Communications to the Editor

New Thermal Reactions of Deuterium-Labeled Bicyclo[3.2.0]hept-2-enes: Bicyclic Skeletal Inversion and Epimerization at C7

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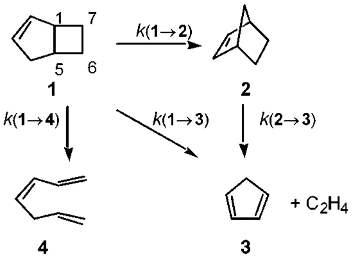
Bicyclo[3.2.0]hept-2-ene (**1**) is thermally converted to bicyclo-[2.2.1]hept-2-ene (**2**), ethylene and cyclopentadiene (**3**), and hepta-1,3(*Z*),6-heptatriene (**4**) through direct, first-order reactions (Scheme 1).(1) The rate constant for decomposition, k_{d}, is equal to $(k(\mathbf{1} \rightarrow \mathbf{2}) + k(\mathbf{1} \rightarrow \mathbf{3}) + k(\mathbf{1} \rightarrow \mathbf{4}))$. Other secondary products evolve with time.

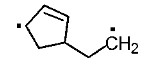
Scheme 1



1 **2** **4** **3**

The stereochemistry of the 1,3-carbon sigmatropic shift converting **1** to bicyclo[2.2.1]hept-2-ene (**2**) has received close attention from two groups.[2,3] Even though the facile retro-Diels−Alder reaction of **2** dictates that its maximum relative concentration during a thermal reaction starting with **1** is less than 2 mol %,[1−4] it has nevertheless been possible to estimate values for rate constants corresponding to migration of C7 with inversion (rate constant k_{i}) and with retention of configuration (k_{r}) by studying deuterium-labeled analogues of **1**. One investigation led to $k_{\mathrm{i}} = (76 \pm 4)\%$ of $(k_{\mathrm{r}} + k_{\mathrm{i}})$ at 276 °C,[2] while the second found $k_{\mathrm{i}} = 89\%$ of $(k_{\mathrm{r}} + k_{\mathrm{i}})$ at 312 °C.[3] Thus, both studies uncovered an appreciable k_{r} component while confirming the dominant k_{i} process for the parent bicyclo[3.2.0]hept-2-ene system.

A detailed theoretical consideration of the isomerization of **1** to **2** and the reaction dynamics of the putative 2-(2-cyclopentene-4-yl)ethyl diradical (**5**) led Carpenter to view the 1,3-carbon shift as a process favoring migration with inversion thanks to dynamic factors, with the conservation of orbital symmetry playing no role.[5] The unusual apparent temperature dependence for reaction stereochemistry was tentatively rationalized as a "bleeding off" of an extended-conformation of diradical **5** to **3** plus ethylene at higher temperatures, thus reducing its contribution to the k_{r} process.



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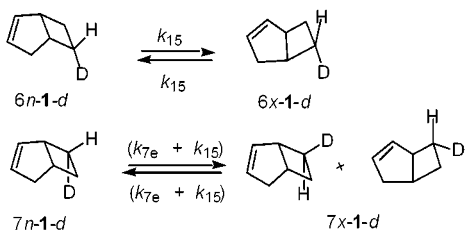
A long-term interest in the thermal chemistry of **1** and more substituted analogues of **1**,[6] and in the fundamental conceptual issues posed by the behavior of reactants having access to numerous kinetically competitive paths leading to alternative products,[7] prompted the present experimental study. It addressed two specific modes of reaction previously unobserved in **1**: a two-centered epimerization at C1 and C5, an automerization process inverting the bicyclic ring system, and a one-centered thermal epimerization at C7. Both thermal stereomutations were considered plausible, although prior work concluded that neither competes with the 1,3 shift to a significant extent.[2,3] These hypothetical stereomutations have now been pursued experimentally, in earnest, using substrates designed and prepared for this specific quest.

Reductions of 6-*d*- and 7-*d*-bicyclo[3.2.0]hepta-2,6-diene[8] with diimide generated in situ by treating anhydrous hydrazine with 30% hydrogen peroxide at −20 °C[9] gave 6-*d*- and 7-*d*-bicyclo-[3.2.0]hept-2-ene, 6*n*-**1**-*d* and 7*n*-**1**-*d.* The bicycloheptene-to-bicycloheptane ratios realized were 7.4:1 and 7.9:1. The labeled bicycloheptenes 6*n*-**1**-*d* and 7*n*-**1**-*d* were isolated and purified by preparative GC, and the endo:exo ratios were determined by ^{2}H NMR at 92.124 MHz: 6*n*-**1**-*d* (δ 1.67):6*x*-**1**-*d* (δ 2.17) = 9.97:1 and 7*n*-**1**-*d* (δ 1.68):7*x*-**1**-*d* (δ 2.32) = 9.12:1.[10]

These samples were heated in the gas phase with nitrogen as bath gas at 275 °C for various periods up to 60 h. Analyses of thermal product mixtures by ^{2}H NMR provided measures of progress toward equilibration of endo and exo epimers. For the 6-**1**-*d* epimers, the equilibration was extremely slow but clearly detectable: the one-way rate constant *k*(6*n*-**1**-*d* to 6*x*-**1**-*d*) was estimated to be $3.6 \times 10^{-8}\,\mathrm{s}^{-1}$. For the 7-**1**-*d* epimers, the equilibration was appreciably faster: *k*(7*n*-**1**-*d* to 7*x*-**1**-*d*) was found to be $5.35 \times 10^{-7}\,\mathrm{s}^{-1}$. Both first-order rate constants were based on five relative mol % versus time kinetic points. Figure 1 illustrates the analytic method and exhibits the clear progress toward equilibration of 7-**1**-*d* epimers; the standard deviation between calculated and observed 7*n*-**1**-*d* values compared with (7*n*-**1**-*d* + 7*x*-**1**-*d*) = 100% was 0.73%.

The very small *k*(6*n*-**1**-*d* to 6*x*-**1**-*d*) rate constant is taken as a measure of ring inversion, or C1,C5 two-center epimerization with rate constant k_{15} (Scheme 2); *k*(7*n*-**1**-*d* to 7*x*-**1**-*d*) = k_{ep} is taken as a measure of ring inversion plus direct one-center epimerization at C7; $k_{\mathrm{ep}} = (k_{15} + k_{7\mathrm{e}})$. Thus, $k_{7\mathrm{e}}$ is estimated to be $5 \times 10^{-7}\,\mathrm{s}^{-1}$ at 275 °C, much smaller than the rate constants $k_{\mathrm{d}} = 8.2 \times 10^{-6}\,\mathrm{s}^{-1}$

Scheme 2



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(1) (a) Frey, H. M.; Cocks, A. T. *J. Chem. Soc. A* **1971**, 2564−2566. (b) Walsh, R.; Wells, J. M. *J. Chem. Soc. Perkin Trans. 2* **1976**, 52−55.

(2) Baldwin, J. E.; Belfield, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 296−297.

(3) Klärner, F.-G.; Drewes, R.; Hasselmann, D. *J. Am. Chem. Soc.* **1988**, *110*, 297−298.

(4) Baldwin, J. E.; Belfield, K. D. *J. Phys. Org. Chem.* **1989**, *2*, 455−466.

(5) Carpenter, B. K. *J. Am. Chem. Soc.* **1995**, *117*, 6336−6344.

(6) (a) Bender, J. D.; Leber, P. A.; Lirio, R. R.; Smith, R. S. *J. Org. Chem.* **2000**, *65*, 5396−5402. (b) Baldwin, J. E.; Leber, P. A. *Tetrahedron Lett.* **2000**, *42*, 195−197.

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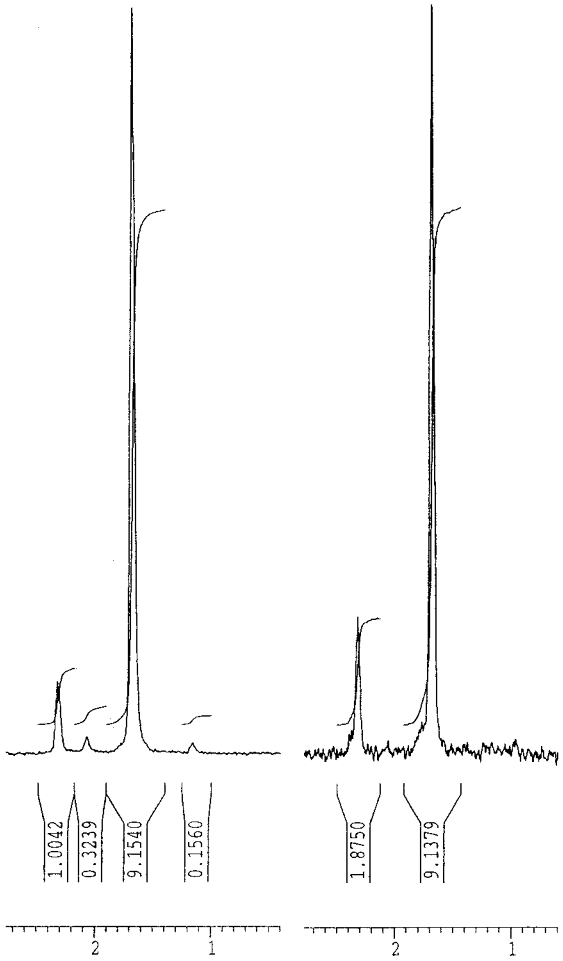
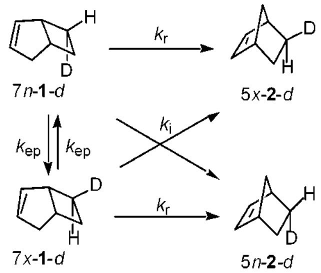


Figure 1. Deuterium NMR spectra for mixtures of 7*x*-**1**-*d* (δ 2.32) and 7*n*-**1**-*d* (δ 1.68): at left, at thermal reaction time 0, in proportions 9.9:90.1; at right, after 40 h at 275 °C, a 17.0:83 mixture.

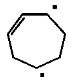
and $k_{1,3} \approx 5.5 \times 10^{-6}$s^{-1} measured at 276 °C,[4] but still quite detectable through the deuterium NMR analytical method employed.

The slow epimerization at C7 (Scheme 3) contributes very little to the overall perceived reaction stereochemistry for the 1,3-carbon shifts over reaction times comparable to those giving maximal relative concentrations of (5*x*-**2**-*d* + 5*n*-**2**-*d*). The appropriate factor to account for the equilibration of 7*n*-**1**-*d* with 7*x*-**1**-*d* (Scheme 3) is $k_d(1 - \exp(-(2k_{ep} + k_d)t))/(2k_{ep} + k_d)(1 - \exp(-k_dt))$, which differs only modestly from unity at t_{max}. At longer times, neglect of this factor would tend to exaggerate the relative importance of the k_r component based on observed ratios of 5-**2**-*d* epimers only slightly. The temperature dependence of k_i:k_r reported earlier[2,3] remains, awaiting careful experimental scrutiny and detailed theory-based explication.

Scheme 3



The ring-inversion process presumably involves a 1-cycloheptene-3,6-diyl diradical (**6**)[11] conformationally suited for achieving the noted reaction. Other conformational versions of **6** may mediate formation of hepta-1,3(*Z*),6-heptatriene (**4**).[12] The slow skeletal inversion process shown by bicyclo[3.2.0hept-2-ene parallels the thermal ring inversion reaction long known for bicyclo[3.1.0]hex-2-enes.[13]



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The thermal epimerization at C7 now observed provides additional support for the diradical-based formulation of the isomerization of **1** to **2** and to the suggested explanation for the temperature-dependent reaction stereochemistry found for this process.[5] Extending the quasi-classical dynamics simulations to include rotations within and reclosures of **5** to both **1** and **2**, and cleavage of **5** to yield cyclopentadiene and ethylene, may be extremely illuminating.

Uncovering the thermal isomerizations interconverting 6*n*-**1**-*d* with 6*x*-**1**-*d* and 7*n*-**1**-*d* to 7*x*-**1**-*d* clarifies the many-faceted reactivity of bicyclo[3.2.0]hept-2-ene (**1**) and may contribute to the serious theoretical efforts being expended to understand these complexities in detail.[5,14] This bicyclic olefin is now revealed to behave much like other vinylcyclobutanes, with one-center and two-center thermal stereomutations occurring at rates comparable to 1,3-carbon shifts.[7b]

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(7) Inter alia, (a) Lewis, D. K.; Glenar, D. A.; Hughes, S.; Kalra, B. L.; Schlier, J.; Shukla, R.; Baldwin, J. E. *J. Am. Chem. Soc.* **2001**, *123*, 996−997. (b) Baldwin, J. E.; Burrell, R. C. *J. Am. Chem. Soc*. **2001**, *123*, 6718−6719.

(8) Baldwin, J. E.; Belfield, K. D. *J. Org. Chem.* **1987**, *52*, 4772−4776.

(9) Mori, K.; Ohti, M.; Sato, A.; Matsui, M. *Tetrahedron* **1972**, *28*, 3739−3745.

(10) Compare the NMR chemical shift assignments provided by Leigh, W. J.; Srinivasan, R. *J. Org. Chem.* **1983**, *48*, 3970−3979.

(11) Uyehara, T.; Takahashi, M.; Kato, T. *Tetrahedron Lett.* **1985**, *26*, 1241−1244.

(12) Doubleday, C. *J. Phys. Chem.* **1996**, *100*, 15083−15086.

(13) (a) Doering, W. von E.; Roth, W. R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 115−122. (b) Doering, W. von E.; Schmidt, K. *Tetrahedron* **1971**, *27*, 2005−2030. (c) Cooke, R. S.; Andrews, U. H. *J. Am. Chem. Soc.* **1974**, *96*, 2974−2980.

(14) Inter alia: (a) Gavezzotti, A.; Simonetta, M. *Tetrahedron* **1975**, *31*, 1611−1617. (b) Fernandez, A. *J. Chem. Phys.* **1985**, *82*, 3123−3126. (c) Carpenter, B. K. *J. Am. Chem. Soc.* **1996**, *118*, 10329−10330. (d) Beno, B. R.; Wilsey, S.; Houk, K. N. *J. Am. Chem. Soc.* **1999**, *121*, 4816−4826. (e) Wilsey, S.; Houk, K. N.; Zewail, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 5772−5786.