WILLIAM MARSH RICE UNIVERSITY

ISOTOPE EFFECTS IN HYDRIDE TRANSFER REACTIONS

by

Reuben Henry Grinstein

A THESIS
SUBMITTED TO THE FACULTY
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF
Doctor of Philosophy

Houston, Texas
June, 1961
Dedicated to the memory of my grandfathers,
Rabbi Henoch Grinstein and Morris Weinstein.
ACKNOWLEDGMENT

I would like to express my grateful appreciation to Professor E.S. Lewis for suggesting this research problem and guiding it to completion.

I am indebted also to Dr. R.B. Turner and Dr. M.G. Ettlinger for their useful advice.

Finally, I would like to thank the William Marsh Rice University, the Robert A. Welch Foundation and the Humble Oil and Refining Company for their generous financial assistance.
TABLE OF CONTENTS

Introduction 1
Methods 18
Results and Conclusions 22
Experimental 41
Summary 59
Bibliography 61

INDEX TO TABLES AND FIGURES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1</td>
<td>Prediction of Isotope Effects from Typical Spectral Data for Hydrogen and Deuterium Compounds</td>
<td>9</td>
</tr>
<tr>
<td>Table 2</td>
<td>Observed Arrhenius Parameters in the Bromination of 2-Carboethoxy-cyclopentanone in Deuterium Oxide</td>
<td>15</td>
</tr>
<tr>
<td>Figure 1</td>
<td>Temperature Variation of Reaction Velocity With and Without Tunnelling Correction</td>
<td>16</td>
</tr>
<tr>
<td>Table 3</td>
<td>Second Order Rate Constants for the Reaction of Pyridine Diphenylborane with Water Measured by Gas Evolution</td>
<td>23</td>
</tr>
<tr>
<td>Table 4</td>
<td>Competitive Isotope Effects in the Reaction of Pyridine Diphenylborane with Labeled Water</td>
<td>23</td>
</tr>
<tr>
<td>Table 5</td>
<td>Arrhenius Parameters for the Competitive Isotope Effects in the Reaction of Pyridine Diphenylborane with Labeled Water</td>
<td>24</td>
</tr>
<tr>
<td>Table 6</td>
<td>Competitive Isotope Effects in the Reaction of Labeled Pyridine Dephenylborane with Water</td>
<td>24</td>
</tr>
</tbody>
</table>
INDEX TO TABLES AND FIGURES
(continued)

Figure 2 Arrhenius Plot of Deuterium and Tritium Isotope Effects in the Reaction of Pyridine Diphenylborane with Labeled Water 25

Table 7 Rate Constants and Isotope Effects for the Reaction of Leuco Crystal Violet H and D with Chloranil 32

Table 8 Arrhenius Parameters for the Reaction of Leuco Crystal Violet with Chloranil 32

Figure 3 Arrhenius Plot of the Rates of Reaction of Protinated and Deuterated Leuco Crystal Violet with Chloranil 33

Figure 4 Arrhenius Plot of Deuterium Isotope Effect in the Reaction of Labeled Leuco Crystal Violet with Chloranil 34

Figure 5 Thermal Conductivity Cell and Vacuum Line Equipment Used in Analysis of Hydrogen Deuteride Gas 47

Figure 6 Detail of Thermal Conductivity Cell and Toepler Pump from Figure 5 48

Figure 7 Schematic Diagram of Electrical System Used in Thermal Conductivity Analysis 49

Figure 8 Detail of Reaction Vessel from Figure 5 50

Figure 9 Reaction Vessel and Ionization Chamber Filling Line for Tritium Isotope Effect Experiments 54
INTRODUCTION

In recent years, nucleophilic substitution reactions have been studied intensively from various viewpoints. Electrophilic substitution reactions have been studied also, but much work is left to be done. The work described in this thesis is on electrophilic substitution on hydrogen, commonly called hydride transfer reactions. Hydrogen isotope effects were used as a means of studying the mechanisms of these reactions.

The field of hydride transfer reactions has been reviewed by Deno, Peterson and Saines (1). Hydride transfer reactions have been found to occur under a wide range of conditions varying from strongly acid to strongly basic solutions. The Cannizzaro reaction (2), which involves the conversion of two molecules of aldehyde into one molecule of the corresponding alcohol, and one of the corresponding acid is an example of a hydride transfer reaction catalyzed by a very strong base. A hydride ion is transferred from one aldehyde molecule to the other.

On the opposite side, Bartlett, Condon and Schneider (3) observed the extremely rapid exchange of hydride ions between alkyl halides and paraffins. For instance, ter.-butyl chloride and isopentane gave isobutane and isopentylchloride.

Dauben, Pearson, Gadecki, Harmon (4) have reported the conversion of cycloheptatriene to tropylium ion by hydride transfer to triphenylmethyl cation. The reaction proceeds under neutral conditions, in any solvent capable of ionizing the triphenylmethyl
salt. They report that triphenylmethyl halides will react in liquid sulfur dioxide, while the fluoborate and perchlorate salts react in acetonitrile.

Doering and Aschner (5) studied the nature of the species transferred in the Meerwein, Pondorf, Verley reduction-Oppenauer oxidation system (6)(7). The reaction involves the reduction of an aldehyde or ketone to an alcohol, or the reverse process, catalyzed by aluminum alkoxides. They measured the kinetics of the oxidation of 2-methylbutanol-1 to 2-methylbutanal. They found that the rates were not affected by free radical inhibitors, such as diphenylamine, thiophenol, or p,p'-bis(dimethylaminophenyl)-amine. Consequently, they concluded that a free radical process was not involved in the reaction.

A very powerful method for studying reaction mechanisms is the use of isotopes. At first, isotopes were used principally as tracers. For instance, Doering and Aschner (5) used deuterium substitution in the 2-methylbutanol-1 on the hydroxyl group, and on carbon 2, as well as using a deuterated solvent. From the reaction mixture, they isolated both alcohol and aldehyde. Neither had any deuterium on carbon 1, though deuterium was easily exchanged on carbon 2 of the aldehyde. Consequently, by excluding the possibility of proton and free radical processes, Doering and Aschner established the validity of the hydride transfer mechanism.

Otvos, Stevenson, Wagner and Beeck (8) used deuterium to study the reaction of isobutane with 2-methylpentene-2 in concentrated sulfuric acid. This is an example of the well known alkylation
reaction used in the manufacture of gasoline. This group demonstrated that the nine methyl group hydrogens readily exchanged with deuterated sulfuric acid, but the tertiary hydrogen would not exchange. They further demonstrated that only the tertiary hydrogen was transferred to the olefin to give isopentane, by replacing the tertiary hydrogen with deuterium, and proving that the isopentane contained one atom of deuterium per molecule.

The second use of isotopes is to study the effects of isotopic substitution on reaction rate. These phenomena, called isotope effects, are commonly divided into primary, and secondary effects. Primary effects are observed when the isotopic bond is broken in the rate determining step, while in secondary effects, the isotopic bond remains intact during the reaction.

The origin of isotope effects can be explained in terms of the theory of absolute reaction rates. This theory, commonly called the transition state theory, is explained thoroughly in Glasstone, Laidler and Eyring (9). According to this theory, there exists an equilibrium between the starting materials, and an "activated complex" (also called the transition state) which subsequently gives rise to the products. The rate constant $k$ for the overall reaction is given by equation 1.

$$k = \frac{K T}{h} \chi K'$$  \hspace{1cm} 1

Where $K$ is the Boltzmann constant, $T$ is the absolute temperature, $h$ is Planck's constant, $\chi$ is a factor that gives the probability that the activated complex will decompose to give products, and $K'$ is the equi-
librium constant between the starting materials, and the activated complex.

Bigeleisen and Wolfsberg (10), Melander (11), Wiberg (12) and Bell (13), among others, have utilized the theory of absolute reaction rates for the prediction of isotope effects. The derivation of equations which follows is a combination of these authors' results.

The term $K'$ can be expressed in terms of the partition functions of the individual species:

$$K' = \frac{\prod_{i}^{n} Q_{i}^{\pm}}{\prod_{i}^{n} Q_{i}^{A} \prod_{i}^{n} Q_{i}^{B}}$$

In equation 2, the individual partition functions, $Q^\pm$ for the transition state, and $Q^A$, $Q^B$ for the reactants, are expressed as the product of separable partition functions for vibrational, rotational, translational and electronic states.

In this thesis, the term "isotope effect" is defined as the ratio of the rate constant of the lighter isotope to that of the heavier. Thus the isotope effect is:

$$\frac{k_{1}}{k_{2}} = \frac{K'_{1}}{K'_{2}} = \frac{\prod_{i}^{n} Q_{i1}^{\pm}}{\prod_{i}^{n} Q_{i2}^{\pm}} \times \frac{\prod_{i}^{n} Q_{i1}^{A}}{\prod_{i}^{n} Q_{i2}^{A}} \frac{\prod_{i}^{n} Q_{i1}^{B}}{\prod_{i}^{n} Q_{i2}^{B}}$$

Assuming that the translational, and electronic partition functions are not seriously affected by isotopic substitutions, equation 3 may be written in more specific terms as:
Where the \( S' \)'s are symmetry numbers, \( A \), \( B \) and \( C \) are moments of inertia, and \( M \) is the mass of the species. \( U \) is a shorthand notation for \( \frac{h}{kT} \), where \( K \) is Boltzmann's constant, \( h \) is Planck's constant, \( T \) is the absolute temperature, and \( \tilde{v} \) is a vibrational frequency.

The assumptions made to simplify equation 3 are valid for most molecules except hydrogen, and in the region of room temperature where most systems are in their electronic ground states.

The activated complex may be treated as if it were a real molecule, except that it has one less degree of vibrational freedom \((3n-7)\). This lost degree of vibrational freedom is equivalent to translation along the reaction co-ordinate. This lost vibration can be thought of as a vibration with a negative Hooke's Law force constant. Instead of being in an energy well, it is on top of a potential hill. Consequently, this mode is sometimes called the imaginary vibration.

Equation 4 has been simplified by Bigeleisen (10) by the application of the Teller-Redlich product rule (14). The effect of the use of this rule is to rewrite the mass and moment of inertia terms as shown in the following equation:

\[
\frac{k_1}{k_2} = \left( \frac{M_1^{3/2}}{M_2^{3/2}} \right)^{\frac{3}{2}} \frac{S_2}{S_1} \left( \frac{A_2 B_2 C_2}{A_1 B_1 C_1} \right)^{\frac{1}{2}} \prod_i e^{-\frac{1}{2}u_i (1-e^{-u_i})} \times \prod_i e^{\frac{1}{2}u_i (1-e^{-u_i})}
\]

\( 4 \)
\begin{align*}
\left( \frac{M_1^* M_2}{M_1^{*2}} \right)^{\frac{3}{2}} \left[ \frac{A^*_1 B^*_1 C^*_1 A^*_2 B^*_2 C^*_2}{A^*_2 B^*_2 C^*_2 A^*_1 B^*_1 C^*_1} \right]^\frac{1}{2} = \left( \frac{m^*_2}{m^*_1} \right)^{\frac{1}{2}} \sum_{i=1}^{3n-6} u_{i1} - u_{i2} \sum_{i=1}^{3n-6} u_{i1} - u_{i2}
\end{align*}

The \( m^* \)'s are the reduced mass of the imaginary vibration of the transition state. In cases where hydrogen is attached to a large residue, \( m^* \) is very close to the isotopic mass.

The resulting equation, known as Bigeleisen's complete equation, is given below:

\begin{align*}
\frac{k_s S_0 S^*_L}{k_s S_0 S^*_L} &= \left( \frac{m^*_2}{m^*_1} \right)^{\frac{1}{2}} \sum_{i=1}^{3n-6} \frac{u_{i2}(1-e^{-u_{i2}})}{u_{i1}(1-e^{-u_{i1}})} \frac{3n-7}{3n-7} \frac{u_{i1}^*(1-e^{-u_{i1}^*})}{u_{i2}^*(1-e^{-u_{i2}^*})} \\
&\quad \times e^{-\frac{1}{2} \left[ \sum_{i=1}^{3n-6} (u_{i1}^*-u_{i2}^*) - \sum_{i=1}^{3n-6} (u_{i1}-u_{i2}) \right]}
\end{align*}

5

The products and summations are taken over all vibrational modes of the starting materials and the transition states. The terms in equation 5 are arranged so that it resembles the Arrhenius equation. In most cases the symmetry numbers (S) cancel.

Early work on the prediction of isotope effects, described by Wiberg (12), was based on two assumptions. The first was that the pre-exponential terms in equation 5 have a value unity. Thus the isotope effect should be due to the exponential term alone. The second assumption was that the imaginary vibration of the transition state corresponds to one real vibration of the isotopic bond in the
starting material. The energy of the other bonds in the starting material was assumed to be unchanged in the transition state. The isotope effect would then be due to the difference in vibrational bond energies of isotope 1 and 2. Since at room temperature, most systems are in their ground state, this method of predicting isotope effects has come to be known as the zero point energy approximation.

There is a possibility that the imaginary vibration of the transition state has no corresponding vibration in the starting material. This situation can be visualized by considering a three body system, AB reacting with C to give A plus BC. In the transition state, there exists a bending vibration, as shown below:

which is related to rotation in the unassociated AB plus C system. If this was the lost vibration, there would be no zero point energy differences between the starting materials and the transition state to give rise to an isotope effect. However, one would have to consider the moment of inertia terms in equation 4 as a possible source of isotope effects. A new rotational partition function would have to be substituted to cover linear and diatomic molecules in place of the one given for nonlinear polyatomic molecules. Also, in the case of triatomic molecules like water, though equation 3 holds, care must be taken to avoid confusion between vibrational and rotational modes.

Again, using the simplified three body system, there exists the
possibility of a symmetrical and unsymmetrical stretching mode in the transition state. Wiberg restricted his consideration to the linear case, and the unsymmetrical stretch as the imaginary vibration.

\[ \text{symmetrical stretch} \quad \text{unsymmetrical stretch} \]

In this case, the symmetrical stretch may be independent of the mass of B and thus cause no trouble. However, in certain cases, the symmetrical stretch may become mass dependent, with the result that the predicted isotope effect would be reduced, since there would be new zero point energy in the transition state to consider.

In practice, the differences in zero point energy, and hence predictions of isotope effects, are calculated from spectral vibrational frequencies. Table 1 gives some typical vibrational frequencies, and the isotope effects calculated from them.
Table 1

Prediction of Isotope Effects from Typical Spectral Data for Hydrogen and Deuterium Compounds

<table>
<thead>
<tr>
<th>Bond</th>
<th>Vibration</th>
<th>R-H $\nu$ (cm$^{-1}$)</th>
<th>$E_0$ (cal/mole)</th>
<th>$k_H/k_D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-H</td>
<td>stretch</td>
<td>2,800</td>
<td>1,150</td>
<td>6.9$^1$</td>
</tr>
<tr>
<td>C-H</td>
<td>bend</td>
<td>2,904</td>
<td>1,193</td>
<td>6.0$^2$</td>
</tr>
<tr>
<td>N-H</td>
<td>stretch</td>
<td>1,299</td>
<td>533</td>
<td>2.4$^2$</td>
</tr>
<tr>
<td>O-H</td>
<td>stretch</td>
<td>3,100</td>
<td>1,270</td>
<td>8.5$^1$</td>
</tr>
<tr>
<td>O-H</td>
<td>stretch</td>
<td>3,300</td>
<td>1,400</td>
<td>10.6$^1$</td>
</tr>
<tr>
<td>B-H</td>
<td>stretch</td>
<td>2,300</td>
<td>945</td>
<td>4.0$^3$</td>
</tr>
</tbody>
</table>

Sources: 1 Wiberg (12)  
2 Shiner and Smith (30) for tertiary H in 1-bromo-2-phenylpropane  
3 Hawthorne and Lewis (24)

The zero point energy approximation method has proved useful in many cases, but frequently the approximations required are unrealistic. The nature of the transition state is unknown, but it is unlikely that all of the zero point energy of a vibration is lost in the transition state. It is even possible that, in some cases, no zero point energy is lost, but rather, the isotope effect comes from the pre-exponential term.

Returning to equation 5, if $(m_2^\pm/m_1^\pm)^\pm = u_1/u_2 = u_1^\pm/u_2^\pm$ and $e^{-u} \ll 1$ as would be the case for the isotopes of hydrogen, then the pre-exponential term should reduce to unity. However, at high temperatures, when $U \ll 1$ and $U^\pm \ll 1$, the products approach unity and the pre-exponential term has the limit of $(m_2^\pm/m_1^\pm)^\pm$. 

This is also true if \( \mathcal{U}_i \equiv \mathcal{U}_z \) and \( \mathcal{U}_i^\pm \equiv \mathcal{U}_z^\pm \).

Bell (13) considers the extreme case where only \( \mathcal{U}_z^\pm \leq 1 \). Now the product term for the transition state would go to unity, and the other two terms would reduce to \( \left( \frac{m_1^*}{m_2^*} \right) \). This case is extreme because it corresponds to no bonding in the transition state. Thus, the extreme range of pre-exponential term values would be, in the case of deuterium, \( \frac{1}{2} \) to \( 1.414 \), and in the case of tritium, \( \frac{1}{3} \) to \( 1.732 \). In both cases, a value near unity is most likely.

In recent years, several attempts have been made to calculate the isotope effects in simple systems from first principles. There are two main difficulties which one encounters when attempting to predict isotope effects. The first involves our lack of knowledge about the exact shape of the energy surface. Even in the simplest cases, such as the reaction of hydrogen atoms with hydrogen molecules, the surface has not been established. There are two methods which are commonly used to approximate the energy surface. The first is Eyring's (9) method, and the second was proposed by Sato (15). Both methods employ London's (16) technique of using the coulombic interactions to calculate energies. Both methods require the use of an empirical parameter. The second drawback is that the functions used to describe the energy surface cannot be integrated exactly, and thus require the use of a computer for numerical solution.

Weston (17) has calculated the values for the reaction of hydrogen atoms with hydrogen molecules. He used the Sato method for determining the energy surface and obtained results in "reasonably good agreement with experimental values."
Shavitt (18) has calculated the rates of ortho-para conversions and isotope exchanges in hydrogen. His results, based on Sato's method also, but adjusting the activation energy to fit experimental values, proved to be unsatisfactory.

Finally, Bigeleisen, Klein, Weston and Wolfsberg (19) have determined both the experimental and theoretical rates for the reaction of hydrogen molecules with chlorine atoms. The two values are in acceptable agreement with one another.

Let us now consider some examples of the use of isotope effects in mechanism studies. Wiberg (20) demonstrated the mechanism of the Cannizzaro reaction using isotopically labeled benzaldehyde. He proposed two mechanisms:

\[
\text{Ph-CHO} + \text{O}^\theta \text{OH} \rightarrow \text{Ph-C-OH}
\]

\[
1 \quad \text{Ph-C-H} + \text{C-\theta} \xrightarrow{k} \text{Ph-CO} + \text{Ph-C-H} + \text{O}^\theta
\]

\[
2 \quad \text{Ph-C-H} + \text{C-\theta} \xrightarrow{k} \text{Ph-C-O-C-\theta} \rightarrow \text{Ph-C-O-C-\theta} + \text{O}^\theta \text{OH}
\]

in each of which the step with rate constant \( k \) is the rate determining step. The difference in the two mechanisms is that in reaction mechanism (1) the carbon-hydrogen bond is broken in this rate determining step and therefore, an isotope effect should be observed. In mechanism (2) this is not the case, and there should be no isotope
effect. Wiberg observed an isotope effect of 1.8, thus eliminating the possibility that the first step in mechanism (2) is rate determining.

Bartlett and McCollum (21) investigated the reduction of triphenylcarbinol by isopropyl alcohol in acid solution. They report an isotope effect of 1.84 measured competitively and 2.58 from the ratio of the individual rate constants.

The base catalyzed reaction of triphenylsilane with proton donors has been studied by Kaplan and Wilzbach (22). They report a deuterium isotope of 1.15 and a tritium isotope effect of 1.26 at 25° C, and 1.29 at 0° C. Brynko, Dunn, Gilman and Hammond (22) studied the reaction of the triphenylsilane in toluene with pipiridine and water. They found the deuterium isotope effect to be 1.46 measured competitively and 1.41 from the ratio of individual rate constants.

Finally, Hawthorne and Lewis (24) reported the deuterium isotope effect in the reaction of pyridine diphenylborane with water to be 6.9 with respect to deuterium in the water and 1.52 with respect to deuterium in the borane.

Each of the above examples is a hydride transfer reaction. In such a reaction, one would expect that the attacking electrophile would be directed towards the region of highest electron density, which is located around a line from the hydrogen atom to the atom to which it is bound. As a consequence, the transition state should be non-linear, and thus, bending vibrations should contribute more to the observed isotope effect than the stretching vibrations. The
resulting isotope effect should be between 1 and 3. For instance, in Table 1, the isotope effect predicted from the loss of one carbon-hydrogen bending vibration is 2.42. Furthermore, the isotope effect could come at least in part from the pre-exponential term.

In the first three examples the authors were expecting a large isotope effect coming from the loss of a stretching vibration. Wiberg (20) thought the value he observed was unreliable because it was so small. Kaplan and Wilzbach tried to explain their observations by saying that the energy lost from the stretching vibration was made up by new bond formation in the products.

Hawthorne and Lewis (24) were the first to suggest that the bending vibration gave rise to the isotope effect, and they also pointed out that it was possible that the pre-exponential term contributed to the isotope effect. In the case of small isotope effects up to \((m_2)^{1/2}\), the pre-exponential term could even account for the whole effect, and the bond need not be broken at all. Consequently, for small isotope effects, one must determine their temperature dependence before deciding on the source of the effect.

A subject which has been deliberately skipped in the correction for the possibility of "tunnelling." In classical theory, an insufficiently energized system cannot surmount a barrier or pass through it. According to quantum mechanics, small particles like hydrogen may have a wave function with a finite value on the other side of the barrier, and thus, the possibility of tunnelling through the barrier must be considered.
The subject of tunnelling correction has been discussed since the postulation of the transition state theory. Wigner (25) proposed intuitively the correction term $\frac{U^2}{24}$ in 1932. More recent authors have attempted a more rigorous determination of the correction factor. Again, work has been hampered by the difficulty of establishing the shape of the energy surface, and consequently the height and width of the barrier.

Bell (26) has attempted to approximate the barrier with a truncated parabola. His results are interesting in that the first term of the series expansion which he derives for the correction factor is the same as Wigner's term.

More exact methods have been employed by Johnson and Rapp (27), Sahvitt (18) and Weston (17). They used an Eckart function (28), which in the symmetrical case looks like a Gauss normal distribution curve, to describe the shape of the barrier. Unfortunately, none of the results published so far are very good.

Recently, two authors have reported experiments presented as evidence of tunnelling. Both reactions involve proton transfer.

Bell, Fendley and Hulett (29) measured the Arrhenius parameters for the isotope effect in the base catalyzed bromination of 2-carboethoxy-cyclopentanone-2-d. The results are listed in Table 2.
Table 2

Observed Arrhenius Parameters in the Bromination of 2-Carboethoxy-cyclopentanone in Deuterium Oxide

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>$D_2O$</th>
<th>$CH_2ClCO_2^-$</th>
<th>$F^-$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_H/k_D$</td>
<td>3.42</td>
<td>3.91</td>
<td>2.66</td>
</tr>
<tr>
<td>$\Delta Ea$ (kcal/mole)</td>
<td>$1.21 \pm 0.08$</td>
<td>$1.45 \pm 0.08$</td>
<td>$2.44 \pm 0.10$</td>
</tr>
<tr>
<td>$A_H/A_D$</td>
<td>$0.44 \pm 0.05$</td>
<td>$0.35 \pm 0.05$</td>
<td>$0.042 \pm 0.008$</td>
</tr>
</tbody>
</table>

Shiner and Smith (30) report the determination of the Arrhenius parameters in the base catalyzed elimination of 1-bromo-2-phenyl-propane. They studied this reaction in hopes of finding evidence for tunnelling, for the mechanism has been known for many years. They report an isotope effect of 7.510 at 25° C with $\Delta Ea$ of 1.79 kcal/mole and $A_H/A_D$ of 0.366.

Bell, Fendley and Hulett argued that the three parameters $k_H/k_D$, $\Delta Ea$, and $A_H/A_D$ should be altered if tunnelling exists.

Since one would expect the hydrogen to tunnel far more than deuterium, because it has half the mass, the value of the hydrogen rate constant should be increased by tunnelling more than the value for the deuterium rate constant. This would result in an increase in value of the observed isotope effect.

Secondly, the activation energy should appear lower in the hydrogen case and the difference in activation energy should be increased.
Finally, the ratio \( \frac{A_H}{A_D} \) should be lowered. The reason can be most easily explained by using Bell's (13) graph.

A is the classical pre-exponential term, and \( A^* \) is the term that would be observed if tunnelling were present. As can be seen from Figure 1, the consideration of a tunnelling correction would result in a lowering of the value of \( A \). Since \( A_H \) would be lowered more, the ratio should be reduced in value.

Bell, Fendley and Hulett, as well as Shiner and Smith, used a comparison of the observed parameters, with the theoretical values, as an argument for the existence of tunnelling in the reactions they measured.
In this thesis, the reaction of pyridine diphenylborane with water and the reactions of 4,4',4''-methylenebis[N,N'-dimethyl-
aniline], (leuco crystal violet), with triphenylmethyl cation and with 2,3,5,6-tetrachlorobenzoquinone, (chloranil), were studied.
METHODS

The first compound studied was pyridine diphenylborane (PDPB) which was synthesized by Hawthorne (31). He prepared the compound by the scheme outlined below:

\[
\begin{align*}
B(\text{OC}_4\text{H}_9)_3 & \rightarrow [\text{Ph}_2\text{BOH}] \quad \text{H}_2\text{NC}_2\text{H}_4\text{OH} \rightarrow \text{Ph}_2\text{BOC}_2\text{H}_4\text{NH}_2 \\
\text{I} & \rightarrow \text{Ph}_2\text{BOC}_2\text{H}_5 \quad \text{LiAIH}_4 \text{Pyridine} \rightarrow (\text{Ph}_2\text{BH})^{-}\text{Py}^+
\end{align*}
\]

In this scheme, the intermediate compound I, \(\beta\) aminoethyl diphenylborinate proved to be quite stable, and was therefore used as a starting material for the subsequent steps.

Hawthorne and Lewis (24) determined the deuterium isotope effect in the reaction of PDPB with water, by measuring the rates of reaction by titrating the remaining PDPB with iodine. Deuterium substitution in the water, and on the borane, was studied at 40° C.

In this laboratory, the isotope effect was determined competitively by isotopic analysis of the product, hydrogen gas. The isotope effect was measured over a temperature range from 0 to 50° C. at ten degree intervals. The four cases of deuterium and tritium substitution on the borane and on the water were investigated.

The hydrogen gas was analyzed in the deuterium case by thermal conductivity. This method of analysis, treated in detail by Daynes (32) is based on the fact that the thermal conductivity of a gas is
a function of the molecular mass. Thus, by using this method, one can easily distinguish between hydrogen and hydrogen deuteride or mixtures of the two.

An apparatus for performing this analysis was constructed after the design of those described by Archer (33), Farkas and Farkas (34), Mabury and Koski (35) and Trenner (36). The detectors used were thermistor beads, and the electrical measurement system was a Wheatstone bridge. The tritium content of the gas was determined with an ionization chamber in conjunction with a vibrating reed electrometer.

In all cases, the reaction was carried to less than ten percent completion, so that the isotope effect could be calculated by the simple formula:

\[
\frac{k_1}{k_2} = \frac{[A_2^0]}{[A_1^0]} \times \frac{[P_1]}{[P_2]}
\]

where \([A_0^0]\) refers to the initial concentration of the compound labeled with isotopes 1 and 2, while the \([P]\)'s refer to the concentrations of the isotopically labeled product.

The second compound chosen for study reflects an attempt to find evidence for tunnelling. Since in electrophilic attack, the transition state should be nonlinear due to attack on the electron cloud, as noted earlier, one should be able to seriously crowd the transition state configuration by steric factors. If the two reactants are large molecules, the reaction site will be shielded by bulky groups and the transition state should be forced to be near linear. The result may increase the likelihood of finding tunnelling.
A clue to such a reaction system should be an unusually high isotope effect. H.J. Dauben, in a private communication, stated that the reaction of triphenylmethyl cations with tri-p-anisylmethane shows an unusually high isotope effect. The reaction of 4,4',4"-methylidinetris [N,N-dimethylaniline], commonly called leuco crystal violet (LCV), with triphenylmethyl cations was chosen for study. The reaction was conducted in acetonitrile solution with triphenylmethyl fluoborate used as the cation source.

There are a variety of methods for preparing LCV. Synthesis by the reduction of the dye, crystal violet, with lithium aluminum hydride was chosen because it is easy to introduce isotopes this way. The triphenylmethyl fluoborate was synthesized by the method described by Dauben, Honnen and Harmon (37). Unfortunately, it was found that the proposed reaction did not follow the expected course.

As a substitute for the triphenylmethyl cation, C.D. Ritchie suggested the use of 2,3,5,6-tetrachlorobenzoquinone (chloranil). Chloranil is an oxidizing agent which has been used by dye chemists for many years. Ritchie (38) has studied this reaction and determined that it is kinetically first order in leuco dye, first order in chloranil and negative one order in acid.

The deuterium isotope effect of this reaction was measured in methanol solution with excess acetic acid. The chloranil is said to catalyze air oxidation of the leuco dye, so precautions were taken to exclude air.

The isotope effect was determined from the ratio of the protium and deuterium rate constants. These rate constants were determined
by measuring the initial rates of formation of crystal violet spectros
copically.
RESULTS AND CONCLUSIONS

The results of the experiments on the reaction of pyridine diphenylborane with water are presented on Tables 3, 4, 5 and 6, and on Figure 2. Table 3 gives the results of the rough measurements of the rate of reaction determined by following the increase of pressure in the reaction vessel. The reactions were made pseudo first order, and the rate constants were calculated by the Guggenheim method (39) described by Frost and Pearson (40). These results suffer from numerous experimental errors, but are useful for rough comparisons. The reaction of pyridine diphenylborane-\textsubscript{1} with protium oxide was examined at six different temperatures between 20 and 40° C. The reaction of the borane with deuterium oxide proved to be too slow to measure conveniently at a variety of temperatures, so the rate was determined at only one temperature (40° C). The rate of reaction of the deuterated borane with ordinary water was also measured at only one temperature (40° C).

The order of the reaction was redetermined by measuring the rates at different concentrations of reactants. Hawthorne and Lewis' (24) conclusion that the reaction is second order overall and first order in the borane and in water was verified.

The value of the second order rate constant at 40° C. for the protinated borane with protium oxide falls in the range of the results reported by Hawthorne and Lewis. The values of the rate constants for the reactions of the protinated borane with deuterium oxide and deuterated borane with ordinary water, are slightly higher.
Table 3

Second Order Rate Constants for the Reaction of Pyridine
Diphenylborane with Water Measured by Gas Evolution

<table>
<thead>
<tr>
<th>Temp. °C</th>
<th>PDPB-h &amp; H₂O kₜₜ x 10⁵</th>
<th>PDPB-h &amp; D₂O kₜₜ x 10⁵</th>
<th>kₜₜ/kₜD</th>
<th>PDPB-d &amp; H₂O kₜₜ x 10⁵</th>
<th>kₜₜ/kₜD</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.0</td>
<td>3.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>29.9</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>34.9</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>39.9</td>
<td>24</td>
<td>4.6</td>
<td>5.2</td>
<td>18</td>
<td>1.3</td>
</tr>
<tr>
<td>45.0</td>
<td>52</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50.1</td>
<td>79</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4

Competitive Isotope Effects in the Reaction of
Pyridine Diphenylborane with Labeled Water

<table>
<thead>
<tr>
<th>Temp. °C</th>
<th>kₜₜ/kₜD</th>
<th>kₜₜ/kₜT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>----</td>
<td>17.7</td>
</tr>
<tr>
<td>8.50</td>
<td>7.38</td>
<td>----</td>
</tr>
<tr>
<td>10.2</td>
<td>----</td>
<td>16.7</td>
</tr>
<tr>
<td>20.0</td>
<td>6.78</td>
<td>13.9</td>
</tr>
<tr>
<td>29.9</td>
<td>6.45</td>
<td>12.6</td>
</tr>
<tr>
<td>39.9</td>
<td>6.04</td>
<td>12.4</td>
</tr>
<tr>
<td>51.4</td>
<td>5.59</td>
<td>----</td>
</tr>
</tbody>
</table>
Table 5

Arrhenius Parameters of the Competitive Isotope Effects in the Reaction of Pyridine Diphenylborane with Labeled Water

<table>
<thead>
<tr>
<th>Parameter</th>
<th>System</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H Only</td>
</tr>
<tr>
<td></td>
<td>H/D Std.dev.</td>
</tr>
<tr>
<td></td>
<td>H/T Std.dev.</td>
</tr>
<tr>
<td>△Ea (kcal/mole)</td>
<td>-20.4 1.15 0.02</td>
</tr>
<tr>
<td>A₁/A₂</td>
<td>0.940 0.031 0.784</td>
</tr>
<tr>
<td>Aₜ⁻¹</td>
<td>4.99 x 10¹¹</td>
</tr>
</tbody>
</table>

Table 6

Competitive Isotope Effects in the Reaction of Labeled Pyridine Diphenylborane with Water

<table>
<thead>
<tr>
<th>Temp. °C.</th>
<th>kₖₕ/kₖₜ D</th>
<th>kₖₕ/kₖ₅ T</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>1.40</td>
<td>1.79</td>
</tr>
<tr>
<td>20.9</td>
<td>1.41</td>
<td>----</td>
</tr>
<tr>
<td>29.9</td>
<td>1.39</td>
<td>1.71</td>
</tr>
<tr>
<td>39.9</td>
<td>1.40</td>
<td>1.77</td>
</tr>
<tr>
<td>49.8</td>
<td>1.41</td>
<td>----</td>
</tr>
</tbody>
</table>
Arrhenius plot of the deuterium (lower line) and tritium (upper line) isotope effects in the reaction of pyridine diphenyl borane with labeled water.
The Arrhenius parameters for the reaction of protinated borane with ordinary water are given on Table 5. The energy of activation (-20.4 kcal/mole) and the pre-exponential term ($4.99 \times 10^{11}$) are in the normal range. The isotope effects calculated from the rate data are smaller than those reported by Hawthorne and Lewis. The apparatus used in these rate measurements was not intended for use in rate studies, and consequently no provision was made to thermostat the glass tubing leading to the manometer. Consequently, the values are subject to error due to changes in room temperature. This is especially true for the reaction with deuterated water, for the measurement required a full day to complete.

Table 4 gives the competitive isotope effects for the reaction of the borane-h, with deuterated and tritiated water. In the deuterium case, the result at 40° C, 6.04, is twelve percent lower than Hawthorne and Lewis' result of 6.90. This difference is not thought to be important. The less accurate result from comparison of rate constants is even lower, namely 5.24.

The discrepancies between the competitive isotope effects and Hawthorne and Lewis' result may be due to secondary isotope effects from the second hydrogen on the oxygen. When the individual rates were measured, hydrogen was the second atom in the hydrogen case, and deuterium in the deuterium case. On the other hand, the competitive isotope effect was determined using a mixture of six parts deuterium oxide to one part protium oxide. Assuming easy exchange, the second atom in either the hydrogen or the deuterium case would most likely have been deuterium. If there is a small positive
secondary isotope effect, the deuterium rate would appear to be lowered with respect to the hydrogen rate, resulting in a higher observed isotope effect. In the competitive effect, secondary effects would tend to be cancelled.

A source of error in the measurement of the isotope effect in the reaction of the borane with labeled water is the possibility of protium contamination in the deuterated water. There are two sources of such contamination. First, there could be exchange with atmospheric moisture. Any serious error from such a source would have shown up in the measurement of the individual rates. No unusual variation was observed. Secondly, the commercial analysis on the deuterated water used could have been in error. (The water used was claimed to be better than 99.5% pure.) Since the standard hydrogen deuteride was prepared from the same water used in the competitive effect measurements, errors due to impure deuterated water should tend to cancel.

Figure 2 shows the data given on Table 4 plotted as log (k_1/k_2) vs. 1/T. The Arrhenius equation may be rewritten in the form

$$\log \left( \frac{k_1}{k_2} \right) = \log \left( \frac{A_1}{A_2} \right) + \frac{\Delta E_A}{2.3R} \frac{1}{T}$$

and it follows that the plot of log k vs. 1/T should give a straight line of slope $\Delta E_A$ and intercept log A, for data which obeys the Arrhenius equation. As can be seen, the points fit the straight line quite well. The Arrhenius parameters were calculated from the slope and intercept of the line which was fitted to the data by the method of least squares.
The value of the tritium isotope effect can be calculated by using the equation (6) derived by Swain, Stivers, Reawer and Schaad (41).

\[
\frac{k_H}{k_T} = \left( \frac{k_H}{k_D} \right)^{1.442}
\]

Using Hawthorne and Lewis' result, the predicted value is 17.2. Using the value from Table 4, a tritium isotope effect of 13.4 is predicted. This is still larger than the observed value of 12.4. The difference can be accounted for by the fact that the derivation of equation 6 was based on the assumptions that the pre-exponential term was unity, and that the hydrogen was attached to a very heavy residue so the reduced mass is the mass of the hydrogen isotope. Actually, the pre-exponential term is slightly less than unity, and the reduced mass for hydrogen attached to oxygen is 0.899 instead of 1.008.

The Arrhenius parameters for the reaction of borane with labeled water are given on Table 5. Judging from the size of the standard deviations, the values are good to about five percent. The value of 1.15 kcal/mole for the deuterium isotope effect activation energy is close to, but significantly less than, the 1.40 kcal/mole predicted from the difference in zero point energy of a typical oxygen-hydrogen
stretching vibration. The theoretical value can be calculated using a typical oxygen-hydrogen stretching frequency of 3,300 (cm⁻¹) as done in Wiberg's review (12). The value of the tritium effect calculated by equation 7 is 1.66 kcal/mole, which is quite close to the experimental value of 1.70 kcal/mole.

The pre-exponential term $A_H/A_D$ is 0.940. This is quite close to the expected value of unity, but considering the value of the standard deviation (0.031), the value is indeed different from unity. The value of 0.784 for $A_H/A_T$ is also significantly less than unity, and is consistent with the deuterium value.

The results of experiments on the reaction of labeled borane with ordinary water are given on Table 6. These results are very interesting for they are essentially temperature independent.

The isotope effect was measured competitively from 0 to 50° C and no variation with temperature was noted within the limits of experimental error. The temperature dependent exponential term of the Arrhenius equation, $k_1/k_2 = A_1/A_2 \exp(-\Delta E_a/RT)$, therefore contributes a negligible amount to the observed isotope effect.

The value for the tritium case was measured at only three different temperatures because it was evident that the results paralleled those for the deuterium case.

In summary, the results for the deuterium and tritium isotope effects reported here are consistent with the transition state (II) proposed by Hawthorne and Lewis on the basis of more limited observations.
Considering the value of the activation energy for the deuterium isotope effect ($\Delta E_a$), one may conclude that about three fourths of the zero point energy of the oxygen-hydrogen stretching vibration is lost in the transition state. On the other hand, the fact that deuterium and tritium isotope effects in the labeled borane case are temperature independent within experimental error is consistent with the assumption that the zero point energies of the borane-hydrogen bond are the same in the transition state as in the starting material. If there were some loss in the zero point energy of the borane bond, one would observe some temperature dependence.

The small isotope effect appears to come mostly from the pre-exponential term. Returning to equation 5 on page 6, if the u's are about the same in the transition state as in the starting materials, which would be the case if the bond remained intact, then a value $(m^+_2/m^+_1)^{1/2}$ is predicted for the pre-exponential term. This value would be 1.414 for the deuterium effect, and 1.732 for the tritium effect.

One may therefore conclude from the data reported that the lost vibration in the transition state is related to the oxygen-hydrogen
stretching vibration, and is unrelated to any of the normal boron-hydrogen vibrations. However, as the system crosses the top of the energy barrier, the boron hydrogen is in motion with respect to the center of gravity of the activated complex.

The theory of absolute reaction rates has served adequately to explain all of the observed phenomena. In turn, these results serve as evidence for the applicability of that theory.

The second compound studied was leuco crystal violet. Its reactions with both chloranil and triphenylmethyl cation were investigated.

The results of the measurements of the rates of reaction of the protinated and deuterated leuco compound with chloranil are to be found on Table 7. The values of the isotope effects computed from these data are also given on Table 7.

Figures 3 and 4 show an Arrhenius plot of the data in Table 7. As can be seen, there is a good fit to the least squares line in all cases.

Table 8 gives the Arrhenius parameters obtained from the analytical expressions for the least squares lines on Figures 3 and 4. The values of the standard deviation for deuterium isotope effect activation energy and the pre-exponential ratio $A_H/A_D$ indicate that the error in measurement is about seven percent.
Table 7
Rate Constants and Isotope Effects for the Reaction of Leuco Crystal Violet H and D with Chloranil

<table>
<thead>
<tr>
<th>Temp. °C</th>
<th>$k_H (av) \times 10^3$ l./mole sec.</th>
<th>Std. dev.</th>
<th>$k_D (av) \times 10^3$ l./mole sec.</th>
<th>Std. dev.</th>
<th>$k_H/k_D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.73</td>
<td>96.77</td>
<td>0.34</td>
<td>8.562</td>
<td>0.34</td>
<td>11.30</td>
</tr>
<tr>
<td>4.81</td>
<td>108.8</td>
<td>9.1</td>
<td>10.07</td>
<td>2.3</td>
<td>10.80</td>
</tr>
<tr>
<td>9.67</td>
<td>141.9</td>
<td>1.7</td>
<td>13.76</td>
<td>2.3</td>
<td>10.31</td>
</tr>
<tr>
<td>14.7</td>
<td>197.6</td>
<td>1.5</td>
<td>19.99</td>
<td>0.98</td>
<td>9.885</td>
</tr>
<tr>
<td>20.0</td>
<td>277.6</td>
<td>2.9</td>
<td>28.38</td>
<td>0.34</td>
<td>9.783</td>
</tr>
<tr>
<td>24.6</td>
<td>342.0</td>
<td>5.9</td>
<td>41.29</td>
<td>0</td>
<td>8.283</td>
</tr>
<tr>
<td>29.9</td>
<td>432.0</td>
<td>0</td>
<td>52.70</td>
<td>0</td>
<td>8.199</td>
</tr>
<tr>
<td>35.1</td>
<td>550.5</td>
<td>2.7</td>
<td>69.82</td>
<td>0</td>
<td>7.885</td>
</tr>
<tr>
<td>39.9</td>
<td>699.4</td>
<td>1.5</td>
<td>92.44</td>
<td>0.79</td>
<td>7.566</td>
</tr>
<tr>
<td>44.7</td>
<td>894.7</td>
<td>4.3</td>
<td>125.6</td>
<td>2.0</td>
<td>7.123</td>
</tr>
</tbody>
</table>

Table 8
Arrhenius Parameters for the Reaction of Leuco Crystal Violet with Chloranil

<table>
<thead>
<tr>
<th>Parameter</th>
<th>System</th>
<th>LCV-h</th>
<th>H/D</th>
<th>LCV-d</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_a$ (kcal/mole)</td>
<td></td>
<td>9.184</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$A$</td>
<td></td>
<td>$6.56 \times 10^9$</td>
<td>$1.83 \times 10^{10}$</td>
<td></td>
</tr>
<tr>
<td>$\Delta E_a$ (kcal/mole)</td>
<td></td>
<td>1.933</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$A_H/A_D$</td>
<td></td>
<td>0.345</td>
<td></td>
<td>0.013</td>
</tr>
</tbody>
</table>
Arrhenius plots of the rates of reaction of protinated (upper line) and deuterated (lower line) leuco crystal violet with chloranil.
Arrhenius plot of the deuterium isotope effect in the reaction of labeled leuco crystal violet with chloranil.

Figure 4
One important source of error is possible protium contamination in the deuterated leuco compound. Using the simple equation below, corrected values for the deuterium isotope effect were calculated.

\[ k_D = \frac{k_{\text{obs.}} \cdot k_H f_H}{1 - f_H} \]

In the above equation, \( k_{\text{obs.}} \) is the measured deuterium rate constant, \( k_D \) the true deuterium rate constant, \( k_H \) the observed hydrogen rate constant, and \( f_H \) the fraction of protium contamination. The new values for the isotope effects were then applied to the Arrhenius equation to obtain the corrected parameters. Using the values for the rate constants given on Table 7, and a two percent protium contamination, a value of 2.48 kcal/mole was calculated for \( \Delta E_a \) which is about twenty-five percent higher than the uncorrected value of 1.93. A value of 0.160 for \( A_H/A_D \), which is about fifty percent lower than the observed value, was obtained.

The results of these experiments are very interesting. First, the isotope effect of 8.3 at 25°C is much larger than the value 6.9 which would be predicted for the complete loss of zero point energy of a typical carbon-hydrogen stretching vibration of 2,800 cm\(^{-1}\). (See Table 1, page 9) If the pre-exponential term were greater than unity, a larger isotope effect would be observed than would come from a normal sized exponential term.

The value for the activation energy for the deuterium isotope effect, however, is also larger than that predicted from spectral data (see Table 1, page 9). The observed value is 1.93 kcal and the
predicted number is 1.15 kcal. Furthermore, the pre-exponential term, the value of which is 0.345, is not greater than unity, but lower than the extreme lower limit of 0.5. If one considers correction for protium contamination, the values are even more deviant from normal.

By Bell's (13) argument, the observation of abnormal values for the isotope effect, the activation energy, and the pre-exponential term, is consistent with the postulation of the existence of tunnelling. If such a mechanism is indeed the case, the comparison of the deuterium and tritium isotope effects should confirm the conclusion, for there is some mass dependence in tunnelling. Hydrogen should tunnel far more than deuterium or tritium.

There are, however, serious difficulties involved with the determination of the tritium isotope effect. Such a determination must be made by competitive methods. It is, however, difficult to measure the tritium content of the product, because the tritium exchanges with the solvent, and large volumes of solvent are required. One is forced, therefore, to measure the activity of the unaltered leuco compound. Such a measurement is most accurate at large extents of completion. The accuracy is dependent upon an exact knowledge of the extent of completion, a difficult thing to determine. An added complication is the fact that the reaction is reversible. The starting material isolated would be contaminated with newly formed protium compound.

The results from the preliminary experiments on the reaction of leuco crystal violet H and D with triphenylmethyl cation proved to be very confusing. In comparing the individual rates, it appeared that
the deuterated compound reacted slightly faster. This peculiar result was at first attributed to the difficulty of preparing solutions of triphenylmethyl fluoborate at accurately known concentrations. To eliminate this source of error, a competitive isotope effect measurement was attempted. A mixture of 1 to 10 of protinated to deuterated leuco crystal violet was allowed to react with triphenylmethyl fluoborate in dry acetonitrile. The product triphenylmethane was isolated in quantitative yield and analyzed for tertiary deuterium by an infrared method. The astounding result was that there was no detectible deuterium in the molecule. Even by making allowances for experimental error, this would have meant that the isotope effect was at least 300. An experiment was immediately attempted using pure deuterated leuco crystal violet. The result was the same, no deuterium was detected in the product. The only conclusion possible is that there is no hydride transfer from the central carbon atom of the leuco compound to the cation.

The observed facts were the formation of a blue color in the reaction solution, and the quantitative yield of triphenylmethane. Furthermore, the characteristic yellow color of triphenylmethyl cation in acetonitrile solution disappeared instantly when mixed with leuco crystal violet. Finally, the spectrum of the blue reaction solution looked more like the monoprotinated form of crystal violet than crystal violet itself.

On the basis of this evidence, the reaction was proposed to proceed by the hydride transfer from one of the methyl groups to the triphenylmethyl cation, as shown in equation 8.
This would account for the formation of the methane. If the cation forms a quaternary ammonium salt with one of the dimethylamino groups, the color would go away, and the triphenylmethyl group would be held close to the hydride donating methyl group. A dye produced by some subsequent oxidation would account for the different spectrum. Slight traces of acid, however, could have distorted the spectrum.

An example of the removal of hydrogen from a carbon attached to nitrogen can be found in the Sommelet reaction (43). In this reaction, aldehydes are produced from primary halides by the action of hexamethylene tetramine in water. The reaction is said to proceed by the scheme outlined below:

\[
R-\text{CH}_2-X + \text{hexamine} \rightarrow R-\text{CH}_2-\text{NH}_2 + \text{etc.}
\]

hexamine $\rightarrow 3\text{CH}_2-\text{NH}$

\[
R-\text{CH}_2-\text{NH}_2 + \text{CH}_2-\text{NH} + H_2O \rightarrow R-\text{CHO} + \text{NH}_3 + \text{CH}_3-\text{NH}_2
\]

Though it has not been definitely proven, it is possible that there is a hydride transfer between the amine and the imine. Triphenylmethyl cation should be as strong an electrophile as an imine, and hence should be able to remove a hydride ion from an amine.
The removal of a hydride ion from a carbon attached to nitrogen is analogous to the removal from carbon attached to oxygen: The latter is found in the Oppenauer oxidation (6). Unfortunately, methanol is not oxidized by this method. Another and better example is the reduction of triphenylmethyl cations by diethylether in the presence of aluminum halides (42).

As a test of the proposed reaction mechanism, an experiment was performed to study the reaction of N,N'-dimethylaniline with triphenylmethyl cation. The two compounds were mixed in dichloromethane, and also in acetonitrile. In both cases, the yellow color of the triphenylmethyl cation disappeared, and a blue color formed slowly. Two fractions were isolated from each solution. The first fraction was triphenylmethane. The second was identified by mass spectrometric methods by the Shell Oil Company. The main component of the second fraction was 4-dimethylaminotetraphenylmethane contaminated with 4-methylaminotetraphenylmethane. If a hydride ion was transferred from a methyl group to the triphenylmethyl cation, the overall result after workup would be demethylation, as shown in equation 8.

Fischer and Leukmann (44) synthesized 4-dimethylaminotetraphenylmethane from N,N'-dimethylaniline and triphenyl carbinol in concentrated sulfuric acid. They also observed coloration in the reaction solution, but overlooked its significance.

A common synthesis of the dye methyl violet, the pentamethyl analogue of crystal violet, is by air oxidation of N,N-dimethylaniline, catalyzed by copper sulfate, or phenol. Presumably, one methyl radical is removed from the amino group by oxidative cleavage,
and converted to formaldehyde. The dye then forms by condensation and subsequent oxidation. The formation of color in the reaction of N,N-dimethylaniline with triphenylmethyl cation may be an analogous reaction.

The detection of triphenylmethane and the demethylated amine from the reaction of N,N-dimethylaniline with triphenylmethyl cation is good evidence for the proposed reaction scheme in the leuco crystal violet case.
EXPERIMENTAL

Synthesis of Pyridine Diphenylborane (PDPB). Pyridine diphenylborane was prepared by the method described by Hawthorne (31) with some small modifications.

Since the borane is unstable to some extent, it was prepared in about ten-gram portions as needed. The very stable β aminoethyl diphenylborinate intermediate was prepared in large quantities, and used as starting material for the final steps.

The modifications of Hawthorne’s procedure are as follows: The easily hydrolized ethyl ester prepared from the β aminoethyl ester was purified in a one plate vacuum still instead of a spinning band column. The quantity of pyridine used was reduced to only 50 mole percent excess, and a tenfold excess of water was used for hydrolysis after the reaction was complete.

The borane was recrystallized from a minimum amount of benzene, using only petroleum ether (30-60° C) as a precipitating agent.

Yields comparable to those reported by Hawthorne were obtained.

Pyridine diphenylborane-d(PDPB-d) was synthesized by an identical procedure using lithium aluminum deuteride.

4,4′,4″-methylidinetriss[N,N-dimethylaniline] (Leuco Crystal Violet) (LCV). This compound was synthesized in small portions because of the difficulties inherent in the use of large volumes of solvent. A typical procedure is as follows:

The reaction was carried out in a 2 liter, 3 neck round bottom flask fitted with a one liter dropping funnel, a Tru-bore stirrer, and
a reflux condenser. The system was thoroughly flushed with dry nitrogen and fitted with drying tubes. The dropping funnel was then filled with a slurry of 8.5 g. of biological stain grade (99% dye content) crystal violet which had been dried at 150° C. for three hours, using 900 ml. of dry tetrahydrofuran as a solvent. One hundred ml. of dry tetrahydrofuran was transferred carefully into the reaction flask. A 1.2 g. portion of lithium aluminum hydride was weighed out and one tenth of this was added to the solvent in the reaction flask. The dye slurry was dropped in, with stirring until the solution in the flask became dark blue. A second portion of the 1.2 g. of hydride was added, whereupon the solution became clear. The process was repeated until all the dye slurry and hydride was used up.

The reaction was stirred overnight, and then most of the solvent was evaporated under reduced pressure. The resulting slurry was taken up in 1 liter of ethyl ether and washed with water until no turbidity was observed in the wash water. The solvent was then completely removed under reduced pressure, and the residue recrystallized from absolute alcohol. Yield 5 g. (66%), m.p. (Fisher Johns block uncorrected) 177-178° C, (reported 175° C).

The deuterated compound was prepared by the same procedure using lithium aluminum deuteride.

**Synthesis of Tritiated Compounds.** The usual procedure for synthesis of LCV and PDPB was modified in the following way to insure maximum inclusion of tritium. Both compounds were synthesized simultaneously to eliminate handling losses. In both cases, tritiated lithium
aluminum hydride was stirred with an excess of the second reagent for at least two hours before adding the unlabeled hydride to achieve maximum reaction. The procedure was as follows:

A solution of 9 mg. of lithium aluminum tritide (10 mc.) in 100 ml. of ether containing a trace of ordinary hydride was prepared in the 3 neck reaction vessel intended for the borane reduction. Not all of the hydride dissolved.

**LCV-t.** Half of the above tritide solution was added to the tetrahydrofuran in the reaction flask set up for LCV synthesis. Care was taken to transfer some of the undissolved solids in the tritide solution. Dye was added in the usual manner, until the solution was dark blue. About 50 ml. of extra dye solution was added and the system was allowed to stir for 2 hours. Ordinary hydride and dye was then added and the synthesis was completed by the usual procedure. A 70% yield was obtained with good tritium content (20,000 counts per minute per milligram in a liquid scintillation counter).

**PDPB-t.** The remainder of the lithium aluminum tritide solution was chilled to -70° C. and 1 ml. of pyridine was added. One half of the solution of 19 g. of ethyl diphenylborinate was added followed by stirring for 2 hours. A solution of 5 g. of lithium aluminum hydride in 500 ml. of dry ether was prepared and added to the chilled solution in the reaction flask, followed by the addition of 9 ml. of pyridine. The synthesis was completed in the usual manner. A normal yield was obtained with good inclusion of tritium (31,000 counts per minute per milligram).
Triphenylmethyl Fluoborate. This compound was synthesized by the method of Dauben, Honnen and Harmon (37).

Solvents and Reagents

Acetonitrile: Practical grade acetonitrile was distilled repeatedly from phosphorus pentoxide in a packed fractionating column until impurities as detected by vapor phase chromatography (Carbowax column) disappeared. The resulting distillate was redistilled in a simple still from phosphorus pentoxide under anhydrous conditions and stored in a dessicator.

Methanol: Brothers Chemical Co. reagent grade absolute methanol was used without further purification.

Acetic Acid: C.P. grade glacial acetic acid was used.

2,3,5,6-tetrachlorobenzoquinone: Commercial C.P. chloranil was re-crystallized once from benzene and used.

Deuterium Isotope Effect in Reaction of PDPB with Water

Apparatus. The analysis of the hydrogen-hydrogen deuteride gas mixture was performed on the apparatus pictured in figure 5. The thermal conductivity chamber was a stainless steel block fitted with two thermistor beads in separate chambers, manufactured by Victoreen Engineering Co., model no. M-182. This device was attached to the glass system by ball and socket joints.

The vacuum was produced by a mechanical pump and a silicone oil diffusion pump. The rest of the associated equipment includes a McLeod gauge (.01 to 25 microns), a Toepler pump, a variety of storage and volumetric bulbs, and sundry one and two arm mercury manometers.
A more detailed view of the thermal conductivity cell and the Toepler pump is provided on figure 6. The left chamber, denoted by the letter S, was filled with standard hydrogen gas. The absolute pressure was measured by manometer C. The only connection between chamber S and chamber U was mercury manometer D. This manometer was used when filling chamber U to the same pressure as S. After this work was completed, an oil manometer was added to achieve greater precision.

The glass tubing on the left hand side of the Toepler pump was 1 mm. capillary tubing. This was provided to reduce the volume, but was later found to be useful in the final adjustment of the pressure in chamber U.

The cell block was wrapped with Tygon tubing and covered with glass wool. Thermostatted water at 40° C. was pumped through the tubing to provide a roughly constant temperature.

A schematic diagram of the electrical measurement system for the thermal conductivity cell is presented on figure 7. Differences in thermal conductivity were measured as a change in the electrical resistance of the thermistor beads. This was accomplished by the use of a Wheatstone bridge with the beads in parallel. In operation, the bridge was used without balancing, the degree of unbalance being measured by a low resistance microammeter (Weston model No. 931). This value was then a measure of the thermal conductivity of the gas. By use of the reversing switch, S-2, the effective range of the microammeter was doubled.
The volumetric bulbs J-1 and J-2 were provided for the preparation of standard hydrogen-hydrogen deuteride mixtures. They were calibrated with mercury before being attached to the system. Their volumes were:

\[
\begin{align*}
J-1 & \quad 9.610 \text{ cc.} \\
J-2 & \quad 19.74 \text{ cc.}
\end{align*}
\]

The reaction vessel N, as seen in detail in figure 8, was constructed from a 50 cc. round bottom flask with a \( 24/40 \) ground glass joint. A side arm with a \( 14/32 \) joint was added. The dropping funnel P was provided with a stopcock on the pressure relief arm, and a condenser jacketed barrel. Manometer 0 was provided for monitoring the pressure inside the reaction vessel.

**Operating Procedure**

**Preparation of Standard Gases.** Commercial tank hydrogen was used as a standard gas. An experiment was performed with PDPB-h and ordinary water to prepare hydrogen gas under experimental conditions. This gas was compared to the tank hydrogen by thermal conductivity, and found to be identical. Pure hydrogen was stored in bulb G.

Pure hydrogen deuteride was prepared by the reaction of lithium aluminum hydride with deuterium oxide in dioxane. The reaction, slowed by cooling, was allowed to go about half way, and the evolved gas discarded for fear of contamination from protium oxide in the water. The reaction was then allowed to go to completion. This gas was stored in bulb H.
Legend to Figures 5, 6 and 8.

A. Liquid Nitrogen Cold Trap
B. Thermal Conductivity Cell
C. Monitoring Manometer
D. Balance Manometer
E, E'. Storage Bulbs
F. Toepler Pump
G. Hydrogen Storage Bulb
H. Hydrogen deuteride Storage Bulb
I. Monitoring Manometer
J-1, J-2. Volumetric Bulbs
K. McLeod Gauge
L. Liquid Nitrogen Cold Trap
M. Condenser
N. Reaction Vessel
O. Monitoring Manometer
P. Dropping Funnel
Thermal conductivity cell and vacuum line equipment used in the analysis of hydrogen deuteride gas.
Figure 6

Detail of thermal conductivity cell and Toepler pump from Figure 5.
Legend to Figure 7.

B \hspace{1cm} \text{Storage Battery (6 volts)}
S-1 \hspace{1cm} \text{On-Off Switch}
S-2 \hspace{1cm} \text{Reversing Switch}
M-1 \hspace{1cm} \text{Voltmeter (range 5 volts)}
M-2 \hspace{1cm} \text{Microammeter (range 100 microamps.)}
T_U \text{ & } T_S \hspace{1cm} \text{Thermistor Beads (unknown and standard cells)}
R-1 \hspace{1cm} \text{Variable Resistor (1500 ohms)}
R-2 \hspace{1cm} \text{Variable Resistor (200 ohms)}
R-3 \hspace{1cm} \text{Variable Resistor (10 ohms)}
R-4 \hspace{1cm} \text{Resistor (230 ohms)}
R-5 \hspace{1cm} \text{Resistor (230 ohms)}
R-6 \hspace{1cm} \text{Resistor (22 ohms)}
R-7 \hspace{1cm} \text{Resistor (10 ohms)}
R-8 \hspace{1cm} \text{Resistor (10 ohms)}
R-9 \hspace{1cm} \text{Variable Resistor (20 ohms)}
Figure 7

Schematic diagram of electrical system used in thermal conductivity analysis.
Figure 8

Detail of reaction vessel from Figure 5.
Preparation of Standard Gas Mixtures was accomplished by the use of the volumetric bulbs. Standard hydrogen deuteride, at relatively high pressure in storage bulb H, was transferred to bulb J-1 at a reduced pressure by successive expansions. Manometer I was provided for pressure measurement. Hydrogen from bulb G was transferred to J-2 by the same method. The two gases were mixed by expansion into Toepler pump F, followed by successive compressions and expansions. Bulb E' was provided for storage of the standard gas mixtures.

Analysis of an Unknown Gas and Calibration of the Cell. Optimum conditions were found to be a working pressure of 3 cm. and a cell temperature of 40° C. Standard reference hydrogen was placed in chamber S at 3 cm. and allowed to remain permanently. No change of pressure was observed over a period of many months, and the meter readings remained relatively constant.

The gas to be analyzed was transferred to chamber U using the Toepler pump. Care was taken to make the pressure in U almost equal to that in S, as measured by manometer D, when the mercury of the Toepler pump was in the capillary part of the left arm. This made the fine adjustment of the pressure easy. It was found that chamber U could be made acceptably free of the previously measured gas by pumping on it for one minute.

The cell was calibrated with samples of pure hydrogen and hydrogen deuteride as well as ten mixtures of the two. Plotting mole percent hydrogen deuteride against the meter reading (in microamperes) produced a slightly curved line which could be approximated by a 10-15° arc of a circle.
In the case of analysis of an unknown gas, a standard mixture of approximately the same concentration was prepared and measured along with pure hydrogen and hydrogen deuteride, every time an unknown gas was measured. The three points thus obtained were used for reference points in drawing the calibration curve. Though the shape of the curve remained relatively constant, meter readings varied slightly from day to day. Memory effects were minimized by making a determination in the fixed sequence: hydrogen; hydrogen deuteride; hydrogen; unknown; hydrogen; standard mixture; and finally hydrogen.

**Competitive Isotope Effect in PDPB-Water Reaction.** Regardless of the site of deuterium substitution, the procedure was the same. The reaction was made pseudo first order by using 1 or 2 millimoles of borane and 100 millimoles of water. The ratio of protinated to deuterated compound was chosen so that the resulting gas was about 50 percent hydrogen deuteride.

Dry borane was weighed into the reaction flask, a teflon covered magnetic stirring bar was added, and the flask attached to the system and the dropping funnel. While the flask was being evacuated, a solution of the water in 10 ml. of dry acetonitrile was placed in the dropping funnel, taking precautions to prevent exchange with atmospheric moisture. The dropping funnel was then sealed and the solution degassed by successive freezings and evacuations. The solution was then admitted to the reaction vessel and refrozen immediately.
The reaction was started by surrounding the reaction vessel with a thermostatted water bath at the desired temperature. The reaction was stopped by instant freezing in liquid nitrogen after about 10 percent reaction with respect to borane. The mixture required about 2 minutes to warm, and at least 15 minutes to react.

The resulting gas was pumped with the Toepler pump through liquid nitrogen trap L into bulb E. This bulb was then immersed in liquid nitrogen to remove the last traces of solvent.

The gas was analyzed as described previously.

Tritium Isotope Effect in Reaction of PDPB with Water

Apparatus. As in the deuterium case, the tritium isotope effect in the reaction of PDPB with water was determined by the method of product analysis. The radioactive product gas was analyzed by measuring the rate of charge of an ionization chamber. A Cary model 32 vibrating reed electrometer and a 250 cc. ionization chamber were used.

The reaction vessel and associated chamber filling equipment may be seen on figure 9. The reaction vessel is of simpler construction than the one for the deuterium study. This modification simplifies the experimental procedure. The reaction vessel T, like the one used in the deuterium study was made from a 50 cc. round bottom flask. The rotating side arm was attached to the neck of the flask by a 14/20 joint. The flask was connected to the system through condenser V. Manometer W was provided for monitoring the gas pressure inside the reaction vessel. The mercury
Legend to Figure 9.

T. Reaction Vessel
V. Condenser
W. Monitoring Manometer
X. Mercury Manometer
Y. Oil Manometer
Z. Ionization Chamber
Reaction vessel and ionization chamber filling line for tritium isotope effect experiments.

Figure 9
manometer X and oil manometer Y were used to measure the pressure of the radioactive gas in the ionization chamber Z.

**Competitive Isotope Effect Measurement Procedure.** PDPB and water were used in the mole ratio of 1 to 100 as in the case of deuterium. About 200 mg. of PDPB was weighed into the reaction flask. A magnetic stirring bar was added, and the flask attached to the system. Ten ml. of dry acetonitrile was added with a syringe. The side arm which had been previously filled with about 900 mg. of water was quickly attached. The water, and acetonitrile were degassed carefully, and mixed by rotating the side arm 180 degrees. The reaction solution was immediately frozen and the reaction vessel again evacuated.

The reaction was started, monitored and stopped in the same way as in the deuterium case. The vessel was immersed in liquid nitrogen for a few minutes, then the coolant was removed so that the tubing could warm, but the reaction mixture was not allowed to melt. The vessel was then reimmersed in nitrogen. This procedure was designed to insure complete solvent condensation.

After chilling the reaction vessel for five minutes, the gas was allowed to expand into the evacuated chamber. The stopcock to the reaction vessel was again closed and the cold gas allowed to warm for 5 minutes to obtain a stable pressure. The oil manometer, which had a long response time, was closed off and the chamber filled to 77 cm. with tank hydrogen gas. The pressure was measured immediately on the mercury manometer and after fifteen minutes on the oil manometer. The initial activity was determined by allowing the reaction to go to completion with respect to the labeled compound.
A small sample of tritiated water was allowed to react completely with a concentrated solution of lithium aluminum hydride in tetrahydrofuran. Samples of the gas produced were measured at various pressures. A graph was prepared by plotting rate of charge versus pressure, and a straight line was drawn through the points. The initial activity for any pressure of gas in the chamber was then easily read from the graph. A similar procedure was used for the case of the tritiated borane, using excess water and acetonitrile as a solvent to generate the tritium labeled hydrogen.

Experiments with Leuco Crystal Violet

Rate of Reaction of Leuco Crystal Violet with Triphenylmethyl Fluoborate. Crude preliminary measurements of the rate of reaction of LCV H & D with triphenylmethyl fluoborate were made by following spectrosopically the change in absorption at 590 m\(\mu\) for two hours. Ten ml. aliquots of an acetonitrile solution, 2 x 10\(^{-5}\) molar in LCV-h and 2 x 10\(^{-5}\) molar in triphenylmethyl fluoborate, were mixed and quickly injected into a 1 cm. silica spectrophotometer cell fitted with a serum stopper. A solution of LCV-d of identical concentration was used with the same fluoborate solution to obtain the deuterium rate constant. The deuterium rate was slightly faster than the protium rate.

Competitive Isotope Effects. A mixture of LCV-h and LCV-d was prepared in the ratio of 1 to 10, H to D. This mixture was dissolved in dry acetonitrile and about mole percent of triphenylmethyl fluoborate was added. After an appropriate amount of time had passed, excess water was added and the triphenylmethane was extracted with
petroleum ether. The ethereal solution was washed with water, dried, and evaporated to dryness. The residue was purified by chromatography over activity I alumina with 30-60°C petroleum ether. A quantitative yield of triphenylmethane was obtained.

The methane was analyzed for deuterium by spectroscopic methods. No signs of absorption were found in the 4.7 micron carbon-deuterium stretching vibration region.

Reaction of Triphenylmethyl Fluoroborate with N,N-dimethylaniline. Two millimoles of N,N-dimethylaniline were combined with an equal amount of triphenylmethyl fluoroborate in 100 ml. of acetonitrile and also 100 ml. of dichloromethane. A dark blue color formed in the solution as the reaction proceeded. After several hours, the solvent was evaporated leaving a colored residue.

The residue was dissolved in petroleum ether and purified by chromatography over alumina. Two main compounds were found. The first was triphenylmethane, identified by its infrared spectrum. The identity of the second compound was established by mass spectrographic analysis by the Shell Oil Company, Deer Park, Texas. They found the compound to be 4-N,N-dimethylaminotetraphenylmethane. They found also a very interesting contaminant, namely, the monomethylamino compound.

The Rates of Reaction of Leuco Crystal Violet H & D with Chloranil. The rates of reaction were measured spectroscopically by following the change of absorption with time of the 590 m/ peak of crystal violet.
Since chloranil catalyzes the air oxidation of the leuco compound, all solutions were carefully de-oxygenated by sweeping with dry nitrogen gas. As a further precaution, the rate constants were determined by measuring the initial rates of reaction.

To help minimize error, the measurements at all temperatures were made with the same three stock solutions. Two of the solutions were $4 \times 10^{-4}$ molar in LCV, one of the protinated and the other of the deuterated compound. The third solution, which was used with either leuco solution was $4 \times 10^{-4}$ molar in chloranil and $4 \times 10^{-1}$ molar in acetic acid. Methanol was the solvent in all cases.

The measurements were made as follows: A 25 ml. aliquot of the LCV solution was combined with 50 ml. of methanol in a 125 ml. Erlenmeyer flask with a ground glass stopper. The solution was swept with nitrogen for 5 minutes. The flask was stoppered and placed in a thermostat. The reaction was started by the addition of 25 ml. of the chloranil solution. A portion of the solution was transferred as rapidly as possible to a 1 cm. silica spectrophotometer cell with a ground glass stopper. The cell was quickly placed in the spectrophotometer and the rate measured. A Cary model 14 recording spectrophotometer equipped with a thermostatted cell compartment was used. The transfer required about one minute, while the initial rate in every case remained linear for at least fifteen minutes.
SUMMARY

The deuterium and tritium isotope effects in the reaction of pyridine diphenylborane with water were measured for the cases of isotopic substitution on the borane and in the water. The temperature coefficients for these isotope effects were determined over the temperature range of 0 to 50°C. A normal large isotope effect, with the expected temperature dependence, was observed in the case of isotopic substitution in the water. A small, temperature independent isotope effect was observed in the case of isotopic substitution on the borane. A model of the transition state was proposed on the basis of these data. The transition state model is non-linear with respect to the three atom system; the hydrogen attached to oxygen in the water, the hydrogen attached to the boron atom and the boron atom. The imaginary vibration of the transition state is related to an oxygen-hydrogen stretching vibration. The isotope effect in the labeled borane case is due to motion of the hydrogen atom, attached to the boron atom, with respect to the center of gravity of the activated complex.

The deuterium isotope effect in the reaction of leuco crystal violet with chloranil was measured at ten different temperatures between 0 and 45°C. The observed isotope effect was unusually high, while the sizes of the Arrhenius parameters for the isotope effect were also abnormal. The activation energy difference (ΔEa) was too high and the pre-exponential term ratio (AH/AH) was below the theoretical limit. These data were interpreted to be evidence for tunnelling.
The reaction of leuco crystal violet with triphenylmethyl cations was studied. Deuterium labeling was used to demonstrate that there is no hydride transfer from the central carbon atom of the leuco compound to the triphenylmethyl cation. The removal of a hydride ion from a methyl group was proposed as an alternate mechanism and substantiated by studying the reaction of a model compound (N,N-dimethylaniline) with triphenylmethyl cation.
BIBLIOGRAPHY


(5) W.E. Doering and T.C. Aschner, ibid., 75, 393 (1953).


(7) A.L. Wilds, ibid., Vol. 2, Ch. 5.


(22) L. Kaplan and K.E. Wilzbach, ibid., 74, 6152 (1952).


(24) M.F. Hawthorne and E.S. Lewis, ibid., 80, 4296 (1958).


(31) M.F. Hawthorne, ibid., 80, 4293 (1958).


(34) A. Farkas and L. Farkas, ibid., A144, 467 (1934).


(36) N.R. Trenner, ibid., 5, 382 (1931).


(39) E.A. Guggenheim, Phil. Mag., 2, 538 (1926).


