1.34	1.40
Et	---	1.37
<u>i</u> -Pr	1.34	1.44
<u>t</u> -Bu	1.40	1.08

Shiner felt that if hyperconjugation were important in causing isotope effects it would seem reasonable to expect a conformational dependence upon such effects. He showed that such an effect did exist in the solvolysis of 2,4,4-trimethyl-2-chloropentane (XIII) and its deuterated methylene analog.⁵⁸ Based on the isotope effect of 1.40 obtained for the solvolysis of t-amyl chloride (III)¹¹ a similar

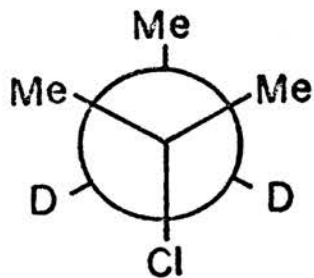


XIII

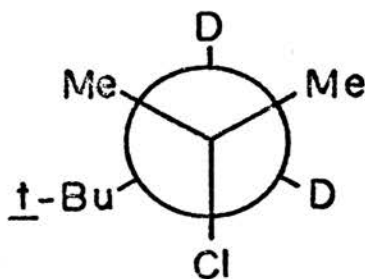
value was expected for XIII; however, the value obtained was 1.08. This difference can be explained by considering the two possible rotational conformations. From the Newman projections shown below it can be seen that the t-butyl group of 2,4,4-trimethyl-2-chloropentane (XIII) can be either trans (XIII-a) or gauche (XIII-b) to chlorine. For the



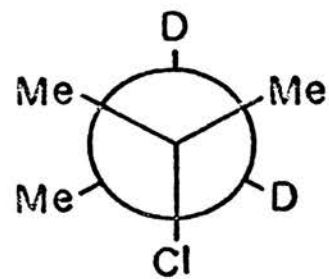
XIII-a



III-a



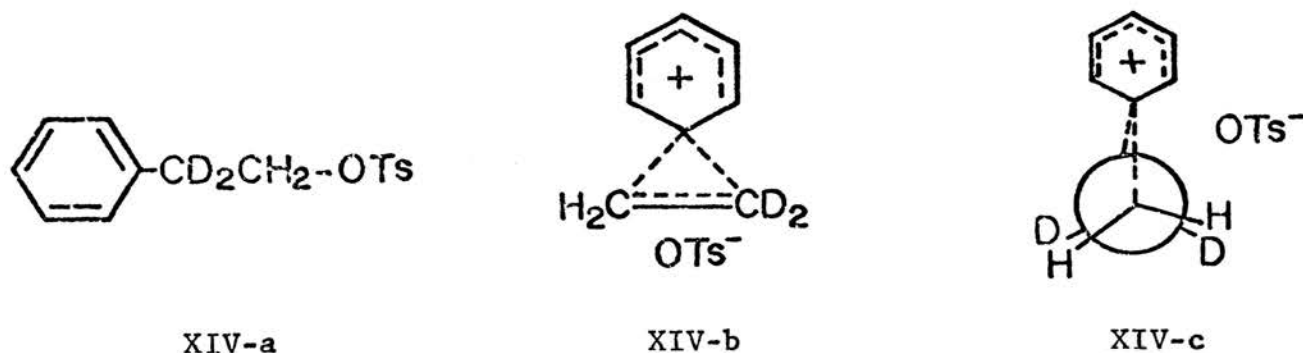
XIII-b



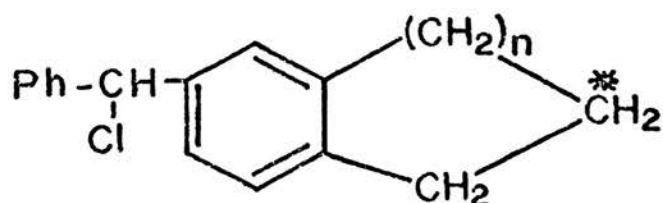
III-b

electrons of the carbon-hydrogen (or carbon-deuterium) bonds to most effectively stabilize the carbonium ion center by overlapping with the developing vacant p-orbital, it is necessary for the t-butyl group to be gauche; however, due to its large size, the t-butyl group is sterically hindered from assuming the gauche conformation (XIII-b). This is not true for t-amyl chloride (III) where, because of the small size of the methyl group, the gauche conformation (III-b) can be assumed. In the trans conformation (XIII-a) the carbon-hydrogen (or carbon-deuterium) bonds are not parallel to the developing vacant p-orbital, so the overlap is lessened. The transition state is therefore not appreciably stabilized by hydrogen as opposed to deuterium, and hence the isotope effect is much lower than expected.

Hyperconjugation and α -hydrogen bonding theories both suggest an angular dependence of the observed isotope effect. Saunders⁵⁹ found support for this idea when he observed that there was no β -deuterium isotope effect in the solvolysis of β -dideutero- β -phenylethyl tosylate (XIV-a). He reasoned that due to phenyl participation the β -carbon-deuterium bonds are not favorably oriented with respect to the developing vacant p-orbital at the reaction center. The transition state of this compound can be represented as either XIV-b or XIV-c as shown below.



Arnold and Truett⁶³ made some observations which support the idea of steric inhibition of hyperconjugation, and they stated that they believed their work to be the first experimental evidence in support of this concept. They measured solvolysis rates for compounds XV-a, XV-b and XV-c at 0° and 25° in 80% acetone-water and obtained the results shown in Table II.



XV-a (n = 1)
 XV-b (n = 2)
 XV-c (n = 3)

in the series $n = 1, 2, 3$ the carbon atom marked C^* is forced further and further from the plane in question and it becomes increasingly more difficult for this planer state to be attained. Therefore, less hyperconjugative stabilization to the reaction center is possible. The decrease in rate of solvolysis in passing through the series XV-a, XV-b and XV-c can be rationalized by the fact that it is becoming increasingly more difficult for the chloride ion to leave because of this decrease in hyperconjugative stabilization of the reaction center.

Winstein, Stevens, and Takahashi⁶⁶ determined the rates of acetolysis of the two 2,2,6,6- d_4 -4-t-butylcyclohexyl tosylates (XVI) shown below, one having an axial tosyl group and the other an equatorial tosyl group. These data are given in Table III.

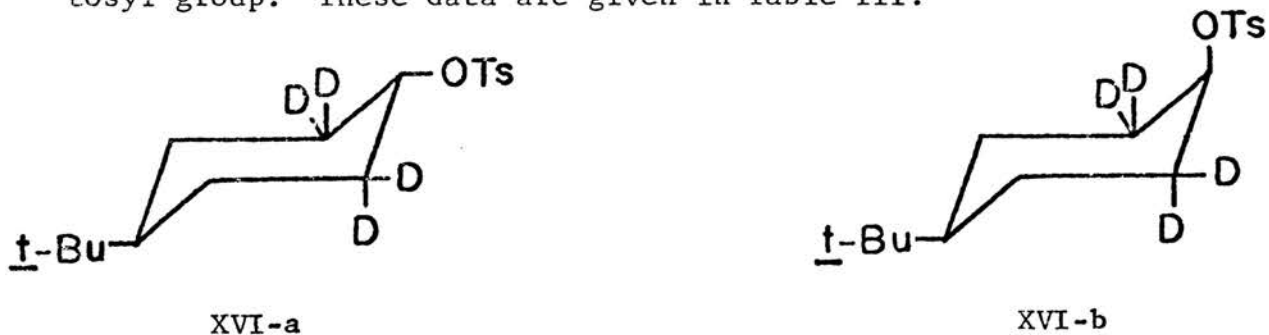


Table III

Isotope Effects in the Solvolysis of the
2,2,6,6- d_4 -4-t-Butylcyclohexyl Tosylate System

Compound	k_H/k_D	k_H/k_D per D
XVI-a	1.96	1.18
XVI-b	2.22	1.22

The comparison of the isotope effects for the two cyclohexyl tosylates shows that the larger effect is observed in the compound with deuterium trans (XVI-b) to the leaving tosyl group. This observation

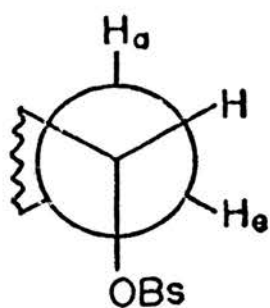
lends support to the argument that hyperconjugation is the cause for secondary deuterium isotope effects since the conformational dependency which was observed for XIII¹¹ was again borne out here. The two cyclohexyl tosylates shown are considered to be the most stable conformations since the t-butyl group would be expected to take an equatorial position.⁶⁷

In 1964, Shiner and Jewett stated that:

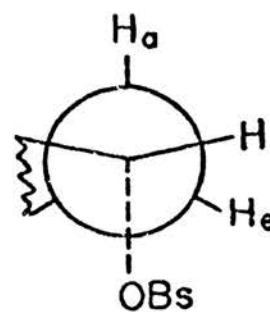
β -Deuterium effects on the rates of a large number of carbonium ion solvolyses can be satisfactorily correlated by the postulate that the governing mode of interaction between the sites of reaction and isotopic substitution is hyperconjugation.⁶² This postulate requires that the maximum rate retardation be observed when the β -C-D bond axis is parallel to the axis of the developing vacant p-orbital.⁶⁸

Shiner and Jewett⁶⁸ made the direct observation of such an effect in the solvolysis of the cis-4-t-butylcyclohexyl brosylate system (XVII), using specifically cis-4-t-butylcyclohexyl brosylate-trans-2-d₁ (single axial β -deuterium) and cis-4-t-butylcyclohexyl brosylate-cis-2-d₁ (single equatorial β -deuterium).

The conformations of the initial state and transition state for this reaction are represented as XVII-a and XVII-b, respectively. The dihedral angle between the carbon-leaving group axis and the β -carbon-hydrogen bond axis is 180° for an axial (a) hydrogen atom and 60° for an equatorial (e) hydrogen atom in both the initial state and the



XVII-a



XVII-b

transition state. If the ring flattens during transition state formation, 1,3-steric interactions involving the leaving group would be reduced, causing the dihedral angle with the axial hydrogen to become less than 180° and that with the equatorial hydrogen less than 60° .

Shiner and Jewett⁶⁸ found that the axial β -deuterium atom slowed the solvolysis rate by a factor of 1.436, whereas the equatorial β -deuterium atom slowed the solvolysis rate by the much smaller factor of 1.096. Thus they showed that the conformational dependence of the β -deuterium effect, predicted by the hyperconjugation postulate, was confirmed in this reaction. It was then suggested that "the large axial β -deuterium effect, though in accord with the hyperconjugation postulate,⁶² might be due to neighboring hydrogen participation which they and others⁶⁹ viewed as an extreme manifestation of a type of electronic interaction also associated with hyperconjugation." In order to confirm this, Shiner and Jewett⁷⁰ determined the effect of substitution of deuterium for each of the four β -hydrogen atoms on the rate of solvolysis of cis-4-t-butylcyclohexyl brosylate (XVII). These data are given in Table IV.

Table IV

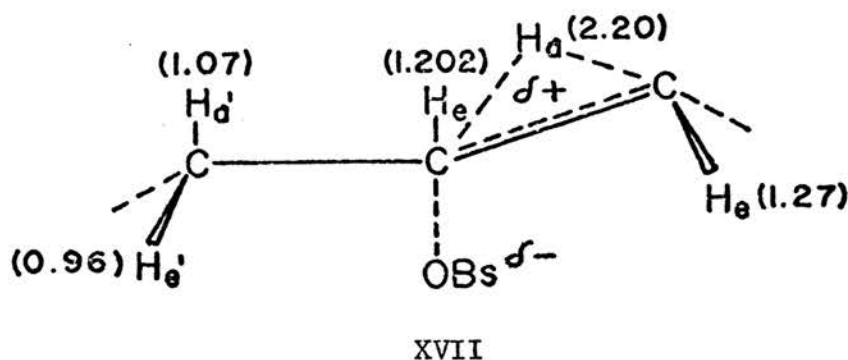
Isotope Effects in the Solvolysis of
cis-4-t-Butylcyclohexyl Brosylates
in 50% Vol. Ethanol-Water at 35°

Deuteration*	k_H/k_D
None	----
α -D, e	1.202
β -D, a	1.436
β -D, e	1.096
β -D (3), a,a,e	2.565
β -D (3), a,e,e	1.784
β -D (4), a,a,e,e	2.862

*a = axial

e = equatorial

From the data in Table IV it can be seen that "successive β -deuterium substitution at conformationally equivalent sites does not lead to cumulative isotope effects, i.e., the solvolytic rate retardation caused by 2,6-diaxial deuteration exceeds the square of that caused by monoaxial deuteration: $\beta\text{-D-a,a,e}/\beta\text{-D-e} = \beta\text{-D-a,a} = 2.565/1.096 = 2.399 > (\beta\text{-D-a})^2 = (1.436)^2 = 2.062$." Shiner and Jewett⁶⁸ stated that one consequence of hydrogen participation is a nonequivalence of the 2- and 6-axial hydrogens in the solvolytic transition state. The preceding analysis of the data tends to indicate that this is the case, although the 2- and 6-axial hydrogens appear equivalent on first inspection of compound XVII. In the following partial structure of XVII the participating hydrogen is shown along with the calculated isotope effects⁷⁰ for replacement of each of the α - and β -hydrogen atoms by deuterium.



The effect of each different β -deuterium atom in the solvolytic transition state may be calculated using an expression of the form

$$(k_H/k_D)_X = 2xx'/(x + x') \quad (3)$$

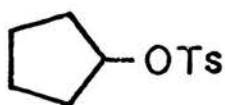
where $(k_H/k_D)_X$ is the experimentally determined isotope effect for substitution of a single deuterium atom ($X = \text{axial or equatorial}$) while x and x' are the effects of the 2- and 6-axial or equatorial isotopic

atoms in the transition state.^{62,70} Such an analysis leads to the isotope effects for replacement of each of the hydrogen atoms by deuterium indicated in the partial structure for XVII. For example, the values 2.20 and 1.07 were calculated by making the following substitutions into Equation 3: $(k_H/k_D)_a = 1.436$ and $xx' = 2.339$. Shiner and Jewett^{68,70} concluded that there was no doubt that these results concerning the nonequivalence of the 2- and 6-axial hydrogens cannot be explained by the simple steric model proposed by Bartell³⁸ as the steric model would predict equivalent effects by each of the axial hydrogens. They further concluded that such grossly noncumulative behavior and the large isotope effect associated with one neighboring (axial) hydrogen⁷¹ are in accord with the theory of neighboring hydrogen participation in the solvolytic transition state. Since this participation is from a secondary hydrogen to an adjacent secondary solvolytic center it is difficult to conceive of any driving force for it other than the formation of a stabilized, bridged, nonclassical intermediate carbonium ion. The absence of extensively rearranged substitution products indicates that the nonclassical ion is unsymmetrically hydrogen-bridged and is separated by an appreciable energy barrier from another presumably similar unsymmetrically hydrogen-bridged, but rearranged, ion. Shiner and Jewett then stated that:

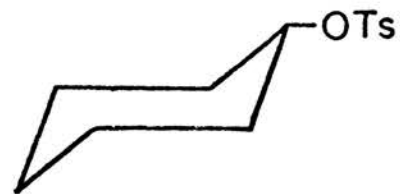
β-Deuterium isotope rate effects thus provide a sensitive probe for nonclassical carbonium ion character in solvolytic transition states and an operational distinction of limited but important applicability between hyperconjugation (cumulative isotope effects from equivalent initial state sites) and participation (noncumulative isotope effects from equivalent initial state sites).⁷⁰

Streitwieser, Jagow, Fahey and Suzuki⁵ have measured the β-deuterium isotope effects in the acetolysis of various deuterated cyclopentyl tosylates (I), and Saunders and Finley⁷² have done the same for the

cyclohexyl tosylate system (XVIII). These systems are shown below and the data are given in Table V.



I



XVIII

Table V

Isotope Effects in the Solvolysis of I and XVIII
in Acetic Acid at 50°

Compound	k_H/k_D	k_H/k_D per D
I-e 2,2,5,5-d ₄	2.06	1.20
I-f <u>trans</u> -2-d ₁	1.16	1.16
I-g <u>cis</u> -2-d ₁	1.22	1.22
XVIII-a 2,2,6,6-d ₄	2.34	1.24
XVIII-b <u>trans</u> -2-d ₁	1.30	1.30
XVIII-c <u>cis</u> -2-d ₁	1.25	1.25

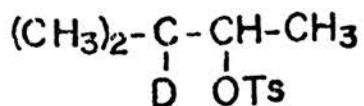
The fact that the isotope effect is very similar in magnitude for both cis- and trans-2-d-cyclopentyl tosylates was interpreted to mean that solvation of the β -hydrogens cannot be responsible for the isotope effect, since the leaving group should hinder solvation of the cis isomer (I-g) and lead to a lower isotope effect.

It is not clear from these data concerning the cyclopentyl system (Table V) whether β -deuterium substitution at conformationally equivalent sites does or does not lead to cumulative isotope effects, i.e., the solvolytic rate retardation caused by tetra-deuteration approximately equals the square of that caused by mono-cis deuteration times the square of that caused by mono-trans deuteration: $2,2,5,5-d_4 = 2.06 \approx 2.01 = (1.22)^2(1.16)^2 = (\text{cis-d}_1)^2(\text{trans-d}_1)^2$.

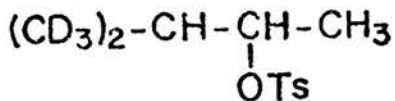
The data of Saunders and Finley (Table V) for the cyclohexyl tosylate system are considerably different from the data for the cyclopentyl system. It is quite clear from the data of Saunders and Finley that successive β -deuterium substitution at conformationally equivalent sites does not lead to cumulative isotope effects, *i.e.*, the solvolytic rate retardation caused by tetra-deuteration is considerably less than the square of that caused by mono-cis deuteration times the square of that caused by mono-trans deuteration: $2,2,6,6-d_4 = 2.34 < 2.64 = (1.25)^2(1.30)^2 = (\text{cis-}d_1)^2(\text{trans-}d_1)^2$. Because of the similarity in structure of the cyclopentyl and cyclohexyl systems one would expect similar isotopic data; however, this was not the case as shown above.

Another interesting difference between the data for the cyclopentyl and cyclohexyl systems was the reversal in magnitude of the cis and trans isotope effects. Based on the fact that trans-2- d_1 -cyclohexyl tosylate had a greater isotope effect than cis-2- d_1 -cyclohexyl tosylate it is possible to conclude, contrary to the cyclopentyl case, that solvation of the β -hydrogens is a possible explanation of the cause of secondary isotope effects.

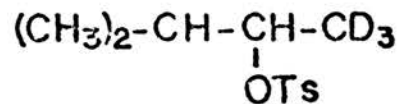
Winstein and Takahashi⁷³ have studied β -deuterium isotope effects in the 3-methyl-2-butyl tosylate system (XIX). They had interest in this system because participation by the lone tertiary hydrogen had been demonstrated by other means.⁷¹ As seen in Table VI, a very large



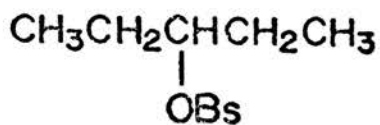
XIX-a



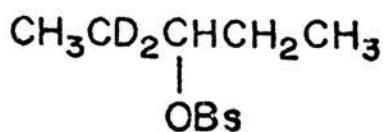
XIX-b



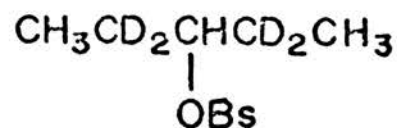
XIX-c



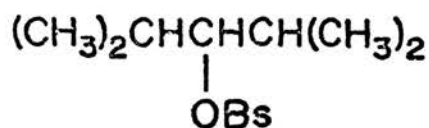
XX-a



XX-b



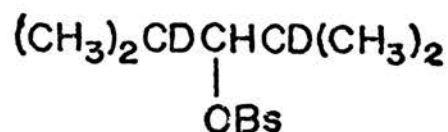
XX-c



XXI-a



XXI-b



XXI-c

Table VII

Isotope Effects in the Solvolysis of Open-Chain Arenesulfonates XX and XXI in 70% Vol. Ethanol-Water at 25°

Compound	k_H/k_D
XX-a	1.0000
XX-b	1.3184
XX-c	1.7365
XXI-a	1.0000
XXI-b	1.3671
XXI-c	2.1179

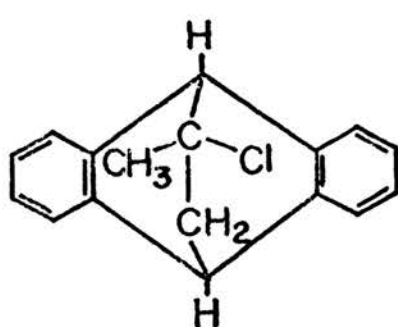
For the case of the 3-pentyl brosylates (XX), the data in Table VII show that successive deuterium substitution leads to cumulative isotope effects, i.e., the solvolytic rate retardation caused by tetra-deuteration approximately equals the square of that caused by di-deuteration: $\text{XX-c} = 1.7365 \approx 1.7383 = (1.3184)^2 = (\text{XX-b})^2$.

Shiner and Stoffer⁷⁴ stated that these results were probably within the limits of experimental error.

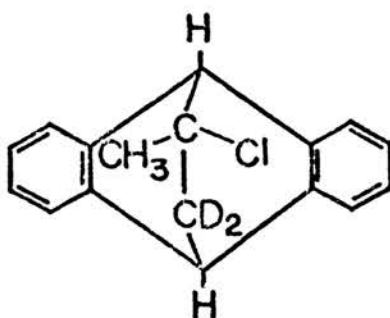
However, in the case of 2,4-dimethyl-3-pentyl brosylates (XXI), the successive deuterium substitution does not lead to cumulative isotope effects, *i.e.*, the solvolytic rate retardation caused by di-deuteration exceeds the square of that caused by mono-deuteration: $XXI-c = 2.1179 > 1.8690 = (1.3671)^2 = (XXI-b)^2$. The effect of each β -deuterium atom in the solvolytic transition state may be calculated using Equation 3. This type of analysis leads to the isotope effects of 1.018 and 2.080 for the replacement by deuterium of the first and second β -hydrogens in 2,4-dimethyl-3-pentyl brosylate (XXI). Similarly, as was suggested in the case of *cis*-4-*t*-butylcyclohexyl brosylate (XVII), the grossly noncumulative behavior observed for XXI is another example of neighboring hydrogen participation in the solvolytic transition state. This is an extreme manifestation of a type of electronic interaction associated with hyperconjugation.⁷⁰

The isotope effect of 2.12 (Table VII) for XXI-c is very close to the isotope effect of 2.26 observed for 3-methyl-2-butyl-3- d_1 tosylate (XIX-a) reported by Winstein and Takahashi (Table VI).⁷³ This is to be expected since the structures of the two compounds are very similar.

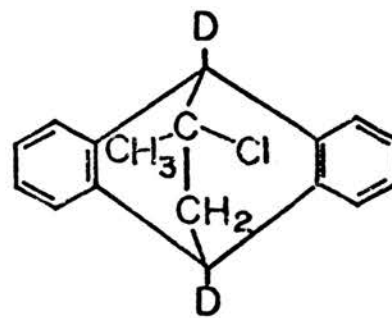
Shiner⁴⁰ has measured the solvolysis rate constants in 60% vol. ethanol-water of compounds XXII-a, XXII-b and XXII-c which are shown below.



XXII-a



XXII-b



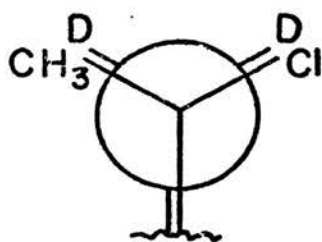
XXII-c

Table VIII

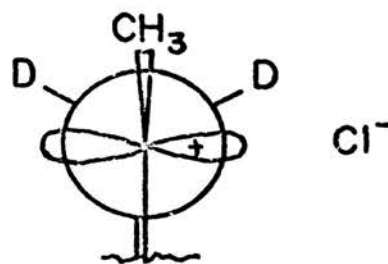
Isotope Effects in the Solvolysis of
XXII-a, XXII-b and XXII-c in 60% Vol. Ethanol-Water at 45°

Compound	k_H/k_D
XXII-a	1.00
XXII-b	1.14
XXII-c	0.986

The results are shown in Table VIII and illustrate the dependence of the isotope effect on steric orientation. The conformations of the initial state XXII-b-1 and the carbonium ion transition state XXII-b-2 are represented as follows:



XXII-b-1

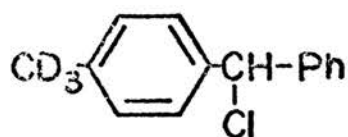


XXII-b-2

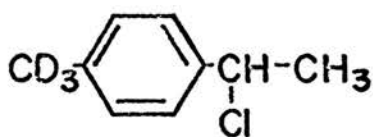
The two carbon-hydrogen (or carbon-deuterium) bonds of the ethano bridge are parallel to the bonds of the α -carbon atom bearing the leaving group (XXII-b-1). However, the isotope effect for XXII-b ($k_H/k_D = 1.14$) is considerably less than that observed for *t*-amyl chloride ($k_H/k_D = 1.40$)¹¹ which has two deuterium atoms in the α -methylene group making orientation for maximum hyperconjugation possible. The bridgehead carbon-hydrogen bond (XXII-c) projects away from and is normal to the developing vacant p-orbital, and in accord with predictions based on the hyperconjugation and α -hydrogen bonding theories no isotope effect of the usual type is observed. The

inverse isotope effect for XXII-c probably represents an inductive effect of deuterium.

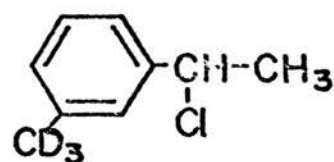
Shiner and Verbanic⁷⁵ observed an isotope effect in the solvolysis of *p*-deutero-methylbenzhydryl chloride (XXIII). Lewis, Johnson and Coppinger⁶⁰ observed a similar effect in *p*-deutero-tolylmethylcarbonyl chloride (XI), however they observed an inverse isotope effect exhibited by *m*-deuterated-tolylmethylcarbonyl chloride (XXIV). These structures are shown below and the results of Shiner and Verbanic⁷⁵ and of Lewis, Johnson and Coppinger⁶⁰ are given in Table IX. What makes these results



XXIII



XI



XXIV

so interesting is that a characteristic of a conjugation effect is that it is transmitted with diminished intensity through an unsaturated system. This characteristic, which is exhibited by these data, is very convincing evidence that hyperconjugation is a possible cause of β -deuterium isotope effects in this system.

Table IX

Isotope Effects in the Solvolysis of
XXIII, XI and XXIV in 80% Acetone-Water

Compound	Temperature	k_H/k_D
XXIII	0°	1.058
XI	50.3	1.01
XXIV	62.4	0.976

Further evidence that hyperconjugation is one of the important phenomena governing secondary isotope effects is the work of Buddenbaum^{76,77} who observed that substitution affects the magnitude of isotope effects. He found that by increasing the electron-donating character of the substituents on the aromatic ring of a series of 1-phenylethyl chlorides (XXV), the β -isotope effect decreased. As shown in Table X, the substituents (R) are much more effective than

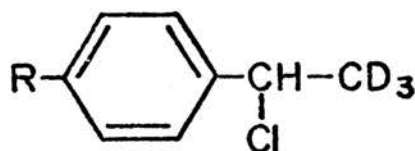


Table X

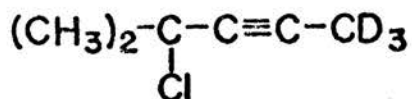
Isotope Effects in the Solvolysis of
XXV at 25°

Solvent	Substituent (R)				
	p-MeO	p-PhO	p-Me	H	p-NO ₂
5% Acetone					1.1966
80% Acetone		1.1590	1.2112		
93% Acetone	1.1334	1.1840			
50% EtOH				1.2240	
60% EtOH				1.2256	
70% EtOH				1.2245	
80% EtOH			1.1988	1.2236	
95% EtOH		1.1638	1.1995		

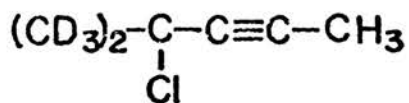
hydrogen in supplying electrons to the reaction center and, therefore, the demand for hyperconjugation is lessened.⁷⁸ The degree of vacancy of the developing p-orbital of the carbonium ion is lessened and the

demand for hyperconjugation is also lessened, thus causing a lower isotope effect.⁷⁹ The substituent effects observed (Table X) are in accord with the hyperconjugation theory of isotope effects. The solvent effects observed by Buddenbaum^{76,77} are also explained by the hyperconjugation theory. As the ability of the solvent to stabilize the quinonoid canonical form of the carbonium ion of XXV decreases, the isotope effect should increase since the demand for hyperconjugation is increased.

Shiner and Kriz⁶¹ felt that despite the remoteness of isotopic substitution from the reaction center, a reasonably large isotope effect should be observed in the solvolysis of 4-chloro-4-methyl-2-pentyne-1,1,1-d₃ (XII) if hyperconjugation were an important mode of interaction in causing the large effects of β -deuterium substitution on solvolysis reactions. In addition, Shiner and Kriz also believed



XII



XII-a

that the solvolysis rate of compound XII-a would be useful in giving a direct comparison between "remote" and β -deuterium substitution in the same direction. It would also make it possible to study the solvent effects on the isotope effect, in view of the criticism of previous "remote" isotope effects on the basis of their large solvent dependence.⁸⁰

As shown in Table XI, β -deuteration was found by Shiner and Kriz⁶¹ to retard the solvolysis rate by an amount similar to that observed for other \underline{t} -alkyl halides.⁸¹ This amount, however, is

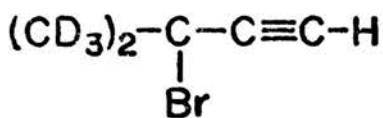
significantly smaller than 1.84, the isotope effect previously observed in the solvolysis of 3-bromo-3-methyl-d₃-1-butyne-4,4,4-d₃ (XXVI).⁷⁹

Table XI

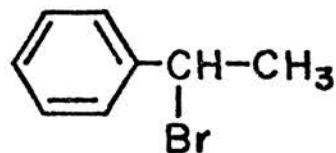
Isotope Effects in the Solvolysis of
XII and XII-a at 25°

Compound	Solvent	k _H /k _D
XII	80% Ethanol	1.092
XII	95% Ethanol	1.0949
XII	70% Acetone	1.087
XII-a	80% Ethanol	1.655

This difference is most likely not due to the difference in leaving group since it has been shown that the β-deuterium isotope effect in the solvolysis of α-phenylethyl bromide (XXVII) is very similar to that for the corresponding chloride.⁸² Thus it may be inferred



XXVI



XXVII

that the difference in β-isotope effects is due to the addition of a methyl group on the end of the triple bond in XII-a, causing, relative to hydrogen, a decrease in β-isotope effect from 1.84 to 1.655. Similar reductions in the β-isotope effect are associated with electron-releasing substituents on the aromatic ring of α-phenylethyl chloride (XXV) and are apparently due to the ability of these groups to disperse the positive charge developed in the transition state and therefore to reduce the demand for hyperconjugation.⁸³

Brown, McDonald, Azzaro, and Koelling observed secondary deuterium isotope effects in the reactions of 2-, 3- and 4-picoline and 2,6-lutidine (XXVIII-XXXI, respectively, as shown below) with alkyl iodides, noting the rates of reaction,⁴¹ and with diborane and boron trifluoride, noting the heats of reaction.¹⁰ The isotope effects on the rates of reaction of the substituted pyridines with alkyl iodides are shown below in Table XII. They postulated that these

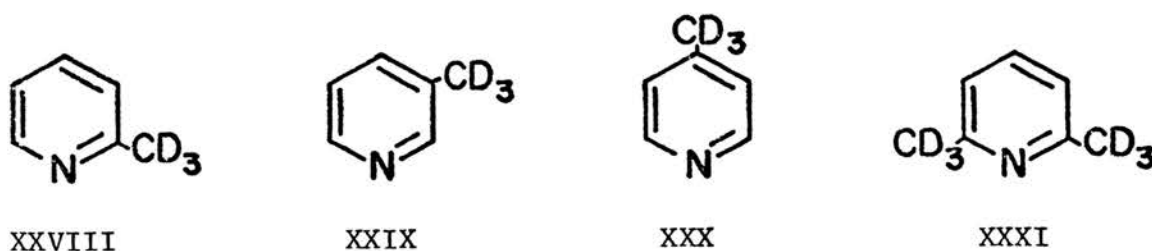


Table XII

Isotope Effects on the Rates of Reaction
of Substituted Pyridines with Alkyl Iodides

Pyridine	Alkyl Iodide	Temp. (T)	$(k_H/k_D)_T$	$(k_H/k_D)_{25^\circ}^*$
XXX	Methyl	25.0	0.999	0.999
XXIX	Methyl	25.0	0.991	0.991
XXVIII	Methyl	25.0	0.970	0.970
XXVIII	Ethyl	75.0	0.965	0.959
XXVIII	Isopropyl	100.0	0.945	0.931
XXXI	Methyl	25.0	0.913	0.913
XXXI	Ethyl	75.0	0.933	0.921
XXXI	Ethyl	100.0	0.935	0.919
4-d ₁	Methyl	25.0	0.988	0.988
d ₅	Methyl	25.0	0.969	0.969

*Corrected to 25° with aid of the expression, $k_H/k_D = \text{EXP}(E_D - E_H)/RT$

effects were due to the smaller steric requirements of deuterium as compared to hydrogen. Brown and McDonald⁴¹ drew the following conclusions from the data which appears in Table XII.

(1) A methyl-d₃ group in either the 4 position ($k_H/k_D = 0.999$) or in the 3 position ($k_H/k_D = 0.991$) has no effect on the rate of reaction over and above the experimental uncertainty (1.00 ± 0.01). A methyl-d₃ group in the 2 position brings about an enhanced rate of reaction well beyond the experimental uncertainty. Thus the 2-picoline system exhibits an inverse secondary deuterium isotope effect.

(2) With methyl iodide as the reacting species the two methyl groups of 2,6-lutidine ($k_H/k_D = 0.913$) appear to exert significantly more than the square of the effect of one methyl group in 2-picoline ($k_H/k_D = 0.970$), i.e., $(k_H/k_D)_{XXXI} = 0.913 \neq 0.941 = (0.970)^2 = (k_H/k_D)_{XXVIII}^2$. However, within the large uncertainty of the ethyl iodide measurements (this uncertainty the result of the necessity to run at elevated temperatures) the effect appears cumulative, i.e., $(k_H/k_D)_{XXXI} = 0.921 \cong 0.920 = (0.959)^2 = (k_H/k_D)_{XXVIII}^2$. The closeness of the observed and calculated isotope effects is very good support for the steric model as a possible explanation of secondary isotope effects, as two methyl groups would be expected to cause the same effect as the square of the isotope effect observed for one methyl group.

(3) The value of the secondary isotope effect appears to increase in the 2-picoline (XXVIII) series as the alkyl iodide is changed from methyl ($k_H/k_D = 0.970$), to ethyl ($k_H/k_D = 0.959$), to isopropyl ($k_H/k_D = 0.931$). However, the same trend is not evident in the series involving 2,6-lutidine (XXXI) with methyl iodide ($k_H/k_D = 0.913$) and ethyl iodide ($k_H/k_D = 0.921$).

(4) Deuteration of the ring in the 4 position of pyridine appears to exhibit an effect ($k_H/k_D = 0.988$) which is of the same order of magnitude as the estimated uncertainty. However, pyridine- d_5 exhibits a small inverse isotope effect ($k_H/k_D = 0.969$).

Interpretation of these results by Brown and McDonald⁴¹ required an analysis of the nature and relative magnitudes of the isotope effects to be expected in these reactions. This analysis was made on the basis of the electronic and steric hypotheses which have been advanced to account for secondary isotope effects. The steric hypothesis suggests that the deuterium atom behaves as though it were smaller than the hydrogen atom.³⁸ Clusius and Weigand⁸⁴ established that the molar volumes of deuterium (D_2) and methane- d_4 at their triple points are considerably smaller than for their hydrogen analogs. On this basis, the steric requirements of methyl- d_3 groups should be significantly smaller than normal methyl groups. The reactivity of the alkyl pyridines was shown by Brown and Cahn⁸⁵ to be sensitive to the steric requirements of the alkyl substituents in the α -position. Therefore, it follows that if the postulated difference in the steric requirements of the methyl- d_3 and normal methyl groups is valid, an enhanced reactivity should be observed for 2-methyl- d_3 -pyridine (XXVIII) and 2,6-dimethyl- d_6 -pyridine (XXXI) over their hydrogen analogs. This was actually the case for all of the alkyl iodides examined (Table XII).

A consequence of the steric interpretation is that the presence of substituents in the 3 and 4 positions, which are relatively remote from the reaction center, should have no influence on the observed rate. This also was actually the case as neither XXIX nor XXX exhibited isotope effects greater than the experimental uncertainty when they were allowed to react with methyl iodide (Table XII).

A further consequence of the steric interpretation is the prediction that the isotope effects in the reactions of the pyridine bases containing α -methyl substituents should increase with the increasing steric requirements of the alkyl iodide. This trend was indeed evident in the isotope effects of 0.970, 0.959 and 0.931 observed in the reactions of 2-picoline (XXVIII) with methyl, ethyl and isopropyl iodide, respectively. A slight reversal of this trend was observed in the reactions of 2,6-lutidine (XXXI) with methyl and ethyl iodide. However, Brown and McDonald felt that the values of 0.913 and 0.920 might well be reversed and still be within the experimental uncertainties of the measurements.

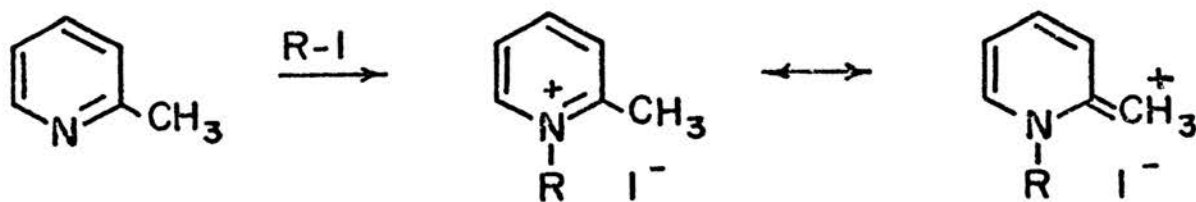
The very small isotope effect observed for 4-picoline (XXX) ($k_H/k_D = 0.999$) clearly supports the conclusion that the 4-methyl- d_3 substituent exerts no significant electronic effect on the reaction rate. In the case of 3-picoline (XXIX), the observed isotope effect ($k_H/k_D = 0.991$) is borderline. However, Brown and McDonald again concluded that the 3-methyl- d_3 substituent exerts no significant electronic effect on the reaction.

With regard to the ring-labeled pyridines, the 0.969 isotope effect observed for pyridine- d_5 was considered to be beyond the experimental uncertainty, but the 0.988 effect observed for pyridine-4- d_1 was just at the limit of the estimated uncertainty. If the latter effect were real, an electronic isotope effect would be indicated. However, it would be impossible in that event to account for a k_H/k_D value as small as 0.969 for the cumulative electronic effect of five deuterium substituents, four of which are much closer to the reaction center than the original 4-deuterium. It appears more reasonable that the 0.969 isotope effect was predominantly a

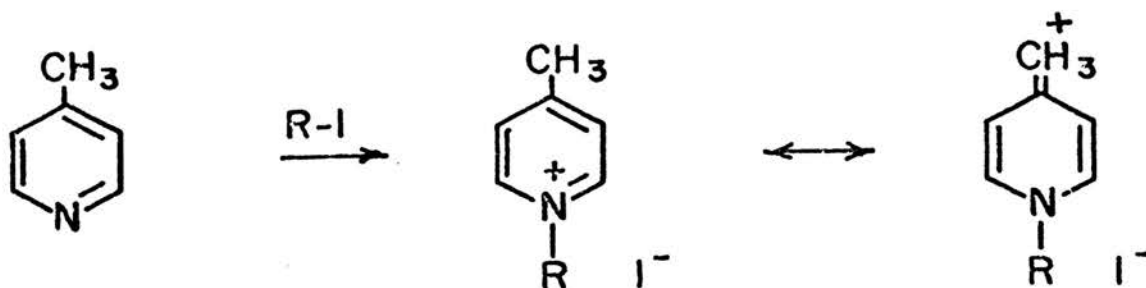
reflection of the smaller steric requirements of the two deuterium atoms in the α -positions.

Predictions resting on a postulated electronic origin for the secondary isotope effect are complicated by opposing theories in the field. In this particular system, a prediction based on a hyperconjugation contribution gives a different answer from one based on an inductive effect.

The nitrogen atom of the various pyridine bases represents a center of developing positive charge in the transition states for the reactions with the alkyl iodide. It might be expected that the positive charge could be stabilized by hyperconjugative contributions from methyl substituents in the 2 and 4 positions, as shown below.



XXVIII



XXX

If this is the case, the introduction of deuterium in these methyl groups would be expected to result in a smaller hyperconjugative contribution and a reduced rate. The effect would be expected to be either much smaller or absent in the 3 position. The observed

effect of deuterium substitution was a rate enhancement restricted to the 2 position (Table XII); therefore, hyperconjugation was not believed to be the basis of the observed secondary isotope effect in the picoline system.

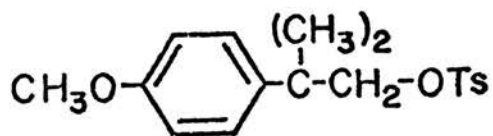
The hypothesis of an inductive isotope effect proposes an enhanced electron-donating ability of deuterium relative to hydrogen. Consequently, a methyl-d₃ group would be expected to stabilize a developing positive center more effectively than would a normal methyl group through the operation of an inductive effect. Thus, this hypothesis also predicts an inverse isotope effect similar to that predicted by the steric interpretation.

The main point of difference in the two proposals as they apply to the reactions under consideration is the requirement of the steric hypothesis that the isotope effect be operative only in the α -position, in the neighborhood of the reaction center, whereas the inductive effect should operate in all three positions of the ring. Both 4-picoline ($pK_a = 6.02$) and 2-picoline ($pK_a = 5.97$) are considerably stronger bases than pyridine ($pK_a = 5.17$).⁸⁶ Obviously the increase must be associated with the electronic effect of the methyl group. Since the effects are comparable for the 4-methyl and 2-methyl substituents, it would appear that on an electronic basis one should anticipate similar effects in the 4 and 2 positions for methyl-d₃ and methyl-d₀ substituents. However, the observed isotope effects of 0.999 for the 4 derivative and 0.970 for the 2 derivative are not in accord with this expectation. Thus the conclusion to be drawn is that for this system a steric effect is operating rather than an electronic effect (hyperconjugative or inductive).

The results obtained for the reactions between 2-, 3- and 4-picoline and 2,6-lutidine (XXVIII-XXXI) and diborane or boron trifluoride, noting the heats of reaction,¹⁰ also support the theory of steric interactions as the cause of secondary deuterium isotope effects.

Tables XIII, XIV and XV show the relative rates of solvolysis of various alkyl brosylates and tosylates in acetic acid and ethanol-water mixtures. The rates are shown so that a correlation can be drawn between brosylates and tosylates as leaving groups in the two solvent systems mentioned. The difference in nucleophilic character of the solvent and solvent ionizing power are not taken into consideration. For a review of these subjects see the articles of Winstein, *et al.*^{87,88}

The rates of solvolysis of *p*-methoxyneophyl tosylate (XXXII)⁸⁹ in both acetic acid and 80% vol. ethanol-water have been determined and the relative rates are shown in Table XIII. From the data it can be inferred that tosylates solvolyze faster in 80% vol. ethanol-water than in acetic acid.



XXXIX

Table XIII

Solvolysis of *p*-Methoxyneophyl Tosylate

<u>Solvent</u>	<u>Relative Rates at 75°</u>
Acetic Acid	1.00
80% vol. Ethanol-water	1.85

The rates of solvolysis of cis- and trans-4-t-butylcyclohexyl tosylates⁹⁰ (XVI-c and XVI-d, respectively) in acetic acid, and of the corresponding brosylates (XXXIII⁹¹ and XVII,⁷⁰ respectively) in 50% vol. ethanol-water have been determined and the relative rates are shown in Table XIV. From the data it can be seen that brosylates solvolyze considerably faster in 50% vol. ethanol-water than do the corresponding tosylates in acetic acid.

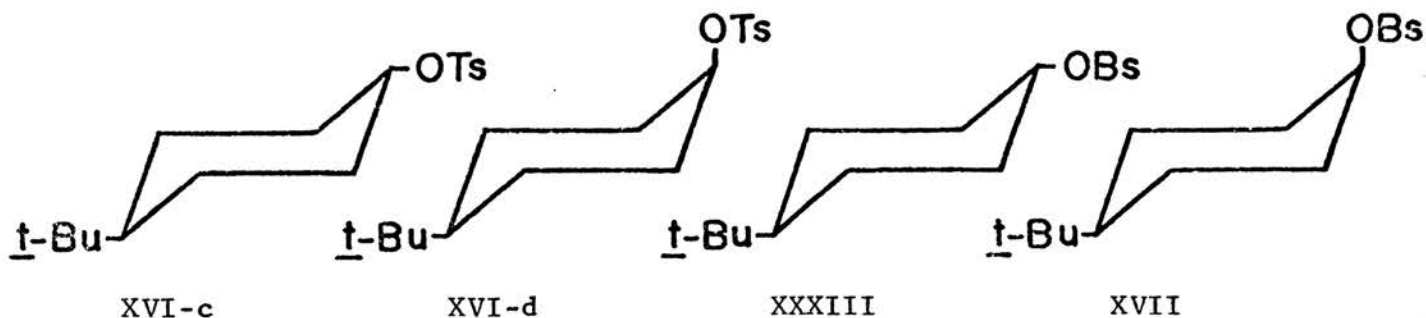


Table XIV

Solvolysis of cis- and trans-t-Butylcyclohexyl
Tosylates and Brosylates

<u>Compound</u>	<u>Solvent</u>	<u>Relative Rate at 35°</u>
XVI-c	Acetic Acid	1.00*
XVI-d	Acetic Acid	3.39*
XXXIII	50% vol. Ethanol-water	109
XVII	50% vol. Ethanol-water	496

*Calculated using $k = Ae^{-E_a/RT}$ to correct to 35°

The rates of solvolysis of iso-propyl and cyclohexyl tosylates and brosylates in 80% vol. ethanol-water and acetic acid have been determined and the relative rates are shown in Table XV.¹⁵ From the data it can be seen that brosylates solvolyze faster in both 80% vol. ethanol-water and in acetic acid than do the corresponding tosylates.

Table XV
Solvolysis of iso-Propyl and Cyclohexyl
Tosylates and Brosylates

Leaving Group	Relative Rates	
	<u>iso</u> -Propyl 80% vol. Ethanol-water at 50°	Cyclohexyl Acetic Acid at 75°
-OTs	1.00	1.00
-OBs	4.28	2.90

It can be seen from the Review of Literature that α -deuterium isotope rate effects appear to depend on the proximity of the leaving group and solvent molecules to the reaction center in the transition state. Also, it is possible to satisfactorily rationalize β -deuterium isotope rate effects in terms of the following: (1) hyperconjugation, α -hydrogen bonding and hydrogen participation, all of which are considered to be varying degrees of the same effect; (2) anharmonicity and inductive effects, the latter considered to be caused by the former; and (3) steric effects.

From the Review of Literature it should be noted that not all β -deuterium isotope rate effects can be attributed to the same cause. However, when attempting to show that one particular cause was responsible for isotope effects it was possible for an investigator to carefully select a number of systems which would illustrate that cause exclusively. It is the author's opinion that in those systems where it appears impossible to rationalize the isotope effect in terms of a single cause it is a combination of the above listed causes, operating in varying degrees, that is responsible for the effects observed.

STATEMENT OF PROBLEM AND PLANNED SOLUTION

As indicated in the Review of Literature, many studies of secondary deuterium isotope effects on the rate of reaction have been carried out. However, only a few papers appeared in the literature concerning deuterium isotope effects in cyclic systems, e.g., acetolysis of deuterated cyclopentyl tosylates,⁵ aqueous ethanolysis of deuterated cis-4-t-butylcyclohexyl brosylates,⁷⁰ aqueous ethanolysis of deuterated trans-4-t-butylcyclohexyl brosylates,⁹¹ and acetolysis of deuterated cyclohexyl tosylates.⁷² It was in reviewing these articles in particular that an interesting discrepancy was noted which seemed to warrant further investigation. In references 70, 72 and 91, all dealing with some form of the cyclohexyl system, it was observed that the isotope effect data obtained was non-cumulative in nature, indicative of hydrogen participation.⁹¹ Also, the isotope effect observed for the cis-mono- β -deuterium isomers was always less than that observed for the trans-mono- β -deuterium isomers. In contrast, however, in reference 5 dealing with the cyclopentyl system just the opposite was observed, i.e., the data appeared cumulative in nature and the cis-isotope effect was greater than that of the trans-isomer. Due to the similarity in structure of the cyclopentyl and cyclohexyl systems, one would expect that very similar isotope effect data would be obtained. Since this was not the case, one might conclude that the observations made for the cyclopentyl system were in error or that the cyclopentyl system is indeed structurally quite different from the cyclohexyl system and therefore different factors govern the isotope effects. It is for these reasons that the author felt a reinvestigation of the solvolysis of the cyclopentyl system should be made.

In order to effectively reinvestigate this system one minor change needed to be made. However, it was felt that this change would not hinder a valid comparison of the results obtained from this investigation with the results of the previous investigation.⁵ Since a conductance method was chosen to monitor the reaction, the solvent was changed to a much lower conducting mixture than the acetic acid which was used in the previous investigation. The solvolyzing media chosen was 70% vol. ethanol-water. The conductance method was selected to make it possible to obtain approximately 0.1% precision.⁹² The precision of the potentiometric titrations used for monitoring the rate of acetolysis of the original work was only about 1%. It was believed that by changing to a monitoring technique which had capabilities of greater precision, arguments could be made in support of, or against, the original work with greater validity.

To make this investigation, brosylates and tosylates of the following alcohols were prepared: cyclopentanol, cyclopentanol-1-d₁, cis-cyclopentanol-2-d₁, trans-cyclopentanol-2-d₁ and cyclopentanol-2,2,5,5-d₄. The tosylates of the alcohols mentioned above are the same compounds studied in the original work. An attempt was made to synthesize 2,2-d₂-cyclopentanol and cis-2-d₁-5,5-d₂-cyclopentanol, however, both syntheses proved unsuccessful.

EXPERIMENTAL

Boiling points and melting points are given in centigrade degrees and are uncorrected unless so stated. Distillations were made using a 6 mm. x 18 in. spinning-band column. Spectra were determined on a Varian A-56/60 nuclear magnetic resonance spectrometer using tetramethylsilane as an internal standard, and on a Perkin-Elmer 137B Infracord Spectrophotometer using a polystyrene film as a reference standard. Refractive indices were determined using a Carl Zeiss Refractometer. Elemental and deuterium analyses were performed by Josef Nemeth of Urbana, Illinois.

Apparatus and Preparation of Solvents

The apparatus and solvents used for the kinetic measurements were prepared as described by Murr^{92,93} with modifications as described by Buddenbaum⁹⁴ and Kriz.⁹⁵

Conductivity Water. Conductivity water of specific conductance $1-2 \times 10^{-7}$ mho was prepared by passing distilled water from a Barnstead Conductivity Water Still through a column packed with Analytical Grade Amberlite MB-1.

Conductivity Ethanol. Commercial absolute ethanol was dried preliminarily for two days with anhydrous calcium sulfate. Two liters of this alcohol was transferred to another dry flask and allowed to react with 12 g. of sodium metal. Another eight liters of this alcohol was decanted from the calcium sulfate into a dry twelve liter flask containing a magnetic stirrer, and to this was added 40 ml. of purified diethyl phthalate and the sodium ethoxide-ethanol solution previously prepared. The alcohol was fractionally distilled from this mixture through a 100 cm. x 2 cm. vacuum-jacketed distillation column packed

with 10 mm. glass helices and fitted with an automatic total condensation, variable take-off head which had an inlet tube for dry, purified nitrogen. A continuous flow of nitrogen was necessary to maintain ethanol of low conductance.

Dry, Purified Nitrogen. Dry, purified nitrogen was prepared by passing prepurified nitrogen, purchased from The Matheson Company, through a 4 cm. x 50 cm. column packed with Linde 5A molecular sieve pellets. The sieves were regenerated by heating to 200° in vacuo for twenty-four hours.

Ethanol-Water Mixture. The composition of binary mixtures used in the study of solvolytic reactions is commonly reported in volume percent. The solvent used in this investigation, 70% vol. ethanol-water, is referred to in volume percent although it was prepared by weight using a 2 kg. capacity, 0.2 mg. sensitivity, Christian Becker balance. The composition in weight percent of the 70% vol. solution was calculated using the densities of water and ethanol at 25° given in the "International Critical Tables."

Conductance Apparatus. Conductances were determined by means of a Jones-Josephs Bridge manufactured by the Leeds and Northrup Company. It was operated and calibrated as described by Murr⁹³ using resistors certified by the National Bureau of Standards. The ratio arms were balanced to equality. Solvent resistances were determined by shunting the cell with three of the 10 kilo-ohm resistors of the bridge in series.

Temperature Control. The conductance bridge, constant temperature bath, nitrogen purification system, ethanol still and water purification column were set up in a room where the temperature was maintained at $25 \pm 2^\circ$. The bath temperature was set at

$25.000 \pm 0.005^{\circ}$ by means of a platinum resistance thermometer calibrated by the National Bureau of Standards and a Muller Temperature Bridge which was calibrated at the time of use.

Conductance Cell. A cell of the type described by Draggett, Bair, and Kraus⁹⁶ and with modifications as made by Murr^{92,93} was used in this investigation.

Cell Constant Determination. Baker-analyzed reagent grade potassium chloride was recrystallized using the method of Draggett, Bair, and Kraus⁹⁶ by precipitating the salt from a saturated aqueous solution by the addition of an equal volume of ethanol. Murr's⁹⁷ method of cell calibration was modified in that ten-fold larger samples of potassium chloride (~ 0.75 g.) were used because the author did not have access to a microbalance. The equation proposed by Lind, Zwolenik, and Fuoss,⁹⁸ and used by Murr, for the calculation of equivalent conductance from concentration data was not used because the determinations were made in a concentration range where this equation did not apply. Instead, a $1.0000 \pm 0.0003 \times 10^{-2}$ demal solution of potassium chloride was prepared and, using the specific conductance of this solution at 25° ($K = 0.00140877$),⁹⁹ the cell constant was determined using Equation 4

$$\Theta = KR \quad (4)$$

where Θ is the cell constant, K is the specific conductance, and R is the resistance measured for this solution. Three determinations were made using this procedure and the cell constant used in this work was the average value obtained from these determinations.

Determination of the Parameters for the Modified Fuoss-Onsager Equation. In the concentration range monitored during the kinetic

runs of Murr,^{92,93} Buddenbaum⁹⁴ and Kriz⁹⁵ it was possible to fit the data to a straight line by using the limiting Onsager conductance equation, Equation 5.¹⁰⁰

$$\Lambda_i = \Lambda_0 - S_a c_i^{1/2} \quad (5)$$

However, it was found in this investigation that when the equivalent conductance (Λ_i) was plotted versus the square-root of the corresponding concentration ($c_i^{1/2}$) the line produced by these points had a slight curvature and could not be satisfactorily fitted by a straight line equation, Equation 5. Therefore, the results were fitted by a least-squares method to a modification of the Fuoss-Onsager conductance equation for unassociated electrolytes, Equation 6.¹⁰¹

$$\Lambda_i = \Lambda_0 - S_a c_i^{1/2} + E c_i \ln c_i + J c_i \quad (6)$$

Since in this investigation resistances were determined for solutions of known concentration, Equation 6 was modified by substituting the defining equation for equivalent conductance ($\Lambda_i = 10^3 \theta / R_i c_i$).¹⁰² This modification is shown as Equation 7.

$$10^3 \theta / R c_i = \Lambda_0 - S_a c_i^{1/2} + E c_i \ln c_i + J c_i \quad (7)$$

The four unknown parameters Λ_0 , S_a , E and J in Equation 7 were determined from resistance and concentration data through the use of a least-squares computer program in conjunction with an IBM 360 computer.

The brosylates of 3-pentanol and cyclopentanol were dissolved in 70% vol. ethanol-water to make solutions of known concentration. The resistance of each of these solutions at $25.000 \pm 0.005^\circ$ was obtained after allowing the solvolysis reaction to go to completion.

The conducting species in this system is the *p*-bromobenzenesulfonic acid produced in the solvolysis reaction, and its concentration was taken to be equivalent to the initial concentration of the alkyl brosylate. This procedure of generating the acid was adopted by necessity because *p*-bromobenzenesulfonic acid is a very unstable compound and decomposes rapidly unless kept in solution. Eleven points scattered over the concentration range of 1×10^{-4} molar to 1×10^{-3} molar were determined by this method. This was the same concentration range monitored during the kinetic runs of this investigation. Conductance measurements are a function of the concentration of the electrolyte present in solution. Since the same electrolyte, *p*-bromobenzenesulfonic acid, was produced in the solvolyses of both alkyl brosylates studied, one would predict that the data obtained for these compounds would have to obey the same conductance equation, Equation 7. This phenomenon was borne out in this investigation.

A similar procedure was adopted for determining the Fuoss-Onsager parameters of Equation 7 with *p*-toluenesulfonic acid as the electrolyte in 70% vol. ethanol-water at 25°. In this investigation cyclopentyl tosylate was allowed to solvolyze in 70% vol. ethanol-water in order to generate the *p*-toluenesulfonic acid electrolyte. The parameters were determined as described above for the *p*-bromobenzenesulfonic acid system, obtaining seventeen points over the same concentration range.

Kinetic Measurements. The cell was filled with 70% vol. ethanol-water and placed in the constant temperature bath. After thermal equilibrium had been established and the conductance of the solvent was found to be satisfactory ($1-2 \times 10^{-7}$ mho), cyclopentyl brosylate

(~ 0.3 g./l. of solvent) was added. The bridge resistance was set to a value corresponding to a *p*-bromobenzenesulfonic acid concentration of about 1×10^{-4} molar. The time (t_0) was noted when the resistance of the solution in the cell equaled this value (R^0). Readings were taken thereafter at roughly fifty second intervals over a period of two and one-half hours (~ 2 half-lives). All observations were made in the manner described for R^0 . The time was measured by a device consisting of a 60 r.p.m. synchronous motor which drove a small, five-digit Veeder Root Reset Counter. The time was direct-reading in seconds. The clock was checked against shortwave Radio Station WWV. A stopwatch was used in conjunction with the clock.

The same procedure was used in monitoring the rate of solvolysis of the cyclopentyl tosylate system in 70% vol. ethanol-water. The size of cyclopentyl tosylate sample was approximately 0.24 g./l. of solvent. Readings were taken at approximately one hundred second intervals over a period of six to eight hours (~ 2 half-lives).

Treatment of Kinetic Data. The least-squares kinetic program described by Buddenbaum¹⁰³ was translated¹⁰⁴ to IBM 360 computer language. The calculations themselves were not changed, but the input and output formats were changed to accommodate the IBM 360 computer.

Deuterium Analyses. Deuterium analyses were made using the Varian A-56/60 nuclear magnetic resonance spectrometer with the procedure as described by Kriz.¹⁰⁵ However, it was felt that these analyses were not adequate for the author to maintain the high precision ($\sim 0.1\%$) of his work. Therefore, the samples were analyzed¹⁰⁶ by combustion of the cyclopentyl brosylate or tosylate

and collection of the water formed to determine the deuterium content by the falling drop technique.

Product Analyses. Product analyses were made using a Varian Aerograph Model 600-D Flame Ionization Gas Chromatograph equipped with a 20 ft. x 1/8 in. column packed with approximately 20% TCEP, i.e., 1,2,3-tris(2-cyanoethoxy) propane, on a substraight of Anakrom SD. Throughout this investigation helium was used as the carrier gas and the column was maintained at 70°.

From the solvolyses of both the cyclopentyl brosylates and tosylates in 70% vol. ethanol-water there were three expected products: cyclopentyl alcohol, cyclopentyl ethyl ether and cyclopentene. Two standard solutions of known concentrations were prepared containing these three materials plus n-butyl alcohol as an internal reference standard. Three 0.5 μ l. samples of both standard solutions were injected into the gas chromatograph, the peak areas were noted, and the mean areas were determined. Three calibration curves were constructed in which the ratio of the area of one of the components, e.g., cyclopentene, to the area of n-butyl alcohol was plotted against the ratio of the moles of that same component to the moles of n-butyl alcohol. In all three plots a straight line was drawn through the two points obtained from the two standard solutions and this line passed through the origin.

Solutions of all of the cyclopentyl brosylates and two of the cyclopentyl tosylates studied in this investigation were prepared and allowed to solvolyze to completion in 70% vol. ethanol-water. The concentration of each solution was approximately 1×10^{-2} molar, the most dilute solution which could be accurately studied on the gas chromatograph. A known amount of n-butyl alcohol was added to

each of the solutions as an internal reference standard. Analysis of these solutions was carried out in a manner similar to that for the standard solutions. Three 0.5 μ l. samples of each solution were injected into the gas chromatograph, the peak areas were noted, and the mean areas were determined. A comparison of these results with the calibration curves made it possible to determine the amount of each component produced in the solvolysis reactions.

The reproducibility obtained between the three samples of any one given solution varied for each component. The cyclopentene peak areas were reproducible to 1-2%. The reproducibility of the cyclopentyl ethyl ether peaks was 2-3%, and this was probably caused by the fact that the ether peak slightly overlapped with the solvent peak. The poorest reproducibility (3-5%) was obtained for the cyclopentyl alcohol and was probably caused by the human error introduced in correcting the areas as these peaks were on the tailing edge of the solvent and did not lie on the base line as did the cyclopentene and cyclopentyl ethyl ether peaks.

Preparation of Compounds

Cyclopentanol. Cyclopentanol was purchased from Matheson Coleman & Bell, and had the following properties: b.p. 138-140 $^{\circ}$ (lit.¹⁰⁷ b.p. 140.85 $^{\circ}$); n_D^{20} 1.4529 (lit.¹⁰⁷ n_D^{20} 1.4530). Nmr spectrum relative to TMS was as follows: singlet 4.97 τ (-OH), triplet 5.77 τ (α -H), doublet or unresolvable singlets 8.33 τ and 8.38 τ (β - and γ -H).

Cyclopentyl Brosylate. Cyclopentyl brosylate was prepared according to the method of Tipson.¹⁰⁸ In a dry flask was placed 0.86 g. (0.01 mole) of cyclopentyl alcohol, 2.81 g. (0.011 mole) of brosyl chloride (p-bromobenzenesulfonyl chloride), and 10 ml. of

pyridine which had been previously dried over anhydrous calcium oxide. The flask was then placed in a refrigerator for 24-48 hours. A few pieces of ice were added followed by 15-20 ml. of water with swirling and cooling. The product was an oil and was separated with a separatory funnel. The aqueous phase was extracted with three 25 ml. portions of ethyl ether, and the ether extracts were combined with the above separated product. The ether solution was washed successively with two 25 ml. portions of each of the following materials: water, 10% sulfuric acid, water, saturated sodium bicarbonate solution, and water. The ether solution was dried over anhydrous calcium sulfate and the ether was removed under vacuum (aspirator) on a RINCO rotory evaporator. The residue was recrystallized from pentane which had been previously passed over alumina to remove any mercaptans present. The pentane also contained decolorizing-charcoal and a trace of sodium carbonate, present to react with any acid which could catalyze decomposition of the brosylate. The melting point was 44-45°.

Anal. Calcd. for $C_{11}H_{13}SO_3Br$: C, 43.29%; H, 4.29%. Found:¹⁰⁶
C, 43.24%; H, 4.26%.

Cyclopentyl Tosylate. Cyclopentyl tosylate was prepared in a manner similar to that described above for cyclopentyl brosylate. A 0.86 g. (0.01 mole) sample of cyclopentyl alcohol was allowed to react with 2.10 g. (0.011 mole) of tosyl chloride (p-toluenesulfonyl chloride) in 10 ml. of dry pyridine. The melting point was 26.5-27.5° (lit.⁵ m.p. 28-29°).

Anal. Calcd. for $C_{12}H_{16}SO_2$: C, 59.97%; H, 6.71%. Found:¹⁰⁶
C, 60.19%; H, 6.84%.

Cyclopentanone-2,2,5,5-d₄. Cyclopentanone was purchased from Eastman Organic Chemicals and had the following properties: b.p. 128-130° (lit.¹⁰⁷ b.p. 130.65°); n_D^{20} 1.4321 (lit.¹⁰⁷ n_D^{20} 1.4347). The following methods were then used in an attempt to synthesize cyclopentanone-2,2,5,5-d₄. Although Method C proved to be the most satisfactory of the three, Method B could have also been used.

Method A. Cyclopentanone-2,2,5,5-d₄ was prepared according to the procedure of Streitwieser, Jagow, Fahey and Suzuki.⁵ A 25.2 g. (0.3 mole) sample of cyclopentanone (1.2 g. atoms of exchangeable H) was mixed with 169 g. (8.77 moles) of deuterium oxide (~63% D₂O, 11.2 g. atoms of exchangeable D) containing 0.1 g. of potassium carbonate and 0.1 g. of sodium chloride. The solution was refluxed overnight. After cooling, the cyclopentanone was separated from the aqueous phase. The aqueous phase was extracted with three 50 ml. portions of anhydrous ethyl ether. The ether extracts were combined with the ketone, dried over anhydrous calcium sulfate, and the ether was removed by distillation through a packed column. It was observed that the residue was of high polymer content, probably Aldol condensation products. Therefore, this method of preparing cyclopentanone-2,2,5,5-d₄ was discontinued.

Method B. A 21 g. (0.25 mole) sample of cyclopentanone (1.0 g. atom of exchangeable H) was dissolved in 500 ml. of purified¹⁰⁹ dioxane containing 100 g. (5.0 moles) of deuterium oxide (9.982 g. atoms of exchangeable D) and 1 g. of dry, freshly distilled triethylamine, b.p. 87-88° (lit.¹¹⁰ b.p. 89-90°). The solution was gently refluxed overnight. Distillation on a packed column removed the triethylamine and water as the dioxane azeotrope, whereupon a new mixture of dioxane, deuterium oxide, and triethylamine was added to the residue.

This procedure was repeated two more times. The residue was distilled on a spinning-band column to give 13.2 g. (0.15 mole, 60% yield) of cyclopentanone-2,2,5,5-d₄. Deuterium analysis by nmr on the dioxane-deuterium oxide mixture used in the final exchange was found to give inconclusive results due to complication of the spectrum by the dioxane. Deuterium analysis by both 60 and 100 mc nmr units on the exchanged ketone also proved unsatisfactory as it was impossible to completely resolve the β - and γ -hydrogen peaks which overlapped one another. Therefore, this method of preparing cyclopentanone-2,2,5,5-d₄ was discontinued since it was believed at the time that deuterium analysis would be made by nmr rather than by the falling-drop technique.

Method C-1. A 21 g. (0.25 mole) sample of cyclopentanone (1.0 g. atom of exchangeable H) was mixed with 100 g. (5.0 mole) of deuterium oxide (9.982 g. atoms of exchangeable D) and 1 g. of dry, freshly distilled triethylamine. The solution was gently refluxed for approximately thirty-six hours, cooled to room temperature, and extracted with three 100 ml. portions of anhydrous ethyl ether. The ether extracts were combined, dried over anhydrous calcium sulfate, and the ether was removed under vacuum (aspirator) on a RINCO rotory evaporator. A new mixture of deuterium oxide and triethylamine was added to the residue, and the above procedure was repeated three more times. The residue was distilled on a spinning-band column to give 11.5 g. (0.131 mole, 52% yield) of cyclopentanone-2,2,5,5-d₄. Deuterium analysis by nmr on the deuterium oxide used in the final exchange indicated the ketone contained 3.984 atoms of deuterium per molecule. Infrared spectrum of cyclopentanone-2,2,5,5-d₄ relative to polystyrene standard gave the following: C-D stretch, doublet 4.67 μ (w) and 4.47 μ (w) (lit.⁵ 4.68 μ (w) and 4.48 μ (w)).

Method C-2. Cyclopentanone-2,2,5,5-d₄ was again prepared according to the procedure given in Method C-1. A 42.0 g. (0.50 mole) sample of cyclopentanone was exchanged six times with 100 ml. portions of deuterium oxide (9.982 g. atoms of exchangeable D) containing a catalytic amount of triethylamine. Obtained from this process was 8.0 g. (0.091 mole, 18.2% yield) of cyclopentanone-2,2,5,5-d₄, b.p. 125-130°. The nmr and infrared spectra for this sample were almost identical to those obtained for the ketone prepared by Method C-1.

Cyclopentanol-2,2,5,5-d₄ (First Preparation). Cyclopentanol-2,2,5,5-d₄ was prepared according to the procedure of Nystrom and Brown.¹¹¹ A solution of 1.52 g. (0.04 mole) of lithium aluminum hydride in 150 ml. of anhydrous ethyl ether was placed in a 500 ml. two-neck flask equipped with a pressure-equalized dropping-funnel, magnetic stirrer, and reflux condenser with drying tube. Before the reaction was started, the system was flushed with dry nitrogen. In the dropping-funnel was placed 8.8 g. (0.1 mole) of cyclopentanone-2,2,5,5-d₄ (from Method C-1) and 50 ml. of anhydrous ether, and this mixture was added dropwise to the hydride solution at such a rate as to produce gentle reflux. Ten minutes after the last addition, water was cautiously added dropwise with continued stirring. The flask was cooled in an ice bath during this latter addition to keep the exothermic decomposition of the excess hydride from becoming too vigorous. The mixture was poured onto 100 ml. of ice water, and to this mixture was added 200 ml. of 10% sulfuric acid. After separation of the ether layer, the aqueous phase was extracted with two 100 ml. portions of ether. The ether extracts were combined, dried over anhydrous calcium sulfate, and the ether was removed by distillation

through a packed column. The remaining residue was distilled on a spinning-band column, using a chaser solvent of dry, freshly distilled diethylcarbitol, b.p. 185-186° (lit.¹¹² b.p. 189°) to give the following: 4.6 g. (0.051 mole, 51% yield) of cyclopentanol-2,2,5,5-d₄; b.p. 135-139°; n_D²⁰ 1.4463. Nmr spectrum relative to -OH proton gave the following: singlet 4.97τ(-OH), singlet 5.80τ(α-H), doublet or unresolvable singlets 8.35τ and 8.40τ(β- and γ-H).

(Second Preparation). Cyclopentanol-2,2,5,5-d₄ was again prepared by the procedure described above. A sample of 8.0 g. (0.091 mole) of cyclopentanone-2,2,5,5-d₄ (from Method C-2) was reduced with 2.0 g. (0.053 mole) of lithium aluminum hydride to give 5.5 g. (0.061 mole, 67% yield) of cyclopentanol-2,2,5,5-d₄, b.p. 135-140°. The nmr and infrared spectra of this sample were almost identical to those obtained for cyclopentanol-2,2,5,5-d₄ in the first preparation.

2,2,5,5-d₄-Cyclopentyl Brosylate (First Preparation). 2,2,5,5-d₄-Cyclopentyl brosylate was prepared from cyclopentanol-2,2,5,5-d₄ (First Preparation) according to the method of Tipson.¹⁰⁸ It had a melting point of 44.3-45.0°. Deuterium analysis¹⁰⁶ showed the brosylate contained 3.718 atoms of deuterium per molecule.

(Second Preparation). 2,2,5,5-d₄-Cyclopentyl brosylate was prepared from cyclopentanol-2,2,5,5-d₄ (Second Preparation) according to the method of Tipson.¹⁰⁸ It had a melting point of 44.2-45.0°. The deuterium content was assumed to be the same as for 2,2,5,5-d₄-cyclopentyl tosylate (3.768 atoms of deuterium per molecule) since both were prepared from the same alcohol.

2,2,5,5-d₄-Cyclopentyl Tosylate. 2,2,5,5-d₄-Cyclopentyl tosylate was prepared from cyclopentanol-2,2,5,5-d₄ (Second Preparation) according to the method of Tipson.¹⁰⁸ It had a melting point of

26.3-27.5°. Deuterium analysis¹⁰⁶ showed the tosylate contained 3.768 atoms of deuterium per molecule.

Cyclopentanol-1-d₁ (First Preparation). Cyclopentanol-1-d₁ was prepared by the same procedure¹¹¹ as described for cyclopentanol-2,2,5,5-d₄. A 10.0 g. (0.119 mole) sample of cyclopentanone was reduced with 1.68 g. (0.04 mole) of lithium aluminum deuteride to give the following: 5.0 g. (0.058 mole, 49% yield) of cyclopentanol-1-d₁; b.p. 137-141°; n_D^{20} 1.4479. Nmr spectrum relative to -OH proton gave the following: singlet 4.97 τ (-OH), singlet 8.35 τ (β - and γ -H). Infrared spectrum relative to polystyrene standard gave the following: C-D stretch, 4.70 μ and 4.63 μ (sh) (lit.⁵ 4.69 μ and 4.63 μ (sh)).

(Second Preparation). Cyclopentanol-1-d₁ was prepared by the procedure shown above. A sample of 8.4 g. (0.10 mole) of cyclopentanone was reduced with 1 g. (0.024 mole) of lithium aluminum deuteride to give 5.2 g (0.06 mole, 60% yield) of cyclopentanol-1-d₁, b.p. 135-140°. The nmr and infrared spectra of this sample were almost identical with those obtained for cyclopentanol-1-d₁ in the first preparation.

1-d₁-Cyclopentyl Brosylate. 1-d₁-Cyclopentyl brosylate was prepared from cyclopentanol-1-d₁ (First Preparation) according to the method of Tipson.¹⁰⁸ It had a melting point of 44.2-45.2°. Deuterium analysis¹⁰⁶ showed the brosylate contained 0.9841 atom of deuterium per molecule.

1-d₁-Cyclopentyl Tosylate. 1-d₁-Cyclopentyl tosylate was prepared from cyclopentanol-1-d₁ (Second Preparation) according to the method of Tipson.¹⁰⁸ It had a melting point of 26.7-27.8°. Deuterium analysis¹⁰⁶ showed the tosylate contained 0.9648 atom of deuterium per molecule.

Cyclopentene Epoxide. Cyclopentene was furnished compliments of the Phillips Petroleum Company, Research Division, Bartlesville, Oklahoma. It had the following properties: b.p. 43.5° (lit.¹¹³ b.p. 44.242°); n_D^{20} 1.4198 (lit.¹¹³ n_D^{20} 1.4225). The following methods were then used in an attempt to synthesize cyclopentene epoxide. Method C proved to be the only satisfactory method of the three.

Method A. By modifying the procedure given in Organic Syntheses, Collective Volume IV,¹¹⁴ an attempt was made to prepare cyclopentene epoxide. A solution of 20.4 g. (0.3 mole) of cyclopentene in 450 ml. of dry, freshly distilled methylene chloride, b.p. $39-40^{\circ}$ (lit.¹¹⁶ b.p. $40-41^{\circ}$), was placed in a one-liter three-neck flask equipped with a pressure-equalized dropping-funnel, magnetic stirrer, thermometer, and reflux condenser with drying tube. The methylene chloride solution was cooled to 20° with an ice bath, and then the cooling bath was removed. A solution of 32.5 g. (0.425 mole) of 40% peracetic acid in acetic acid containing 5.0 g. of sodium acetate-trihydrate and 5 ml. of acetic anhydride was added dropwise and with stirring to the reaction mixture during a period of fifteen minutes. The resulting mixture was stirred overnight, during which time the temperature was not allowed to rise above 35° . The contents of the flask were poured into 500 ml. of water, and the organic layer was separated. The aqueous phase was extracted with two 150 ml. portions of methylene chloride. The methylene chloride extracts were combined, washed with two 100 ml. portions of 10% aqueous sodium carbonate and then with two 100 ml. portions of water, and dried over anhydrous magnesium sulfate. The methylene chloride was removed by distillation through a packed column. The cyclopentene

epoxide should have remained as a residue. However, since no residue remained, no appreciable amount of epoxide was obtained by this method.

Method B. By modifying the procedure given in Organic Syntheses, Collective Volume IV,¹¹⁵ an attempt was made to prepare cyclopentene epoxide. In a one-liter three-neck flask equipped with a pressure-equalized dropping-funnel, magnetic stirrer, thermometer, and reflux condenser with drying tube was placed a solution of 27.2 g. (0.4 mole) of cyclopentene, 115 ml. of 30% aqueous hydrogen peroxide, and 400 ml. of freshly distilled methanol, b.p. 63-64° (lit.¹¹⁷ b.p. 64.96°). After the mixture was cooled to 15° with an ice bath, 33 ml. (0.2 mole) of 6 normal aqueous sodium hydroxide was added, dropwise and with stirring, over a period of one hour. During the addition, the temperature of the reaction mixture was maintained at 15-20° with a bath of cold water (the reaction will not begin below 15°). After the addition was complete, the resulting mixture was stirred for three hours while the temperature was maintained at 20-25°. The reaction mixture was poured into 500 ml. of water and extracted with two 400 ml. portions of ethyl ether. The ether extracts were combined, washed with water, and dried over anhydrous magnesium sulfate. The ether was removed by distillation through a packed column. The cyclopentene epoxide should have remained as a residue. However, since no residue remained, no appreciable amount of epoxide was obtained by this method.

Method C. Cyclopentene epoxide was prepared according to the procedure of Emmons and Pagano.¹¹⁸ In a 250 ml. two-neck flask equipped with a pressure-equalized dropping-funnel, magnetic stirrer, and reflux condenser with drying tube was placed a solution of 8.2 ml. (0.3 mole) of 90% hydrogen peroxide and 50 ml. of dry, freshly

distilled methylene chloride. After the mixture was cooled to 5° with an ice bath, 50.8 ml. (0.36 mole) of trifluoroacetic anhydride was added over a period of ten minutes. The peroxytrifluoroacetic acid so obtained was stirred for fifteen minutes while the temperature was maintained at 0-5°. In a 500 ml. two-neck flask equipped with a pressure-equalized dropping-funnel, magnetic stirrer, and reflux condenser with drying tube was placed 95 g. (0.9 mole) of sodium carbonate, 13.6 g. (0.2 mole) of cyclopentene, and 200 ml. of methylene chloride. The cold solution of peroxytrifluoroacetic acid made previously was transferred to the dropping-funnel, and was added to the well-stirred cyclopentene solution over a period of thirty minutes. During the addition, the solvent boiled vigorously and it was necessary to use a condenser cooled with ice water maintained at 5° to prevent escape of the olefin. After the addition was complete, the mixture was heated under reflux for a period of thirty minutes. The insoluble salts were removed by filtration and the filter cake was washed with methylene chloride. The filtrate was combined with the reaction mixture, and the methylene chloride was removed by distillation through a packed column. The residue was distilled on a spinning-band column using a chaser solvent of dry, freshly distilled s-tetrachloroethane, b.p. 144-145° (lit.¹¹⁹ b.p. 146°), to give the following: 7.11 g. (0.084 mole, 42% yield) of cyclopentene epoxide; b.p. 96-100° (lit.¹¹⁸ b.p. 98-100°); n_D^{20} 1.4330 (lit.¹¹⁸ n_D^{20} 1.4341).

trans-Cyclopentanol-2-d₁. trans-Cyclopentanol-2-d₁ was prepared by the same procedure¹¹¹ as described for cyclopentanol-2,2,5,5-d₄. A 5.0 g. (0.0595 mole) sample of cyclopentene epoxide was allowed to react with 1.68 g. (0.04 mole) of lithium aluminum deuteride to

give the following: 2.1 g. (0.0242 mole, 41% yield) of trans-cyclopentanol-2-d₁; b.p. 136-141°; n_D²⁰ 1.4489. Nmr spectrum relative to -OH proton gave the following: singlet 4.97τ(-OH), singlet 5.63τ(α-H), singlet 8.23τ(β- and γ-H). Infrared spectrum relative to polystyrene standard gave the following: C-D stretch, 4.60μ (lit.⁵ 4.62μ).

2-d₁-trans-Cyclopentyl Brosylate. 2-d₁-trans-Cyclopentyl brosylate was prepared according to the method of Tipson.¹⁰⁸ It had a melting point of 44.0-44.9°. Deuterium analysis¹⁰⁶ showed the brosylate contained 0.9971 atom of deuterium per molecule.

2-d₁-trans-Cyclopentyl Tosylate. 2-d₁-trans-Cyclopentyl tosylate was prepared according to the method of Tipson.¹⁰⁸ It had a melting point of 26.2-27.2°. The deuterium content was assumed to be the same as for 2-d₁-trans-cyclopentyl brosylate (0.9971 atom of deuterium per molecule) since both were prepared from the same alcohol.

cis-Cyclopentanol-2-d₁ (First Preparation). cis-Cyclopentanol-2-d₁ was prepared according to the procedure of Finley and Saunders.¹²⁰ Into a dry, three-neck flask equipped with a pressure-equalized dropping-funnel, magnetic stirrer, nitrogen bubbler tube, and reflux condenser with drying tube was placed 11.4 g. (0.08 mole) of freshly distilled boron trifluoride ethyl etherate, b.p. 122-124° (lit.¹²¹ b.p. 125-126°), and 100 ml. of anhydrous ethyl ether. This mixture was refluxed with stirring under a dry nitrogen atmosphere for about thirty minutes in order that any excess boron trifluoride might react with the ether. This precaution was taken because in previous attempts to run this reaction the excess boron trifluoride, probably acting as a Lewis acid, catalyzed the polymerization of cyclopentene. The flask was cooled to room temperature and 10.2 g. (0.15 mole) of cyclopentene was added to the reaction mixture. In the dropping-

funnel was placed 2.1 g. (0.05 mole) of lithium aluminum deuteride in 100 ml. of anhydrous ether, and this suspension was added to the reaction mixture over a period of about three hours. This addition led to a very exothermic reaction and the condenser had to be cooled with ice water maintained at 5° in order that the olefin would not boil away. The mixture was then refluxed for approximately two hours to make sure that the reaction had gone to completion. The reaction mixture was cooled to room temperature, water was added to destroy excess diborane-d₆, and then the mixture was treated with 40 ml. (0.12 mole) of 3 molar aqueous sodium hydroxide and 20 ml. (0.862 mole) of 30% hydrogen peroxide. The mixture was filtered and the filtrate was extracted with three 50 ml. portions of ether. The ether solution was washed successively with two 25 ml. portions of each of the following materials: water, 10% sulfuric acid, water, saturated sodium bicarbonate solution, and water. The ether solution was dried over anhydrous calcium sulfate and the solvent was removed under vacuum (aspirator) on a RINCO rotary evaporator. The residue was distilled on a spinning-band column, using a chaser solvent of dry, freshly distilled diethylcarbitol, to give the following: 4.0 g. (0.046 mole, 31% yield) of cis-cyclopentanol-2-d₁; b.p. 136-140°; n_D²⁰ 1.4497. Nmr spectrum relative to -OH proton gave the following: singlet 4.97τ(-OH), poorly resolved triplet 5.62τ(α-H), doublet or very poorly resolved singlets 8.22τ and 8.25τ(β- and γ-H). Infrared spectrum relative to polystyrene standard gave the following: C-D stretch, 4.56μ (lit.⁵ 4.56μ).

(Second Preparation). cis-Cyclopentanol-2-d₁ was prepared by the procedure shown above. A sample of 10.2 g. (0.15 mole) of cyclopentene was reduced with diborane-d₆ produced from 11.4 g.

(0.08 mole) of boron trifluoride ethyl etherate and 2.1 g. (0.05 mole) of lithium aluminum deuteride to give the following: 4.4 g. (0.051 mole, 34% yield) of cis-cyclopentanol 2-d₁; b.p. 135-140°. The nmr and infrared spectra of this sample were almost identical to those obtained for cis-cyclopentanol-2-d₁ in the first preparation.

2-d₁-cis-Cyclopentyl Brosylate. 2-d₁-cis-Cyclopentyl brosylate was prepared from cis-cyclopentanol-2-d₁ (First Preparation) according to the method of Tipson.¹⁰⁸ It had a melting point of 44.0-44.7°. Deuterium analysis¹⁰⁶ showed the brosylate contained 0.9919 atom of deuterium per molecule.

2-d₁-cis-Cyclopentyl Tosylate. 2-d₁-cis-Cyclopentyl tosylate was prepared from cis-cyclopentanol-2-d₁ (Second Preparation) according to the method of Tipson.¹⁰⁸ It had a melting point of 25.8-27.0°. Deuterium analysis¹⁰⁶ showed the tosylate contained 0.9440 atom of deuterium per molecule.

Cyclopentyl Ethyl Ether. Cyclopentyl ethyl ether was prepared by modifying the procedure given in Vogel.¹²² A sample of 15.5 g. (0.674 mole) of "molecular" sodium was prepared by refluxing sodium in a xylene solution. The xylene was completely replaced by 100 ml. of anhydrous ethyl ether. A reflux condenser and dropping-funnel were attached to the flask, and a solution of 56.8 g. (0.66 mole) of cyclopentanol and 50 ml. of anhydrous ether was added slowly with stirring. The reaction mixture was allowed to reflux overnight to complete the formation of the sodium alkoxide. A 108 g. (0.692 mole) sample of ethyl iodide was added dropwise to the alkoxide with stirring. The reaction mixture was refluxed for 24 hours with a blue solid precipitating out as the reaction progressed. The solid was removed by filtration, the ether was removed under vacuum (aspirator)

on a RINCO rotory evaporator, and the remaining residue was distilled on a spinning-band column using a chaser solvent of dry, freshly distilled diethyl carbitol to give the following: 6.8 g. (0.06 mole, 9% yield) of cyclopentyl ethyl ether; b.p. 120-122° (lit.¹²³ b.p. 122°); n_D^{20} 1.426 (lit.¹²³ n_D^{20} 1.423).

2-Cyclopentenone. 2-Cyclopentenone was purchased from Aldrich Chemical Company, and had the following refractive index: n_D^{20} 1.4827. Nmr spectrum relative to TMS was as follows: multiplet 2.50 τ (α -vinyl H), multiplet 4.22 τ (β -vinyl H), multiplet 7.82 τ (β -methylene H), and multiplet 8.22 τ (α -methylene H). Infrared spectrum of 2-cyclopentenone relative to polystyrene standard gave the following: C=O stretch 5.90 μ and C=C stretch 6.30 μ .

5,5-d₂-2-Cyclopentenone. A 5 g. (0.061 mole) sample of 2-cyclopentenone (0.12 g. atom of exchangeable H) was mixed with 50 g. (2.5 moles) of deuterium oxide (4.991 g. atoms of exchangeable D) and 0.1 g. of brosyl chloride. The solution was stirred at room temperature for approximately two weeks. The solution was extracted with three 50 ml. portions of anhydrous ethyl ether. The ether extracts were combined, dried over anhydrous calcium sulfate, and the ether was removed under vacuum (aspirator) on a RINCO rotory evaporator. A new mixture of deuterium oxide and brosyl chloride was added to the residue, and the above procedure was repeated. To avoid thermally inducing polymerization, the residue was not distilled at this point but was placed in a freezer until needed. Obtained from this procedure was 2.5 g. (0.037 mole, 60% yield) of 5,5-d₂-2-cyclopentenone. The nmr spectrum for this sample was almost identical to that for 2-cyclopentenone except that there was no peak at 8.22 τ (α -methylene H). There was no appreciable difference between the infrared spectra of these two compounds.

Cyclopentanol (Model reaction for the preparation of 2,2-d₂-cyclopentanol). Cyclopentanol was prepared by the same procedure¹¹¹ as described for cyclopentanol-2,2,5,5-d₄. A 5 g. (0.061 mole) sample of 2-cyclopentenone was reduced with 2 g. (0.053 mole) of lithium aluminum hydride to give the following: 4.5 g. (0.052 mole, 85% yield) of cyclopentanol; b.p. 134-141°. The nmr spectrum was extremely complex but did indicate qualitatively that the 2-cyclopentenone had been reduced to a mixture of approximately 70% cyclopentanol and 30% of what appeared to be cyclopentenol.

5,5-d₂-2-Cyclopentenol. An unsuccessful attempt was made to prepare 2,2-d₂-cyclopentanol by the procedure given above for the reduction of 2-cyclopentenone to cyclopentanol. A 2.5 g. (0.037 mole) sample of 5,5-d₂-2-cyclopentenone was allowed to react with 1 g. (0.026 mole) of lithium aluminum hydride to give the following: 2.1 g. (0.024 mole, 65% yield) of 2,2-d₂-cyclopentenol; b.p. 135-141°. The nmr spectrum for this sample was very complex, however it did indicate that none of the desired product, 2,2-d₂-cyclopentanol, was produced but rather that 5,5-d₂-2-cyclopentenol had been produced.

5,5-d₂-2-Cyclopentenyl Brosylate. 5,5-d₂-2-Cyclopentenyl brosylate was prepared according to the method of Tipson.¹⁰⁸ No physical properties were determined for this brosylate. However, it was noted that it was a liquid at -15° and a solid at -78°.

1-Cyclopentenyl Acetate (Model reaction for the preparation of 2,2,5-d₃-1-cyclopentenyl acetate). 1-Cyclopentenyl acetate was prepared according to the procedure of Hagemeyer and Hull.¹²⁴ In a 100 ml. flask equipped with a packed column fitted with a total condensation take-off head was placed 16.8 g. (0.20 mole) of cyclopentanone, 56 g. (0.56 mole) of iso-propenyl acetate and

0.2 g. of *p*-toluenesulfonic acid·mono-hydrate. The mixture was heated at such a temperature that a by-product of acetone continuously distilled from the reaction mixture. After approximately three hours an additional 14 g. (0.14 mole) of *iso*-propenyl acetate was added to the reaction mixture and heating was continued for approximately twelve hours at total reflux. The acetone was removed by distillation. The reaction mixture was cooled to room temperature, diluted with 100 ml. of ether, and was washed with two 100 ml. portions of a saturated solution of aqueous sodium bicarbonate. The ether solution was dried over anhydrous calcium sulfate and the ether was removed under vacuum (aspirator) on a RINCO rotary evaporator. The remaining residue was distilled on a packed column under vacuum using a chaser solvent of diethylcarbitol to give the following: 13.5 g. (0.107 mole, 53.6% yield) of 1-cyclopentenyl acetate; b. p. 64-68° (30 mm. Hg); n_D^{20} 1.4478. Infrared spectrum of 1-cyclopentenyl acetate relative to polystyrene standard gave the following: C=O stretch 5.68 μ and C=C stretch 6.00 μ .

Cyclopentanol (Model reaction for the preparation of *cis*-2-d₁-5,5-d₂-cyclopentanol). An unsuccessful attempt was made to prepare cyclopentanol by the reduction of 1-cyclopentenyl acetate with diborane followed by hydrolysis with aqueous acetic acid. The diborane reduction procedure was a modification of that used for the preparation of *cis*-cyclopentanol-2-d₁.¹²⁰ A 6.75 g. (0.0536 mole) sample of 1-cyclopentenyl acetate was allowed to react with diborane produced from 11.4 g. (0.08 mole) of boron trifluoride ethyl etherate and 2.1 g. (0.05) mole of lithium aluminum hydride. The diborane was generated externally and transferred by a stream of dry nitrogen into the reaction vessel which contained the 1-cyclopentenyl acetate.

The reaction mixture was hydrolyzed with 20 ml. of acetic acid followed by 20 ml. of water and was heated to reflux for approximately three hours. The excess water and acetic acid were removed from the reaction mixture by distillation using a chaser solvent of diethylcarbitol. A black solid residue remained in the diethylcarbitol and indicated decomposition of the products. No attempt was made to identify the residue. None of the desired product, cyclopentanol, was produced by this procedure.

Cyclopentanol (Model reaction for the preparation of cis-2-d₁-5,5-d₂-cyclopentanol). An unsuccessful attempt was made to prepare cyclopentanol by the reduction of 1-cyclopentenyl acetate with biimine followed by hydrolysis with aqueous acetic acid. The procedure followed for this attempted synthesis was that of Corey and Mock.¹²⁵ A 6.75 g. (0.0536 mole) sample of 1-cyclopentenyl acetate was placed in 100 ml. of anhydrous ethanol and to this was added 15 g. (0.072 mole) of anthracene-9,10-biimine. The solution was heated to reflux for 30 minutes at which time a second 15 g. sample of the anthracene biimine was added. Heating was continued for an additional thirty minutes. The reaction mixture was cooled, hydrolyzed by adding 20 ml. of water followed by 20 ml. of acetic acid, and was heated to reflux for three hours. Distillation of the reaction mixture using a chaser solvent of diethylcarbitol resulted in similar decomposition of products as mentioned in the above procedure for the preparation of cyclopentanol. None of the desired product, cyclopentanol, was produced by this procedure.

EXPERIMENTAL RESULTS

Table XVI
Cell Constants

<u>Cell</u>	<u>Cell Constant</u>
250 ml.	0.6307
500 ml.	0.3600

Table XVII
Parameters Used in Fuoss-Onsager Equation
(Equation 6)

<u>Electrolyte*</u>	<u>Λ_o</u>	<u>S_a</u>	<u>E</u>	<u>J</u>
p-Bromobenzenesulfonic Acid	89.247	114.27	265.71	2494.5
p-Toluenesulfonic Acid	89.090	145.40	485.56	4002.8

*In 70% vol. ethanol-water at 25°

Table XVIII
Solvolysis Rates and Isotope Effects
for Cyclopentyl Brosylates in 70% Vol. Ethanol-Water at 25°

<u>Cyclopentyl Brosylate</u>	<u>Run No.</u>	<u>Observed Rate $k \times 10^4$ (sec⁻¹)</u>	<u>Corrected Rate* $k \times 10^4$ (sec⁻¹)</u>	<u>k_H/k_D^*</u>
Normal	1	2.8031 ± 0.0015	-----	-----
	2	2.7991 ± 0.0011		
	3	2.8009 ± 0.0004		
	4	2.8024 ± 0.0004**		
	Av.	2.8014 ± 0.0023		
1-d ₁ -	1	2.3682 ± 0.0003	2.3603	1.1869
	2	2.3664 ± 0.0006		
	Av.	2.3673 ± 0.0009		
<u>cis</u> -2-d ₁ -	1	2.4308 ± 0.0004	2.4290	1.1533
	2	2.4332 ± 0.0007		
	Av.	2.4320 ± 0.0012		
<u>trans</u> -2-d ₁ -	1	2.3756 ± 0.0009	2.3735	1.1803
	2	2.3739 ± 0.0005		
	Av.	2.3747 ± 0.0009		
2,2,5,5-d ₄ -	1	1.5639 ± 0.0008	1.4837	1.8881
	2	1.5617 ± 0.0005		
	Av.	1.5628 ± 0.0011		

*Corrected to 100% deuterium in the position(s) under consideration, with aid of the expression $k_{corr.} = f_D k_{D obs.} + (1 - f_D) k_H$.

**Data shown in appendix.

Table XIX

Solvolysis Rates and Isotope Effects for
Cyclopentyl Tosylates in 70% Vol. Ethanol-Water at 25°

<u>Cyclopentyl Tosylate</u>	<u>Run No.</u>	<u>Observed Rate k x 10⁵ (sec⁻¹)</u>	<u>Corrected Rate* k x 10⁵ (sec⁻¹)</u>	<u>k_H/k_D*</u>
Normal	1	5.1270 ± 0.0021		
	2	5.1346 ± 0.0018		
	Av.	5.1308 ± 0.0038	-----	-----
1-d ₁ -	1	4.3600 ± 0.0020		
	2	4.3661 ± 0.0041		
	Av.	4.3630 ± 0.0031	4.3350	1.1836
<u>cis</u> -2-d ₁ -	1	4.4726 ± 0.0036		
	2	4.4692 ± 0.0011		
	Av.	4.4709 ± 0.0017	4.4318	1.1577
<u>trans</u> -2-d ₁ -	1	4.3671 ± 0.0010		
	2	4.3597 ± 0.0032		
	Av.	4.3634 ± 0.0037	4.3611	1.1765
2,2,5,5-d ₄ -	1	2.8406 ± 0.0012		
	2	2.8350 ± 0.0024		
	Av.	2.8378 ± 0.0028	2.7201	1.8863

*Corrected to 100% deuterium in the position(s) under consideration, with aid of the expression $k_{\text{corr.}} = f_{\text{D}} k_{\text{D obs.}} + (1 - f_{\text{D}}) k_{\text{H}}$.

Table XX

Products of Solvolysis of
Cyclopentyl Brosylates in 70% Vol. Ethanol-Water

<u>Cyclopentyl Brosylate</u>	<u>Products (% of Total)</u>		
	<u>Cyclopentene</u>	<u>Cyclopentanol</u>	<u>Cyclopentyl Ethyl Ether</u>
Normal	22.1	45.9	32.0
1-d ₁ -	19.9	47.5	32.6
<u>cis</u> -2-d ₁ -	21.8	44.5	33.7
<u>trans</u> -2-d ₁ -	19.5	45.5	35.0
2,2,5,5-d ₄ -	14.0	44.1	41.9

DISCUSSION

In order to make a comparison with the work of Streitwieser, Jagow, Fahey and Suzuki⁵ it was necessary to synthesize the same compounds used by them in the original work. Therefore, the tosylates of cyclopentanol and its 1-d₁, cis-2-d₁, trans-2-d₁ and 2,2,5,5-d₄ analogs were synthesized. With the exception of cis-2-d₁-cyclopentanol, all of the alcohols were prepared by procedures identical to those used in the original work. The cis-2-d₁ alcohol was prepared by reducing cyclopentene with diborane-d₆ and oxidizing with alkaline hydrogen peroxide.¹²⁰ This procedure is well documented by Brown^{126,127} who has determined that the diborane reduction nearly always gives 97% (or more) pure cis-addition. The procedure used for the preparation of cis-2-d₁-cyclopentanol in the original work was to first prepare the trans-2-d₁-cyclopentanol, conversion of this alcohol to the tosylate, treatment of the tosylate with tetramethylammonium acetate in dry acetone and hydrolysis with aqueous base. Since the diborane procedure used in this investigation requires three fewer steps than the procedure used in the original investigation, it is believed that the cis-isomer is stereochemically as pure as, if not purer than, that produced by the procedure of Streitwieser, Jagow, Fahey and Suzuki.

In addition to the tosylates mentioned above it was decided that a more thorough comparison could be made by studying the same basic system with a different, but similar, leaving group. Therefore, the brosylates of the same five cyclopentyl alcohols mentioned above were synthesized for this purpose. It was felt that by studying the cyclopentyl system with a second leaving group any unique characteristics of the tosyl group would be exposed.

The isotope effect results and rate constants for this investigation are shown in Tables XVIII and XIX. From the results it can be seen that there is very close agreement between the isotope effects for the brosylate and tosylate of any one given isotopically substituted cyclopentyl alcohol, e.g., the greatest difference exhibited was that of 0.38% for the cis-compounds. This close agreement indicates that when changing from one leaving group to another structurally similar leaving group there is a negligible influence on the isotope effect. From the results it can also be seen that cyclopentyl brosylate solvolyzes 5.5 times as fast as cyclopentyl tosylate. When compared with similar data for the iso-propyl system this relative rate seems quite reasonable since iso-propyl brosylate solvolyzes 4.3 times as fast as iso-propyl tosylate in 80% vol. ethanol-water at 50° (Table XV).

The kinetic procedure adopted for this investigation was that proposed by Murr and Shiner⁹² in which the rate of solvolysis was monitored by a conductance technique. They determined the precision of this technique to be ~0.03%. The cell constants used for this investigation were accurate to ~0.03%, this error being due to the inability to weigh the potassium chloride any more accurately. It was possible to maintain the constant temperature bath used in this study at $25.000 \pm 0.005^\circ$ (0.02%). The clock used was checked regularly and was found to be quite accurate. The estimated uncertainty in time is 0.01% or less. The parameters determined for the Fuoss-Onsager equation were limited by the precision with which the brosylates and tosylates could be weighed. These weights were required in order to calculate the concentrations of electrolyte in solution. The estimated precision of these parameters is ~0.1%. From the least-squares computer program written by Buddenbaum¹⁰³ and used for the

calculation of the first order or pseudo first order rate constants in this investigation, it was possible to obtain values reproducible within a range of 0.05-0.1%. The rate constants shown in Tables XVIII and XIX are the mean value of a minimum of two replicate runs and it is estimated that their uncertainty is no greater than the reproducibility for obtaining them, i.e., 0.05-0.1%. The isotope effects, however, should be more certain than the rate constants due to a cancellation of errors in taking the ratio of the rate constants.

From the error analysis shown above it can be seen that every attempt was made to make the final results as precise as possible. However, the determining factor governing the precision of the rate constants obtained was found to be the precision of the deuterium analyses, ¹⁰⁶ ~0.1 atom % for the mono-deuterium compounds and ~0.05% for the d₄-compounds. The following example illustrates how this error affects the isotope effect. The isotope effect, k_H/k_D , reported for cis-2-d₁-cyclopentyl brosylate (Table XVIII) is 1.1533. By taking into account the ± 0.1 atom % precision this value can vary from 1.1557 to 1.1519. A similar analysis for the other mono-deuterated compounds indicates a similar precision.

It is difficult to estimate the preciseness of the rate constants given for the d₄-compounds. They were corrected to 100% deuterium in the four β-positions by assuming that the only other species present was the d₃-compound as opposed to the presence of some d₂-, d₁- and d₀-contaminants. Since the rate of solvolysis of the d₃-compound was not known, it had to be calculated. It was calculated by assuming that the cyclopentyl brosylate and tosylate systems exhibited cumulative nature. This appears to be a valid assumption since the solvolytic

rate retardation caused by tetra-deuteration approximately equals the square of that caused by mono-cis deuteration times the square of that caused by mono-trans deuteration: $2,2,5,5-d_4$ -brosylate = $1.8881 \approx 1.8530 = (1.1533)^2(1.1803)^2 = (\text{cis-2-}d_1\text{-brosylate})^2(\text{trans-2-}d_1\text{-brosylate})^2$. Similarly for the tosylate system: $2,2,5,5-d_4$ -tosylate = $1.8863 \approx 1.8552 = (1.1577)^2(1.1765)^2 = (\text{cis-2-}d_1\text{-tosylate})^2(\text{trans-2-}d_1\text{-tosylate})^2$. Although the observed and calculated isotope effects for the d_4 -compounds are not equal within the experimental uncertainty, they only differ by $\sim 1.9\%$ and $\sim 1.7\%$ for the brosylate and tosylate, respectively. Most systems which are considered noncumulative in nature have calculated and observed isotope effects differing by 10-15%.^{70,72} Therefore, based on the small differences observed for the cyclopentyl system, it is felt that the assumption of cumulative behavior is valid.

In order to check the accuracy of the correction technique mentioned above, a new sample of the d_4 -alcohol was synthesized. The brosylate of this alcohol was prepared and its rate of solvolysis was determined. The deuterium content of the first d_4 -brosylate was 92.95% and that of the second was 94.20%. The isotope effect calculated for the first d_4 -brosylate was 1.8881 and that of the second was 1.8876. From this analysis the correction technique appears to be quite satisfactory. For purposes of comparison the other extreme was assumed, i.e., that the only contaminant present in the d_4 -brosylate was the d_0 -brosylate. This yields a corrected d_4 -isotope effect of 1.9071. Based on this small difference ($1.9071 - 1.8881 \approx 0.02$) ($\sim 1\%$), the assumptions of cumulative behavior and the presence of only a d_3 -contaminant seem reasonable. Based on the factors mentioned above it appears that the rate constants for the d_4 -compounds are precise to at least 0.2%.

The kinetic procedure used by Streitwieser, Jagow, Fahey and Suzuki⁵ was to monitor the rate of solvolysis by a potentiometric titration technique, which they estimated to be precise to ~1%. No mention was made concerning the precision of their deuterium analyses, but it is assumed that these were more precise than was their kinetic procedure. In view of this information it appears that the results of this investigation are more precise than those obtained in the original work.

The results of both the original investigation (Table V) and this investigation indicate that the cyclopentyl system exhibits cumulative or almost cumulative behavior. The most striking difference between the results of the two studies is the reversal in magnitude of the cis- and trans-isotope effects. As opposed to the work of Streitwieser, Jagow, Fahey and Suzuki,⁵ this investigation and the investigations of several others^{70,72,91} indicate that the isotope effect of the trans-isomer is greater than the isotope effect of the cis-isomer. This is the order that would be predicted, based on the theory that the β -hydrogens can hydrogen-bond to specific solvent molecules and lead to an elimination driving force. If this is the case, the trans-hydrogens should be more effectively involved and subsequently weakened more than the cis-hydrogens; therefore, substitution of a trans-hydrogen by deuterium should produce a greater isotope effect.¹⁶ From the work of Saunders and Finley,⁷² the results of which are shown in Table V, it can be seen that for the acetolysis of cyclohexyl tosylates the trans-isotope effect is greater than that of the cis-isomer. This order of magnitude is in agreement with the results of this investigation. More important, however, is the fact that in the work of Saunders and Finley the

solvolyses were carried out in acetic acid, as were also the solvolyses of Streitwieser, Jagow, Fahey and Suzuki. This indicates that there is no special characteristic of the acetic acid medium as opposed to ethanol-water which can account for the reversal in magnitude of the cis- and trans-isotope effects observed in the two solvolysis systems.

From Tables XVIII and XIX it can be seen that the differences between the cis- and trans-isotope effects are small, i.e., 0.0270 for the brosylates and 0.0188 for the tosylates. However, it is believed that these are true differences because of the high precision of this investigation. The variation in brosylate and tosylate differences ($0.0270 - 0.0188 = 0.0082$) is quite puzzling but can be rationalized in the following ways: (1) The variation is of the same order of magnitude as the experimental uncertainty. (2) The possibility exists that there is a change in the extent of ring puckering when changing from a brosyl to a tosyl group. The latter explanation seems unlikely, however, since the brosyl and tosyl group are so similar in structure.

The product analysis is shown in Table XX. Since 70% vol. ethanol-water is a fairly good nucleophilic solvent and only weakly basic, the greater percentage of substitution products over elimination products was expected. This was confirmed as shown in Table XX. Because water is a better nucleophile than ethanol, a higher percentage of substitution products would be expected with water than with the co-solvent. This was found to be true for all of the compounds studied and the results are shown in Table XX. The presence of an almost equal number of water molecules and

ethanol molecules in the solvent explains the closeness of the alcohol percentages to the ether percentages.

Because carbon-deuterium bonds are stronger than carbon-hydrogen bonds²⁵ it is more difficult for a carbon-deuterium bond to be broken to produce an olefin. This fact was borne out as expected since the olefin fraction for the d_4 -compound was considerably smaller than for the other compounds analyzed. The olefin fraction should have been even lower than the 14% reported as no attempt was made to correct for deuterium composition (~93% in the d_4 -compound). It was also expected that the trans-brosylate would yield a lower olefin fraction on solvolysis than would the cis-2- d_1 and d_0 -compounds. This was the case and the results serve as an argument for the idea of specific solvation of the β -hydrogens as a possible cause for β -deuterium isotope effects.

As described in the Review of Literature, secondary β -deuterium isotope rate effects can be rationalized in terms of three classical effects: hyperconjugation, induction and steric effects. The cyclopentyl system was analyzed in terms of these three effects. If hyperconjugation were the predominant cause of the β -isotope effects observed for the cyclopentyl system, one would have to expect a decrease in solvolysis rate with the introduction of deuterium in the β -positions. This was the case for all of the β -deuterium substituted compounds studied (Tables XVIII and XIX). Also, if hyperconjugation were responsible for the β -isotope effects observed, the isotope effects should be subject to the same stereochemical influences observed for other hyperconjugative systems (Table I). It appears that this is also the case as the cis- and trans-isotope effects observed are very similar in magnitude to those isotope

effects shown in other hyperconjugative systems (Table I). The cumulative or nearly cumulative behavior exhibited by the cyclopentyl system in this investigation is also support for the hyperconjugation postulate.⁷⁰

In analyzing the results in terms of inductive effects the following must be taken into consideration. The carbon-deuterium bond being shorter than the carbon-hydrogen bond, deuterium appears to be a better electron donor than hydrogen.²⁸ This requires that the developing carbonium ion in the transition state of the solvolysis reaction be stabilized more by deuterium than by hydrogen. This would result in an inverse isotope effect, *i.e.*, $k_H/k_D < 1$. However, it can be seen from the results in Tables XVIII and XIX that only normal isotope effects were observed ($k_H/k_D > 1$), so any inductive influences that might be present in the cyclopentyl system are masked by the presence of a greater effect in the opposite direction.

In analyzing the results in terms of steric effects several factors must be considered. The steric isotope effect is due to the smaller size of deuterium as compared to hydrogen. In the cyclopentyl system one is concerned with a secondary carbon atom at the reaction center, therefore, the possibilities of unimolecular and bimolecular kinetics have to be taken into account. If the reaction is unimolecular, *i.e.*, development of a full-fledged carbonium ion in the transition state, then only a very small isotope effect should be observed for the cis- and trans- β -deuterium compounds since the substituting group can approach from either side of the ring system. The isotope effects of 1.15 and 1.18 observed for the cis- and trans-isomers, respectively (Tables XVIII and XIX), are of the normal magnitude (see Tables III, IV and V) and are

considered to be larger than those expected for the unimolecular-steric postulate mentioned above. If the reaction is bimolecular, i.e., displacement of the leaving group by a solvent molecule in the transition state, then the trans- β -deuterium compound should react faster than the cis- β -deuterium or d_0 -compounds due to the smaller deuterium atom on the same side of the ring as the entering solvent molecule. Also, the cis- β -deuterium compound should react at approximately the same rate as the d_0 -compound since they both have two hydrogens on the same side of the ring as the entering solvent molecule. It can be seen from Tables XVIII and XIX that the results for this investigation are in opposition to the above mentioned facts as the trans-compound reacted slower than the cis-compound. The cis-compound in turn reacted considerably slower than the d_0 -compound. From this it appears that a steric effect is not operating in this system.

Attempts were made to synthesize both 2,2- d_2 -cyclopentanol and cis-2- d_1 -5,5- d_2 -cyclopentanol, but unfortunately these attempts proved unsuccessful. Since the model reaction was reasonably successful, no logical explanation can be given for failure in the preparation of the d_2 -compound. It is not surprising, however, that the technique adopted for the preparation of the d_3 -compound proved unsuccessful. The method required stereospecific reduction of the carbon-carbon double bond of 1-cyclopentenyl acetate in a cis-manner. The two reducing agents chosen for this were diborane¹²⁰ and biimine,¹²⁵ both known to give cis-reduction products. The reduction of an enol acetate with diborane was attempted by Brown¹²⁸ and found to be unsuccessful. A survey of biimine reductions showed that tri-substituted double bonds and polar double bonds result in very poor yields

of reduction product.¹²⁹ Both of these limitations are present in the 1-cyclopentenyl acetate system. In light of these observations it seems certain that a poor selection was made in choosing the 1-cyclopentenyl acetate as a base compound for the synthesis of cis-2-d₁-5,5-d₂-cyclopentanol.

Initially it was not known whether the cyclopentyl system exhibited cumulative or noncumulative isotope effects. Had the system been noncumulative in nature, it was believed that the d₂- and d₃-compounds would be useful in determining the extent of hydrogen participation in the transition state.⁷⁰ Since the studies with the cis-, trans- and d₄-compounds showed the absence of noncumulative behavior (Tables XVIII and XIX) it is felt that the d₂- and d₃-compounds would have yielded no significant information.

CONCLUSION

The α - and β -deuterium isotope rate effects for the solvolysis of cyclopentyl brosylates and tosylates in 70% vol. ethanol-water at 25° have been determined. There is very close agreement between the isotope effects for the brosylate and tosylate of any one given isotopically substituted cyclopentyl alcohol. From this it can be concluded that a change from one leaving group to another structurally similar leaving group causes a negligible influence on the isotope effect.

It can be further concluded that because of the apparent cumulative behavior exhibited by the cyclopentyl system, the best explanation of the cause of secondary β -deuterium isotope rate effects in this system is the hyperconjugation postulate.

Finally, it was determined that the trans-isotope effect was larger than the cis-isotope effect for both the cyclopentyl brosylate system and the cyclopentyl tosylate system. From this it can be concluded that the results obtained by Streitwieser, Jagow, Fahey and Suzuki⁵ for the acetolysis of the cyclopentyl tosylate system were in error. In addition, contrary to the conclusion of Streitwieser, Jagow, Fahey and Suzuki,⁵ specific solvation of the β -hydrogens leading to an elimination driving force cannot be entirely ruled out as a possible explanation of secondary β -deuterium isotope rate effects.

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