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Thermal Chemistry of Bicyclo[4.2.0]oct-2-enes

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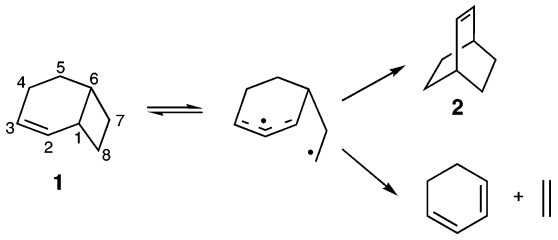

At 300 °C, bicyclo[4.2.0]oct-2-ene (**1**) isomerizes to bicyclo[2.2.2]oct-2-ene (**2**) via a formal [1,3] sigmatropic carbon migration. Deuterium labels at C7 and C8 were employed to probe for two-centered stereomutation resulting from C1−C6 cleavage and for one-centered stereomutation resulting from C1−C8 cleavage, respectively. In addition, deuterium labeling allowed for the elucidation of the stereochemical preference of the [1,3] migration of **1** to **2**. The two possible [1,3] carbon shift outcomes reflect a slight preference for migration with inversion rather than retention of stereochemistry; the *si*/*sr* product ratio is ∼1.4. One-centered stereomutation is the dominant process in the thermal manifold of **1**, with lesser amounts of fragmentation and [1,3] carbon migration processes being observed. All of these observations are consistent with a long-lived, conformationally promiscuous diradical intermediate.

Introduction

Vinylcyclopropanes and vinylcyclobutanes undergo ring expansion reactions to cyclopentenes and cyclohexenes, respectively, via formal [1,3] sigmatropic carbon migrations. With appropriately labeled substrates, four stereochemically distinct [1,3] products may be observed. They are conventionally denoted as *si*, *sr*, *ai*, and *ar*, where *s* or *a* refers to suprafacial or antarafacial topology of the π-system and *r* or *i* refers to retention or inversion of configuration at the migrating carbon. According to the Woodward−Hoffmann paradigm, *si* and *ar* products may be privileged as orbital symmetry-allowed concerted reactions, whereas *sr* and *ai* may not.[1] Because of geometrical constraints present in various bicyclic vinylcyclobutanes, such as those under investigation herein, antarafacial processes are geometrically prohibited. Thus, *si*/*sr* ratios have been used as a measure of the degree of orbital symmetry control in their [1,3] sigmatropic rearrangements.[2a]

Many thermal studies of bicyclo[3.2.0]hept-2-enes have been reported.[2] While the mixed stereochemical results exhibited by these vinylcyclobutane derivatives have met with various interpretations—competing orbital symmetry allowed and forbidden reactions,[2a] competing concerted and stepwise mechanisms,[2b,f,h] or even partitioning of a short-lived diradical[2e]—recent experimental[3,4] and theoretical[5,6] investigations have suggested that these reactions are almost certainly mediated by short-lived, nonstatistical diradical intermediates that partition to multiple products from a common shallow plateau on the potential energy surface.

A cross-system comparison of the thermal chemistry of bicyclo[2.1.1]hex-2-enes, bicyclo[3.2.0]hept-2-enes, and sub-

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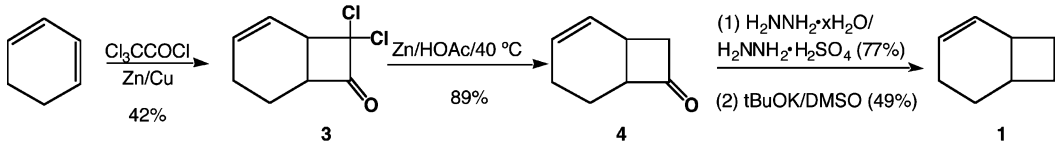
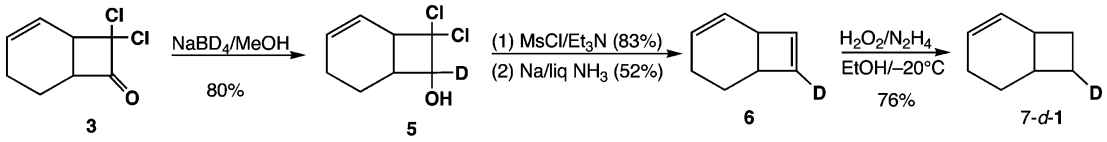
SCHEME 1. Synthesis of 1



SCHEME 2. Synthesis of 7-*d*-1



stituted monocyclic vinylcyclobutanes in a recent review[7] identified the bicyclo[4.2.0]oct-2-enes as a logical bridge between the more geometrically constrained bicyclo[2.1.1] and -[3.2.0] compounds and the more conformationally flexible monocyclic vinylcyclobutanes. As a consequence of this analysis, three hypotheses concerning the thermal behavior of vinylcyclobutanes were articulated:[8] (1) the *si*/*sr* ratio should correlate inversely with the degree of conformational freedom of the vinylcyclobutane, (2) an *exo*-methyl stereochemical marker on the migrating carbon should slow the rate of rotation about the bond between that carbon and its adjacent carbon in a short-lived diradical intermediate, as compared to the rate of rotation of that fragment having deuterium rather than *exo*-methyl as the marker,[9,10] and thus should form products having a higher *si*/*sr* ratio, and (3) fragmentation and a one-centered epimerization or stereomutation should increasingly compete with [1,3] shifts in vinylcyclobutanes having greater conformational flexibility.

Two of the aforementioned predictions have already been subjected to experimental verification.[8] Leber and co-workers noted that both predictions (1) and (3) were valid for a series of methyl-substituted bicyclic vinylcyclobutane derivatives; comparison of the kinetic behavior of 8-*exo*-methylbicyclo-[4.2.0]oct-2-ene with 7-*exo*-methylbicyclo[3.2.0]hept-2-ene and 5-*exo*-methylbicyclo[2.1.1]hex-2-ene showed that, indeed, the increase in flexibility accompanying increased ring size led both to a smaller *si*/*sr* ratio and to greater total participation of the fragmentation and stereomutation processes in the thermal manifold. This earlier work did not subject prediction (2) to an experimental evaluation.

The present report details thorough kinetic analyses of bicyclo[4.2.0]oct-2-ene (**1**), 7-*d*-bicyclo[4.2.0]oct-2-enes (7-*d*-**1**), and 8-*d*-bicyclo[4.2.0]oct-2-enes (8-*d*-**1**). This work represents a further validation of predictions (1) and (3) and an initial test of prediction (2). Explicit comparisons to the thermal chemistry of other deuterium-labeled vinylcyclobutanes will be made, as well as comparisons between methyl-labeled and deuterium-labeled vinylcyclobutanes.

Results

Syntheses. The synthesis of bicyclo[4.2.0]oct-2-ene (**1**), as shown in Scheme 1, started with the precursor 8,8-dichlorobicyclo[4.2.0]oct-2-en-7-one (**3**), which was prepared in moderate yield from 1,3-cyclohexadiene and trichloroacetyl chloride according to a previously published procedure.[11] Dechlorination with zinc in acetic acid[11] afforded bicyclo[4.2.0]oct-2-en-7-one (**4**) in 89% yield. Low-temperature Wolff−Kishner reduction[12] of **4** via the intermediacy of its hydrazone derivative gave bicyclo[4.2.0]oct-2-ene (**1**). Spectral data recorded for **3** and **4**, both known compounds, were in agreement with the literature.[11,13] In contrast, compound **1**, while known,[14,15] has been subjected to rigorous spectral analysis for the first time. Not only are high-field ^{1}H NMR chemical shifts consistent with previously reported low-field values, but ^{13}C NMR data including a DEPT pulse sequence have provided a compelling structure proof for **1**.

The synthesis of both epimers of 7-*d*-**1** (Scheme 2) commenced from compound **3**. Using a methodology previously documented for site-specific deuterium labeling of bicyclo[3.2.0]-hepta-2,6-dienes,[16] compound **3** was subjected to the following reaction sequence: reduction with $NaBD_4$ in methanol to alcohol **5**, mesylation with methanesulfonyl chloride and triethylamine, and treatment with Na in liquid ammonia to 7-*d*-bicyclo[4.2.0]-octa-2,7-diene (**6**). d_0-Analogues of **5**[13] and **6**[17] are known compounds; full spectral characterization was secured for **6**, the direct precursor to 7-*d*-**1**. Compound **6** was converted to 7-*d*-**1** by a novel selective reduction using diimide generated in situ by treatment of hydrazine with hydrogen peroxide at −20 °C.[18] Based on ^{2}H NMR, it was shown that this reduction occurred

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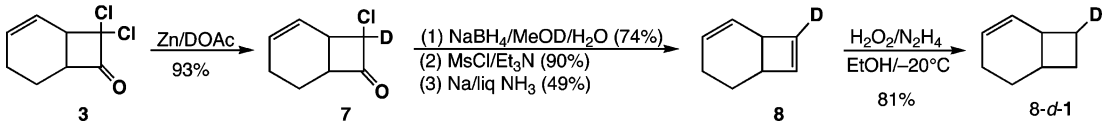
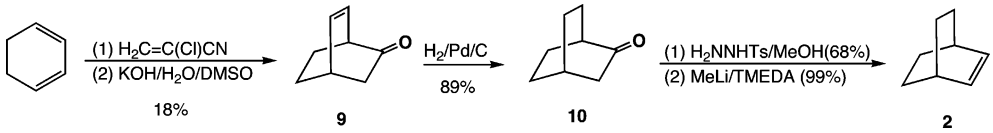
SCHEME 3. Synthesis of 8-*d*-1



SCHEME 4. Synthesis of 2



preferentially from the exo face of the C7−C8 π-bond: 7-*n*-*d*-**1** (δ 1.77):7-*x*-*d*-**1** (δ 1.91) = 4.8:1.[18,19]

The synthesis of 8-*d*-**1** epimers (Scheme 3) was accomplished via a similar methodology. After selective reduction of **3** with zinc in AcOD to afford 8-*d*-8-chlorobicyclo[4.2.0]oct-2-en-7-one (**7**), a reaction sequence analogous to that employed in the synthesis of **6** gave first an alcohol using $NaBH_4$ in CH_3OD and ultimately 8-*d*-bicyclo[4.2.0]octa-2,7-diene (**8**), which differs from **6** only in the position of the deuterium label. Using the aforementioned kinetically controlled diimide reduction, **8** was efficiently converted to 8-*d*-**1**. Hydrogen was preferentially delivered from the exo face of the cyclobutene π-bond: 8-*n*-*d*-**1** (δ 1.63):8-*x*-*d*-**1** (δ 2.23) = 5.9:1.[19]

The independent syntheses of 7-*d*-**1** and 8-*d*-**1** as well as selected NOE experiments with unlabeled **1** were employed to achieve partial assignment of the proton resonances in **1**. ^{2}H NMR results for 7-*d*-**1** and 8-*d*-**1** confirmed the assignments of the C7 and C8 proton signals. Differentiations between absorptions for endo and exo hydrogens on C7 and C8 were suggested by the synthetic method used to prepare these compounds, and assignments were confirmed with NOE experiments. When the proton signal at δ 2.64 assigned to the bridgehead hydrogen on C1 was irradiated, enhancement of the absorption at δ 2.23 (*exo*-H at C8) was observed. Similarly, irradiation of a peak at δ 2.59, due to the bridgehead hydrogen on C6, enhanced the resonance at δ 1.91 (*exo*-H at C7). The endo proton resonances at both of these positions exhibit the expected shielding effect of the proximal double bond;[20] comparatively, the *endo*-H at C8 (δ 1.63) is more shielded than the *endo*-H at C7 (δ 1.77) due to its closer proximity to the shielding cone of the π-bond.

The synthesis of **2** (Scheme 4) originated with the known compound bicyclo[2.2.2]oct-5-en-2-one (**9**) prepared by Diels−Alder reaction of 1,3-cyclohexadiene and 2-chloroacrylonitrile followed by base-catalyzed hydrolysis.[21] Hydrogenation of **9** over a Pd catalyst yielded bicyclo[2.2.2]octan-2-one (**10**), another known compound[22] that was converted to **2** by a two-step Shapiro modification of the Bamford−Stevens reaction via the intermediacy of its tosylhydrazone derivative.[23] Compound **2** is well-known, and the spectral data obtained for a pure sample of this material closely matched the reported literature values.[22,24] Of particular interest are the ^{1}H NMR chemical shifts of the exo and endo hydrogens in **2** at δ 1.48 and 1.21, respectively.

Thermal Reactions. Thermal reactions of **1**, 7-*d*-**1**, 8-*d*-**1**, and **2** were carried out in a well-conditioned thermal bulb at 300.0 °C.[2h] Preparative GC provided **1** of greater than 99.5% purity, and seven kinetic runs starting with this purified reactant **1** were followed. These runs spanned a time range of 3−45 h, corresponding to between 19% and 89% conversion of **1** to products and greater than 3 half-lives. Thermal reactions starting with **1** were also carried out at 275.0 and 315.0 °C to define activation parameters. The Arrhenius plot yielded the activation parameters $E_a = 51.8 \pm 0.3$ kcal/mol and $\log A = 14.9 \pm 0.1$.

Samples of 7-*d*-**1** and 8-*d*-**1** were heated for varying lengths of time up to 30 h, and the resultant kinetic runs were analyzed by ^{2}H NMR. Whereas 7-*d*-**1** was studied to detect a possible two-centered stereomutation at the C1−C6 bond, 8-*d*-**1** was examined to probe for a possible one-centered stereomutation at C8 and to derive explicit stereochemical data for the [1,3] carbon migration of C8 from C1 to C3. The principal results of the thermal study of 7-*d*-**1** and 8-*d*-**1** at 300 °C have already been communicated.[19]

The potential for retro Diels−Alder fragmentation of **2** was investigated by following four kinetic runs starting with **2**. After 240 h at 300.0 °C, only 10% of **2** had reacted. There was no appreciable thermal loss of **2** at 45 h, corresponding to the duration of the longest kinetic runs of **1**. Because of the prohibitively slow rate of the retro Diels−Alder reaction of **2**, and the fact that activation parameters have previously been reported for this reaction,[25] further thermal study was not pursued. The limited kinetic data secured for loss of **2** led to a rate constant at 300 °C of 1.3 ($\pm$0.1) $\times$ 10^{-7} s^{-1}, a value reasonably close to the 1.8 $\times$ 10^{-7} s^{-1} calculated using the Arrhenius parameters reported by Huybrechts based on a more extensive thermal study of **2** over the temperature range of 275−360 °C.[25]

The data obtained through kinetic runs starting with **1** at 300 °C led to the first-order rate constants for loss of starting material (k_0), formation of **2** (k_{13}), and fragmentation to give ethylene plus 1,3-cyclohexadiene (k_f) tabulated in Table 1. The experimental first-order rate constants for parallel first-order reactions in Table 1 correspond to the thermal reactions depicted in Scheme 5, and the relationship $k_0 = k_{13} + k_f$. Compound **2** is essentially thermally inert over the time period for which the thermal chemistry of **1** was observed, as the value calculated for the retro Diels−Alder reaction is slower than k_0 by 2 orders of magnitude.

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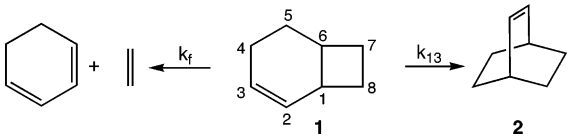
TABLE 1. Parallel First-Order Rate Constants ($\times 10^6$ s) for 1

temp (°C)	k_0[a]	k_{13}[b]	k_f[c]	k_{13}/k_f
275	1.7 ± 0.2	0.5	1.2	0.42
300	13.9 ± 0.3	4.26	9.60	0.44
315	44.1 ± 0.6	13.2	30.9	0.43

[a] Rate constant for overall loss of **1**, where $k_0 = k_{13} + k_f$. [b] Rate constant for [1,3] shift of **1** to **2**. [c] Rate constant for fragmentation of **1** to 1,3-cyclohexadiene and ethylene.

SCHEME 5. Thermal Reactions of Unlabeled 1



A possible two-centered epimerization at C1−C6 might have been detected with the aid of a specific deuterium label at C7, as outlined in Scheme 6. The endo isomer of 7-*d*-**1**, 7-*n*-*d*-**1**, served as a probe of this stereomutation, and overall "ring-flip". It was not detected.

The absence of appreciable two-centered stereomutation was, however, advantageous in that thermal isomerization of 7-*d*-**1** as a mixture of 7-*x*-*d*-**1** and 7-*n*-*d*-**1** allowed unambiguous determination of the ^{2}H NMR chemical shifts of 5-*x*-*d*-**2** and 5-*n*-*d*-**2** (Scheme 7). The ^{2}H NMR chemical shifts of δ 1.51 and 1.24 for 5-*x*-*d*-**2** and 5-*n*-*d*-**2**, respectively, correspond well to the ^{1}H NMR shifts observed for **2** (*vide supra*).

Scheme 8 illustrates the thermal reactions that were observed starting from the epimers of 8-*d*-**1**; 8-*n*-*d*-**1** and 8-*x*-*d*-**1** interconvert via one-centered stereomutations, or epimerizations, at C8; the one-way rate constant k_{8e} defined in Scheme 8 is 3.06×10^{-5} s^{-1}. Both epimers of 8-*d*-**1** undergo [1,3] carbon migration to 5-*d*-**2** epimers with a slight preference for migration with inversion of stereochemistry: $k_{si} = 2.46 \times 10^{-6}$ s^{-1}, $k_{sr} = 1.80 \times 10^{-6}$ s^{-1}, and $k_{13} = k_{si} + k_{sr} = 4.26 \times 10^{-6}$ s^{-1}; $k_{si}/k_{sr} \approx 1.4$. In addition, 8-*d*-**1** fragments directly to 1,3-cyclohexadiene and *d*-ethylene: $k_f = 9.60 \times 10^{-6}$ s^{-1}. The progression of decreasing importance of rate constants is in the following order: $k_{8e} > k_f > k_{13}$.[19]

The absence both of octatriene isomers in product mixtures and a "ring-flip" two-center stereomutation has been cited as evidence that **1** does not undergo kinetically competitive C1−C6 bond cleavage.[19] It is possible, however, to envision a degenerate [1,3] rearrangement of **1** involving C1−C6 bond cleavage; that is, C6 could migrate from C1 to C3. A careful examination of the ^{2}H NMR spectra for thermal runs performed on 8-*d*-**1** excludes this possibility as well. This hypothetical rearrangement, should it occur, would transform 8-*x*-*d*-**1** to 4-*x*-*d*-**1**, which would exhibit a ^{2}H NMR signal at ca. δ 2.0 due to an *exo*-allylic deuterium. No such peak was observed throughout the thermal study of 8-*d*-**1**.

Discussion and Conclusions

An examination of the first-order rate constants in Table 1 shows that at all temperatures k_f is greater than k_{13}. Not only is the k_{13}/k_f ratio significantly less than 1, but it is also constant. Although one might expect fragmentation to increase as temperature increases, that is not observed at least over this fairly narrow 40 °C temperature range. Activation parameters have been determined for both the [1,3] isomerization and fragmentation processes based on the rate constants in Table 1. For conversion of **1** to **2**, $E_a = 52.6 \pm 0.7$ kcal/mol and $\log A = 14.7 \pm 0.3$. Relative to the activation parameters for [1,3] rearrangement, those for fragmentation of **1** are quite comparable: $E_a = 52.0 \pm 0.3$ kcal/mol and $\log A = 14.8 \pm 0.1$. This remarkable similarity is consistent with the two products from **1** sharing the same rate-determining step to form a diradical intermediate common to both thermal products.

Gajewski has previously explicated the two major criteria of concert, one energetic and one stereochemical.[26] The energetic test implicates a nonconcerted reaction whenever the experimental E_a value is about equal to or larger than the bond dissociation energy of the C−C bond being broken. The activation parameters determined for overall loss of **1** (E_a = 51.8 kcal/mol; $\log A = 14.9$) are comparable to those reported for vinylcyclobutane (E_a = 49.3 kcal/mol; $\log A = 14.5$).[27,28] For the vinylcyclobutane to cyclohexene isomerization, the experimental E_a value is 47.5 ± 0.5 kcal/mol, essentially identical to the E_a = 47.9 kcal/mol barrier estimated using a thermochemical model for complete C1−C2 bond rupture to form a strain-free diradical intermediate.[28] Gajewski asserted that the activation free energies for almost every [1,3] shift are 5−10 kcal/mol higher than required for a simple bond homolysis, a generalization consistent with [1,3] carbon shifts being stepwise nonconcerted processes.[26] Fundamentally, the vinylcyclobutane reaction fails the energetic criterion of concert.

What then of the stereochemical criterion of concert? Despite Gajewski's admonition that stereoselectivity is a necessary but insufficient criterion for concert,[26] the almost complete stereoselectivity of the [1,3] shift in 5-*exo*-methylbicyclo[2.1.1]hex-2-ene (first entry in Table 2) has been oft-cited in support of a concerted mechanism for the vinylcyclobutane-to-cyclohexene rearrangement. Given the three hypotheses enumerated previously, an examination of the stereochemical data in Table 2 reveals that the contribution from the symmetry-allowed *si* pathway decreases with an increase in conformational flexibility of the bicyclic vinylcyclobutanes.[8] The *si*/*sr* ratio decreases going down Table 2 for both the methyl- and the deuterium-substituted series, suggesting that the conformational agility of the molecule contributes to the stereochemical outcome of the [1,3] shift. Thus, the first hypothesis is further substantiated by extension to the more conformationally flexible bicyclo[4.2.0]-oct-2-enes.

The second hypothesis, which relates to the stereochemical effect of the substituent on the migrating carbon, states that a substituent such as an exo methyl group on the migrating carbon can retard the rate of rotation about the C−CHCH$_3$ bond in the diradical intermediate and thus increase the *si*/*sr* ratio. Conversely, replacing methyl with deuterium, as was done in this study, will decrease the *si*/*sr* ratio. That is, in fact, what is observed. For the bicyclo[4.2.0]oct-2-enes, an *exo*-methyl label affords *si*/*sr* = 2.4;[8] a deuterium label, *si*/*sr* = 1.4.[19] The generality of this trend can be validated by comparing the entries in Table 2. Moreover, the data in Table 2 provide compelling

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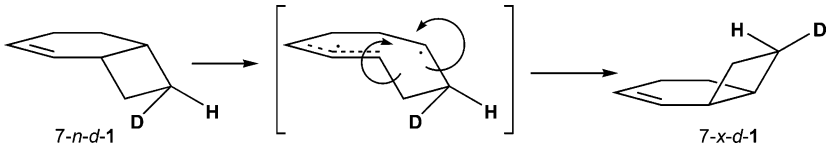
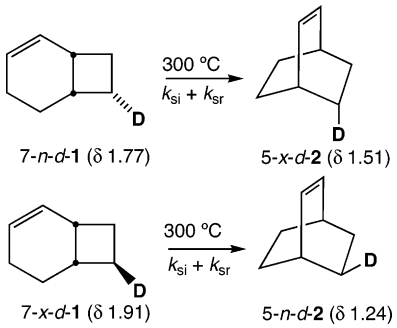
(31) Baldwin, J. E.; Fede, J.-M. *J. Am. Chem. Soc.* **2006**, *128*, 5608−5609.

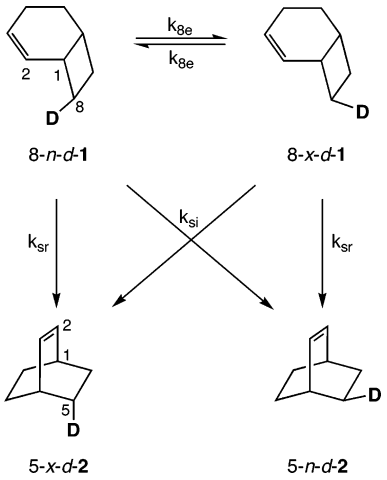
SCHEME 6. Undetected C_1-C_6 Double Stereomutation of 7-*d*-1



SCHEME 7. Thermal Conversion of 7-*d*-1 Epimers to 5-*d*-2 Epimers



SCHEME 8. Kinetic Scheme for 8-*d*-1



evidence that the [1,3] shift of bicyclic vinylcyclobutanes fails the stereochemical criterion of concert.

The third and final hypothesis states that the combined extent of stereomutation and fragmentation should increase at the expense of the [1,3] isomerization as the bicyclic vinylcyclobutane becomes more conformationally supple. To examine the validity of this hypothesis for a series of bicyclic and monocyclic vinylcyclobutanes, the relative contributions of each of the three major exit channels available to vinylcyclobutanes, the [1,3] migration, one-centered stereomutation or epimerization, and fragmentation, are compared in Table 3.

The exit channel data in Table 3 strikingly complement the stereochemical data in Table 2 by supporting the conclusion that the bicyclo[2.1.1]hex-2-enes are anomalous. The total amount of epimerization and fragmentation combined increases dramatically as the conformational flexibility of a bicyclic vinylcyclobutane increases going down Table 3. For the bicyclic vinylcyclobutanes, the [1,3] isomerization process gradually becomes less important relative to epimerization and to a lesser extent fragmentation. The relative amount of fragmentation is comparable for both bicyclo[3.2.0]hept-2-ene and bicyclo[4.2.0]-oct-2-ene. Comparing the bicyclic and the monocyclic vinylcyclobutanes shows that fragmentation becomes the dominant

TABLE 2. Stereochemistry for [1,3] Shifts Shown by Bicyclic Vinylcyclobutanes

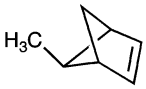
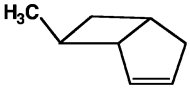
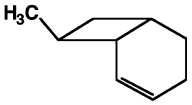
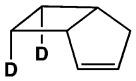
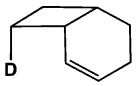
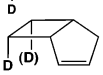
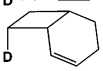
Reactant	% *si*	% *sr*	*si*/*sr*	Ref
	99.5	0.5	200	29
	87	13	7	2h
	71	29	2.4	8
	98	2	50	30
	76	24	3	2e
	58	42	1.4	this work

TABLE 3. Relative Percent Contribution of Three Major Exit Channels: [1,3] Carbon Shifts, Epimerizations, and Fragmentations

Reactant	%[1,3]	%Ep	%Fr	Rel. Rates	Ref.
	100	0	0	[1,3] only	30
	60	11	29	[1,3]>Fr>Ep	2g,18b
	11	67	22	Ep>Fr>[1,3]	this work
	23	29	48	Fr>Ep>[1,3]	31

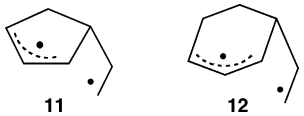
mode of reaction for monocyclic systems. The existence on the vinylcyclobutane potential energy surface of a trans-diradical intermediate, from which isomerization to cyclohexene is geometrically prohibited, undoubtedly contributes to the dominance of the fragmentation exit channel for monocyclic vinylcyclobutanes.[6c] Not only do the data in Table 3 substantiate the final hypothesis, but they illustrate that the balance between the three dominant exit channels available to the diradical intermediate is easily altered by the conformational flexibility of the reactant vinylcyclobutanes and, by extension, of the related diradicals themselves.

The relative order of importance of rate constants for the three reaction manifolds for four vinylcyclobutanes is indicated in the next to last column of Table 3. The essentially rigid bicyclo-[2.1.1]hex-2-ene experiences [1,3] rearrangement exclusively. As soon as the bicyclic framework permits even modest

conformational mobility, fragmentation and epimerization become significant. Still, the [1,3] product is the dominant exit channel for bicyclo[3.2.0]hept-2-ene. In contrast, the isomerization is far less important for bicyclo[4.2.0]oct-2-ene (**1**), for which epimerization is favored. It appears that subtle differences in the dynamic factors associated with bond rotation in closely related diradicals allow the intermediate to partition among the various exit channels in myriad ways. The greater is the distance between the migrating carbon and the migration terminus,[8] the more time the diradical has to explore conformational space before reformation of a C−C bond or cleavage of a second C−C bond defines a product.

The fate of the diradical experiencing an inward trajectory[5,6] of the migrating carbon accompanying bond homolysis is largely determined by dynamic factors.[5] The existence of a long-lived diradical residing in a deeper local energy minimum that is protected from immediate isomerization to **2** or fragmentation to 1,3-cyclohexadiene and ethylene is consistent with the low *si*/*sr* ratio ≈ 1.4, suggesting there is sufficient time for C7−C8 bond rotation before C8 reaches C3 in the [1,3] migration (Scheme 9). Although residual bonding has been postulated as a basis for the preference for the *si* product,[5b,6c] internal rotation destroys residual bonding.[4b] Perhaps there still remains a small contribution from a rapid direct inward trajectory leading exclusively to the *si* product or from a subset of the diradical population with greater angular momentum.

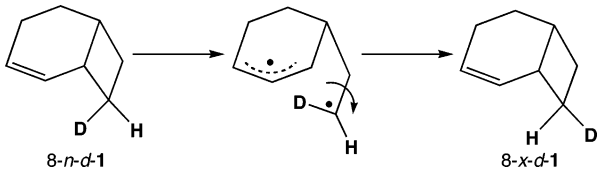
While compound 8-*n*-*d*-**1** exhibits little preference for 5-*n*-*d*-**2**, the orbital-symmetry allowed *si* product (Scheme 8), the diradical intermediate has a far greater tendency to reclose to the less thermodynamically stable **1** (with corresponding epimerization at C8) than to isomerize to the more thermodynamically stable **2**: $k_{8e} > k_f > k_{13}$.[19] This suggests that the conspicuous difference in rate order (Table 3) reported for the bicyclo[3.2.0]hept-2-enes ($k_{13} > k_f > k_{7e}$) as compared to the bicyclo[4.2.0]oct-2-enes is a consequence of different diradical lifetimes, not rotational rates or diradical stabilities, for **11** and **12**. A sufficiently high-energy barrier protecting the diradical intermediate formed by C1−C8 bond homolysis of **1** from either isomerization to **2** or fragmentation can account for the difference in lifetimes for **11** and **12**. If a shallow minimum on a potential energy surface has associated with it wider exit channels,[6c] then a steeper minimum will produce narrower exit channels, favoring reclosure to starting material. Using Carpenter's terminology, the inefficiency of the direct trajectory favors a reflected trajectory due to the facility of internal bond rotation in the diradical intermediate.[5b]



11 **12**

Given the kinetic dominance of epimerization at C8 evident in product mixtures (Scheme 8) and an *si*/*sr* ratio close to one for the two [1,3] shifts, any rationale championing orbital symmetry control of the thermal isomerizations observed becomes untenable. The small *si*/*sr* rate ratio corresponds to a paltry difference in activation energy of less than 0.4 kcal/mol. Not only does the low *si*/*sr* ratio provide a compelling refutation of orbital symmetry control of the [1,3] sigmatropic rearrangement, but also the low *si*/*sr* ratio and the competition between the three exit channels constitute rigorous experimental support for a long-lived, conformationally promiscuous diradical intermediate on the potential energy surface.

SCHEME 9. Epimerization at C_8 in 8-*d*-1



Experimental Section

8,8-Dichlorobicyclo[4.2.0]oct-2-en-7-one (3). To a mixture of 70 g of zinc−copper couple (0.75 mol) in 25.0 mL of 1,3-cyclohexadiene (0.262 mol) and 200 mL of anhydrous diethyl ether was added a solution of 100 g of trichloroacetyl chloride (0.550 mol) and 100 mL of dimethoxyethane (DME) over a period of 1 h. The reaction was stirred overnight at room temperature. The resulting mixture was filtered through a sintered glass funnel, and the solid was washed several times with hexane. The organic phase was washed sequentially with 0.5 N HCl, 5% NaOH, water, and brine; filtered through a plug of silica gel and charcoal; dried with $MgSO_4$; evaporated under reduced pressure; and subjected to bulb-to-bulb distillation at 1−2 Torr (55−60 °C) to afford 20.9 g of **3** (42%). IR (cm^{-1}): 3050 (w), 1800 (s), 1650 (w), 705 (s). MS (*m*/*z*): 194 (1%), 192 (4%), 190 (M^+, 6%), 155 (14%), 127 (15%), 91 (33%), 79 (27%), 55 (100%). ^1H NMR (500 MHz, $CDCl_3$): δ 1.61 (1H, m), 1.95 (1H, m), 2.00 (1H, m), 2.07 (1H, m), 3.41 (1H, m), 4.07 (1H, m), 5.84 (1H, m), 6.05 (1H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.6 (CH_2), 20.7 (CH_2), 44.1 (CH), 53.2 (CH), 86.6 (CCl_2), 122.9 (=CH), 132.3 (=CH), 196.6 (C=O).

Bicyclo[4.2.0]oct-2-en-7-one (4). To a mixture of 12.13 g of zinc dust (0.186 mol) in 60 mL of absolute ethanol and 25 mL of TMEDA was added 11.8 mL of glacial acetic acid (0.206 mol) over 10 min. After addition of a solution of 6.00 g (31.4 mmol) of **3** in 12.6 mL of glacial acetic acid (0.219 mol), the reaction was heated to 40 °C and stirred overnight. The reaction mixture was passed through a sintered glass funnel, exercising care to avoid exposing the pyrophoric zinc to air until it had been quenched by the addition of water. The solids were washed thoroughly with 50:50 pentane:ether before the organic layer was washed successively with 1 N HCl, saturated $NaHCO_3$, water, and brine and then dried with $MgSO_4$. Solvent was evaporated under reduced pressure, affording 3.43 g (28.1 mmol, 89%) of **4**. IR (cm^{-1}): 3050 (w), 1780 (s), 1650 (w), 690 (m). MS (*m*/*z*): 122 (<1%), 91 (4%), 80 (100%), 79 (79%). ^1H NMR (300 MHz, $CDCl_3$): δ 1.49 (1H, m), 1.94 (3H, m), 2.53 (1H, dt), 2.85 (1H, m), 3.20 (1H, ddd), 3.49 (1H, m), 5.78 (1H, m), 5.87 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.3 (CH_2), 21.1 (CH_2), 22.8 (CH), 51.9 (CH_2), 57.2 (CH), 128.2 (=CH), 128.8 (=CH), 211.8 (C=O).

Bicyclo[4.2.0]oct-2-ene (1). To a solution of 3.77 g of hydrazine sulfate (29.1 mmol) in 10.5 mL of hydrazine hydrate was added 3.43 g (28.1 mmol) of **4** over 15 min. The reaction mixture was stirred overnight at 65 °C, extracted with ether, dried over $MgSO_4$, and evaporated under reduced pressure to yield 2.95 g (21.7 mmol, 77%) of bicyclo[4.2.0]oct-2-en-7-one hydrazone. IR (cm^{-1}): 3460 (w), 3200 (w), 3020 (w), 2930 (m), 1590 (w), 1540 (w), 700 (s). To a solution of 1.58 g (14.1 mmol) of freshly sublimed potassium *tert*-butoxide in 25 mL of anhydrous DMSO was added 1.39 g (9.24 mmol) of hydrazone over 5 h. After being stirred overnight, the reaction was quenched with ice cold water (5 mL) and the product was extracted into pentane. The organic phase was washed several times with water to remove all residual DMSO, dried with $MgSO_4$, and purified by short-path distillation to give 0.489 g (4.53 mmol, 49%) of **1** as a colorless liquid. IR (cm^{-1}): 3010 (w), 1650 (w), 700 (s). MS (*m*/*z*): 108 (2%), 91 (6%), 80 (100%), 79 (51%), 77 (51%). ^1H NMR (500 MHz, $CDCl_3$): δ 1.48 (2H, m), 1.61 (1H,

m), 1.73 (1H, dq), 1.87 (1H, m), 1.97 (1H, m), 2.08 (1H, m), 2.19 (1H, dq), 2.59 (1H, m), 2.64 (1H, br s), 5.73 (1H, m), 5.79 (1H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (CH_2), 22.4 (CH_2), 24.0 (CH_2), 27.8 (CH_2), 32.7 (CH), 33.0 (CH), 126.8 (═CH), 130.9 (═CH).

7-*d*-8,8-Dichlorobicyclo[4.2.0]oct-2-en-7-ol (5). To a solution of 4.738 g of **3** (24.9 mmol) and 30 mL of MeOH at 0 °C was added 0.90 g of $NaBD_4$ (27 mmol) over 2 h. The reaction was warmed to rt and stirred overnight. The reaction was extracted with ether, washed sequentially with 1 N HCl, H_2O, saturated $NaHCO_3$, H_2O, and brine, and then dried with $MgSO_4$. Evaporation at reduced pressure afforded 3.864 g (20.0 mmol, 80%) of **5**. IR (cm^{-1}): 3300 (br, m), 3050 (w), 1650 (w), 860 (s), 710 (s).

7-*d*−Bicyclo[4.2.0]octa-2,7-diene (6). To a solution of 3.864 g (20.0 mmol) of **5**, 4 mL of triethylamine, and 100 mL of CH_2Cl_2 at 0 °C was added 3.1 mL of methanesulfonyl chloride (40 mmol) over 15 min. The reaction was warmed to rt, stirred overnight, extracted into CH_2Cl_2, washed sequentially with 1 N HCl, water, saturated $NaHCO_3$, water, and brine, and then dried over $MgSO_4$. Evaporation at reduced pressure afforded 3.20 g (16.6 mmol, 83%) of mesylate. IR (cm^{-1}): 3020 (w), 1650 (w), 1360 (s), 1170 (s), 710 (s). After condensing ca. 500 mL of ammonia, 1.84 g of sodium metal (80 mmol) was added to the liquid ammonia in small pieces over 15 min at −78 °C to yield an intense blue reaction mixture. A solution of 3.20 g (16.6 mol) of mesylate in 40 mL of anhydrous THF was slowly added to the reaction, which was then allowed to stir at −78 °C for 5 h before slowly warming to −35 °C. The reaction was then cooled to −60 °C, and sufficient NH_4Cl was added until the blue color dissipated. The reaction was then allowed to warm slowly; before all of the ammonia had evaporated, 100 mL of pentane and 100 mL of water were added. The reaction was extracted with pentane, washed sequentially with 1 N HCl, water, saturated $NaHCO_3$, water, and brine, and then dried with $MgSO_4$. Short-path distillation afforded 0.923 g (8.63 mmol, 52%) of **6**. IR (cm^{-1}): 3020 (m), 1630 (w), 710 (s). MS (*m*/*z*): 107 (27%), 92 (42%), 79 (100%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.34 (1H, tt), 1.76 (1H, m), 1.86 (1H, br m), 2.00 (1H, br m), 3.12 (1H, m), 3.25 (1H, m), 5.83 (2H, m), 5.86 (1H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (CH_2), 25.8 (CH_2), 41.4 (CH), 42.0 (CH), 128.0 (═CH), 129.2 (═CH), 136.2 (═CH), 137.7 (═CD). ^{2}H NMR (92 MHz, $CHCl_3$): δ 6.08.

7-*d*-Bicyclo[4.2.0]oct-2-ene (7-*d*-1). To a solution of 0.923 g (8.63 mmol) of **6** and 30 mL of absolute ethanol was added 0.27 mL (8.63 mmol) of anhydrous hydrazine. The reaction was cooled to −20 °C, and then 1 mL aliquots of 30% hydrogen peroxide were added to the reaction mixture every 2 h while reaction progress was monitored by GC. After 6 h, an additional 0.27 mL of anhydrous hydrazine was added. Water (20 mL) was added to the reaction after >80% conversion was achieved. Short-path distillation afforded 0.715 g (6.56 mmol, 76%) of crude 7-*d*-**1**, which was obtained in >99% purity by preparative GC (8' × 1/4" 20% DC-710 on Chrom P, 70 °C). IR (cm^{-1}): 3020 (m), 2190 (w), 1640 (w), 690 (s). MS (*m*/*z*): 109 (3%), 92 (4%), 80 (100%), 79 (53%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.48 (2H, m), 1.61 (1H, m), 1.73 (0.18H, m), 1.87 (0.82H, m), 1.97 (1H, m), 2.08 (1H, m), 2.19 (1H, dq), 2.59 (1H, m), 2.64 (1H, br s), 5.73 (1H, m), 5.79 (1H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (CH_2), 22.0 (CHD), 24.0 (CH_2), 27.7 (CH_2), 32.6 (CH), 33.0 (CH), 126.8 (═CH), 130.9 (═CH). ^{2}H NMR (92 MHz, $CHCl_3$): δ 1.77 (82%), 1.91 (18%).

8-*exo*-*d*-8-*endo*-Chlorobicyclo[4.2.0]oct-2-en-7-one (7). To a solution of 9.22 g (48.5 mmol) of **3** in 100 mL of *d*-acetic acid was slowly added 3.2 g of zinc dust (49 mmol). The reaction was stirred until the gray color of zinc was observed to disappear. When the reaction was deemed complete by GC−MS, it was cooled to 0 °C before ice water was added to the reaction vessel. After three successive extractions with ether, the organic phase was washed sequentially with saturated sodium bicarbonate, water, 1 N HCl, water, and brine, and then dried with $MgSO_4$. Evaporation at reduced pressure afforded 7.08 g (45.1 mmol, 93%) of **7**. MS (*m*/*z*): 157 (2%), 129 (6%), 79 (27%), 55 (100%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.57 (1H, m), 2.03 (2H, m), 2.09 (1H, m), 3.23 (1H, br m), 3.61 (1H, br m), 5.77 (1H, m), 6.02 (1H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.1 (CH_2), 20.7 (CH_2), 29.8 (CH), 53.0 (CH), 62.4 (CDCl), 123.0 (═CH), 131.2 (═CH), 202.8 (C═O). The ^{13}C NMR data matched the literature values for 8-*endo*-chlorobicyclo-[4.2.0]oct-2-en-7-one.[13]

8-*d*-Bicyclo[4.2.0]octa-2,7-diene (8). Compound **8** was prepared according to the procedure for the preparation of **6**. Starting with 5.24 g (33.4 mmol) of **7**, 40 mL of *d*-methanol, and 5.58 g (134 mmol) of $NaBH_4$, 3.95 g (24.7 mmol, 74%) of alcohol was isolated. IR (cm^{-1}): 3400 (br, m), 2920 (m), 2220 (w), 1640 (w), 705 (s). MS (*m*/*z*): 159 (1%), 103 (16%), 80 (100%), 57 (31%). From 3.95 g (24.7 mmol) of alcohol, 7 mL of triethylamine, and 7.74 mL of methanesulfonyl chloride (0.1 mol) was isolated 5.24 g (22.2 mmol, 90%) of mesylate derivative. IR (cm^{-1}): 2930 (w), 2300 (w), 1350 (s), 1180 (s). The diene was prepared from 5.24 g of mesylate (22.2 mmol) as per the procedure for **6**. Short-path distillation afforded 1.16 g (10.9 mmol, 49%) of **8**. IR (cm^{-1}): 3020 (w), 1640 (w), 700 (s), 670 (s). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.33 (1H, tt), 1.75 (1H, m), 1.85 (1H, m), 1.99 (1H, m), 3.11 (1H, br s), 3.24 (1H, m), 5.82 (2H, m), 6.08 (1H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (CH_2), 25.8 (CH_2), 41.4 (CH), 42.1 (CH), 128.0 (═CH), 129.2 (═CH), 136.4 (═CD), 137.6 (═CH). ^{2}H NMR (92 MHz, $CDCl_3$): δ 5.92.

8-*d*-Bicyclo[4.2.0]oct-2-ene (8-*d*-1). Compound 8-*d*-**1** was prepared according to the procedure for the preparation of 7-*d*-**1**. Starting with 1.164 g (10.9 mmol) of **8**, crude 8-*d*-**1** (0.962 g, 8.83 mmol) was isolated in 81% yield. Purity greater than 99% was achieved via preparative GC. IR (cm^{-1}): 3010 (w), 1640 (w), 730 (s). MS (*m*/*z*): 109 (2%), 92 (3%), 80 (100%), 79 (51%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.49 (2H, m), 1.59 (0.15H, m), 1.72 (1H, m), 1.87 (1H, m), 1.98 (1H, m), 2.08 (1H, m), 2.18 (0.85H, dq), 2.59 (1H, m), 2.65 (1H, br s), 5.74 (1H, m), 5.79 (1H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (CH_2), 22.3 (CH_2), 24.1 (CH_2), 27.5 (CHD), 32.7 (CH), 32.9 (CH), 126.8 (═CH), 130.9 (═CH). ^{2}H NMR (92 MHz, $CHCl_3$): δ 2.23 (15%), 1.63 (85%).

Bicyclo[2.2.2]oct-5-en-2-one (9). To a solution of 27 mg of hydroquinone in 20 mL (0.18 mol) of 1,3-cyclohexadiene was added 10 mL (11 g, 0.12 mol) of 2-chloroacrylonitrile (pretreated with potassium hydroxide pellets from which it was decanted before addition). After refluxing overnight in the dark at 90−100 °C, an additional 10 mL of 1,3-cyclohexadiene was added, and the reaction mixture was again refluxed overnight. The brown reaction mixture was diluted with 15 mL of CH_2Cl_2, and the resultant solution was filtered through a short silica gel column and then concentrated under reduced pressure to yield 6.9 g of a dark brown liquid. IR (cm^{-1}): 3040 (w), 2240 (w), 1650 (w), 710 (s). To a solution of the viscous residue in 95 mL of DMSO was slowly added an aqueous solution of 11.6 g of KOH in 20 mL of water over 4 h with continuous stirring. Stirring was continued for an additional 20 h; the addition of 200 mL of water was followed by five successive extractions with pentane. The organic extract was then washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to afford 2.6 g (0.021 mol, 18% overall) of compound **9** as a white crystalline solid (mp 85−88 °C). IR (cm^{-1}): 3040 (w), 1725 (s), 1610 (w), 700 (s). MS (*m*/*z*): 122 (23%), 80 (100%), 79 (88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.48 (m, 1H), 1.55 (m, 1H), 1.67 (m, 2H), 1.83 (m, 1H), 2.00 (m, 1H), 2.96 (m, 1H), 3.10 (br m, 1H), 6.17 (t, 1H), 6.45 (t, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 22.5 (CH_2), 24.2 (CH_2), 32.3 (CH), 40.5 (CH_2), 48.5 (CH), 128.4 (═CH), 137.0 (═CH), 213.2 (C═O).

Bicyclo[2.2.2]octan-2-one (10). A solution of 0.68 g (5.6 mmol) of **9** in 50 mL of absolute ethanol, to which ca. 0.2 g of 10% Pd/C was added, was placed in a Parr apparatus and subjected to medium-pressure hydrogenation for 2 h. After the reaction mixture was filtered through a sintered glass funnel, it was diluted with water, extracted with ether, washed with water, dried with $MgSO_4$, and concentrated under reduced pressure to yield 0.62 g (5.0 mmol,

89%) of **10** as a white solid (mp 169−172 °C). IR (cm^{-1}): 1720 (s), 1670 (w). MS (*m*/*z*): 124 (54%), 81 (36%), 80 (100%). ^1H NMR (500 MHz, $CDCl_3$): δ 1.58 (m, 2H), 1.69 (m, 2H), 1.79 (m, 4H), 2.13 (m, 1H), 2.22 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.3 (CH_2), 24.7 (CH_2), 27.9 (CH), 42.3 (CH), 44.7 (CH_2), 218.1 (C═O).

Bicyclo[2.2.2]oct-2-ene (2). To a solution of 1.86 g (10.0 mmol) of *p*-toluenesulfonylhydrazide in 50 mL of methanol was added 0.62 g (5.0 mmol) of **10**. After sitting overnight, the resultant white crystals were filtered, washed with 1:1 pentane:ether, and dried in a vacuum oven to yield 0.99 g (3.4 mmol, 68%) of tosylhydrazone (mp 214−215 °C). IR (cm^{-1}): 3210 (m), 1650 (w), 1320 (s), 1170 (s), 670 (s). Under nitrogen atmosphere, 3.4 mL of 1.6 M MeLi in ether (5.4 mmol) was added via syringe to a solution of 0.76 g (2.6 mmol) of tosylhydrazone in 25 mL of TMEDA in an ice bath. After the reaction was allowed to warm and stir overnight, it was cooled to −30 °C, quenched with water, and extracted successively with pentane. The organic layer was washed with water, 3 M NaOH, 1 N HCl, water, and brine, dried over $MgSO_4$, and concentrated by short-path distillation to give a colorless waxy solid. To facilitate transfer, the waxy solid was dissolved in ca. 5 mL of pentane; 99% yield of **2** was based on GC analysis of this pentane solution. IR-(cm^{-1}): 1620 (w). MS (*m*/*z*): 108 (18%), 80 (100%), 79 (47%). ^1H NMR (500 MHz, $CDCl_3$): δ 1.21 (br d, 4H), 1.48 (br d, 4H), 2.46 (br m, 2H), 6.23 (dd, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.7 (CH_2), 29.5 (CH), 134.3 (═CH).

Gas-Phase Reactions. Thermal reactions were conducted in an apparatus described previously.[2h] Thermolysis samples were analyzed by GC on an HP cross-linked methyl silicone column (50 m × 0.2 mm i.d. × 0.10 μm film thickness) operating at an initial temperature of 60 °C held for 1 min followed by a temperature ramp of 0.5 °C/min to a maximum temperature of 120 °C. Retention times (min) were as follows: **2** (9.0), **1** (10.0), and the internal standard cyclooctane (11.8). Concentrations of fragments 1,3-cyclohexadiene and ethylene were determined by difference as compared to a time zero sample for each kinetic run.

Thermal runs of deuterium-labeled compounds were removed using standard vacuum line transfer and dissolved in chloroform that had been purified by washing with concd H_2SO_4 and water and then distilling from calcium hydride. ^2H NMR spectra were acquired at 92.15 MHz.

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Supporting Information Available: ^2H NMR spectrum of 7-*d*-**1** and its thermal reaction mixture; tables of mole fractions for thermal runs of **1** at 275, 300, and 315 °C and the associated first-order rate plots; copies of an Arrhenius plot and a sample GC chromatogram for the gas-phase thermal decomposition of **1**. Copies of ^1H NMR and ^{13}C NMR spectra of compounds **1**, 7-*d*-**1**, 8-*d*-**1**, **2**, **6**, and **8** can be found in the SI section of ref 17. This material is available free of charge via the Internet at http://pubs.acs.org.

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