VALIDITY OF SOME APPROXIMATION PROCEDURES USED IN THE THEORETICAL CALCULATION OF ISOTOPE EFFECTS

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INTRODUCTION

This discussion of isotope effects on rate constants will be carried out within the framework of transition state theory. Consideration of unimolecular reactions at low pressures is excluded. Isotope effects on transmission coefficients and on tunnelling will generally be ignored. The energy of an N-atomic molecule is described in terms of $3N$ independent degrees of freedom corresponding to three translations, three rotations (only two for a linear molecule), and $3N - 6$ vibrations ($3N - 5$ for a linear molecule), with the electronic energy, of course, taken as isotope-independent. The vibrations will be treated within the harmonic approximation and the translations and the rotations will be treated as classical degrees of freedom. One of the vibrational degrees of freedom in the transition state (with zero or imaginary frequency designated by $\nu_L^{\ddagger}$) does not correspond to genuine vibration and is treated in the standard manner of transition state theory. Reference should be made to the literature for discussion of these assumptions[1-3].

For simplicity, the case in which only one of the reactants is isotopically substituted will be considered. The isotopic rate ratio k_1/k_2 at temperature T is then given by[1]

$$
\frac{k_1}{k_2} =
$$

$$
\frac{\left[\frac{I_{A_2}I_{B_2}I_{C_2}}{I_{A_1}I_{B_1}I_{C_1}}\right]^{1/2}\left(\frac{M_2}{M_1}\right)^{3/2}}{\left[\frac{I_{A_2}^{\ddagger}I_{B_2}^{\ddagger}I_{C_2}^{\ddagger}}{I_{A_1}^{\ddagger}I_{B_1}^{\ddagger}I_{C_1}^{\ddagger}}\right]^{1/2}\left(\frac{M_2^{\ddagger}}{M_1^{\ddagger}}\right)^{3/2}} \times \frac{\prod_i^{3N-6}\frac{[1-\exp(-u_{1i})]}{[1-\exp(-u_{2i})]}}{\prod_i^{3N^{\ddagger}-7}\frac{[1-\exp(-u_{1i}^{\ddagger})]}{[1-\exp(-u_{2i}^{\ddagger})]}} \times \frac{\exp\left[\sum^{3N-6}(u_{1i}-u_{2i})/2\right]}{\exp\left[\sum^{3N^{\ddagger}-7}(u_{1i}^{\ddagger}-u_{2i}^{\ddagger})/2\right]}
$$

$$
\tag{1}
$$

$$
= \frac{\nu_{1L}^{\ddagger}}{\nu_{2L}^{\ddagger}} \times \frac{\prod^{3N-6}\frac{u_{2i}}{u_{1i}}}{\prod^{3N^{\ddagger}-7}\frac{u_{2i}^{\ddagger}}{u_{1i}^{\ddagger}}} \times \frac{\prod^{3N-6}\frac{[1-\exp(-u_{1i})]}{[1-\exp(-u_{2i})]}}{\prod^{3N-7}\frac{[1-\exp(-u_{1i}^{\ddagger})]}{[1-\exp(-u_{2i}^{\ddagger})]}} \times \frac{\exp\left[\sum^{3N-6}(u_{1i}-u_{2i})/2\right]}{\exp\left[\sum^{3N^{\ddagger}-7}(u_{1i}^{\ddagger}-u_{2i}^{\ddagger})/2\right]} \tag{2}
$$

Q

Here, by convention, 1 and 2 refer to light and heavy isotopic species, respectively; the numerators refer to isotopically substituted reactant; ‡ refers to transition state; I's are principal moments of inertia and M's are molecular masses; $u = h\nu/kT$ where ν is a normal vibrational frequency, h is Planck's constant and k Boltzmann's constant (u is dimensionless; with ν in cm^{-1}, $u = 1 \cdot 4385\ \nu/T$). The transition state products and sums are over the $3N^{\ddagger} - 7$ real (genuine) frequencies. $\nu_L{}^{\ddagger}$ refers to the zero or imaginary frequency of the transition state which is sometimes referred to as the frequency of decomposition. The symmetry numbers s which give rise only to purely classical statistical factors have been omitted here and subsequently. Equations (1) and (2) are completely equivalent and one may be obtained from the other by means of the Teller–Redlich product rule[1]. Equation (2) shows that the high temperature limit (also the classical limit) of the isotope effect is $\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}$ since at high temperature, $u \to 0$, $\exp\ (u_1 - u_2)/2 \to 1$, and $1 - \exp\ (-u_{1i})/1 - \exp\ (-u_{2i}) \to u_{1i}/u_{2i}$.

The first ratio of ratios in equation (1), which is completely equivalent to $\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}$ multiplied by the ratio of ratios of u's (which will be referred to as VP) in equation (2), arises from the translational and rotational partition functions and will be designated as MMI. The second ratio of ratios, involving $1 - \exp\ (-u)$ factors, arises from excitation of vibrations and will be referred to as EXC. The last term arises from the vibrational zero-point energies and will be designated as ZPE. The equations can then be written, $k_1/k_2 = (MMI) \times (EXC) \times (ZPE) = (\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}) \times (VP) \times (EXC) \times (ZPE)$.

METHOD OF CALCULATION

In order to use equations (1) or (2) for the calculation of k_1/k_2 corresponding to given knowledge or assumptions about force fields of reactant and transition state, one needs to know the normal vibrational frequencies (ν_{1i}, ν_{2i}, $\nu_{1i}{}^{\ddagger}$, $\nu_{2i}{}^{\ddagger}$) of all the molecular species involved. The calculation of the normal vibrational frequencies corresponding to a given force field is very tedious for all except very small molecules, if carried out by hand or with a desk calculator. Consequently, exact calculations with equations (1) or (2) have been carried out in the past only for small molecules.

The availability of large digital computers has changed this situation. Schachtschneider[4] has written a machine programme for calculating the normal harmonic vibrational frequencies of molecules which employs the FG matrix method of Wilson[5]. It is now quite feasible to calculate the frequencies of a molecule containing as many as thirty atoms. The input data consist of molecular geometries, atomic masses, and force constants. I's and M's are automatically calculated by the computer. We have modified the Schachtschneider programme so that isotope effects on rate constants or on equilibria are also automatically calculated. An IBM 7094 computer was used for the computations. The rate isotope effect is calculated within the framework of equation (1). The products and sums are taken over all the real frequencies. The transition state automatically has $3N^{\ddagger} - 7$ real frequencies. In the case of an equilibrium, the transition state quantities in the denominator of equation (1) are replaced by reaction product quantities, and the products and sums are taken over the $3N - 6$ real frequencies

of the reaction product. $(MMI)/[\Pi(u_{2i}/u_{1i})/\Pi(u_{2i}^{\ddagger}/u_{1i}^{\ddagger})]$ is automatically evaluated by the programme. (It is again emphasized that the products are taken over the real frequencies). For the case of a reaction rate, this ratio equals $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ [see equations (1) and (2)], while for an equilibrium it is unity. In most of our computations, we have worked with models yielding $\nu_{L}^{\ddagger}$ equal to zero so that the above procedure is the method by which we have obtained $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$. If one is dealing with a reaction model in which the $\nu_{L}^{\ddagger}$'s are not zero (but imaginary) or with an equilibrium, then the latter machine calculation serves as a convenient check on the machine computation of the vibrational frequencies.

MODEL CALCULATIONS

The above computing machine programmes have been employed to study isotope effects in some model systems. The calculations on these model systems will be used here to discuss approximation procedures which have been developed for the consideration of isotope effects. These approximations include both procedures to calculate isotope effects corresponding to given models of reactants and transition states and also methods to deduce information about transition states from experimental results. In the subsequent discussion[6], we shall use the model systems to gain some knowledge about secondary isotope effects. The general philosophy of these calculations has not been to attempt to reproduce theoretically a given experimental finding nor to deduce something about the specific properties of a given transition state in a certain reaction. We are instead attempting to gain some understanding about kinetic isotope effects within the transition state framework.

The model reactions studied include the following: (i) RX → (RX)‡, (ii) RX + X → (RX$_2$)‡, and (iii) CH$_2$(COOH)$_2$ → (CH$_2$COOH—COOH)‡. R here is an alkyl group. X has a mass of eighty. The bond angles in the RX reactants were chosen tetrahedral with bond distances R(CC) = 1·54 Å, R(CH) = 1·09 Å, R(CX) = 1·91 Å. In the (RX)‡ transition state, the CX bond was usually broken. This situation is sometimes designated by (R—X)‡. A zero frequency of decomposition was achieved in this case by setting the diagonal CX stretching force constant $f_{CX}^{\ddagger}$ equal to zero (with no interaction force constant between the CX stretching coordinate and any other coordinate). Sometimes, instead, a CC bond or a CH bond has been broken by setting the relevant force constant ($f_{CC}^{\ddagger}$ or $f_{CH}^{\ddagger}$) equal to zero. The geometrical arrangement of the (RX)‡ transition state has usually been kept the same as in the reactant [(MMI) = 1·000]. Consideration of lengthening, in the transition state, of the bond to be broken or of even more serious geometric changes does not alter general conclusions, as will be explicitly pointed out in the following discussion[6]. In the (RX$_2$)‡ transition state, the geometrical arrangement about the carbon atom to which the two X atoms are attached is a trigonal bipyramid with XCX angle = 180°, H(C)CX angles = 90°, H(C)CH angles = 120°, R(CH) = 1·09 Å, R(CC) = 1·54 Å, R(CX) = 2·25 Å. In other ways, the geometry of R is the same in reactant and transition state. The zero frequency of decomposition $\nu_{L}^{\ddagger}$ was achieved here by one of two different methods. In the first, one CX bond in (RX$_2$)‡ was broken by just setting one diagonal CX stretching force

constant (say $f_{CX_1^\ddagger}$) equal to zero (with $f_{CX_2^\ddagger} > 0$). In the second method, $\nu_L^\ddagger$ corresponds to motion in which one CX distance is decreasing and the other is increasing. The zero $\nu_L^\ddagger$ was achieved by setting $f_{CX_1^\ddagger} = f_{CX_2^\ddagger} = f_{12}^\ddagger$ where $f_{12}^\ddagger$ is the interaction force constant between the two stretching coordinates. The CX-bond-breaking transition state for $(RX)^\ddagger$ might correspond to transition states in S_N1 reactions while the $(RX_2)^\ddagger$ transition states described above might correspond to transition states in S_N2 reactions. The third type of model reaction considered corresponds to the breaking of a carbon–carbon bond in malonic acid. We use this reaction as a model for a decarboxylation reaction. A reasonable geometry was chosen for the reactant[7]. The transition state geometry was left the same as the reactant geometry, although again we have carried out other calculations in which the CC bond to be broken was enlarged in the transition state. The zero $\nu_L^\ddagger$ was usually achieved here by setting the relevant $f_{CC^\ddagger} = 0$.

Needless to say, the force constants in a given molecular species are independent of isotopic substitution[1]. Within the philosophy of these calculations, no attempt has been made to pick "best" force fields for reactants. Reactant force fields (and transition state force fields, for that matter, except for the $f_{12}^\ddagger$ interaction force constant mentioned above) have usually been chosen to include only diagonal force constants, denoted by $f_{coordinate}$, (i.e., a so-called valence force field) for bond stretches, bond-angle bends, torsions, and out-of-plane wags. The force constants used for the reactant alkyl groups and for reactant malonic acid are reasonable† but specific ones might be wrong by a factor of two when comparison is made with real systems. We have, in fact, at times used different force constants for the same reactant in different calculations. X might be a bromine atom, but no special significance should be attached to its mass, or even to the fact that both X atoms in $(RX_2)^\ddagger$ possess the same mass, except that it is much heavier than an H atom. Thus, while there might be some quantitative change in the isotope effect if X were replaced by a polyatomic organic group, such replacement would not lead us to new qualitative conclusions. We are anticipating, in part, here and below, the results of the later section on cut-off procedure. RX force constants were sometimes chosen as though X were bromine but at other times more arbitrarily. The magnitudes of the bending force constants coupling X to the alkyl group were in the range of magnitudes of usual bending force constants. Qualitatively, the isotope effect depends largely on force constant differences at the isotopic position(s) between reactant and transition state. Generally, lower force constants in the transition state than in the reactant lead to isotope effects $k_1/k_2 > 1$, while higher force constants lead to $k_1/k_2 < 1$. While some of the force fields used are indicated in the tables in this and in the following[6] discussion, we have generally listed only the important force constant differences between reactant and transition state. Some of the force constant changes which were made between reactants and transition states were necessary to obtain the one zero (or imaginary§)

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† The " reasonable " force constants used in the present and in the subsequent paper[6] are not based completely on any one source but they are based in large part on compilations of force constants such as found in reference 4.

§ All of the calculations explicitly presented in this paper correspond to zero values of $\nu_L^\ddagger$. Some calculations leading to imaginary values of $\nu_L^\ddagger$ have been carried out; these do not alter any of the present conclusions.

frequency which characterizes the transition state (as discussed above), while other changes were made just to investigate the consequence on the isotope effect. We have not necessarily asked the question whether these latter force constant changes have reasonable physical bases. We have generally attempted to avoid the drawing of conclusions which depend on some peculiarity in the chosen force fields. We are aware of the possible pitfalls in drawing conclusions from model calculations, and we hope that we have avoided such pitfalls.

THE LOW TEMPERATURE APPROXIMATION

At low temperature, the vibrational excitation factor EXC is unity. We will refer to

$$k_1/k_2 = (MMI) \times (ZPE) \qquad (3)$$

as the low temperature approximation. Once a model for a transition state has been assumed, MMI may be calculated just on the basis of geometrical considerations and the masses of the atoms. If it is then possible to calculate or to estimate ZPE†, equation (3) can be applied to obtain k_1/k_2. Conversely, if equation (3) is valid, ZPE may be obtained from experimental data at one temperature if MMI is "known". If experimental data are available over a range of temperatures, both MMI and ZPE might be deduced.

EXC will be less than unity, at a given temperature, if all the frequencies of the reactants are so large that the corresponding $1 - \exp(-u)$ factors may be considered unity while the transition states possess lower frequencies which are excited. In considerations of more complicated situations, one must always bear in mind that at very high temperatures $(EXC) = (VP)^{-1} = (MMI)^{-1} \times (v_{1L}^{\ddagger}/v_{2L}^{\ddagger})$.

Table 1 shows that the low temperature approximation is generally a good approximation at 50°K. Cases 1 and 2 correspond to the same transition state. For the hydrogen isotope effect, the lowering of HCX bending force constant in the transition state with respect to reactant appears to determine the negative deviation from unity in EXC at room temperature. On the other hand, for the carbon isotope effect, the disappearance of the low frequency, which is essentially a CX stretching frequency, in the transition state (it "goes over" into the frequency of decomposition $v_L^{\ddagger}$) makes the major contribution to EXC at room temperature and leads to EXC larger than unity. Case 6 corresponds to CH bond break and EXC differs very little from unity even at room temperature. However, case 11 also corresponds to CH bond break but $(EXC) = 0.918$ at 300°K. Case 11 is typical of a number of cases in the table where MMI is larger than unity white at room temperature EXC is smaller than unity. One should not draw the conclusion that large MMI will invariably yield EXC less than unity because models could easily be constructed which do not show this trend. Moreover, MMI equal to unity does not necessarily mean EXC close to unity as evidenced by case 10, where an increase in torsional force constants in the transition state has led to a considerably smaller contribution from the

† Some attempts to calculate isotope effects on zero-point energies in molecules without calculating all the normal vibrational frequencies have been undertaken[8]. The application of these methods to transition states and to the evaluation of ZPE needs further investigation.

Table 1. The low temperature approximation

Case[a]	Isotopic reactant	$T(°K)$	k_1/k_2 eq. (1)	MMI	ZPE	EXC	(MMI) × (ZPE)	AMMI	AZPE	$\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}$
1	CD_3X	50 300 500	13·41 1·502 1·254	1·000 1·000 1·000	13·41 1·541 1·296	1·000 0·974 0·967	13·41 1·541 1·296	0·94	1·59	1·079
2	$^{14}CH_3{}^2X$	50 300	1·808 1·112	1·000 1·000	1·808 1·104	1·000 1·007	1·808 1·104	1·02	1·09	1·054
3	$^{14}CH_3X$	300	1·118	0·991	1·119	1·008	1·109	1·02	1·10	1·054
4	$^{14}CH_3X$	300 2000	1·105 1·060	1·113 1·113	1·060 1·009	0·937 0·944	1·180 1·123	1·03	1·07	1·059
5	CD_3X	50 300 2000	0·1904 0·855 1·076	1·271 1·271 1·271	0·1508 0·730 0·954	0·993 0·921 0·888	0·1917 0·928 1·212	1·17	0·73	1·086
6	CD_3X	50 300	$1·462 \times 10^5$ 7·28	1·000 1·000	$1·462 \times 10^5$ 7·26	1·000 1·002	$1·462 \times 10^5$ 7·26	1·01	7·21	1·391
7	CD_3CH_2X	300	1·251	1·131	1·208	0·916	1·366	1·03	1·21	1·039
8	$^{14}CH_3CH_2X$	50 300	1·053 1·029	1·042 1·042	1·015 1·002	0·996 0·986	1·058 1·044	1·03	1·00	1·027
9	$^{13}COOH$ CH_2 $COOH$	300	1·028	1·000	1·040	0·989	1·040	0·99	1·04	1·005
10	$(CD_3)_2CHX$	300 2000	1·413 1·117	1·000 1·000	1·105 1·015	1·278 1·101	1·105 1·015	1·45	0·97	1·039
11	CD_3CH_2X	300	6·96	1·131	6·70	0·918	7·58	1·02	6·82	1·405

a Only the changes in force constants between reactant and indicated transition state involving the isotopic position(s) and the breaking bond will be described below.

Case 1: $(CD_3—X)\ddagger$; $f_{CX} = 2\cdot9$, $f_{HCX} = 0\cdot62$; $f_{CX}\ddagger = 0\cdot0$ md/Å, $f_{HCX}\ddagger = 0\cdot37$ md-Å.

Case 2: $(^{14}CH_3—X)\ddagger$; same as case 1.

Case 3: $(^{14}CH_3—X)\ddagger$; CH_3 group flat in transition state: $f_{CX} = 2\cdot9$, $f_{HCX} = 0\cdot62$; $f_{CX}\ddagger = 0\cdot0$ md/Å, $f_{HCX}\ddagger = 0\cdot405$ md-Å.

Case 4: $(^{14}CH_2X_2)\ddagger$; $f_{CX} = 2\cdot9$, $f_{HCX} = 0\cdot62$; $f_{CX_2}\ddagger = f_{CX_1}\ddagger = f_{12}\ddagger = 2\cdot0$ md/Å, $f_{HCX}\ddagger = 0\cdot41$ md-Å.

Case 5: $(CD_3X_2)\ddagger$; same as case 4.

Case 6: $(CD_3X)\ddagger$; CH bond break; $f_{CH} = 5\cdot1$; $f_{CH}\ddagger$ (breaking bond) $= 0\cdot0$ md/Å.

Case 7: $(CD_3CH_2X_2)\ddagger$; $f_{CX} = 2\cdot9$, $f_{CH} = 4\cdot8$, $f_{CCX} = 0\cdot62$; $f_{CX_1}\ddagger = f_{CX_2}\ddagger = f_{12}\ddagger = 2\cdot0$, $f_{CH}\ddagger = 4\cdot5$ md/Å, $f_{CCX}\ddagger = 0\cdot31$ md-Å.

Case 8: $(^{14}CH_3CH_2X_2)\ddagger$; same as case 7.

Case 9: $(CH_3COOH—^{13}COOH)\ddagger$; $f_{CC} = 4\cdot4$; $f_{CC}\ddagger$ (breaking bond) $= 0\cdot0$ md/Å, CO stretching force constants have been raised in transition state, wagging and CCC bending force constants involving the isotopic carbon atom have been lowered in the transition state.

Case 10: $[(CD_3)_2CH—X]\ddagger$; described in reference 6, Table 6.

Case 11: $(CD_3CH_2X_2)\ddagger$; CH bond break; $f_{CH} = 4\cdot8$; $f_{CH}\ddagger$ (breaking bond) $= 0\cdot0$ md/Å. This case corresponds to a hypothetical reaction $CD_3CH_2X + X \to (CD_3CH_2X_2)\ddagger$ in which one of the CH bonds on the β carbon atom is broken in the transition state.

torsions in the transition state to EXC than from these torsions in the reactant. EXC in case 9 is also large compared to the total magnitude of the isotope effect. Here force constants which "determine" low frequencies in the reactant have been lowered further in the transition state. One should, of course, remember, as already noted, that at very high temperatures EXC becomes equal to the inverse of MMI times $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$.

Table 1 also lists apparent values of MMI (denoted AMMI) and apparent values of ZPE (denoted AZPE) which were obtained by assuming that the temperature-dependence of the isotope effect is indeed given by equation (3). The procedure which is employed now is typical of one of the uses to which we have put the results of model calculations. The model calculation k_1/k_2 results are used as though they were experimentally observed isotope effects and subjected to a type of analysis to which experimental data might be subjected. The approximate values so obtained for certain quantities are compared with the values which these quantities are actualy known to have in the model system. It was possible to fit a plot of ln (k_1/k_2) *versus* $1/T$ over a limited temperature span reasonably well by a straight line. The straight line used for the present purposes was the one which connects the points at 300 and 325°K but this line usually fits the point even at 400°K quite well. The infinite temperature intercept of this straight line was designated as ln (AMMI) and AZPE was determined at 300°K from k_1/k_2 = (AMMI) × (AZPE).

The low temperature approximation does perform reasonably at room temperature in some cases. The judgement on how well it performs depends on the accuracy which is expected. There are some cases in *Table 1* where the approximation is quite poor. The AMMI values determined from the room temperature values of isotopic rates in *Table 1* do not appear to give generally reliable information about MMI. In the subsequent discussion[6], these values are referred to as *A*. The AZPE values in *Table 1* show a similarity to the actual ZPE values and, at least for the model cases here, it is possible to obtain some idea of the isotope effect on the zero-point energy difference from the temperature dependence of the rate isotope effect.

Further comment on case 4 appears appropriate at this point. Melander[2] has considered carbon isotope effects in S_N2 reactions and has indicated that these may be large compared to carbon isotope effects in S_N1 reactions (see case 2) essentially because of the large magnitude of MMI in the former. Actually, we find that we can consider case 4 in two steps: (1) $^{14}CH_3X +$ $X \rightleftharpoons {}^{14}CH_3X_2$, (2) $^{14}CH_3X_2 \rightarrow ({}^{14}CH_3X_2)^{\ddagger}$. The first step is an equilibrium step with (MMI) = 1·113 while the second step is the reaction step, now with (MMI) = 1·000. Some calculations have been carried out in which, in the first step, all six $f_{HCX}^{\ddagger}$ and both $f_{CX}^{\ddagger}$ in CH_3X_2 were set equal to one-half the corresponding values in CH_3X. The isotope effect in the equilibrium step is now found to be 1·005 at 300°K. The cause of the isotope effect in the over-all reaction must now be found in the force constant changes at the isotopic position during the reaction step 2†. It is of interest that case 5 gives rise to an inverse isotope effect in spite of the large value of MMI

† We note that, within the philosophy of the present calculations, we have not attempted to determine for what kinds of force fields, S_N2 type reactions would correspond to higher isotope effects than S_N1 type reactions.

which corresponds to this case. These examples have been pointed out to show the general dangers which may be inherent in considering only one or another factor in equation (1).

THE HIGH TEMPERATURE APPROXIMATION

For sufficiently small values of $u = h\nu/kT$, equation (2) (in logarithmic form) can be expanded in powers of $1/T$. The first non-vanishing term involves $1/T^2$ and is given below[1, 9]

$$\ln\ (k_1/k_2) = \ln\ (\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}) + (1/24)\{\sum_{}^{3N-6} (u_{1i}^2 - u_{2i}^2) - \sum_{}^{3N\ddagger-7} (u_{1i}^{\ddagger 2} - u_{2i}^{\ddagger 2})\}$$

$$= \ln\ (\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}) + (1/24)(h/2\pi kT)^2 \sum_i (a_{ii} - a_{ii}^{\ddagger})(m_{1i}^{-1} - m_{2i}^{-1})$$

$$= \ln\ (\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}) + (1/24)(h/2\pi kT)^2 \{ \sum_{\substack{i,j \\ \text{reactant}}} f_{ij}(g_{1,ij} - g_{2,ij})$$

$$- \sum_{\substack{i,j \\ \ddagger}} f_{ij}^{\ddagger}(g_{1,ij} - g_{2,ij})^{\ddagger}\} \tag{4}$$

The second and third forms of equation (4) contain the Wigner tunnelling correction term[1]. $a_{ii} - a_{ii}^{\ddagger}$ refers to the difference in the three diagonal Cartesian force constants of atom i between the reactant and the transition state and m refers to atomic mass. The sum in the second formulation need only include the isotopically substituted atom(s). In the third formulation, f_{ij} refers to the usual force constants ($2V = \sum f_{ij}q_iq_j$) and g_{ij} to the corresponding G-matrix elements of Wilson[5]. The sums need only be over those coordinates q_i, q_j which both involve the same isotopically substituted atom. The second and third formulation have great appeal since they enable one to calculate an isotope effect just from a knowledge of force fields, geometries, and atomic masses. As has been pointed out, equation (4) just represents the first term in an expansion. The complete series converges for all $u < 2\pi$. Because of the slowness of the convergence of the series near its limit of convergence and because $u < 2\pi$ is very restrictive at room temperature, the complete series has not been found of general utility. Equation (4) should be valid for both u and $\Delta u = u_1 - u_2$ small. In order to extend the validity of equation (4) to larger u, it has been proposed[1] to replace $1/24$ by $\bar{\gamma}/24$. $\bar{\gamma}$ is defined in terms of the Bigeleisen–Mayer function $G(u)$ by $\bar{\gamma} = 12G(\bar{u})/\bar{u}$,where $\bar{u}$ refers to some average frequency which is responsible for the isotope effect. A table of $12G(u)/u$ has been calculated[9] and one can determine that for large u, corresponding to high frequency, γ is small while it tends to unity for small u. By definition, $\bar{\gamma}$ is temperature dependent.

We have shown previously[7] that the application of the gamma-bar method to carbon isotope effects in the decarboxylation of malonic acid (with just a simple CC-bond-rupture transition state) shows only qualitative agreement with the exact calculation by means of equation (1). While a frequency of ~800 cm^{-1} in the reactant involving (in part) CC stretching motion seemed to be the one no longer present in the transition state, it was found that, in the region between 300 and 500°K, $\bar{\gamma}$ corresponding to

$\sim$1450 cm^{-1} was necessary to fit the data designated by k_1/k_2 while $\bar{\gamma}$ ($\sim$1800 cm^{-1}) was necessary for $k_1/2k_3$. Perusal of calculated frequencies shows that the difference in the isotope effect on frequencies between reactants and transition states for reactions of this type involves a wide range of frequencies.

In *Table 2*, results are shown of applications of the high temperature approximation to some primary carbon isotope effects and some secondary hydrogen isotope effects. It has been assumed here that $\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}$ is known. The determination of $\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}$ does indeed present a problem (see next section). When one compares approximate k_1/k_2 values with exactly calculated ones, one should bear in mind that one should really compare deviations from the limiting value $\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}$. Values of k_1/k_2 at 300°K calculated with $\bar{\gamma} = 1$ are shown. So long as CH stretching force constants are not involved in the force constant changes between reactants and transition states, the agreement between the exact and calculated k ratios in the table might be described at least as fair (depending on degree of accuracy desired). As expected, the agreement improves at higher temperature. Thus, one calculates at 500°K in case 1, $k_1/k_2(\bar{\gamma} = 1) = 1\cdot0751$ while the exact value is 1·0722. The table also shows the $\bar{\gamma}$ values at 300°K and the frequencies to which they correspond. $\bar{\gamma}$'s corresponding to such frequency are found to give k ratios in reasonable (sometimes better, sometimes worse) agreement with exact k ratios over a temperature range (300–500°K). The average frequencies are higher than one would anticipate. Thus, the CX stretching frequency which disappears in the transition state in cases 1 and 2 has a value of $\sim$600 cm^{-1}. $\bar{\gamma}$ corresponding to 600 cm^{-1} equals 0·885 at 300°K†. Since the $\bar{\gamma}$ derived from the k ratio for case 1 equals 0·751, it is seen that the use of the 600 cm^{-1} value would remove of the order of 50 per cent of the discrepancy between the deviation of the exact k ratio from $\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}$ and the deviation, from $\nu_{1L}{}^{\ddagger}/\nu_{2L}{}^{\ddagger}$, of the k ratio computed with $\bar{\gamma}$ equal to unity. The "anomalously reasonable" average frequency in case 4 comes about in spite of the fact that there are large positive and negative shifts in isotope effects on frequencies over a large frequency region. In order that the average frequency as calculated by us should have meaning, it is really necessary that either isotopic shifts in u values or differences of individual isotope-dependent u's between reactant and transition state should be small. Neither one of those conditions is well met by case 5, a secondary deuterium isotope effect. In case 6, where the shift in frequencies between reactant and transition state might be expected to be smaller, we find an average

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† We have examined the calculated reactant and transition state frequencies for case 1 (*Table 2*) which corresponds to simple CX bond break. Besides the isotope effect on the zero-point energy difference between reactant and transition state which results in the 600 cm^{-1} region from the disappearance of the CX stretching frequency, there is a sizeable effect in the bending frequency region $\sim$1400 cm^{-1}. Thus, if only the calculated isotope effect in the 600 cm^{-1} frequency is assumed to contribute to the vibrational terms in equation (1) (see reference 2 for discussion of this type of approximation), one obtains $k_1/k_2 = 1\cdot079$ at 300°K which must be compared with the exactly calculated value 1·099. Similarly, the carbon isotope effect in the CH bond break (case 7, *Table 2*) is calculated to be 1·056 at 300°K if only the calculated isotope effect on the CH stretching frequency which disappears is used (exact value is 1·035). On the other hand, for a primary hydrogen isotope effect in a similar reaction (case 6, *Table 1*), the one frequency approximation yields $k_1/k_2 = 7\cdot44$ at 300°K while the exact value is 7·28. The general quantitative significance of one-frequency approximations in equation (1) is thus somewhat dubious even for simple bond breaks.

Table 2. Investigations of the gamma-bar method

Case	Isotopic reactant	Transition state[a]	Force constant change at isotopic position(s)	Change[b]	k_1/k_2, exact	300°K $\bar\gamma = 1$[e]	$\bar\gamma$ (calc. at 300°K)[f]	$\bar\nu$ (cm^{-1})	$\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$
1	$^{14}CH_3X$	A	CX	$2.9 \to 0.0$	1·0989	1·1144	0·751	1000	1·0535
2	$^{14}CH_3X$	A	CX	$2.9 \to 0.0$	1·1116	1·1379	0·696	1170	1·0535
3	$^{14}CH_3X$	A	$\left\{\begin{array}{l}\text{HCX}\\\text{CX}\end{array}\right.$	$0.62 \to 0.37$ $4.0 \to 0.0$	1·1141	1·1384	0·722	1090	1·0535
4	$^{14}CH_3X$	B	See below[c]		1·1052	1·1125	0·866	660	1·0585
5	CD_3X	A	HCX	$0.62 \to 0.37$	1·5020	1·8024	0·645	1340	1·0785
6	$CH_3CD_2CH_2X$	C	$\left\{\begin{array}{l}\text{CH}\\\text{HCH}\end{array}\right.$	$4.5 \to 4.36$ $0.53 \to 0.445$	1·1244	1·4146	0·333	3280	1·0027
7	$^{14}CH_3X$	D	CH	$4.8 \to 0.0$[d]	1·0346	1·1008	0·333	3270	1·0030

[a] $A = (R - X)^{\ddagger}$
$B = (RX_2)^{\ddagger}$
$C = (RX_2)^{\ddagger}$ with $f_{CX_1}^{\ddagger} = 0·0, f_{CX_2}^{\ddagger} = 4·0$ md/Å
$D = (RX)^{\ddagger}$, break one CH bond

[b] Units: stretching force constants, md/Å, bending force constants, md/Å

[c] $f_{CX} = 2·9, f_{HCX} = 0·62; f_{CX_1}^{\ddagger} = f_{CX_2}^{\ddagger} = f_{11}^{\ddagger} = 2·0$ md/Å, $f_{HCX}^{\ddagger} = 0·41$ md/Å

[d] Attention is called to the fact that f_{CH} in the reactant here equals 4·8 md/Å while in the most of the cases above and also in case 6, *Table 1*, which refers to the same reaction, a value of 5·1 md/Å was used. The analysis of the present case with $f_{CH} = 5·1$ md/Å is entirely similar. We have pointed out this situation to emphasize that we have at times used somewhat different force fields even for the same reactant.

[e] Calculated with equation (4).

[f] The calculated values of $\bar\gamma$ and $\bar\nu$ at 500°K for cases 1–7, respectively, follow: 0·866, 1090 cm^{-1}; 0·833, 1260 cm^{-1}; 0·851, 1170 cm^{-1}; 0·971, 470 cm^{-1}; 0·816, 1340 cm^{-1}; 0·51^6, 1340 cm^{-1}; 0·509, 3210 cm^{-1}. **3150**

frequency of 3280 cm^{-1} in spite of the fact that $\sim1/3$ of the contribution to the coefficient of $\bar{\gamma}/24$ arises from the change in the HCH force constant (which contributes principally to lower frequencies). In general, the application of the "gamma-bar method" as used here will become more confusing if force constants which contribute mainly to large frequencies and force constants which contribute mainly to small frequencies are changed at the same time, especially if one set of force constants increases between reactant and transition state and the other set decreases. $\bar{\gamma}$ corresponding to a shift in force constants which affect high frequencies will tend to be small, while $\bar{\gamma}$ corresponding to a shift in force constants which affect low frequencies will tend to be large. One could contrive a situation where: (i) force constants corresponding to high frequencies are increased in the transition state with respect to reactant (this increase by itself would tend to give an inverse isotope effect—but with small value of $\bar{\gamma}$) and (ii) force constants corresponding to low frequencies are decreased in the transition state (this latter decrease by itself would tend to give a normal isotope effect with larger value of $\bar{\gamma}$), in such a way that the coefficient of $\bar{\gamma}/24$ in equation (4) vanishes. The over-all isotope effect in such a situation might be considerably larger than $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$. Case 9 of *Table 1* is an example of such a situation. The gamma-bar method in the simple form presented here (*i.e.*, an equation with just one $\bar{\gamma}$; see reference 1) must fail completely in this situation.

Once an isotope effect has been obtained for a model system and $\bar{\gamma}$ has been calculated as in *Table 2*, the gamma-bar method may be used very successfully to predict how further force constant changes will affect the isotope effect. Thus, for instance, according to equation (4), changes in force constants not involving the isotopic position(s) should not change the isotope effect; within limits, this is found to be the case. Also it is found, as predicted by equation (4), that the actual values of the force constants corresponding to coordinates even involving the isotopic position(s) are not very important, within limits, so long as these force constants have the same values in reactant and in transition state.

For general qualitative reasoning about isotope effects, we find the high temperature approximation and its very simple modification very useful. For quantitative applications, methods for determining the average frequency *a priori* have still to be found. We also know that there are situations where the simple procedure will break down.

$\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$—THE RATIO OF THE FREQUENCIES OF DECOMPOSITION

The factor $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ has received considerable attention[1] during the past decade†. At one time it was thought that, for simple bond rupture, the isotopic frequency ratio $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ is equal to the ratio of the square roots of the reduced masses of the atoms forming the bond being broken (Slater

† Since $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ is the high temperature limit of the isotope effect and because of the way in which this factor appears in equation (4) and in some related equations, $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ has sometimes been referred to as the "temperature-independent factor". This somewhat unfortunate nomenclature has led some workers[10] to conclude that an equation of the form $k_1/k_2 = (\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}) \times$ (ZPE) may be implied. The latter formulation is, of course, not generally meaningful.

value). Subsequently, it was thought that the reduced mass corresponding to the two fragment masses instead of the two atomic masses should be used (fragment value). If we regard as simple bond rupture the case where the stretching force constant of the bond to be broken is set equal to zero in the transition state, we actually find that the fragment value is correct only if the centres of mass of the two fragments lie on the extensions of the line corresponding to the broken bond, as in $CD_3X \rightarrow (CD_3—X)^{\ddagger}$. Otherwise, the fragment value is only an approximation since there will be relative rotation of the two fragments in addition to relative translation in the decomposition motion; the malonic acid decarboxylation model is an example of the latter situation. If the usual designation of isotopic rate constants for malonic acid decarboxylation is used, $^{12}CH_2(^{12}COOH)_2 \xrightarrow{k_1} {}^{12}CO_2, {}^{12}CH_2(^{12}COOH)$

$(^{13}COOH) \xrightarrow{k_3} {}^{13}CO_2$, then $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ for $k_1/2k_3$ equals $1 \cdot 0054$, while the fragment value is $1 \cdot 0062$ and the Slater value is $1 \cdot 0198$. Values of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ for many model reactions are given in the tables of this paper and of the subsequent paper[6]. While the interpretation of the numerical values of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ is of interest, we do not intend to pursue this question further here.

Since the value of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ throws some light on the nature of the transition state, there has been interest in the determination of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ from experimental data in the region in the vicinity of room temperature (where most experiments are carried out). We want to look critically at the methods, which have been used principally for carbon isotope effects. For convenience, the discussion is restricted to isotope effects with (ZPE) > 1.

The methods which have been proposed for determining or bracketing the value of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ include[11, 12]: (i) extrapolation of a straight-line plot of ln (k_1/k_2) versus $1/T$ to infinite temperature to yield a lower limit to ln $(\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger})$, (ii) similar extrapolation versus $1/T^2$ to yield an upper limit to ln $(\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger})$, (iii) similar extrapolation, within the framework of the $\bar{\gamma}$ method, versus $\bar{\gamma}/T^2$, and (iv) the Yankwich–Weber–Ikeda[13, 14] (YWI) "semi-empirical" method. Methods (i) and (ii) are indeed valid at high temperatures where equation (4) is valid. Method (iii) gives the correct result if the value of the average frequency is known and if the $\bar{\gamma}$ method is applicable to the isotope effect; we have already pointed out the difficulty connected with the problem of the average frequency.

In a temperature region in which the isotope effect is expressible by equation (3), method (i) extrapolates to ln (MMI) which does not necessarily bear any relationship to ln $(\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger})$. In intermediate temperature regions, one can show that method (i) could lead to extrapolations higher or lower than ln $(\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger})$, which need not even lie between ln $(\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger})$ and ln (MMI). The use of method (ii) in the region where equation (3) is applicable yields ln $(\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger})$ = ln (MMI) + (ZPD)$/(T_1 + T_2)$, where ZPD is the isotope effect on the zero-point energy difference between reactant and transition state in units of °K, and T_1 and T_2 are the two temperatures through which the straight line is drawn†. Thus, if the zero-point

† Over a limited temperature range (T_1, T_2), one can fit an equation of the form $\alpha + \beta/T$ reasonably well by an expression $A + B/T^2$, and vice versa. Simple algebraic manipulations show then $B = \beta T_1 T_2/(T_1 + T_2)$, $A = \alpha + \beta/(T_1 + T_2)$, or inversely, $\beta = B(T_1 + T_2)/T_1 T_2$, $\alpha = A - B/(T_1 T_2)$.

energy factor is made to increase without changing $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ or the other factors in the rate ratio expression, the apparent value of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ or, more properly, the apparent value of its upper limit, from method (ii), will increase.

In the YWI method, the isotope effect is written $k_1/k_2 = (\text{TIF}) \times (\text{TDF})$ where TIF (temperature-independent factor) refers to $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ and TDF (temperature-dependent factor) refers to the rest of equation (2). YWI sought to establish a relationship between the temperature dependence of ln (k_1/k_2), in a given temperature range $(10^3/T = 3\cdot00$ to $2\cdot75)$, expressed by Δ ln (k_1/k_2), and the value of TDF at the mean value of $1/T$. With a limited number of model calculations, Yankwich and Ikeda[14] obtained a narrow range of plots of $\langle$ln $(\text{TDF})\rangle_{\text{av.}}$ versus Δ ln (k_1/k_2) with slopes $\sim 6\cdot5$– $9\cdot0\dagger$. In cases where Δ ln (k_1/k_2) values are too high to be used with these plots, we employ $\langle$ln $(\text{TDF})\rangle_{\text{av.}} = \Delta$ ln $(k_1/k_2) \times (0\cdot16 \pm 0\cdot02)^{-1}$ in the temperature range $10^3/T = 2\cdot75$–$2\cdot50$ as suggested by Yankwich and Weber[13]. The use of actual model calculations in the YWI method may compensate for a good deal of the error inherent in the other methods for determining $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$. Still, the answers obtained only have meaning if the actual experimental situation lies within the range of the models employed by YWI.

Table 3 presents some results corresponding to the isotopic rate ratio in the decarboxylation of malonic acid previously denoted as $k_1/2k_3$. Similar results have been obtained with ^{13}C-substitutions in other positions in malonic acid. We follow here the previously discussed procedure of subjecting the isotope effects calculated by the digital computer for various force field assumptions to the same kind of analysis to which one might subject experimental data (i.e., methods (i)–(iv), above). Calculated data from 275 to 500°K were employed. As with experimental results, there was usually no difficulty in making the straight line plots required, at least through the points in the upper hundred degrees of the temperature region.

Case I corresponds to the normal reactant force field and transition state force field previously used by the authors[7]. Transition state geometry and reactant geometry are the same. The carbon–carbon bond is broken in the transition state by lowering the relevant f_{CC} from $4\cdot4$ md/Å in the reactant to zero in the transition state. Cases II and III are similar to case I except that both carbon–carbon stretching force constants in the reactant were given the value $8\cdot8$ (case II) and $13\cdot2$ md/Å (case III). These cases were carried out to show that one obtains the result expected when the zero-point energy isotope effect is increased. Case IV is again similar to case I, but in the transition state, carbon–oxygen stretching force constants were lowered in order to increase the zero-point energy isotope effect. Case V corresponds to the normal reactant force field; the force constants in the transition state were adjusted to yield a large value of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ (the decomposition coordinate does, in fact, almost correspond to the so-called Slater coordinate[1]) but the over-all isotope effect was kept approximately the

†This method bears some relation to the high temperature approximation equation (4), which yields in this temperature range $\langle$ln $(\text{TDF})\rangle_{\text{av.}} = \Delta$ln $(k_1/k_2) \times 5\cdot75$. If equation (3) were valid, one would obtain $\langle$ln $(\text{TDF})\rangle_{\text{av.}} = \Delta$ln $(k_1/k_2) \times 11\cdot5 + $ ln (VP).

Table 3. Comparison of exact and derived values of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ for $k_1/2k_3$ in the decarboxylation of malonic acid

Case[a]	$10^4 \ln (\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger})$					$10^4 \ln (k_1/2k_3)$		$10^4 \ln$ (ZPE)
	Exact	$1/T$ plot	$1/T^2$ plot	$\bar{\gamma}$ method	YWI method	350°K	500°K	500°K
I	54	−12	89	79	90 ± 10	253	173	174
II	54	−31	132	98	122 ± 23	402	272	282
III	54	−31	174	111	163 ± 40	526	356	369
IV	54	−56	175	145	172 ± 44	571	381	402
V	202	44	215	196	172 ± 22	446	330	309

[a] Cases are explained in text.

same as in some of the other cases. In the use of the $\bar{\gamma}$ method here, the "historic"[1, 7] value of 900 cm^{-1} was employed for the average frequency in cases I, IV, and V. In cases II and III, where higher values of carbon–carbon stretching force constants were used in the reactants, values of 1300 cm^{-1} and of 1600 cm^{-1}, respectively, were employed. The values of ln $(\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger})$ obtained in the various cases are listed in *Table 3*. The $1/T$ plots do give lower limits here but the absolute values are not very useful. It should be noted that both positive and negative deviations from ln (MMI) $= 0$ occur. The $1/T^2$ plot does not consistently lead to the low actual value of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ in cases I–IV which must be compared with the high value in case V. The increase of ZPE does, as expected, increase the apparent value of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ (or rather its upper limit). The YWI method does not perform much better than the $1/T^2$ extrapolation. The $\bar{\gamma}$ method performs best, especially in cases II and III where some compensation has been introduced by making the indicated changes in the average frequency. As already mentioned, if the proper value of the average frequency were known, this method would yield the correct results.

The conclusion to be drawn from these considerations is that there are no *generally* valid methods available today for estimating $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ from measurements of rates in the vicinity of room temperature. In cases where one has some *a priori* feeling about the nature of the transition state, either the YWI procedure using model calculations or the $\bar{\gamma}$ method may function quite well.

CUT-OFF PROCEDURE

As the molecules involved in the computations become larger, the computations become more cumbersome and consume more computer time. There is some final limit for molecular size above which it is no longer feasible to make computations even with a high-speed computer. Also, there may be cases where the reaction centre is part of a large molecule whose exact nature is not known. There is, therefore, good cause for looking for methods of employing calculations with smaller molecules (or model molecules) to predict the results which would have been obtained in calculations with larger molecules. We have, so far, only carried out some preliminary investigations of this topic. All of these investigations have involved secondary isotope effects.

In the subsequent paper[6] secondary isotope effects in the absence of force constant changes at the isotopically substituted positions are discussed. This discussion leads one to suspect that, in the calculation of secondary isotope effects, the computational results would be little affected by large changes in that part of the molecule (either in reactant or in transition state) further removed from the isotopic atom(s) than two bonds, including, possibly, complete cut-off of all of these parts of the molecule. If $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ in the "cut-off" calculation and in the original calculation differed, one would expect to have to introduce a correction for just this factor to obtain the same effect in the cut-off case as in the original molecule computation. One should not, of course, cut off parts of the molecule containing atoms which are involved in coordinates coupling them to the isotopic positions

if there are changes in the force constants of these coordinates (such changes contribute to the over-all isotope effect).

Table 4 presents some data for the model reaction n-$CH_3CD_2CH_2X$ + X → (n-$CH_3CD_2CH_2X_2$)‡ where the indicated changes in CH stretching force constants and in HCH bending force constants on the β carbon atom were made between the reactant and the transition state. The last two

Table 4. Cut-off calculations for $CH_3CD_2CH_2X$ + X → ($CH_3CD_2CH_2X_2$)‡[a]

A. Values of isotope effect k_1/k_2

T(°K)	Reactant "molecule"				
	n-$CH_3CD_2CH_2X$[b]	C–CD_2CH_2X[c]	CHD_2CH_2X[d]	C–CD_2–C[e]	CD_2[f]
50	1·8763	1·8669	1·8762	2·0190	2·1224
200	1·1920	1·1918	1·1915	1·1917	1·2061
300	1·1244	1·1244	1·1255	1·1222	1·1296
500	1·0689	1·0690	1·0699	1·0661	1·0683
1000	1·0271	1·0272	1·0279	1·0243	1·0245
$\nu_{1L}^‡/\nu_{2L}^‡$	1·0027	1·0028	1·0035	1·0000	1·0000

B. Decomposition of isotope effect at 300°K

MMI	1·0725	1·0756	1·1005	1·0000	1·0000
EXC	0·9547	0·9533	0·9321	0·9982	0·9965
ZPE	1·0982	1·0966	1·0973	1·1242	1·1336

[a] Reactant: f_{CX} = 4·0, f_{CD} = 4·5 md/Å, f_{DCD} = 0·53 md-Å; transition state: $f_{CX_1}^‡$ = 0·0, $f_{CX_2}^‡$ = 4·0, $f_{CD}^‡$ = 4·36 md/Å, $f_{DCD}^‡$ = 0·445 md-Å.
[b] $CH_3CD_2CH_2X$ + X → ($CH_3CD_2CH_2X_2$)‡
[c] C–CD_2CH_2X + X → (C–$CD_2CH_2X_2$)‡
[d] CHD_2CH_2X + X → ($CHD_2CH_2X_2$)‡
[e] C–CD_2–C ⇌ C–C*D_2–C
[f] CD_2 ⇌ C*D_2

calculations actually just refer to calculations of isotopic equilibrium constants with the same force constant changes at the isotopic positions, i.e., C–CD_2–C ⇌ C–C*D_2–C, CD_2 ⇌ C*D_2 (* indicates force constant changes). In these two calculations, no $\nu_L^‡$ appears and, consequently, the apparent value of $\nu_{1L}^‡/\nu_{2L}^‡$ equals unity. It is seen that in the room temperature region only the last calculation (CD_2) performs at all unsatisfactorily. The C–CD_2–C calculation does give somewhat high values at very low temperatures. The first two cases have almost identical $\nu_{1L}^‡/\nu_{2L}^‡$. The introduction of a correction for $\nu_{1L}^‡/\nu_{2L}^‡$ values into the third and fourth cases (e.g., multiply fourth case by 1·0027) brings these into closer agreement with the first case at room temperature and above. Attention is drawn to the fact that the MMI factors for the equilibrium cases are quite different, not because of equilibrium, but because no X atom is added. Again it is evident that only the triple product (MMI) × (EXC) × (ZPE) is important.

A number of other, similar cut-off calculations have yielded similar results. It is of interest that when one examines the calculated frequencies for different "cut-off reactions", which all yield similar isotope effects, one finds different isotope effects on vibrational frequencies in different frequency regions.

Some computations have been carried out in order to test the importance of $\nu_{1L}^‡/\nu_{2L}^‡$ on the cut-off procedure. CD_3CH_2X + X → ($CD_3CH_2X_2$)‡ has been studied both as a reaction (i.e., 20 real frequencies in $CD_3CH_2X_2$) with $\nu_{1L}^‡/\nu_{2L}^‡$ = 1·0387 and as an equilibrium (i.e., 21 real frequencies in

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$CD_3CH_2X_2$) with no $\nu_L^{\ddagger}$ appearing. The force constant changes at the isotopic positions were kept the same. The ratio of the isotope effect on the rate to that on the equilibrium is within 0·4 per cent of $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ at 200°K and within 0·1 per cent at 300°K.

Obviously, further study on cut-off procedures is necessary in order to define the real limits of such procedures. Study on primary isotope effects is especially necessary. (Some such study has already been carried out by Sharp and Johnston[15]). For the present, we are much encouraged by our preliminary results.

CONCLUSIONS

Computer programmes for the evaluation of kinetic isotope effects, on the basis of given reactant and transition state force fields, have been employed to study some of the approximation procedures which have been used in the theoretical treatment of isotope effects. The general danger of just considering one part or another of the theoretical equations has been pointed out. The interplay of the three factors which make up equation (1) suggests further search for expansion methods which express the isotope effect even at room temperature directly in terms of force constants, geometries, and masses†. The high temperature equation and the so-called gamma-bar equation have been found of great qualitative utility, but there exists some question about their general quantitative usefulness in the room temperature region at present. Difficulties involved in obtaining the isotopic frequency ratio of the decomposition frequencies from room temperature region experiments have been pointed out. Indications have been obtained that the isotope effects for very large molecular systems can be studied theoretically by working with smaller molecules.

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† Some work in this direction may be found in reference 9, as has already been mentioned.