JOC Article

Thermal Reactions of 8-Methylbicyclo[4.2.0]oct-2-enes: Competitive Diradical-Mediated [1,3] Sigmatropic, Stereomutation, and Fragmentation Processes

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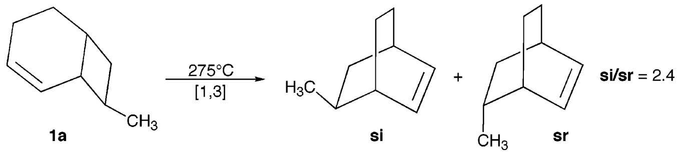

At 275 °C, 8-*exo*-methylbicyclo[4.2.0]oct-2-ene (**1a**) undergoes a [1,3] sigmatropic rearrangement to 5-methylbicyclo[2.2.2]oct-2-enes, of which the orbital symmetry-allowed *si* product is only marginally favored over the forbidden *sr* product; that is, *si*/*sr* is 2.4. Accompanying the [1,3] shift are significant amounts of epimerization and fragmentation. The 8-endo epimer **1b**, which yields no [1,3] product, experiences primarily direct fragmentation and secondarily epimerization. A diradical intermediate can account for all such observations.

Introduction

The vinylcyclobutane-to-cyclohexene rearrangement has been formally classified as a [1,3] sigmatropic rearrangement. For a vinylcyclobutane appropriately labeled at both the migrating carbon and migration terminus, four discrete [1,3] products exist: *si*, *sr*, *ai*, and *ar*, where *s* or *a* refer to suprafacial or antarafacial involvement of the π system and where *i* or *r*, inversion or retention, designate the stereochemical outcome with respect to the migrating carbon as it moves across the π system. According to the Woodward–Hoffmann selection rules,[1] the *si* and *ar* products are symmetry-allowed; *sr* and *ai*, symmetry-forbidden. Only *si* and *sr* products, however, are geometrically accessible in structurally constrained bicyclic vinylcyclobutanes. Thus, the *si*/*sr* ratio has been viewed as a measure of the degree of orbital symmetry control or concertedness of the [1,3] carbon migration of bicyclic vinylcyclobutanes.

While numerous experimental studies[2–7] of the [1,3] sigmatropic rearrangement of bicyclo[3.2.0]hept-2-enes have been conducted, there is only one prior literature reference to bicyclo[4.2.0]oct-2-ene thermal chemistry. In 1973, Berson and Holder reported[8] the results of a gas-phase thermal study of the 8-*exo*- and 8-*endo*-methyl epimers of 7-*endo*-acetoxy-8-methylbicyclo[4.2.0]oct-2-ene. Although Berson and Holder acknowledge a competing epimerization reaction, there is no mention of either retro-Diels–Alder reactions of the bicyclo[2.2.2]octenes or of Diels–Alder recombination reactions that are known to complicate the analysis of the analogous bicyclo[3.2.0] compounds.[2b] With respect to the significant issue of [1,3] stereochemistry, Berson and Holder cite an *sr*/*si* value of 0.45 (*si*/*sr* = 2.2) for the 8-*exo*-methyl epimer and *sr*/*si* of 12 (*si*/*sr* = 0.08) for the 8-*endo*-methyl epimer.

Experimental[9,10] and theoretical[11,12] reappraisals of the “not obviously concerted” vinylcyclobutane-to-cyclohexene

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[8] Berson, J. A.; Holder, R. W. *J. Am. Chem. Soc.* **1973**, *95*, 2037–2038.

[9] (a) Baldwin, J. E.; Burrell, R. C. *J. Am. Chem. Soc.* **2001**, *123*, 6718–6719. (b) Baldwin, J. E.; Burrell, R. C. *J. Am. Chem. Soc.* **2003**, *125*, 15869–15877.

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[11] (a) Carpenter, B. K. *J. Org. Chem.* **1992**, *57*, 4645–4648. (b) Carpenter, B. K. *J. Am. Chem. Soc.* **1995**, *117*, 6336–6344.

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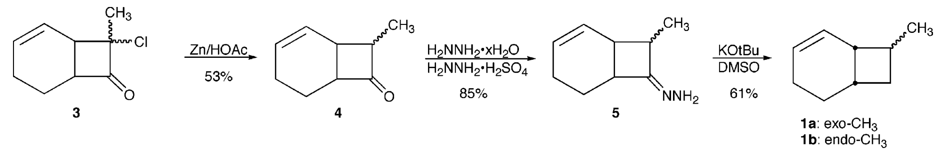
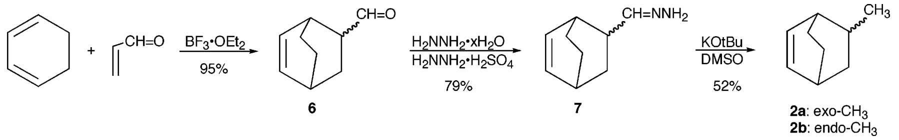
10.1021/jo051505g CCC: $30.25

SCHEME 1. Synthesis of 1



SCHEME 2. Synthesis of 2



rearrangement have proffered an alternative to a concerted orbital symmetry-controlled mechanism: a conformationally promiscuous diradical intermediate on a relatively flat potential energy surface. A review[13] of this recent work has led to several important postulates for bicyclic vinylcyclobutanes: (1) the *si*/*sr* ratio should correlate with the conformational flexibility of the π system, (2) a methyl substituent on the migrating carbon slows down the rate of rotation relative to a deuterium substituent in a short-lived diradical and thus results in a higher *si*/*sr* ratio, and (3) fragmentation and stereomutation will compete with [1,3] shifts in conformationally labile diradicals.

We wish to report herein the results of a thorough kinetic analysis of 8-*exo*-methylbicyclo[4.2.0]oct-2-ene (**1a**) and 8-*endo*-methylbicyclo[4.2.0]oct-2-ene (**1b**) and, as a corollary, to subject the aforementioned predictions to experimental verification. A direct comparison of the stereochemical and kinetic results with those of other methyl-labeled vinylcyclobutanes will also be made.

Results

Syntheses. A mixture of the 8-methyl epimers **1a** and **1b** was prepared by subjecting 8-methylbicyclo[4.2.0]oct-2-en-7-one[14] (**4**) to a two-step cyclobutanone reduction sequence[15] based on low-temperature Wolff−Kishner reduction of the hydrazone derivative **5**. Because the direct conversion of 1,3-cyclohexadiene and methylketene, generated by treatment of propionyl chloride with triethylamine, resulted in compound **4** in only 4−5% yield, we opted instead to initiate the synthesis of **1** from the 8-chloro-8-methylbicyclo[4.2.0]oct-2-en-7-one[14] (**3**) precursor (Scheme 1). As the latter ketene cycloaddition proceeded in 63% yield and the subsequent zinc reduction[16] in 53% yield, the overall yield of 33% for the two-step sequence was far superior to the one-step variation.

Because compounds **3** and **4** have been reported in the literature previously, only compound **1** was subjected to rigorous structure proof. Using preparative GC, **1a** was obtained free of **1b**. Base-catalyzed epimerization, which has been noted previously,[7] routinely occurs during the low-temperature Wolff−Kishner reaction sequence. Thus, the methyl ketone **4**, primarily endo, is converted to mostly 8-*exo*-methylbicyclo[4.2.0]oct-2-ene (**1a**), making the purification and isolation of **1b** from **1a** difficult. Thus, it was more convenient to acquire spectra of pure **1a** as well as of a mixture of **1a** and **1b**.

The synthesis of **2** (Scheme 2), as an epimeric mixture, is based on the application of the two-step low-temperature Wolff−Kishner reduction[15] to compound **6**, the Diels−Alder cycloadduct of 1,3-cyclohexadiene, and acrolein. The Lewis acid-catalyzed reaction, using either aluminum trichloride[17] or boron trifluoride,[18] proceeds in good to excellent yield, limited only by the gradual evaporative loss of acrolein during the course of the reaction. Spectral elucidation relies primarily on ^{13}C NMR values that closely match those reported in the literature.[19]

Differentiation between the 5-*exo*- (**2a**) and 5-*endo*-methylbicyclo[2.2.2]oct-2-ene (**2b**) epimers is based on ^{1}H and ^{13}C NMR characterization.[20−22] Although the *endo*-methyl hydrogens experience a typical shielding environment,[23] the ^{13}C NMR chemical shift for the *endo*-methyl in **2b** is 23.1 ppm compared to 20.5 ppm for the *exo*-methyl in **2a**.[21]

Thermolysis Reactions. Gas-phase thermal reactions of **1a**, **1b** (contaminated with 4−7% **1a**), and a mixture of **2a** and **2b** have been performed in a well-conditioned kinetic bulb[24] at 275.0 °C. As there was an ample amount of pure **1a**, obtained at greater than 99.5% purity by preparative GC, eight kinetic points between 0.5 and 24 h, corresponding to between 7 and 68% conversion, were determined. A representative capillary GC chromatogram for the thermal reaction of **1a** is shown in Figure 1. Given the facile epimerization of **1b** to **1a** and the relative dearth of **1b**, only four kinetic runs of 1, 2, 3, and 4 h were done over ca. 1 half-life for **1b**. The thermal behavior of **1a** was also monitored at a temper-

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[22] Grob, C. A.; Sawlewicz, P. *Helv. Chim. Acta* **1984**, *67*, 1859−1867.

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[24] Gajewski, J. J.; Chou, S. K. *J. Am. Chem. Soc.* **1977**, *99*, 5696−5707.

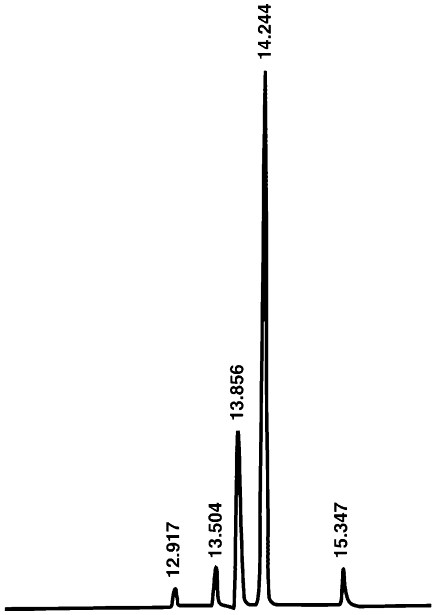


FIGURE 1. Capillary GC chromatogram for thermolysis of **1a** with elution order **2b**, **2a**, **1a**, internal standard (propylcyclohexane), and **1b**. (Chromatogram traced for clarity; see the Supporting Information for the original.)

TABLE 1. Rate Constants ($\times 10^5$ s) Derived Using Simplified Parallel First-Order Reactions Model

compd	T (°C)	$k_d{}^a$ (k'_d)^b	$k_{1,1}$ ($k'_{1,1}$)	$k_{1,3}$ (si)	$k_{1,3}$ (sr)	k_f (k'_f)
1a	275	1.25 ± 0.04	0.38	0.12	0.05	0.70
	300	8.0 ± 0.3	1.2	0.7	0.3	5.8
	315	20 ± 1	2.2	2.2	1.0	15
1b	275	4.1 ± 0.2	0.9			3.2

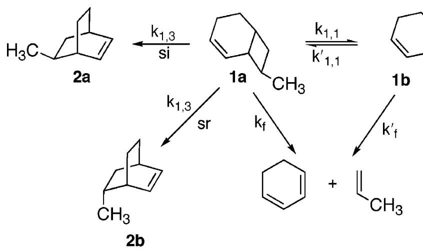
[a] Rate of overall decomposition of **1a**. [b] Rate of overall decomposition of **1b**.

ature of 300 °C to probe for any temperature dependence in the *si/sr* ratio and to follow the kinetics for 5 half-lives. Given the ca. 15 h half-life of **1a** at 275 °C, the higher temperature enabled us to examine **1a** more conveniently over an extended time frame. Thermal reactions of **1a** at 315 °C were also run at 1 h intervals for a total of 3 h to allow determination of Arrhenius parameters.

A prior report of the activation parameters for the retro-Diels–Alder reactions[25] of **2a** and **2b** has allowed us to predict that **2a** and **2b** are thermally inert at 275 °C. Nonetheless, we heated a mixture of **2a** and **2b** for intervals up to 24 h to show experimentally that the concentrations of **2a** and **2b** are invariant over 24 h at 275 °C.

The experimental first-order rate constants given in Table 1 correspond to thermal interconversions depicted in the kinetic scheme (Scheme 3). As shown in Scheme 3, **1a** and **1b** epimerize with each other. In addition, **1a** undergoes both [1,3] sigmatropic rearrangement to **2a** and **2b** and direct fragmentation to 1,3-cyclohexadiene and propene whereas **1b** experiences only direct fragmentation. All experimental first-order rate constants are given in Table 1 (k values refer to rate constants for **1a**; k' values refer to those for **1b**).

SCHEME 3. Kinetic Scheme[a]



[a] $k_{1,1}$ = rate of epimerization of **1a** to **1b**. $k'_{1,1}$ = rate of epimerization of **1b** to **1a**. $k_{1,3}$ = rate of [1,3] sigmatropic rearrangement of **1a** to **2a/2b**. k_f = rate of direct fragmentation of **1a** to 1,3-cyclohexadiene and propene. k'_f = rate of direct fragmentation of **1b** to 1,3-cyclohexadiene and propene.

TABLE 2. Rate Constants ($\times 10^5$ s) Derived Using Runge–Kutta Numerical Integration

compd	T (°C)	k_d (k'_d)	$k_{1,1}$ ($k'_{1,1}$)	$k_{1,3}$ (si + sr)	k_f (k'_f)
1a	275	1.5	0.7	0.2	0.6
	300	11.0	2.2	1.5	7.3
1b	275	4.3	1.0		3.3

Monitoring the disappearance of reactant **1a** or **1b** versus time has resulted in the rate constant for overall decomposition, k_d or k'_d, respectively. Approximate experimental values for $k_{1,1}$ (or $k'_{1,1}$), $k_{1,3}$, and k_f (or k'_f) have been obtained from the slopes of linear plots of product mole fraction versus $1 - e^{-k_d t}$. This simplified rate model proved satisfactory for obtaining accurate *si* (**1a** → **2a**) and *sr* (**1a** → **2b**) rate constants (Scheme 3). A Runge–Kutta four-step numerical integration[26] (calculated using an Excel spreadsheet) has afforded modestly different rate constants, as reported in Table 2, presumably yielding improved $k_{1,1}$ and $k'_{1,1}$ values.

Molecular Modeling. Molecular modeling (AM1) permitted an examination of the low energy conformers of the following series of compounds: vinylcyclobutane, bicyclo[3.2.0]hept-2-ene, and bicyclo[4.2.0]oct-2-ene. It is apparent that the second ring in bicyclo[3.2.0]hept-2-ene and bicyclo[4.2.0]oct-2-ene limits the distance between the migrating carbon, C7 and C8, respectively, and the migration terminus C3. The magnitude of this gap, not surprisingly, increases in the following order: 3.15 Å for the conformer of vinylcyclobutane that would afford an allylic diradical with cisoid stereochemistry, 3.38 Å for the single low-energy conformer of bicyclo[3.2.0]hept-2-ene, and 3.57 Å, the average distance (of 3.47 and 3.67 Å) for the two low-energy conformers of bicyclo[4.2.0]oct-2-ene. Whereas the cyclopentene ring in bicyclo[3.2.0]hept-2-ene is virtually planar, the cyclohexene ring in bicyclo[4.2.0]oct-2-ene is decidedly puckered, giving rise to two low energy conformers (see the Supporting Information). This conformational flexibility in the six-membered ring has the consequence of increasing the gap between the migrating carbon and the migration terminus.

Spartan ′04 calculations have also been performed on the compounds listed in Table 3, which provides a compilation of stereochemical results for a series of bicyclic and monocyclic vinylcyclobutanes. The only

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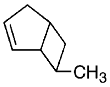
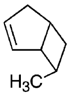
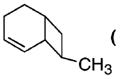
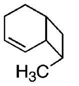
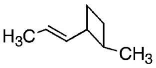
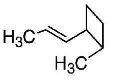
(25) Huybrechts, G.; Ngoy, G. *Int. J. Chem. Kinet.* **1975**, *7*, 775–784.

(26) Carpenter, B. K. *Determination of Organic Reaction Mechanisms*; Wiley: New York, 1984; pp 76–81.

TABLE 3. Stereochemistry of [1,3] Shifts in Vinylcyclobutanes

exo-CH_3	si(%)	sr(%)	si/sr	endo-CH_3	si(%)	sr(%)	si/sr	ref.
 **(8a)**	87	13	6.8	 **(8b)**	1	99	0.01	7
 **(1a)**	71	29	2.4	 **(1b)**	0	0	N/A	this work
	64	36	1.8		26	74	0.35	9a

significant difference, compared to the nonmethylated hydrocarbons, is that the average distance between the migrating carbon C8 and the migration terminus in compound **1a** is 3.49 Å, 0.11 Å greater than the 3.38 Å in **8a**.

TABLE 4. Kinetic Comparison[a] of 8-Methylbicyclo[4.2.0]oct-2-ene (1) and 7-Methylbicyclo[3.2.0]hept-2-ene (8), 275 °C

	exo-CH_3		*endo*-CH_3	
	1a	**8a**	**1b**	**8b**
k_d (×10^5 s)	1.5	1.5	4.3	1.0
$k_{1,3}$ (%)	15	94		40
$k_{1,1}$ (%)	47	5	23	38
k_f (%)	38	1	77	12
	$k_{1,1} > k_f > k_{1,3}$	$k_{1,3} \gg k_{1,1} > k_f$	$k_f > k_{1,1}$	$k_{1,3} \approx k_{1,1} > k_f$

[a] Based on Runge−Kutta rate constants.

Discussion and Conclusions

The crucial stereochemical probe resulting from this study, the *si/sr* ratio of **1a**, is robust because the retro-Diels−Alder reactions of **2a** and **2b** are 3 orders of magnitude slower than k_d and at least 200 times slower than $k_{1,3}$. This conclusion has been supported experimentally by showing that the concentrations of **2a** and **2b** are constant over a 24 h thermal investigation at 275 °C and by confirming invariant concentrations of **2a** and **2b** using a Runge−Kutta numerical analysis based on calculated retro-Diels−Alder rate constants (from literature activation parameters)[24] as inputs. An experimental *si/sr* ratio of 2.4 for **1a** has been determined at both 275 and 300 °C; the value of *si/sr* at 315 °C is 2.3. Thus, the *si/sr* value does not vary appreciably with temperature, a fact consistent with our prior observation[7] for 7-*exo*-methylbicyclo[3.2.0]hept-2-ene (**8a**).

The earlier prediction that the magnitude of the *si/sr* ratio correlates with the relative flexibility of the π system[13] is borne out by the cumulative results in Table 3. The *si/sr* ratio for **1a** is lower than that of **8a** by a factor of 3. More significantly, however, is the remarkable similarity in the *si/sr* ratio of 2.4 for **1a** and the *si/sr* value of 1.8 reported earlier by Baldwin and Burrell for a methyl-labeled monocyclic vinylcyclobutane (Table 3).

In the related study of 7-*endo*-acetoxy-8-*exo*-methylbicyclo[4.2.0]oct-2-ene, Berson reports a similar stereochemical ratio, *si/sr* = 2.2. Given that we have studied **1a** at three different temperatures, we have calculated Arrhenius parameters ($E_a = 44.3 \pm 1.5$ kcal/mol; $\log A = 12.8 \pm 0.6$) that are similar but not identical to those cited by Berson[27] for 7-*endo*-acetoxy-8-*exo*-methylbicyclo-[4.2.0]oct-2-ene: $E_a = 46.7$ kcal/mol; $\log A = 13.2$. In addition, we have determined Arrhenius parameters specifically for the **1a** → **2a** + **2b** transformation: $E_a = 46.3 \pm 1.9$ kcal/mol and $\log A = 12.7 \pm 0.7$, values close to those corresponding to the overall rate of disappearance of **1a**.

For 7-*endo*-acetoxy-8-*endo*-methylbicyclo[4.2.0]oct-2-ene Berson and Holder report[8] an *sr/si* value of 12 (*si/sr* = 0.08). Compound **1b**, the analogue without the *endo*-acetoxy substituent, yields no observable **2a** or **2b**. Conceivably, the small amount of [1,3] observed by Berson and Holder was derived from the 8-*exo*-methyl epimer formed by epimerization at C8. Alternatively, the steric effect caused by the 7-*endo*-acetoxy and 8-*endo*-methyl substituents could have favored a conformer in which the migrating carbon C8 might have positioned itself closer to the migration terminus.

The difference in the [1,3] rate constants for the *si* and *sr* pathways, the **1a** → **2a** or **1a** → **2b** conversions, respectively, translates to a calculated difference in transition state energy of less than 1 kcal/mol. This value is remarkably close to one calculated previously by Houk et al. for the energy difference between the *si* and *sr* transition states of bicyclo[3.2.0]hept-2-ene.[12b]

A kinetic comparison between **1a** and **8a** in Table 4 shows that the [1,3] shift, which was dominant for **8a**, only marginally competes with fragmentation and epimerization in **1a**. Molecular modeling of **1a** compared to **8a** provides a rationale for the diminished [1,3] contribution to the overall thermal manifold. The additional 0.1 Å gap between the migrating carbon and the migration terminus is apparently sufficient to advantage direct fragmentation and epimerization over the [1,3] shift. That such processes can indeed compete with the [1,3] sigmatropic rearrangement further strengthens the presupposition of an incipient diradical intermediate. There is no difference in the k_d values for **1a** and **8a**, merely a difference in the allocation of the various exit channels from their corresponding diradical intermediates. Regardless of how the resultant diradical intermediate distributes itself among the various products, both **1a** and **8a** produce diradicals with equivalent energy costs. This observation

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[27] Berson, J. A. *Acc. Chem. Res.* **1972**, *5*, 406−414.

TABLE 5. Kinetic Comparison[a] of 1a at 275° and 300 °C

	275 °C	300 °C
k_d ($\times 10^5$ s)	1.5	11.
$k_{1,3}$ (%)	15	14
$k_{1,1}$ (%)	47	20
k_f (%)	38	66
	$k_{1,1} > k_f > k_{1,3}$	$k_f > k_{1,1} > k_{1,3}$

[a] Based on Runge−Kutta rate constants.

is in agreement with the third prediction (vide supra) from the recent review[13] of vinylcyclobutane thermal chemistry.

The inward dynamic trajectory that both Carpenter[11b] and Houk[12] have predicted for bicyclo[3.2.0]hept-2-ene and its derivatives is favored in **1a** as well, if both [1,3] and [1,1] sigmatropic processes are linked to this motion. The increased separation between the migrating carbon and the migration terminus for the [1.3] rearrangement might well permit a greater extent of rotation before closure to the bicyclo[2.2.2] molecular framework, thus accounting for the lower *si*/*sr* ratio of **1a** compared to that of **8a** (Table 3). The inward trajectory, however, is completely ineffective for **1b** due to the extreme van der Waals repulsion between the *endo*-methyl substituent on the migrating carbon and either an *endo*-H on C4 or an *endo*-H on C5 (see the Supporting Information). By default, outward rotation of C8, the migrating carbon, during the bond-breaking event favors fragmentation over epimerization by a factor of 3 to 1. Fragmentation, which is virtually nonexistent in **8a** and only a minor contributor to the thermal profile of 7-*endo*-methylbicyclo[3.2.0]hept-2-ene (**8b**), is actually competitive with epimerization for **1a** and becomes the major thermal event for **1b**. As fragmentation becomes more prominent, there is correspondingly less [1,3] migration. The following $k_{1,3}/k_f$ ratios provide a compelling comparison between the thermal behavior of the corresponding bicyclo[3.2.0] and [4.2.0] compounds: **8a**, 150; **8b**, 3; **1a**, 0.4; **1b**, 0.

Doering has provided an apt characterization of “noninteractive singlet diradicals”[10b] with excited vibrational states accessible only when all residual bonding between the migrating carbon and the migration origin is destroyed by internal rotation. The consequence of this internal rotation is that “orbital overlap vanishes and with it rule by Woodward and Hoffmann.” Doering also enunciates “the principle of least rotational involvement” and its corollary, which is that a larger number of internal rotations for a given diradical species diminishes its contribution to the product distribution. The diradical species that forms from **1a** and closes to **2a** and **2b** exhibits only a modest selectivity toward **2a**, indicative of a greater propensity toward rotation. This also provides a strong rationale for the minor amount of **2a** and **2b**, the [1,3] migration products, in the thermal manifold of **1a** and the complete absence of **2a** and **2b** in the thermal profile of **1b**.

A comparison of Runge−Kutta rate constants for **1a** at 275 and 300 °C can be found in Table 5. For the resultant Runge−Kutta rate constants at 300 °C, there is greater uncertainty because compound **1b** has not been studied at 300 °C due to its limited quantity. The reported Runge−Kutta rate constants represent an average of three reasonable “fits” that do not differ substantially; that is, in all cases $k_f > k_{1,1} \geq k_{1,3}$. A Runge−Kutta numerical analysis has not been conducted on the thermal data for **1a** at 315 °C due to the limited number of data points.

Whereas the [1,3] contribution remains relatively constant at both 275 and 300 °C, an observation conceptually consistent with a nonstatistical[11b] diradical intermediate, the amount of fragmentation relative to epimerization increases directly with temperature. This phenomenon suggests that both epimerization and fragmentation might be linked to a statistical diradical intermediate that yields more fragmentation at higher temperature due to the greater entropic favorability of fragmentation over isomerization. If this is indeed the case, one might conclude that **1b**, given the complete absence of **2a** and **2b** at 275 °C, cannot generate a nonstatistical diradical intermediate as a consequence of the extreme steric crowding caused by the *endo*-methyl substituent.

Of the three postulates formulated in an *Accounts of Chemical Research* review paper on the vinylcyclobutane-to-cyclohexene rearrangement,[13] two are unambiguously supported by the results of the current study. The low *si*/*sr* ratio of 2.4 for **1a** is consistent with a model of a conformationally flexible bicyclic vinylcyclobutane. As shown dramatically in Table 3, the *si*/*sr* ratio for **1a** is closer to that of the corresponding monocyclic vinylcyclobutane than it is to that of the bicyclic vinylcyclobutane **8a**. The dominance of epimerization and fragmentation in the thermal reactions accessible to **1a** and the exclusive presence of these two processes for **1b** confirm the prediction that the presence of stereomutation and fragmentation implicates a diradical process. What remains to be tested is the assumption of a lower *si*/*sr* ratio when the migrating carbon is labeled with a deuterium in lieu of a methyl, which due to its greater size is expected to slow the rate of rotation in the incipient diradical. The results of our investigation of 8-d$_1$-bicyclo-[4.2.0]oct-2-ene are forthcoming.

Experimental Section

Detailed general experimental procedures can be found in ref 7.

8-Chloro-8-methylbicyclo[4.2.0]oct-2-en-7-one (3). To a solution of 50 mL of 1,3-cyclohexadiene (0.52 mol) and 31 mL of 2-chloropropionyl chloride (0.32 mol) in 75 mL of chloroform was added a solution of 35 mL of triethylamine (0.25 mol) in 25 mL of chloroform dropwise over ca. 6 h. The reaction was then stirred overnight at room temperature. After removal of the chloroform via simple distillation and the triethylamine hydrochloride by vacuum filtration, the filtrate was washed successively with water and brine and dried over $MgSO_4$. Vacuum distillation afforded 26.9 g (63%) of compound **3** as an isomeric mixture (54:46 ratio by GC), which was isolated as a viscous oil: IR (cm^{-1}) 3010 (w), 1780 (s), 710 (m), 700 (m); MS (*m/z*) 172 (M + 2, 2), 170 (M, 6), 135 (14), 80 (38), 79 (54), 55 (100).

8-Methylbicyclo[4.2.0]oct-2-en-7-one (4). To a mixture of 11.6 g (177 mmol) of zinc dust in 23.5 mL (151 mmol) of TMEDA and 59 mL of absolute ethanol was added 12 mL (0.21 mol) of glacial acetic acid over ca. 10 min. After addition of a solution of 5.55 g (32.5 mmol) of compound **3** in 13 mL of acetic acid over ca. 10 min, the reaction mixture was warmed to 40 °C and stirred overnight. Exercising care to minimize exposure of the activated zinc to air, the mixture was first filtered through a sintered-glass funnel, and the zinc residue was then washed with water to deactivate the zinc. The filtrate was washed successively with 1 N HCl, $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated under reduced pressure to afford 2.36 g (53%) of compound **4**, 88% endo by GC. IR (cm^{-1}) 3020 (w), 1780 (s), 1640 (w), 700 (m). The exo- and endo-epimers were separated by flash chromatography on silica gel by elution with 95:5 pentane/ether. 8-*exo*-Methylbicyclo[4.2.0]-oct-2-en-7-one (**4a** as a mixture with **4b**): MS (*m/z*) 136 (10), 107 (100), 91 (78), 79 (87), 77 (48); ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.0, 128.2, 128.0, 60.3, 54.2, 31.5, 21.4, 20.0, 14.6 (*exo*-CH_3). 8-*endo*-Methylbicyclo-[4.2.0]oct-2-en-7-one (**4b**): MS (*m/z*) 136 (42), 107 (59), 91 (100), 79 (100), 77 (77). ^1H NMR (300 MHz, $CDCl_3$) δ 5.94 (m, 1H), 5.75 (m, 1H), 3.59 (br m, 1H), 3.41 (ddq, 1H), 3.00 (br m, 1H), 1.98 (m, 3H), 1.50 (m, 1H), 1.00 (d, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 130.1, 125.5, 55.4, 55.2, 27.6, 21.3, 18.5, 8.8 (*endo*-CH_3).

Using the same methodology as in the preparation of **3** but substituting 26 mL (0.30 mol) of propionyl chloride for 2-chloropropionyl chloride resulted in only 1.7 g (5%) of compound **4**, 97% endo by GC.

8-Methylbicyclo[4.2.0]oct-2-en-7-one Hydrazone (5). To a solution of 2.4 g (18 mmol) of hydrazine sulfate in 7.0 mL of hydrazine hydrate was added 1.2 g (8.9 mmol) of compound **4**. After the reaction mixture was heated overnight at 65 °C, it was extracted three times with ether, washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Compound **5** (1.16 g, 85%) was used without further purification: IR (cm^{-1}) 3370 and 3260 (m, NH_2), 3020 (w), 1610 (m, C=N), 720 (s).

8-Methylbicyclo[4.2.0]oct-2-ene (1). To a solution of 2.21 g (19.7 mmol) of potassium *tert*-butoxide in 25 mL of anhydrous DMSO was added a solution of 1.16 g (7.6 mmol) of compound **5** via syringe over 4–5 h. After being stirred overnight, the reaction mixture was quenched with water and extracted with pentane. The organic extract was then washed seven times with water, dried over $MgSO_4$, and concentrated by simple distillation. The crude product (0.57 g, 61%) consisted of a 93:7 (as determined by GC) mixture of **1a**/**1b**, respectively: IR (cm^{-1}) 3015 (w), 700 (s). 8-*exo*-methylbicyclo[4.2.0]oct-2-ene (**1a**): MS (*m/z*) 122 (1), 81 (9), 80 (100), 79 (58), 77 (14). ^1H NMR (500 MHz, $CDCl_3$) δ 5.75 (d, 2H), 2.50 (sextet, 1H), 2.20 (br t, 1H), 2.01 (dt, 2H), 1.93 (m, 1H), 1.82 (m, 1H), 1.59 (m, 1H), 1.53 (M, 2H), 1.12 (d, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.1 (HC=), 126.8 (HC=), 40.4 (HC), 36.8 (HC), 30.5 (H_2C), 28.9 (HC), 25.3 (H_2C), 22.1 (H_2C), 21.3 (H_3C). 8-*endo*-methylbicyclo[4.2.0]oct-2-ene (**1b**): MS (*m/z*) 122 (0.5), 81 (9), 80 (100%), 79 (54), 77 (12); ^1H NMR (300 MHz, $CDCl_3$) δ 5.90 (m, 1H), 5. 66 (br d, 1H), 0.84 (d, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.4, 127.8, 36.3, 33.6, 29.9, 29.6, 22.6, 21.2, 16.7 (H_3C).

Bicyclo[2.2.2]oct-5-ene-2-carboxaldehyde (6). To a solution of 14.5 mL (120 mmol) of 1,3-cyclohexadiene in 100 mL of toluene was added 1.66 mL (12.6 mmol) of anhydrous $AlCl_3$ followed by a solution of 1.67 mL (90% Aldrich, 22.5 mmol) of acrolein in 100 mL of toluene. After being stirred at 40 °C for 2 days, an additional increment of 1.67 mL of acrolein was added. The next day, the cooled reaction mixture was poured into ice–water. The aqueous layer was then extracted with ether, which was washed with $NaHCO_3$ and dried over Na_2SO_4. Distillation of the volatiles resulted in 3.7 g (60%) of crude **6**, which was used without further purification.

Alternatively, to a solution of 5.5 mL (90%, 74 mmol) of acrolein, 15.0 mL (97%, 153 mmol) of cyclohexadiene, and 82.0 mL of anhydrous ether was added by syringe over a period of 10 min 4.0 mL (32 mmol) of boron trifluoride diethyl etherate. After being stirred overnight, the reaction mixture was quenched with water and then extracted three times with ether, washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to afford 9.4 g (95%) of crude **6**, 80:20 endo/exo by GC analysis. Spectral characterization was performed on a sample consisting of a mixture of isomers that was subjected to chromatographic purification by elution from silica gel with 90:10 hexane/ethyl acetate: IR (cm^{-1}) 3040 (w), 1725 (s), 700 (s). Bicyclo[2.2.2]oct-5-en-2-*endo*-carboxaldehyde (major epimer): MS (*m/z*) 136 (12), 108 (14), 80 (53), 79 (100); ^1H NMR (500 MHz, $CDCl_3$) δ 9.43 (d, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.2, 136.3, 130.8, 51.1, 30.9, 29.4, 26.9, 25.3, 24.9. Bicyclo[2.2.2]oct-5-en-2-*exo*-carboxaldehyde (minor epimer): MS (*m/z*) 136 (1), 80 (52), 79 (100), 58 (55). ^1H NMR (500 MHz, $CDCl_3$) δ 9.74 (d, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.6, 135.8, 133.6, 50.4, 30.5, 29.7, 25.5, 25.0, 21.3.

Bicyclo[2.2.2]oct-5-ene-2-carboxaldehyde Hydrazone (7). To a solution of 6.5 g (44 mmol) of hydrazine sulfate in 12 mL of hydrazine hydrate was added 3.6 g (26 mmol) of compound **6**. After the reaction mixture was heated overnight at 65 °C, it was extracted three times with ether, washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Compound **7** (3.14 g, 79%) was used without further purification: IR (cm^{-1}) 3370 and 3200 (m, NH_2), 3020 (w), 1630 (m, C=N), 700 (s).

5-Methylbicyclo[2.2.2]oct-2-ene (2). To a solution of 2.6 g (24 mmol) of potassium *tert*-butoxide in 15 mL of anhydrous DMSO was added a solution of 3.1 g (21 mmol) of compound **7** in 5 mL of anhydrous DMSO via syringe over 5 h. After being stirred overnight, the reaction mixture was quenched with water and extracted with pentane. The organic extract was then washed seven times with water, dried over $MgSO_4$, and concentrated by simple distillation to afford 1.3 g (52%) of compound **2**, which consisted of a 23:77 mixture of **2a**/**2b**, respectively. 5-*exo*-methylbicyclo[2.2.2]oct-2-ene (**2a**): MS (*m/z*) 122 (7), 80 (100), 79 (46); ^1H NMR (300 MHz, $CDCl_3$) δ 6.4 (t, 1H), 6.2 (t, 1H), 2.4 (br s, 1H), 2.2 (br s, 1H), 1.8 (m, 1H), 1.5 (m, 2H), 1.4 (m, 1H), 1.2 (m, 1H), 1.1 (m, 1H), 1.0 (d, 3H), 0.9 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.6, 133.1, 35.6, 34.8, 30.6, 30.3, 26.2, 20.5 (CH_3), 18.8. 5-*endo*-Methylbicyclo-[2.2.2]oct-2-ene (**2b**): MS (*m/z*) 122 (7), 80 (100), 79 (43). ^1H NMR (300 MHz, $CDCl_3$) δ 6.2 (t, 1H), 6.1 (t, 1H), 2.4 (br s, 1H), 2.2 (br s, 1H), 1.7 (m, 2H), 1.5 (m, 1H), 1.4 (m, 1H), 1.2 (m, 2H), 0.8 (d, 3H), 0.7 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.2, 132.2, 36.5, 35.8, 32.1, 30.3, 26.5, 24.2, 23.1 (CH_3).

Gas-Phase Reactions. Thermal reactions were conducted in a previously described apparatus.[7] 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 0.6 °C/min to a maximum temperature of 100 °C. Retention times (min) were as follows: **2b** (12.92), **2a** (13.50), **1a** (13.86), the internal standard propylcyclohexane (14.24), **1b** (15.35), as in Figure 1. Concentrations of fragments 1,3-cyclohexadiene and propene were determined by difference compared to a time zero sample for each kinetic run.

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Supporting Information Available: Copies of first-order kinetic rate plots for **1a** and **1b**; NMR spectra for **1a** and **1b**; tables of mole fractions for thermal runs of **1a**, **1b**, and a mixture of **2a** and **2b**; low energy conformations for **1a** and **1b** generated from Spartan ′04 for Macintosh. This material is available free of charge via the Internet at http://pubs.acs.org.

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