THE MAGNITUDE OF THE PRIMARY KINETIC ISOTOPE EFFECT FOR COMPOUNDS OF HYDROGEN AND DEUTERIUM

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I. INTRODUCTION

The "deuterium isotope effect" has become one of the most important of the tools which physical-organic chemists employ in the elucidation of the mechanisms of chemical reactions. The theory of the magnitude of these effects is well advanced. But a partial failure of communications between physical chemists and organic chemists has led to a situation where a serious theoretical misunderstanding, or perhaps one should say a dilemma, has plagued the interpretation of the experimental data.

In general, when a bond to hydrogen or deuterium is broken in the rate-controlling step of a reaction, the rate constant, k_H, for the reaction of the hydrogen compound exceeds the constant, k_D, for the same reaction of the corresponding deuterium compound. Baldly stated—and oversimplified—the dilemma is this: Eyring's theory of reaction rates and the crudest first-order approximation to the theory of isotope effects apparently lead to the prediction, for linear transition states, of a ratio k_H/k_D in excess of 6, whereas many of the experimental results which have been obtained show that this ratio of rate constants may be only slightly greater than unity. The explanation conventionally offered for these low values of the kinetic isotope effect will here be shown to conflict with the absolute rate theory.

Excellent reviews (19, 32, 46) have discussed the application of the "deuterium isotope effect" to organic chemistry, have tabulated (9, 46) much of the available data, and have shown how to justify a large k_H/k_D ratio in terms of the vibrational zero-point energy of the molecules involved. The explanation for both small and large isotope effects is implicit in the complete equations for the kinetic isotope effect as originally published by Bigeleisen and Mayer (6), and has been carefully considered in recent papers of Bigeleisen (7) and of H. S. Johnston (22, 25). This review examines the theoretical dilemma of the organic chemist and offers a simplified solution based on the work of Johnston.

II. THE FIRST APPROXIMATION

Before the theory of small deuterium isotope effects is considered, the conventional first approximation is presented in Section II for the calculation of the ratio k_H/k_D. A few pertinent experimental data are reviewed in Section III. Some special cases, and some more general ones, are discussed in Section IV. The "dilemma" is set forth at the end of that section, and the qualitative and quantitative aspects of the theory in Sections V and VI. The reader already familiar with the field can economically skip directly to these last two sections.

For brevity, the theory is discussed in terms of carbon-hydrogen and carbon-deuterium bonds, but it will of course apply to bonds with other elements than carbon and by a simple extension to compounds of tritium.

Eyring's theory for reaction rates (18) assumes that the reactants are in equilibrium with an "activated complex" or "transition state," and that this complex subsequently decomposes, in the rate-controlling step of the overall process, into products. The transition state is distinguished from ordinary chemical molecules in that one of its vibrations has been replaced by an internal translation.

Consider a reaction which involves the transfer of a hydrogen atom[1] from a carbon-hydrogen bond in a molecule A—H to another molecule, B. As a first approximation, one of the degrees of freedom in A—H may be considered as a carbon-hydrogen stretching vibration. This vibration becomes translational motion, as the hydrogen atom moves from A to B in the transition state.

The major portion of the kinetic isotope effect arises from contributions to the activation energy from changes in zero-point energy which occur when the reactants are converted to an activated complex. The stretching vibration of A—H is quantized with a frequency ν_H and an associated zero-point vibration energy of $\frac{1}{2}h\nu_H$. Assuming a carbon-hydrogen stretching frequency of 2900 A., the zero-point energy is about 4.15 kcal./mole. The corresponding carbon-deuterium frequency, ν_D, is about 2100 A. and the zero-point energy about 3.0 kcal./mole. The difference in zero-point energy, $\frac{1}{2}h\nu_H - \frac{1}{2}h\nu_D \simeq 1.15$ kcal./mole. If this stretching vibration becomes, in the activated complex, a degree of translational freedom, the vibration is lost. Therefore $\frac{1}{2}h\nu_H^* - \frac{1}{2}h\nu_D^* = 0$, where ν_H^* and ν_D^* represent the (zero) frequencies for the stretching vibration of the C—H and C—D bonds in the activated complex. The net difference in activation energy for the reaction of AH and AD is then just 1.15 kcal./mole; at 300°K. this corresponds to a factor of 7 in rate. This simplified theory cannot easily account for smaller ratios of k_H/k_D in reactions which proceed via a linear transition state.

III. THE EXPERIMENTAL FINDINGS

Many reactions show deuterium isotope effects near 300°K. of 6 or more. For example, the ratio k_H/k_D for the bromination of acetone (36) is 7.7, for the bromination of nitromethane (35) is 6.5, and for the bromination of nitroethane (49) is 10. The ratio for the oxidation of isopropyl alcohol with chromic acid (44) varies with experimental conditions from 6.9 to 8.4. The ratio for the oxidation by permanganate of benzaldehyde in neutral aqueous solution (45) is 7, for the oxidation by permanganate of formate ion (48) is 7.4, and for the oxidation of desoxybenzoin by selenious acid (12) is about 6; the chromic acid oxidation of phenyl-*tert*-butylcarbinol in 86.5 per cent aqueous acetic acid gives a kinetic isotope effect (20) for deuterium of 14, and the permanganate oxidation of phenyltrifluoromethylcarbinol (40) in alkali one of 16. The attack of methyl radicals from diacetyl peroxide on toluene shows an isotope effect (15), measured from the methane produced, of nearly 9. The reaction of the lithium salt of cyclohexylamine with α-deuteroethylbenzene shows an isotope effect (41) for deuterium of 12 ± 3, and the bromination of ethyl cyclopentane-2-carboxylate, catalyzed by fluoride ion (24) at −20°C., a value for k_H/k_D of 10. (The large value of this last isotope effect has been cited as evidence for "tunnelling" (4, 24).) These reactions with large isotope effects are of varied chemical types and include ionization reactions, oxidation-reduction reactions with several different reagents, and a free-radical reaction.

The oxidation of ethanol to acetaldehyde with bromine (26) shows an intermediate isotope effect of 4; the cyclization (11) of the *N*-chloro derivative of methylamylamine-4-*d* by a free-radical pathway shows a k_H/k_D of 3.5. The elimination of trimethylamine from *n*-butyltrimethylammonium ion (39) gives a similar intermediate isotope effect, and the elimination reactions (37) with alkali from $C_6H_5CD_2CH_2X$ show ratios of k_H/k_D which vary from 8.0 (for X = tosyl in *tert*-butyl alcohol at 30°C.) to 3.0 (for X = $\overset{+}{N}(CH_3)_3$ in ethanol at 50°C.). Isotope effects for many free-radical reactions in the gas phase have been listed by Trotman-Dickenson (43); in particular, at 182°C., the reaction of $CH_3\cdot$ with acetone proceeds 2.5 times as rapidly as does the reaction between $CD_3\cdot$ and hexadeuteroacetone, and the reaction of $CH_3\cdot$ is 3 times as fast with H_2 as with D_2. Provided that the major factor in the isotopic rate effect arises from the contributions of zero-point energy to the activation energy, these rate factors at 182°C. correspond to ratios of 4 to 5 at 25°C.

On the other hand, many kinetic isotope effects are considerably smaller than those cited above. The ratio for the Cannizzaro reaction (45) is only 1.8, that for the oxidation of isopropyl alcohol by bromine (42) only 2.8, and that for the oxidation of isopropyl alcohol by the triphenylmethyl cation (2) is 1.8–2.6. Furthermore, the reaction of water with the diphenylborane-pyridine complex (21) gives a kinetic isotope effect of 1.5 and the acid-catalyzed rearrangement of methylallyl alcohol to isobutyraldehyde (1) a ratio k_H/k_D of 1.2–1.5. The rate of adsorption for hydrogen on platinum black exceeds the rate for deuterium by a factor (30) of about 1.5 at 18°C. The ratio k_H/k_D for the neutralization of organometallic compounds with water or alcohol is near unity or in some cases slightly less than unity (33). Not all of the examples cited above are mechanistically clear; other examples of low isotope effects are even less useful for the purpose of this exposition, for there is reason to question whether a bond to hydrogen is broken in the rate-controlling step. In this category, the ratio k_H/k_D for the reaction of triphenylsilane (27) with water is 1.15, and the formation of fluorenone from ring-labeled *o*-phenylbenzoic acid (13) shows an isotope effect of 1.4 in sulfuric acid and of 3 in hydrofluoric acid. The formation of fluorenone by

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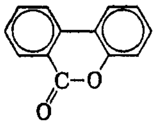
[1] No distinction is here intended between H^+, $H\cdot$, and H^-; the term "hydrogen atom" is used for all. A and B are atoms or groups of atoms, but for the purpose of this review they have no structure.

the oxidation of *o*-phenylbenzaldehyde with di-*tert*-butyl peroxide (14) gives a ratio, k_H/k_D, of 1.4, the formation of fluorenone by the diazotization of *o*-phenylbenzylamine (14) a ratio of 1.1, and the formation of the lactone



by the thermal decomposition of the peroxide of *o*-phenylbenzoic acid (14) a ratio of 1.3. In the benzoylation of aniline and of *N*,*N*-dideuteroaniline (16), the ratio k_H/k_D of 0.86 is probably a secondary isotope effect.

Among the most important examples, for the purposes of the present disscusion, are those of Wiberg and Slaugh (47), who studied the free-radical chlorination and bromination of deuterotoluenes. Their work amplified earlier contributions to the subject (8). They found that the k_H/k_D ratio for the removal of a hydrogen atom from the methyl group of toluene by bromine atoms at 77°C. is 4.6, by chlorine atoms (under slightly different conditions) is 1.3, and by $SO_2Cl\cdot$ radicals is 1.4. In free-radical brominations with *N*-bromosuccinimide, k_H/k_D was 4.9 for toluene, 2.7 for ethylbenzene, and 1.8 for cumene.

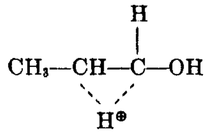
The reactions discussed above are not concerned with solvent isotope effects (6, 46) nor (in general) with secondary isotope effects (38). No attempt has been made here to give an exhaustive list of experimental results, or even to supplement earlier reviews (9, 19, 46). Rather a few examples have been cited to show that the kinetic isotope effect for deuterium varies in magnitude from 1 to 16 (or more) and that both polar and free-radical processes may show isotope effects of different size.

IV. EXPLANATIONS FOR LOW k_H/k_D RATIOS

A. *Some special cases*

In certain special cases, the low ratios of k_H/k_D may be adequately explained. These are irrelevant to the main argument in this article and are briefly discussed only for the sake of completeness. First of all, the kinetic isotope effect obtains only when a bond to a hydrogen atom is broken (or formed) in the rate-controlling step of a reaction. Melander (31) could account for the absence of an isotope effect in the nitration of toluene by postulating that the reaction occurs by way of a cyclohexadiene intermediate. Provided that the rate-controlling step in nitration is the addition of NO_2^+ to the aromatic system to produce this intermediate, no isotope effect should be observed, since a carbon-hydrogen bond is not broken in the rate-controlling step of the process. This explanation has received strong substantiation in Zollinger's work on the aromatic coupling reaction (50). In the presence of bases which can easily remove a hydrogen ion, the rate-controlling step of this reaction is the addition of the diazonium cation to the aromatic system, and the reaction, by analogy with nitration, shows almost no kinetic isotope effect. However, when little base is present, the removal of the proton is no longer fast relative to the condensation process, but becomes rate-controlling; in these circumstances, an isotope effect as large as a factor of 6.55 has been observed. Further, this hypothesis is consistent with much other data concerning the mechanism of aromatic substitution (10, 29). Although this explanation is valid where used, many of the small isotope effects cited in Section III do not fall within this special class.

A broader category of reactions where the isotope effect will be small contains those which proceed internally, by way of "triangular" transition states (21, 28). In these reactions, the bond in A—H is not stretched to its breaking point; rather it is bent so that the hydrogen atom may become attached to another part of the molecule, A. An excellent example is that of Bartlett and Anderson (1), where the transition state probably has the geometry shown below. E. S. Lewis



and his collaborators have pointed out (21, 28) that in such reactions, it may more nearly be said that a bending rather than a stretching is converted to translational motion. Since vibration frequencies for bending are much lower than those for stretching, the zero-point energy lost in the transition state (and hence the contribution of zero-point energy to the activation energy) will be small. Some of the examples cited in Section III fall in this category, but of course many do not; in particular, the attacks of bromine and chlorine atoms on toluene (47) probably occur by way of linear transition states.

B. *General theory*

A general explanation for a spectrum of values of the ratio k_H/k_D is that the theory offered in Section II is oversimplified to the point of absurdity. The "back-of-an-envelope" calculation is concerned with the zero-point energy of only one vibration; it does not take into account the entire partition function of the reactants or of the activated complex; it does not take into account the rate of "translation" across the barrier; it does not take into account the possibility of isotope effects on the "transmission coefficient"; and it does not take into account the "tunnelling" of hydrogen through the barrier.

The assumption was made that the only vibration of importance is the stretching of the bond A—H. This motion is not even a proper vibration, since the "normal vibrations" of the molecule will include motions of all the atoms, and not a vibration of one bond. Even if the normal vibrations are approximated by a set of bond vibrations, the bending as well as the stretching modes for the C—H bond should be taken into account. Furthermore, in a polymolecular reaction, new vibration frequencies are introduced into the transition state. Two nonlinear molecules, which have n and m atoms, respectively, have altogether 6 degrees of rotational freedom, 6 degrees of translational freedom, and $3n + 3m - 12$ degrees of vibration. When combined with an activated complex, they have only 3 degrees of rotational freedom and 4 of translation, but $3n + 3m - 7$ vibrations; 5 new vibrations (or internal rotations) have been introduced into the transition state. In a proper treatment, all of these should be taken into account.

More precisely,

$$\frac{k_H}{k_D} = \frac{Q_D Q_H^{\ddagger}}{Q_H Q_D^{\ddagger}} \tag{1}$$

where the Q's and $Q^{\ddagger}$'s are the partition functions for the molecules AH and DH and for the activated complexes AHB and ADB. Moreover, for the computation of isotope effects involving hydrogen, deuterium, and tritium, important tunnelling effects (3, 7, 25) must also be determined. In special cases the partition functions have been evaluated, and moderately complete calculations of isotope effects have been performed in which all or most of these complexities have been taken into account; the reactions of hydrogen atoms with hydrogen molecules (17), of methyl radicals with hydrogen molecules (34), and of chlorine atoms with hydrogen molecules (5) have been reviewed by Bigeleisen and Wolfsberg (7), and the reaction of methyl radicals with ethane by Johnston (25). Although these calculations are important contributions to physical chemistry, they do not offer a qualitative or pictorial understanding of variations in the magnitudes of isotope effects.

C. An earlier explanation

Organic chemists have had an ingenious explanation for the low values of k_H/k_D, which runs something as follows. The bond in A—H may be only partially broken in the transition state. Then it will retain some strength and maintain a definite vibration frequency, so that the zero-point energy for the hydrogen compound in the transition state will exceed that for the corresponding deuterium compound. The contribution of the zero-point energy is a double difference:

$$\begin{aligned}\Delta\text{ZPE} = {} & \text{ZPE (reactants, hydrogen)} - \\ & \text{ZPE (reactants, deuterium)} - \\ & [\text{ZPE (activated complex, hydrogen)} - \\ & \text{ZPE(activated complex, deuterium)}]\end{aligned}$$

Consequently, it has been argued that in the case above, ΔZPE is less than it would have been if the bond between A and H had been completely broken in the activated complex. The kinetic isotope effect need not, therefore, be large.

But this argument, as stated, is in direct conflict with the theory of absolute rates (18). The derivation of Eyring's equation requires that the vibration in question become translation, and no compromise with this point is possible which will preserve the essential outlines of the transition-state theory. The "calculation" of Section II assumes Eyring's formulation and the explanation above denies it; both ideas cannot be incorporated in the same treatment. The purpose of the present article is to point a way, short of a complete solution of every problem in terms of partition functions, to a reconciliation of the absolute rate theory with low kinetic isotope effects. The theory, outlined in Sections V and VI, is a simplified version of that of H. S. Johnston; his publications, and those of Bigeleisen, go far beyond these considerations. A less mathematical but essentially equivalent treatment has been offered by Melander (32).

V. THE SECOND APPROXIMATION

Consider the reaction

$$\text{AH} + \text{B} \rightleftarrows \text{A}\cdots\text{H}\cdots\text{B} \rightarrow \text{A} + \text{HB} \tag{2}$$

where A· · ·H· · ·B is a linear transition state restricted to the x-axis. This assumption amounts to ignoring bending vibrations; further, A and B are regarded as structureless groups. (Here and subsequently, the equations will generally be written for hydrogen, and parallel equations for deuterium will be assumed.) If A· · ·H· · ·B were a linear molecule (rather than an activated complex), it would have two stretching vibrations, a symmetrical and an antisymmetrical one.

$$\underset{\text{Symmetric}}{\leftarrow\text{A}\quad\text{H}\quad\text{B}\rightarrow} \qquad \underset{\text{Antisymmetric}}{\leftarrow\text{A}\quad\text{H}\rightarrow\ \leftarrow\text{B}}$$

Neither of these corresponds to the stretching vibration of A—H or B—H. If A· · ·H· · ·B is a transition state, one of these vibrations becomes translation, as required by Eyring's theory. But the other vibration is retained. Now, if this vibration is truly symmetrical, A and B move in opposite directions, and the hydrogen atom remains motionless. The vibration frequency is therefore independent of whether hydrogen or deuterium is present in the complex, and the formation of the transition state leads to a change in zero-point energy of 1.15 kcal./mole, as suggested in Section II. However, when the strengths of the partial bonds of H to A and to B are not equal, the so-called "symmetrical" vibration will no longer consist merely of the motion of A and B; the hydrogen atom will move, too. (This is easily seen, for example, where H is bonded much more tightly to A than to B.) Therefore the vibration frequency must depend to some extent on the mass of the central atom, i.e., on whether it is hydrogen or deuterium. The "symmetric" vibration will have a zero-point energy for hydrogen different from that for deuterium, and this difference will decrease the contribution of zero-point energy to the activation energies for the reactions of AH and AD. Consequently, the isotope effect will be small. At first, this may sound something like the organic chemists' notion that the isotope effect will be lowered when the bond is only partially broken in the transition state. But more closely analyzed, the ideas are quite different. The vibration in A—H corresponds neither to the real nor to the imaginary vibration of A—H—B. The bond which is present in the transition state, and which contributes to its zero-point energy, is one which does not exist in either the reactants or the products; it is a vibration peculiar to the activated complex. The distinction is shown schematically in figure 1.

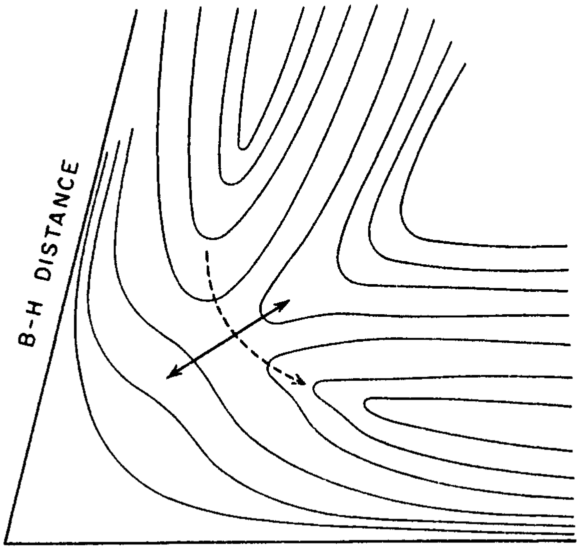
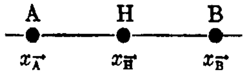


FIG. 1. Schematic representation of a contour map for the energy of a transition state, A—H—B. The double-headed arrow shows the "symmetric" vibration, the dotted arrow the direction for reaction.

VI. A SIMPLIFIED MATHEMATICAL TREATMENT

A. The exponential term

These ideas are much better expressed quantitatively than qualitatively. Let us place the groups A, H, and B in one-dimensional space, and describe by x_A, x_H, and x_B the *displacements* of these atoms from their equilibrium positions in a molecule which later will be equated to the transition state.



Let the force constant for the stretching of the bond between A and H be called $\mathbf{k}_1$, and that for the stretching of the bond between H and B be called $\mathbf{k}_2$. In contrast to the situation in simple molecules, where similar bond stretchings may be nearly independent, the motions in the activated complex are necessarily strongly coupled; the coupling constant is called β. Therefore the potential energy, V, for the molecule AHB is given by equation 3.

$$V = \tfrac{1}{2}\mathbf{k}_1(x_H - x_A)^2 + \tfrac{1}{2}\mathbf{k}_2(x_B - x_H)^2 + \beta(x_H - x_A)(x_B - x_H) \quad (3)$$

One can calculate the force on A, H, and B as the negative partial derivatives of the potential with respect to the displacement coördinates:

$$\frac{\delta V}{\delta x_A} = -F_A = -\mathbf{k}_1(x_H - x_A) - \beta x_B + \beta x_H \quad (4)$$

$$\frac{\delta V}{\delta x_H} = -F_H = \mathbf{k}_1(x_H - x_A) - \mathbf{k}_2(x_B - x_H) + \beta x_B - 2\beta x_H + \beta x_A \quad (5)$$

$$\frac{\delta V}{\delta x_B} = -F_B = \mathbf{k}_2(x_B - x_H) + \beta x_H - \beta x_A \quad (6)$$

Now

$$F = m\mathbf{a} = m\,\frac{\mathrm{d}^2x}{\mathrm{d}t^2} \quad (7)$$

where m is the mass of any atom, $\mathbf{a}$ is acceleration, and t is time. In order to find the acceleration, it will be assumed that the particles A, H, and B move in normal vibrations with harmonic motion, or

$$x = L\sin 2\pi\nu t + N\cos 2\pi\nu t \quad (8)$$

so that

$$\mathrm{d}^2x/\mathrm{d}t^2 = -\lambda x,\ \text{where } \lambda = 4\pi^2\nu^2 \quad (9)$$

Combining equations 4, 5, and 6 with 7 and 9,

$$(m_A\lambda - \mathbf{k}_1)x_A + (\mathbf{k}_1 - \beta)x_H + \beta x_B = 0 \quad (10)$$

$$(\mathbf{k}_1 - \beta)x_A + (m_H\lambda - \mathbf{k}_1 - \mathbf{k}_2 + 2\beta)x_H + (\mathbf{k}_2 - \beta)x_B = 0 \quad (11)$$

$$\beta x_A + (\mathbf{k}_2 - \beta)x_H + (m_B\lambda - \mathbf{k}_2)x_B = 0 \quad (12)$$

These constitute three homogeneous linear equations in the three unknowns x_A, x_H, and x_B, and they can be simultaneously valid if, and only if, the determinant of equation 13 is zero.

$$\begin{vmatrix} m_A\lambda - \mathbf{k}_1 & \mathbf{k}_1 - \beta & \beta \\ \mathbf{k}_1 - \beta & m_H\lambda - \mathbf{k}_1 - \mathbf{k}_2 + 2\beta & \mathbf{k}_2 - \beta \\ \beta & \mathbf{k}_2 - \beta & m_B\lambda - \mathbf{k}_2 \end{vmatrix} = 0 \quad (13)$$

Equation 13 can be expanded to equation 14:

$$m_Am_Hm_B\lambda^3 - (m_Am_H\mathbf{k}_2 + m_Am_B\mathbf{k}_1 + m_Am_B\mathbf{k}_2 + m_Hm_B\mathbf{k}_1 - 2m_Am_B\beta)\lambda^2 + (m_A + m_H + m_B)(\mathbf{k}_1\mathbf{k}_2 - \beta^2)\lambda = 0 \quad (14)$$

Equation 14 contains no constant term, so that one factor of the equation is

$$\lambda = 0 \tag{15}$$

This solution is the familiar one for similar exercises (23) and corresponds to the translation of the "molecule" AHB in the one-dimensional space along the x-axis. If AHB represents an activated complex rather than a molecule, absolute rate theory demands that a second frequency be zero or imaginary, i.e., one of the vibrations must become translation. A second value of λ can be set equal to zero if the last term in equation 14 vanishes, i.e.,

$$\mathbf{k}_1\mathbf{k}_2 - \beta^2 = 0 \tag{16}$$

In equation 16 $\mathbf{k}_1\mathbf{k}_2 - \beta^2$ is set equal to zero. If the coupling constant, β, between the stretching of AH and of HB (see equation 3) is small, $\mathbf{k}_1\mathbf{k}_2 - \beta^2$ is positive, and both of the frequencies calculated from equation 14′ are real (when λ is factored from equation 14, the resulting quadratic equation may be called 14′). Under these conditions, AHB corresponds to a molecule and not to an activated complex, since any displacement of the atoms is met by a restoring force, and the molecule merely vibrates. However, when (as in equation 16) the quantity $\mathbf{k}_1\mathbf{k}_2 - \beta^2$ vanishes, one of the values of λ in equation 14′ becomes zero, and therefore (since by definition $\lambda = 4\pi^2\nu^2$) one of the frequencies in AHB becomes zero, i.e., a vibration becomes translation. But if the coupling constant, β, is very large, $\mathbf{k}_1\mathbf{k}_2 - \beta^2$ becomes negative rather than zero. Inspection shows that under these conditions, one of the quadratic roots for λ in equation 14′ is necessarily negative. Since $\lambda = 4\pi^2\nu^2$, the negative value of λ corresponds to an imaginary frequency, ν^*. The imaginary frequency represents translational motion.

The differential equation for simple harmonic motion corresponds to the oscillation of a particle in a parabolic potential well and requires a positive force constant and a real vibrational frequency. A transition state, however, corresponds to the situation where a particle moves under the influence of a potential function with a maximum rather than a minimum at the position where the complex "exists." There is no restoring force to hold the complex together; on the contrary, the force constant for the motion is negative, and the potential function is concave downward, not upward. A negative force constant will yield an imaginary vibrational frequency. The more sophisticated theory of isotope effects assumes that $\mathbf{k}_1\mathbf{k}_2 - \beta^2$ is negative, and the frequency ν^* imaginary rather than zero. The simpler treatment here presented nevertheless goes a long way toward illustrating the essential ideas involved in the more elaborate work.

Equation 16 states that the coupling constant in the activated complex is the square root of the product of the two other force constants. When equation 16 is valid, equation 14 reduces to equation 17:

$$\lambda = 4\pi^2\nu^{\ddagger 2} = \frac{\mathbf{k}_1}{m_A} + \frac{\mathbf{k}_2}{m_B} + \frac{\mathbf{k}_1 + \mathbf{k}_2 - 2\sqrt{\mathbf{k}_1\mathbf{k}_2}}{m_H} \tag{17}$$

Equation 17 shows the influence of isotopic mass upon the frequency (and hence upon the zero-point energy) of the "symmetric" vibration in the transition state.

When $\mathbf{k}_1 = \mathbf{k}_2 = \mathbf{k}$, equation 17 becomes:

$$\lambda = 4\pi^2\nu^{\ddagger 2} = \mathbf{k}\left(\frac{1}{m_A} + \frac{1}{m_B}\right) \tag{18}$$

The mass of the hydrogen atom does not enter this expression; hence the frequency is unchanged on isotopic substitution. At this level of approximation, the bond lengths for the transition state do not enter the calculation; the zero-point energy for the two isotopic activated complexes will be the same provided that the force constants, $\mathbf{k}_1$ and $\mathbf{k}_2$, are equal.

But suppose the force constants are not equal. If, for example, $\mathbf{k}_1 \gg \mathbf{k}_2$, equation 17 reduces to equation 19:

$$\lambda = 4\pi^2\nu^{\ddagger 2} = \mathbf{k}_1\left(\frac{1}{m_A} + \frac{1}{m_H}\right) \tag{19}$$

Here the mass of the hydrogen (or deuterium) atom enters into the expression for the frequency of the "symmetrical" vibration; furthermore, since m_A and m_B are presumably large compared to the mass of either a hydrogen or a deuterium atom, the frequencies $\nu_H^\ddagger$ and $\nu_D^\ddagger$ will be almost in inverse ratio to the square roots of the masses of the isotopes. For example, if $m_A = 12$, $m_B = 16$, and $\mathbf{k}_1 = 10\mathbf{k}_2$, then the frequencies $\nu_H^\ddagger$ and $\nu_D^\ddagger$ will lie in the ratio of 1.32:1. The situation is similar if $\mathbf{k}_2 \gg \mathbf{k}_1$. If the magnitude of $\nu_H^\ddagger$ is large, the difference between the zero-point energy of A—H—B and A—D—B may be as large as that between AH and AD, and the contribution of zero-point energy to the activation energy may vanish.

B. The preëxponential term

For the reaction of AH with B, through the linear activated complex A—H—B, equation 1 can be expanded to equation 20.

$$\frac{\mathrm{k}_H}{\mathrm{k}_D} = \frac{\nu_H^*}{\nu_D^*}\,\frac{\nu_{AD}}{\nu_{AH}}\,\frac{\nu_H^\ddagger}{\nu_D^\ddagger}\,e^{\Delta \mathrm{ZPE}/RT} \tag{20}$$

Here ν_H^* and ν_D^* are the (zero) frequencies of the vibrations of the transition state which become translational motion, ν_{AH} and ν_{AD} are the stretching frequencies of the one-dimensional molecules AH and AD, and $\nu_H^\ddagger$ and $\nu_D^\ddagger$ are the frequencies of the real vibration in the transition states of AHB and ADB. The derivation of this equation is indicated in the Appendix.

In order to evaluate the preëxponential factor in equation 20, the indicated frequencies must be found, and in particular the quotient of null frequencies, $\nu^*_{\mathrm{H}}/\nu^*_{\mathrm{D}}$, must be estimated by solving equation 14 as a quadratic in λ, obtaining the ratio of the frequencies for the antisymmetric vibrations of AHB and ADB, and then allowing $\mathbf{k}_1\mathbf{k}_2 - \beta^2$ to approach zero, so that the frequencies ν^*_{H} and ν^*_{D} each approach zero.

When λ is factored from equation 14, the residue is a standard quadratic equation, of the form

$$a\lambda^2 + b\lambda + c = 0 \tag{21}$$

where $c = (m_{\mathrm{A}} + m_{\mathrm{H}} + m_{\mathrm{B}})(\mathbf{k}_1\mathbf{k}_2 - \beta^2)$. When c is small (in the present example it will be allowed to approach zero), the solutions to equation 21 are $\lambda = -b/a$ and $\lambda^* = -c/b$. The frequency corresponding to λ has already been found (equation 17). Then

$$\lambda^* = \frac{(m_{\mathrm{A}} + m_{\mathrm{H}} + m_{\mathrm{B}})(\mathbf{k}_1\mathbf{k}_2 - \beta^2)}{m_{\mathrm{A}}m_{\mathrm{H}}\mathbf{k}_2 + m_{\mathrm{A}}m_{\mathrm{B}}\mathbf{k}_1 + m_{\mathrm{A}}m_{\mathrm{B}}\mathbf{k}_2 + m_{\mathrm{H}}m_{\mathrm{B}}\mathbf{k}_2 - 2m_{\mathrm{A}}m_{\mathrm{B}}\beta} \tag{22}$$

Equation 22 may be simplified with the aid of equations 17 and 23

$$m_{\mathrm{A}} + m_{\mathrm{H}} + m_{\mathrm{B}} = M \tag{23}$$

where M is the molecular weight of the activated complex. So

$$\lambda^* = 4\pi(\nu^*)^2 = \frac{M}{m_{\mathrm{A}}m_{\mathrm{H}}m_{\mathrm{B}}} \cdot \frac{(\mathbf{k}_1\mathbf{k}_2 - \beta^2)}{\lambda} \tag{24}$$

where ν^* is the zero "frequency" of the antisymmetric "vibration." In the quotient of λ^*_{H} by λ^*_{D}, the term $\mathbf{k}_1\mathbf{k}_2 - \beta^2$ appears in both numerator and denominator; as the term is allowed to approach zero (see equation 16), the quotient is nevertheless represented by equation 25.

$$\frac{\lambda^*_{\mathrm{H}}}{\lambda^*_{\mathrm{D}}} = \frac{M_{\mathrm{H}}}{M_{\mathrm{D}}}\,\frac{m_{\mathrm{D}}}{m_{\mathrm{H}}}\,\frac{\lambda_{\mathrm{D}}}{\lambda_{\mathrm{H}}} = \frac{M_{\mathrm{H}}}{M_{\mathrm{D}}} \cdot \frac{m_{\mathrm{D}}}{m_{\mathrm{H}}} \cdot \frac{\dfrac{\mathbf{k}_1}{m_{\mathrm{A}}} + \dfrac{\mathbf{k}_2}{m_{\mathrm{B}}} + \dfrac{\mathbf{k}_1 + \mathbf{k}_2 - 2\sqrt{\mathbf{k}_1\mathbf{k}_2}}{m_{\mathrm{D}}}}{\dfrac{\mathbf{k}_1}{m_{\mathrm{A}}} + \dfrac{\mathbf{k}_2}{m_{\mathrm{B}}} + \dfrac{\mathbf{k}_1 + \mathbf{k}_2 - 2\sqrt{\mathbf{k}_1\mathbf{k}_2}}{m_{\mathrm{H}}}} \tag{25}$$

If $\mathbf{k}_1 = \mathbf{k}_2$, i.e., if the force constants binding H (or D) to A and B are equal, then

$$\frac{\lambda^*_{\mathrm{H}}}{\lambda^*_{\mathrm{D}}} = \frac{M_{\mathrm{H}}}{M_{\mathrm{D}}}\,\frac{m_{\mathrm{D}}}{m_{\mathrm{H}}} \tag{26}$$

Since M_{H} does not differ much from M_{D},

$$\frac{\nu^*_{\mathrm{H}}}{\nu^*_{\mathrm{D}}} \simeq \sqrt{2} \tag{27}$$

Under these conditions, the quotient $\nu_{\mathrm{AD}}/\nu_{\mathrm{AH}}$ is approximately equal to $1/\sqrt{2}$, and the quotient $\nu^{\ddagger}_{\mathrm{H}}/\nu^{\ddagger}_{\mathrm{D}}$ equals 1. The latter follows because, when the force constants $\mathbf{k}_1$ and $\mathbf{k}_2$ are equal, the symmetric vibration is independent of the isotope involved (see equation 18). The entire preëxponential term of equation 20 is then unity.

However, if $\mathbf{k}_1 \gg \mathbf{k}_2$, then

$$\frac{\lambda^*_{\mathrm{H}}}{\lambda^*_{\mathrm{D}}} \simeq \frac{M_{\mathrm{H}}}{M_{\mathrm{D}}}\,\frac{m_{\mathrm{D}}}{m_{\mathrm{H}}}\left[\frac{\mathbf{k}_1}{m_{\mathrm{A}}} + \frac{\mathbf{k}_1}{m_{\mathrm{D}}}\right]\Big/\left[\frac{\mathbf{k}_1}{m_{\mathrm{A}}} + \frac{\mathbf{k}_1}{m_{\mathrm{H}}}\right] \tag{28}$$

Since $m_{\mathrm{A}} \gg m_{\mathrm{D}}$, m_{H}, equation 28 reduces, approximately, to equation 29.

$$\frac{\lambda^*_{\mathrm{H}}}{\lambda^*_{\mathrm{D}}} = \frac{(\nu^*_{\mathrm{H}})^2}{(\nu^*_{\mathrm{D}})^2} = 1 \tag{29}$$

Here again the preëxponential factor is approximately unity, since the ratio of the frequencies of the "symmetric" vibration now "cancels" the ratio of the frequencies for the molecules AH and AD, and the ratio $\nu^*_{\mathrm{H}}/\nu^*_{\mathrm{D}}$ is 1. Regardless, then, of the ratio of the force constants, the preëxponential factor estimated for this simplified model is near unity.[2] In any real example, wherever the force constants in the activated state are widely different, the rate ratio, $\mathrm{k_H}/\mathrm{k_D}$, will tend toward 1, and will be small because of the small difference in zero-point energy and because of a preëxponential factor near unity. An alternative approach to the same conclusion has been offered by Melander (32).

For example, in the chlorination of toluene (47), the transition state is presumably linear and may resemble closely a chlorine atom and a toluene molecule; that is to say, the maximum in the energy barrier may occur before very much lengthening of the C—H bond has taken place, or very much binding between hydrogen and chlorine. The absolute rate theory demands that, in the transition state, one vibration is completely converted to translational motion. But this motion is largely that of the carbon and chlorine atoms, and the hydrogen atom takes little part in it, although it is the atom transferred. Furthermore, the "symmetrical" vibration in the transition state, where the carbon and chlorine atoms move either together or apart without rupture of the activated complex, is distinguished by the large motion of the hydrogen atom. It is this "symmetric" vibration which contributes zero-point energy to the transition state and accounts for the low ratio of $\mathrm{k_H}/\mathrm{k_D}$ which is observed.

Obviously, this theory of a linear one-dimensional transition state is highly simplified. Most activated complexes are not linear, none is one-dimensional, and all of them will have bending vibrations which should be taken into account. Further, the extreme approxi-

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[2] It should be stressed again (see Appendix) that this approximation holds only for those temperatures sufficiently low that the terms in the vibrational partition function of the form $1 - e^{-h\nu_i/kT}$ are near unity. At very high temperatures this approximation no longer holds, and in the limit, the preëxponential factor approximates $\nu^*_{\mathrm{H}}/\nu^*_{\mathrm{D}}$. However, this limit lies in a region of temperature where few if any organic compounds exist, and so this special case is of little experimental interest.

mations here made can apply only to problems of the isotope effects for hydrogen, deuterium, and tritium. The proper solution to other problems may require a complete evaluation of all the partition functions, the $\nu_{\mathrm{H}}^{*}/\nu_{\mathrm{D}}^{*}$ ratio, and the tunnelling effect. Nevertheless, the simple treatment justifies the use of the absolute rate theory in those cases with a linear transition state, where a low kinetic isotope effect has been found, and provides a bridge between the oversimplified first approximation and the complete but rather unwieldy mathematical solutions of the problem of the kinetic isotope effect.

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APPENDIX

A brief description is here added concerning the derivation (6) of equation 20. The application of Eyring's absolute rate theory (18) to the relative rates of reactions of isotopic molecules leads to equation 1, where the Q for each molecule or activated complex may be expanded as the product of translational, rotational, and vibrational partition functions (but with neglect of tunnelling). The quotients of the translational and rotational partition functions for isotopic molecules may be expressed in terms of vibrational frequencies and the masses, m_i, of the various atoms by equating the classical and quantum-mechanical partition functions at high temperatures. Since the potential functions for isotopic molecules are the same, the ratio of the total classical partition functions for isotopic molecules

$$Q_{\text{classical}}/Q'_{\text{lassical}} \text{ reduces (6) to } \prod^{i} \left(\frac{m_i}{m'_i}\right)^{3/2} \tag{20a}$$

and when T is large, the ratio of vibrational partition functions,

$$Q_{\text{vib}}/Q'_{\text{vib}} = \prod^{i} \left(\frac{e^{-h\nu_i/2kT}}{1 - e^{-h\nu_i/kT}}\right) \Big/ \prod^{i} \left(\frac{e^{-h\nu'_i/2kT}}{1 - e^{-h\nu'_i/kT}}\right)$$

$$\text{reduces to } \prod^{i} \frac{\nu'_i}{\nu_i} \tag{20b}$$

where k is Boltzmann's constant, and the primed constants refer to those for isotopically substituted molecules.

Then, for high temperatures, equating the complete classical and quantum-mechanical partition functions leads to an expression of the form of equation 20c for each reactant and transition state.

$$\frac{Q_{\text{trans}}Q_{\text{rot}}}{Q'_{\text{trans}}Q'_{\text{rot}}} = \prod^{i} \frac{\nu_i}{\nu'_i} \prod^{i} \left(\frac{m_i}{m'_i}\right)^{3/2} \tag{20c}$$

At room temperature and above, the translational and rotational partition functions are well approximated by their high-temperature limits, so equation 20c may generally be used.

In evaluating the functions, a question arises as to the number of vibrations to be counted. For the vibrational partition functions of the transition state of ordinary, nonlinear molecules, only $3n - 7$ vibrations may be included, since one degree of freedom (the decomposition along the reaction coördinate) has already been taken specifically into account in the derivation (18) of Eyring's equation. Since, however, the ordinary translational and rotational motions are not specially treated in the absolute rate equation, the quotient in equation 20c must be obtained as if the activated state were an ordinary molecule. The product in equation 20c must therefore include not only $3n - 7$ real vibrations of each transition state but the imaginary vibrations $\nu^{‡*}$ and $\nu'^{‡*}$ as well. Insertion of the rotational and translational functions from 20c into equation 1 leads to equation 20d

$$\frac{\text{k}}{\text{k}'} = \frac{\nu^{‡*}}{\nu'^{‡*}} \left[\prod^{3n-6} \frac{\nu'}{\nu} \prod^{3n-7} \frac{\nu^{‡}}{\nu'^{‡}} \frac{Q'_{\text{vib}}Q^{‡}_{\text{vib}}}{Q_{\text{vib}}Q'^{‡}_{\text{vib}}} \right] \tag{20d}$$

for a unimolecular reaction or a bimolecular reaction where one reactant is an atom. On substituting the vibrational partition functions from equation 20b into equation 20d, the equation for the ratio of the rate constants is obtained.

However, the transition state AHB has only one real vibration, and the group B is assumed to have no vibration, i.e., it behaves like an atom. Furthermore, for this particular case, the quotient of terms of the form $1 - e^{-h\nu_i/kT}$ (from equation 20b) may be approximated by unity, since the frequencies of stretching carbon to hydrogen (or carbon to deuterium) bonds are high. With these simplifications, equation 20d easily reduces to equation 20.