

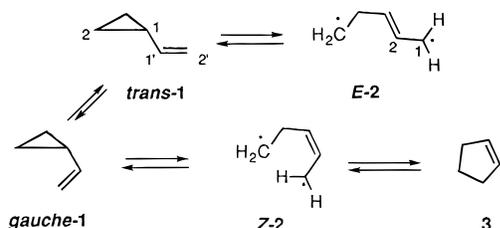
Thermal Stereomutations and Vinylcyclopropane-to-Cyclopentene Rearrangement of 2-Methylene-3-spirocyclopropanebicyclo[2.2.1]heptane

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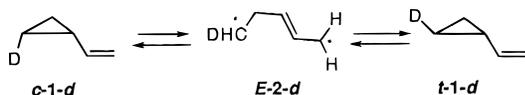
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In 1963, soon after the thermal conversion of vinylcyclopropane (**1**) to cyclopentene (**3**) was first reported,¹ it was recognized that homolysis of a C1–C2 bond in **1** might lead to both (*E*)- and (*Z*)-2-pentene-1,5-diyl diradicals (**E-2**, **Z-2**).² The former could not proceed readily to cyclopentene, while the latter, the “fruitful” alternative, might be only slightly higher in energy, and then require but little further energy to give the [1,3] carbon shift product **3**.²



Four years later the thermal equilibration of *cis* and *trans* isomers of 1-vinyl-2-*d*-cyclopropane (**c-1-d**, **t-1-d**) was uncovered and found to be faster than the structural isomerization.³ While the diradical **E-2-d** could have served conveniently to rationalize this facile stereomutation, the question as to whether stereomutation and the slower [1,3] carbon migration might occur through one common or two separate reaction manifolds could only be noted, not resolved.³



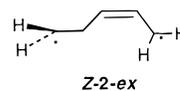
Stereomutations of substituted vinylcyclopropanes are typically much faster than structural isomerizations, a fact complicating stereochemical studies of the [1,3] carbon migrations.^{4,5} Yet information on the stereochemical course of vinylcyclopropane-to-cyclopentene rearrangements has been secured for a number of monocyclic systems: they isomerize with some preference for suprafacial, inversion (*si*) stereochemistry but with substantial contributions from suprafacial, retention (*sr*), antarafacial, inversion (*ai*), and antarafacial, retention (*ar*) paths as well.^{4,5}

Theoretical investigations of the parent rearrangement have located only a single transition structure linking vinylcyclopropane

with cyclopentene.⁶ Yet four stereochemically distinct products are formed in kinetically controlled processes!^{4,5} A 1-vinyl-2,2'-*d*₂-cyclopropane may give four stereoisomers of 3,4-*d*₂-cyclopentene through passages through four distinct versions of that single transition structure, all isometric⁷ (but for the labels), two pairs of diastereomeric enantiomers (when the deuterium labels are considered).⁵ Conformational flexibility available to a 1,5-*d*₂-labeled **Z-2** diradical permits one starting material to reach all four transition structures in the transition region without the intervention of intermediates.^{6e,f}

Recent direct dynamic quasi-classical trajectory calculations for rearrangement of the parent system based on these understandings have provided an account of overall stereochemistry in striking agreement with experimental results.^{8–10} The experimental relative rate constants were found to be $k_{si} = 40\%$, $k_{sr} = 23\%$, $k_{ar} = 13\%$, and $k_{ai} = 24\%$, with estimated experimental uncertainties of ± 2 to 3%, at 300 °C;⁸ the relative percent yields calculated from trajectories initiated at three saddle points were $si = 45 \pm 4$, $sr = 28 \pm 3$, $ar = 12 \pm 3$, and $ai = 24 \pm 3$.⁹

Just how stereomutations fit in this picture remains only partly clarified. The latest theoretical work has found a transition structure for a **Z-2** conformer corresponding to a one-center epimerization at C2, and another, an extended **Z-2** form (**Z-2-ex**), that could accommodate epimerization at C1, both lower in energy than the transition structure leading to cyclopentene.^{6e,f} Thus access to **E-2** diradicals might not be required for stereomutations. Vinylcyclopropanes limited to *gauche* conformational forms and to **Z-2** diradical conformational options might still exhibit facile stereomutations.¹¹



2-Methylene-3-spirocyclopropanebicyclo[2.2.1]heptane (**4**) was selected as a suitable substrate to test this inference. Thermal isomerization of **4** would be expected to give tricyclo[5.2.1.0^{2,6}]-dec-2(6)-ene (**5**) as a reactive intermediate, which through a retro Diels–Alder reaction would provide the known tetrahydropentalenes **6** and **7**.¹² The geometrically limited vinylcyclopropane **4** was readily prepared from 3-methylenenorbornanone, through Simmons-Smith¹³ and then Wittig reactions. At 309 °C in a gas-phase static reactor with pentane as a bath gas it isomerized and

(6) (a) Quirante, J. J.; Enríquez, R.; Hernando, J. M. *J. Mol. Struct. (THEOCHEM)* **1990**, *204*, 193–200. (b) Quirante, J. J.; Enríquez, R.; Hernando, J. M. *J. Mol. Struct. (THEOCHEM)* **1992**, *254*, 493–504. (c) Houk, K. N.; Li, Y.; Evansck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682–708. (d) Houk, K. N. *Acc. Chem. Res.* **1995**, *28*, 81–90. (e) Davidson, E. R.; Gajewski, J. J. *J. Am. Chem. Soc.* **1997**, *119*, 10543–10544. (f) Houk, K. N.; Nendel, M.; Wiest, O.; Storer, J. W. *J. Am. Chem. Soc.* **1997**, *119*, 10545–10546.

(7) (a) Mislow, K. *Bull. Soc. Chim. Belg.* **1977**, *86*, 595–601. (b) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994; p 1201.

(8) (a) Baldwin, J. E.; Villarica, K. A.; Freedberg, D. I.; Anet, F. A. L. *J. Am. Chem. Soc.* **1994**, *116*, 10845–10846. (b) Baldwin, J. E.; Villarica, K. A. *J. Org. Chem.* **1995**, *60*, 186–190.

(9) Doubleday, C.; Nendel, M.; Houk, K. N.; Thweatt, D.; Page, M. J. *J. Am. Chem. Soc.* **1999**, *121*, 4720–4721.

(10) For perspectives on reaction dynamics in some organic reactions, see: (a) Carpenter, B. K. *Acc. Chem. Res.* **1992**, *25*, 520–528. (b) Carpenter, B. K. *Am. Sci.* **1997**, *85*, 138–149. (c) Carpenter, B. K. *Angew. Chem., Int. Ed.* **1998**, *37*, 3340–3350.

(11) Stereochemical studies on two 1-ethynylbicyclo[4.1.0]heptane to bicyclo[4.3.0]non-1(9)-ene isomerizations have shown that antarafacial utilization of the allylic moiety does occur, even when extended **Z-2-ex** diradical conformations are not accessible, see: (a) Baldwin, J. E.; Bonacorsi, S. J.; Burrell, R. C. *J. Org. Chem.* **1998**, *63*, 4721–4725. (b) Baldwin, J. E.; Burrell, R. C. *J. Org. Chem.* **1999**, *64*, 3567–3571.

(12) Pauli, A.; Meier, H. *Chem. Ber.* **1987**, *120*, 1617–1620.

(13) Olah, G. A.; Reddy, V. P.; Rasul, G.; Prakash, G. K. S. *J. Org. Chem.* **1992**, *57*, 1114–1118.

(1) (a) Vogel, E. *Angew. Chem.* **1960**, *72*, 4–26, note 162; Vogel, E.; Palm, R.; Ott, K. H., unpublished. (b) Overberger, C. G.; Borchert, A. E. *J. Am. Chem. Soc.* **1960**, *82*, 1007–1008, 4896–4899.

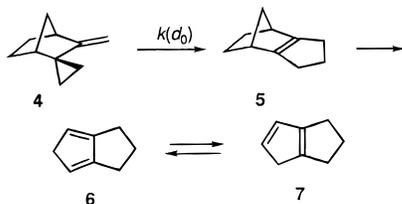
(2) Doering, W. von E.; Roth, W. R. *Tetrahedron* **1963**, *19*, 715–737.

(3) (a) Willcott, M. R.; Cargle, V. H. *J. Am. Chem. Soc.* **1967**, *89*, 723–724. (b) Cargle, V. H. Ph.D. Dissertation, University of Houston, 1969. (c) Willcott, M. R.; Cargill, R. L.; Sears, A. B. *Prog. Phys. Org. Chem.* **1972**, *9*, 25–98. (d) Willcott, M. R.; Cargle, V. H. *J. Am. Chem. Soc.* **1969**, *91*, 4310–4311.

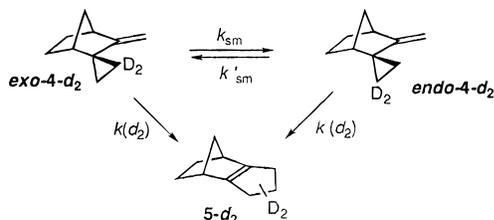
(4) Baldwin, J. E., in *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed., John Wiley & Sons: Chichester, 1995; Vol. 2, pp 469–494 and references therein.

(5) Baldwin, J. E. *J. Comput. Chem.* **1998**, *19*, 222–231 and references therein, including many of the numerous review articles on the vinylcyclopropane-to-cyclopentene rearrangement.

gave rise to the bicyclic dienes **6** and **7**, with rate constant $k(d_0) = 2.26 \times 10^{-6} \text{ s}^{-1}$ (5 kinetic points, GC analyses, $R^2 = 0.989$).



A sample of **4-d₂** (*exo-4-d₂* (deuterium at δ 0.49 and 0.79); *endo-4-d₂* (δ at 0.65 and 0.69) = 86.7:13.3, by ^2H NMR spectroscopy at 92.1 MHz) was obtained through the same sequence, using CD_2I_2 in place of CH_2I_2 in the first step. The rate constant for the structural isomerizations converting *exo-4-d₂* and *endo-4-d₂* to **5-d₂** (and on to **6-d₂** and **7-d₂**) at 309 °C was slightly slower for the labeled reactant: $k(d_2) = 1.8 \times 10^{-6} \text{ s}^{-1}$.¹³ Thermal stereomutations interconverting *exo-4-d₂* and *endo-4-d₂* were followed by ^2H NMR spectroscopy: the percent diastereomeric excess— $100(\text{exo-4-d}_2 - \text{endo-4-d}_2)/(\text{exo-4-d}_2 + \text{endo-4-d}_2)$ —as a function of time (73.4, 47.4, 23.2, 12.2, and 3.0, after 0, 1, 3, 5, and 20 h) showed that stereomutations were much faster. The function $\text{endo-4-d}_2(t) - \text{endo-4-d}_2(20 \text{ h})$ was well-modeled through a simple exponential function, giving $(k_{\text{sm}} + k'_{\text{sm}}) = 1.18 \times 10^{-4} \text{ s}^{-1}$ ($R^2 = 0.999$).

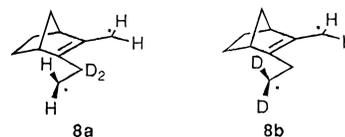


After 20 h (more than 12 half-lives), *exo-4-d₂*:*endo-4-d₂* was found to be 51.5:48.5, so that $k_{\text{sm}} = 5.7 \times 10^{-5} \text{ s}^{-1}$ and $k'_{\text{sm}} = 6.1 \times 10^{-5} \text{ s}^{-1}$. The slight $k_{\text{sm}}, k'_{\text{sm}}$ inequality might be taken as indicative of some preference for C3–C(exo) versus C3–C(endo) bond cleavage and normal secondary deuterium kinetic isotope effects, but the calculated difference is small: if there is any preference at all, it is very minor.

For *exo-4-d₂* and **4** $k_{\text{sm}}:k(d_0)$ is ~ 25 , a ratio similar to one found for vinylcyclopropanes **c-1-d** and **1**: the stereomutation rate constant $k_{\text{ct}} = k(\text{cis-to-trans})$ for **c-1-d** is $2.5 \times 10^{-4} \text{ s}^{-1}$ at 309

°C,³ $k(\mathbf{1} \rightarrow \mathbf{3})$ at this temperature is $7.7 \times 10^{-6} \text{ s}^{-1}$,¹⁵ and the ratio $k_{\text{ct}}:k(\mathbf{1} \rightarrow \mathbf{3})$ is ~ 32 .

The geometrical constraints imposed on the vinylcyclopropane sub-system in *exo-4-d₂* do not impede the stereomutation process governed by k_{sm} to any significant extent, demonstrating that access to *E-2* diradicals is not required for such epimerizations. Extended diradical transition structures analogous to **Z-2-ex** such as **8a** and **8b**—structures that are unlikely to have any mutually stabilizing interactions between the two radical entities—seem thoroughly satisfactory alternatives. They appear to be readily accessible from **4-d₂** and to be of substantially lower energy than the diradicaloid transition structures involved in [1,3] shift reactions leading to **5-d₂**, just as implied by theory for the parent system.^{6e,f}



The kinetic results found in the present work answer the question posed by Wilcott and Cargle in 1967:³ stereomutations shown by vinylcyclopropanes may occur through both **Z-2** and **E-2** reaction manifolds. The diradical transition structures implicated in these stereomutations would be devoid of special radical–radical stabilizing effects. Our results are in complete harmony with the most recent theory based on CASSCF/6-31G* and CASSCF–(4,4)/6-31G* calculations, which find **Z-2-ex** some 2.7–3.2 kcal/mol below the transition structure for rearrangement to cyclopentene (“**TS13**”^{6e} or “[**1a,3s**]TS, the transition state for the *si* shift”^{6f}). Whatever “energy of concert” may be associated with the transition structure for the vinylcyclopropane rearrangement it seems more than overshadowed by other geometrically and electronically dictated energy-costly influences.

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

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(14) The ratio $k(d_0)/k(d_2)$ is not known with much precision, for the rate constants were derived from limited data.

(15) Lewis, D. K.; Charney, D. J.; Kalra, B. L.; Plate, A. M.; Woodard, M. H.; Cianciosi, S. J.; Baldwin, J. E. *J. Phys. Chem. A* **1997**, *101*, 4097–4102.