

ands coordinated to the transition-metal catalyst, e.g., hydrogen bonding between the hydroxyl group on the phosphine ligand and the carbonyl group of a prochiral carbonyl compound in the hydrogenation or coordination of an amino group on the ligand with the magnesium atom on a Grignard reagent in the cross-coupling reaction. Thus, chiral ferrocenylphosphines are superior to others in that structural modification can be readily made by introduction of a desired functional group on to the side chain according to the demand of the reaction type. In the field of asymmetric synthesis by stoichiometric chiral reagents, high stereoselectivity has been sometimes attained by the stereocontrol based on the attractive interactions, e.g., chelation in the asym-

metric alkylation by Meyers.³² This type of stereocontrol should be more extensively applied to asymmetric synthesis with homogeneous transition-metal catalysts, which will certainly bring about much higher stereoselectivity. Our current interest is in development of new catalyst systems efficient for catalytic asymmetric reactions other than those described here.

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(32) Meyers, A. I. *Acc. Chem. Res.* 1978, 11, 375.

Temperature Dependence of the Primary Kinetic Hydrogen Isotope Effect as a Mechanistic Criterion

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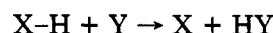
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Organic chemists have traditionally applied the primary isotope effect as a mechanistic criterion by measuring k_H/k_D at a single, convenient temperature. This single value is then invested with significance, being related to whether it is large, small, or intermediate; it also suffices to establish whether H transfer is occurring in the rate-determining step of the mechanism.

Various efforts have been made to correlate the size of this single value of k_H/k_D with the occurrence of hydride, proton, or hydrogen atom transfer with no outstanding success. The failure to take advantage of existing theoretical treatments¹ that teach a broader significance of the temperature dependence of k_H/k_D is probably related to experimental difficulties in obtaining, over a sufficient temperature range, k_H/k_D data of the accuracy and precision demanded.

Several categories of transition states (hereafter abbreviated TS) of H-transfer reactions may be discerned through application of the "full" criterion, meaning the temperature dependence of the kinetic isotope effect (TDKIE). The development of techniques^{2,3} that afford the required precision in measurements of k_H/k_D over extensive ranges of temperature has created a position from which the transition states of common H-transfer processes may be characterized by means of the "full"

criterion. It is useful to review the origins of the temperature-dependence of k_H/k_D based on a simple two-dimensional TS model of a three-center process⁴ (where X and Y may be atoms or molecules):



Background

The TDKIE criterion is ultimately based on the Arrhenius relation:

$$k_H/k_D = A_H/A_D \exp(-[\Delta E_a]_D^H/RT) \quad (1)$$

Two categories of transition states can be defined in

(1) (a) M. E. Schneider and M. J. Stern, *J. Am. Chem. Soc.*, **94**, 1517 (1972); (b) R. P. Bell, *Chem. Soc. Rev.*, **3**, 513 (1974); E. F. Caldin, *Chem. Rev.*, **69**, 135 (1969).

(2) H. Kwart and J. J. Stanulonis, *J. Am. Chem. Soc.*, **98**, 4009 (1976). The high-precision method of measuring isotope effects developed here depends on the use of a (nonmagnetic) quadrupole mass spectrometer that is characterized by a very short time of flight of the isotopic masses of interest. This assures that two such masses can be compared under virtually identical conditions of ionization and collection. This instrument is coupled to a computer programmed to look at two discrete mass peaks in rapid succession and deduce the ratio of their intensities. If a relatively constant pressure of substrate flowing into the ionization chamber for several minutes is maintained, thousands of mass ratio data are gathered by the computer, which is also programmed to perform several statistical operations on these data before expressing the average isotopic mass ratio of a block. A number of blocks consisting of several thousand mass ratio measurements are taken, spaced at intervals of time to detect the occurrence of such vagaries as memory effects and drifts in tuning and calibration factors.

(3) H. Kwart, S. F. Sarnar, and J. H. Olson, *J. Phys. Chem.*, **73**, 4056 (1969). This reference describes in full detail the structure of a gold coil microreactor specially suited for high-temperature gas-phase reaction kinetics with negligible wall effects.

(4) (a) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961); (b) J. Bigeleisen, *Pure Appl. Chem.*, **8**, 217 (1964); (c) R. C. Melander and W. H. Saunders, Jr., "Reaction Rates of Isotopic Molecules", Wiley, New York, 1980.

Harold Kwart did his undergraduate work at Brooklyn College and had started graduate work with Harold C. Urey at Columbia University when World War II interfered. During the war, he was involved in isotope studies on the Manhattan Project. In 1945, he commenced graduate work to the Ph.D. at Harvard University, where Paul D. Bartlett was his mentor. After 2 years of postdoctoral work at Harvard, he joined the faculty of Bryn Mawr College. In 1951 he moved to the University of Delaware, where he is now H. Fletcher Brown Professor of Organic Chemistry.

terms of the Westheimer derivation^{4a} of the kinetic hydrogen isotope effect:

(a) A symmetrical TS of linear H transfer between the reaction centers X and Y occurs in which the restoring forces on both sides of the hydrogen being transferred are equal or nearly so. This situation, which is often observable in a so-called concerted TS, gives rise to a maximum isotope effect with the observed activation energy difference, $[\Delta E_a]_D^H$, equal to the initial state zero point (zp) energy difference between corresponding H and D bonds; the latter, designated as $[\Delta E_0]_D^H$, is directly obtainable from IR data; i.e., $[\Delta E_a]_D^H = [\Delta E_0]_D^H$. The value of A_H/A_D for this case varies narrowly between the limits $0.7-2^{1/2}$ and has been calculated^{1a} to have a practical upper limit of 1.2. The activation barrier of reaction is characterized as broad, reflecting a large distance of separation of the reaction centers X and Y between which the H is being transferred in the TS.

(b) An unsymmetrical TS of linear H transfer, defined as one in which there is residual motion of the H in the TS, is associated with an activation energy difference that is somewhat less than the zero point energy difference, and normally it is measurably less. This is due to the fact that, when there is motion of the transferring atom (H or D) in the TS, we must reckon with the TS zp energy differences, designated as $[\Delta E_0^*]_D^H$. Since $[\Delta E_a]_D^H = [\Delta E_0^*]_D^H - [\Delta E_0^*]_D^H$, the observed will be somewhat less than the initial-state zp, energy difference, i.e., $[\Delta E_a]_D^H < [\Delta E_0]_D^H$. (No case has yet been found of an unsymmetrical TS of linear H transfer in which $[\Delta E_a]_D^H = 0$, although this is conceivable.) The A_H/A_D in this case is also limited to values between 0.7 and $2^{1/2}$; it is generally understood that this range of A_H/A_D values is characteristic of linear H-transfer processes with broad barriers.

A third category of linear H-transfer mechanisms comprises cases in which the distance of separation of X from Y in the TS becomes quite small, i.e., a narrow or thin reaction barrier. Beyond a critical degree of narrowness, the top of the classical reaction barrier will not be attained in all systems because of the occurrence of tunneling. In the case of a broad, flat-topped barrier, the uncertainty in the location of the highly energetic H and D particles, born of the Heisenberg uncertainty principle, is never greater than the width of the barrier. However, for a narrow, steeply curved barrier top, a point along the reaction coordinate may be reached where the uncertainty in the location of the vibrating particle is greater than the barrier width. At this level of energy the particle will be found on the product side of the barrier without having surmounted the energy requirements for classical passage over the top of the barrier. Such are the circumstances, in general, which give rise to the expression "tunneling through a narrow barrier". In fact, procedures have been developed⁵ for computing the barrier dimensions, including the separation of X and Y centers when tunneling is involved.

The criteria to be applied for detection of tunneling (again) depend upon accurate measurement of k_H/k_D as a function of temperature. Since it is the curvature of the Arrhenius plot which demonstrates experimen-

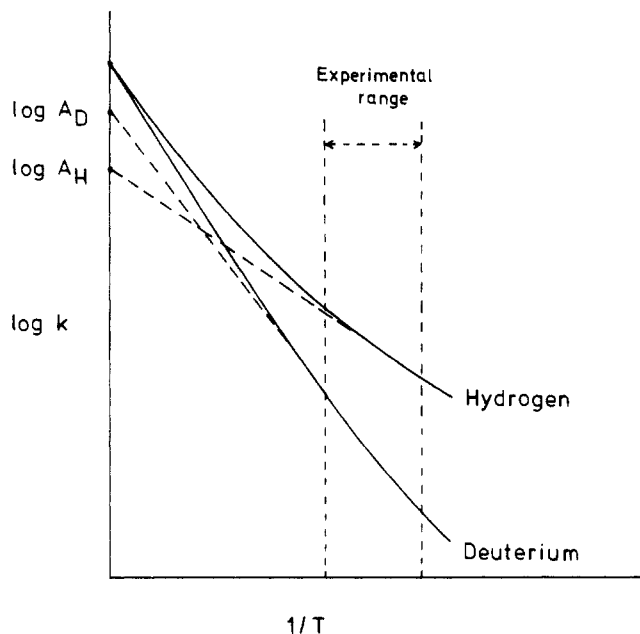


Figure 1. Arrhenius plots with incidence of tunneling of H and D.

tally the incidence of tunneling, it will be realized from Figure 1 that such a pathway of linear H transfer is identified by two distinctive findings:⁶ (a) $[\Delta E_a]_D^H \gg [\Delta E_0]_D^H$, and (b) $A_H/A_D \ll 0.7$. It must be emphasized that these are the apparent, experimentally determined parameters derived from linear Arrhenius plots in the normal range of measurement (see Figure 1), the slopes and intercepts being computed according to eq 1 without any allowance for the possibility of curvature outside the temperature range investigated.

It is necessary to insert a caveat concerning interpretation of the tunneling process. Tunneling is not a mechanistically distinguishable path paralleling other reaction paths or partitioning the mechanism among competing paths. In other words, it is not an additional way of traversing the reaction barrier; rather, it is a correlation applicable to barriers only when the crossing is treated classically. We must be aware also that calculations of barrier dimensions⁶ from A_H/A_D data may be an artifact since the relation to real barriers is still to be shown definitively. Strictly speaking, *we cannot conceive of a TS structure associated with tunneling H transfer*.⁷

A fourth category of TS structure is recognized in a nonlinear H-transfer process. In contradistinction to linear H transfer, in which the amplitudes of stretching vibration are limited by the distance of separation of X and Y, the amplitudes of H vibration are considerably less restricted in a bent TS. Thus, the H is likely to be in motion in a bent TS, even more so than for an unsymmetrical, linear H transfer where $[\Delta E_a]_D^H$ is less than $[\Delta E_0]_D^H$. Therefore, if the sum of $[\Delta E_0^*]_D^H$ for all the TS modes equals the sum of $[\Delta E_0^*]_D^H$ for all the reactant modes of the reference H, then the isotope

(5) (a) R. P. Bell, *Trans. Faraday Soc.*, **54**, 1 (1959). (b) E. F. Caldin, M. Kasparian, and G. Tomalin, *Trans. Faraday Soc.*, **64**, 2802 (1968); E. F. Caldin and G. Tomalin, *ibid.*, **64**, 2814, 2823 (1968).

(6) See, however D. J. McLennan, *Aust. J. Chem.*, **32**, 1883 (1979), whose model calculations show that somewhat higher $[\Delta E_a]_D^H$ and lower A_H/A_D values than normal are obtained with loose, symmetrical transition states. It is suggested that such experimental results might falsely be invoked to be indicative of tunneling, but it also is to be emphasized that such structures apply primarily to H^+ transfers in solution.

(7) V. K. Babamov and R. A. Marcus, *J. Chem. Phys.*, **74**, 1791 (1981); see particularly Figures 1 and 2 in this article.

Table I
Summary of TDKIE Parameters and Their Corresponding TS Classifications

TS category	k_H/k_D	$[\Delta E_a]_D^H$	A_H/A_D
linear H-transfer symmetrical	"maximum" ($\sim 6-8$ at 25°C)	$= [\Delta E_0]_D^H \rightarrow \text{CH} = 1.15 \text{ kcal}$	1 ($0.7-2^{1/2}$)
linear H-transfer unsymmetrical	less than maximum ($\sim 2-5$ at 25°C)	$\leq [\Delta E_0]_D^H \sim 0.3-1 \text{ kcal}$	1 ($0.7-2^{1/2}$)
linear H-transfer tunneling	more than "maximum" (>9 at 25°C)	$\leq [\Delta E_0]_D^H \sim 1.5-6 \text{ kcal}$	< 0.6
nonlinear H-transfer bent	$> 2^{1/2}$	~ 0	$2^{1/2} \rightarrow \sim 6$ (thus far)

effect will tend to be temperature independent and its magnitude determined only by A_H/A_D . Since the zp E_0 of the H bending modes are normally 3-4 times smaller than for stretching, and since the bending modes are those principally undergoing change in the bent TS, even if there were a difference, $\Sigma[\Delta E_0^*]_D^H - \Sigma[\Delta E_0^*]_D^H$, it could only be very small, corresponding to a virtually temperature independent k_H/k_D .

The distinctive feature of the bent TS, however, lies not so much in its temperature independence, because unsymmetrical, linear H-transfer processes also tend toward small $[\Delta E_a]_D^H$ values; rather, it is the extraordinarily large values of A_H/A_D , usually much greater than the theoretical limit of $2^{1/2}$, (discussed above), that have empirically been identified as the hallmark of the bent TS.

It must be emphasized, however, that this conclusion has as yet not been rigorously derived from the principles of transition-state theory. Some lines of argument which appear to rationalize the observation that a temperature-independent isotope effect greater than $2^{1/2}$, i.e., $A_H/A_D \geq 2^{1/2}$, is to be associated with a bent TS in a single-step reaction process have been advanced, and model calculations have been cited which appear to justify this rationalization.⁸

Before considering experimental data that serve both to calibrate and to support these conclusions regarding the bent TS, let us summarize the TDKIE parameters that identify each of the four categories of H-transfer TS's (see Table I). Thus far, with the use of high precision methods of k_H/k_D measurement,^{2,3} only these categories and no shadings or intermediate classifications of TS geometry in H-transfer reactions have been recognized experimentally, though such possibilities have not been excluded.

Applications of the TDKIE Criteria

These criteria have not been frequently applied in the past. Most of these criteria applications have occurred in studies of intermolecular proton transfer. Most of the cases that involve quantum mechanical tunneling have been exhaustively reviewed.^{1b,9,10} An example of simple, intermolecular hydrogen transfer, previously studied by Wiberg and Motell,¹¹ which proved to occur by a linear, symmetrical mechanism, will be treated in a later section.

Linear Transition States without a Tunnel Correction. *The Retroene Thermolysis.* All the fol-

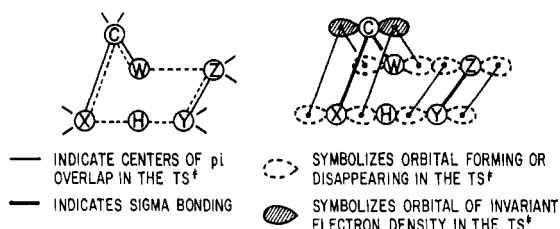
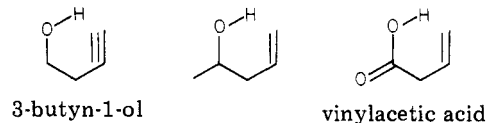
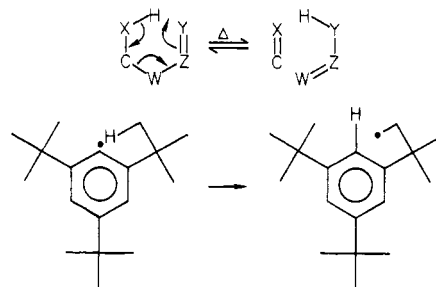


Figure 2. Bonding in the pericyclic transition state of the ene and retroene reactions.

lowing examples studied¹² have very similar activation parameters despite large differences in the acidities of their O-H bonds and in the hybridization of the centers of their respective pericyclic TS's. The isotope effects



of these reactions measured over a ca. 100°C range were virtually identical; $[\Delta E_a]_D^H \approx 1.3 \text{ kcal} = [\Delta E_0]_D^H$ for the O-H bond, and $A_H/A_D \approx 1.0$. These data require that the H transfer take place from oxygen to a π -carbon center (of nonspecific hybridization) separated by a relatively large distance over a broad activation barrier. In general, the retroene (and presumably also the corresponding ene reaction) sketched below has require-



ments that are not accommodated by a planar TS, as commonly supposed.¹³ They are, however, fitted nicely to the structure of a pericyclic¹⁴ TS represented with orbital symmetry conservation in Figure 2.

Similar results were obtained in studies of analogous retroene thermolyses, namely, the thermal β -cis-elimination reactions of carboxylic acid derivatives such as esters¹⁵ and carbamates.¹⁶ These reactions proceed through opposite-direction, rate-determining H-transfer steps in which C-H in the reactant converts to O-H in

(8) H. Kwart, M. W. Brechbiel, R. M. Acheson, and D. C. Ward, *J. Am. Chem. Soc.*, **104**, 4671 (1982). See this article also for references and discussion of a model calculation that intrinsically relates A_H/A_D to the angle of H transfer at a single (constant) temperature, i.e., a temperature-independent k_H/k_D .

(9) (a) H. S. Johnson, *Adv. Chem. Phys.*, **3**, 131 (1960); (b) M. D. Harmony, *Chem. Soc. Rev.*, **1**, 211 (1972).

(10) R. P. Bell, "The Proton in Chemistry", Chapman and Hall, London, 1973, Chapter 12. See also ref 1b.

(11) K. B. Wiberg and E. L. Motell, *Tetrahedron*, **19**, 2009 (1963).

(12) H. Kwart and M. C. Latimore, *J. Am. Chem. Soc.*, **93**, 3770 (1971).

(13) See, for example, A. Viola, J. H. MacMillan, R. J. Proverb, and B. L. Yates, *J. Am. Chem. Soc.*, **93**, 6967 (1971).

(14) (a) M. J. S. Dewar, *Angew. Chem., Int. Ed. Engl.*, **10**, 761 (1971); *Tetrahedron, Suppl.*, **8**, 1, 75 (1966); (b) M. J. S. Dewar and W. W. Schoeller, *J. Am. Chem. Soc.*, **93**, 1481 (1971); (c) W. V. E. Doering and R. Roth, *Tetrahedron*, **18**, 67 (1962).

(15) A. T. Blades and P. W. Gilderson, *Can. J. Chem.*, **38**, 1407 (1960).

(16) H. Kwart and J. Slutsky, *J. Chem. Soc., Chem. Commun.*, 1183 (1972).

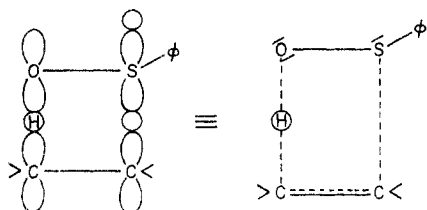
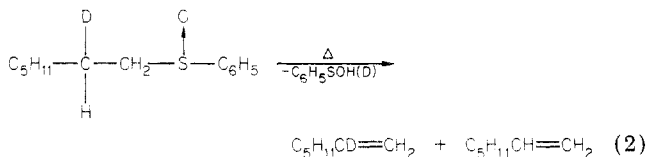


Figure 3. Sulfoxide thermolysis TS: pericyclic orbital diagram.

the product. The thermolysis reactions of benzyl allyl, benzyl propargyl, and alkyl allyl ethers, to which the full isotope effect criterion has also been applied,¹⁷ provide further examples of symmetrical linear H transfer between two carbon centers. In such cases $[\Delta E_a]_D^H = [\Delta E_0]_D^H = 1.1$ kcal and $A_H/A_D = 1.0 \pm 0.2$.

All these data support a generalized pericyclic process^{17a} encompassing a host of familiar thermolysis reactions that are now classifiable as retroene by virtue of a commonly structured, nonplanar TS of linear H transfer as represented in Figure 2, where W, X, Y, and Z can be carbon, nitrogen, or oxygen. The process corresponding to the thermodynamic reverse of this, known as the ene reaction,¹⁸ must of course take place via the identical TS. A number of recent studies, however, have discussed a "super" ene reaction that does not occur via the concerted, pericyclic TS established by the isotope effect data considered above. These cases are treated in a subsequent section.

The Thermal β -Cis-Elimination Reaction of Aliphatic Sulfoxides. (see eq 2). Stereochemical and



kinetic evidence¹⁹ proves this reaction occurs via a thermally induced, cyclic process of H transfer. The isotope effect measured²⁰ over the temperature range 403–503 K was entirely consistent with the TS structure of a planar, 5-membered, cyclic mechanism of linear H transfer; $[\Delta E_a]_D^H = [\Delta E_0]_D^H = 1.15$ kcal/mol and $A_H/A_D = 0.76$. This conclusion is expressed in the orbital diagram of the pericyclic^{14a} TS, Figure 3. Clearly, the greater length of the C–S bond and its freedom from steric influence are the most important factors in accommodating the twin requirements of coplanarity of the five centers in the TS and linear H transfer. However, when steric factors arising from substitution at carbon are introduced, such as in α -branched alkyl sulfoxides, the oxygen and carbon centers between which the H transfer must occur are brought much closer together in the TS. The "corset effect", discussed by Maier²¹ in connection with the properties of sub-

(17) H. Kwart, S. F. Sarnar, and J. Slutsky, *J. Am. Chem. Soc.*, **95**, 5242 (1973).

(18) (a) H. M. R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 556 (1969). (b) V. W. Oppolzer and V. Snieckus, *Angew. Chem.*, **90**, 506 (1978). (c) E. C. Keung and H. Alper, *J. Chem. Educ.*, **49**, 97 (1972).

(19) See, for examples: (a) C. A. Kingsbury and D. J. Cram, *J. Am. Chem. Soc.*, **82**, 1819 (1960); (b) J. R. Shelton and K. E. Davis, *Int. J. Sulfur Chem.*, **8**, 197 (1973).

(20) H. Kwart, T. J. George, R. Louw, and W. Ultee, *J. Am. Chem. Soc.*, **100**, 3927 (1978).

(21) G. Maier, S. Pfriem, U. Schafer, R. Matusch, *Angew. Chem., Int. Ed. Engl.*, **17**, 520 (1978).

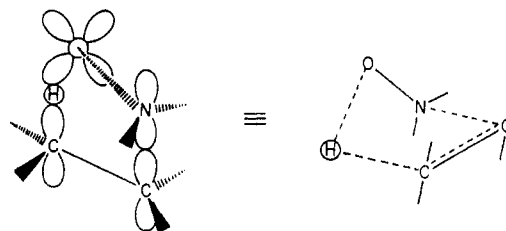
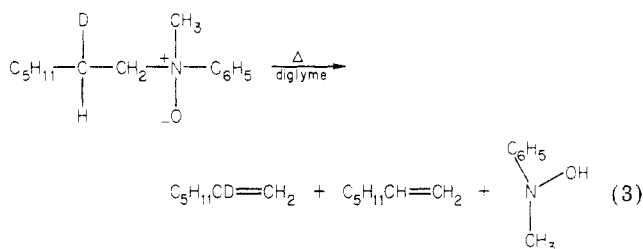


Figure 4. Amine oxide thermolysis TS*.

stituted tetrahedranes, is another expression of such steric influences of very bulky groups, like *tert*-butyl, in a cyclic TS. This corresponds to narrowing of the reaction barrier and is attended by an increased probability of tunneling. Such an occurrence was shown²² in the case of ethyl *tert*-butyl sulfoxide, for which the TDKIE parameters were found to be $[\Delta E_a]_D^H = 3.1$ kcal/mol and $A_H/A_D = 0.07$, which identify⁶ a tunneling process of linear H transfer.

Bent vs. Unsymmetrical Linear H-Transfer Transition States. *The thermal β -cis-elimination mechanism of amine oxides* (see eq 3) has been fre-



quently discussed²³ in terms of a cyclic, planar TS, analogous to that of the sulfoxide elimination, on the basis of stereochemical and substituent effect considerations. The temperature dependence of k_H/k_D was therefore applied as a test of this assumed mechanistic relationship to sulfoxide thermolysis.

However, when the thermolysis of the related amine oxide (eq 3) was studied²⁰ in the noncoordinating solvent diglyme at temperatures ranging from 363 to 484 K, it was found that the isotope effect did not change with temperature; $[\Delta E_a]_D^H = 0$ and $A_H/A_D = 2.209 \pm 0.007$ over the entire 120 K range. The conclusion to be drawn from these results is that the TS of this concerted reaction is bent and nonplanar. A structure for comparison with the normal TS of sulfoxide thermolysis (Figure 3) is given in Figure 4.

This kind of identification of the bent TS, by determining $[\Delta E_a]_D^H$ to be very small and A_H/A_D greater than 1.2, obviously requires data of very high precision and accuracy. Such concerns can be documented by an example in which the temperature dependence of an amine oxide thermolysis was estimated by direct, titrimetric measurements of rate rather than by the preferred^{1c} competition methods employed here.²⁰ In their titrimetric study of (phenylethyl)dimethylamine oxide thermolysis rates in solutions of Me_2SO (containing water or butanol as cosolvent), Chiao and Saunders²⁴ reported the TDKIE parameters $[\Delta \Delta H^\ddagger]_D^H = 0.3\text{--}1.6$ kcal/mol and $[\Delta \Delta S^\ddagger]_D^H = 0\text{--}3$ eu, with an error

(22) J. W. A. M. Janssen and H. Kwart, *J. Org. Chem.*, **42**, 1530 (1977).

(23) A. C. Cope, E. Ciganek, C. F. Howell, and E. E. Schweizer, *J. Am. Chem. Soc.*, **82**, 4663 (1960).

(24) W. B. Chiao and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **100**, 2802 (1978).

Table II
Temperature Dependence of k_H/k_D in Thermolysis of
 $C_6H_{11}CHDCH_2N(O)(CH_3)_2$ in Me_2SO Solution^a

temp, °C	k_H/k_D
170.0 ± 0.1	2.517
160.0 ± 0.1	2.561
139.9 ± 0.1	2.665
130.0 ± 0.1	2.720
120.0 ± 0.1	2.778
100.0 ± 0.1	2.919

^a Calculated quantities: $[\Delta E_a]_D^H = 0.695$ kcal/mol;
 $A_H/A_D = 1.14$; correlation coefficient = 0.9999.

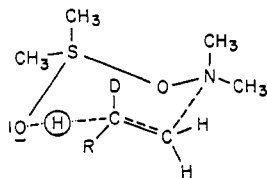


Figure 5. Unsymmetrical TS of Me_2SO -mediated β elimination of amine oxides.

probability of up to 5 eu.

The possibility of a variation of k_H/k_D with solvent in this reaction was adumbrated in early observations by Cram and co-workers,²⁵ which indicated that the use of Me_2SO solvent greatly accelerates the thermolysis of amine oxides. In order to evaluate this possibility we undertook to study the temperature dependence of eq 3 in a large excess of Me_2SO containing a total of approximately 1.6 mol of water/mol of the amine oxide, utilizing the competitive method previously employed.²⁰ Under these circumstances the water normally associated with the amine oxide is completely sequestered.

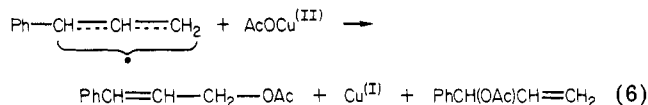
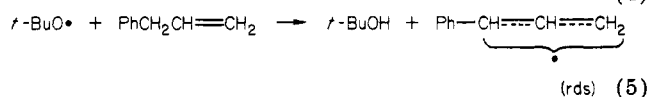
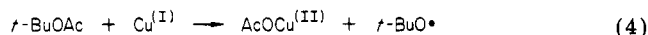
The data²⁶ listed in Table II, show a regular variation of k_H/k_D with temperature, in distinction to the temperature invariant values gathered in previous studies using the noncoordinating solvent diglyme. The activation parameters ($[\Delta E_a]_D^H = 0.695$ kcal/mol and $A_H/A_D = 1.14$) support the conclusion that the change to the coordinating solvent Me_2SO brought about a significant alteration in TS structure. In the altered TS the H-transfer takes place linearly between the carbon and oxyanion centers of the solvent-coordinated substrate. The looser, chair conformation of a 7-membered TS shown in Figure 5 is able to achieve the geometric requirements for linear H-transfer, whereas the more constricted 5-membered TS in Figure 4 cannot. The greater length of the S-O bonds also serves to accommodate a reaction barrier width great enough to permit linear H transfer without tunneling.

Furthermore, since $[\Delta E_a]_D^H$ is little more than half as great as $[\Delta E_0]_D^H$, we have here an example of an asymmetric TS, i.e., a product-like or reactant-like TS of linear H transfer, probably the former. These circumstances are fostered by the ability of Me_2SO to stabilize the carbanion character developing in the course of H transfer.

Radical abstraction of allylic hydrogen is a very facile process. Under ordinary bimolecular circumstances hydrogen atom abstraction from carbon prefers to take place with linear geometry, as evidenced by the data gathered by Wiberg and Motell¹¹ in studies of the tem-

perature dependence of k_H/k_D in the radical chlorination of methane; $[\Delta E_a]_D^H = [\Delta E_0]_D^H = 1.3$ kcal/mol; $A_H/A_D = 1.09$.

The allylic acetoxylation reaction²⁷ is known to involve abstraction of allylic hydrogen by *tert*-butoxy radical in the rate-determining step²⁸ (rds in the following example); see eq 4-6. As a probe of the role of



the adjacent double bond in the TS of this process, k_H/k_D was measured²⁹ at intervals over a 90 °C temperature range. The isotope effect was found to be essentially temperature independent ($k_H/k_D = 2.90 \pm 0.06$). Since A_H/A_D is therefore very much greater than the maximum of 1.2 for linear H-transfer processes,³⁰ a cyclic process of H abstraction, involving a bent TS, following initial complexation of the *tert*-butoxy radical with the allylic double bond, possibly obtains.

Recent secondary (k_H/k_D)_α experiments,³¹ using $\text{PhCH}_2\text{CD}=\text{CH}_2$ and $\text{PhCH}_2\text{CH}=\text{CD}_2$, support the concept of preliminary complexing of the nucleophilic radical *t*-BuO· with the allylic double bond. Since (k_H/k_D)_α is inverse at both C-1 and C-2 and the magnitudes of the respective effects are sufficiently different, it was possible to suggest that a preliminary charge-transfer complex was formed between the radical and the olefinic centers lying close to the TS of the H abstraction. Such complexing has been frequently detected by means of the same secondary KIE criteria for both polar and radical addition reactions of the double bond.³²⁻³⁴ Moreover, a preliminary bridging interaction between either nucleophilic or electrophilic radicals and orbitals has been justified by frontier orbital considerations^{35,36} for allylic H abstraction. The results presented above may be regarded as experimental support for this postulate.

The Superene Reaction. As discussed earlier, application of the TDKIE criterion has verified a symmetrical, linear H-transfer, pericyclic TS for the regular ene reaction. This is generally a poor-yielding preparative procedure requiring elevated temperatures (>150

(27) For a full discussion of this reaction, see G. Sosnovsky and S. O. Lawesson, *Angew. Chem., Int. Ed. Engl.*, **3**, 269 (1964).

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(29) H. Kwart, D. A. Benko, and M. E. Bromberg, *J. Am. Chem. Soc.*, **100**, 7093 (1978).

(30) Preexponential factors calculated for five model reactions^{1a} show that A_H/A_D lies between 0.75 and 1.2. It was also calculated previously^{1b} that, when $A_H/A_D = 1.2$, tunneling is unimportant; see J. H. Kim and K. T. Leffek, *Can. J. Chem.*, **52**, 592 (1974), for a fuller discussion of maxima and minima of A_H/A_D values in linear H-transfer processes.

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(36) K. N. Houk, "Frontiers of Radical Chemistry", W. A. Pryor, Ed., Academic Press, New York, 1980, pp 60-67.

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(26) H. Kwart and M. Brechbiel, *J. Am. Chem. Soc.*, **103**, 4650 (1981).

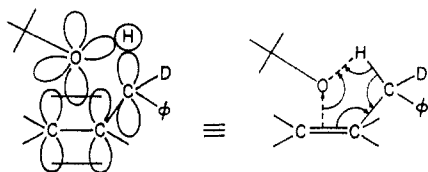
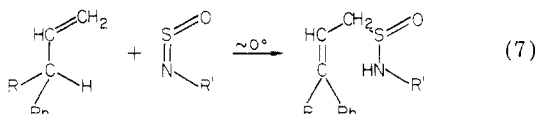


Figure 6. Bent TS* of allylic hydrogen abstraction.

°C) and protracted reaction times.¹⁸ A class of enophiles featuring multiply bonded heteroatoms at the reaction sites has been found to possess superenophilic properties. They rapidly and nearly quantitatively convert appropriate olefins to the expected ene reaction products at near ambient temperatures.

The TDKIE criteria have now been applied to several such cases. It has been found that the reaction course is considerably different from that in the regular ene.³⁷ Thus, the superene reaction described by eq 7 is char-



acterized by a temperature-independent $k_H/k_D = 2.863$ over a long temperature range, which is indicative of a bent TS. Ancillary evidence supports the rapid, reversible formation of a four-membered charge-transfer complex between the superene reactants. The observed regio- and stereoselectivity, taken together with the evidence for a bent TS following upon the formation of the CT complex, have led to the proposal of a pseudopericyclic process.³⁸ Therein, the unshared pair on the nitrogen that abstracts the H in the TS exchanges roles with the electron pair with which the nitrogen was bonded to the sulfur.

Another example recently studied³⁹ involves a carbonyl enophile with strongly electron-withdrawing substituents. For the ene reaction of dialkyl mesoxalates,⁴⁰ a classical pericyclic mechanism, modified by a slight deviation from linear H transfer in which the concerted TS occurs somewhat displaced along the reaction coordinate toward the character of the product,^{41,42} was assigned.

In our study of the TDKIE³⁹ of the reactions of diethyl mesoxalate and allylbenzene, the temperature-independent $k_H/k_D = 2.557 \pm 0.015$ suggests that the TS is bent, which is not in keeping with the earlier, classical pericyclic TS proposal. Moreover, the secondary $(k_H/k_D)_\alpha$ effects evaluated at both ends of the allylic double bond, $((k_H/k_D)_\alpha = 0.950 \pm 0.001$ per D at both C-1 and C-2), are both identical and inverse. These results again provide the basis for proposing a pseudopericyclic^{37,38} TS preceded by the formation of a symmetrically structured four-membered preliminary CT complex (see Figure 6).

Sigmatropic H Rearrangements: Extraordinary A_H/A_D Values. Acyclic conjugated pentadienes un-

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(42) L. M. Stephenson and M. Orfanopoulos, *ibid.*, **46**, 2200 (1981).

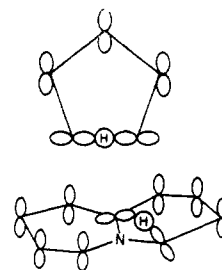
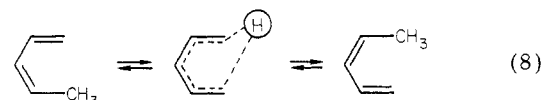


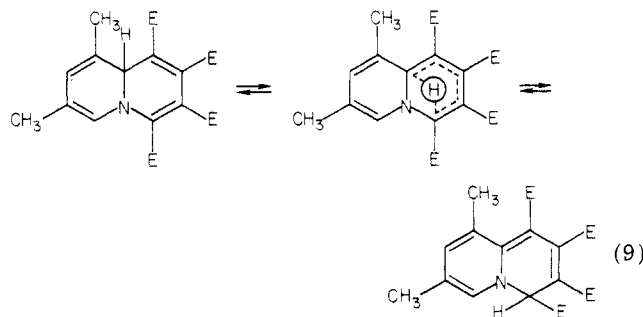
Figure 7. Acyclic linear sigmatropic H transfer (a, upper) and intracyclic nonlinear sigmatropic H transfer (b, lower).

dergoing 1,5-sigmatropic rearrangement have been regularly formulated⁴³ in the literature with a bent TS of H transfer. However, in the particular case shown in eq 8 a temperature-dependent isotope effect, where



$[\Delta E_a]_D^H = [\Delta E_0]_D^H$ and $A_H/A_D \cong 1$, has been determined,⁴³ though its significance in relation to the geometry of the TS depicted in Figure 7 was not recognized.

However, there are cases in which a 1,5-sigmatropic H transfer is clearly constrained by the rigid, cyclic geometry of the pentadienic framework to occur in a bent TS such as is shown in Figure 7b; the corresponding case in point shown in eq 9 was selected as



a test of the thesis that a bent TS will afford a temperature-independent k_H/k_D larger than $2^{1/2}$.

The results obtained⁸ not only fulfilled the expectations of our thesis inasmuch as temperature independence was observed over a >60 °C range, but the value of $A_H/A_D = 5.113 \pm 0.016$ was the largest one realized to that date. Apparently, the largest values of A_H/A_D are to be associated with bent transition states in which the nonlinear H transfer occurs at larger angles (but less than 180°). Model calculations have been cited⁸ that support the conclusion of a direct relationship between the size of A_H/A_D and the transfer angle.

Since tunneling is generally associated with extraordinarily large values of k_H/k_D , the thought might occur that these extraordinarily large values of A_H/A_D could stem from tunneling in a bent TS. This thought, however, must be rejected since tunneling can be noted only where k_H/k_D is temperature dependent, and, as we have seen here, in a bent TS the k_H/k_D is an isenthalpic quantity. Apparently tunneling in reactions of complex, multiatom molecules in solution does not occur when the H-transfer process is nonlinear, although this may

(43) W. R. Roth and J. König, *Liebigs Ann. Chem.*, **699**, 24 (1966).

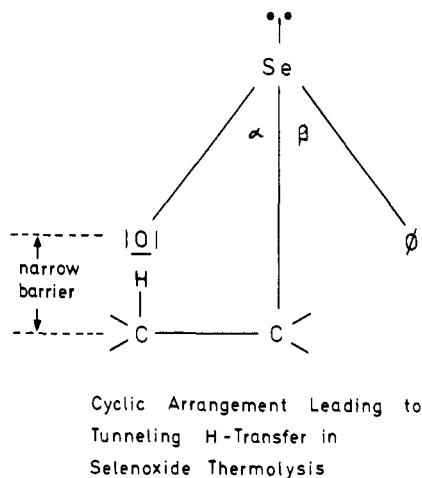
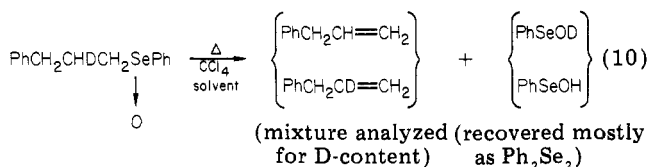


Figure 8.

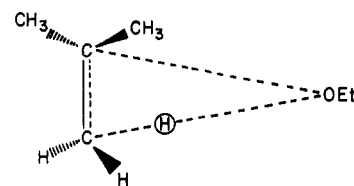
not be a prohibition in very simple structures in gas phase reactions.

Linear Transition States with a Major Tunnel Correction. The thermal β -cis-elimination mechanism of selenoxide-mediated olefin formation (see eq 10) has achieved great popularity as a means of introducing the double bond into complex organic structures via a stereospecific syn elimination.⁴⁴ The popularity of this procedure is related to the greatly diminished activation requirement compared to the corresponding sulfoxide elimination. To ascertain the origins of the rate increase that follows upon the replacement of sulfur by selenium, we measured the temperature dependence of k_H/k_D utilizing the competitive isotope effect method expressed by eq 10.



The experimental values⁴⁵ ($[\Delta E_a]_D^H = 2.52$ kcal/mol and $A_H/A_D = 0.092$) are clearly indicative of a tunneling pathway of β elimination. They are to be referenced to the isotope effect parameters found for highly hindered sulfoxides,^{23b} with which they are quite comparable in magnitude. In such sulfoxides, tunneling has been regarded as the consequence of steric deformation bringing into close proximity the centers involved in H transfer.

Using the VSEPR model^{46,47} as the basis for structuring the cyclic TS in keeping with these data requires that we take into account two important factors: (a) the considerable lengthening of the C-Se compared to the C-S bonds, and (b) the electropositive nature of the selenium which is responsible for a large degree of electron release from this central element in the cyclic TS, and, therefore, a diminished extent of bonding, electron-pair repulsions. Thus, even the bulkiest substituents on the selenium are mutually less repulsive

Figure 9. TS* structure in the thermolysis of *t*-BuOEt.

than those on sulfur, and when the repulsions arising from the nonbonding pairs are taken into consideration, a very considerable narrowing of the bond angles α and β depicted in Figure 8 is made understandable. Consequently, the lowering of the activation energy for thermal cis elimination attending the substitution of sulfur by selenium is to be correlated with a severe shortening of the distance of separation of the H-transfer reaction centers, the factor that brings about hydrogen tunneling much below the top of the semi-classical reaction barrier.

Some spectacular examples of tunneling in intramolecular H transfer have recently been observed. In the thermolysis of *tert*-butyl ethyl ether to isobutene and ethanol, reaction has been postulated to take place via a rectangular 4-membered TS on the basis of stoichiometric and activation parameter measurements.⁴⁸ This proposal, however, is at variance with data obtained in the course of measurements⁴⁹ of k_H/k_D over a 70 °C temperature range for $\text{C}_4\text{D}_9\text{OCH}_2\text{CH}_3$, $\text{C}_4\text{H}_9\text{O-CD}_2\text{CH}_3$, and $\text{C}_4\text{H}_9\text{OCH}_2\text{CH}_3$ pyrolyses.

Rather than a rectangular (bent) TS, which should have exhibited a temperature-independent isotope effect, it was found that $[\Delta E_a]_D^H = 5.7$ kcal, very much greater than $[\Delta E_0]_D^H$, and $A_H/A_D = 0.07$. It is noteworthy that if the reaction could be made to occur at ambient temperatures it would exhibit a k_H/k_D of >1000 .

The k_H/k_D value for substitution on the α -carbon of the ethyl moiety was found to correspond to a very small secondary D-isotope effect.⁵⁰ The magnitudes of the primary isotope effect parameters found are consistent only with linear H transfer occurring in a tunneling process. After correction for the secondary deuterium isotope effect due to the nontransferring deuterium,⁵¹ the reaction barrier dimensions could be computed from the data by a modified Bell-Caldin method;⁵ the calculated barrier width, 0.830 Å, is indicative of the closeness of the reaction centers between which the H is linearly transferred.

These results and other activation energy considerations are consonant with considerable extension (ionization) of the $-\text{C}^{\delta+}\cdots\text{OEt}^{\delta-}$ bond prior to H tunneling from the β -carbon to the now closely juxtaposed ether oxygen bearing a large degree of negative charge (see Figure 9).

A dramatic example of tunneling in the course of cyclic H transfer has been detected by Ingold and his collaborators⁵² in the isomerization of sterically hindered radicals. An aryl radical was converted intramolecularly to an alkyl radical through linear migration

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(48) N. J. Daly and C. Wentrup, *Aust. J. Chem.*, **21**, 1535 (1968).

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(50) See E. A. Halevi, *Prog. Phys. Org. Chem.*, **1**, 109 (1963).

(51) Corrected for the effects observed by V. J. Shiner and J. S. Humphrey, Jr., *J. Am. Chem. Soc.*, **84**, 2416 (1963).

(52) G. Brunton, J. A. Gray, D. Griller, L. R. C. Barclay, and K. U. Ingold, *J. Am. Chem. Soc.*, **98**, 6803 (1976); **100**, 4197 (1978).

of hydrogen from a methyl group, separated by a series of bonds in a cyclic array, which situated the transferring atom in close proximity to the initial radical center. A case in point is the isomerization of 2,4,6-tri-*tert*-butylphenyl radical.

The isomerization was observed over a very long temperature range ($-26 \rightarrow -245$ °C). It was possible under these conditions to recognize unequivocally curvature of the Arrhenius plot, a large difference in the activation energies, $[\Delta E_a]_D^H \gg 1.3$, and a large, inverse ratio of the preexponential factors ($A_H/A_D = 0.1 \rightarrow 0.01$) for H and D transfer. The experimentally determined k_H/k_D values rise from 80 at -30 °C to 13 000 at -150 °C, which is significantly larger than the maximum classical $k_H/k_D = 260$ at -150 °C.

Concluding Remarks

The applications of the mechanistic criteria discussed above represent only a small sample of a growing number of cases. The large majority of these cases, thus far, involve cyclic processes of intramolecular H transfer, although in theory as well as known practice there is no evident restriction from application to intermolecular H transfer. The most visible accomplishments of this kinetic isotope effect approach to elucidating mechanistic features are the following: (1) the identification of tunneling and the factors which bring about the alteration in the dimensions of the reaction barrier;

(2) the direct characterization of transition-state geometry, i.e., linear or angular H transfer, and some first hand perception of the factors that control this previously neglected TS property; (3) the emergence of a "definite" criterion of concertedness in H-transfer processes, wherein the magnitudes of $[\Delta E_a]_D^H$ and A_H/A_D are invoked in a quantitative way; (4) the basis for a call to reevaluate many earlier mechanistic conclusions derived from a single temperature measurement of k_H/k_D and an "eyeball" interpretation of such results. Values of A_H/A_D of extraordinary magnitude tend to vitiate this common practice among organic chemists interpreting isotope effects. Moreover, until suitable procedures of model calculations can be developed to account rigorously for temperature-independent isotope effects of extraordinary magnitude, previously calculated single temperature k_H/k_D values must be viewed with some suspicion. Whether an isotope effect is large, small, or intermediate (which is the language commonly used in such discussions) is devoid of significance until its temperature dependence is also known.

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Novel Radical Anions and Hydrogen Atom Tunneling in the Solid State

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While it has long been recognized that the exposure of solids to γ or X radiation at low temperatures results in the production of trapped radicals, it is perhaps less well-known that this technique has enabled the discovery of several novel and unusual paramagnetic

species. In this Account we are concerned largely with the characterization and chemical significance of the radical anions and radical-anion pairs formed from acetonitrile, methyl halides, and dimethyl sulfoxide.

Initially, these studies were severely complicated by the occurrence of hydrogen atom abstraction reactions by methyl radicals at low temperatures. Far from having only nuisance value, however, these reactions proved to be of intrinsic interest and provided an ideal proving ground for the demonstration of quantum tunneling.

Experimental Aspects

Because γ or X-ray photons have high energies (1.17 and 1.33 MeV from ^{60}Co), it is a common misconception that molecules in an absorber are subjected to an extremely energetic process devoid of chemical specificity.

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