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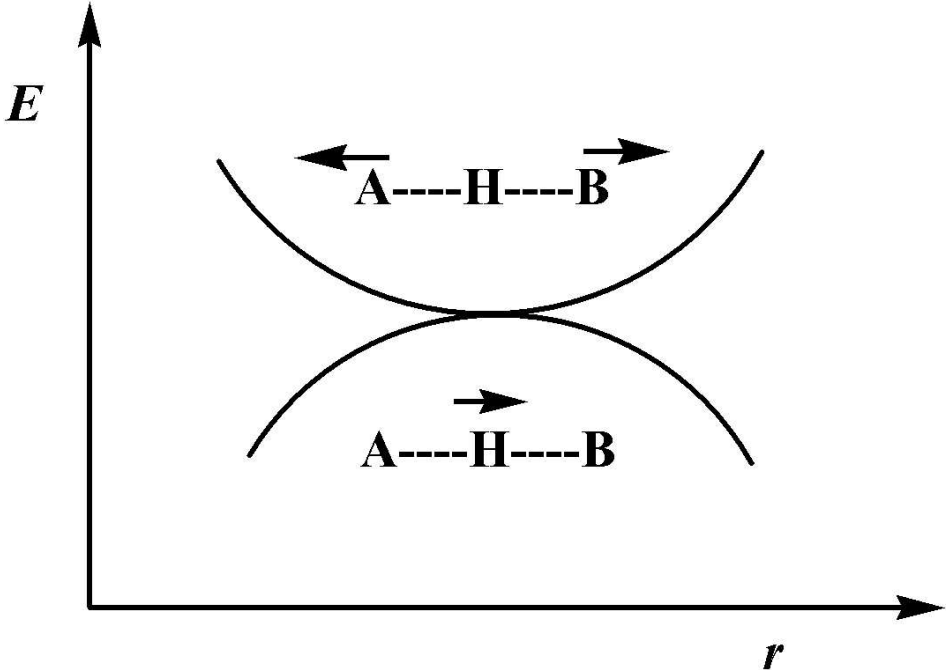
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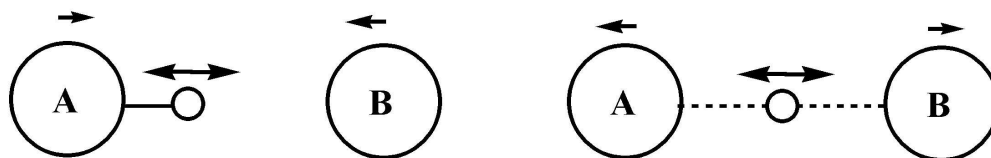
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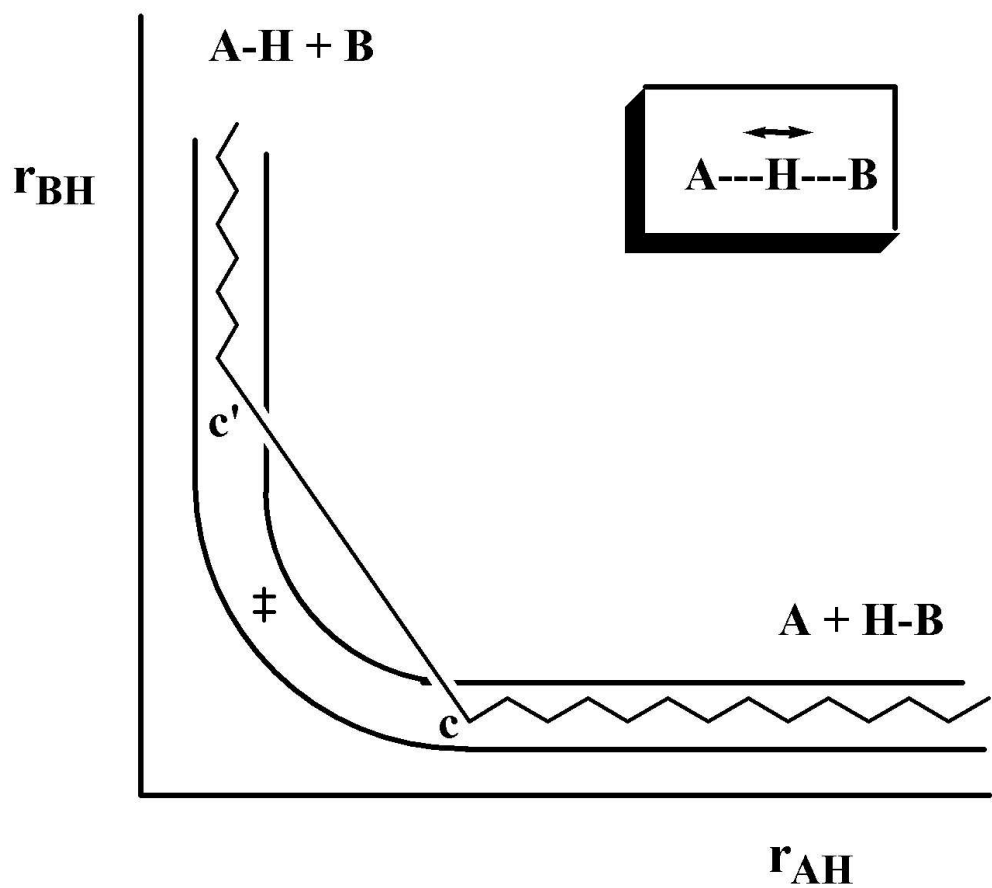




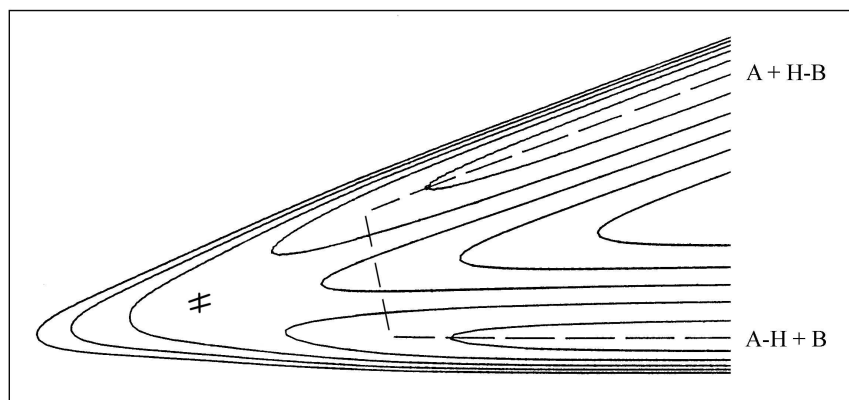
Reaction coordinate and 'real' vibrations of the transition state
80x58mm (360 x 360 DPI)



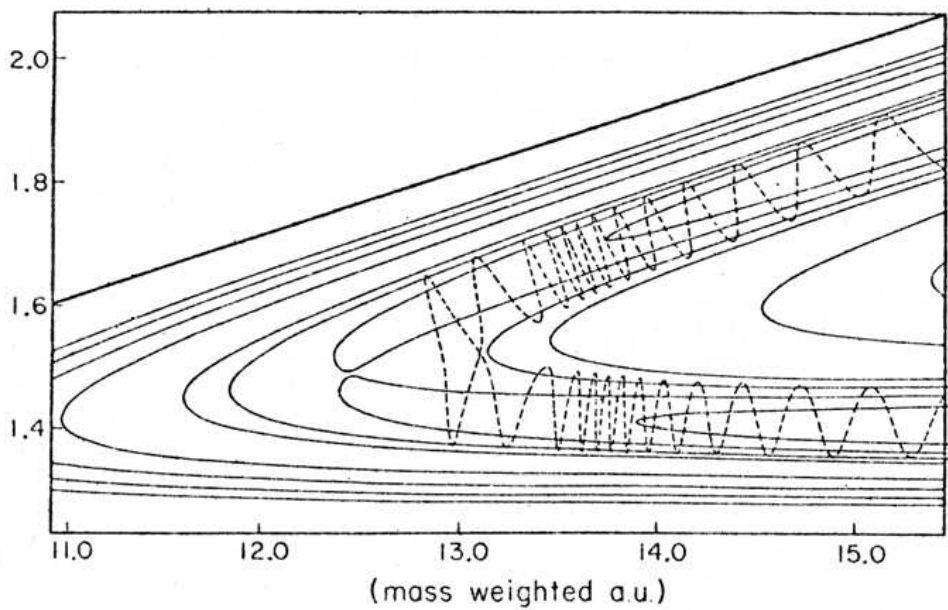
Collinear collision complexes (a) early stage (b) at point of rebound
155x27mm (360 x 360 DPI)



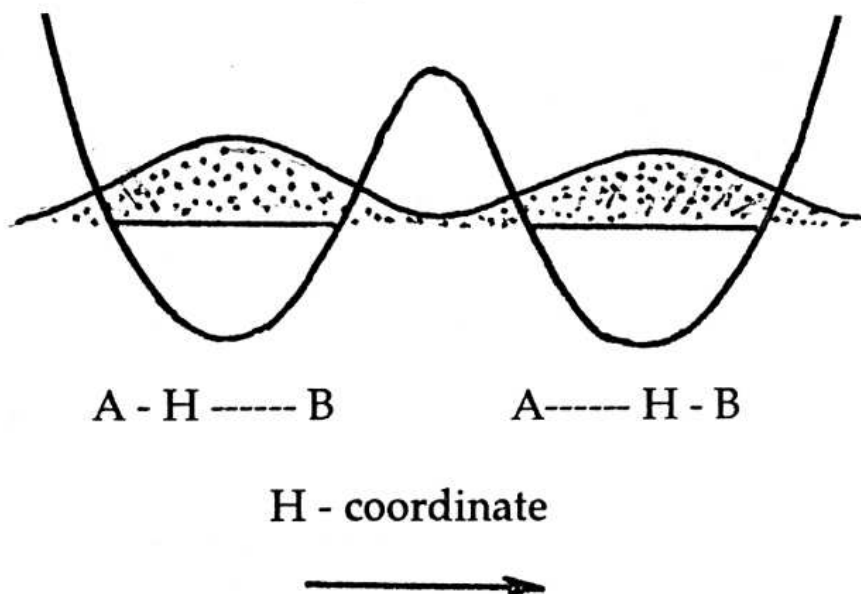
Reaction coordinate diagram showing the vibrational motion of hydrogen within a collision complex leading to tunnelling
91x80mm (360 x 360 DPI)



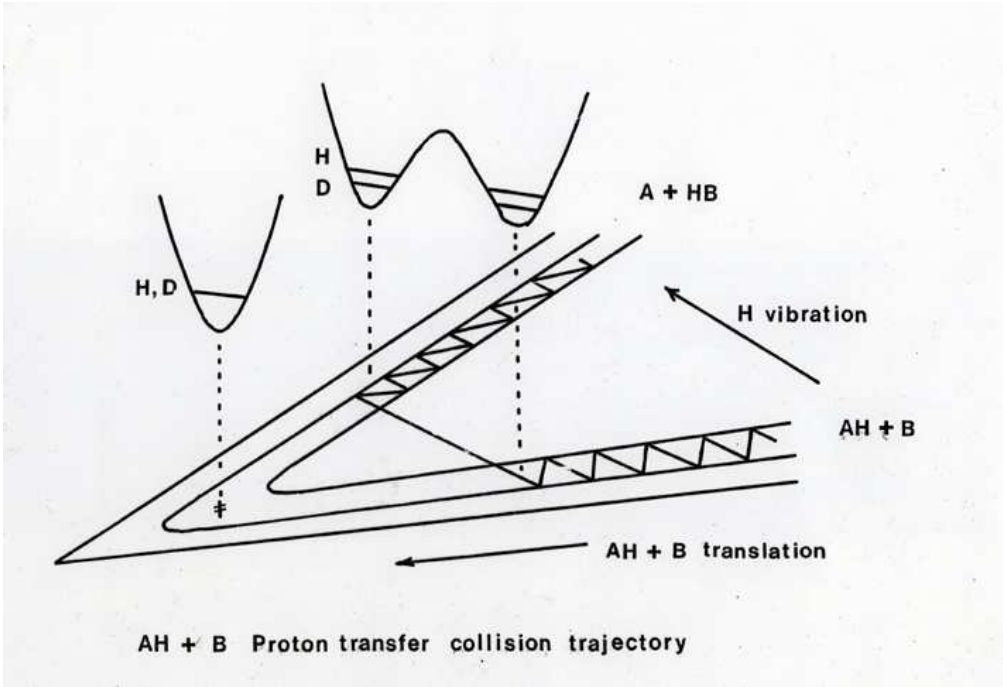
Potential energy surface showing minimum energy and tunnelling pathways
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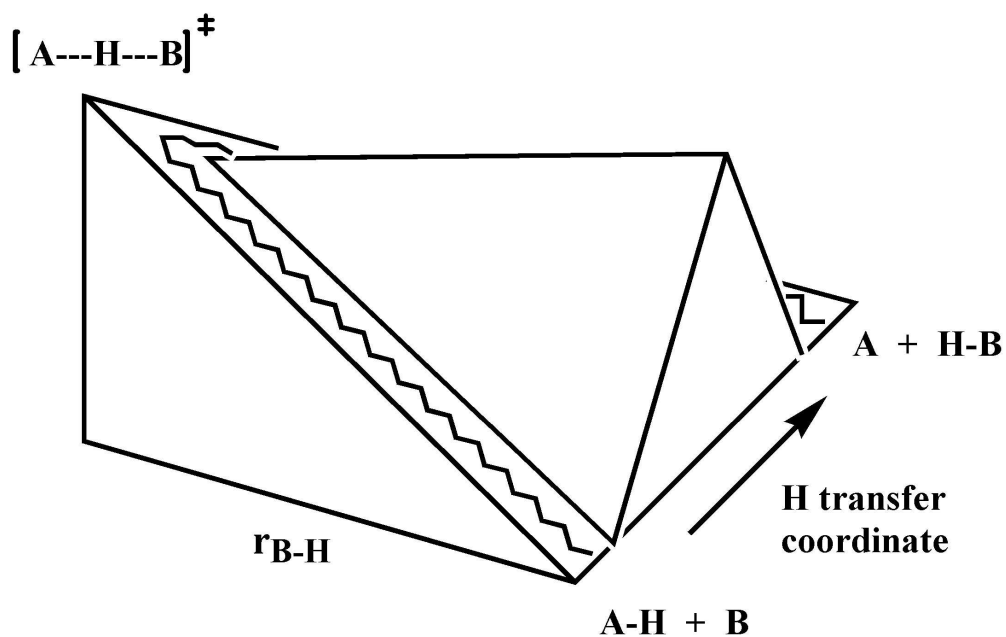
Calculated trajectory (dashed line) of collision complex subject to tunnelling²⁷
187x115mm (96 x 96 DPI)



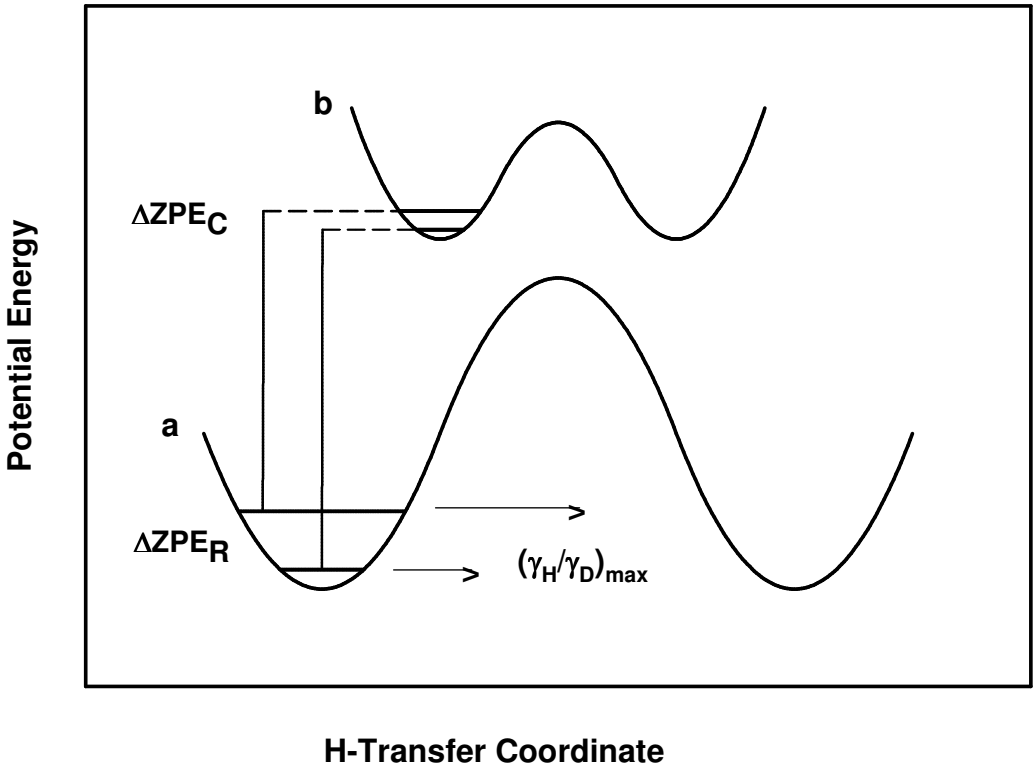
Cross section along tunnelling coordinate cc' in Figure 3 showing overlap of zero point vibrational wave functions
187x134mm (96 x 96 DPI)



Projection of cuts across a potential surface onto a skewed reaction coordinate for hydrogen transfer at the transition state and along a tunnelling coordinate
187x128mm (96 x 96 DPI)



Classical barrier to reaction and a 'non-tunnelling' reaction trajectory
153x98mm (360 x 360 DPI)



A pictorial representation of zero point energy and tunnelling contributions to primary hydrogen isotope effects

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ABSTRACT

The interpretation of primary hydrogen isotope effects in terms of isotopic sensitivities of zero point energies in the reactants and transition state is reviewed. The reader is reminded that the transition state for a hydrogen transfer reaction corresponds to the position of maximum energy on the minimum energy path defined by the motion of the heavy atoms between which hydrogen is transferred. Tunnelling occurs through the potential energy barrier separating the reactant and product channels of the potential energy surface for this reaction. It is a consequence of rapid vibrational motion of the hydrogen within a collision complex and the overlap of vibrational wave functions between reactant and product sides of the barrier. Comparing zero point energies of a tunnelling complex and a hydrogen bond confirms results of calculations indicating that the zero point energy of the complex is likely to be less than that of the reactants. It follows that there should be a compensation between contributions from zero point energy changes and tunnelling which may explain why tunnelling rarely leads to very large isotope effects at ambient temperatures. The isotopic sensitivity of the zero point energy of the transition state is discussed in terms of variations in force constants of reacting bonds within a three-centre model. A shift in isotopic sensitivity from the reaction coordinate mode to real stretching vibration as the structure of the transition state becomes more reactant- or product-like, which provides a basis for the Westheimer effect, contrasts with the behaviour of hydrogen bonds, for which there is no change in isotopic sensitivity of the two stretching modes.

INTRODUCTION

It is more than fifty years since Bigeleisen and Wolfsberg interpreted primary hydrogen isotope effects in terms of differences in isotopically sensitive zero point energies between reactants and transition state.¹ In 1961 Westheimer took that interpretation a step further by identifying the stretching vibration associated with the transferring proton (not representing the reaction coordinate) as a key factor controlling the magnitude of the isotope effect.² It was argued that for a symmetrical transition state, in which the force constants to the reacting hydrogen atom are the same, there is no motion of hydrogen in this vibration and consequently no change in zero point energy upon substitution of deuterium for hydrogen.²⁻⁴ For a symmetrical transition state therefore the full effect of a zero point energy change in the hydrogen stretching vibration of the reactant was expressed in the isotope effect, which achieved a maximum value in the range $k_H/k_D = 7-10$ depending on the vibration frequency of the reactant and the extent to which isotopically sensitive bending vibrations were cancelled between reactants and transition state.⁴⁻⁶ For reactant and product like transitions states k_H/k_D was presumed to approach 1.0 and a (small) equilibrium isotope effect respectively.

The notion that primary hydrogen isotope effects possessed maximum values (the Westheimer or Melander-Westheimer effect)²⁻⁴ strongly influenced experimental investigations in the following twenty years. A considerable effort was expended in demonstrating that measurements of k_H/k_D for a series of related proton transfers, such as the base-promoted ionisation ketones and nitroalkanes, did indeed exhibit a maximum when plotted against equilibrium constants if these were varied over a sufficiently wide range.⁷⁻⁹

Today greater interest is focused on the contribution of quantum mechanical tunnelling than zero point energy to hydrogen isotope effects,¹⁰⁻¹⁴ as witnessed by the symposium in print of which this paper forms a part. Historically, tunnelling has been a focus of many experimental and theoretical studies of hydrogen transfer reactions in the gas phase.¹⁵⁻¹⁹ A main concern of these papers was with quantum corrections to a transition state theory based calculation of reaction rate constants for semi-empirical potential energy surfaces arising both

from tunnelling at low temperatures and reflection back of collision complexes crossing the energy barrier at high temperatures.²⁰⁻²⁴ Surprisingly there is little or no mention of the Westheimer effect among the many studies of isotope effects for gas phase hydrogen transfer reactions. This must be partly a consequence of the lack of series of reactions within which the reactivity or equilibrium constants can be varied systematically in the manner possible for organic reactions in solution.

While the main principles governing tunnelling were worked out in the years before or soon after Westheimer's treatment of zero point energies,¹⁵⁻¹⁹ the conclusions reached were published in papers which sometimes included a significant mathematical treatment of the topic. One widely read text book in which they were discussed was H.S. Johnston's "Gas Phase Reaction Rate Theory".¹⁵ However, a principal focus of this text was on the then new studies of reactive molecular scattering made possible by the development of molecular beams and studies of infrared chemiluminescence, as well as the first serious computer-based statistical simulations of reaction rates. Despite its importance, it is perhaps not surprising that this did not reach a wider audience of experimental organic and inorganic chemists. The purpose of the present paper is not to present new experimental or theoretical results but to provide a straightforward introduction to tunnelling complementary to the Westheimer-Melander treatment of zero point energy.

Early Treatments of Tunnelling

The name of R. P. Bell is associated with early treatments of tunnelling and his monograph published in 1980 still provides the best introduction to the topic.²⁵ At a time before computers gave fairly easy access to multidimensional potential energy surfaces, Bell developed approximate treatments of tunnelling based on one dimensional energy barriers and derived a quantum correction to the reaction coordinate mode of a hydrogen-transfer transition state bearing a close analogy with the zero point energy correction to the orthogonal stretching vibration^{5,6} which was the main focus of Westheimer and Melander's treatment. These two vibrations are shown schematically for a saddle point and transition state in Fig 1. The curvature of the potential energy surface along the reaction coordinate

can be represented by a negative force constant f and associated with an imaginary vibration frequency ν_L^\ddagger . The relationship between f and ν_L^\ddagger is shown in eqs 1 and 2 where f refers to the curvature of a quadratic potential energy surface, E is the potential energy, r is a displacement along the reaction coordinate and μ the reduced mass. The value of ν_L^\ddagger is a significant parameter characterising permeability to tunnelling. Thus a high curvature (large f and large imaginary value of ν_L^\ddagger [in units $i \text{ sec}^{-1}$]) implies a 'thin' barrier and consequently greater correction for tunnelling through the barrier relative to passage over it.

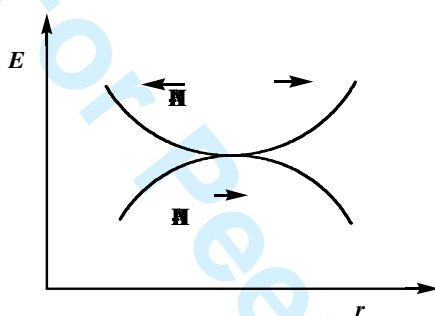


Figure 1 Reaction coordinate and 'real' vibrations at a transition state

$$d^2E/dr^2 = -f \quad (1)$$

$$\nu_L^\ddagger = (1/2\pi)\sqrt{f/\mu} \quad (2)$$

While the attempt to simplify and develop a mathematically tractable treatment of tunnelling in the 1950s was understandable and necessary, in the long run an emphasis on tunnelling as a correction to a transition state-based reaction rate may have been misleading. As outlined below for the most commonly studied transfer of a hydrogen between heavy atoms the principal pathways for tunnelling do not lie along the reaction coordinate and the barrier subject to tunnelling does not correspond to the 'classical' minimum energy path. Thus although an assessment of tunnelling based on this barrier provides a convenient and pragmatic correction to a transition state-based rate constant for relatively small amounts of tunnelling, it is perhaps not the best starting point for understanding the origin of tunnelling.

A PICTORIAL MODEL FOR TUNNELLING

To represent tunnelling qualitatively and pictorially it is helpful to recognise (a) that the one-dimensional energy barrier normally shown for a reaction, which represents a cross section along the minimum energy path (and reaction coordinate) of a potential energy surface, differs from the barrier through which tunnelling occurs, and (b) that the atomic and molecular motions leading to passage over this barrier also differ from those leading tunnelling. These points can be demonstrated by considering representative trajectories of reacting molecules and the potential energy barriers to their reaction.

Reaction coordinate for hydrogen transfer

The reaction coordinate for a hydrogen transfer corresponds to the collision of two 'heavy' atoms (or molecules) to one of which a hydrogen atom is attached. In figure 2 the heavy atoms are shown as A and B. In the course of a collision they approach each other quite 'slowly' in comparison with the motion of the much lighter hydrogen atom. The difference in masses indeed allows us to a good approximation to separate the two motions. Fig 2 is intended to show that on the time scale of the collision the hydrogen is vibrating rapidly between the two atoms.

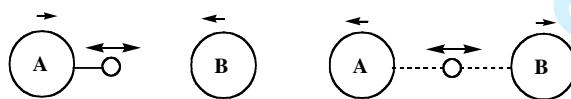


Figure 2 Collinear collision complexes for hydrogen transfer: (a) early-stage (b) at point of rebound

The transfer of a hydrogen atom ($A-H + B \rightarrow A + H-B$) is illustrated in Fig 3 on a reaction coordinate diagram from which all but two potential energy contours bounding the minimum energy path for reaction have been omitted. The position of the maximum in energy along this pathway is indicated by the symbol \ddagger representing the transition state. The rapid motion of the hydrogen within the collision complex is indicated by the zig-zag path of a

collision trajectory in which the vibration of A-H is dominant as the reactants approach each other and of B-H as the products separate.

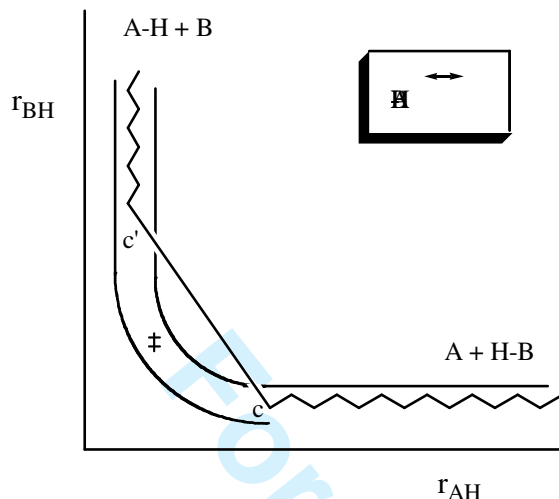


Figure 3 Reaction coordinate diagram showing the vibrational motion of hydrogen within a collision complex leading to tunnelling

The collision trajectory shown does not pass through the transition state but cuts the 'corner' at which it lies. The corner-cutting pathway is denoted cc' and corresponds to motion of the hydrogen between the two heavy atoms while their positions remain fixed (i.e. the increase in r_{AH} equals the decrease in r_{BH}). As shown below, reaction complexes which follow this pathway are tunnelling through an energy barrier. They lead to an increase in reaction rate because the tunnelling occurs at a lower energy than that of the transition state. The reaction path through the transition state surmounts a 'semi-classical' reaction barrier (also shown below) without resort to tunnelling because at the transition state there is no further barrier hindering transfer of the proton. The barrier is 'semi-classical' (or 'quasiclassical'²⁶) because although it does not involve tunnelling it does include the zero point energies of the transition state and reactants.

For a symmetrical (linear) transition state there is no appreciable motion of hydrogen independently of the heavy atoms other than that constrained by stretching or bending vibrations. For a collinear reactive collision following the minimum energy path for reaction the transition state is at or close to the point of rebound of the reacting molecules. From this point the hydrogen 'rides on the back' of the reagent B along the

product energy channel having been delivered to the transition state attached to A. For a proton transfer, because of the high energy of a bare proton, the combined bonding of A and B to the proton along the reaction path is strongly conserved.

Potential energy surfaces.

Most of the features of a qualitative description of tunnelling are contained in Fig 3. The figure shows that tunnelling hydrogens do not pass through the transition state and that the barrier with which tunnelling is associated differs from that along the reaction coordinate.²⁷ The difference in barriers may be shown by including the potential energy as contours as in Fig 4. In this figure the curvature of the reaction coordinate is distorted to allow the use of mass-weighted coordinates. The progress of a (classical) molecular collision can then be represented by a single line tracing the trajectory of a 'billiard ball' directed on to the surface with the appropriate energies of translational and vibrational motion. However, note that, as usual, only linear configurations of the A-H-B collision complex are represented and that the dashed line traces the minimum energy path for reaction up to and following displacement of the hydrogen by tunnelling.

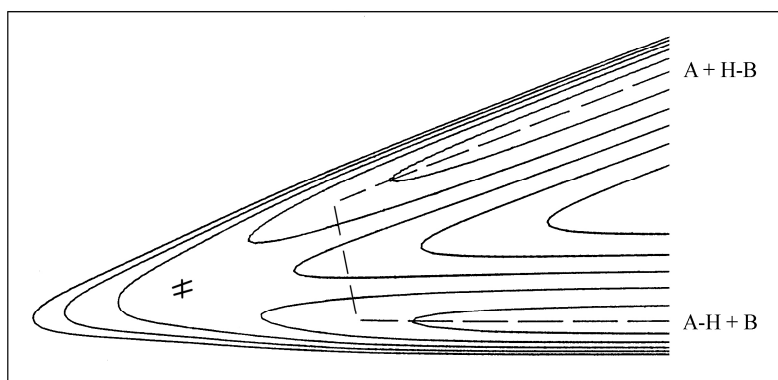


Figure 4 Potential energy surface showing minimum energy and tunnelling pathways

The trajectory of a molecular collision leading to tunnelling is shown in figure 5 reproduced from a paper of Babamov and Marcus in 1981.²⁸ It can now be seen that the zig-

zag pathway of the trajectory implies that at the limit of each vibration the hydrogen impacts on the barrier separating the reactant and product channels. It is at the points of impact that tunnelling is liable to occur. As implied above, tunnelling is easier when the barrier is thinner and it can be seen that this is true when the collision complex is closer to the transition state.

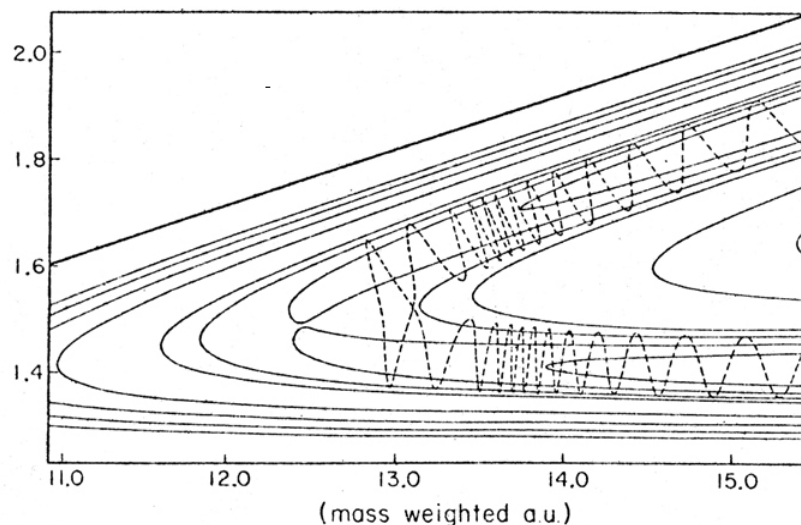


Figure 5 Calculated trajectory (dashed line) of collision complex subject to tunnelling.²⁸

Whether or not in practice transfer of the hydrogen occurs by tunnelling will depend on the temperature and rate of reaction. At sufficiently high temperatures and for fast reactions (with low energy barriers) a large proportion of collisions will possess sufficient energy to surmount the 'normal' or heavy-atom reaction barrier without tunnelling. Other things being equal tunnelling should be most important for slow reactions at low temperatures or with high barriers. Good recent examples of both situations are provided by double proton transfers in hydrogen-bonded carboxylic acid dimers discussed in this issue by Horsewill²⁹ and by the intramolecular transfer of a proton of the carbene hydroxymethylene to form formaldehyde ($\text{HOCH}_2 \cdot \rightarrow \text{O}=\text{CH}_2$) at 11 °K in an argon matrix.³⁰

The reaction trajectory in Fig 5 is an idealised one. The reaction rate is determined by averaging over a great variety of collisions with different initial translational and, indeed, rotational energies, as well as for non-collinear collisions. Moreover, the

representation of the tunnelling trajectory by a straight line through the energy barrier strictly implies that the proton moves fully independently of the heavy atoms. If this were true the angle between the reactant and product channels of the surface would be zero. In practice typical angles are 15° for transfer of a hydrogen and 30° for the corresponding transfer of deuterium between carbon, oxygen or nitrogen atoms.²⁶ Moreover the sharp curvature of the reaction path and relatively independent motion of the tunnelling hydrogen in Figs 4 and 5 is characteristic of hydrogen transfer between heavy atoms. The behaviour of the well studied isotope exchange of hydrogen molecules and hydrogen atoms is less straightforward in that the tunnelling involves motion of three atoms implying a curved trajectory in e.g. Fig. 3.^{26,31} It is also an approximation to suggest that semi-classical and tunnelling rates of reaction are fully separable.²⁶

Quantum mechanical description of tunnelling.

To complete a description of tunnelling an explanation of the barrier penetration is required. This arises from the existence of zero point (and higher) energy levels for the vibrating hydrogen atom in the reactant and product reaction channels. The vibrations are associated with wave functions which allow extension of the bond to hydrogen beyond its classical limits. In Fig 6 these zero point energies and the associated vibrational wave functions are shown for a cross section through the surface along the tunnelling reaction path cc' in Fig. 3 and extending across the reactant and product channels to the edges of the potential energy surface. The cross section is a double well potential which includes configurations of the collision complex in the reactant (A-H---B) and product (A---H-B) reactant channels, for which the A-B distance is the same but the position of the proton differs. The figure shows a symmetrical reaction in which A and B are equivalent or nearly so.

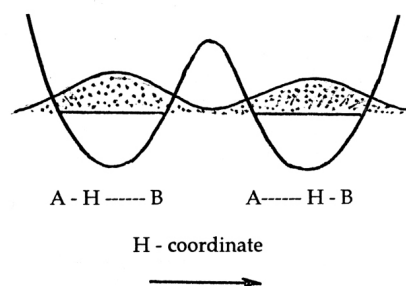


Figure 6 Cross section along tunnelling coordinate cc' in Fig 3 showing overlap of zero point vibrational wave functions

Tunnelling between the two configurations is possible if there is significant overlap of the wave functions. This can occur (a) if the barrier between the channels is sufficiently thin (b) if the energies of the vibrations are closely matched. Strictly speaking the symmetrical situation shown corresponds to 'coherent' tunnelling which is most commonly associated with reversible phenomena such as inversion of a molecule of ammonia. Transfer of hydrogen atoms would normally be represented by incoherent tunnelling where the energy levels differ (and the product is of lower energy than the reactant). Then matching of energy levels may be achieved for reactions in solution by coupling with solvent interactions, especially for proton transfer for which there will normally be a strong solvent interaction with an atom bearing a positive or negative charge in the reactants or products. However, even in the gas phase matching may be achieved at an appropriate distance between the heavy atoms within a collision complex.

The energy levels in Fig 4 correspond most obviously to zero point energies, but the discussion appears not to be qualitatively changed if some or many reaction trajectories involve vibrational excitation. In principle such excitation should favour tunnelling, as it allows access to a thinner barrier and more favourable overlap of wave functions. Moreover for an unsymmetrical barrier and highly exothermic reaction it is likely that hydrogen transfer will occur from the zero point energy level of the reactant to a vibrationally excited state of the product, even for reaction over the (semi) classical energy barrier.³⁵

It should be added that most computational treatments of hydrogen transfer include tunnelling not as the resonance phenomenon illustrated in Fig. 6 but as a hydrogen atom impinging on an energy barrier, as considered by Bell. Much of the above discussion, which emphasises the particle rather than wave character of the proton, is more appropriate to that concept. Strictly speaking Fig 6 represents a condition of resonance in which the hydrogen is delocalised between reactant and product states and relaxation of the heavy atoms of the collision complex relocalises it in its reactant or product structure.

Good introductions to the different ways of analysing tunnelling are provided in the introductions to several papers in this symposium including references 26, 29 and 32. Also pertinent are papers by Siebrand³³ and Kutznetsov.³⁴ A fundamental problem is to sum contributions over a range of energies and structures of collision complexes. While rate constants based on transition state theory provide a good approximation to quantised trajectory calculations on potential energy surfaces when tunnelling is not taken into account it has been much more difficult to find a correspondingly convenient approximation for calculating a rate constant when tunnelling is important.

Tunnelling by deuterium can be expected to be less effective than for hydrogen because the larger mass of deuterium implies a more localised vibrational wave function with less overlap between configurations of collision complexes in reactant and product valleys. In addition, the lower zero point energy of a bond to deuterium implies that the vibrating atom is impinging on the barrier to atom transfer at a lower energy and hence greater barrier width than the hydrogen.

Finally, two more representations of potential energy surfaces for hydrogen transfer between heavy atoms are shown in Figs 7 and 8. Fig 7 shows a projection of the double well potential of Fig 6 on a reaction coordinate diagram based on Fig 4 including an idealised reaction trajectory corresponding to tunnelling between the wells. Also shown is the disappearance of the double well, and hence of a barrier to proton transfer, at the transition state (the cross section for the single well should be at right angles to that for the double well

for the symmetrical reaction shown). The direction of a proton transfer trajectory with the positions of the A and B atoms fixed is shown by the arrow labelled 'H-vibration'.

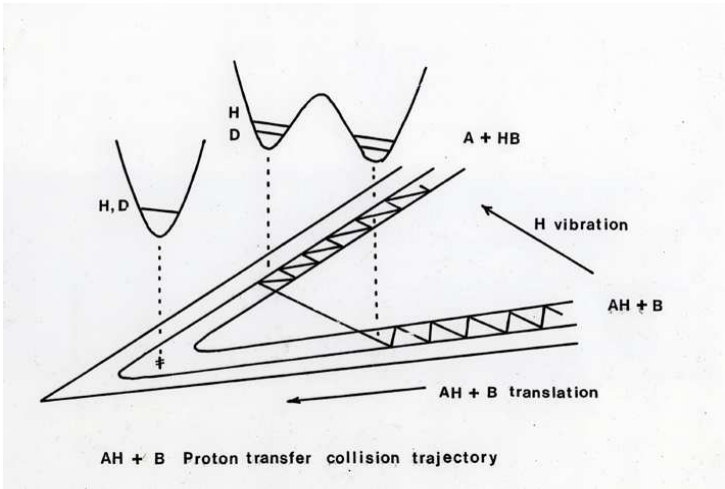


Figure 7 Projection of cuts across a potential energy surface onto a skewed reaction coordinate for hydrogen transfer at the transition state and along a tunnelling coordinate

Fig 8 is a schematic representation of the classical barrier for a heavy atom collision leading to transfer of a hydrogen without tunnelling. Again note that there is no independent movement of the hydrogen along this reaction coordinate. The hydrogen is compressed in the collision between the heavy atoms and in principle rebounds with either A or B with approximately equal probability for a collision trajectory reaching the transition state.

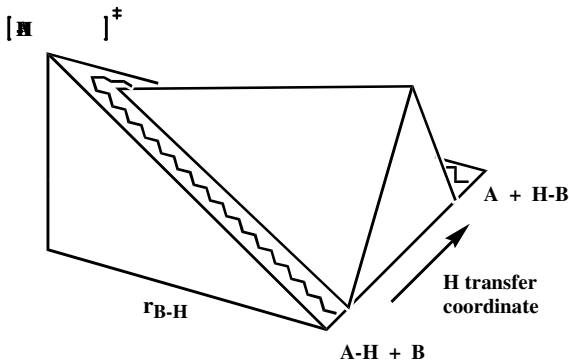


Figure 8 Classical barrier to reaction and a 'non-tunnelling' reaction trajectory

TUNNELLING AND ZERO POINT ENERGY

The barrier to the reaction in Fig. 8 is classical rather than semi-classical because no zero point energies are shown. In practice collision complexes do have zero point energy. For the reaction $A-H + B \rightarrow A + H-B$, the zero point energy of a reactant-like complex should approximate that of the A-H vibration and that of a product-like complex the B-H vibration. The zero point energy can be seen as providing a variable 'flat bottom' above the valley floors of a potential energy surface corresponding to the minimum energy pathway between reactant and products. It is then interesting to ask how the magnitude of this zero point energy varies with the geometry of collision complexes based on an analogy with hydrogen bonds or from calculations for theoretical or semi-empirical potential energy surfaces.¹⁸

Studies of O-H---O hydrogen bonds in crystals allow access to a wide range of geometries.^{35,36} In general, hydrogen bonding reduces the frequency of the covalent O-H stretching vibration and introduces a low frequency vibration which corresponds to a hindered translation in the limit of a very weak hydrogen bond. For the few symmetrical hydrogen bonds known, such as HF_2^- ,^{37,38} the vibrations conform to the characteristic symmetric and asymmetric stretching vibrations we associate with other linear three centre symmetrical molecules such as CO_2 .

The changes in geometry for different strengths of hydrogen bonds have been considered to map the reaction coordinate of a proton transfer reaction.^{39,40} In a similar way we might take the changes in vibration frequency as mapping the variation in isotopically sensitive zero point energy along this coordinate. If the vibration frequencies of alcohols in the gas phase and of carboxylic acid-carboxylate anion complexes in the solid state offer suitable guides we can say that this frequency decreases from 3600 cm^{-1} for a covalent O-H bond to 700 cm^{-1} for hydrogen symmetrically bound between two oxygen atoms. These measurements apply to equilibrium configurations of hydrogen bonds, but there is some indication that 'dynamic' compression of bond distances in molecular collisions affect the vibration frequencies similarly.⁴¹ While it is a large step from equilibrium measurements for hydrogen bonds between electronegative atoms to a collision complex for a proton or

hydrogen transfer from a carbon atom, it seems reasonable to suppose that a similar loss of zero point energy accompanies compression of (say) a C-H bond in a molecular collision.

If we consider the relationship between contributions from zero point energy and tunnelling to an isotope effect it has sometimes been supposed that the two effects augment each other. However, if we examine limiting cases for which, on the one hand, all collision complexes pass over an energy barrier and, on the other, all hydrogen atoms tunnel through it, it seems more reasonable to conclude that the two contributions are complementary.

Thus, in the first limit the isotope effect is given by eq 3, in which ΔZPE^\ddagger and ΔZPE_R are differences in H and D isotopic zero point energies in the transition state and reactants respectively, kT is the thermal energy, and for simplicity contributions from changes in isotopic partition functions are neglected.

$$k_H/k_D = e^{-(\Delta ZPE^\ddagger - \Delta ZPE_R)/kT} \quad (3)$$

For the second limit we suppose that reaction occurs from the bottom of the reactant valley of a potential energy surface and that the zero point energy of the reacting collision complex is not appreciably perturbed from that of the reactants. The isotope effect is then expressed as in eq 4 by the ratio of tunnelling (transmission) coefficients for the H and D isotopes, γ_H/γ_D . The ratio can be treated as an upper limit $[(\gamma_H/\gamma_D)_{\max}]$ because the width of the proton transfer barrier for a reactant-like collision complex is large and because the (zero point) energy separation between H and D complexes is at a maximum. The difference in zero point energy does not contribute directly to tunnelling but it implies a narrower effective barrier for hydrogen than deuterium. This is illustrated in Figure 9a.

$$k_H/k_D = (\gamma_H/\gamma_D)_{\max} \quad (4)$$

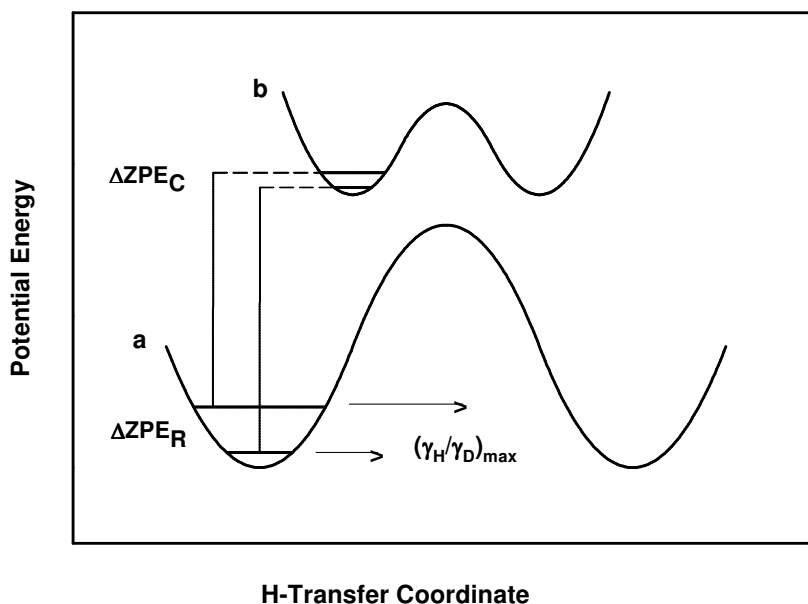


Fig 9 Energy barriers for hydrogen tunnelling: (a) for a reactant-like collision complex (A-H----B) and (b) a collision complex closer to the transition state (A--H---B) . The hydrogen transfer coordinates for the complexes correspond to cross sections at different points on the 'heavy atom' coordinate of Fig 8. As indicated in fig 8 (and figs 4, 5 and 7) the energy maximum for barrier (b) should be lower than that for (a). For clarity in a one-dimensional representation energy curve (b) is displaced vertically.

More generally the isotope effect will reflect a combination of zero point energy and tunnelling contributions corresponding to a collision complex which is intermediate in structure between reactants and transition state. H and D zero point energies and the barrier to hydrogen transfer for such a complex are shown in Fig 9b. Now the isotope effect depends not only on tunnelling but on the difference in zero point energies of the complex and reactant, $\Delta ZPE_C - \Delta ZPE_R$. The contribution of the two factors is expressed in eq 5. Because the barrier to hydrogen transfer for the complex is narrower and the difference in energy of H and D complexes is smaller, the tunnelling contribution to the isotope effect, γ_H/γ_D , is less than for a more reactant-like complex. However, this reduced tunnelling contribution is offset by a favourable zero point energy effect.

$$k_{\text{H}}/k_{\text{D}} = (\gamma_{\text{H}}/\gamma_{\text{D}}) e^{-(\Delta\text{ZPE}_{\text{C}} - \Delta\text{ZPE}_{\text{R}})/kT}$$

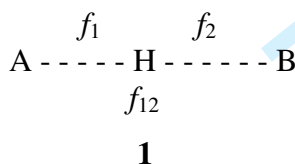
In practice rate constants represent many reaction trajectories with tunnelling occurring from a range of structures of collision complexes. However, if tunnelling and zero point energy contributions vary between the above limits it is clear that the zero point energy term should be smaller where $\gamma_{\text{H}}/\gamma_{\text{D}}$ is larger and vice versa. In other words one can envisage a pay off between zero point energy and tunnelling contributions to isotope effects, so that as tunnelling increases the zero point energy effect is reduced. The compensation between the two effects could offer an explanation as to why large primary hydrogen isotope effects (i.e. > 10) at ordinary temperatures (near 25°) are not common and that measured isotope effects remain within the semiclassical limits implied by zero point energy changes even where the contribution of tunnelling is appreciable.

This argument based on hydrogen bonds is an intuitive one, but it is consistent with calculations for potential energy surfaces, e.g. of the $\text{H} + \text{H}_2$ isotope exchange reaction.¹⁸ Indeed changes in zero point energies along the reaction coordinate (and corresponding differences in vibrational energies between isotopic collision complexes) are implicitly taken into account in tunnel corrections based on such surfaces. This variation in zero point energies is similar to, but not quite the same as, that used by Westheimer to explain the dependence of isotope effects on the location of the transition state for hydrogen transfer along a reaction coordinate. Moreover, as indicated below, and by measurements of equilibrium isotope effects, the net change in isotopic zero point energy accompanying formation of a hydrogen bond is likely to be less than that for a transition state. If that is the case, the extent to which tunnelling is offset by zero point energy changes may be quite limited.

Zero point Energy at the Transition State

At the transition state, zero point energy contributes to the reaction barrier and semi-classical isotope effects arise from a difference of H and D zero point energies between the reactants and transition state. While it seems possible to estimate zero point energies associated with the reaction channels leading to the transition state by analogy with hydrogen bonding, the situation for the transition state itself is different

At the transition state the potential energy surface for a reaction corresponds to a saddle point. The quadratic region of the saddle point may be analysed in terms of the stretching vibrations of a linear three centre model with force constants to the reacting hydrogen f_1 and f_2 and interaction force constant f_{12} as depicted in **1**. When the model represents a transition state the curvature along the reaction coordinate must be negative and the frequency corresponding to this curvature is then imaginary. This is true when $f_{12} > \sqrt{f_1 f_2}$.



For a symmetrical transition state with $f_1 = f_2$ there is no zero point energy difference between the notional H and D frequencies corresponding to motion orthogonal to the reaction coordinate and the contribution of this zero point energy to the reaction barrier is the same for both isotopes. This is similar to the situation for a hydrogen bond except that the isotopically sensitive frequency is now an imaginary value corresponding to the reaction coordinate.

To consider the isotopic sensitivity of the ‘real’ vibration and reaction coordinate mode of the transition state it is relevant to be reminded that their combined sensitivity is controlled by the product rule.^{1,42} In a single dimension for a triatomic collinear collision complex this is expressed in eq 6, in which ω and ω^\ddagger represent real and imaginary

frequencies (in cm^{-1}) of the two stretching vibrations and m and M are masses of hydrogen isotopes and isotopic collision complexes respectively.

$$\frac{\omega_{\text{H}}\omega_{\text{H}}^{\ddagger}M_{\text{H}}^{1/2}}{\omega_{\text{D}}\omega_{\text{D}}^{\ddagger}M_{\text{D}}^{1/2}} = \frac{m_{\text{H}}^{1/2}}{m_{\text{D}}^{1/2}} \quad (6)$$

For hydrogen bonds we expect isotopic sensitivity to be confined to a single vibration, characteristically the vibration of higher frequency. However for a sufficiently large interaction constant, i.e. as f_{12} approaches $(f_1 + f_2)/2$, both vibrations become isotopically sensitive. Indeed, as f_{12} approaches $(f_1 + f_2)/2$ closely (and f_1 and f_2 have similar values) isotopic sensitivity is again confined to a single vibration, but this is now the vibration with lower frequency. As f_{12} becomes equal to $\sqrt{f_1 f_2}$ this frequency passes through zero and increases again as an imaginary frequency (for $f_{12} > \sqrt{f_1 f_2}$).

For a symmetrical transition state $f_1 = f_2$, and $(f_1 + f_2)/2 = \sqrt{f_1 f_2}$. In this case, as we have seen, there is no motion of hydrogen in the real stretching vibration of the transition state. For unsymmetrical transition states, the force constants f_1 and f_2 differ. Then $(f_1 + f_2)/2$ is greater than $\sqrt{f_1 f_2}$, and this inequality becomes more pronounced as the disparity between f_1 and f_2 increases. A consequence is that there is a shift in isotopic sensitivity from the reaction coordinate mode to the real stretching vibration of the transition state. Thus the small isotope effects envisaged by Westheimer for reactant- or product-like transition states arise both from an increasing magnitude and increasing isotopic sensitivity of the real vibration and associated zero point energy at the transition state.

An extended analysis of the influence of stretching and interaction force constants on both isotopic sensitivity and bond displacements for the vibrations of a three centre model has been provided by Albery.⁴³ He points out that variations in isotopic sensitivity of the zero point energy are associated with a change in reaction coordinate from the isotopically insensitive translational approach of the reactants for a highly reactant-like transition state to a practically independent (and isotopically sensitive) motion of the hydrogen atom in a symmetrical transition state. As noted above, this behaviour contrasts

with that of hydrogen bonds for which the larger stretching frequency ν_s is expected to show full isotopic sensitivity for all degrees of symmetry or asymmetry.

The relationship between force constants, masses and frequencies for these vibrations is conveniently summarised in an appendix to H. S. Johnston's book¹⁵ and reproduced below.

Gas Phase and Solution

In principle the discussion provided above applies to gas phase reactions, which normally involve transfer of hydrogen atoms. Most studies of isotope effects and tunnelling apply to proton or hydride transfer reactions in polar solvents, especially water.¹⁻¹³ Generally, it has been supposed that collision complexes of reactants in solution or for enzymes do not differ fundamentally from those in the gas phase, although the translational motions associated with a molecular collision in the gas phase may be replaced by a weak stretching vibration (hindered translation) of a hydrogen bond in solution. However, the potential energy surface for the reaction will be strongly influenced by the solvent or protein environment, especially for ionic reactions.

A reasonable view of interactions of reactants with the solvent is that reorientation of solvent molecules to accommodate developing charges accompanying a reaction occur prior to or following the covalent bond-making and bond-breaking step of a reactive molecular collision. However, within the time frame of a 'heavy atom' collision (or hindered translation) relaxation of solvent molecules can occur along preformed hydrogen bonds or orientated lone pair interactions with (e.g.) a centre of developing positive charge.

A point discussed for tunnelling in solution and enzymatic reactions is the influence of fluctuating solvent interactions in achieving a matching of vibrational energy levels between reactant and product reaction channels of the potential energy surface (fig 3) thereby facilitating tunnelling. This falls outside the scope of the present discussion but is addressed in other papers of this symposium in print.

Conclusion

The main purpose of this analysis is to provide a qualitative description of a plausible relationship between contributions to primary hydrogen isotope effects from zero point energy and tunnelling. The Westheimer-Melander effect has provided a historic guide for experimental investigations of hydrogen isotope effects. Marrying this zero point energy-based analysis to a not too naïve representation of tunnelling might be considered one challenge presented for this symposium.

It can certainly be claimed that the revival of interest in tunnelling has been stimulated by experimental measurements for enzyme-catalysed reactions.⁴⁵ The measurements have raised the question of whether enzymes might facilitate tunnelling. With some notable exceptions⁴⁵⁻⁴⁷ it seems fair to say that this question has been addressed more actively by computational or theoretical chemists^{26,33,48} than by organic or inorganic chemists undertaking measurements of isotope effects for non-enzymatic reactions. It would be a useful upshot of the symposium if more experimentalists were encouraged to take an interest in the field.

NOTE ON THREE CENTRE MODEL (1) AND HYDROGEN BONDS

Convenient relationships between frequencies of stretching vibrations, isotopic masses and force constants for a linear three atom model for a hydrogen bond or hydrogen transfer transition state (1 above) have been provided by H. S. Johnston¹⁵ and are reproduced in eqs 4 - 6 below. The two vibration frequencies are represented by λ_1 and λ_2 , where $\lambda = 4\pi^2 c^2 \omega^2$ and c is the velocity of light ($\omega = \nu/c$). As a minor simplification the masses of A and B are taken as equal (m) and presumed to be at least ten times greater than the mass of hydrogen m_H .

$$\lambda_1 = \frac{1}{2}[B + (B^2 - 4C)^{1/2}]$$

$$\lambda_2 = \frac{1}{2}[B - (B^2 - 4C)^{1/2}]$$

$$B = (f_1 + f_2)/m + (f_1 + f_2 - 2f_{12})/m_H$$

$$C = (f_1 f_2 - f_{12}^2)(2m + m_H)/m^2 m_H$$

It is apparent that when m is sufficiently large C and λ_2 approach zero. Usually $m \gg m_H$ and λ_2 is then very much less than λ_1 . The value of λ_1 becomes comparable to λ_2 only when f_{12} approaches $(f_1 + f_2)/2$ and B become small. Values of C and λ_2 also fall to zero when $f_{12} = \sqrt{f_1 f_2}$. When $f_{12} > \sqrt{f_1 f_2}$, C and λ_2 become negative and the frequency ω_L^\neq corresponding to λ_2 is imaginary.

When the interaction constant f_{12} is not too large it is evident that B is isotopically sensitive ($B_H/B_D \rightarrow m_H/m_D$) because $m \gg m_H$. In the normal case that C is also small only λ_1 will show appreciable isotopic sensitivity. This is typical of hydrogen bonds. Thus for the symmetrical hydrogen bond of the bifluoride ion the stretching frequencies $\omega_a^H = 1452$ and $\omega_s^H = 600 \text{ cm}^{-1}$ for HF_2^- , and $\omega_a^D = 1040$ and $\omega_s^D = 600 \text{ cm}^{-1}$ for DF_2^- are well fitted by the (harmonic) force constants $f_1 = f_2 = 2.32$ and $f_{12} = 1.71 \times 10^5 \text{ dynes/cm}$.

In the case of HF_2^- the interaction force constant f_{12} is quite large. However, it is only as f_{12} approaches $(f_1 + f_2)/2$ that relative magnitudes and typical isotopic sensitivities of λ_1 and λ_2 break down. Then B becomes isotopically insensitive and there is a switch in sensitivities and relative magnitudes between λ_1 and λ_2 . At extreme values of $f_{12} \geq \sqrt{f_1 f_2}$, $C = 0$ or is negative and the three centre model now represents a transition state.

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