

Steric Effects and the Secondary Isotope Effect

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Numerous secondary deuterium isotope effects have been reported in recent years. Shiner¹¹ presented a chart relating the origins of such effects. Inductive effects,^{4,5,13} hyperconjugative effects^{4,5,8,11,13} and non-bonded interactions^{1,7} have been suggested and vigorously debated. Each side has supported its effect with experimental data and theoretical considerations. Another group of workers prefer to argue within the framework of the Bigeleisen expression.^{2,11} It should be reemphasized that all of the foregoing effects and others can be contained within the Bigeleisen formulation. Such effects can be included into the partition functions.

Bartell¹ has signaled attention to the mass-sensitive amplitudes of vibration or steric effect. *We wish to expand upon this suggestion to provide an order of magnitude of the effect and to suggest that it will also account for both normal and inverse secondary isotope effects.*

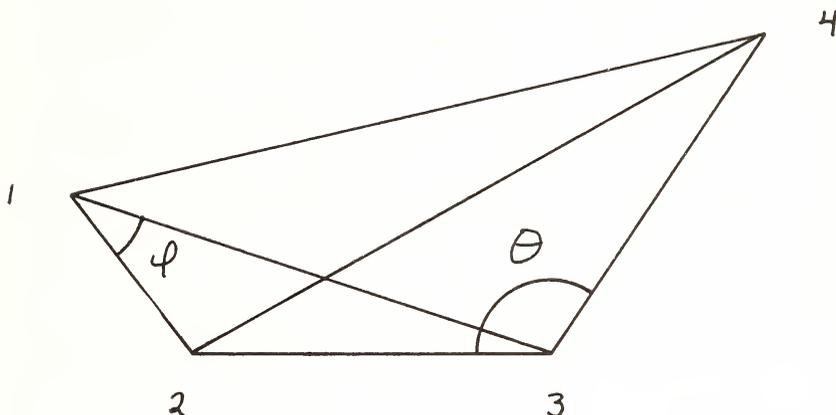


Figure 1

Consider the model (Fig. 1) :

where position one represents a hydrogen or a deuterium, position three represents the reactive site, four the incoming or outgoing reactant, and r_{ij} is the distance between i and j . Centers 2,3,4 define the xy plane with center 3 as the origin. The location of center 1 will be given by (x,y,z) though calculations are made in spherical polar coordinates. The interaction between i and j will be given by:

$$\phi_{\text{total}} = \phi_{\text{repulsion}} + \phi_{\text{attraction}}$$

Expressed in Mie's formulation (Fig. 2) :

The various parameters (D, σ, m, n) can be estimated from scattering functions⁶ or Lennard-Jones and Morse curves. All force constants are considered in the harmonic approximation and all off-diagonal elements are set nearly equal to zero.

The overall energy, E_H , of the system is then estimated for a given set of r_{ij} 's and angles ϕ and θ . Then r_{12} is shortened 0.001 Å to 0.010 Å to account for the anharmonicity upon substitution of deuterium. The energy, E_D , is then recalculated. The difference, $E_H - E_D$, is then the

$$\phi_{ij} = \frac{D_e \epsilon_{ij}}{n_{ij} - m_{ij}} \left[\frac{n_{ij}}{m_{ij}} \right] \frac{1}{n_{ij} - m_{ij}} \left[\frac{\sigma_{ij}}{r_{ij}} \right] n_{ij} - \left[\frac{\sigma_{ij}}{r_{ij}} \right] m_{ij}$$

$n_{ij} > m_{ij}$

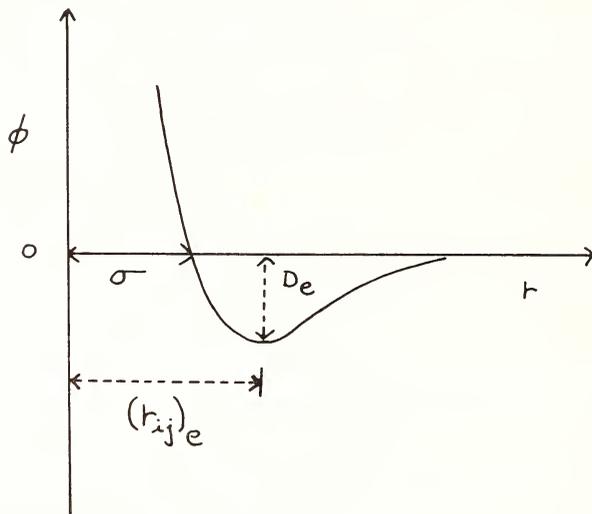


Figure 2

estimate of the steric effect. This comparison is quite convenient due to the cancellation of so many of the parameters. The most critical set of parameters is, of course, for the r_{14} and r_{12} interaction. The values of this difference range from about -200 to 200 cal./mole, dependent upon the orientation of the vector ϕ_{12} to ϕ_{14} and the distance, r_{14} . This is also seen from the graph of the potential function. If $r_{1j} > (r_{1j})_e$, the slope is positive. If $r_{1j} < (r_{1j})_e$, the slope is negative. Thus both small normal secondary isotope effects ($k_H/k_D > 1$) and small inverse effects ($k_H/k_D < 1$) can be explained and order of magnitude is of the order of a 200 cal. per hydrogen or less. If $r_{1j} = (r_{1j})_e$, k_H/k_D would be one. An isokinetic situation is also present if θ_{12} is orthogonal to θ_{14} . The effect is very small if r_{14} is large and also if center 1 is shielded from 4 by center 2. The general model will account for the α -effect by shortening r_{13} , the β -effect by shortening r_{12} and the γ (ζ , etc)-effect by lengthening r_{12} .

A simpler two center model¹² also gives the correct order of magnitude. Though both of the present models are static, they are comparable to Bartell's method of using the mean-square of the amplitude times the second derivative of the potential function. He considers only the region where this derivative is positive. The present model has ascribed the

differences $\Delta\Delta F^\ddagger$, of a given reaction mainly to non-bonded interactions. As the model is static, strain arising from torsion and bending modes cancel in the first approximation. Kinetic energy terms, though important, have been neglected. The parameters were adjusted to give an activation energy of about 20 kcal, an average value for reactions studied near room temperature. Isotopic substitution has been assumed to give no difference in the Arrhenius frequency factor.¹¹

As first suggested by Bartell this type of model works quite well for the dissociation of trimethylamine-trimethylboron.⁹ This type of reaction is known to have large steric requirements.³ Much of our fundamental understanding of steric effects has been due to Brown's thorough investigations in such systems.

Mislow¹⁰ has claimed that a steric explanation based on the size of deuterium compared to hydrogen is not compatible with data on attempted asymmetric reduction of ketones. This reaction is of very low steric requirement as seen comparing the $\Delta\Delta F^\ddagger$ observed (170 cal./mole) upon substitution of a methyl group for a hydrogen atom.¹⁰ Using the data on substitution of methyl for hydrogen in amine-boron complexes as a reference and then estimating the parameters of methyl-hydrogen interaction in Mislow's reduction, a crude estimate of the potential functions for ketone reduction can be made. On such a basis, the maximum steric isotope effect, k_H/k_D , is estimated to be only 1.0006 which is to be compared with the observed value 1.0000 ± 0.0002 . It is concluded that Mislow's system is too insensitive to the steric effects and does not constitute a crucial experimental case to rule upon the non-existence of such effects.

In conclusion, it is now noted that all the various origins of the secondary isotope effect predict small effects. The problem still remains as to dissection of the isotope effect into three or more separate effects in a given system.

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