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

LETTERS 2005 Vol. 7, No. 23 5195–5197

ORGANIC

John E. Baldwin,[†] Andrew R. Bogdan,[‡] Phyllis A. Leber,^{*,‡} and David C. Powers[‡]

Department of Chemistry, Syracuse University, Syracuse, New York 13244, and Department of Chemistry, Franklin and Marshall College, Lancaster, Pennsylvania 17604

phyllis.leber@fandm.edu

Received August 18, 2005

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 diradicalmediated 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 1969⁶ (Table 1, entry 1), contributed prominently to an almost universal

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

compound	t(°C)	<i>si</i> (%)	<i>sr</i> (%)	si/sr	ref.
H ₃ C	120– 150	99.5	0.5	200	6
H ₃ C	250– 300	87	13	6.8	10
H ₃ C	275– 315	71	29	2.4	12
	315	0	100	0	this work

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

(6) Roth, W. R.; Friedrich, A. Tetrahedron Lett. 1969, 31, 2607-2610.

[†] 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.

⁽³⁾ Woodward, R. B.; Hoffmann, R. The Conservation of Orbital Symmetry; Academic Press: New York, 1970.

⁽⁴⁾ Frey, H. M. Adv. Phys. Org. Chem. 1966, 4, 148-193.

⁽⁵⁾ Frey, H. M.; Walsh, R. Chem. Rev. 1969, 69, 103-124.

^{10.1021/}ol052004k CCC: \$30.25 © 2005 American Chemical Society Published on Web 10/19/2005

(si) reaction stereochemistry. 6-endo-Acetoxybicyclo[3.2.0]hept-2-enes labeled with an exo-deuterium⁷ or an exo-methyl⁸ 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 6.8¹⁰ (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-8exo-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 confirmed¹² that 8-exo-methylbicyclo[4.2.0]oct-2ene 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-ene¹⁴ 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 ($k_d = 2.0 \times 10^{-4} \text{ s}^{-1}$ at 315 °C¹²).

Entry to the tricyclic system in compound 1 was achieved by photochemical cycloaddition of cyclopentene and 2-cy-



clohexenone^{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 modification¹⁸ of the Bamford-Stevens reaction gave compound 1, and the structure was confirmed by a ¹³C 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 (CH₂), 32.6 (CH₂), 25.6 (CH₂), 25.0 (CH₂), 21.4 (CH₂). 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 ¹³C 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 ¹³C NMR spectra (recorded for CCl₄ solutions) have been reported in the literature.¹⁹ A simple ¹³C 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 LiAlH₄, conversion of the resultant alcohols to mesylate derivatives, and further reduction with LiEt₃BH. Substitution of LiEt₃BH for LiAlH₄ was necessitated by the observation of both substitution and elimination products with LiAlH₄.

⁽⁷⁾ Berson, J. A.; Nelson, G. L. J. Am. Chem. Soc. 1967, 89, 5503-5504.

⁽⁸⁾ Berson, J. A.; Nelson, G. L. J. Am. Chem. Soc. 1970, 92, 1096-1097.

⁽⁹⁾ Berson, J. A. Acc. Chem. Res. 1972, 5, 406-414.

⁽¹⁰⁾ Bender, J. D.; Leber, P. A.; Lirio, R. R.; Smith, R. S. J. Org. Chem. 2000, 65, 5396-5402. (11) Berson, J. A.; Holder, R. W. J. Am. Chem. Soc. 1973, 95, 2037-

²⁰³⁸

⁽¹²⁾ Bogle, X. S.; Leber, P. A.; McCullough, L. A.; Powers, D. C. J. Org. Chem. 2005, 70, in press.

⁽¹³⁾ Carpenter, B. K. J. Am. Chem. Soc. **1995**, 117, 6336–6344. (14) (a) Clemans, G. B. J. Org. Chem. **1973**, 38, 3459–3461. (b) Clemans, G. B.; Blaho, J. K. J. Org. Chem. 1987, 52, 1621-1622.

⁽¹⁵⁾ Cantrell, T. S. J. Org. Chem. 1974, 39, 3063-3070.

⁽¹⁶⁾ Eaton, P. E. J. Am. Chem. Soc. **1962**, 84, 2454–2455. (17) Lange, G. L.; Gottardo, C. Magn. Reson. Chem. **1996**, 34, 660– 666.

⁽¹⁸⁾ Lightner, D. A.; Gawronski, J. K.; Bouman, T. D. J. Am. Chem. Soc. 1980, 102, 5749-5754.

⁽¹⁹⁾ Salomon, R. G.; Folting, K.; Streib, W. E.; Kochi, J. K. J. Am. Chem. Soc. 1974, 96, 1145-1152.

⁽²⁰⁾ Fringuelli, F.; Guo, M.; Minuti, L.; Pizzo, F.; Taticchi, A.; Wenkert, E. J. Org. Chem. 1989, 54, 710-712.

⁽²¹⁾ Masjedizadeh, M. R.; Dannecker-Doerig, I.; Little, R. D. J. Org. Chem. 1990, 55, 2742-2752.



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 ¹³C 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**) = $(k_f + k_{sr}) = 4.4 \times 10^{-6} \text{ s}^{-1}$, k_{sr} (for the isomerization **1** \rightarrow **2**) = 1.4 × 10⁻⁶ s⁻¹, and $k_f = 3.0 \times 10^{-6} \text{ s}^{-1}$ (Scheme 3). The k_f/k_{sr} ratio is 2.1.



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 $k_{\rm f}/(k_{\rm sr} + k_{\rm si})$ 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

Acknowledgment. We thank the NSF for support of this work through CHE-0244103 and CHE-0211120 at Syracuse University and CHE-0075097 at Franklin & Marshall College and acknowledge the Donors of the American Chemical Society Petroleum Research Fund for partial support of this research at Franklin & Marshall College.

OL052004K

⁽²²⁾ Takaishi, N.; Fujikura, Y.; Inamoto, Y. J. Org. Chem. 1975, 40, 3767–3772.

⁽²³⁾ Inamoto, Y.; Aigami, K.; Takaishi, N.; Fujikura, Y.; Tsuchihasahi, K.; Ikeda, H. J. Org. Chem. 1977, 42, 3833–3839.

⁽²⁴⁾ Murakhovskaya, A. S.; Stepanyants, A. U.; Zimina, K. I.; Aref'ev, O. A.; Epishev, V. I. Bull. Acad. Sci. USSR, Div. Chem. Sci. 1975, 24, 847–849.

 ⁽²⁵⁾ Baldwin, J. E.; Burrell, R. C. J. Org. Chem. 1999, 64, 3567–3571.
(26) Leber, P. A.; Baldwin, J. E. Acc. Chem. Res. 2002, 35, 279–287.