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Thermal Isomerization of *cis,anti,cis*-Tricyclo[6.3.0.0^{2,7}]undec-3-ene to *endo*-Tricyclo[5.2.2.0^{2,6}]undec-8-ene

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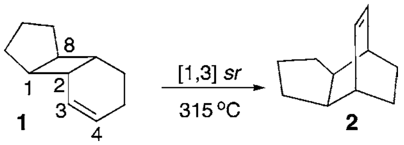
ABSTRACT

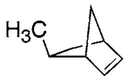
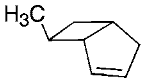
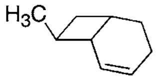
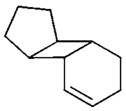


The gas-phase thermal isomerization of *cis,anti,cis*-tricyclo[6.3.0.0^{2,7}]undec-3-ene (1) to *endo*-tricyclo[5.2.2.0^{2,6}]undec-8-ene (2) at 315 °C occurs cleanly through a symmetry-forbidden [1,3] suprafacial,retention (*sr*) pathway.

Woodward and Hoffmann's 1965 seminal communication on sigmatropic rearrangements dealt primarily with hydrogen shifts; [1,3] carbon migrations were mentioned only tangentially in a footnote.[1] A more detailed consideration of sigmatropic rearrangements including carbon shifts was provided in 1969.[2,3] Despite the fact that Frey had already formulated a mechanistically attractive analysis of the vinylcyclobutane-to-cyclohexene isomerization as a diradical-mediated process,[4,5] Woodward and Hoffmann's paradigm, when applied to [1,3] carbon sigmatropic migrations,[2,3] proved appealing to many. Serious debate over the importance of orbital symmetry control in such thermal isomerizations has continued into the present century.

An isomerization of a bicyclic vinylcyclobutane, the conversion of 5-*exo*-methylbicyclo[2.1.1]hex-2-ene to 6-*exo*-methylbicyclo[3.1.0]hex-2-ene reported in 1969[6] (Table 1, entry 1), contributed prominently to an almost universal acceptance of the Woodward−Hoffmann interpretation of vinylcyclobutane-to-cyclohexene conversions as concerted [1,3] sigmatropic rearrangements, for the strongly favored product corresponded to the allowed suprafacial inversion

Table 1. Stereochemistry of [1,3] Shifts for Bicyclic and Tricyclic Vinylcyclobutanes

compound	*t* (°C)	*si*(%)	*sr*(%)	*si/sr*	ref.
	120–150	99.5	0.5	200	6
	250–300	87	13	6.8	10
	275–315	71	29	2.4	12
	315	0	100	0	this work

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[†] Syracuse University.
[‡] Franklin and Marshall College.
(1) Hoffmann, R.: Woodward, R. B. *J. Am. Chem. Soc.* **1965**, *87*, 4389−4390.
(2) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781−853.
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(*si*) reaction stereochemistry. 6-*endo*-Acetoxybicyclo[3.2.0]hept-2-enes labeled with an *exo*-deuterium[7] or an *exo*-methyl[8] substituent at the migrating carbon C7 similarly showed that [1,3] carbon shift products were formed with more inversion than retention: the reported *si*/*sr* values were >19 for the *exo*-deuterium-labeled reactant and 9.3 for the *exo*-methyl substrate.[9] A recent investigation of 7-*exo*-methylbicyclo-[3.2.0]hept-2-ene found that it isomerized with an *si/sr* ratio of 6.8[10] (Table 1, entry 2).

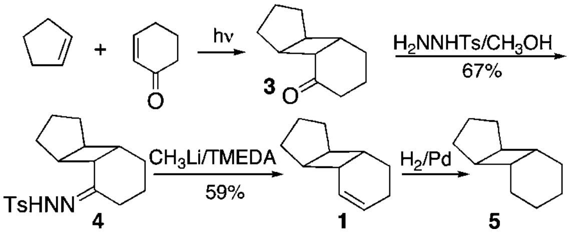
Only one prior investigation of the thermal chemistry of a bicyclo[4.2.0]oct-2-ene has appeared in the literature. In 1973, Berson and Holder reported that 7-*endo*-acetoxy-8-*exo*-methylbicyclo[4.2.0]oct-2-ene isomerized to substituted bicyclo[2.2.2]octenes with only modest selectivity favoring the symmetry-allowed *si* pathway ($si/sr = 2.2$).[11] We have recently confirmed[12] that 8-*exo*-methylbicyclo[4.2.0]oct-2-ene gives isomeric [1,3] carbon shift products reflecting a similar *si/sr* ratio, 2.4 (Table 1, entry 3).

Thus, bicyclic vinylcyclobutane systems isomerize through [1,3] carbon shifts to give two products reflecting *si* and *sr* reaction stereochemistry, with the *si* outcome strongly or at least modestly favored (Table 1, entries 1−3), a preference interpreted by Carpenter in terms of dynamic rotational effects.[13] In these systems, antarafacial pathways (*ar* or *ai*) are geometrically inaccessible for they would lead to thermochemically disadvantaged products.

The present work involved designing, making, and studying the thermal chemistry of a tricyclic vinylcyclobutane **1** for which three of the four canonical [1,3] pathways would be geometrically prohibited. According to AM1 calculations, a *si* pathway from **1** to *trans*-5,6-trimethylenebicyclo[2.2.2]-oct-2-ene[14] would be endothermic by 12.2 kcal/mol while an *sr* reaction leading to **2** would be exothermic by 10.2 kcal/mol. An *sr* shift would not be inevitable—**1** might prove thermally stable, or it might decompose only through fragmentation.

The cyclopentane substructure within **1** would restrict the [1,3] shift possibilities, and it would tend to make thermal cleavage of the C1−C2 bond to afford an alkyl, allylic diradical intermediate more difficult through restricting rotation about the C1−C8 bond. Thus, reduction of the rate constant for thermal decomposition of **1** might be expected, compared with the fragmentation and [1,3] isomerizations observed in some model systems, such as 8-*exo*-methylbicyclo-[4.2.0]oct-2-ene ($k_d = 2.0 \times 10^{-4}$ s^{-1} at 315 °C[12]).

Scheme 1



Entry to the tricyclic system in compound **1** was achieved by photochemical cycloaddition of cyclopentene and 2-cyclohexenone[15,16] with a 450-W medium-pressure mercury lamp (Scheme 1). The reaction was allowed to proceed to at least 75% conversion. The photochemical cycloadduct isolated had spectral data matching those reported for this known structure.[17] Chromatographic purification of the cycloadduct facilitated formation of the tosylhydrazone derivative; its relatively narrow melting point range (130−134 °C) signified a fairly high degree of purity. The Shapiro modification[18] of the Bamford−Stevens reaction gave compound **1**, and the structure was confirmed by a ^{13}C NMR DEPT pulse sequence: δ 131.3 (=CH), 126.8 (=CH), 46.0 (CH), 40.5 (CH), 35.8 (CH), 35.2 (CH), 32.9 (CH$_2$), 32.6 (CH$_2$), 25.6 (CH$_2$), 25.0 (CH$_2$), 21.4 (CH$_2$). Further characterization of compound **1** was achieved by catalytic reduction to *cis*,-*anti*,*cis*-tricyclo[6.3.0.0^{2,7}]undecane (**5**), which yielded a ^{13}C NMR spectrum with only six peaks: δ 43.2, 35.2, 32.2, 26.6, 26.3, 20.7. While the $C_{11}H_{18}$ saturated tricyclic hydrocarbon is not a known compound, the *cis*,*anti*,*cis* and *cis*,*syn*,*cis* analogues with 10 and 12 carbons and their ^{13}C NMR spectra (recorded for CCl_4 solutions) have been reported in the literature.[19] A simple ^{13}C NMR additivity model predicts δ 41.4, 33.8, 32.7, 26.6, 24.5, 22.6 for the *cis*,*anti*,*cis*-isomer of tricyclo[6.3.0.0^{2,7}]undecane, in reasonable agreement with the experimental values. In additional support of this structural assignment of **1**, the reaction sequence of Scheme 1 starting with the cycloaddition of cyclohexene with cyclohexenone led to the known *cis*,*anti*,*cis*-tricyclo[6.4.0.0^{2,7}]-dodecane.[19]

The precursor of compound **2** was accessed by Diels−Alder cycloaddition of 1,3-cyclohexadiene and 2-cyclopentenone using aluminum trichloride as a catalyst.[19] Subsequent reduction of ketone **6**[20] to compound **2** was accomplished via the following three-step sequence:[21] treatment with $LiAlH_4$, conversion of the resultant alcohols to mesylate derivatives, and further reduction with $LiEt_3BH$. Substitution of $LiEt_3BH$ for $LiAlH_4$ was necessitated by the observation of both substitution and elimination products with $LiAlH_4$.

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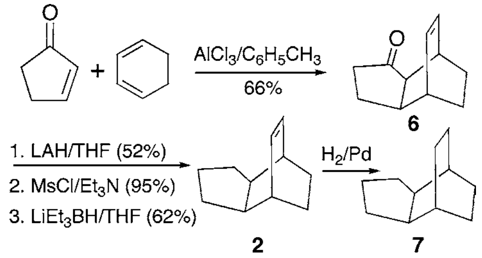
Scheme 2



This sequence of reactions (Scheme 2) gave the endo isomer of compound **2**, a known compound.[22] Catalytic hydrogenation of **2** converted it to another known compound (**7**) with six nonequivalent carbons: δ 41.1, 30.0, 28.1, 27.2, 26.6, 20.3. These ^{13}C NMR chemical shifts match those reported in the literature. [23,24]

The thermal reactions of **1** were followed at 315 °C using pentane as a bath gas and a gas-phase static reactor.[25] Reaction time versus relative concentration data were secured through capillary GC analyses; the internal standard cyclodecane, product **2**, and reactant **1** were well resolved and eluted in that order (Figure 1). Product mixtures were exceptionally clean; minor side products were not seen. Data from six kinetic runs gave rate constants k_d (for first-order loss of **1**) = $(k_f + k_{sr}) = 4.4 \times 10^{-6}$ s^{-1}, k_{sr} (for the isomerization $\mathbf{1} \rightarrow \mathbf{2}$) = 1.4×10^{-6} s^{-1}, and $k_f = 3.0 \times 10^{-6}$ s^{-1} (Scheme 3). The k_f/k_{sr} ratio is 2.1.

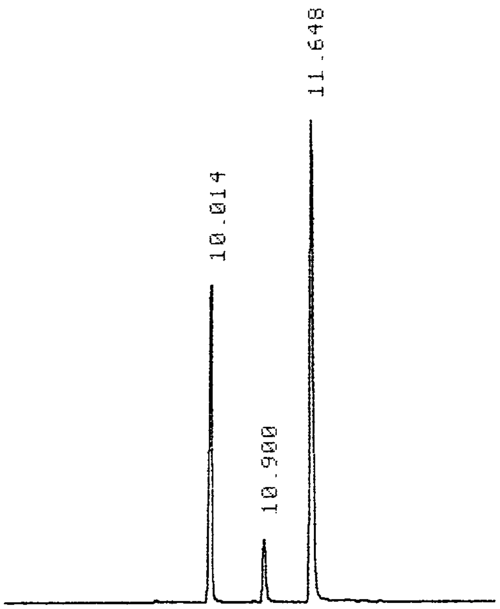
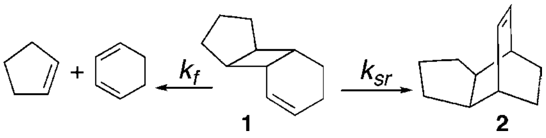


Figure 1. Capillary GC analysis of gas-phase thermal reaction mixture from **1** after 19 h at 315 °C: from left to right, internal standard cyclodecane, **2**, and **1**.

Scheme 3



The simplest mechanistic explanation for the thermal behavior of **1** is homolytic cleavage of the C1−C2 bond to generate an alkyl, allylic diradical intermediate that partitions itself between potential reformation of **1**, formation of the [1,3] *sr* isomerization product **2**, and fragmentation. The [1,3] shift in compound **1** is more competitive with fragmentation than in 8-*exo*-methylbicyclo[4.2.0]oct-2-ene (Table 1, entry 3), which at 315 °C affords predominantly fragmentation with lesser amounts of the [1,3] shift products and epimerization in a ratio of 74:15:11, respectively; the $k_f/(k_{sr} + k_{si})$ ratio is 4.9.[12]

In summary, the tricyclic vinylcyclobutane **1** undergoes thermal isomerization exclusively through an *sr* pathway; the *si/sr* value is 0 (Table 1, entry 4). Notably, this is the first such example of a vinylcyclobutane labeled with an *exo*-alkyl substituent on the migrating carbon that proceeds without any contribution from the *si* pathway. The geometrical constraints in **1** force a symmetry-forbidden suprafacial, retention outcome without greater fragmentation or lesser [1,3] carbon-shift contributions.

The conversion of **1** to **2** provides another example of a vinylcyclobutane-to-cyclohexene isomerization taking place through a short-lived diradical intermediate giving products in proportions influenced by geometrical constraints and dynamic factors, rather than by more or less control by orbital symmetry influences.[26]

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