

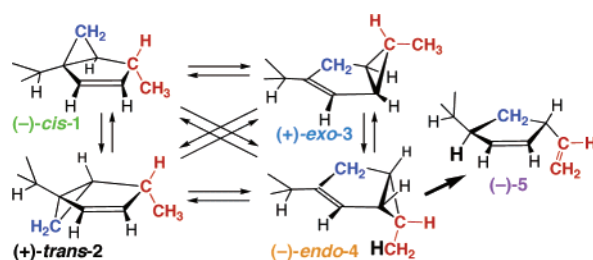
Kinetics of Thermal Rearrangements in the Δ^2 -Thujene System: A Full Quadrisection of a Perturbed Bicyclo[3.1.0]hex-2-ene

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Further insight into the behavior of suppositional diradicals in a caldera is sought in the thermal rearrangements among the four “ Δ^2 -thujenes”, two 1-isopropyl-4-methylbicyclo[3.1.0]hex-2-enes [(*-*)-*cis*-**1** and (*+*)-*trans*-**2**] and two isomers, *exo*- and *endo*-3-isopropyl-6-methylbicyclo[3.1.0]hex-2-ene [(*+*)-*exo*-**3** and (*-*)-*endo*-**4**]. Optically pure *trans*-3-isopropyl-5-vinylcyclopentene (**5**) is the final, strongly thermochemically favored product, the result of an intramolecular homodienyl shift of a methyl hydrogen atom in (*-*)-*endo*-**4**. The set of twelve specific rate constants, four sets of three each, that define the interrelations among the four isomers has been extracted from data acquired starting from each isomer. An attractive mechanistic hypothesis involving an intermediate diradical of iso conformation, common, for example, to both (*-*)-*cis*-**1** and (*+*)-*exo*-**3** (as educts), that proceeds to an anticonformer common to both (*+*)-*trans*-**2** and (*-*)-*endo*-**4** does not lead to a satisfactory rationalization of the product distribution. Addition of a second mechanistic conceptual scheme, that of a diradical-in-transit behaving as if there were a measure of continuous bonding (for example, (*+*)-*trans*-**2** proceeding directly to (*-*)-*cis*-**1**), improves agreement with experiment. Over a 30 °C range of temperature, there is no credible change in product distribution.

Introduction

The contrast between the superficial simplicity of intermolecular homolysis of a carbon–carbon covalent bond into a pair of radicals and their recombination and the complexity of the intramolecular analogue continues to evade mechanistic clarification and the development of a modicum of understanding of the variation of product distribution in response to introduction of substituents. The critical, qualitative difference lies in the internal rotational component—seemingly irrelevant in the intermolecular instance, but the key element in the intramolecular analogue. The failure over the past several decades to have reached a satisfying understanding of at least semiquantitative predictive value—intellectual control—does not detract from, but rather emphasizes, the fundamental importance of the challenge.

In that area of thermal rearrangements including monocyclic vinylcyclopropanes, many painstaking experiments have failed to provide a satisfying degree of understanding of the factors controlling distribution of products.^{1,2} Vinylcyclopropanes of the bicyclo[3.1.0]hex-2-ene type have been examined in the thought that the greater restraint on internal rotations imposed by the bicyclic system leads to a reduction in the number of possible products and might in consequence lead to the emergence of a clearer understanding of their formation. Exclusion of *trans*-substituted cyclopropanes and the conversion of ring enlargements to a pair of degenerate rearrangements follow from this simplification. The maximum number of

(1) Baldwin, J. E. *Chem. Rev.* **2003**, *103*, 1197–1212.
(2) Doering, W. von E.; Barsa, E. A. *J. Am. Chem. Soc.* **2004**, *126*, 12353–12362.

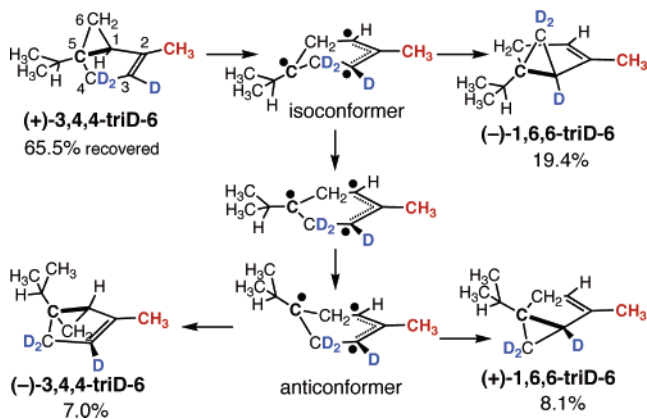


FIGURE 1. Thermal rearrangements of a Δ^3 -thujene: potential symmetry of its hypothetical planar diradical intermediate broken by three deuterium atoms.

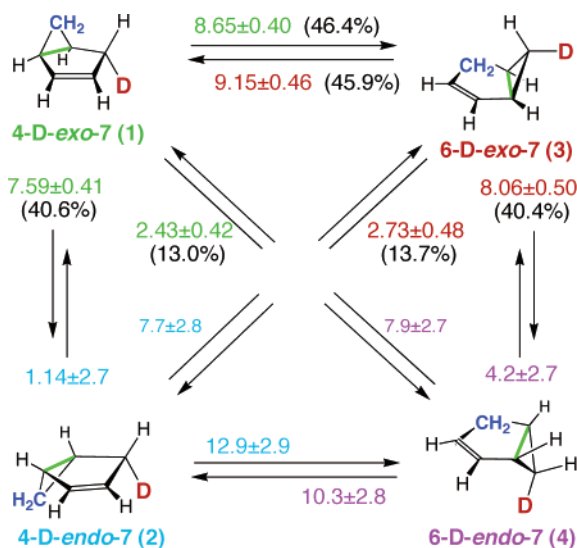
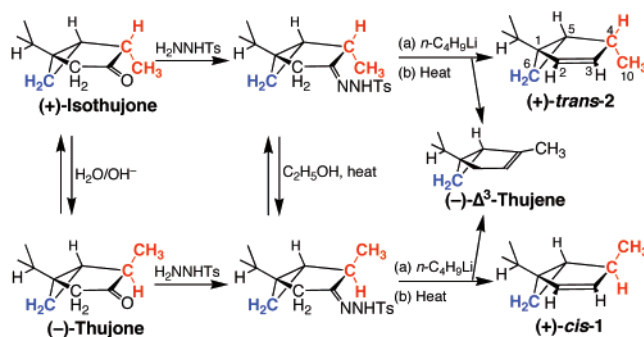


FIGURE 2. Reaction pathways of 4-deuteriobicyclo[3.1.0]hex-2-ene at 255 °C reported by Baldwin and Keliher⁶ starting from **1** and **3** (fractions given in percent). Values of specific rate constants as recalculated by the Fink–Marquardt program are given in units of 10^{-5} s^{-1} .

reaction paths in optimally labeled examples is reduced to four. By contrast, the complexity inherent in monocyclic vinylcyclopropanes is apparent from the 14 competitive reaction paths revealed by suitable labeling.² This paper concerns the behavior of Δ^2 -thujene. It is the first example in which the kinetics of all four interconversions have been elucidated independently.

Previous studies in the bicyclic area have involved Δ^3 -thujene (Figure 1)³ and the parent bicyclo[3.1.0]hex-2-ene (Figure 2),^{4,5} the latter an elegant and definitive contribution by Baldwin and Keliher.⁶ A good case has been made for a rate-determining entry into a caldera of intermediary diradicals, emergence from which generates products related to educts either by retention

SCHEME 1. Preparation



of the original conformation (*iso* conformation) or by conversion to an *anti* conformation by internal torsions (see Figure 1). This conceptual scheme has recently received strong theoretical support from a computational investigation by Suhrada and Houk^{7a} and a remarkable quantitative validation from the dynamic trajectory simulation of Doubleday, Suhrada, and Houk.^{7b}

In the earlier study of the Δ^3 -thujenes, an inherent symmetry in the diradicals demanded that the two products from the anti conformational diradical be formed in equal amounts (Figure 1, (-)-3,4,4-triD-6, 7.0%, and (+)-1,6,6-triD-6, 8.1%). In a preliminary study of the Δ^2 -thujenes, initiated mainly because of their concurrent availability, it was observed that (+)-*trans*-2 and (-)-*endo*-4 had been formed from (-)-*cis*-1 also in equal amounts.⁸ When Baldwin and Keliher discovered that the two products, 4-D-*endo*-7 and 6-D-*endo*-7 from 4-D-*exo*-7, were formed in unequal amounts, a thorough examination of the thermal behavior of the other three isomers of Δ^2 -thujenes became irresistible. Interest was the greater because equality would carry with it the mechanistic implication that the anti conformers of the diradical intermediate were the common precursor of two of the products. In experimental practice, the Δ^2 -thujenes allowed entrance into the caldera from each of the four interconvertible isomers and elucidation of a complete quadrisection.

Results

Pyrolysis of the dry lithium salts of the *p*-tolylsulfonylhydrazones of the naturally occurring, readily available, and interconvertible (+)-isothujone and (-)-thujone (Scheme 1) make both diastereomeric Δ^2 -thujenes, 1-isopropyl-4-methylbicyclo[3.1.0]hex-2-ene, (+)-*trans*-2 and (+)-*cis*-1, respectively, easily available. Detracting from the attractiveness of the substantially higher yields of this preparative method in contrast to those from an older method³ is the ease with which the two *p*-tosylhydrazones are themselves interconvertible. However, compensation is found in the sensitivity of the relative distribution among the four bicyclo[3.1.0]hex-2-enes to experimental conditions, advantage of which can be taken as outlined in Table S-1 in the Supporting Information.

The two thujenes (+)-*cis*-1 and (+)-*trans*-2 are epimeric at the C-4 atom bearing the methyl group ("red" in Scheme 1) and are not interconvertible under the conditions either of their

(3) (a) Doering, W. von E.; Lambert, J. B. *Tetrahedron* **1963**, *19*, 1989–1994. (b) Doering, W. von E.; Schmidt, E. K. G. *Tetrahedron* **1971**, *27*, 2005–2030.

(4) Grimme, W. Cited in Doering, W. von E.; Roth, W. R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 115–122.

(5) Cooke, R. S.; Andrews, U. H. *J. Am. Chem. Soc.* **1974**, *96*, 2974–2980.

(6) Baldwin, J. E.; Keliher, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 380–381.

(7) (a) Suhrada, C. P.; Houk, K. N. *J. Am. Chem. Soc.* **2002**, *124*, 8796–8797. (b) Doubleday, C.; Suhrada, C. P.; Houk, K. N. *J. Am. Chem. Soc.* **2006**, *128*, 90–94.

(8) Schmidt, E. K. G. Ph.D. Dissertation, Yale University, 1968; *Diss. Abstr. Int., B* **1970**, *30*, 3573; order no. 7002797.

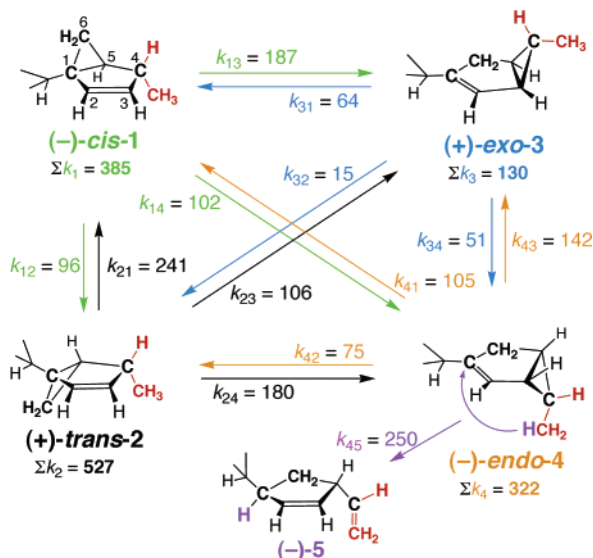


FIGURE 3. Thermal rearrangements of the Δ^2 -thujenes shown with specific rate constants at 237 °C given in units of 10^{-7} s^{-1} . Sums of the three rate constants (Σk_n) emanating from each educt are also shown.

preparation or their thermally induced rearrangements. Thus, two enantiomeric sets of products can be generated under kinetic control.

Thermal rearrangements occur at convenient rates between 200 and 240 °C. A true equilibrium is not reached among the four bicyclo[3.1.0]hex-2-enes of the same enantiomeric set because *endo-4* proceeds uniquely, competitively, irreversibly, and stereospecifically by a concerted 1,5-homodieryl, intramolecular hydrogen transfer from the methyl group at C-6 to C-1 to the thermodynamically most stable isomer, *trans-3-isopropyl-5-vinylcyclopentene* (**5**). The complete stereospecificity makes the formation of either enantiomer of **5** available in optically pure form depending on whether (+)-*trans-2* or (+)-*cis-1* is the educt. A comparable example has been reported by Crowley in the rearrangement of 2,3,6,6-tetramethylbicyclo[3.1.0]hex-3-ene, obtained from the photorearrangement of the two *trans*-alloocimenes to 3-isopropenyl-4,5-dimethylcyclopentene.⁹

Isolation and purification of the four stereoisomers is accomplished by preparative GC of a partially rearranged material resulting from heating (+)-*cis-1* or (+)-*trans-2* at 237 °C for 2 h. Quantitative analysis is accomplished by capillary GC. For the study of the kinetics, each of the four isomers is heated for lengths of time sufficient to reach a steady state (pseudoequilibrium). The resulting data at 237 and 207 °C are given in Tables S-2 and S-3 in the Supporting Information.

Calculation of the thirteen specific rate constants (three each from the three educts (-)-*cis-1*, (+)-*trans-2*, and (+)-*exo-3* and four from (-)-*endo-4*, Figure 3) is accomplished by the program KINETIC of Fink, which also allows calculation of uncertainties of each specific rate constant at the 95% confidence level.¹⁰ The program permits calculation from the four sets of collected data of relative concentrations/times of reaction simultaneously up to a total of 150 data. As we ended up with more than that many in the study at 237 °C, four separate calculations were

TABLE 1. Specific Rate Constants and Enthalpies of Activation for the Thermal Rearrangements of the Four Δ^2 -Thujenes at 207.0 and 237.0 °C in the Gas Phase

rate constant ^a	$k^{b,c}$		E_a^d
	207 °C	237 °C	
k_{12}	5.58 ± 0.69	96 ± 9.7	46.28
k_{13}	11.6 ± 0.60	181 ± 4.1	44.68
k_{14}	6.49 ± 0.73	102 ± 8.9	44.75
k_{21}	14.4 ± 0.73	241 ± 4.7	45.76
k_{23}	5.62 ± 0.64	106 ± 9.1	47.68
k_{24}	11.1 ± 0.78	180 ± 6.2	45.29
k_{31}	4.07 ± 0.31	64.0 ± 8.3	44.78
k_{32}	0.80 ± 0.32	14.7 ± 38.4	47.34
k_{34}	3.22 ± 0.31	50.9 ± 10.2	44.83
k_{41}	7.31 ± 1.15	105 ± 11.3	43.35
k_{42}	5.03 ± 1.17	74.9 ± 16.6	43.91
k_{43}	10.2 ± 1.07	142 ± 6.9	42.84
k_{45}	23.3 ± 0.97	250 ± 2.8	38.58

^a See Figure 3 for the definition of k . ^b Rate constants are the weighted averages of the values appearing in Table S-4 in units of 10^{-7} s^{-1} . ^c Uncertainties are at the 95% confidence level. ^d Energies of activation in kilocalories per mole.

made in each case using all the points from one educt and five to seven from each of the other three. This problem did not arise in the study at 207 °C. As revealed in Table S-4 in the Supporting Information, the results of the four calculations differ but slightly. The specific rate constants from experiments at 207 and 237 °C are collected in Table 1, as are the derived enthalpies of activation. The average of all values (excluding that from k_{45}) is $45.0 \pm 1.4 \text{ kcal/mol}$ (standard error). Especially to be noted are the greater uncertainties in precision when (+)-*exo-3*, the thermodynamically most stable of the four bicyclo[3.2.0]hexenes, is the educt.

Discussion

Monocyclic systems of the vinylcyclopropane and vinylcyclobutane classes reacting in a not obviously concerted way have involved too many variables of the internal rotational type to allow a useful level of understanding to be gained.^{11,12} The existence of concert in many thermal rearrangements reduces the number of internal rotational elements in general to four, the choices among which have been totally mastered by the insight of Woodward and Hoffmann.¹³ The constraint imposed by the bicyclic nature of the Δ^2 -thujenes likewise reduces the number of internal rotational elements.

The caldera—a nonspecific term for the collection of accessible diradicals acting as intermediary between educt and products¹⁴—in this hypothetical mechanism is entered by stretching the weakest bond of the cyclopropane ring to its bond-dissociative energy level and creating noninteractive diradicals having no bonding overlap between their two components. Such diradicals, for example, having equal bond distances between C-5 (the secondary radical) and C-3 and C-1 (the stabilized

(11) Doering, W. von E.; Cheng, X-h.; Lee, K-w.; Lin, Z-s. *J. Am. Chem. Soc.* **2002**, *124*, 11642–11652.

(12) The achievement of so-called “intellectual control” of the mechanism in organic chemistry has been limited to those areas where consideration of two or three independent variables has sufficed. In areas where many variables of the internal rotational type seem to be involved, intellectual control has remained obstinately elusive.

(13) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim, Germany, 1970; p 121.

(14) Northrop, B. N.; Houk, K. N. *J. Org. Chem.* **2006**, *71*, 3–13.

(9) Crowley, K. J. *J. Org. Chem.* **1968**, *33*, 3679–3686.

(10) Marquardt, D. W. *J. Soc. Ind. Appl. Math.* **1963**, *11*, 431–441. We thank Dr. R. Fink for a copy of the program KINETIK, which permits optimization by the Marquardt procedure of kinetic schemes with up to seven components.

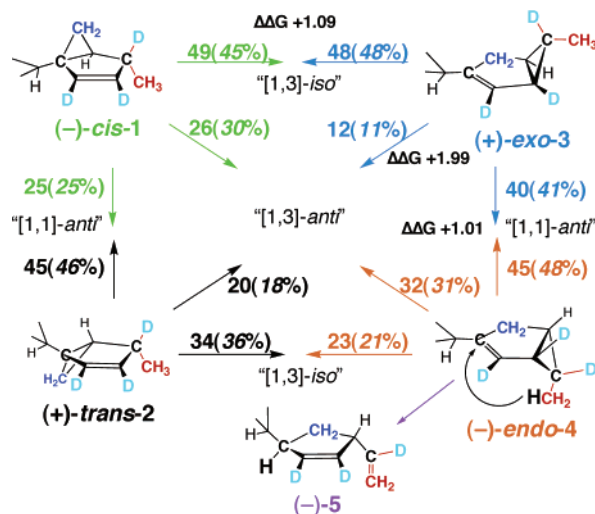


FIGURE 4. Distribution of products (%) from the rearrangement at 237 °C of the all-protium “ Δ^2 -thujenes” (Roman bold) and of the 2,3,4- and 1,2,6-trideuterium derivatives (italic bold, in parentheses). Differences in free energy relative to (+)-*exo-3* are given in kilocalories per mole.

TABLE 2. Fractions (%) of the Three Types of Rearrangements Undergone by Bicyclo[3.1.0]hexenes

educt	[1,3]-iso ^a	[1,1]-anti ^a	[1,3]-anti ^a
4-D- <i>exo-7</i> ^{b,c}	48 (0.0) ^d	36 (0.0)	16 (0.0)
(-)- <i>cis-1</i> ^e	49 (+1.1)	25 (+0.9)	26 (-0.1)
(+)- <i>trans-2</i> ^e	34 (-1.0)	45 (-0.9)	20 (-2.0)
(+)- <i>exo-3</i> ^e	48 (+1.1)	40 (+1.0)	12 (+2.0)
(-)- <i>endo-4</i> ^e	23 (+0.9)	45 (-1.0)	32 (+0.1)
(+)-3,4,4-triD-6 ^f	56	20	23

^a See the text for definitions. ^b Reference 6. ^c Recalculated as 46.0%, 40.5%, and 13.5% (Figure 2). ^d In parentheses are the differences in free energy in kilocalories per mole (see Figure 4). ^e Figure 3. ^f Reference 3b (Figure 1).

allylic radical),¹⁵ are removed from control by orbital symmetry. This scheme is the same as that introduced by Doering and Schmidt^{3b} to accommodate the behavior of Δ^3 -thujene, a bicyclo[3.1.0]hexene uninformed by the additional asymmetric carbon atom of the Δ^2 -thujenes (compare Figures 1 and 3).

From the ratios of the specific rates of reaction for interconversions among (-)-*cis-1*, (+)-*exo-3*, (-)-*endo-4*, and (+)-*trans-2* (Table 1), differences in free energies of formation at 237 °C are calculated (Figure 4). (Differences in enthalpies of activation have not been determined with sufficient precision.) Relative to $\Delta\Delta G$ of (+)-*exo-3* set to 0.00 kcal mol⁻¹, these are [(-)-*cis-1*] +1.09 kcal mol⁻¹, [(-)-*endo-4*] +1.01 kcal mol⁻¹, and [(+)-*trans-2*] +1.99 kcal mol⁻¹. Have the kinetically controlled distributions among products been influenced by these thermochemical differences? Although the rearrangements of the most stable isomer, (+)-*exo-3*, and (-)-*endo-4* seem to support this suggestion, that of (+)-*trans-2* does not, while that of (-)-*cis-1* is ambiguous (see Table 2).

When the kinetic data of Table 1 are presented as fractions (%) of the three products from each of the four Δ^2 -thujenes as educts (Figure 4), it emerges clearly that no single intermediate-in-common (for example, a planar diradical or its equivalent such as a mixture of conformers at an equilibrium established

prior to exit from the caldera by covalent bond formation) can represent more than 10% of the picture. It is also clear in two cases that the major product appears to result from breaking and remaking the same bond, (+)-*trans-2* to (-)-*cis-1* and (-)-*endo-4* to (+)-*exo-3*, but this is not true of the interconversion of (-)-*cis-1* and (+)-*exo-3* or of (+)-*trans-2* and (-)-*endo-4*. The hypothesis of passage to an anti conformation by way of a coplanar conformation (see Figure 2), from which identical ratios of the two products would result in the loss of any memory of origin, is also wanting. While this prediction is consistent with the conversion of (-)-*cis-1* to (+)-*trans-2* and (-)-*endo-4*, it is inconsistent with the other three conversions.

Among the other usual suspects for gaining mechanistic insight, temperature dependence of product ratios is nonexistent within experimental uncertainties, a characteristic also found by Baldwin and Keliher with the paradigm.⁶ Whether examination over the much larger range of temperature required to reveal significant differences as small as 2 kcal mol⁻¹ would be productive is problematic. In light of the failure of pressure to influence product ratios in an arguably more favorable example, we doubt that an investigation of the effect of pressure would reveal a significant correlation.¹⁶

Grasping for vestiges of Woodward–Hoffmann considerations of orbital symmetry in this or other not obviously concerted rearrangements has led nowhere. Even here, where attainment of the zero overlap between the allyl and secondary radicals associated with the planar, symmetrical stage can easily be avoided and thus retain a modicum of bonding throughout the bond-breaking, bond-making process, any encouragement found in the instance of (+)-*trans-2* rearranging to (-)-*cis-1* and of (-)-*endo-4* rearranging to (+)-*exo-3* is erased in the corresponding reverse reactions.

All the standard approaches to mechanism fail to consolidate into a coherent conceptual scheme for understanding and predicting product distribution as a function of constitutional perturbation (gaining intellectual control), this despite the ease with which their enthalpies of activation can usually be estimated.

The interaction of Doubleday on the theoretical side and Baldwin on the experimental side has led to a clarification of the two paradigms of vinylcyclopropane^{17,18} and bicyclo[3.1.0]hex-2-ene.^{5,6,7b} In both, the quantitative agreement between experimental and theoretical ratios among products is spectacular. In providing the basis for identifying schemes for assessing quantitatively or qualitatively the effects of structural perturbations, these scientists have made a fundamental contribution. The question of why the distribution among the three products in bicyclo[3.1.0]hex-2-ene is 48%, 36%, and 16% has no more meaning in organic chemistry than the question of why the bond dissociation energy of ethane to a pair of methyl radicals is 91 kcal mol⁻¹. As practitioners of a perturbational science, organic chemists and their theoretical allies aspire to gain intellectual control over the effect of various types of perturbation. In ethane, such questions as what the effect of the changes is, for example, to hexaphenylethane, to hexamethylethane, and to hexa-1,5-diene have been satisfactorily addressed. The classical successes have generally involved electronic and steric changes on enthalpies of formation and activation.

(16) Klärner, F.-K.; Wurche, F.; Doering, W. v. E.; Yang, J.-d. *J. Am. Chem. Soc.* **2005**, *127*, 18107–18113.

(17) Baldwin, J. E.; Villarica, K. A.; Freedberg, D. I.; Anet, F. A. L. *J. Am. Chem. Soc.* **1994**, *116*, 10845–10846.

(18) Doubleday: C. *J. Phys. Chem. A* **2001**, *105*, 6333–6341.

(15) Roth, W. R.; Bauer, F.; Beitat, A.; Ebbrecht, T.; Wüstefeld, M. *Chem. Ber.* **1991**, *124*, 1453–1460.

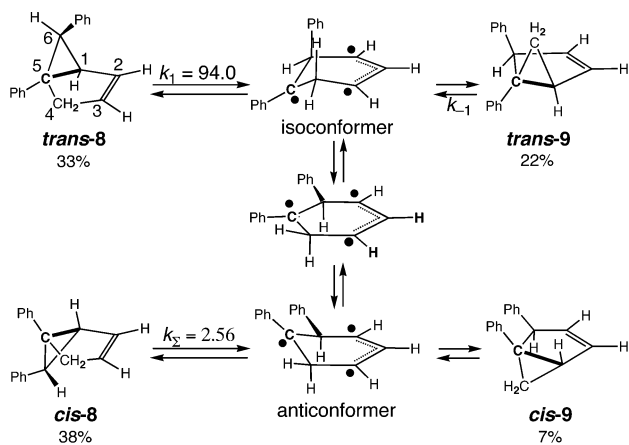


FIGURE 5. Interconversions among four diphenylbicyclo[3.1.0]hex-2-enes. Relative concentrations at equilibrium at 201 °C are recorded in percent. Rate constants at 180 °C are given in units of 10^{-5} s^{-1} : k_1 from the fast equilibration between *trans*-8 and *trans*-9 and k_2 from the rearrangement of *cis*-8 to the sum of the other three isomers.

In the present work, perturbation by an isopropyl group at C-1 and a methyl group at C-4 leads, as expected from conventional experience, to little change in the overall rates. The challenge lies in predicting (explaining) the effect on the paradigmatic ratios. The relevant data are collected in Table 2. The three types of rearrangement are designated “[1,3]-iso”, the breaking of a 1,5-bond and making of the 3,5-bond with retention of conformation (e.g., rearrangement of (–)-*cis*-1 to (+)-*exo*-3 and of (–)-*endo*-4 to (+)-*trans*-2), “[1,1]-anti”, rearrangement by inversion of conformation (e.g., (–)-*cis*-1 to (+)-*trans*-2), “[1,3]-anti” (e.g., (–)-*cis*-1 to (–)-*endo*-4), and [1,1]-iso, the unobservable but calculable identity reaction (see Figure 4). (Doubleday et al. use a slightly different nomenclature to describe the same situation.^{7b}) We note that the average values, [1,3]-iso: $43 \pm 12\%$, [1,1]-anti: $35 \pm 10\%$, and [1,3]-anti: $22 \pm 7\%$, cluster around the values for the paradigm 4-D-*exo*-7. It may be significant that the iso conformational, [1,3]-iso, and [1,1]-anti processes are the more favored, while the less favored is the [1,3]-anti process, which is comprised of both readjustments of geometry.

With respect to the four Δ^2 -thujenes, the charge is the prediction of how the introduction of isopropyl at C-1 and methyl at C-4 into the paradigm is expected to lead to departures from the 48:36:16 ratios reported for the paradigm. What constitutes a significant departure depends at the moment on the magnitude of the observed uncertainties in the dynamic calculation and the experimental determinations. It also depends on a subjective decision. If the uncertainties in the ratios of the rates of the competing reactions are, say, 5%, are departures exceeding 10%, 20%, or 2-fold to be considered significant? Depending on one’s decision, the examples in Table 2 show no departures worthy of discussion, or perhaps the example of (–)-*endo*-4 does.

By contrast, the example of 5,6-diphenylbicyclo[3,1,0]hex-2-ene communicated by Swenton and Wexler¹⁹ (Figure 5) reveals a dramatic departure from the paradigm. Within a time sufficient to have established equilibrium at 130 °C between the two components *trans*-8 and *trans*-9, only 2% crossover to *cis*-8 and *cis*-9 by processes [1,1]-anti and [1,3]-anti is observed,

(19) Swenton, J. S.; Wexler, A. *J. Am. Chem. Soc.* **1971**, *93*, 3066–3068.

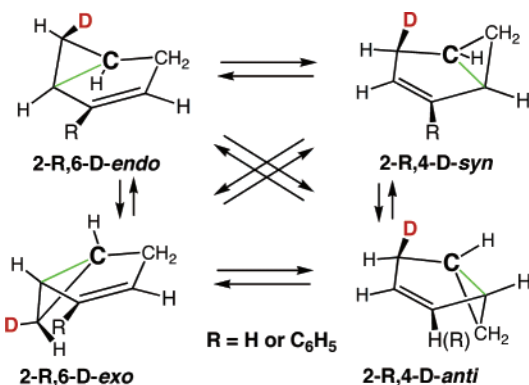


FIGURE 6. Rearrangements of 2-H- and 2-phenyl-6-deuteriobicyclo[3.1.0]hex-2-enes.

despite an unexceptional ratio of 55:45 of the two pairs (at 201°C). In an exemplary discussion, Swenton and Wexler ascribe the acceleration of rate brought about by the 5-phenyl group to stabilization by the benzyl resonance and the dramatic slowing of the crossover to a steric repulsion between the two phenyl groups as they approach closer to each other in the torsion needed to achieve the planar diradical functioning as the transition region between the iso conformer and the anti conformer. In this intermediary region, the radical-stabilizing phenyl group is being forced partially out of the plane by the adjacent phenyl group.

Whether the slowness of the crossover is predictable in terms of a dynamic trajectory analysis may be some time in the answering, but meanwhile, as implied in the Swenton–Wexler analysis, conventional steric factors may well serve in apposite cases to provide an understanding of the effect of constitutional perturbations. If the isopropyl group in the Δ^2 -thujenes is sterically too small a perturbation, others such as that of three (or four) methyl (alkyl) groups at positions 1, 5, and 6 (6) may deserve a look.

The quantitatively successful dynamic trajectory treatment comes without any qualitative guidance for the prediction of the relation between constitutional perturbations and distribution of products. At the moment, the only accessible approach may be empirical. Might perturbations at positions not directly involved in the bond-breaking, bond-making processes influence the distribution? Significant changes in the frequencies of the normal vibrational modes that couple with excitation of the cyclopropane-breaking modes might alter the patterns of entry into the caldera and thus the eventual distribution among products.

Examples of such “tertiary” constitutional effects (compare secondary kinetic isotope effects) are limited. In the readily accessible trideuterio- Δ^2 -thujenes of Figure 4, the two deuterium atoms at positions 2 and 4 qualify as perturbations possibly affecting the frequencies of normal vibrational modes to an appreciable extent. But whether they influence those modes critical to the ultimate distribution among products is not clear. The experimental results, shown in parenthesized italics in Figure 4, reveal no consistent effect. Further pursuit of this approach might involve more substantial perturbations at positions 2, 4, and 6, which are not directly involved at the site of reaction. Such a comparison might involve an R group such as a phenyl at position 2 (Figure 6). A phenyl group, although nodal in the hypothetical allyl portion of the diradical, might change the absolute values of the rate constants slightly, but a

large effect on the relative distribution among the four products could be ascribed to a tertiary effect.

Experimental Section

Preparation of (+)-*cis*-1 and (+)-*trans*-2. Preparation of mixtures of α - and β -thujenes from (+)-isothujone and (–)-thujone by pyrolysis at 140 °C of the lithium salts of the corresponding tosylhydrazones has already been described in detail.^{3b} Fractions from the initial isolation, rich in Δ^2 -thujenes, are redistilled from the spinning band column to give almost pure (+)-*cis*-1 (bp₇₆₀ \approx 146.5 °C), (+)-*trans*-2 (bp₇₆₀ \approx 149.5 °C), and pure Δ^3 -thujene (bp₇₆₀ = 152.5 °C).

Ratios among (+)-*cis*-1, (+)-*trans*-2, and Δ^3 -thujene were sensitive to conditions as explicated in Table S-1. These reactions were effected in a 25 mL, two-necked, round-bottomed flask with a magnetic stirrer. Immediately after the additions at 30–35 °C, which took \sim 30 s, solvent was removed in the vacuum of a water aspirator, leaving a salt which was freeze-dried for \sim 1 h. The flask was then placed in an oil bath at 140 °C and pyrolyzed at \sim 13 Torr. The thujenes were trapped at –75 °C and analyzed by GC on column A at 70 °C. The results of the various modifications to this procedure are given in Table S-1.

The final procedure employed follows. A solution of 6.48 g of tosylhydrazone in 30 mL of anhydrous THF was treated with 14.5 mL of 1.6 N *n*-butyllithium in hexane (1.1 molar equivalents) at rt under argon. After the now red solution had been stirred for 2 h, an additional 14.5 mL of 1.6 N *n*-butyllithium was added dropwise. After being stirred for a further 10 min, the solution was treated with 3 mL of water and extracted with two 15 mL portions of pentane. Concentration and distillation at \sim 140 °C yielded 1.96 g (72%) of a mixture of *cis*- and *trans*- Δ^2 -thujene and Δ^3 -thujene in the ratio 100:47:9 (by ¹H NMR).

Thermal Reaction of Δ^2 -Thujenes. Samples of pure (+)-*cis*-1 and (+)-*trans*-2 were sealed in separate ampules of Pyrex glass and heated simultaneously at \sim 237 °C in a tubular furnace. On analysis by GC (column A), each reaction mixture showed the same five peaks, their intensities differing depending on the starting thujene. Pure samples of *cis*-1, *trans*-2, **5**, *exo*-3, and *endo*-4 were collected by preparative GC employing a 6 m column of 26.8% PCEP (1,2,3-tris(2-cyanoethoxy)propane on 60/80 mesh Chromosorb P) at 80 °C with He as a carrier gas flowing at 60 mL of He/min. Retention times at 50 mL of He/min for *cis*-1, *trans*-2, **5**, *exo*-3, and *endo*-4 are 5.62 (relative retention time 1.00), 6.00 (1.07), 7.22 (1.28), 8.81 (1.57), and 10.48 (1.86) min, respectively. Specific rotations, NMR spectra, IR spectra, and mass spectra follow.

Data for (+)-*(1S,4S,5R)*-1-isopropyl-4-methylbicyclo[3.1.0]-hex-2-ene [(+)-*cis*-1]: [α]_D²⁵ +85.6 (absolute EtOH); [α]_D²⁴₅₄₆ +101.4 (*c* 5.8, CHCl₃); MS (70 eV) *m/z* (rel intens) 136 (25, parent), 121 (57), 109 (10), 107 (15), 105 (12), 94 (10), 93 (100, base), 92 (15), 91 (33), 79 (31), 77 (34), 65 (7), 43 (37), 41 (23), 39 (17); ¹H NMR δ 5.82 (dd, *J* = 5.4, 1.8 Hz, 1H), 5.32 (d, *J* = 5.4 Hz, 1H), 2.43 (q, *J* = 7.2 Hz, 1H), 1.30 (quintet, *J* = 7.2 Hz, 1H), 1.01 (d, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 7.2 Hz, 4H), 0.89 (d, *J* = 7.2 Hz, 3H), 0.71 (dd, *J* = 8.4, 3.6 Hz, 1H), 0.12 (t, *J* = 3.6 Hz, 1H); ¹³C NMR δ 133.9, 133.4, 43.1, 41.7, 31.0, 28.2, 22.6, 22.3, 21.1, 21.0.

Data for (+)-*(1S,4R,5R)*-1-isopropyl-4-methylbicyclo[3.1.0]-hex-2-ene [(+)-*trans*-2]: [α]_D^{19.5} +30.8 (neat); *d*₄²² 0.822 (micro-pycnometer); IR (cm⁻¹) 3055, 3035, 1602, 1026; MS (70 eV) *m/z* (rel intens) 136 (25, parent), 121 (58), 109 (19), 107 (19), 105 (14), 94 (9), 93 (100, base), 92 (17), 91 (42), 79 (29), 77 (35), 65 (9), 43 (45), 41 (30), 39 (20); ¹H NMR δ 5.78 (dd, *J* = 6.0, 1.8 Hz, 1H), 5.14 (d, *J* = 6.0 Hz, 1H), 3.10 (quintet, *J* = 6.6 Hz, 1H), 1.35 (quintet, *J* = 6.6 Hz, 1H), 1.19 (m, 1H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.44 (m, 1H), 0.20 (t, *J* = 3.6 Hz, 1H); ¹³C NMR δ 134.7, 133.8, 42.6, 41.6, 31.0, 25.3, 21.0, 20.8, 17.2, 17.1.

Data for (–)-*(1S,5R,6R)*-3-isopropyl-6-methylbicyclo[3.1.0]-hex-2-ene [(–)-*exo*-3]: [α]_D²⁰ –61.8 (*c* 0.86, CCl₄) (when derived from (+)-*cis*-1); IR (cm⁻¹) 3066 (m), 3054 (s), 3030 (s), 1623 (m), 1469 (s), 1388 (m), 1379 (m) (identical to compound **V** of Doering and Lambert^{3a}); ¹H NMR δ 5.55 (t, *J* = 1.8 Hz, 1H), 2.48 (dd, *J* = 16.8, 7.2 Hz, 1H), 2.22 (d, *J* = 16.8 Hz, 1H), 2.14 (quintet, *J* = 7.2 Hz, 1H), 1.48 (quartet, *J* = 3.0 Hz, 1H), 1.17 (sextet, *J* = 3.0 Hz, 1H), 0.94 (m, 10 H), 0.26 (m, 1H); ¹³C NMR δ 149.1, 124.9, 36.4, 31.9, 29.6, 25.2, 23.8, 21.9, 21.8, 17.3.

Data for (+)-*(1R,5S,6R)*-3-isopropyl-6-methylbicyclo[3.1.0]-hex-2-ene [(+)-*endo*-4]: [α]_D²¹ +147 (*c* 0.37, CCl₄) (when derived from (+)-*cis*-1); IR (cm⁻¹) 3053 (m), 3035 (s), 3019 (m), 1630 (m), 1460, 1461 (s), 1380 (s), 1366 (s), 848 (vs), 829 (m, sh), 780 (vs), 734 (s); MS *m/z* 136 (parent), 93 (base); ¹H NMR δ 5.27 (s, 1H), 2.37 (dd, *J* = 16.8, 8.4 Hz, 1H), 2.19 (quintet, *J* = 7.2 Hz, 1H), 1.98 (d, *J* = 16.8 Hz, 1H), 1.87 (m, 1H), 1.43 (m, 1H), 0.97 (t, *J* = 7.2 Hz, 6H), 0.85 (s, 4H); ¹³C NMR δ 152.2, 120.2, 32.0, 29.9, 28.3, 22.3, 22.1, 19.7, 16.1, 6.4.

Data for *trans*-3-isopropyl-5-vinylcyclopentene (5**):** [α]_D²⁰ +191 (*c* 0.20, CCl₄) (when derived from (+)-*cis*-1); IR (cm⁻¹) 3076 (s), 3054 (s), 1815 (m), 1633 (s), 1608 (m), 1463 (s), 1370, 1359 (m) (identical to compound **VI** of Doering and Lambert^{3a}); MS *m/z* 136 (parent), 93 (base); ¹H NMR δ 5.75 (m, 1H), 5.68 (m, 1H), 5.64 (m, 1H), 5.01 (dq, *J* = 17.3, 1.2 Hz, 1H), 4.91 (dq, *J* = 9.6, 1.2 Hz, 1H), 3.24 (m, 1H), 2.45 (m, 1H), 1.70 (m, 2H), 1.41 (sextet, *J* = 6.6 Hz, 1H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 6.6 Hz, 3H); ¹³C NMR δ 142.8, 134.7, 134.0, 113.0, 52.5, 49.9, 34.9, 32.9, 20.7, 20.6.

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Supporting Information Available: Table S-1 showing the dependence of the products on the preparation conditions of thujenes, Tables S-2 and S-3 summarizing untreated data from the kinetic studies, and Table S-4 giving alternative calculations of kinetic data at 237 °C. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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