by ^{1}H NMR was constant throughout the nitrogen extrusion process) ^{1}H NMR data for **19**: ($CDCl_3$) δ (Me_4Si) 1.96 (br m, 10 H), 3.45 (d of t, $J = 4$ and 7 Hz, 1 H), 5.05 (d, $J = 7$ Hz, 2 H), 9.14 (d, $J = 4$ Hz, 1 H); ^{1}H decoupling, irradiation at δ 3.45 gives 1.96 (br m, 10 H), 5.05 (s, 2 H), 9.14 (s, 1 H); irradiation at δ 5.05 gives 1.96 (br m, 10 H), 3.45 (d, $J = 4$ Hz, 1 H), 9.14 (d, $J = 4$ Hz, 1 H); irradiation at δ 9.14 gives 1.96 (br m, 10 H), 3.45 (t, $J = 7$ Hz, 1 H), 5.05 (d, $J = 7$ Hz, 2 H). The IR ($CDCl_3$) of the mixture of **16c** and **19** showed 2738 cm^{-1} and a broad carbonyl band, 1700–1725 cm^{-1}. Attempted purification of aldehyde **19** was thwarted by its instability.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Institutes of Health for support of this work. We also thank Dr. C. E. Costello for mass spectra.

Supplementary Material Available: Procedures for the preparation of several materials (as indicated above) (4 pages). Ordering information is given on any current masthead page.

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(3) Rastetter, W. H. *J. Am. Chem. Soc.* **1976**, *98*, 6350.

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(6) Rastetter, W. H.; Richard, T. J. *Tetrahedron Lett.* **1978**, 2999.

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(9) Although it might appear that trans double bond bonds would be formed if the Cope rearrangement were to occur via a transoid transition state, the dihedral angle between each epoxide C–H bond and the adjacent vinyl substituents in the transoid conformation (see, e.g., **3b**, Scheme II) is approximately 65°, which would allow cis double bond formation in the rearrangement product. See also Birladeanu, L.; Harris, D. L.; Winstein, S. *J. Am. Chem. Soc.* **1970**, *92*, 6387, especially footnote 13.

(10) Vogel, E.; Günther, H. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 385.

(11) A similar effect is seen with 2,7-dimethyloxepin and two related, interconverting oxepin oxides; see ref 5.

(12) The synthesis and chemistry of *syn*-2-hydroxyindan 3a,7a-oxide is described in the following: Rastetter, W. H.; Lewis, M. D.; Richard, T. J.; Adams, J. *J. Org. Chem.*, in press.

(13) For the parent, *sym*-oxepin oxide, the rate of Cope rearrangement is not quite rapid enough to produce fluxional NMR behavior; see ref 3 and 4.

(14) This argument, applied to homotropilidenes, was first advanced by Doering and Roth in their classic papers on thermal rearrangements. von E. Doering, W.; Roth, W. R. *Tetrahedron* **1963**, *19*, 715. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 115.

(15) Grimme, W. *J. Am. Chem. Soc.* **1973**, *95*, 2381.

(16) See, for example, Birladeanu, L.; Harris, D. L.; Winstein, S. *J. Am. Chem. Soc.* **1970**, *92*, 6387. Günther, H.; Pawliczek, J. B.; Ulmen, J.; Grimme, W. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 517. Klein, H.; Kursawa, W.; Grimme, W. *ibid.* **1973**, *12*, 580.

(17) See Cheng, A. K.; Anet, F. A. L.; Mioduski, J.; Meinwald, J. *J. Am. Chem. Soc.* **1974**, *96*, 2887, and references cited therein.

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(19) Equilibration of *sym*-2,7-dideuteriooxepin oxide with *sym*-4,5-dideuteriooxepin oxide at 39.8 °C requires ca. 3000 (see ref 4); in principle, an enzyme could accelerate or retard this rate.

(20) Details of the indicated procedures are available in the microfilm supplement to this paper; see paragraph at end of paper regarding supplementary material.

(21) Giovannini, E.; Wegmüller, H. *Helv. Chim. Acta* **1958**, *41*, 933.

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Quantitative Prediction of Structure–Reactivity Relationships for Unimolecular Reactions of Unsaturated Hydrocarbons. Development of a Semiempirical Model

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Contribution from the Department of Chemistry, Cornell University,
Ithaca, New York 14853. *Received December 18, 1978*

Abstract: A simple theoretical model that has previously been used to make qualitative predictions about substituent and benzannelation effects on the rates of thermal pericyclic reactions has now been shown to give quantitative results for a variety of unsaturated hydrocarbon reactions. These reactions include pericyclic and biradical transformations as well as simple homolytic fission to discrete radicals. Substituent effects on the rates of the pericyclic and biradical reactions can be predicted with an uncertainty (least-squares standard deviation) of ±1.7 kcal/mol, while for homolytic fissions the uncertainty is ±4.4 kcal/mol. Possible contributors to the success of the model are discussed. Applications of the model to the Cope rearrangement, Dewar benzene ring opening, and bicyclo[3.2.0]hept-6-ene ring opening are also considered.

A procedure based on simple Hückel molecular orbital (HMO) theory has recently been shown to provide some insight into the qualitative effects of substituents[1] and of benzannelation[2] on the rates of pericyclic reactions. We now report that the same approach provides a quantitative description of these structure–reactivity relationships if one considers only unsaturated hydrocarbon reactants. In addition, the model is found to be applicable to a number of radical and biradical reactions.

The technique involves selection of appropriate models for the reactant and transition state, and then evaluation of the Hückel π-electron energy (E_π) for each. If ΔE_π is defined as the difference in π-electron energy between the model transition state and reactant, the quantity $\Delta\Delta E_\pi$ is then the difference in ΔE_π for two reactions whose rates (or, more specifically, activation enthalpies) are to be compared. In the case of cyclobutene ring openings, it has been noted previously[2] that there is an apparent linear relationship between $\Delta\Delta E_\pi$ and $\Delta\Delta H^{\ddagger}$, the change in observed activation enthalpy that occurs upon replacement of the cyclobutene double bond by an annelated benzene ring or a pair of exocyclic methylene groups. Since the original investigation covered only four sets of reactions, it was not clear whether this relationship was fortuitous or genuine. The present work extends the investigation to 24 examples of widely varying hydrocarbon reactions and results in a linear $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ relationship covering a range of >50 kcal/mol in $\Delta\Delta H^{\ddagger}$.

The data are classified by reaction type and will be discussed in separate sections. Since the experimental data are drawn from many different sources, some reporting activation energy

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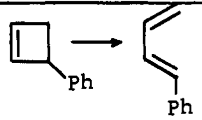
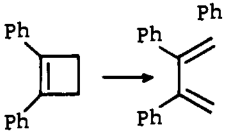
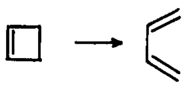
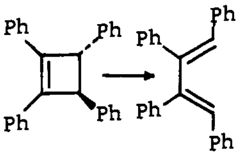
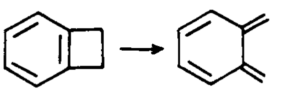
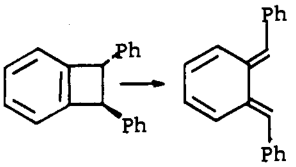
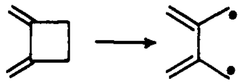
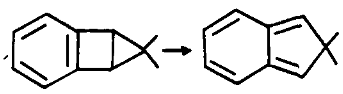
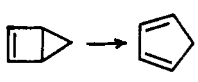
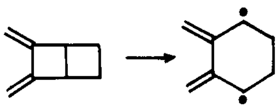
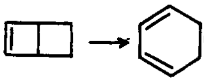
Table I. Cyclobutene and Related Ring Openings

Reaction	Reference Reaction (ΔE_π, $\Delta H^\ddagger$)	$\Delta\Delta E_\pi(\lvert\beta\rvert)$	$\Delta\Delta H^\ddagger$(kcal/mol)	Literature Reference
	 (-3.657, 31.6)	-0.361	-6.3	6
		+0.142	-0.5	7
		-0.620	-11.2	8
		+0.362	+6.4	2,9,50
		-0.412	-11.0	10
		+0.611	+14.1	11
	 (-2.000, 26.2)	-0.381	-7.6	2,12
	 (-2.000, 32.2)	-0.736	-14.7	13,14

and some activation enthalpy, it has been necessary to convert the data to a common base. We have elected to use activation enthalpy. Activation energies have been converted to activation enthalpies by subtraction of RT, where T is the mean temperature of the kinetic runs.[3] Where this temperature was not reported, T was taken to be the temperature at which the unimolecular rate constant would be 10^{-4} s^{-1}.

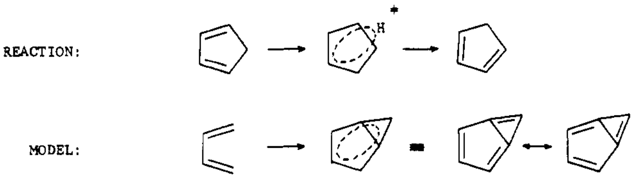
Pericyclic Reactions

(a) Cyclobutene Ring Openings. As described earlier,[2] we have assumed that unconstrained cyclobutenes will open in a conrotatory fashion and that the transition state for this process can be modeled by the π orbitals of the corresponding Möbius cyclobutadiene.[4] For cyclobutene itself the calculated value of ΔE_π is thus the difference between the Hückel π-electron energies of Möbius cyclobutadiene and ethylene, viz. $-3.657\lvert\beta\rvert$. The observed activation enthalpy is 31.6 kcal/mol.[5] In Table I the cyclobutene ring opening has been used as a reference for comparison with the conrotatory opening of substituted analogues. The differences in ΔE_π and in $\Delta H^\ddagger$ between the reaction under consideration and the reference reaction are recorded under the $\Delta\Delta E_\pi$ and $\Delta\Delta H^\ddagger$ columns, respectively.

When a cyclobutene is annelated about the 3,4 bond by a three- or four-membered ring, we have assumed that its ring opening will be constrained to be disrotatory and that the transition state for this process is best modeled by the π orbitals of a Hückel cyclobutadiene.[4] The reference reaction is then the ring opening of bicyclo[2.1.0]pentene or bicyclo[2.2.0]hexene, as appropriate.

For 3,4-disubstituted cyclobutenes, only the trans isomers have been considered, since they alone can undergo a conrotatory ring opening without serious steric interference.

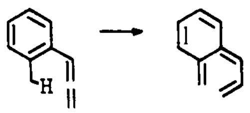
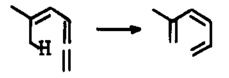
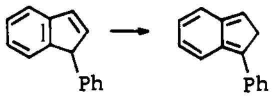
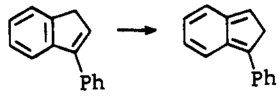
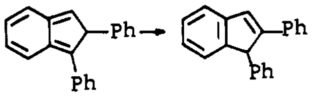
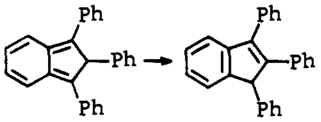
(b) [1,5]-Hydrogen Migrations. One of the more intriguing observations to be made during the course of this work is that a migrating hydrogen atom can be represented by a standard π center in our model and that changes in $\Delta H^\ddagger$ upon structural variation of the reactant are predicted as accurately as for reactions that involve only carbon-centered orbitals. Thus, the model transition state for [1,5]-hydrogen migration in cyclopentadiene is bicyclo[3.1.0]hexatriene.



$\Delta E_\pi = -3.918\lvert\beta\rvert$

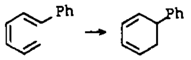
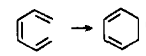
The calculated $\Delta\Delta E_\pi$ and observed $\Delta\Delta H^\ddagger$ for a variety of [1,5]-hydrogen shifts are recorded in Table II. In the second and third entries of Table II we have been forced to use the indene to isoindene rearrangement as a reference rather than the preferable (structurally simpler) degenerate [1,5]-hydrogen migration of cyclopentadiene. The rates of 1-phenyl-

Table II. [1,5]-Hydrogen Migrations

Reaction	Reference Reaction (ΔE_π, $\Delta H^{\ddagger}$)	$\Delta\Delta E_\pi(\lvert\beta\rvert)$	$\Delta\Delta H^{\ddagger}$ (kcal/mol)	Literature Reference
	 (-3.528, 23.9)	+0.270	+4.9	16,17
		-0.368	-4.8	15
		-0.039	-1.5	15
	 (-3.918, 21.2)	-0.446	-8.6	18
		-0.368	-7.3	18

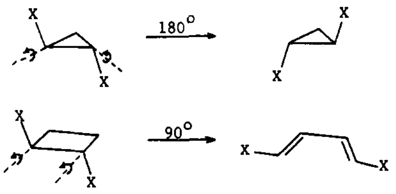
and 3-phenylindene rearrangements were reported only in terms of rate enhancements over the unsubstituted indene, not as absolute rate constants.[15] For the purposes of the present work these rate enhancements were converted to $\Delta\Delta G^{\ddagger}$ values at the temperature quoted and then, assuming negligible difference in $\Delta S^{\ddagger}$ between substituted and unsubstituted indenes, $\Delta\Delta G^{\ddagger}$ equated to $\Delta\Delta H^{\ddagger}$.

(c) Electrocyclic Ring Closure of (*Z*)-1,3,5-Hexatrienes. We could find quantitative data for only one unsaturated hydrocarbon-substituted hexatriene ring closure, viz., 1-phenyl-1,3,5-hexatriene.[19] The effect of the phenyl group is very small and not particularly well described by our model. However, we include it here for the sake of completeness. This reaction could not be included in our statistical evaluation of multiparameter vs. single parameter models (see section on treatment of data), since it was the only member of its class.

Reaction	Reference Reaction (ΔE, $\Delta H^{\ddagger}$)	$\Delta\Delta E_\pi$	$\Delta\Delta H^{\ddagger}$
	 (-1.012, 29.1)	+0.088	-0.9

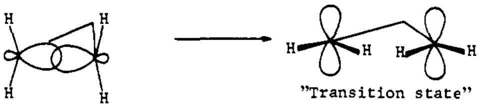
Biradical Reactions: Cyclopropane Stereomutation

One important distinction between cyclopropane stereomutation and an electrocyclic reaction such as cyclobutene ring opening is that in the former at least one methylene group must execute a 180° rotation, whereas in the latter only a 90° rotation is involved.

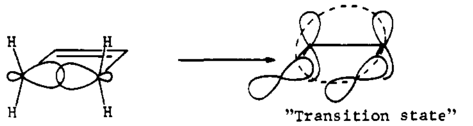


If the cyclopropane stereomutation were a single-step reaction, the transition state would necessarily occur at a rotation of 90°. In fact, there is some controversy about whether the species derived by rotating two methylene groups of cyclopropane through 90° is a transition state or an intermediate. Recent work[20] suggests that if it is an intermediate it cannot be in a very deep potential well. Consequently, the error in activation enthalpy derived by assuming such a species to be a transition state is unlikely to be large.

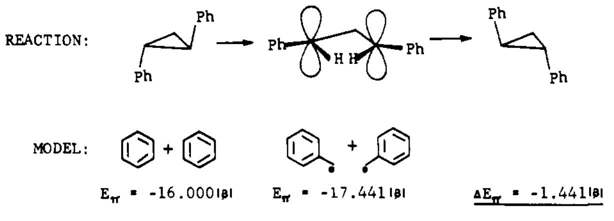
We assume that the residual bonding between two cyclopropane methylene groups that have executed a 90° rotation is negligible, especially since the reaction coordinate probably involves a substantial increase in the CCC angle:



This is to be contrasted with the cyclobutene ring opening, where the transition state necessarily occurs at a rotation of <90° and considerable residual bonding would be expected:[21]



These differences are reflected in our models for the respective transition states, illustrated in each case by the vicinal diphenyl derivative.



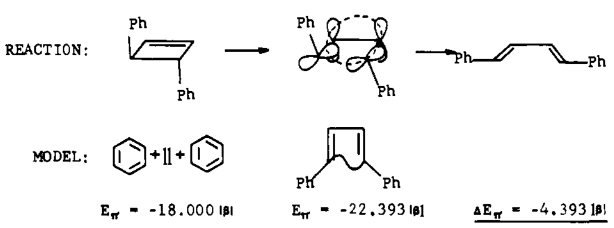
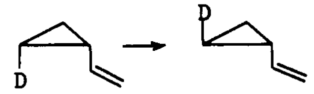
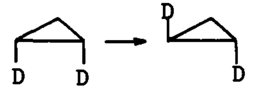
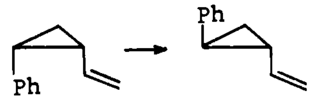
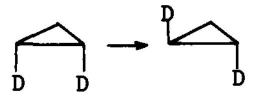
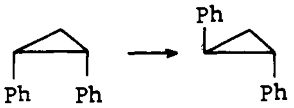
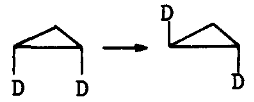
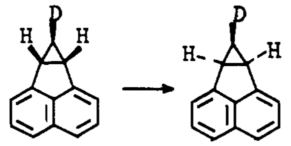
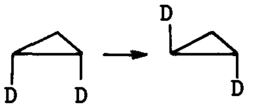
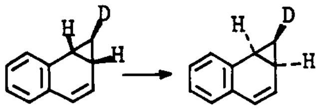
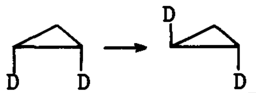


Table III. Cyclopropane Stereomutations

Reaction	Reference Reaction (ΔE_π, $\Delta H^{\ddagger}$)	$\Delta\Delta E_\pi(\lvert\beta\rvert)$	$\Delta\Delta H^{\ddagger}$ (kcal/mol)	Literature Reference
	 (0.000, 63.7)	-0.828	-16.4	10,25
		-1.549	-31.7	26
		-1.441	-31.0	27
		-1.587	-29.7	10
		-2.103	-44.8	23

Of course one can imagine a complete spectrum of potential energy surfaces for ring-opening reactions with varying degrees of bonding between the termini at the transition state. Presumably, as the ring-opened species becomes more stable (with respect to the reactant), the transition state should occur earlier and involve more bonding between the methylene carbons. Since our model allows only three values for the resonance integral of the breaking bond at the transition state (+1, 0, or −1 β units), one might anticipate that there would be difficulty in accommodating a range of transition states. Surprisingly we have not found this to be the case. A value of +1 (or −1 for an out-of-phase overlap) seems to accommodate the pericyclic reactions, while an assumption of zero bonding between the termini seems to account for substituent effects on the rates of cyclopropane stereomutations. In this regard the benzannelated norcaradienes represent a potentially instructive class. The ring opening of norcaradiene is an exothermic reaction and should clearly be treated as a pericyclic process with substantial bonding between the termini still present in the transition state. On the other hand, the ring opening of benzonorcaradiene is endothermic,[23] and the question arises whether to use a pericyclic ($\beta = +1$) or acyclic[24] ($\beta = 0$) model for the transition state. The acyclic model with cyclopropane as the reference standard does give a good quantitative description of the activation enthalpy. One can conjecture that the pericyclic model with norcaradiene as reference would have worked equally well. Unfortunately, the activation enthalpy for ring opening of norcaradiene is not known and so we are unable to test this hypothesis.

The cyclopropane stereomutations included in our analysis are listed in Table III.

Homolytic Cleavage Reactions

In view of the fact that the $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ relationship appears to encompass both pericyclic and biradical reactions, it is interesting to ask whether simple homolytic fission to two separate radicals can be included in the correlation. As shown in Table IV, it would appear that such is the case.

Treatment of Data

The slopes of the four $\Delta\Delta H^{\ddagger}/\Delta\Delta E_\pi$ (Tables I-IV) are recorded in Table V, along with the standard deviations of each fit. The standard deviations in $\Delta\Delta H^{\ddagger}$ for the first three reaction types range from 1.09 to 1.90 kcal/mol, which is outside the probable error of the measurements (an error of ±1.0 kcal/mol in the experimental values of $\Delta\Delta H^{\ddagger}$ seems reasonable). The radical reactions have a standard deviation of 2.11 kcal/mol, which is well within the estimated uncertainties of about 5 kcal/mol in each $\Delta H^{\ddagger}$.[28] The unfavorable discrepancy between the individual experimental errors for the first three reaction types and the (larger) deviations in $\Delta\Delta H^{\ddagger}$ calculated from the model suggests an error inherent to the model, such that even with perfect experimental data fitting errors of about 1.0 kcal/mol may be expected. Nevertheless, this residual error seems surprisingly small given the obvious crudity of the model.

Although there is a wide spread in the slopes, the standard deviations of the slopes are also large and one may reasonably question whether the entire data set of 24 points could be adequately correlated by a single line through the origin. When the individual points were weighted in accordance with their estimated uncertainty (1.0 and 5.0 kcal/mol as described above) the calculated regression line is:

$$\Delta\Delta H^{\ddagger} = 20.33\ \Delta\Delta E_\pi \qquad \text{(weighted)}$$

$$\sigma_{\Delta\Delta H^{\ddagger}}\ \text{(pericyclic + biradical reactions)} = 1.66\ \text{kcal/mol}$$

$$\sigma_{\Delta\Delta H^{\ddagger}}\ \text{(simple radical reactions)} = 4.35$$

$$\sigma_{\text{slope}} = 0.58\ \text{kcal/(mol}\cdot\lvert\beta\rvert)$$

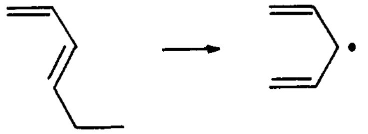
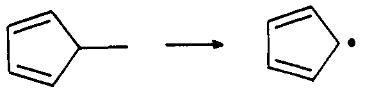
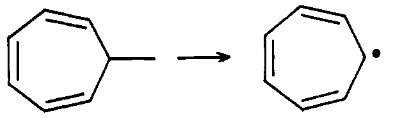
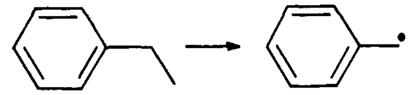
If all of the weights are set equal to unity the equation becomes:

$$\Delta\Delta H^{\ddagger} = 19.31\Delta\Delta E_\pi \qquad \text{(unit weights)}$$

$$\sigma_{\Delta\Delta H^{\ddagger}} = 2.25\ \text{kcal/mol}$$

$$\sigma_{\text{slope}} = 0.47\ \text{kcal/(mol}\cdot\lvert\beta\rvert)$$

Table IV. Homolytic Cleavage Reactions (All Experimental Data from Reference 28)

Reaction	Reference Reaction (ΔE_π, $\Delta H^\ddagger$)	$\Delta\Delta E_\pi(\lvert\beta\rvert)$	$\Delta\Delta H^\ddagger$(kcal/mol)
 + • CH_3	$C_2H_6 \rightarrow 2H_3C\bullet$ (0.000, 88.2)	-0.828	-12.6
 + • CH_3	$C_2H_6 \rightarrow 2H_3C\bullet$	-1.464	-24.0
 + • CH_3	$C_2H_6 \rightarrow 2H_3C\bullet$	-0.992	-18.7
 + • CH_3	$C_2H_6 \rightarrow 2H_3C\bullet$	-1.382	-24.0
 + • CH_3	$C_2H_6 \rightarrow 2H_3C\bullet$	-1.555	-27.0
 + • CH_3	$C_2H_6 \rightarrow 2H_3C\bullet$	-0.721	-16.4

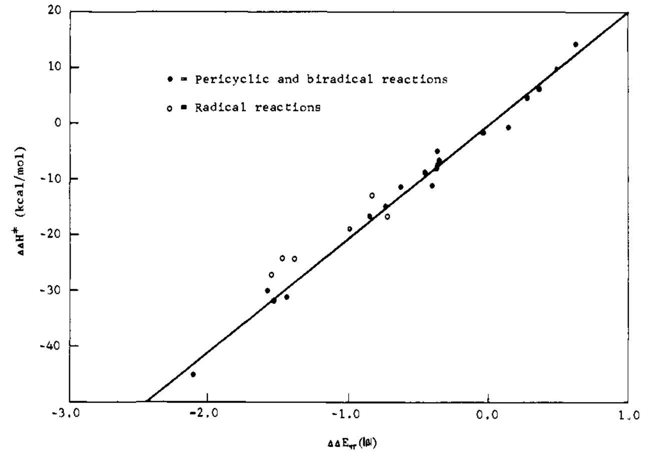


Figure 1.

Table V. Comparison of $\Delta\Delta H^\ddagger/\Delta\Delta E_\pi$ Plots for Pericyclic, Biradical and Radical Reactions

reaction type	no. of points	slope, kcal/(mol·$\lvert\beta\rvert$)	$\sigma_{\Delta\Delta H^\ddagger}$	σ_{slope}
pericyclic				
(a) cyclobutene ring openings	8	20.22	1.90	1.38
(b) [1,5]-hydrogen migrations	5	17.77	1.09	1.47
biradical	5	20.57	1.78	0.51
homolytic fission	6	17.45	2.11	0.72

The question to be answered is whether the use of four independent slopes for the four reaction types results in a statistically significant improvement in the fit. Such problems can be addressed by applying the *F* test,[29] which inquires whether the decrease in the calculated variance on using four slopes in place of one could occur by chance (say with 95% probability) or whether the improvement is so marked that it is statistically improbable that it appears by chance (say with less than 5% random occurrence). When the data have unequal weights, the unweighted variance must be replaced by the "generalized *R* factor", but the logic is unchanged.

With an unweighted analysis (of dubious significance given the known larger uncertainties in the radical reaction $\Delta H^\ddagger$s), the one-parameter model can just be rejected at the 95% confidence level. With weighted points the *F* value calculated for 24 points with 20 df compared to a model with 3 constrained parameters is 1.066, corresponding to a confidence level of 39%. This says that the increase in weighted residuals on constraining 3 parameters is neither large enough (i.e., greater than 3.10) to reject the 1-parameter treatment, nor small enough (less than 0.115) to reject the 4-parameter model. In short, there is no statistically significant basis from the available data and assumed weights for choosing one model over the other. Until additional data prove otherwise, it would appear wiser to use the weighted one-parameter model both for its simplicity and as a way to avoid underestimating the errors for predicted $\Delta\Delta H^\ddagger$s. In summary, then:

$$\Delta\Delta H^\ddagger = 20.33\Delta\Delta E_\pi$$

± 1.7 kcal/mol (pericyclic and biradical reactions)

and

$$\Delta\Delta H^\ddagger = 20.33\ \Delta\Delta E_\pi$$

± 4.4 kcal/mol (dissociation to simple radicals)

Errors are expressed as standard deviations in $\Delta\Delta H^\ddagger$ rather than standard deviations in the slope, since there is no evidence for increasing error with increasing distance from the origin. The weighted one-parameter regression line is displayed graphically in Figure 1.

Theoretical Interpretation

Observation of a quantitative correlation between $\Delta\Delta E_\pi$ and $\Delta\Delta H^\ddagger$ has to be reconciled with a number of uncomfortable facts:

(1) It is well known that the approximations of simple Hückel molecular orbital theory are so severe that, with a few notable exceptions (vide infra), the method is unable to give accurate quantitative descriptions of molecular properties.

(2) The present work deals with biradical intermediates and forbidden reaction transition states, both known to require the use of extensive configuration interaction (CI) to arrive at a proper description of the wave functions and relative state energies.[30,31] Our model uses no CI.

(3) The model transition states used in the present work cannot correspond to the real transition states in terms of the magnitude of overlap between adjacent orbitals. In particular, we have allowed only three values (+1, 0, and −1 β units) for the resonance integral between a pair of orbitals. This cannot be the case in reality.

One may reasonably ask, then, how a theoretical model that is so obviously faulty can provide a quantitative description of structure-reactivity relationships in the reactions of unsaturated hydrocarbons.

In trying to answer this question it must be emphasized that the $\Delta\Delta E_\pi/\Delta\Delta H^\ddagger$ correlation is purely empirical and that a complete understanding of its origin is not yet at hand. Rather we will argue by analogy and attempt to show that a correlation of this type is at least plausible.

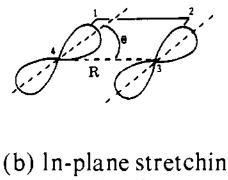
One major contributor to the success of the procedure must surely be the "double difference" technique employed. Thus, by comparing the calculated activation enthalpies for two structurally related reactions one is presumably "cancelling out" a variety of errors that would surely be present in the calculation for a single reaction. In this regard the technique can be likened to that commonly employed in linear free-energy relationships where one considers the relative effect of a particular structural change on two related reactions.[32]

It is also instructive to compare the $\Delta\Delta E_\pi/\Delta\Delta H^\ddagger$ correlation with the good quantitative description of aromatic hydrocarbon resonance energies by HMO theory.[33] Here too the delocalization energy/resonance energy plot is concerned with differences between calculated quantities vs. differences between experimental quantities. (Delocalization energy is the difference in calculated π-electron energy between the fully delocalized molecule and a localized model, while empirical resonance energy is typically the difference in experimental enthalpy of hydrogenation between the aromatic molecule itself and a localized, nonaromatic model.) The linear $\Delta\Delta E_\pi/\Delta\Delta H^\ddagger$ relationship described in the present work seems to be showing that the accurate description of the structural dependence of thermodynamic properties by HMO theory can be extended to a description of kinetic (transition state) properties. It is certainly striking that the value of $|\beta|$ derived from the $\Delta\Delta E_\pi/\Delta\Delta H^\ddagger$ plot (20 kcal/mol) is so close to the values derived from the aromatic resonance energy plots (16-20 kcal/mol).[33]

A much more difficult problem is the obvious inaccuracy of the transition-state models used to derive the $\Delta\Delta E_\pi/\Delta\Delta H^\ddagger$ relationship. While the models must be incorrect in detail they apparently contain some grain of truth that allows quantitative calculation of structure-reactivity relationships. Clearly it would be desirable to find out what this property is, since it presumably represents the essence of success of the technique.

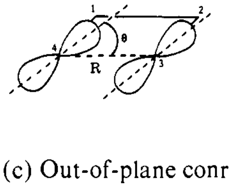
One approach to the problem is to investigate the effect of choosing different transition-state models on the $\Delta\Delta E_\pi/\Delta\Delta H^\ddagger$ relationship. In particular it would be desirable to try to identify the feature or features distinguishing a "good" transition-state model from a "poor" one. We have investigated this question for benzocyclobutene and bismethylenecyclobutane ring openings (both referred to the ring opening of cyclobutene itself as the standard reaction). In each case five different ring-opening pathways (and hence five different transition-state models) were considered. In the summaries of these reaction pathways shown below, α is a parameter measuring the extent of reaction; $\alpha = 0$ for reactant and $\alpha = 1$ for the product. The resonance integrals β_σ and β_π are assumed to be directly proportional to the overlap integrals $S_{\sigma\sigma}$ and $S_{\pi\pi}$.[34]

(a) In-plane conrotation with simultaneous stretching of the 3,4 bond:



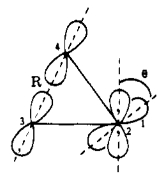
$\theta = 90\alpha$
$R = (1.54 + 1.2\alpha)$ Å
$\beta_{12} = 1.0$
$\beta_{14} = \sin\theta$
$\beta_{23} = -\sin\theta$
$\beta_{34} = \beta_\sigma \cos^2\theta - \beta_\pi \sin^2\theta$

(b) In-plane stretching of the 3,4 bond from 1.54 to 2.36 Å followed by in-plane conrotation without further change in the 3,4 internuclear distance:



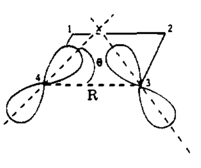
$\theta = 90\alpha$
$R = 2.364$ Å
$\beta_{12} = 1.0$
$\beta_{14} = \sin\theta$
$\beta_{23} = -\sin\theta$
$\beta_{34} = \beta_\sigma \cos^2\theta - \beta_\pi \sin^2\theta$

(c) Out-of-plane conrotation:



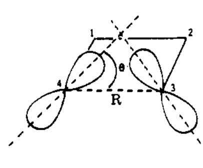
$\theta = 90\alpha$
$R = (1.54 + 1.7\alpha)$ Å
$\beta_{12} = \cos\theta$
$\beta_{14} = -\sin\theta$
$\beta_{23} = \sin\theta$
$\beta_{34} = \beta_\sigma$

(d) In-plane disrotation with simultaneous stretching of the 3,4 bond:



$\theta = 90\alpha$
$R = (1.54 + 1.2\alpha)$ Å
$\beta_{12} = 1.0$
$\beta_{14} = \sin\theta$
$\beta_{23} = \sin\theta$
$\beta_{34} = \beta_\sigma \cos^2\theta + \beta_\pi \sin^2\theta$

(e) In-plane stretching of the 3,4 bond from 1.54 to 2.36 Å followed by in-plane disrotation without further change in the 3,4 internuclear distance:



$\theta = 90\alpha$
$R = 2.364$ Å
$\beta_{12} = 1.0$
$\beta_{14} = \sin\theta$
$\beta_{23} = \sin\theta$
$\beta_{34} = \beta_\sigma \cos^2\theta + \beta_\pi \sin^2\theta$

If there is an exact linear correlation:

$$\Delta\Delta H^\ddagger\,(\text{obsd}) = m\Delta\Delta E_\pi$$

for a particular model, then one should find that for two different reactions:

$$\frac{\Delta\Delta H^\ddagger(1)}{\Delta\Delta H^\ddagger(2)} = \frac{\Delta\Delta E_\pi(1)}{\Delta\Delta E_\pi(2)} \equiv r$$

The advantage of taking this kind of ratio is that one cancels out the model-dependent slope m, allowing a more meaningful comparison between different models. Thus one would like to know, for example, how the r value obtained from the Möbius cyclobutadiene-based transition-state model for conrotatory ring opening of cyclobutene derivatives compares with the r values for conrotatory pathways a-c. In addition, it would appear to be desirable to investigate the variation of r with α

Table VI[a]

	conrotatory pathways									disrotatory pathways					
	a			b			c			d			e		
α	A	B	r	A	B	r	A	B	r	A	B	r	A	B	r
0.0	0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0		0.0	0.0	
0.1	0.0225	0.0140	1.61	0.0307	0.0188	1.63	0.0088	0.0057	1.54	−0.0171	−0.0083	2.06	−0.0237	−0.0108	2.19
0.2	0.0938	0.0576	1.63	0.1185	0.0719	1.65	0.0386	0.0248	1.56	−0.0711	−0.0343	2.07	−0.0950	−0.0431	2.20
0.3	0.2160	0.1304	1.66	0.2504	0.1495	1.67	0.0943	0.0599	1.57	−0.1680	−0.0804	2.09	−0.2137	−0.0974	2.19
0.4	0.3803	0.2242	1.70	0.4085	0.2388	1.71	0.1764	0.1107	1.59	−0.3160	−0.1501	2.11	−0.3768	−0.1551	2.43
0.5	0.5613	0.3220	1.74	0.5723	0.3273	1.75	0.2779	0.1721	1.61	−0.4458	−0.1734	2.57	−0.1682	0.1384	−1.22
0.6	0.7211	0.4042	1.78	0.7244	0.4057	1.78	0.3774	0.2316	1.63	0.0284	0.4206	0.07	0.1480	0.4777	0.31
0.7	0.7979	0.4682	1.70	0.7965	0.4683	1.70	0.4676	0.2857	1.64	0.3954	0.5091	0.78	0.3844	0.5101	0.75
0.8	0.7714	0.5082	1.52	0.7252	0.5131	1.41	0.5401	0.3304	1.63	0.6176	0.5246	1.18	0.5459	0.5320	1.03
0.9	0.7819	0.5292	1.48	0.6834	0.5398	1.27	0.5907	0.3644	1.62	0.7490	0.5327	1.41	0.6392	0.5446	1.17
1.0	0.8096	0.5334	1.52	0.6696	0.5486	1.22	0.6178	0.3880	1.59	0.8096	0.5334	1.52	0.6696	0.5486	1.22

r values from model	
conrotation	1.69
disrotation	1.93
single rotation	0.69

[a] $A = \Delta\Delta E_\pi$ for bismethylenecyclobutane; $B = \Delta\Delta E_\pi$ for benzocyclobutene.

in order to determine whether points on the potential energy profile other than the transition state could provide a $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ correlation. In principle, r should be equal to the ratio of experimental $\Delta\Delta H^{\ddagger}$ values for the two reactions in question. However, since none of the models will give a perfect $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ correlation, this need not be true in practice. In particular a model that gives a value of r close to the experimental one for a particular pair of reactions need not be the model that gives the best fit to experimental data over all the reactions considered. Our interest here is to use r as a parameter for comparison of the model used in developing the empirical $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ relationship with the somewhat more detailed models outlined in a–e.

The calculations on pathways a–e for benzocyclobutene and bismethylenecyclobutane are summarized in Table VI. A number of striking features can be seen in Table VI. Firstly, for the conrotatory pathways a–c, r is quite constant over a large range of α, implying that points other than the transition state could give a $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ correlation. This is in strong contrast to the disrotatory pathways d–e where a sharp discontinuity occurs at $\alpha \simeq 0.5$. This discontinuity can be traced to a HOMO–LUMO crossing that occurs in the forbidden (disrotatory) pathway, but which does not occur for the allowed (conrotatory) mode.[35] Note that points beyond the transition state of the allowed reaction, even the product, give r values that are reasonably close to the value derived from the original model. This is clearly not the case for the forbidden pathways. One can expect, therefore, that the concept of "thermodynamic driving force", in which one attempts to deduce the rate of a reaction from the stability of the product, is likely to be qualitatively correct for allowed reactions but not for forbidden reactions. Experimental evidence appears to support this contention.[2]

A second interesting observation is that the value of r varies little between conrotatory pathways a–c, despite their very different transition-state geometries, and is very close to the value obtained from the Möbius cyclobutadiene based model for the conrotation transition state. Similarly, the value of r (for $0 < \alpha < 0.5$) is quite constant between disrotatory pathways d and e and is again close to the value derived from the model transition state. It is also noteworthy that these values of r are each very different from that obtained for a third type of mechanism, single methylene rotation.

While this kind of numerical experiment does not constitute a formal proof, it does provide support for a number of tentative conclusions. (1) It appears that r is approximately constant for a number of possible transition-state geometries belonging to the same topological set. There are, however, significant changes in r with change in orbital topology of the transition state. (2) The model transition states based on the π-isoconjugate hydrocarbon, while not corresponding to points on any of the potential energy profiles calculated in a–e, do retain the orbital topology information and do appear to give r values close to those derived from the more detailed treatment. (3) In view of (1) and (2) above it would appear that orbital topology may be very important in determining the value of r and hence may be a significant contributor to the success of the $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ correlation.

Applications of the $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ Relationship. The most obvious use of the relationship is to predict the activation enthalpy for a pericyclic, radical, or biradical reaction of a hydrocarbon, provided, of course, that one has the data for a suitable reference reaction. In Table VII are listed a few more or less arbitrarily chosen examples.

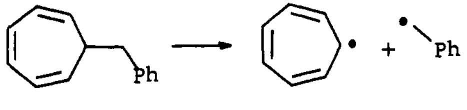
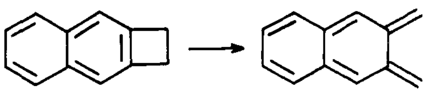
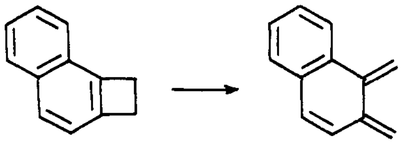
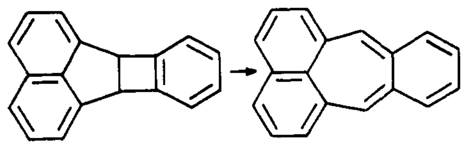
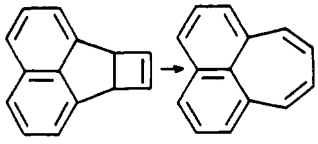
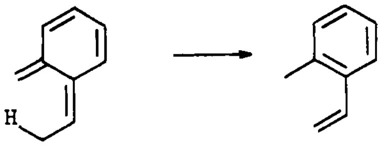
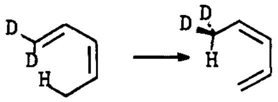
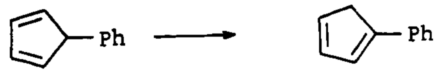
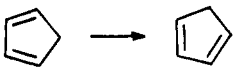
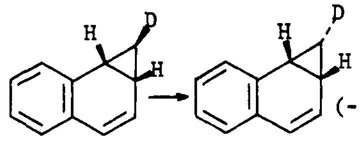
A somewhat more conjectural application of the procedure is to use the comparison between observed and calculated $\Delta\Delta H^{\ddagger}$ values as a criterion for evaluating the probability that a particular reaction is proceeding by a concerted pericyclic mechanism. If the observed $\Delta\Delta H^{\ddagger}$ for a reaction differs by a statistically significant amount ($>3\sigma$, say) from that calculated on the basis of a pericyclic model, one may suspect that the assumed mechanism is incorrect. It is important to point out, however, that the $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ correlation has been derived from a rather limited set of reactions and there is no proof that it applies to all pericyclic reactions of neutral hydrocarbons (although considering the diversity of the reactions that do fit it seems a reasonable assumption). Consequently, if a new reaction fails to obey the $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ correlation it should be taken as an indication, but not a proof, that the mechanism may be different from that presumed in applying the model.

We have found three sets of reactions that deviate significantly from the $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ correlation, and, in each case, there is indeed some question about the mechanism of the process.

Dewar Benzene and Related Ring Openings (Table VIII). As noted earlier,[2] the Dewar benzene and related ring openings are very poorly correlated by the $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ relationship. It seems probable that this is because the reactions are not simple pericyclic processes—a conclusion arrived at independently by other workers.[40,43] Sadly, the present procedure does not enable one to deduce what the mechanism is, merely what it probably is not.

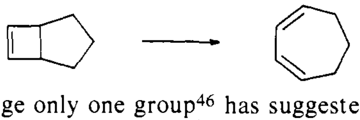
Cope Rearrangement. The $\Delta\Delta E_\pi/\Delta\Delta H^{\ddagger}$ correlation can

Table VII

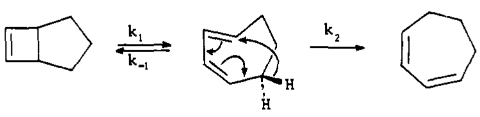
Reaction	Predicted $\Delta H^{\ddagger}$ (kcal/mol)	Reference Reaction (ΔE_{π}, $\Delta H^{\ddagger}$)	Literature Reference
	42.1	$C_2H_6 \longrightarrow 2H_3C\bullet$ (0.000, 88.2)	28
	40.3	 (-3.657, 31.6)	5
	37.2		5
	33.7	 (-3.163, 38.5)	39
	31.3	 (-3.528, 35.4)	38
	14.0	 (-3.918, 21.2)	36
	13.4	 (-3.258, 18.9)	23

hold only if the mechanism of a particular transformation is invariant with respect to substitution. (In this regard it can again be likened to a linear free-energy relationship such as the Hammett equation.) If a reaction has two or more paths separated by only a small energy gap, it may be possible for substitution to cause a change (gradual or sudden) from one mechanism to another. It has recently been suggested that the Cope rearrangement is just such a reaction.[44] The proposed alternate pathways are a pure pericyclic [3,3]-sigmatropic shift and a stepwise reaction proceeding via a cyclohexane-1,4-diyl biradical. Gajewski[44] has suggested that the mechanism may vary between these extremes depending upon substitution. This proposal is certainly consistent with our observation that neither a pericyclic model nor a biradical model alone allows a good $\Delta\Delta E_{\pi}/\Delta\Delta H^{\ddagger}$ fit for all substitution patterns (Table IX). It seems probable that there may be other such "variable mechanism" reactions (the Diels-Alder reaction looks like a prime candidate, for example) that could be identified through a study of the effect of unsaturated hydrocarbon substituents.

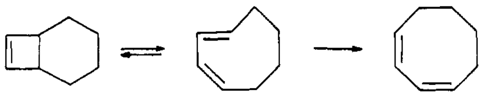
Ring Opening of Bicyclo[3.2.0]hept-6-ene Derivatives. The ring opening of bicyclo[3.2.0]hept-6-ene to *cis,cis*-1,3-cycloheptadiene has been supposed by most workers to be a forbidden disrotatory or a biradical process:[45]



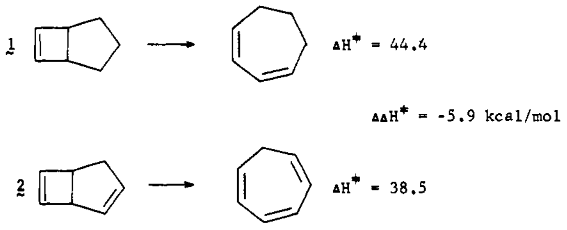
To our knowledge only one group[46] has suggested that the mechanism may involve an allowed conrotatory ring opening followed by a [1,5]-hydrogen shift:



In 1969, McConaghy and Bloomfield[46] reported that just such a process occurs for the next higher homologue, bicyclo[4.2.0]oct-7-ene:



Application of the $\Delta\Delta E_{\pi}/\Delta\Delta H^{\ddagger}$ relationship becomes apparent when one considers the effect of introducing a second double bond on the activation enthalpy for ring opening of **1**:



A forbidden disrotatory model leads to the prediction of a decrease in activation enthalpy of 12.2 kcal/mol upon introduction of the second double bond, while a biradical model predicts $\Delta\Delta H^{\ddagger} = -13.0$ kcal/mol. The observed $\Delta\Delta H^{\ddagger}$ of -5.9 kcal/mol differs from these calculated values by 3.8 and 4.3 σ, respectively, leading us to conclude that neither is a

Table VIII

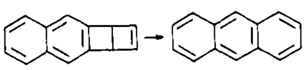
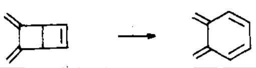
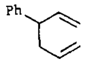
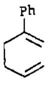
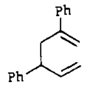
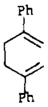
Reaction	$\Delta\Delta H^{\ddagger}_{calc}$[a] (kcal/mol)	$\Delta\Delta H^{\ddagger}_{obs}$	diff/σ[e]
	7.4	0.0[b]	4.4
	8.7	2.0[c]	4.0
	12.4	-5.8[d]	11.0

Table IX

Reactant	$\Delta\Delta H^{\ddagger}$calc (pericyclic)	$\Delta\Delta H^{\ddagger}$calc (biradical)	$\Delta\Delta H^{\ddagger}$obs	diff/σ (pericyclic)	diff/σ (biradical)
	-7.8	0.0	-3.0	2.9	1.8
	0.8	-6.0	-1.9	1.6	2.5
	-7.0	-6.0	-6.6	0.2	0.4
	1.6	-12.0	-10.2	8.2	1.1

satisfactory model for the true reaction mechanism.[47] There would be no point in comparing observed and calculated effects of the second double bond for the conrotatory ring opening if the [1,5]-hydrogen shift were the rate-determining step for the McConaghy-Bloomfield mechanism. Work of Wiberg[48] and Christl[49] suggests that this may well be the case. They have shown that the bicyclo[1.1.0]butane derivatives **3** and **4** undergo thermal rearrangement to **1** and **2**, respectively, and have strongly implicated *cis,trans*-1,3-cycloheptadiene and *cis,cis,trans*-1,3,5-cycloheptatriene as intermediates in these reactions:

3 

4 

These results suggest that $k_{-1} \gg k_2$ in the McConaghy-Bloomfield mechanism, making the [1,5]-hydrogen shift rate determining by definition.

The quantitative effect of the extra double bond on the activation enthalpy for [1,5]-hydrogen shift is hard to determine in such highly distorted systems. However, if the differences in strain energy and distortion between the *cis,trans*-diene and *cis,cis,trans*-triene are ignored, the $\Delta\Delta E_{\pi}/\Delta\Delta H^{\ddagger}$ relationship leads to the prediction of $\Delta\Delta H^{\ddagger} = -7.4$ kcal/mol, in reasonable agreement (0.9σ) with the observed value.

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