

## Activation Parameters for Three Reactions Interconverting Isomeric 4- and 6-Deuteriobicyclo[3.1.0]hex-2-enes

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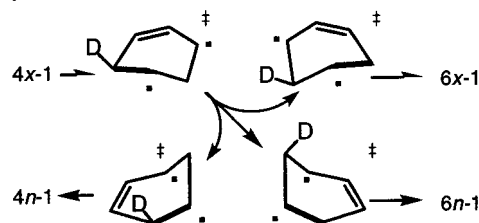
The thermal equilibration of 4,4-*d*<sub>2</sub>- and 6,6-*d*<sub>2</sub>-bicyclo[3.1.0]-hex-2-enes uncovered by Doering and Grimme<sup>1</sup> has been extended through in-depth studies of similar isomerizations in deuterium-labeled and non-racemic 2-methyl-5-isopropylbicyclo[3.1.0]hex-2-enes ( $\Delta^3$ -thujenes)<sup>2,3</sup> and bicyclo[3.1.0]hex-2-enes.<sup>4</sup> These classic investigations identified three different paths leading to distinct degenerate products. The equilibrations take place through [1,3]-carbon shifts with *retention, suprafacial* and *inversion, antarafacial* stereochemistry and a two-centered epimerization resulting in enantiomerization of the bicyclic skeleton—a “ring-flip” process. Rate constants for these paths are here designated as  $k_r$ ,  $k_i$ , and  $k_f$ .

These stereochemical and kinetic results also afforded clear mechanistic insights, as outlined by Doering and Schmidt.<sup>3</sup> A reactant suffers cleavage of the C1–C5 bond to form an intermediate diradical, having independent allylic and unconjugated radical entities. The product distribution is dictated by competitive conformational changes experienced by the diradical prior to its demise as it finds an exit channel. The incremental barrier separating the most important conformational forms of the diradical derived from  $\Delta^3$ -thujene is small, some 1.2 kcal/mol.

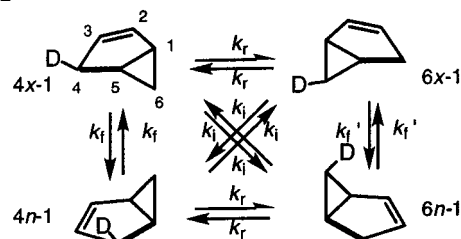
Cooke and Andrews in 1974<sup>4</sup> reported that the gas-phase isomerizations of 2,4-*exo-d*<sub>2</sub>-bicyclo[3.1.0]hex-2-ene at 318 °C take place with  $k_r > k_f > k_i$  in about 51:38:11 proportions. Since that work the degenerate isomerizations of bicyclo[3.1.0]hex-2-enes have been neglected, both experimentally and theoretically, even as substantial progress toward understanding vinylcyclopropane-to-cyclopentene isomerizations has been made.<sup>5–7</sup> Were those understandings directly applicable to the isomerizations of bicyclo[3.1.0]hex-2-enes, one would picture the reactions as involving first C1–C5 bond cleavage; the transition structure would presumably have *C*<sub>1</sub> symmetry (but for one or more isotopic labels). Dynamic control would lead the diradical formed directly or in part indirectly to three exits from a relatively broad, flat potential energy surface, each transition structure being isometric and isoenergetic with the entry structure (Scheme 1). The four transition structures linking conformationally evolving short-lived diradicals with one entry and three different exit channels, or one isomer with three other stereoisomeric products, would not be in thermal equilibrium, and transition-state theory would not be relevant. Dynamic factors rather than the detailed topography of small dips and ridges on that surface would dictate stereochemical outcomes and rate-constant proportions.

The potential importance of this degenerate isomerization for emerging understandings of entropy control or dynamic control in diradical-mediated reactions<sup>7–9</sup> and for the conceptual issues associated with transition regions having convex surfaces or “caldera” characteristics<sup>10</sup> prompted the present kinetic work to define activation parameters for the  $k_r$ ,  $k_f$ , and  $k_i$  processes in the parent system. Secondary objectives included testing for a kineti-

Scheme 1



Scheme 2



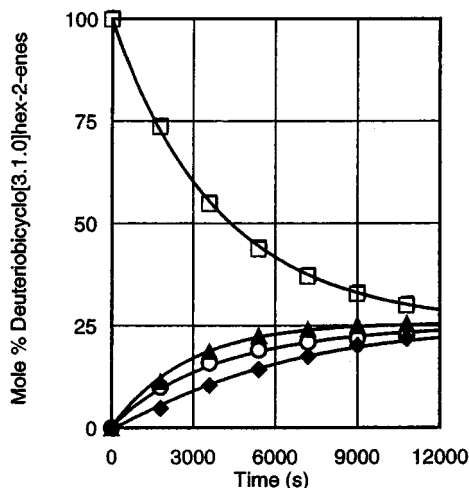
cally competitive one-center epimerization at C6 (through a reversible cleavage of C1–C6;  $k_{6c}$ )<sup>11</sup> and for possible deuterium isotope effect on rate constants. Quasi-classical direct dynamics calculations on the diradical structures involved in vinylcyclopropane rearrangements have revealed that diradical isotopomers may have somewhat different dynamical properties and partition to distinct products in significantly different proportions;<sup>7</sup> might the same novel effect be found experimentally for the degenerate isomerizations of deuterium-labeled bicyclo[3.1.0]hex-2-enes?

These objectives were pursued through preparations of 4-*exo*- and 6-*exo-d*-bicyclo[3.1.0]hex-2-enes (4x-1 and 6x-1) and kinetic studies of the thermal isomerizations they exhibit. The synthesis of 4x-1-*d* was completed through a highly stereoselective reduction of bicyclo[3.1.0]hex-3-en-2-one<sup>12</sup> from the *exo* face of the molecule (LiAlD<sub>4</sub>, CuI, THF, HMPA, –78 °C)<sup>13</sup> followed by a ketone-to-olefin functional group transformation<sup>14</sup> and purification by preparative GC. According to <sup>1</sup>H NMR spectral comparisons with unlabeled bicyclo[3.1.0]hex-2-ene, the 4x-1 secured was free of the 4*n* isomer and of any significant *d*<sub>0</sub>-component. The 6x-1 starting material was obtained through a longer route, involving 5-(*E*)-*d*-pent-4-enoic acid, the related  $\alpha$ -diazo ketone, and 6-*exo-d*-bicyclo[3.1.0]hexan-2-one as significant intermediates.<sup>15</sup> The GC-purified hydrocarbon was estimated to be about 4% *d*<sub>0</sub>; the labeled substrate was about 97:3 6*x*:6*n* according to <sup>1</sup>H and <sup>2</sup>H NMR analyses.

Gas-phase kinetic runs starting with 4x-1 at 224.9, 240.1, and 255.0 °C gave concentration-versus-time profiles for the four isomers that could be modeled well by applying Scheme 2, with  $k_f = k_f'$ . Each of the four mol % functions at any temperature, according to that kinetic scheme, is equal to  $25(1 \pm \exp(-\lambda_1 t) \pm \exp(-\lambda_2 t) \pm \exp(-\lambda_3 t))$ ; the  $\pm$  coefficients are known and the  $\lambda_i$  constants may be found by fitting data using least-squares calcula-

**Table 1.** Thermal Isomerizations of 4-*exo-d*-Bicyclo[3.1.0]hex-2-ene Modeled Using Kinetic Scheme 2<sup>a</sup>

T (°C)	(k <sub>r</sub> + k <sub>i</sub> )	(k <sub>i</sub> + k <sub>e</sub> )	(k <sub>r</sub> + k <sub>e</sub> )	k <sub>r</sub>	k <sub>i</sub>	k <sub>e</sub>
224.9	0.96	1.26	0.78	0.72	0.54	0.24
240.1	3.6	4.5	2.8	2.7	1.9	0.9
255.0	12.3	16.2	10.2	9.10	7.05	3.15

<sup>a</sup> Rate constants × 10<sup>5</sup> s.**Figure 1.** Concentration-versus-time profiles for thermal reaction mixtures derived from 4*x*-1 at 255.0 °C. The isomers are labeled 4*x*-1(□), 4*n*-1(○), 6*x*-1(▲), and 6*n*-1(◆).

tions to single exponential decays. For example: mol % values for [4*n*-1 + 6*x*-1] isomers at any time are equal to 50(1 - exp(-λ<sub>2</sub>t)). From the three λ<sub>i</sub> values the three rate constants may be calculated, for λ<sub>1</sub> = 2(k<sub>r</sub> + k<sub>i</sub>), λ<sub>2</sub> = 2(k<sub>r</sub> + k<sub>e</sub>), and λ<sub>3</sub> = 2(k<sub>i</sub> + k<sub>e</sub>). The results obtained are summarized in Table 1.

The analytical method used for estimating the mol % values was <sup>1</sup>H NMR at 300 MHz. The four protons at C4 and C6 have well separated chemical shifts<sup>16</sup> and T<sub>1</sub> relaxation times shorter than 5 s; 30 s delays between pulses were employed.

The early runs were conducted at 240 °C; the later product mixtures from reactions at 225 and 255 °C with careful spin calibrations provided more precise data. The quality of the match between data and kinetic modeling may be judged from Figure 1 for 255.0 °C runs from 4*x*-1. The rms error between observed and calculated mol % values over the 24 data points was 0.46%. For the three sets of data, the rms error over 72 points was 0.56%. Arrhenius plots indicated little change in calculated rate-constant ratios with temperature: the k<sub>r</sub>:k<sub>i</sub>:k<sub>e</sub> proportions were about 48:36:16, similar to the proportions reported by Cooke and Andrews.<sup>4</sup> The calculated activation parameters were E<sub>a</sub> 43.8, 44.3, 44.8 kcal/mol and log A 14.1, 14.2, 14.1, respectively, essentially identical values, differing by less than probable error limits, consistent with a rate-determining formation followed by a partitioning of a common intermediate. These parameters may be compared with those reported for the racemization of (-)-Δ<sup>3</sup>-thujene, E<sub>a</sub> = (43.4 ± 0.5) kcal/mol and log A = (14.3 ± 0.2).<sup>3</sup>

The patterns of data from kinetic runs initiated with 6*x*-1 were expected to be identical if there were no significant k<sub>6e</sub> component, or to deviate appropriately if the converse were true. The kinetic evolution of isomers starting from 4*x*-1 would depend mostly on k<sub>r</sub>, k<sub>i</sub>, and k<sub>e</sub>, and be relatively insensitive to k<sub>6e</sub>. Starting from 6*x*-1, however, the direct interconversion between 6*x*-1 and 6*n*-1 for the racemic materials studied would depend significantly on both k<sub>r</sub> and k<sub>6e</sub>.<sup>17</sup>

The thermal reaction data secured with 6*x*-1 (97% 6*x*, 3% 6*n*) as starting material showed that k<sub>6e</sub> plays no kinetically important role at these temperatures and time domains, and that no significant isotopomer-specific deuterium isotope effects are involved. If there is any k<sub>6e</sub> contribution it must be relatively minor, and to measure it reliably alternative experimental approaches would need to be employed.

The interconversions of 4-*d*- and 6-*d*-labeled bicyclo[3.1.0]hex-2-enes through the three paths identified by Doering and co-workers and by Cooke and Andrews occur with essentially identical activation energies and preexponential factors. The first two are the simplest known degenerate [1,3] carbon shifts; the three together seem an ideal case for theory-based studies of the behavior of diradical structures launched onto relative flat potential energy surfaces having alternative exit channels. Relevant theory defining the potential energy surface and dynamic effects for conformationally various diradical intermediates involved in the degenerate isomerizations of bicyclo[3.1.0]hex-2-enes crossing that surface are anticipated with keen interest.

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**Supporting Information Available:** Kinetic data, kinetic plots, and <sup>1</sup>H NMR spectra (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- Were k<sub>6e</sub> of kinetic significance, λ<sub>2</sub> and λ<sub>3</sub> would depend on all four rate constants: λ<sub>2</sub>, λ<sub>3</sub> = (k<sub>r</sub> + k<sub>i</sub> + 2k<sub>r</sub> + k<sub>6e</sub>) ± ((k<sub>r</sub> - k<sub>i</sub>)<sup>2</sup> + k<sub>6e</sub><sup>2</sup>)<sup>1/2</sup>.

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