Mechanisms of Elimination Reactions. XI. Theoretical Calculations of Isotope Effects in Elimination Reactions[1]

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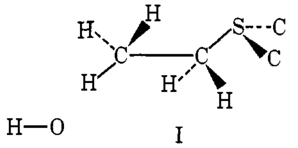
Abstract: Deuterium and sulfur isotope effects have been calculated for E2 reactions of hydroxide ion with ethyldimethylsulfonium ion, using the Wolfsberg–Schachtschneider *FG* matrix program. The dependence of the isotope effects on transition-state force constants (including off-diagonal *F* matrix elements used to achieve a zero or imaginary reaction coordinate frequency) was explored. The deuterium isotope effect goes through a maximum when the proton is half-transferred, and is not strongly affected by the extent of weakening of the carbon–sulfur bond. Similarly, the sulfur isotope effect increases with increasing extent of carbon–sulfur bond weakening, and does not depend much on the extent of proton transfer. Less reassuring are two other observations. The deuterium isotope effect can be changed drastically by changes in the degree of coupling (off-diagonal *F* matrix elements) of the proton-transfer motion with other atomic motions, and the sulfur isotope effect can remain very small until the stretching force constant of the carbon–sulfur bond has decreased to less than half of its original value. The implications of these results for the use of isotope effects in determining transition-state structures are discussed.

For some time, we have been interested in kinetic isotope effects as a means of exploring the structure of the transition state in elimination reactions.[3] Especially promising results have been obtained by combining deuterium and sulfur,[4,5] and deuterium and nitrogen[6] isotope effects. Discussions of such results assume that the deuterium isotope effect is determined primarily by the extent of proton transfer, and the sulfur or nitrogen isotope effect primarily by the degree of weakening of the bond to the leaving group. Theoretical calculations of proton-transfer isotope effects based on a three-center[7] and somewhat more complex[8] model have been reported. Some calculations of sulfur isotope effects on rather simplified models for sulfonium ion decomposition are also in the literature.[9] These results, however, give no information on whether there is any interdependence of isotope effects when both carbon–sulfur cleavage and proton transfer are part of the reaction coordinate motion. Our main aim in undertaking the present work was to provide evidence on this point. Among previous examples of such calculations on multicenter reactions, the work of Goldstein[10a] and Seltzer[10b] is especially noteworthy.

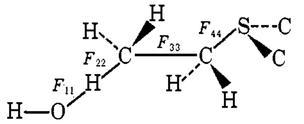
Models and Methods

The ground state was taken as ethyldimethylsulfonium ion plus hydroxide ion (I). Bond angles at carbon



I

were assumed to be tetrahedral, and the C–S–C bond angles were taken as 105°.[11] The C–S bond lengths were taken as 1.82 Å, and the other bond lengths (r_{CC}, 1.54 Å; r_{CH}, 1.09 Å; r_{OH}, 0.958 Å) were taken from a standard compilation.[12] A transition state was chosen that had the same bond lengths (except for the reacting bonds) and the same bond angles as the reactant (II).



II

All bond lengths were kept constant through the entire series of calculations, and changes in bond strength were introduced by varying only the force constants. The "compromise" set of bond lengths for the reacting bonds were r_{CS}, 2.10 Å; r_{CC}, 1.52 Å; r_{CH}, 1.21 Å; r_{OH}, 1.20 Å. This method is justified by the numerical calculations of Stern and Wolfsberg,[13] who showed that changes in bond lengths and bond angles without concomitant changes in force constants had very little influence on isotope effects.

Force constants for the ground and transition states are listed in Table I. Ground-state force constants were taken from the literature[11,14,15] or were reasonable guesses based on literature data. Torsional force constants were kept very low to minimize their influence on

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[2] Eastman Kodak Fellowship, 1966–1967.

[3] Early work is discussed by W. H. Saunders, Jr., in "The Chemistry of Alkenes," S. Patai, Ed., Interscience Division, John Wiley & Sons, Inc., New York, N. Y., 1964, Chapter 2.

[4] A. F. Cockerill and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **89**, 4985 (1967).

[5] A. F. Cockerill, *J. Chem. Soc., B*, 964 (1967).

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[7] A. V. Willi and M. Wolfsberg, *Chem. Ind.* (London), 2097 (1964); W. H. Saunders, Jr., *ibid.*, 663 (1966).

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[9] W. H. Saunders, Jr., *Chem. Ind.* (London), 1661 (1963).

[10] M. J. Goldstein and M. L. Thayer, Jr., *J. Am. Chem. Soc.*, **87**, 1933 (1965); S. Seltzer and S. G. Mylonakis, *ibid.*, **89**, 6584 (1967).

[11] H. Siebert, *Z. Anorg. Allgem. Chem.*, **273**, 161 (1953).

[12] "Tables of Interatomic Distances and Configuration in Molecules and Ions," Special Publications No. 11 and 18, The Chemical Society, London, 1958 and 1965.

[13] M. Wolfsberg and M. J. Stern, *Pure Appl. Chem.*, **8**, 225 (1964).

[14] J. H. Schachtschneider and R. G. Snyder, *Spectrochim. Acta*, **19**, 117 (1963).

[15] E. B. Wilson, Jr., J. C. Decius, and P. Cross, "Molecular Vibrations," McGraw-Hill Book Co., Inc., New York, N. Y., 1955, pp 175–176.

the isotope effect. Stretching force constants of reacting bonds in the transition state were varied from 0 to 100% of their normal values by ZN or $1 - ZN$, where ZN ranges between 0 and 1.00. Bond-bending force constants involving reacting bonds were varied in the same fashion in the absence of any compelling theoretical reason for doing otherwise. A function varying as $ZN(1 - ZN)$ was used for the linear C–H–O bend and the torsional involving this system.

The HCSC torsional was varied as $1 - ZN$. Very low frequencies resulted at high ZN, which caused excessive rounding errors in the calculation of vibrational partition function ratios. Consequently, an approximation devised for partition functions for internal rotation[16] was used when the frequency of the torsional motion fell below 25 cm^{-1}.

A computer program devised by Schachtschneider[14] for calculating vibrational frequencies by the FG matrix method and modified by Wolfsberg[13] to calculate isotope effects was adapted to the University of Rochester IBM 360 Model 50 computer. Force constants of the reacting bonds were arbitrarily varied, both separately and simultaneously, so as to simulate the various possible structures for the E2 transition state.[3]

A zero or imaginary reaction coordinate frequency for the transition state was attained by setting that block of the determinant of the F matrix containing the stretching force constants of the reacting bonds equal to zero by the introduction of appropriate off-diagonal elements, since[17]

$$|FG| = |F|\cdot\mu_1\mu_2\cdots\mu_f = \lambda_1\lambda_2\cdots\lambda_f \qquad (1)$$

Using the labeling of structure II, let

$$\begin{vmatrix} F_{11} & F_{12} & 0 & 0 \\ F_{12} & F_{22} & F_{23} & 0 \\ 0 & F_{23} & F_{33} & F_{34} \\ 0 & 0 & F_{34} & F_{44} \end{vmatrix} = DF_{11}F_{22}F_{33}F_{44} \qquad (2)$$

where D is zero or negative. If we define the off-diagonal elements as follows

$$F_{12} = A(F_{11}F_{22})^{1/2} \qquad (3)$$

$$F_{23} = B(F_{22}F_{33})^{1/2} \qquad (4)$$

$$F_{34} = C(F_{33}F_{44})^{1/2} \qquad (5)$$

substitute eq 3–5 into eq 2, and expand the determinant, we get

$$1 - C^2 - B^2 - A^2 + A^2C^2 = \mathrm{D} \qquad (6)$$

The parameters A–C enable us to calculate permissible combinations of off-diagonal elements for any given value of D. This may be regarded as measures of the extent to which the stretching motions of the reacting bonds are coupled to each other. To simplify our task we assumed $D = 0$ and $B = C$ for most of the calculations.

No corrections for proton tunneling[18–20] were applied. A tunneling correction is not required, of course, for $D = 0$ (flat potential barrier), which includes most of the calculations in this study. Even for those cases where $D \neq 0$, we felt that current uncertainty over the proper method of calculating tunneling corrections[20] made it inadvisable to introduce this variable into an already very complex situation.

Table I. Assumed Force Constants for Ground and Transition States[a]

Type of force constant	Value in ground state	Value in transition state
HO str (OH^-)	7.8	7.8
HO str[b]	0.0	$7.8ZN$
CH str[c]	4.7	$4.7(1 - ZN)$
CC str[d]	4.7	6.58
CS str[e]	3.14	$3.14(1 - ZN)$
CS str[f]	3.14	3.14
CH str	4.7	4.7
HOH bd	0.0	$0.69ZN$
HCC bd[g]	0.606	$0.606(1 - ZN)$
HCC bd	0.606	0.606
HCH bd[g]	0.541	$0.541(1 - ZN)$
HCH bd	0.541	0.541
CCS bd	0.25	$0.25(1 - ZN)$
HCS bd	0.522	$0.522(1 - ZN)$
CSC bd[h]	0.294	$0.294(1 - ZN)$
CSC bd	0.294	0.294
HOHCC tors[i]	0.0	$0.04ZN(1 - ZN)$
HCCS tors	0.02	0.02
HCSC tors	0.01	$0.01(1 - ZN)$
CHO bd[j]	0.0	$0.32ZN(1 - ZN)$

[a] Values are in mdyn/Å. [b] Forming OH bond (F_{11} in structure II of text). [c] Breaking CH bond (F_{22} in structure II of text). [d] F_{33} in structure II of text. [e] Breaking CS bond (F_{44} in structure II of text). [f] S-methyl bond. [g] One HC is breaking bond. [h] One CS is breaking bond. [i] Linear OHC taken as axis of torsional motion. [j] Linear bend.

Results and Discussion

We present here a selection of our results intended to illustrate the main conclusions drawn from these calculations. All isotope effects quoted are at the same temperature (25°).

Table II shows the variation of the deuterium isotope effect with extent of proton transfer. The expected maximum[7] is observed. Our results differ from the three-center model[7] in that k_H/k_D at the maximum is not independent of whether the reaction coordinate frequency is zero or imaginary. This is to be expected, for the three-center model possesses only one real stretching frequency, a symmetric stretch in which the proton does not move when it is equally bound to origin and terminus. By contrast, our model has numerous real stretching frequencies in which the proton moves, including that corresponding to the symmetric stretch in the three-center model. Consequently, the

Table II. Deuterium Isotope Effects and Extent of Proton Transfer[a]

	k_H/k_D		
ZN for CH and OH[b,c]	$A = 0.95$[d] $D = 0.0$	$A = 0.95$ $D = -0.2$	$A = 1.05$[d] $D = -0.2$
0.2	2.54	2.57	3.09
0.4	4.13	4.31	5.68
0.6	5.90	5.35	6.84
0.8	4.09	4.32	5.35

[a] At 25°. [b] Decrease with increasing extent of proton transfer. [c] ZN for CS assumed constant at 0.9 (90% broken). [d] $B = C$ assumed throughout.

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(16) D. R. Herschbach, H. S. Johnston, K. S. Pitzer, and R. E. Powell, *J. Chem. Phys.*, **25**, 736 (1956).

(17) See ref 15, p 183.

(18) E. Wigner, *Z. Physik. Chem.*, **19B**, 203 (1932).

(19) R. P. Bell, *Trans. Faraday Soc.*, **55**, 1 (1959).

(20) H. S. Johnston and D. Rapp, *J. Am. Chem. Soc.*, **83**, 1 (1961).

Table III. Influence of the Coefficient A on Deuterium and Sulfur Isotope Effects[a]

A^{b-e}	k_H/k_D	$[(k_{32}/k_{34}) - 1]100$
0.95	5.90	1.15
0.90	4.42	1.35
0.50	1.76	1.50

[a] See footnote a, Table II. [b] $D = 0$ throughout. [c,d] See corresponding footnotes, Table II. [e] ZN for CH and OH assumed constant at 0.6.

two isotopic transition states still differ in zero-point energy at the maximum and the isotope effect can be changed by manipulating the off-diagonal force constants. The three-center model clearly oversimplifies the real situation in its prediction of an invariant maximum value of k_H/k_D. Increase in A increases k_H/k_D.[21]

Table III shows the effect of wider variations in A. While the sulfur isotope effect does not vary markedly, there is a dramatic decrease in k_H/k_D with decrease in A. This result carries the disquieting implication that k_H/k_D may not be a reliable measure of the extent of proton transfer in the transition state. Intuitively, one might expect A to be large where proton transfer is the major component of the reaction coordinate motion (E1cB-like reaction), and to decrease as one progresses toward a more concerted process and finally on to an E1-like reaction. The limiting case would be that where proton transfer is a negligible component of the reaction coordinate and the hydrogen isotope effect secondary rather than primary. Proton transfer is unlikely to have progressed very far under these circumstances, so that a small isotope effect is expected for an E1-like reaction both from the value of A and the extent of proton transfer. In an E1cB-like process, the A value should be large, but the isotope effect will be small because the proton is more than half-transferred. One can usually distinguish E1-like from E1cB-like transition states by substituent effects.[3] Thus, variation in k_H/k_D caused by variation in the contribution of proton transfer to the reaction corrdinate motion (as measured by A) probably will not seriously affect qualitative conclusions based on the three-center model for proton transfer.

The source of this decrease in k_H/k_D with A is revealed by an examination of the detailed results. The proton-transfer motion becomes a less important component of the reaction-coordinate frequency, but a more important component of the real frequencies of the transition state. Consequently, there is an increased spread between zero-point energies of the isotopic transition states. This cancels part of the zero-point energy difference between the isotopic reactants, resulting in a decreased zero-point energy contribution to the deuterium isotope effect.

Table IV. Influence of the Coefficient Ratio C/B on Deuterium and Sulfur Isotope Effects[a]

ZN for CH and OH[b−e,h]	k_H/k_D[f] and $[(k_{32}/k_{34}) - 1]100$[g] for $C/B =$ 2.0	1.0	0.5
0.2	2.50 (1.22)	2.54 (1.05)	2.54 (0.95)
0.6	5.08 (1.40)	5.90 (1.15)	6.04 (0.85)
0.8	3.96 (1.05)	4.09 (0.72)	4.09 (0.73)

[a−d] See corresponding footnotes, Table II. [e] $D = 0$ throughout. [f] Top figure on each line is deuterium isotope effect. [g] Lower figure in parentheses is sulfur isotope effect. [h] $A = 0.95$ throughout.

The ratio C/B represents the relative extents to which the CS and CH stretches, respectively, are coupled to the CC contraction in the reaction coordinate motion. Intuitive expectations are not obvious here, except that a value of C/B near unity might be associated with a highly concerted reaction. In any event, the influence of this ratio (Table IV) is not great on either the deuterium or sulfur isotope effects, except when $ZN = 0.6$. Examination of the eigenvectors of the reaction coordinate frequency and the real frequencies reveals an interesting effect. As expected, the contribution to the reaction coordinate of the CS stretch increases, and of the proton-transfer decreases, as C/B increases. The major factor in the isotope effect change, however, lies in a real frequency in which reverse changes in the magnitudes of the eigenvectors occur. This frequency is more sensitive to substitution of H for D when C/B is large. The zero-point energy difference between isotopic species in the transition state becomes larger, decreasing the isotope effect. By the same line of reasoning, the increase in the sulfur isotope effect with increasing C/B can be explained.

One of the most important questions is whether the sulfur isotope effect is dependent on the extent of proton transfer, and the deuterium isotope effect on the strength of the CS bond in the transition state. Normally, force-constant changes remote from the position of isotopic substitution have a negligible influence on the isotope effect.[13] This generalization cannot *a priori* be trusted in the present case, however, for the CH and CS stretching motions are coupled by off-diagonal elements in the F matrix. Consequently, we tested the validity of this assumption by the calculations reported in Table V.

Table V. Influence of Carbon–Sulfur Bond Strength and Extent of Proton Transfer on Sulfur and Deuterium Isotope Effects[a]

	$[(k_{32}/k_{34}) - 1]100$[c] and k_H/k_D[d] when ZN for CH and OH[b] is			
ZN for CS[b,e]	0.1	0.4	0.6	9.0
0.1	−0.14	−0.27	−0.15 (6.09)	−0.14
0.4	0.05	0.03	0.14	0.14
0.6	0.23	0.27	0.36	0.34
0.9	0.73	1.15	1.15 (5.90)	0.99
0.95	0.75	1.36	1.32 (5.34)	1.10

[a,b] See corresponding footnotes, Table II. [c] Top figure in each line is sulfur isotope effect. [d] Lower figure in parentheses in column 4 is k_H/k_D. [e] $A = 0.95$, $B = C$, $D = 0$ throughout.

The figures in parentheses in column 4 show that k_H/k_D is rather insensitive to the amount of CS bond weakening except when the bond is more than 90% broken. Even then, the change is not sufficient to constitute a serious complication in interpretation of k_H/k_D. Reading across any line of the table discloses a similar insensitivity of the sulfur isotope effect to the extent of

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(21) If $B = C$, then assuming $A = 1.0$ and $D = 0$ requires $B = C = 0$, and decreasing A increases B and C. Only positive values of A, B, and C have physical meaning, for only then are the atoms constrained to move in the proper directions to give products in the reaction coordinate motion.

proton transfer. Only when the CS bond is more than 90% broken is the variation much beyond normal experimental error in determination of sulfur isotope effects. It is intriguing to note the maximum near half-transfer of the proton, making the sulfur and deuterium isotope effects analogous in this respect. The observation is probably of no mechanistic utility, however, for changes in the extent of proton transfer are unlikely to occur without concomitant changes in CS bond strength.[4]

The most striking feature of Table V is the unexpected behavior of the sulfur isotope effect with respect to changes in the CS bond strength. The effect is inverse at first, and becomes significantly greater than zero only when the CS bond is about half-broken. After that it rises more rapidly to a maximum of 1.3–1.4%, a reasonable value in the light of available experimental results.[22] While the sulfur isotope effect increases with increasing weakening of the CS bond, as expected, the relationship is not even close to linear.

These calculations do provide a plausible explanation for a rather puzzling set of experimental results. The sulfur[4] and deuterium[5] isotope effects in the reaction of 2-phenylethyldimethylsulfonium ion with hydroxide ion in water–dimethyl sulfoxide change so as to indicate that the extents of both CH and CS stretching are decreasing with increasing dimethyl sulfoxide concentration. The sulfur isotope effect decreases to a value of 0.11% at 20 mol %, while the deuterium isotope effect continues changing up to 84 mol % dimethyl sulfoxide, the highest concentration studied. It is now obvious from the calculations that the 0.11% need not represent a nearly intact CS bond, and that the extent of CS stretching may still be decreasing, along with the extent of CH stretching, between 20 and 84 mol % of dimethyl sulfoxide.

One might object that it is improper to speak of CS bond strength only in terms of the stretching force constant, for the off-diagonal term (interaction between CS and CC stretches) also functions to hold the atoms together.[23] Granting this point, we still feel our usage is legitimate and proper. Certainly the character of the CS bond is changing, as the stretching force constant decreases, in a manner which makes decomposition to products progressively easier. The constraints on the sulfur atom resulting from the off-diagonal term merely represent the condition that it must move "in step" with other atoms so as to give products.

While there is no reason to doubt the nonlinear trend in sulfur isotope effect as a function of CS bond strength, too much significance should not be attached to the absolute magnitudes. In particular, the inverse effects found for the models with nearly intact CS bonds do not arise from zero-point energy effects, but from a moments-of-inertia ratio which is inverse to the extent of 0.3%. This phenomenon undoubtedly results simply from the different bond lengths, and hence different centers of mass, of reactants, and transition states. It is a constant factor which might well be less obtrusive in a more realistic model, so we cannot say whether inverse sulfur isotope effects from this source would be found experimentally.

The influence on k_H/k_D of a model which gives an imaginary reaction coordinate frequency was explored briefly in Table II. In Table VI, we present the effect of a similar model on the sulfur isotope effect. Note that constant A requires that B and C increase as D becomes more negative. The sulfur isotope effect is somewhat smaller for imaginary than for zero reaction coordinate frequencies, but the decrease does not continue beyond small negative values of D (low absolute magnitudes of the imaginary frequency).

Table VI. Influence of Imaginary Reaction Coordinate Frequencies on Sulfur Isotope Effects[a]

	$[(k_{32}/k_{34}) - 1]100$ for D =		
ZN for CS[b,c]	0.0	−0.2	−0.5
0.6	0.27	0.16	0.13
0.9	1.15	0.68	0.67
0.95	1.36	0.76	0.73

[a] See footnote *a*, Table II. [b] ZN for CH assumed constant at 0.6. [c] $A = 0.95$, $B = C$ throughout.

Perhaps the most important results of these calculations are the observations that the sulfur isotope effect may remain small until the CS bond is extensively weakened, and that k_H/k_D may be strongly influenced by the extent of coupling of the proton transfer with other atomic motions. The number of parameters that can change the isotope effect clearly make it impossible to draw even semiquantitative conclusions about transition-state structure from single measurements of isotope effects. Comparisons of isotope effects between two systems that differ widely in structure or environment are also risky. One should not be too pessimistic, however, for the parameters that we have treated as independent variables in these calculations will very likely be interdependent in an actual physical situation. Thus, systematic changes in some structural or environmental feature of a reaction (basicity of reagent, for example[4,5]) can be expected to yield qualitatively interpretable results. Isotopic substitution at a number of different positions in the same molecule may even yield semiquantitative information about transition-state structure under favorable conditions. Since the bimolecular elimination reaction is a particularly complex process, the applicability of isotope effects to other mechanistic studies need not necessarily be compromised by ambiguities found in this study.

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(22) See ref 3 and 4, and other papers quoted therein.

(23) This argument was called to our attention by Professor M. J. Goldstein.