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Thermal [1,5] Hydrogen Sigmatropic Shifts in *cis,cis*-1,3-Cyclononadienes Probed by Gas-Phase Kinetic Studies and Density Functional Theory Calculations

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Abstract: The kinetics of gas-phase thermal [1,5] hydrogen shifts interconverting the five isomeric monodeuterium-labeled *cis,cis*-1,3-cyclononadienes have been followed at four temperatures from 240 to 287 °C. The activation parameters found were $E_a = 37.1 \pm 0.8$ kcal/mol, log A $= 11.6 \pm 0.3$, $\Delta H^{\ddagger} = 36.0 \pm 0.8$ kcal/mol, and $\Delta S^{\ddagger} = -9.0 \pm 0.3$ eu. Density functional theory based calculations have provided geometries and energies for the ground-state cyclononadiene conformational isomers, for the transition states linking one to another, and for the transition states for [1,5] hydrogen shifts responsible for isomerizations among the five labeled dienes. A generalized formulation of the Winstein-Holness equation is presented and applied to the complex system, one that involves 11 ground-state conformers, 10 transition states separating them, and five transition states for [1,5] hydrogen shifts. The value for the empirical E_a derived from calculated mole fractions of ground-state conformers and calculated energies for specific ground-state conformers and [1,5] hydrogen shift transition structures was 37.5 kcal/mol, in excellent agreement with the experimentally obtained activation energy. The significance of conformational options in various ground states and transition structures for the [1,5] hydrogen shifts is considerable, an inference that may well have general applicability.

Introduction

A number of structural isomerizations observed more than 100 years ago were correctly formulated in the 1950s and early 1960s as transformations involving thermal dienyl [1,5] shifts of hydrogen in acyclic and in cyclic dienes.[1,2] These reports from many laboratories established that the isomerizations were intramolecular and, for the cyclic dienes and trienes, the [1,5] hydrogen transannular shifts clearly involved a single face of the dienyl system. Nearly simultaneously thermal [1,7] hydrogen shifts were perceived to be responsible for the interconversion of precalciferol and calciferol (previtamin D_2 and vitamin D_2).[3] These [1,7] shifts were thought to involve hydrogen transfers from one face to the other of the π system through a helical transition structure.[3b,c] With the advent of proton NMR spectroscopy and the availability of deuterium-labeled reagents useful for preparing labeled dienes, it became possible to follow reaction kinetics for degenerate [1,5] hydrogen shifts. Such early kinetic work on isomerizations of cyclic reactants included studies of cycloheptatriene,[4] cyclopentadiene,[5] and *cis,cis*-1,3-cyclooctadiene.[6] In the absence of isotopic labeling the [1,5] hydrogen shifts in these systems could not lead to a discernible reaction product, but thanks to studies starting from 7-*d*-

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(1) For a general review of [1, 5] hydrogen shifts, see Hasselmann, D. *Houben-Weyl, Methods of Organic Chemistry*; Thieme: Stuttgart, 1995; Vol. E 21d, pp 4421−4430.

(2) (a) Grundmann, C.; Ottmann, G. *Liebigs Ann. Chem.* **1953**, *582*, 163−177. (b) Doering, W. von E.; Laber, G.; Vonderwahl, R.; Chamberlain, N. F.; Williams, R. B. *J. Am. Chem. Soc.* **1956**, *78*, 5448. (c) Alder, K.; Jungen, H.; Rust, K. *Liebigs Ann. Chem.* **1957**, *602*, 94−117. (d) Nozoe, T.; Mukai, T.; Tezuka, T. *Bull. Chem. Soc. Jpn.* **1961**, *34*, 619−674. (e) ter Borg, A. P.; van Helden, R.; Bickel, A. F. *Recl. Trav. Chim. Pays-Bas* **1962**, *81*, 591−598. (f) Büchi, G.; Burgess, E. M. *J. Am. Chem. Soc.* **1962**, *84*, 4, 3104−3109. (g) Mironov, V. A.; Sobolev, E. V.; Elizarova, A. N. *Dokl. Akad. Nauk SSSR* **1962**, *143*, 1112−1115. (h) Mironov, V. A.; Sobolev, E. V.; Elizarova, A. N. *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* **1962**, 2077−2078. (i) Wolinski, K J.; Chollar, B.; Baird, M. D. *J. Am. Chem. Soc.* **1962**, *84*, 2775−2779. (j) Mironov, V. A.; Sobolev, E. V.; Elizarova, A. N. *Tetrahedron* **1963**, *19*, 1939−1958. (k) ter Borg, A. P.; Kloosterziel, H. *Recl. Trav. Chim. Pays-Bas* **1963**, *82*, 741−756. (l) ter Borg, A. P.; Kloosterziel, H. *Pays-Bas* **1963**, *82*, 1189−1196. (m) Glass, D. S.; Zirner, J.; Winstein, S. *Proc. Chem. Soc.* **1963**, 276−267. (n) Watthey, J. W. H.; Winstein, S. *J. Am. Chem. Soc.* **1963**, *85*, 3715−3716. (o) Roth, W. R. *Liebigs Ann.* **1964**, *671*, 10−25; 25−31. (p) Weth, E.; Dreiding, A. S. *Proc. Chem. Soc.* **1964**, 59−60. (q) McLean, S.; Hayes, R. *Tetrahedron Lett.* **1964**, 2385−2390. (r) Marvell, E. N.; Caple, G.; Schatz, B. *Tetrahedron Lett.* **1965**, 385−389. (s) McLean, S.; Hayes, R. *Tetrahedron* **1965**, 2329−2342. (t) Nozoe, T.; Takahaski, K. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 665−674. (u) Tochtermann, W.; Schnabel, G.; Mannschreck, A. *Z. Naturforsch. B* **1966**, *21*, 897−898.

(3) (a) Velluz, L.; Amiard, G.; Goffinet, B. *Bull. Soc. Chim. Fr.* **1955**, 1341−1348. (b) Havinga, E.; Schlatmann, J. L. M. A. *Tetrahedron* **1961**, *16*, 146−152. (c) Schlatmann, J. L. M. A.; Pot, J.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1964**, 83, 1173−1184. (d) Havinga, E. *Experientia* **1973**, *29*, 1181−1193.

(4) (a) ter Borg, A. P.; Kloosterziel, H.; van Meurs, N. *Proc. Chem. Soc.* **1962**, 359. (b) ter Borg, A. P.; Kloosterziel, H.; van Meurs, N. *Recl. Trav. Chim. Pays-Bas* **1963**, *82*, 717−740.

(5) Roth, W. R. *Tetrahedron Lett.* **1964**, 1009−1013.

(6) Glass, D. S.; Boikess, R. S.; Winstein, S. *Tetrahedron Lett.* **1966**, 999−1008.

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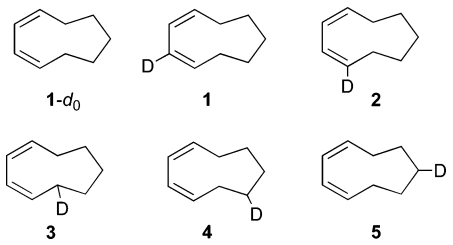
cycloheptatriene, 1,2,3,4,5-d_5-cyclopentadiene, and 5-*d*-cyclooctadiene, rate constants and activation parameters could be found. These kinetic studies were very demanding experimentally, for the instrumentation at hand was far less powerful than the NMR resources routinely available today. They depended on ^{1}H spectra and Varian NMR 40-MHz and A-60 spectrometers, the state-of-the-art instruments of the day. Yet good initial estimates of activation parameters were obtained.

Woodward and Hoffmann discussed these known [1,5] and [1,7] hydrogen shifts in 1965 in their seminal analysis and generalized formulation of sigmatropic reactions.[7] They rationalized why [1,3] hydrogen shifts had not been observed, why [1,5] shifts should be suprafacial and were seen to be suprafacial, and deduced that [1,7] hydrogen shifts should be antarafacial. These stereochemical characteristics of [1,5] and [1,7] hydrogen shifts were later confirmed in an acyclic substituted pentadienyl[8] and in heptatrienyl reactants.[9] This part of the background is of importance to the development of orbital symmetry theory for [1,5] hydrogen shifts. It rationalizes nicely the suprafacial stereochemistry invariably seen in cyclic and acyclic reactants. Thanks to the relatively low activation energies observed, and the inferred large energies of concert, one may be confident that these reactions are concerted.

The present work combined theoretical and experimental assessments of [1,5] hydrogen shifts in *cis,cis*-1,3-cyclononadiene (**1**-d_0) and the [1,5] hydrogen shifts responsible for thermal isomerizations among the five possible mono-deuterium-labeled cyclononadienes (**1** to **5**).



This study may be considered a direct extension of related work on [1,5] shifts shown by deuterium-labeled C5 to C8 *cis,cis*-1,3-cycloalkadienes.[10] While an initial assessment offered by Glass, Boikess, and Winstein suggested that dienyl [1,5] hydrogen shifts in six, seven, eight, and nine-membered rings have comparable rates and activation energies,[6] subsequent studies have demonstrated that [1,5] hydrogen shifts in *cis,cis*-1,3-cycloalkadienes are characterized by different activation parameters.[10] Through this first kinetic investigation of such shifts in deuterium-labeled *cis,cis*-1,3-cyclononadienes, and a theory-based analysis of the reactions, one hopes to gain data relevant to an understanding of just how geometrical constraints forced by $-(CH_2)_n-$ tethers linking C1 and C5 in *cis,cis*-1,3-cycloalkadienes, and in the respective transition structures for [1,5] hydrogen shifts, modify reactivity.

(7) Woodward, R. B.; Hoffmann, R. *J. Am. Chem. Soc.* **1965**, *87*, 2511−2513.
(8) Roth, W. R.; König, J.; Stein, K. *Chem. Ber.* **1970**, *103*, 426−439.
(9) (a) Hoeger, C. A.; Okamura, W. H. *J. Am. Chem. Soc.* **1985**, *107*, 268−270. (b) Hoeger, C. A.; Johnston, A. D.; Okamura, W. H. *J. Am. Chem. Soc.* **1987**, *109*, 4690−4698.
(10) (a) Baldwin, J. E.; Leber, P. A.; Lee, T. W. *J. Org. Chem.* **2001**, *66*, 5269−5271. (b) Hess, B. A., Jr. *Int. J. Quantum Chem.* **2002**, *90*, 1064−1070. (c) Hess, B. A., Jr; Baldwin, J. E. *J. Org. Chem.* **2002**, *67*, 6025−6033. (d) Baldwin, J. E.; Raghavan, A. S. *J. Org. Chem.* **2004**, *69*, 8128−8130, and *J. Org. Chem.* **2005**, *70*, 4218. (e) Baldwin, J. E.; Chapman, B. R. *J. Org. Chem.* **2005**, *70*, 337−380.

Other aspects of thermal [1,5] hydrogen shifts—the importance of tunneling,[11] deuterium kinetic isotope effects,[12] substituent effects on reaction rates,[13] and all manner of theoretical approaches to the geometry and bonding characteristics of transition structures[13]—continue to receive serious attention. These shifts are responsible for an array of novel rearrangements[14] and synthetically useful applications.[15] Such aspects of [1,5] hydrogen shift chemistry will not be of direct relevance here, for the primary concerns of this combined experimental and theoretical investigation of [1,5] hydrogen shifts in *cis,cis*-1,3-cyclononadienes relate to the challenging complexities of this system, thanks to its size and conformational flexibilities. The conformational options available to the ground-state reactants, and the several kinetically competitive transition structures contributing to the overall [1,5] shifts, turn out to require inclusion of a Winstein−Holness approach to the kinetic analysis[16] and derivation of a theory-based activation energy.

Results

Kinetic Scheme. At equilibrium the mono-deuterium-labeled isomers **1** to **5** will be present in the proportions 1:1:2:2:1, ratios defined by the number of hydrogens of each sort that might be substituted by a deuterium atom. Relating all possible hydrogen shifts with the net isomerizations each would effect reveals that the kinetic scheme constitutes a linear array of reversible first-order reactions governed by rate constants *k*, 2*k*, or 4*k* (Figure 1).

In Figure 1 each rate constant reflects the number of hydrogen atoms in one isomer that could shift to give the adjacent isomer. A [1,5] deuterium shift would not be seen, and hence primany k_H/k_D effects are not an issue. Secondary k_H/k_D effects are neglected, just as they have been in similar kinetic studies for smaller cycloalkadienes.

From the kinetic scheme of Figure 1 the time dependence of mole percent concentrations of the five isomers at any time *t* is

(11) (a) Thoburn, J. D.; Peles, D. N. *Abstracts of Papers*; American Chemical Society: Washington, D.C.; 231st ACS National Meeting, Atlanta, GA, United States, March 26−30, 2006; COMP-220. (b) Doering, W. von E.; Zhao, X. *J. Am. Chem. Soc.* **2006**, *128*, 9080−9085.
(12) (a) Ikeda, H.; Ushioda, N.; Inagaki, S. *Chem. Lett.* **2001**, 166−167. (b) Pye, C. C.; Poirier, R. A. *Can. J. Chem.* **2005**, *83*, 1299−1305. (c) Doering, W. von E.; Keliher, E. J.; Zhao, X. *J. Am. Chem. Soc.* **2004**, *126*, 14206−14216.
(13) (a) Hess, B. A., Jr.; Schaad, L. J.; Pancir, J. *J. Am. Chem. Soc.* **1985**, *107*, 149−154. (b) Kahn, S. D.; Hehre, W. J.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 8291−8292. (c) Saettel, N. J.; Wiest, O. *J. Org. Chem.* **2000**, *65*, 2331−2336. (d) Singh, P. M.; Lyngdoh, R. H. D. *Indian J. Chem. A* **2001**, *40*, 682−686. (e) Okajima, T.; Imafuku, K. *J. Org. Chem.* **2002**, *67*, 625−632. (f) Alabugin, I. V.; Manoharan, M.; Breiner, B.; Lewis, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 9329−9342. (g) Buck, H. *Int. J. Quantum Chem.* **2004**, *97*, 808−814. (h) Hayase, S.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem, Soc.* **2004**, *126*, 10028−10034. (i) López, C. S.; Faza, O. N.; de Lera, A. R. *Org. Lett.* **2006**, *8*, 2055−2058.
(14) (a) Doering, W. von E.; Rosenthal, J. W. *J. Am. Chem. Soc.* **1966**, *88*, 2078−2079. (b) Hashimoto, K.; Amano, A. *Chem. Lett.* **1975**, 721−724. (c) Oth, J. F. M.; Gilles, J.-M. *J. Phys. Chem. A* **2000**, *104*, 7980−7994. (d) Hopf, H.; Wolff, J. *Eur. J. Org. Chem.* **2001**, 4009−4030. (e) Hopf, H.; Kampen, J.; Bubenitschek, P.; Jones, P. G. *Eur. J. Org. Chem.* **2002**, 1708−1721. (f) Hoepfner, T.; Jones, P. G.; Ahrens, B.; Dix, I.; Ernst, L.; Hopf, H. *Eur. J. Org. Chem.* **2003**, 2596−2611. (g) Lewis, F. D.; Sajimon, M. C.; Zuo, X.; Rubin, M.; Gevorgyan, V. *J. Org. Chem.* **2005**, *70*, 10447−10452.
(15) (a) Jones, D. W.; Thompson, A. M. *J. Chem. Soc., Chem. Commun.* **1988**, 1095−1096. (b) Allen, A.; Gordon, D. M. *Indian J. Chem. B* **1999**, *38*, 269−273. (c) Sugimura, T.; Kohno, H.; Nagano, S.; Nishida, F.; Tai, A. *Chem. Lett.* **1999**, **11**, 1143−1144. (d) Dehnhardt, C.; McDonald, M.; Lee, S.; Floss, H. G.; Mulzer, J. *J. Am. Chem. Soc.* **1999**, *121*, 10848−10849. (e) Verma, S. K.; Fleischer, E. B.; Moore, H. W. *J. Org. Chem.* **2000**, *65*, 8564−8573. (f) Martins, J. C.; Van Rompaey, K.; Wittmann, G.; Toemboely, C.; Toth, G.; De Kimpe, N.; Tourwe, D. *J. Org. Chem.* **2001**, *66*, 2884−2886. (g) Alajarín, M.; Sánchez-Andrada, P.; López-Leonardo, C.; Alvarez, A. *J. Org. Chem.* **2005**, *70*, 7617−7623. (h) Alajarín, M.; Vidal, A.; Ortín, M.-M. *Tetrahedron* **2005**, *61*, 7613−7621.
(16) Winstein, S.; Holness, N. J. *J. Am. Chem. Soc.* **1955**, *77*, 5562−5578.

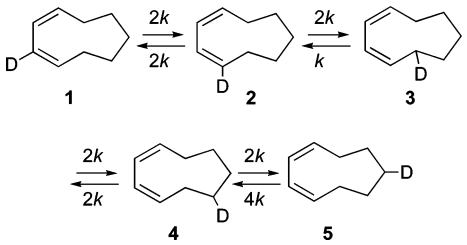


Figure 1. Kinetic scheme for the interconversion of mono-deuterium-labeled *cis*,*cis*-1,3-cyclononadienes, where *k* is the first-order rate constant for the shift of one hydrogen.

defined by the linear nonhomogeneous differential equations

$$
\begin{array}{lcccccc}
-\mathrm{d}(\mathbf{1})/\mathrm{d}t & = & 2k(\mathbf{1}) & -2k(\mathbf{2}) & & & \\
-\mathrm{d}(\mathbf{2})/\mathrm{d}t & = & -2k(\mathbf{1}) & +4k(\mathbf{2}) & -k(\mathbf{3}) & & \\
-\mathrm{d}(\mathbf{3})/\mathrm{d}t & = & & -2k(\mathbf{2}) & +3k(\mathbf{3}) & -2k(\mathbf{4}) & \\
-\mathrm{d}(\mathbf{4})/\mathrm{d}t & = & & & -2k(\mathbf{3}) & +4k(\mathbf{4}) & -4k(\mathbf{5}) \\
-\mathrm{d}(\mathbf{5})/\mathrm{d}t & = & & & & -2k(\mathbf{4}) & +4k(\mathbf{5})
\end{array}
$$

These equations, wherein all concentrations are functions of time, have a simple matrix form: the derivatives of mole percent concentrations with respect to time (a 1×5 column matrix) are equal to the 5×5 rate coefficient matrix **K** times the concentration matrix $\mathbf{A}(t)$.

$$
\begin{bmatrix} -\mathrm{d}(\mathbf{1})/\mathrm{d}t \\ -\mathrm{d}(\mathbf{2})/\mathrm{d}t \\ -\mathrm{d}(\mathbf{3})/\mathrm{d}t \\ -\mathrm{d}(\mathbf{4})/\mathrm{d}t \\ -\mathrm{d}(\mathbf{5})/\mathrm{d}t \end{bmatrix} = \begin{bmatrix} 2k & -2k & 0 & 0 & 0 \\ -2k & +4k & -k & 0 & 0 \\ 0 & -2k & +3k & -2k & 0 \\ 0 & 0 & -2k & +4k & -4k \\ 0 & 0 & 0 & -2k & +4k \end{bmatrix} \times \begin{bmatrix} \mathbf{1}(t) \\ \mathbf{2}(t) \\ \mathbf{3}(t) \\ \mathbf{4}(t) \\ \mathbf{5}(t) \end{bmatrix}
$$

To find the solutions of the associated homogeneous equations we assume that at $t = 0$ the concentrations are fixed, and therefore,

$$
\left.\frac{\mathrm{d}A_i(t)}{\mathrm{d}t}\right|_{t=0} = 0\text{tth?9q:0and} \quad A_i(t)|_{t=0} \equiv A_i(0), \qquad \text{for } i = 1,2, ..., 5
$$

which gives the constant coefficients of unknown *k* and a set of linear homogeneous equations. Nontrivial solutions are obtained from the condition that the determinantal equation $\det|\mathbf{K}\text{-}\lambda\mathbf{I}| = 0$, where **I** is the identity matrix and λ are the unknown eigenvalues. Solving this equation with the aid of the linear algebra software provided by Maple[17] for the case when $A_1(0) = \mathbf{1}(0) = 100\%$ provides the eigenvalues $\lambda_1 = 0$, $\lambda_2 = 0.8706k$, $\lambda_3 = 3.081k$, $\lambda_4 = 5.625k$, and $\lambda_5 = 7.424k$, and the five eigenfunctions, (the eigenvectors), often collected as a 5×5 matrix **B**.

The particular solutions of the initial set of equations have an exponential form, which results from a simple integration over time. The general solutions of the differential equations are the linear combinations of the particular solutions. From these, concentrations of each isomer can be calculated at any time *t*, given the single rate constant *k*.

$$\mathbf{1}(t) = 14.29 + 51.39\exp(-\lambda_2 t) + 15.24\exp(-\lambda_3 t) + 18.55\exp(-\lambda_4 t) + 0.54\exp(-\lambda_5 t)$$

$$\mathbf{2}(t) = 14.29 + 29.02\exp(-\lambda_2 t) - 8.24\exp(-\lambda_3 t) - 33.62\exp(-\lambda_4 t) - 1.46\exp(-\lambda_5 t)$$

$$\mathbf{3}(t) = 28.57 - 11.96\exp(-\lambda_2 t) - 38.05\exp(-\lambda_3 t) + 17.52\exp(-\lambda_4 t) + 3.92\exp(-\lambda_5 t)$$

$$\mathbf{4}(t) = 28.57 - 41.76\exp(-\lambda_2 t) + 9.77\exp(-\lambda_3 t) + 10.62\exp(-\lambda_4 t) - 7.21\exp(-\lambda_5 t)$$

$$\mathbf{5}(t) = 14.29 - 26.69\exp(-\lambda_2 t) + 21.27\exp(-\lambda_3 t) - 13.07\exp(-\lambda_4 t) + 4.21\exp(-\lambda_5 t)$$

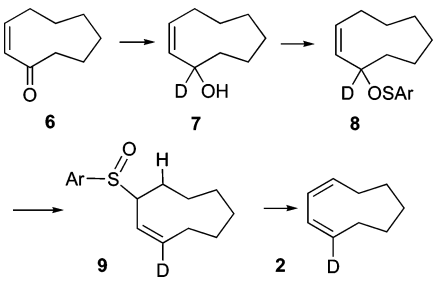
The coefficients of the exponential functions are evaluated following a standard procedure[18] and described in a symbolic way by the equation

$$\boldsymbol{A}(t) = \mathbf{B} \times \mathrm{diag}(\exp(-\lambda_1 t), \exp(-\lambda_2 t), \exp(-\lambda_3 t), \exp(-\lambda_4 t), \exp(-\lambda_5 t)) \times \mathbf{B}^{-1} \times \boldsymbol{A}(0)$$

The kinetic profile expected, portrayed in graphical form in Figure 2, has the dimensionless parameter *kt* along the *x* axis. This behavior should be observed at all temperatures.

Synthesis. Among the various synthetic routes to mono-deuterium-labeled cyclononadienes those which offered promise of giving one specific isomer were of primary interest. Two routes seemed attractive possibilities for meeting this objective.

The first took advantage of chemistry developed by Reich and Wollowitz.[19] Reduction of cyclononenone (**6**)[20] with $NaBD_4$ in the presence of $CeCl_3$[21] gave the deuterium-labeled allylic alcohol (**7**); condensation of this alcohol with 2,4-dinitrobenzenesulfenyl chloride in CH_2Cl_2/Et_3N gave rise to the corresponding sulfenate ester (**8**). It proceeded to isomerize through a five-centered, six-electron process, a [2,3] sigmatropic rearrangement, to afford an allylic sulfoxide (**9**), which then gave the C1 deuterium-labeled isomer **2** through a thermal syn elimination.



The second route utilized the addition of DBr to 1,2-cyclononadiene (**10**)[22−24] to provide 2-*d*-3-bromocyclononene (**11**). Dehydrobromination of **11** with *t*-BuOK in 15% DMSO/

(17) Linear algebra, in Maple 9.5; Waterloo Maple, Inc.: Waterloo, Canada.

(18) Baldwin, J. E.; Leber, P. A.; Lee, T. W. *J. Chem. Educ.* **2001**, *78*, 1394−1399.
(19) Reich, H. J.; Wollowitz, S. *J. Am. Chem. Soc.* **1982**, *104*, 7051−7059.
(20) Mehta, G. *Org. Prep. Proced. Int.* **1970**, *2*, 245−248.
(21) Davis, M. W.; Crabtree, R. H. *J. Org. Chem.* **1986**, *51*, 2655−2661.
(22) Skattebøl, L.; Solomon, S. *Organic Synthesis*; Wiley & Sons: New York, 1973; Collect. Vol. V, pp 306−310.
(23) Moorthy, S. N.; Singh, A.; Devaprabhakara, D. *J. Org. Chem.* **1975**, *40*, 3452−3453.
(24) Hammond, G. S.; Warkentin, J. *J. Am. Chem. Soc.* **1961**, *83*, 2554−2558.

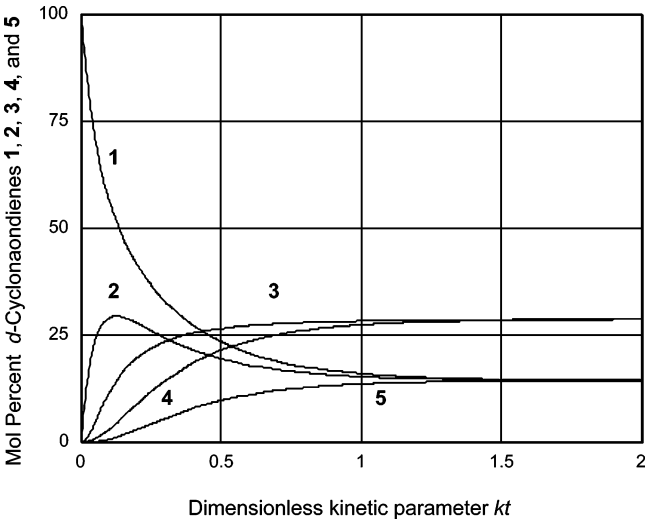
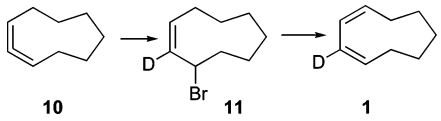


Figure 2. Calculated kinetic profiles for isomerizations of monodeuterium labeled *cis,cis*-1,3-cyclononadienes **1** to **5** with **1**($t = 0$) = 100%.

ether gave the C2 deuterium-labeled isomer **1**.[25] The position of the deuterium label in **1** is determined by its location in **11**, whether the elimination of HBr is a 1,2- or a 1,4-process, or takes place through both alternatives.



Syntheses through these two routes using $NaBH_4$ and HBr, respectively, rather than the deuterium-labeled reagents, led to authentic **1**-d_0. Preparative GC using a β,β-ODPN column and relatively low injector, column, and detector temperatures provided clean samples for record spectra and for all kinetic experiments. The proton NMR spectrum of **1**-d_0 confirmed its structure and stereochemistry. The vinylic proton absorption multiplets were centered at δ 5.7 (C2,C3 H) and 5.3 (the more complicated multiplet, for C1,C4 H). The upfield absorptions were observed at δ 2.12 (4H), 1.62 (2H), and 1.47 (4H), in agreement with data reported in the literature.[26]

The deuterium NMR spectrum of **1** showed but a single absorption, at δ 5.9, confirming the specificity of the labeling. Isomer **1** rather than isomer **2** was selected for the kinetic study based on convenience of purification and with a eye to the kinetic scheme: **1** is at one end of the linear sequence of reversible first-order reactions linking the five isomers (Figure 1).

Reaction Kinetics. Initial experiments following gas-phase thermal isomerizations of **1** in the presence of pentane as a bath gas proved frustrating, for the product mixtures scrutinized by ^{2}H NMR spectroscopy at 92.1 MHz reflected substantial losses of deuterium-labeled cyclononadienes relative to pentane and distributions of isomers inconsistent with the patterns of kinetic behavior anticipated from theory (Figure 2). Particularly annoying were variable, too-large proportions of **1** relative to the intensities and distributions of absorptions for the other isomers predicted by theory. After more than a dozen trial kinetic runs it became clear that thermal reaction product mixtures formed in the kinetic bulb were not being transferred efficiently through the vacuum system to a liquid nitrogen-cooled u-tube, and some starting material, isomer **1**, was not reaching the evacuated kinetic bulb when it was "injected" and this component of the sample was not being removed completely from the vacuum line prior to a collection of a product mixture. Both of these contributions to flawed kinetic data stem from a common factor: a hydrocarbon as large as cyclononadiene can be remarkably resistant to transfer under vacuum, for its adhesion to glass counterbalances its equilibrium vapor pressure. Once these difficulties were diagnosed, corrective actions were taken, and they proved successful.

Injections of samples of **1** in pentane were introduced directly into the middle of the thermostated kinetic bulb through a septum and through the bore of the stopcock atop that bulb with the aid of a gastight syringe fitted with a 10-cm needle, and the stopcock to the bulb was closed as time zero was noted. A second stopcock, separating the injection port and the first stopcock from the vacuum line, was then opened, and whatever residual **1** might have been left between kinetic bulb and vacuum line was pumped away, with some warming of the relevant portions of the line with a heat gun. Thus, all of isomer **1** within a product mixture had indeed been subjected to the thermal reaction conditions; no unreacted **1** temporarily adhering to glass in the interstitial space accessible to the septum and between the two stopcocks eventually found its way into the u-tube used to collect thermal reaction product mixtures. The vacuum line was reconfigured so as to diminish the distance between the kinetic bulb and the u-tube, and between the u-tube and the transfer connection used to move a collected product mixture into an NMR tube containing degassed $CHCl_3$. By minimizing the glass surface area product mixtures had to traverse before being examined by NMR, fair amounts of the cyclononadienes could be obtained from kinetic runs starting with ~7 mg of **1** in ~240 μL of pentane. By taking great care to ensure that product mixtures were not contaminated by **1** that had not reached the kinetic bulb and not been removed from the vacuum system prior to collecting a product mixture, erratic excess contributions from isomer **1** in product mixtures ceased to be manifested. The relative proportions of each isomer in product mixtures could be determined by ^{2}H NMR, as exemplified by the spectrum shown in Figure 3, and trustworthy kinetic data could be secured.

A series of five or six independent kinetic runs at each of four temperatures provided four sets of mole percent concentration data for isomers **1**−**5** versus time. All data points in a set were compared with theory-based concentrations based on a single variable, the rate constant k. By minimizing the root-mean-square deviation with the aid of the "solver" routine in Excel, the best value of k was determined. Figure 4, for kinetic runs at 287.0 °C, demonstrates the fair agreement between experimentally determined mole percent concentration data points and the theoretical functions calculated based on the best value of the single kinetic variable parameter found; the optimal value of the rate constant k at this temperature was 1.23×10^{-3} s^{-1}.

All kinetic data based on ^{2}H NMR analyses of thermal product mixtures are tabulated in the Supporting Information provided. The temperature-dependent rate constants for a [1,5]

(25) Agarwal, S. K.; Moorthy, S. N.; Mehrotra, I.; Devaprabhakara, D. *Indian J. Chem. B* **1977**, *15*, 563−564.
(26) (a) Shumate, K. M.; Neuman, P. N.; Fonken, G. J. *J. Am. Chem. Soc.* **1965**, *87*, 3996. (b) Stierman, T. J.; Johnson, R. P. *J. Am. Chem. Soc.* **1985**, *107*, 3971−3980. (c) Leigh, W. J.; Zheng, K.; Clark, K. B. *J. Org. Chem.* **1991**, *56*, 1574−1580.

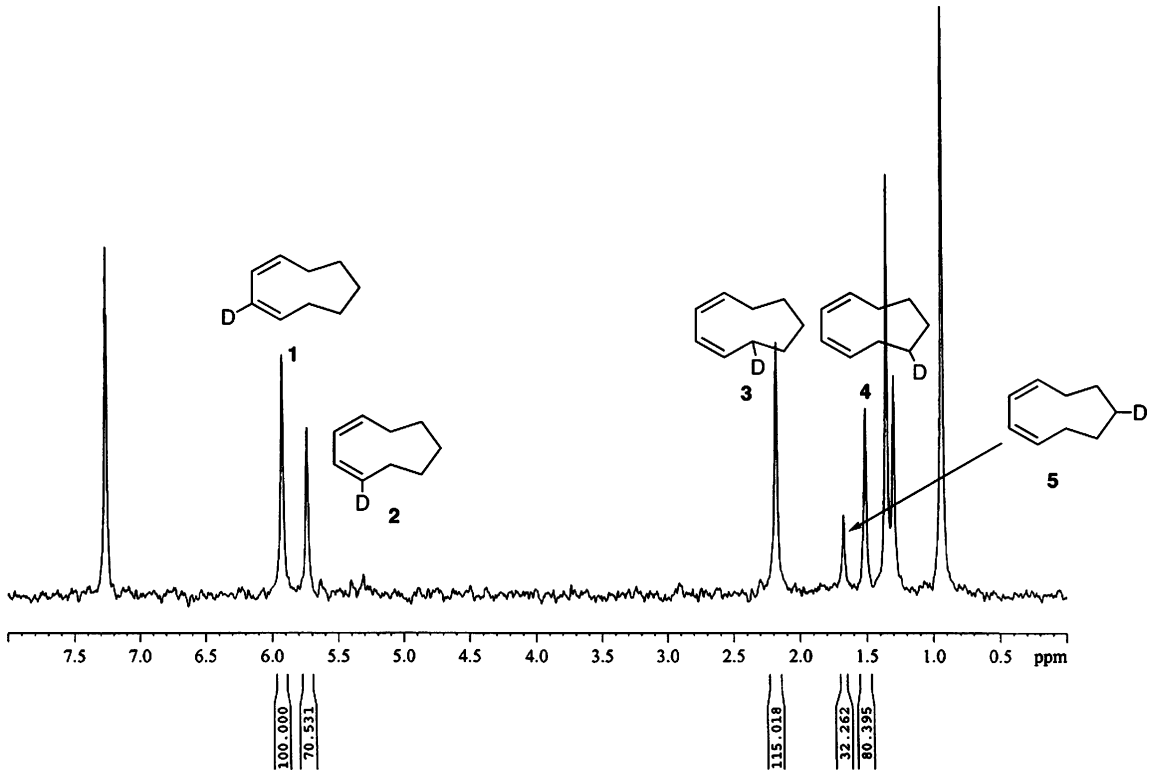


Figure 3. ^{2}H NMR spectrum of the thermal reaction mixture formed by heating isomer **1** in the gas phase at 287.0 °C for 911 s. The chemical shifts for deuterium singlets for the isomers are at δ 5.92 (**1**), 5.73 (**2**), 2.18 (**3**), 1.67 (**5**), and 1.51 (**4**). The unlabeled peaks are contributed by natural abundance deuterium in solvent $CHCl_3$ (δ 7.26) and pentane (δ 0.93, 1.29, and 1.35).

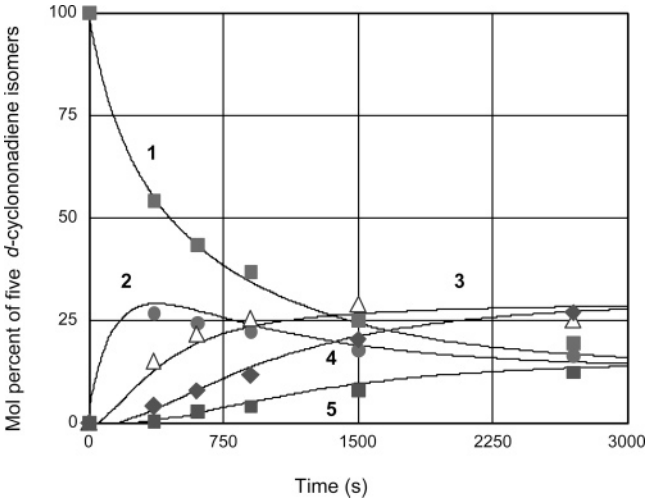


Figure 4. Kinetic data at 287.0 °C and theoretical functions for isomers **1**−**5** calculated with the best-fit rate constant $k = 1.23 \times 10^{-3}$ s^{-1}.

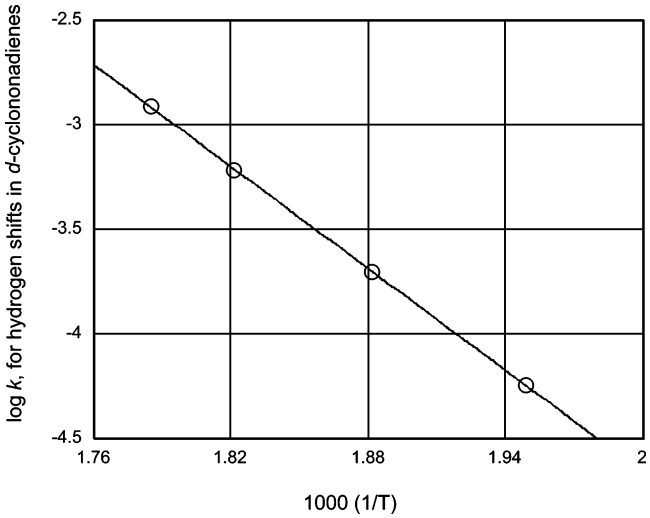


Figure 5. Arrhenius plot for rate constants for a [1,5] hydrogen shift in monodeuterium-labeled *cis,cis*-1,3-cyclononadienes. The activation parameters are $E_a = 37.1$ kcal/mol and $\log A = 11.6$.

hydrogen shift in *cis,cis*-1,3-cyclononadiene determined from the data were 5.72×10^{-5} s^{-1} at 240.0 °C, 1.97×10^{-4} s^{-1} at 258.3 °C, 6.01×10^{-4} s^{-1} at 276.0 °C, and 1.23×10^{-3} s^{-1} at 287.0 °C. The Arrhenius plot based on these rate constants and temperatures (Figure 5) provides the activation parameters $E_a = 37.1$ kcal/mol and $\log A = 11.6$. A Eyring plot of ln(k/T) versus $1/T$ leads to $\Delta H^{\ddagger} = 36.0$ kcal/mol and $\Delta S^{\ddagger} = -9.0$ eu. Were the experimental rate constant accurate to ±5%, the activation parameters and estimated uncertainties would be[27] $E_a = 37.1 \pm 0.8$ kcal/mol, $\log A = 11.6 \pm 0.3$, $\Delta H^{\ddagger} = 36.0 \pm 0.8$ kcal/mol, and $\Delta S^{\ddagger} = -9.0 \pm 0.3$ eu.

Density Functional Calculations. The relatively large ring present in *cis,cis*-1,3-cyclononadiene is likely to give rise to a number of possible conformers. Therefore, to obtain a calculated activation energy for the [1,5] hydrogen shift in **1** that can be compared with the experimentally obtained activation energy, one must carry out a conformational study of this system. This was done through calculations using GAUSSIAN 98W[28] and the density functional method employing B3LYP, Becke's three-parameter hybrid method[29] with the Lee−Yang−Parr correlation

(27) Benson, S. W.; O'Neal, H. E. *Kinetic Data on Gas-Phase Unimolecular Reactions*; National Standard Reference Data Series, 21; National Bureau of Standards: Washington, D.C., 1970; p 9.
(28) Frisch, M. J.; et al. Gaussian, Inc.: Pittsburgh, PA, 1998.
(29) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652.

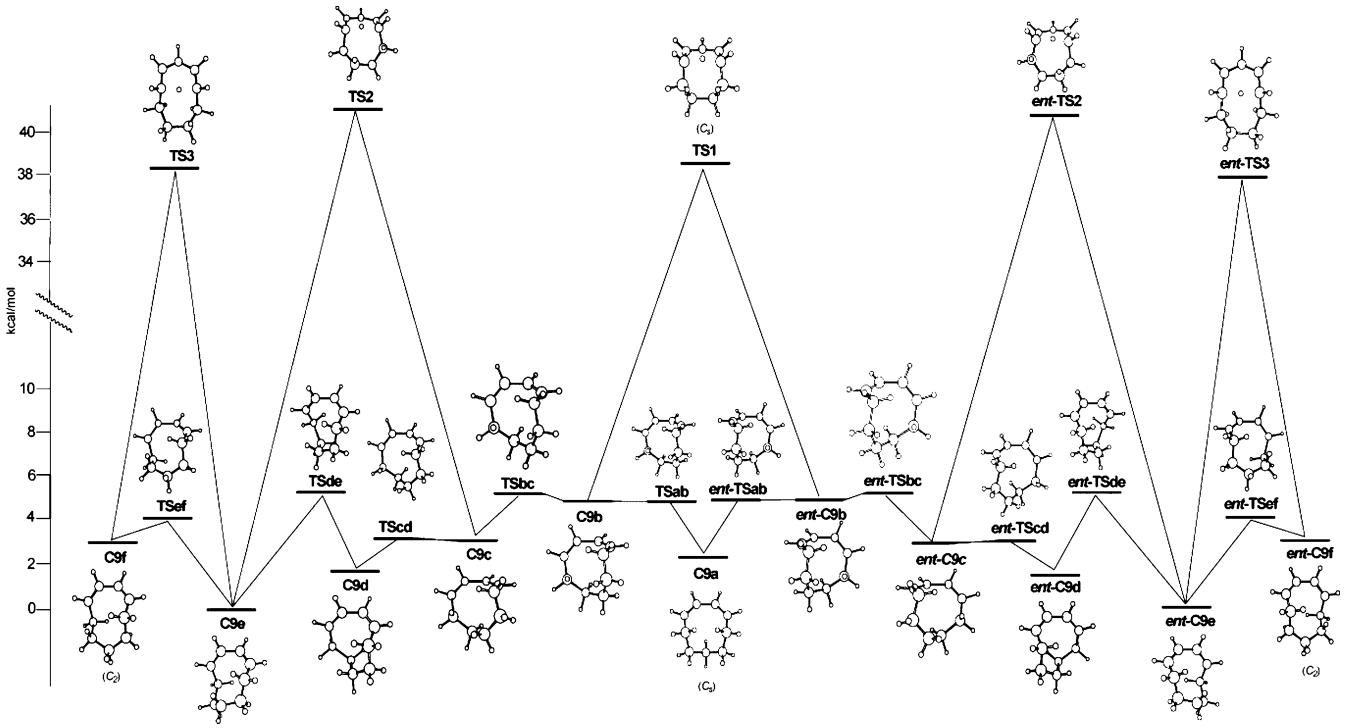


Figure 6. Minima and transition structures located on the *cis,cis*-1,3-cyclononadiene potential energy surface. The prefix *ent* indicates that the structure is an enantiomer of a structure shown on the left-hand side of the figure.

functional[30] and the 6-31G* basis set.[31] Stationary points were characterized by computation of second derivatives. Energies reported here include zero-point energy corrections calculated with unscaled B3LYP/6-31G* frequencies obtained analytically with G98W. Intrinsic reaction coordinate calculations[32] were used to determine reaction pathways. The results of these calculations are summarized in Figure 6.

Six conformers (**C9a**−**C9f**) were located, and they differed in energy by as much as 5 kcal/mol with **C9e** being the most stable and **C9b** the least stable. Of these six conformers five can exist as enantiomeric pairs, with the sixth, **C9a**, having a plane of symmetry. They are all (11 structures) shown in the lower part of Figure 6 with **C9a** "separating" the enantiomeric pairs. We were also able to successfully locate the transition structures linking these conformers with one another, and their structures are shown in the middle part of Figure 6 designated by **TSmn**, where m and n denote which conformers are linked by the transition structure. All exist as enantiomeric pairs. IRC calculations[32] were performed on all of these transition structures to confirm which two conformers each transition structure linked.

As was found in the case of [1,5] hydrogen shifts in *cis,cis*-1,3-cyclooctadiene,[10c] not all conformers of **1** are capable of undergoing the [1,5] hydrogen shift, because some have geometries unfavorable for this reaction. As a consequence only three transition structures (**TS1**−**TS3**) were located, and these are shown at the top of Figure 6. IRC calculations showed that **TS1**, a structure of C_s symmetry, links the enantiomeric pair of conformers, **C9b** and ***ent*-C9b**, with an activation energy of 33.4 kcal/mol; **TS2** links **C9c** and **C9e** with an activation energy of 38.4 kcal/mol from **C9c** and 41.4 kcal/mol from **C9e**; and **TS3** links **C9e** and **C9f** with an activation energy of 37.9 kcal/mol from **C9e** and 34.9 kcal/mol from **C9f**.

On examining these three transition structures it is apparent that they differ primarily in conformational aspects of the four sp^3 hybridized carbons (butane-like), since in all of them the geometry of the five carbons (pentadienyl system) and migrating hydrogen are very similar. The structures of **TS2** and **TS3** correspond roughly to the two gauche conformers of butane, although they are not equivalent (i.e., not mirror images), since as seen in Figure 6 they each link diastereomeric conformers, namely **TS2** links **C9c** and **C9e**, **TS3** links **C9e** and **C9f**. On the other hand **TS1** links the enantiomers of **C9b** and therefore must contain a plane of symmetry, the presence of which is necessary to interconvert two enantiomers. The consequence of this is that the butane part of the structure is eclipsed, which is clearly seen in the structure of **TS3**.

Structural images of the 14 distinct (not mirror-image related) C_9H_{14} species shown in Figure 6 and discussed above are provided in the Supporting Information with bond length and bond angle data.

Reaction Path Complexities and a Generalized Winstein−**Holness Analysis.** Because of the large number of conformers and several reaction pathways available to them, to calculate the activation energy that corresponds to the measured activation energy one has to take into account the several transition structures that lead to [1,5] hydrogen shifts as well as the concentrations of all the conformers present at equilibrium. This problem was originally addressed by Winstein and Holness as they derived what is now known as the Winstein−Holness (W−H) equation (eq 1) for two conformers in equilibrium with

(30) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, 37, 785−789.
(31) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213−222.
(32) Gonzalez, C.; Schlegel, H. B. *J. Chem. Phys.* **1989**, *90*, 2154−2161; *J. Phys. Chem.* **1990**, *94*, 5523−5527.

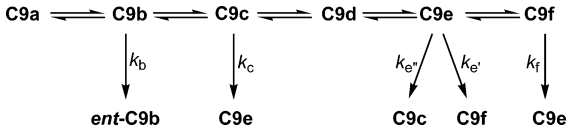


Figure 7. Schematic drawing of the [1,5] hydrogen shifts in *cis,cis*-1,3-cyclononadienes where *k*'s are the rate constants leading through a hydrogen shift to another conformer.

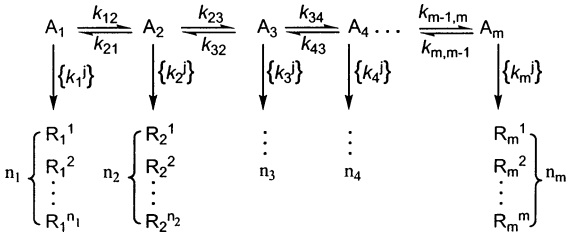


Figure 8. Kinetic network involving m ground-state conformers in equilibrium. The number of competing first-order reactions for conformer A_i, is denoted by n_i and in general $j = 1, ..., n_i$.

each one undergoing a reaction.[16,33]

$$k_{exp} = N_a k_a + N_b k_b \quad (1)$$

In the case of two conformational isomers at equilibrium, the empirical rate constant, k_{exp}, is expressed as a sum of the products of the mole fractions, N_a and N_b, of two conformers at equilibrium and rate constants, k_a and k_b, for the two reactions leading to two different transition structures. It is assumed here that the rates of reaction are much slower than the rate of interconversion of the two conformers. However, with the cyclononadiene reactions at issue here, the situation is much more complex. As seen in Figure 6, there are not just two structurally and energetically distinct conformers in equilibrium, but six: five pairs of enantiomers and one achiral form. Only four of these lead to possible [1,5] hydrogen shifts, as shown schematically in Figure 7. Therefore the original W−H equation has to be generalized if the concept behind it is to be applied to a case involving more than two conformers and two reactions. Fortunately, this can be done relatively easily.

Consider the general case of conformers in equilibrium with one another and some or all of them undergoing first-order reactions, including competing first-order reactions of the same conformer, as in Figure 8.

The rate constants for the conformational interconversions and the rate constants for reactions satisfy the Curtin−Hammett/Winstein−Holness conditions:

$$k_{i,i+1} \text{ and } k_{i+1,i} \gg k_i^j \quad \text{for } i = 1, \ldots m \text{ and } j = 1, \ldots n_i$$

For each product (R_i^j) we have the equation

$$\frac{d[R_i^j]}{dt} = k_i^j[A_i] \text{ for } j = 1, ..., n_i$$

For example for the conformer $i = 1$ and n_1 different products

$$\frac{d[R_1^1]}{dt} = k_1^1[A_1], \frac{d[R_1^2]}{dt} = k_1^2[A_1], ..., \frac{d[R_1^{n_i}]}{dt} = k_1^{n_i}[A_1]$$

Now let us define

$$R_i = \sum_j^{n_i} R_i^j$$

where n_i is the number of reaction products of A_i with their rate constants for formation k_i^j with $j = 1,..., n_i$.

Summing up gives

$$\frac{d[R_1]}{dt} = k_1[A_1] \quad \text{where } k_1 = \sum_{j=1}^{n_1} k_1^j$$

In general we have for each reaction the following equations

$$\frac{d[R_i]}{dt} = k_i[A_i] \quad \text{and } k_i = \sum_{j=1}^{n_i} k_i^j \quad \text{for } n_i > 0,$$

otherwise $k_i = 0$

For all *m* conformers we have

$$\sum_{i=1}^{m} \frac{d[R_i]}{dt} = \sum_{i=1}^{m} k_i[A_i]$$

The empirical total reaction rate constant k_{W-H} is defined through the equation

$$\frac{d[\text{all} - \text{products}]}{dt} = k_{W-H} \sum_{i=1}^{m} [A_i]$$

thus

$$k_{W-H} \sum_{i=1}^{m} [A_i] = \sum_{i=1}^{m} k_i[A_i]$$

which gives

$$k_{W-H} = \sum_{i=1}^{m} k_i[A_i] / \sum_{i=1}^{m} [A_i]$$

Introducing the mole fractions of the conformers

$$N_i = [A_i] / \sum_{i=1}^{m} [A_i], \quad \text{with the property } \sum_i^m N_i = 1$$

finally we have

$$k_{W-H} = \sum_{i=1}^{m} k_i N_i$$

where *m* is the number of conformers and

$$k_i = \sum_{j=1}^{n_i} k_i^j \quad \text{for } n_i > 0, \quad \text{otherwise } 0$$

For example, if $m = 6$, $n_1 = 1$, $n_2 = 2$, $n_3 = 0$, $n_4 = 1$, $n_5 = 1$, $n_6 = 0$, as in Figure 9, the rate constant for the sum of all

(33) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994; pp 647−655.

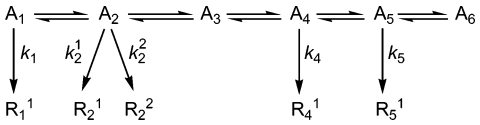


Figure 9. Hypothetical kinetics network for interconverting conformers and multiple reaction paths to products according to the generalized Winstein−Holness equation derived.

first-order reactions from the set of conformers is given by

$$k_{W-H} = k_1N_1 + (k_2^1 + k_2^2)N_2 + k_4N_4 + k_5N_5$$

For the cyclononadiene network of Figure 7, the experimentally accessible rate constant for a [1,5] shift of a single hydrogen, k_{exp}, is given by

$$k_{exp} = N_b k_b + N_c k_c + N_e(k_{e'} + k_e) + N_f k_f \qquad (2)$$

Using the Arrhenius equation (eq 3)

$$k = A\, e^{-E_a/RT} \qquad (3)$$

one can rewrite eq 2 in terms of activation energies E_a. For the five reactions depicted in Figure 7, and the assumption that the Arrhenius factor (A) is the same for all five reactions, we have

$$e^{-E_a^{exp}/RT} = N_b\, e^{-E_a^b/RT} + N_c\, e^{-E_a^c/RT} + N_e(e^{-E_a^{e'}/RT} + e^{-E_a^e/RT}) + N_f\, e^{-E_a^f/RT} \qquad (4)$$

Equation 4 allows the calculation of the empirical activation energy, E_a^{exp}, from the calculated mole fractions of the conformers and activation energies. Using mole fractions obtained from the DFT computed equilibrium constants along with computed activation energies for the five reactions shown in Figure 7, one obtains an empirical activation energy (E_a^{exp}) of 37.5 kcal/mol, in remarkably good agreement with that obtained experimentally, 37.1 ± 0.8 kcal/mol. When an empirical activation energy, E_a^{exp}, was calculated based on enthalpies rather than zero-point corrected energies, the agreement with the experimental value was within about 0.1 kcal/mol of the experimental value, 37.1 kcal/mol, an insignificant improvement, given the estimated uncertainty of the activation energy defined by the Arrhenius plot.

When analyzing eq 4 it is possible to see the distinct contributions to E_a^{exp} of each of the five reactions depicted in Figure 7. Not surprisingly the major contributor is the reaction **C9e** → **C9f** via **TS3**, since the mole fraction present of **C9e** at equilibrium is computed to be 0.90, though the activation energy for this reaction (37.9 kcal/mol) lies in the middle range of the five computed activation energies. Two other reactions (**C9f** → **C9e** and **C9b** → ***ent*-C9b**) make significant contributions to the empirical activation energy, even though their mole fractions present at equilibrium are less than 0.01. However, both of these reactions have computed activation energies, 34.9 and 34.4 kcal/mol, respectively, that are significantly lower than that for the dominant contributor, **C9e** → **C9f**. The total effect of these two contributions gives an empirical activation energy lower than one would have obtained using only the dominant contributor.

Conclusions

This combined experimental and theory-based investigation of the conformational and [1,5] hydrogen shift-mediated degenerate isomerizations of *cis,cis*-1,3-cyclononadiene has provided mutually reinforcing understandings of the structure−reactivity issues involved. Eleven ground-state conformational isomers are in thermal equilibrium; eight of these may give rise to [1,5] hydrogen shifts through one or two of the five distinct isomeric transition structures. Calculated mole fractions of the ground-state conformations based on relative energies, and E_a values from differences in specific ground-state conformer/specific transition structure pairs, give rise to a calculated empirical E_a value, 37.5 kcal/mol, in fine agreement with the experimentally derived value, E_a = 37.1 ± 0.8 kcal/mol. The agreement lends support to the judgment derived from the theoretical results that conformational aspects of ground-state species and of alternative transition structures for [1,5] hydrogen shifts are significant determinates of overall reactivity. Even conformational details in parts of the cyclic transition structures remote from the essential "core" structural element, the pentadienyl system bridged by a migrating hydrogen, may well affect activation parameters significantly.

Experimental Section

Deuterium NMR spectra at 92.1 MHz were recorded by Mr. David Kiemle on a DPX- 600 Bruker Avance spectrometer at the State University of New York College of Environmental Science and Forestry in Syracuse.

Mass spectrometric analyses were obtained on a Hewlett-Packard 5890 series instrument connected to an Intel Pentium 1 computer equipped with Windows software HP G1701AA version A.02.00. Analytical GC was done using a HP 5890 series II instrument with a flame ionization detector, a HP 3396 series II integrator, and a capillary cross-linked 5% PH ME siloxane 25-m × 0.2-mm × 0.3-μm column. Preparative GC work was done on a Varian Aerograph A 90-P3 instrument using a 2.3-m × 0.64-cm 20% β, β' ODPN column at 65 °C and a HP 3392 A integrator.

2-*d*-3-Bromocyclononene (11). 1,2-Cyclononadiene[22] (**10**; 1.22 g, 0.01 mol) in 20 mL of pentane in a three-necked 100-mL round-bottomed flask under a nitrogen atmosphere was cooled to 15−20 °C. Deuterium bromide generated from 200 mg of D_2O (0.01 mol) and 2 g of acetyl bromide (0.016 mol) was passed into this solution through a dropping funnel in 10 min.[23,24] The reaction was allowed to run for about 2 h, and then the reaction mixture was washed thoroughly with aqueous Na_2CO_3 and dried over Na_2SO_4. The pentane solution was filtered and concentrated by distillation to give crude 2-*d*-3-bromocyclononene in 70% yield. MS *m*/*z* 201, 203 (M^+) (Calcd for $C_9H_{13}BrD$, M^+ 201, 203).

2-*d*-*cis,cis*-1,3-Cyclononadiene (1).[25] A portion of the crude cyclic bromide **11** from the above reaction (0.46 g, 2.2 mmol), in 15% DMSO/ether (5 mL) was added to *t*-BuOK (0.50 g, 4.6 mmol) in 15% DMSO/ether (15 mL) under a dry nitrogen atmosphere at 20 °C with stirring. The reaction was run for 5 h, then quenched with 10 mL of ice water containing acetic acid. This mixture was extracted twice with pentane, dried over Na_2SO_4, filtered, and concentrated by distillation to give ≈ 70% of crude labeled diene. 2-*d*-*cis*,*cis*-1,3-Cyclononadiene (**1**) was isolated and purified by preparative GC: ^{1}H NMR: δ 5.8−6.0 (δ, 1.5 H), 5.6−5.8 (m, 2H), 2.2−2.1 (s, 4H), 1.7−1.6 (s, 2H), 1.5−1.4 (s, 4H). ^{2}H NMR: only one singlet, at δ 5.92. Analytical GC: homogeneous product. Repetitions of this dehalogenation reaction and preparative GC provided sufficient **1** for kinetic studies.

***cis,cis*-1,3-Cyclononadiene (1-d_0)**[26] was prepared from **10** by way of 3-bromocyclononene in the same way; ^{1}H NMR: δ 5.8−6.0 (d, 2 H), 5.6−5.8 (m, 2H), 2.2−2.1 (m, 4H), 1.6−1.7 (m, 2H), 1.4−1.5 (m, 4H) (ref 26b, lit. ^{1}H NMR: δ 5.90 (d, 2H), 5.71 (q, 2H), 2.2−2.1 (m, 4H), 1.7−1.6 (m, 2 H), 1.54−1.46 (m, 4H). ^{13}C NMR: δ 133.1, 127.6, 29.6, 29.4, and 26.0.

Gas-Phase Thermal Rearrangements. Gas-phase kinetic experiments were conducted using a static reactor attached to a vacuum line similar in design and components to a setup described elsewhere.[34]

A 3% solution of preparative GC-purified deuterium-labeled cyclononadiene (100% isomer **1**) in distilled pentane was prepared and stored in a 5-mL screw-cap vial fitted with a 20-mm Mininert syringe valve. About 250 μL of this solution (containing ~7 mg of **1**) was injected through a septum into an evacuated thermostated 300-mL Pyrex kinetic bulb using a gastight syringe fitted with a 10-cm needle, and the stopcock to the bulb was closed. The stopwatch used to measure reaction time was started, and a second stopcock, separating the injection port and the first stopcock from the vacuum system, was opened. During the reaction full vacuum was applied to all of the line beyond the first stopcock, to remove whatever residual **1** that had been injected but not been sealed in the kinetic bulb and that may have adhered to glass between the two stopcocks. After the desired time, the stopcock bypassing the u-tube was closed, the stopwatch was stopped, and the stopcock sealing the kinetic bulb was opened. The thermal reaction mixture was allowed to collect in a u-tube immersed in liquid nitrogen under active vacuum. This transfer typically took 25−30 min. The stopcocks connecting the u-tube to the vacuum line were then closed, and the product mixture collected in the u-tube was transferred to an NMR tube containing 250−300 μL of chloroform that had been degassed prior to the transfer, following the freeze-and-thaw process repeated three times. Once the thermal mixture was collected in the NMR tube with the use of a liquid nitrogen-cooled Dewar, the tube was sealed using a propane torch, and the sample was analyzed using ^{2}H NMR. A representative spectrum of a reaction mixture is shown in Figure 3.

(34) (a) Baldwin, J. E.; Burrell, R. C. *J. Org. Chem.* **1999**, *64*, 3567−3571. (b) Baldwin, J. E.; Burrell, R. C. *J. Org. Chem.* **2002**, *67*, 3249−3256.

Acknowledgment. We thank the National Science Foundation for support at Syracuse University, through CHE-0211120 and CHE-0514376, and David J. Kiemle for his invaluable assistance.

Supporting Information Available: Four tables of kinetic data, three kinetic plots, a photograph of the gas-phase kinetic setup on the vacuum line, calculated geometries and energies of *cis,cis*-1,3-cyclononadiene ground-state conformers, transition structures for conformational interconversions, and transition structures for [1,5] hydrogen shifts (14 files), graphical representations of the 14 structures with bond lengths and bond angles, and a complete reference citation for Gaussian 98W, ref 28. This material is available free of charge via the Internet at http://pubs.acs.org.

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