Stereochemistry of the Thermal Isomerizations of *trans*-1-Ethenyl-2-phenylcyclopropane to 4-Phenylcyclopentene

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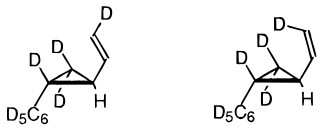
Received April 26, 1996[⊗]

Abstract: The stereochemical course of the thermal isomerization of *trans*-1-ethenyl-2-phenylcyclopropane to 4-phenylcyclopentene at 216.4 °C in the gas phase has been uncovered through syntheses and kinetic studies based on chiral d_9-labeled analogs. This example of the vinylcyclopropane-to-cyclopentene rearrangement takes place with the participation of all four stereochemically distinct paths, the relative contributions (±3%) being 58% *si*, 8% *ar*, 24% *sr*, and 10% *ai*. The stereochemical outcome is determined by alternative diradical transition structures of comparable energy, rather than by orbital symmetry control.

Introduction

The thermal isomerization of *trans*-1-ethenyl-2-phenylcyclopropane (*t*-**1**-d_0) to 4-phenylcyclopentene (**2**-d_0) is a well-known vinylcyclopropane rearrangement; it is accompanied by cis, trans interconversion between *t*-**1**-d_0 and *c*-**1**-d_0 (Scheme 1).[1]

The kinetic situation is more complicated than implied by the simple outline of Scheme 1, for both cis and trans versions of **1**-d_0 occur in enantiomeric forms, and each rate constant for vinylcyclopropane rearrangement, k and k', could have four components corresponding to four stereochemical paths. Thus, the kinetic situation is one involving 28 rate constants or, less dauntingly, 13 independent kinetic parameters. Any experimental determination of reaction stereochemistry for the vinylcyclopropane rearrangement would need to employ isotopic labeling and chiral substrates, and deal with the inherent kinetic complexities of the situation. This challenge has now been met using the chiral d_9-labeled substrates (1*S*,2*R*)-**1**-*E* and (1*S*,2*R*)-**1**-*Z*.



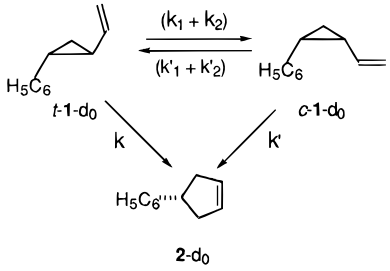
(1*S*,2*R*)-**1**-*E*

(1*S*,2*R*)-**1**-*Z*

The thermal stereomutation reactions[2] for the vinylcyclopropane (1*S*,2*R*)-**1**-*E* are shown explicitly in Scheme 2. This chiral trans starting material may be expected to undergo both cis−trans isomerization and loss of enantiomeric excess as (1*R*,2*S*)-**1**-*E* forms. Each of the four isomers in Scheme 2 would have time-dependent relative concentrations, and each could react to give four different isomers of d_9-labeled 4-phenylcyclopentene.

The relationships among the immediate precursor, stereochemistry of the cyclopentene product, and reaction stereochemistry (suprafacial or antarafacial, *s* or *a*, participation of the allyl unit; retention or inversion, *r* or *i*, at the migrating carbon, C2) for (1*S*,2*R*)-**1**-*E* are summarized in Scheme 3. Similar correlations for other isomers of **1**-*E* and **1**-*Z* reactants are easily constructed.

Scheme 1



One substantial technical difficulty inherent in this system is presented by the fact that the deuterium-labeled 4-phenylcyclopentene products cannot be analyzed through GC or chiral GC, a powerful method we have used to define rection stereochemistry for other instances of the vinylcyclopropane rearrangement.[3−6] And there is a further complication not encountered in earlier work with deuterium-labeled vinylcyclopropanes[7] or *trans*-1-ethenyl-2-methylcyclopropanes:[3,8,9] products may form from cis as well as from trans isomers. Thus, one must plan on an analytical strategy for the cyclopentene products independent of GC or chiral GC or, of course, polarimetry, a strategy able to sort out reaction mixtures containing four isomeric products, each of which could be derived from four different vinylcyclopropanes. Further, the analytical methods employed would have to be sensitive enough to permit one to acquire stereochemical information on very small (∼1 mg) samples of the cyclopentenes, for thermal reactions run to higher conversions form more and more products from stereorandom reactants, and are stereochemically less informative.

In Ghatlia's stereochemical investigation of the vinylcyclopropane rearrangement of (−)-(1*R*,2*R*)-1-(2′-(*Z*)-deuterioethenyl)-2-methylcyclopropane,[9] cyclopentene products were con-

[⊗] Abstract published in *Advance ACS Abstracts,* August 15, 1996.

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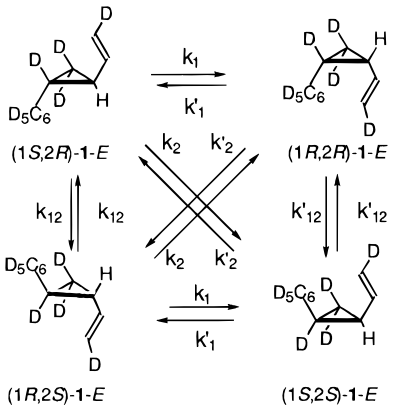
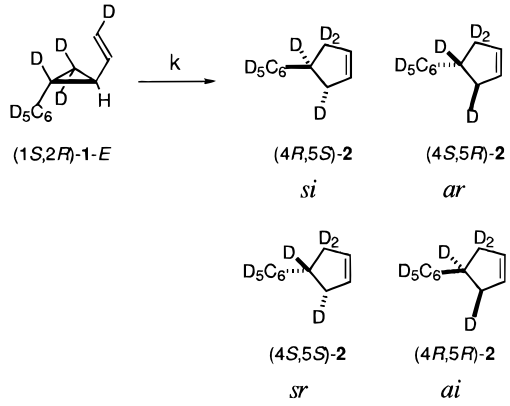
S0002-7863(96)01377-7 CCC: $12.00

Scheme 2



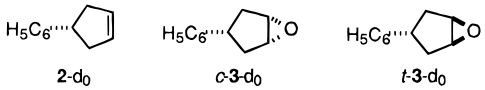
Scheme 3



verted to cyclopentane oxides, and these oxides were analyzed by ^{2}H NMR spectroscopy with the aid of an added chiral lanthanide shift reagent. A similar approach was envisioned for the present work, but for practical reasons, ^{1}H NMR was adopted as the spectroscopic tool. The required discrimination between enantiotopic hydrogens was established, stereochemical assignments based on a deuterium-labeled 4-phenylcyclopentene of known absolute stereochemistry were made, and the substrates selected for the study were prepared and isomerized.

Results

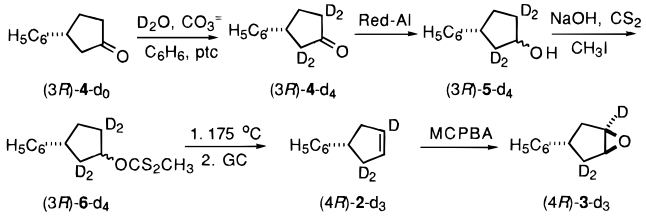
Syntheses. Authentic samples of the cis and trans isomers of 1-ethenyl-2-phenylcyclopropane (*c*-**1**-d_0, *t*-**1**-d_0) and of 4-phenylcyclopentene (**2**-d_0) were prepared following published procedures.[1,10] Oxidation of **2**-d_0 with *m*-chloroperbenzoic acid (MCPBA) in CH_2Cl_2 gave a 1:9 mixture of *c*-**3**-d_0 and *t*-**3**-d_0,



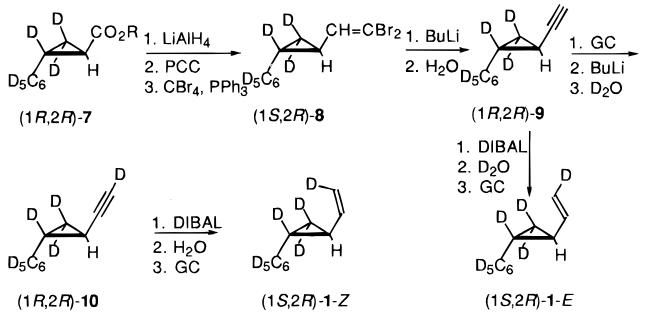
a mixture difficult to separate by preparative GC. A sample of the cis epoxide was secured by treating **2**-d_0 with an aqueous solution of *N*-bromosuccinimide followed by dehydrohalogenation of the intermediate bromohydrin with NaOH.

A chiral deuterium-labeled analog of epoxide *t*-**3**-d_0, *trans*-(4*R*)-phenylcyclopentene-1,3,3-d_3 oxide ((4*R*)-**3**-d_3), was prepared from (3*R*)-(+)-phenylcyclopentanone[11] as outlined in Scheme 4. Ketone (3*R*)-**4**-d_0 was converted to (3*R*)-**4**-d_4 using a biphasic system containing K_2CO_3, D_2O, C_6H_6, and cetyltri-

Scheme 4



Scheme 5



methylammonium bromide as a phase transfer catalyst.[12] The extent of deuterium incorporation in the two α positions was about 99%, judging from the loss of proton NMR absorption intensity at δ 2.4 and 2.7. Reduction of ketone (3*R*)-**4**-d_4 with Red-Al in benzene gave a mixture of diastereomeric alcohols (3*R*)-**5**-d_4,[13] which were converted to the xanthate esters (3*R*)-**6**-d_4 using *n*-Bu_4NHSO_4 as a phase transfer catalyst.[14,15]

The olefins formed through pyrolysis of the xanthates (3*R*)-**6**-d_4 at 175 °C were distilled from the reaction vessel as they formed and collected in a cold trap. The chiral, deuterium-labeled 4-phenylcyclopentene (4*R*)-**2**-d_3 was separated from the isomeric (3*R*)-phenylcyclopentene-2,5,5-d_3 byproduct and purified by preparative GC. Oxidation with MCPBA converted (4*R*)-**2**-d_3 to (4*R*)-**3**-d_3.

The chiral deuterium-labeled 1-ethenyl-2-phenylcyclopropanes required for this stereochemical investigation were prepared following well-established precedents (Scheme 5). Styrene-d_8 was condensed with (±)-menthyl diazoacetate[16] in the presence of a chiral copper aldimine catalyst derived from L-alanine to provide a 15:85 mixture of cis and trans isomers of (±)-menthyl 2-phenylcyclopropanecarboxylates, enriched in the (1*R*,2*R*)-**7** isomer.[17] The corresponding aldehyde, obtained through a $LiAlH_4$ reduction followed by a pyridinium chlorochromate oxidation, was converted to dibromide (1*S*,2*R*)-**8** with CBr_4 and triphenylphosphine.[18,19]

Dibromide (1*S*,2*R*)-**8** was dehydrochlorinated with *n*-BuLi in pentane to yield alkyne (1*R*,2*R*)-**9**.[18] A distilled sample

(10) 4-Substituted cyclopentenes usually give a preponderance of the trans epoxide when oxidized by MCPBA: (a) Crossley, N. S.; Darby, A. C.; Henbest, H. B.; McCullough, J. J.; Nicholls, B.; Stewart, M. F. *Tetrahedron Lett.* **1961**, *12*, 398−403. (b) Henbest, H. B. *Proc. Chem. Soc.* **1962**, 74−75. (c) Henbest, H. B. *Proc. Chem. Soc.* **1963**, 159−165. (d) Sohar, P.; Bernath, G. *Acta Chim. Acad. Sci. Hung.* **1975**, *87*, 285−291.

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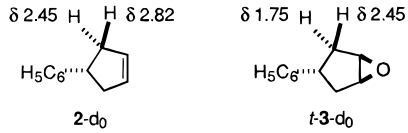
containing both alkyne (1*R*,2*R*)-**9** and some (1*R*,2*S*)-**9** was reacted with 1 equiv of DIBAL in pentane.[20,21] Reaction of the organoaluminum intermediate with an excess of D_2O afforded a mixture containing the expected olefins, unreacted alkynes, and some overreduced compounds. Olefinic products were isolated by preparative GC on a TCEPE column, and then (1*S*,2*R*)-**1**-*E* and (1*S*,2*S*)-**1**-*E* were separated from each other by GC on an Apiezon L column. Partially separated samples of the olefins were chromatographed again to yield analytically pure (1*S*,2*R*)-**1**-*E*. The ^{1}H NMR analysis of a homogeneous sample of (1*S*,2*R*)-**1**-*E* indicated 96% deuterium incorporation at the terminal vinyl position, C2′, with *E* stereochemistry:[9,22] the observed coupling constant between the trans hydrogens on C1′ and C2′ was 17 Hz.

When alkynes (1*R*,2*R*)-**9** and (1*R*,2*S*)-**9** were separated by preparative GC, and (1*R*,2*R*)-**9** was reduced with 1.5 equiv of DIBAL over a longer reaction period, a slightly higher yield of (1*S*,2*R*)-**1**-*E* was realized, and it was easily obtained as a homogeneous sample through a simple GC purification using a TCEPE column, but ^{1}H NMR spectroscopy revealed a lower (85%) incorporation of deuterium label. The extended reaction time may have allowed more d_0 olefin to be formed through a reductive elimination of the organoaluminum intermediate prior to reaction of that intermediate with D_2O.

The (1*S*,2*R*)-**1**-*Z* substrate was prepared (Scheme 5) from a sample of GC-purified (1*R*,2*R*)-**9** by way of the d_9 alkyne (1*R*,2*R*)-**10** (99% deuterium at the alkynyl position, after two exchanges), which was reduced with 1.2 equiv of DIBAL for 16 h and then treated with H_2O. Olefin (1*S*,2*R*)-**1**-*Z* was isolated in pure form from the product mixture by preparative GC. The ^{1}H NMR spectrum showed a coupling constant of 10 Hz between the two cis vinyl hydrogens on C1′ and C2′. Small samples of (1*S*,2*R*)-**1**-*E* and (1*S*,2*R*)-**1**-*Z* from each synthetic route were subjected to oxidation with $KMnO_4$ followed by treatment with diazomethane to yield methyl *trans*-2-phenylcyclopropanecarboxylates enriched in the (1*R*,2*R*) enantiomer.[3,4] Chiral GC analyses, utilizing a Cyclodex B column at 100 °C, revealed the enantiomeric excess values of these samples to be 52%, the (1*R*,2*R*) enantiomer eluting first. For analyses of the methyl *cis*-2-phenylcyclopropanecarboxylates, the Lipodex E column was used; the (1*R*,2*S*)-(-) enantiomer[23] eluted first.

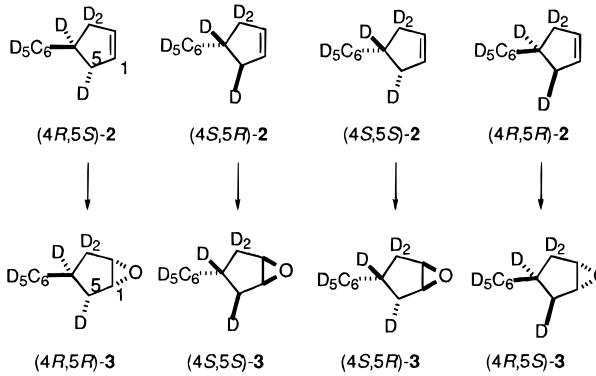
Chemical Shift Assignments for Methylene Protons in 2-d_0 and *t*-3-d_0. The proton NMR spectrum of 4-phenylcyclopentene (**2**-d_0) shows methylene proton absorptions at δ 2.45 and 2.82.[10] In the related trans epoxide, *t*-**3**-d_0, the methylene resonances come at δ 1.75 and 2.45. Expectations based on chemical shifts observed for protons in similar compounds provided the tentative assignments shown in the annotated structures below



2-d_0 *t*-**3**-d_0

associating the proton cis to phenyl with the signal at δ 2.45 in the cyclopentene and at δ 1.75 ppm in the epoxide.

Scheme 6



Experimental evidence relevant to these assignments was obtained through NOE and lanthanide shift reagent studies. The benzylic proton in epoxide **3**-d_0 is at δ 3.0; NOE difference spectra[24] showed that irradiation of the signal at δ 3.0 resulted in a positive NOE effect for the δ 2.45 signal and no appreciable response for the δ 1.75 absorption, thus indicating a cis relationship between H(benzylic) and H(at δ 2.45). Utilizing the chiral lanthanide shift reagent tris[3-[(heptafluoropropyl)-hydroxymethylene]-(+)-camphorato]europium(III), Eu(hfc)$_3$, it was possible to measure the relative downfield shifts of the signals initially centered at δ 1.75 and 2.45 in the ^{1}H NMR spectrum of **3**-d_0. One would expect that with increased additions of Eu(hfc)$_3$ the resonances for the proton cis to the epoxide function would shift downfield faster than the signals for the other methylene hydrogen.[25,26] Plots of increments of Eu(hfc)$_3$ versus chemical shifts for the two protons initially at δ 1.75 and 2.45 showed that the δ 2.45 proton moved downfield more that 50% faster than the absorption originally at δ 1.75, thus lending further support for an assignment of the proton at δ 2.45 as the one cis to the epoxide oxygen, and cis to the benzylic hydrogen. Finally, when labeled 4-phenylcyclopentenes from thermal isomerizations of (1*S*,2*R*)-**1**-*E* and (1*S*,2*R*)-**1**-*Z* were obtained, the proton NMR absorptions at δ 2.45 and 2.82 had unequal intensities, corresponding to the alternative stereochemical possibilities for the CHD unit. The related epoxides showed the same inequalities, and confirmed that the proton at δ 2.45 in the cyclopentene is at δ 1.75 in the trans epoxide.

Chiral Lanthanide Shift Reagent Studies. Experiments with several chiral shift reagents and *c*-**3**-d_0, *t*-**3**-d_0, and (4*R*)-**3**-d_3 were conducted to learn whether an NMR distinction between enantiotopic hydrogens in 4-phenylcyclopentene could be made indirectly, by way of the related trans epoxides (Scheme 6).[27] The best results were obtained using Eu(hfc)$_3$ that had been dried under vacuum several days before use. Careful addition of small quantities of Eu(hfc)$_3$ at the beginning of an analysis allowed a sure tracking as signals shifted downfield. Once partial resolution had been attained, larger quantities of Eu(hfc)$_3$ could be added to resolve the NMR absorptions of enantiotopic protons fully.

When incremental amounts of Eu(hfc)$_3$ were added to a $CDCl_3$ solution of the achiral trans epoxide **3**-d_0, the oxirane hydrogens moved downfield most rapidly, and were resolved, the benzylic hydrogen moved downfield, the hydrogens cis to the oxygen of the epoxide function were shilfted downfield and

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Table 1. Relative Concentrations of Vinylcyclopropanes and Cyclopentenes from Thermal Reactions of *c*-**1**-*E* at 216.4 °C

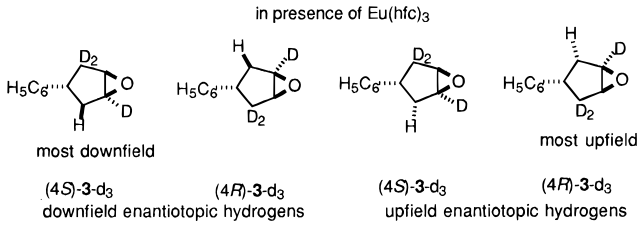
time (min)	[*t*-**1**-*E*]	[*c*-**1**-*E*]	[**2**]
0	10.0	90.0	0
10	39.6	60.4	0
20	61.3	37.4	1.3
45	78.2	19.4	2.4
60	78.9	17.8	3.3
90	79.7	16.0	4.3

Table 2. Relative Concentrations of Vinylcyclopropanes and Cyclopentenes from Thermal Reactions of (1*S*,2*R*)-**1**-*E* at 216.4 °C

time (min)	[*t*-**1**-*E*]	[*c*-**1**-*E*]	[**2**]
0	100.0	0.0	0.0
20[a]	87.4	12.0	0.6
45[a]	83.1	15.3	1.6
60[a]	83.7	14.3	2.0
60[b]	81.7	15.7	2.6
75[b]	81.3	15.7	3.0

[a] 96% deuterium incorporation at C2′. [b] 85% deuterium incorporation at C2′.

Scheme 7



were resolved, and the related geminal hydrogens (originally at δ 1.75) moved downfield less quickly, but at high concentrations of shift reagent they too were separated. Some interference from the aromatic protons in the molecule complicated the observed resonances for these signals, a complication avoided with C_6D_5 in place of C_6H_5 in the d_9-labeled systems used in the stereochemical experiments. Similar NMR studies with the cis epoxide *c*-**3**-d_0 showed that, when enough shift reagent had been added, NMR signals from it did not overlap with any signals from protons of *t*-**3**-d_0; thus, epoxidation reaction mixtures of reaction products containing *c*-**3**-d_0 and *t*-**3**-d_0 in a 1:9 ratio may be analyzed using Eu(hfc)$_3$ and ^{1}H NMR without prior separation of diastereomers, when ^{1}H NMR enantiotopic H-cis-to-benzyl-H absorptions have been shifted downfield to at least δ 13.0.

When a sample of (4*R*)-**3**-d_3 of 75% ee (by chiral GC of one diastereomer of precursor (3*R*)-**5**-d_4) was investigated with the aid of Eu(hfc)$_3$, resolved ^{1}H NMR signals for both enantiotopic versions of both sorts of methylene protons were obtained. In both cases, the less intense C5-H enantiotopic proton of the (4*S*)-phenyl stereoisomer was downfield of the resonance due to the enantiotopically related proton in the (4*R*)-phenyl system (Scheme 7).

Kinetic Data and Rate Constants. The thermal reactions of (1*S*,2*R*)-**1**-*E*, (1*S*,2*R*)-**1**-*Z* and *c*-**1**-*E* at 216.4 °C were run in the gas phase in sealed ampules. Samples of *c*-**1**-*E* were obtained from thermal reaction mixtures of (1*S*,2*R*)-**1**-*E*; they were purified to 90:10 cis:trans by preparative GC, sealed in ampules along with a minimun amount of spectral grade pentane, and isomerized at 216.4 °C. The results of analytical GC assessments of product mixtures are summarized in Tables 1 and 2.

The data of Tables 1 and 2 can be modeled with integrated functions (eqs 1 and 2) appropriate for the kinetic situation at hand (Schemes 1 and 2). A least-squares fit of the data with the aid of suitable software[28] gives optimal values for the

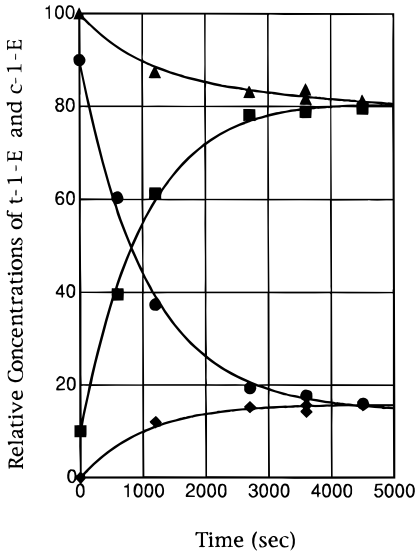


Figure 1. Relative concentrations of *t*-**1**-*E* and *c*-**1**-*E* from thermal isomerizations of 1-ethenyl-2-phenylcyclopropanes as functions of time using the data of Tables 1 and 2.

$$[t\text{-}\mathbf{1}\text{-}E](t) = A_1(e^{-\lambda_1 t}) + A_2(e^{-\lambda_2 t}) \quad (1)$$

$$[c\text{-}\mathbf{1}\text{-}E](t) = B_1(e^{-\lambda_1 t}) + B_2(e^{-\lambda_2 t}) \quad (2)$$

parameters λ_1 and λ_2 common to all four relative concentration versus time plots (Figure 1). The coefficients A_1 and A_2 (and B_1 and B_2) are not independent, for the sum must equal the initial relative concentration of the isomer.

All four calculated functions and the data points are shown in Figure 1. In each, $\lambda_1 = 9.4 \times 10^{-4}$ s^{-1} and $\lambda_2 = 1.0 \times 10^{-5}$ s^{-1}. The A_1 (or B_1) parameters and R^2 values for the four plots were -75.1 and 0.998 (*t*-**1**-*E*, Table 1), 74.9 and 0.987 (*c*-**1**-*E*, Table 1), 15.4 and 0.984 (*t*-**1**-*E*, Table 2), and -16.7 and 0.987 (*c*-**1**-*E*, Table 2).

The expressions for *t*-**1**-*E* and *c*-**1**-*E* may be integrated and used to provide an equation for the relative concentration of the 4-phenylcyclopentenes **2** as a function of time (eq 2):

$$[\mathbf{2}](t) = k((A_1/\lambda_1)(1 - e^{-\lambda_1 t}) + (A_2/\lambda_2)(1 - e^{-\lambda_2 t})) + k'((B_1/\lambda_1)(1 - e^{-\lambda_1 t}) + (B_2/\lambda_2)(1 - e^{-\lambda_2 t})) \quad (3)$$

Here k is the rate constant for all four [1,3] shift paths from the *trans*-vinylcyclopropanes, and k' is the rate constant for all [1,3] shift paths from the *cis*-vinylcyclopropanes. Using the data from Tables 1 and 2, one can plot the concentration of **2** as a function of time starting with either 90% *c*-**1**-*E* (Table 1) or 100% *t*-**1**-*E* (Table 2); the data points and calculated functions are shown in Figure 2. The best fits were found using the parameters $k = 5.7 \times 10^{-6}$ s^{-1} and $k' = 1.43 \times 10^{-5}$ s^{-1}.

With the aid of these best-fit rate constants and eq 3, one may calculate the relative concentrations and proportions of 4-phenylcyclopentene products derived for cis and trans isomers of the cyclopropane reactants over any time interval. Some calculated values for these relative concentrations that will be convenient to have at hand are gathered in Table 3.

Determinations of enantiomeric excess values for the recovered vinylcyclopropanes (1*S*,2*R*)-**1**-*E* and (1*S*,2*S*)-**1**-*E* were made by chiral GC analyses of the corresponding methyl esters, obtained through oxidations followed by esterifications with diazomethane. These observed ee values, relative concentration differences for the enantiomers of *t*-**1**-*E*, and weighted time-

(28) Deltagraph Pro 3, DeltaPoint, Inc., Monterey, CA 93940.

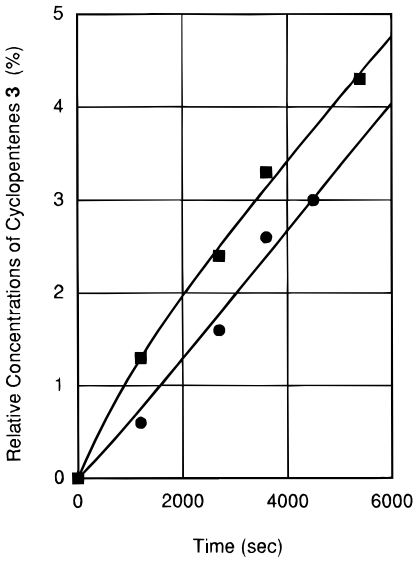


Figure 2. Relative concentrations of **2** as functions of time from 90% *c*-**1**-*E* (squares) and 100% (1*S*,2*R*)-**1**-*E* (filled circles). The data points were fit with eq 2, using the *A*, *B*, and λ parameters found through the least-squares calculations of Figure 1, to provide the new parameters $k = 5.7 \times 10^{-6}$ s^{-1} and $k' = 1.43 \times 10^{-5}$ s^{-1}.

Table 3. 4-Phenylcyclopentene Products **2** Derived from Cis and Trans Isomers of **1**-*E*

reactant	time (min)	[**2**] total	[**2**] from *c*-**1**-*E*	[**2**] from *t*-**1**-*E*	% from *t*-**1**-*E*
t-**1**-*E*	45	1.77	0.40	1.37	77.3
t-**1**-*E*	60	2.39	0.60	1.80	75.0
t-**1**-*E*	75	3.01	0.80	2.21	73.5
c-**1**-*E*	75	3.76	2.07	1.69	44.9

averaged values of ee for (1*S*,2*R*)-**1**-*E* at various reaction times (*P*(*t*) values) are recorded in Table 4.

The samples of the cis isomer (1*S*,2*S*)-**1**-*E* formed through the stereomutations of (1*S*,2*R*)-**1**-*E* were found to be racemic, or nearly racemic. If the cis isomer in reaction mixtures were always racemic, then one would expect [(1*S*,2*R*)-**1**-*E*] − [(1*R*,2*S*)-**1**-*E*] to follow a single exponential decay; the best single-exponential-function match to the experimental data was given by [(1*S*,2*R*)-**1**-*E*] − [(1*R*,2*S*)-**1**-*E*] = 52.2 exp($-3.21 \times 10^{-4}t$) ($R^2 = 0.997$). The weighted time-averaged enantiomeric excess values (*P*(*t*)) for recovered (1*S*,2*R*)-**1**-*E* were calculated from the expression $P(t) = (52.2 \int \exp(-3.21 \times 10^{-4}t)(15.4 \exp(-9.4 \times 10^{-4}t) + 84.6 \exp(-1 \times 10^{-5}t))\,dt)/\int(15.4 \exp(-9.4 \times 10^{-4}t) + 84.6 \exp(-1 \times 10^{-5}t))\,dt$. Although the ee values for recovered (1*S*,2*R*)-**1**-*E* decrease quite rapidly, the *P*(*t*) values show a more moderate time-dependent diminution.

Table 5 shows the distribution between pairs of cyclopentene products (4*R*,5*S*)-**2** + (4*S*,5*R*)-**2** and (4*S*,5*S*)-**2** + (4*R*,5*R*)-**2** formed during thermal isomerizations of (1*S*,2*R*)-**1**-*E* and of *c*-**1**-*E*. The percentages of each isomer were estimated by ^{1}H NMR analyses of preparative GC-purified samples. Fortunately, isotope-induced chemical shift perturbations were large enough so that C(5)HD proton absorptions did not overlap with the minor C(5)H$_2$ resonances. Thus, the relative integrated signal intensities in Table 5 reflect the d_9-labeled systems only; no "corrections" were needed to adjust for the lack of 100% deuterium incorporation at C2′ in starting materials.

From the product ratios of Table 5, one may calculate the rate constant ratios $(k_{si} + k_{ar})/k$ and $(k'_{si} + k'_{ar})/k'$, since one already has values for k and k' and may calculate the relative concentrations of 4-phenylcyclopentene products formed from *t*-**1**−*E* and from *c*-**1** *E* over the given reaction times (Table 4). Using each of the three product ratios from (1*S*,2*R*)-**1**-*E* as starting material with the single product ratio from *c*-**1**-*E* (Table 5), the rate constant ratios are found to be $(k_{si} + k_{ar})/k = 0.66 \pm 0.01$ and $(k'_{si} + k'_{ar})/k' = 0.52 \pm 0.01$.

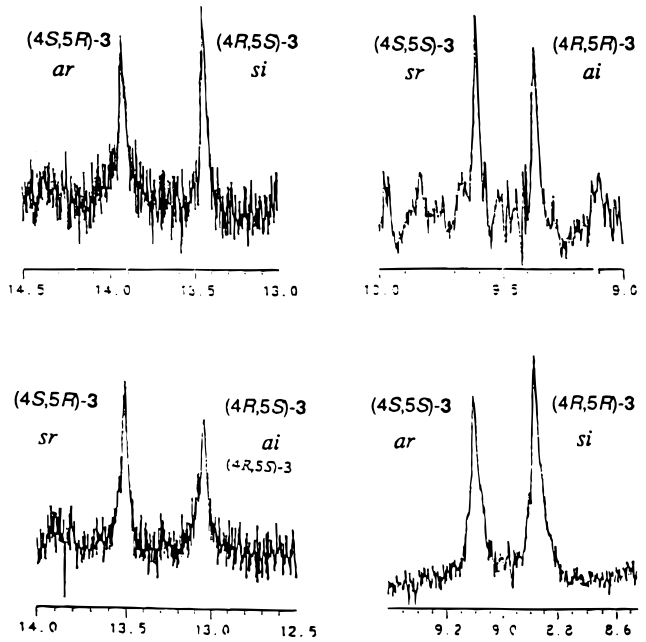


Figure 3. ^{1}H NMR spectra in the presence of Eu(hfc)$_3$ for epoxides **3** in 4-phenylcyclopentenes **2** isolated from thermal reaction mixtures: at top, from 45-min reaction of (1*S*,2*R*)-**1**-*Z*; at bottom, from 60-min reaction of (1*S*,2*R*)-**1**-*E*.

Samples of d_9-labeled 4-phenylcyclopentenes from thermal reactions of (1*S*,2*R*)-**1**-*E* and (1*S*,2*R*)-**1**-*Z* were converted to the corresponding trans epoxides, which were analyzed by ^{1}H NMR in the presence of variable proportions of Eu(hfc)$_3$. The observed ^{1}H NMR signals for enantiotopic protons provided the numerical values summarized in Table 6. Figure 3 displays segments of Eu(hfc)$_3$ resolved ^{1}H NMR spectra for the epoxides **3** stemming from the 45-min reaction of (1*R*,2*S*)-**1**-*Z* and the 60-min thermal reaction of (1*R*,2*S*)-**1**-*E*.

Reaction Stereochemistry. From the experimental evidence summarized above one may calculate rate constants for each of the four stereochemically distinct paths leading from one enantiomer of a d$_9$-labeled *trans*-1-ethenyl-2-phenylcyclopropane to a d$_9$-labeled 4-phenylcyclopentene. The logic and method for these calculations follow precedents detailed in earlier publications.[3,4,6−9] One only has to correct the observed preferences for one enantiomer (Table 6) for the contributions from racemic d_9-labeled *cis*-1-ethenyl-2-phenylcyclopropane and for the *P*(*t*) of the trans reactant. For example, for the 60-min product mixture, referring to Tables 3 and 4, 19.5% ($100 \times (25 \times 0.48)/(25 \times 0.48 + 75 \times 0.66)$) of the pair of enantiomers (4*R*,5*R*)-**3** and (4*S*,5*S*)-**3** comes from racemic cis reactants, and 80.5% from *t*-**1**-*E* having a weighted time-averaged ee (*P*(*t*)) of 31.5%. Thus, the ratio of enantiomers formed directly from the enantiomeric trans substrates is $(59 - 0.5 \times 19.5):(41 - 0.5 \times 19.5) = 61.2:38.8$. The fraction $k_{si}/(k_{si} + k_{ar})$, say *f*, may then be calculated simply, for $(100 + P(t))f + (100 - P(t))(1 - f) = 2 \times 61.2$; from the value of *f* found, the relative value of k_{si} follows: $0.855 \times 0.66 = 0.564$, the value recorded (in percentage terms) along with the other calcluated k_{rel} values in Table 7.

The average values of relative rate constants in Table 7 show consistency, but the calculated standard deviations underestimate the likely uncertainties; when the estimated uncertainty in the $(k_{si} + k_{ar})/k$ ratio is included, all relative rate constants are estimated to be reliable to ± 3%, and the values used in the following discussion, 58% *si*, 8% *ar*, 24% *sr*, and 10 *ai*, are

Table 4. Observed, Calculated, and Time-Averaged Enantiomeric Excess Values for Recovered (1*S*,2*R*)-**1**-*E* and (1*S*,2*S*)-**1**-*E* after Thermal Reactions at 216.4 °C

time (min)	(1*S*,2*R*)-**1**-*E* ee (obs, %)	[(1*S*,2*R*)-**1**-*E*] − [(1*R*,2*S*)-**1**-*E*][a]	[(1*S*,2*R*)-**1**-*E*] − [(1*R*,2*S*)-**1**-*E*][b]	*P*(*t*)[c]	(1*S*,2*S*)-**1**-*E* ee (obs, %)
0	52.2	52.2	52.2	52.2	
20	40.0	35.4	35.5	43.5	8
45	28.0	23.4	21.9	35.3	4
60	19.0	15.6	16.4	31.5	0
75	14.4	11.7	12.3	28.2	0

[a] (ee (%) of (1*S*,2*R*)-**1**-*E*/100) [*t*-**1**-*E*]. [b] Calculated with [(1*S*,2*R*)-**1**-*E*] − [(1*R*,2*S*)-**1**-*E*] = 52.2 exp(−3.21 × 10^{-4}t). [c] See text.

Table 5. Observed Relative Percentages of Cyclopentene Products **2** Formed During the Thermal Reactions of (1*S*,2*R*)-**1**-*E* and *c*-**1**-*E*

reactant	time (min)	[(4*R*,5*S*)-**2** + (4*S*,5*R*)-**2**][a]	[(4*S*,5*S*)-**2** + (4*R*,5*R*)-**2**][b]
(1*S*,2*R*)-**1**-*E*	45[c]	63	37
(1*S*,2*R*)-**1**-*E*	60[d]	61.3	38.7
(1*S*,2*R*)-**1**-*E*	75[e]	60.6	39.4
c-1-*E*	75[e]	56	44

[a] ^{1}H NMR relative intensity at 2.45 ppm. [b] ^{1}H NMR relative intensity at 2.82 ppm. [c] 96% deuterium incorporation at C2′ in the starting material. [d] 85% deuterium at C2′. [e] 90% cis isomer; 91% deuterium C2′, recovered from thermal product mixtures starting from (1*S*,2*R*)-**1**-*E* of 85% or 96% deuterium at C2′.

Table 6. Relative Concentrations of Stereoisomeric Epoxides **3** Derived from 4-Phenylcyclopentene-d_9 Thermal Rearrangement Products

reactant	time (min)	[(4*R*,5*R*)-**3**]: [(4*S*,5*S*)-**3**]	[(4*S*,5*R*)-**3**]: [(4*R*,5*S*)-**3**]
(1*S*,2*R*)-**1**-*Z*[a]	45	43:57	38:62
(1*S*,2*R*)-**1**-*E*[b]	45	60:40	56:44
(1*S*,2*R*)-**1**-*E*[c]	60	59:41	54:46
(1*S*,2*R*)-**1**-*E*[c]	75	59:41	52:48

[a] 99% deuterium incorporation at C2′ for (1*S*,2*R*)-**1**-*Z*. [b] 96% deuterium incorporation at C2′. [c] 85% deuterium incorporation at C2′.

understood to be associated with such uncertainties. The rate constants themselves may be calculated, for $k = (k_{si} + k_{ar} + k_{sr} + k_{ai}) = 5.7 \times 10^{-6}$ s^{-1}.

Discussion and Conclusion

Through syntheses of labeled chiral 1-ethenyl-2-phenylcyclopropane reactants and a reference compound for establishing absolute stereochemical assignments for enantiotopic protons in 4-phenylcyclopentenes, and through exercising suitable analytical methods, this kinetic and stereochemical study arrived at experimentally based values for the rate constants for the four paths leading from (1*S*,2*R*)-**1**-*E* or (1*S*,2*R*)-**1**-*Z* to four stereoisomers of **2**.

The mechanistic significance or interpretation of these results depends in part on theory, in part on related stereochemical findings. According to the Woodward−Hoffmann theory,[29] if the vinylcyclopropane-to-cyclopentene isomerization were concerted and controlled by the constraints and the energetic benefits of orbital symmetry control, it should take place exclusively through the "allowed" *si* and *ar* paths. The reaction stereochemistry favors these paths, but only very modestly; the $(k_{si} + k_{ar})$:$(k_{sr} + k_{ai})$ ratio is 66:34, corresponding to a $\Delta\Delta G^{\ddagger}$ of only 0.65 kcal/mol. (The $(k'_{si} + k'_{ar})$:$(k'_{sr} + k'_{ai})$ ratio for the isomerizations from the cis isomer is estimated to be 52:48, corresponding to no appreciable energetic preference at all.) Since the $k_{sr} + k_{ai}$ components are very much in evidence, and the $k_{si} + k_{ar}$ components do not enjoy any substantial energy-of-concert advantage over the "forbidden" paths, one must conclude that this vinylcyclopropane-to-cyclopentene rearrangement is not controlled by any conservation-of-orbital-symmetry consideration.

Comparisons with the stereochemical characteristics of related substituted vinylcyclopropane-to-cyclopentene rearrangements provide further insight. There are now seven examples (summarized in Table 8) of vinylcyclopropane rearrangements that have been studied in sufficient detail to learn the relative importance of all four paths, and these examples establish a clear pattern. Over a substantial range of substituents at *trans*-C2 and *E*-C2′ positions, all four possible reaction paths participate. The pattern emerges from stereochemical results obtained for different systems representing a range of kinetic complexities, studied with different analytical methods by different experimentalists, utilizing several different data reduction strategies. The essential result, the fairly consistent pattern of stereochemical outcomes, does not at this stage seem vulnerable to some undetected and unsuspected systematic error in one or another of these experimental efforts.[30,31]

Just why this pattern of stereochemical proclivities should be so generally maintained is another question, one that presently remains elusive. Further experimental and theoretical work seems required before a fully developed mechanistic understanding of the vinylcyclopropane-to-cyclopentene isomerization may be gained, and investigations designed to contribute toward that goal are in progress.

Experimental Section

General Procedures. Tetrahydrofuran was freshly distilled from benzophenone and sodium as required. Methylene chloride, pentane, and hexanes were stored over dried 4A molecular sieves for several days before use. Pyridine and DMSO were freshly distilled from CaH_2 and stored over dry 4A molecular sieves. Diethyl ether was either distilled from $LiAlH_4$ and stored over molecular sieves or used directly from a newly opened container. Carbon disulfide was stored over 4A molecular sieves for several weeks before use. Dry benzene was secured through distillation.

Measurements of enantiomeric excess values by chiral GC employed a HP 5890A gas chromatograph with a FID detector interfaced to an HP 3396 Series II or a HP 3392A integrator. All chiral GC analyses were done using either a fused silica Cyclodex B capillary column (methylated β-cyclodextrin as the stationary phase; J & W Scientific, 30 m × 0.26 mm i.d.) or a fused silica Lipodex E capillary GC column (octakis(2,6-di-*O*-pentyl-3-*O*-butyryl)-γ-cyclodextrin as the stationary phase; Macherey-Nagel, 50 m × 0.25 mm i.d.). The injection port temperatures were maintained at 160 × °C and the detector block at 300 °C. Optimal GC separations were achieved on the Cyclodex B column with a column head pressure of 25 psi.

The ^{1}H NMR and ^{13}C NMR spectra were recorded for $CDCl_3$ solution containing 0.1% Me_4Si on a General Electric 300 MHz QE-300 or 500 MHz spectrometers. Other instrumentation used in this work has been detailed elsewhere.[3,4]

(29) (a) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781−853. (b) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry;* Verlag Chemie: Weinheim, 1971; pp 120−122.

(30) Vinylcyclopropanes substituted with a *tert*-butyl group at C1′ appear to react with other stereochemical characteristics; see: (a) Gajewski, J. J.; Warner, J. M. *J. Am. Chem. Soc.* **1984**, *106*, 802−803. (b) Gajewski, J. J.; Squicciarini, M. P. *J. Am. Chem. Soc.* **1989**, *111*, 6717−6728. (c) Gajewski, J. J.; Olson, L. P. *J. Am. Chem. Soc.* **1991**, *113*, 7432−7433. (d) Gajewski, J. J.; Olson, L. P.; Willcott, M. R. *J. Am. Chem. Soc.* **1996**, *118*, 299−306.

(31) Compare Carpenter, B. K. *Acc. Chem. Res.* **1992**, *25*, 520−528.

Table 7. Relative Rate Constants (%) for Distinct Paths Followed in the Thermal Isomerizations of (1*S*,2*R*)-**1**-*Z* and (1*S*,2*R*)-**1**-*E* to 4-Phenylcyclopentenes-d_9 at 216.4 °Ct

time (min)	reactant[a]	k_{si}	k_{ar}	k_{sr}	k_{ai}
45	(1*S*,2*R*)-**1**-*Z*	58.7	7.3	24.8	9.2
45	(1*S*,2*R*)-**1**-*E*	55.7	10.3	25.4	8.6
60	(1*S*,2*R*)-**1**-*E*	56.4	9.6	23.5	10.5
75	(1*S*,2*R*)-**1**-*E*	59.6	6.4	20.7	13.3
		av 57.6 ± 1.8	8.4 ± 1.8	23.6 ± 2.1	10.4 ± 2.1

Table 8. Complete Stereochemical Studies of Thermal Rearrangements of Chiral *trans*-1-((*E*)-2′-R′-Ethenyl)-2-R-cyclopropanes to 3-R′-4-R-Cyclopentenes

R	R′	ref	*T* (°C)	*si* (%)	*ar* (%)	*sr* (%)	*ai* (%)
D	D	7	300	40	13	23	24
CH_3	D	9	284.6	55	15	18	13
CH_3	CH_3	8	296.5	65	8	22	5
CH_3	C_6H_5	3	250	60	10	19	11
C_6D_5	D		216.4	58	8	24	10
C_6H_5	CH_3	4	234.4	44	20	25	11
C_6H_5	C_6H_5	6	160	67	12	17	4

***trans*-4-Phenylcyclopentene Oxide (*t*-3-d_0).** To a 15-mg (0.1 mmol) sample of 4-phenylcyclopentene (**2**-d_0) in 2 mL of CH_2Cl_2 was added 90 mg (0.25 mmol) of 50% MCPBA. The reaction mixture was stirred overnight under N_2, and then subjected to a conventional workup. Analytical GC of the concentrate indicated two new products in a 1:9 ratio. Data for the major isomer, *t*-**3**-d_0, after purification by GC on a 15% SE-30 on Chromosorb W column: GC−MS, *m*/*z* (relative abundance) 160 (M^+, 29), 142 (29), 131 (28), 117 (100), 115 (76), 104 (37), 103 (28), 91 (44), 77 (36), 51 (28), 39 (26); ^{1}H NMR δ 7.35 (m, 5H), 3.62 (s, 2H), 3.01 (quintet, J = 8.9 Hz, 1H), 2.48 (dd, J = 7.5, 14 Hz, 2H), 1.77 (dd, J = 10.3, 14 Hz, 2H); ^{13}C NMR δ 148.5, 128.4, 127.3, 126.2, 56.6, 37.7, 35.7.

***cis*-4-Phenylcyclopentene Oxide (*c*-3-d_0).** To 80 mg (0.56 mmol) of 4-phenylcyclopentene (**2**-d_0) and 1 mL of water cooled to 0 °C was added 100 mg (0.56 mmol) of NBS with stirring. The reaction mixture was warmed to 40 °C for 2 h and then transferred to a separatory funnel. The resulting halohydrin was extracted from the aqueous solution with three 10-mL portions of ether. The ether extracts were washed with brine, dried, filtered, and concentrated, and the concentrate was combined with 1 mL of 30% NaOH. The reaction mixture was stirred for 20 h at rt and then extracted with two 25-mL portions of pentane. The pentane solution was dried over Na_2SO_4, filtered, and concentrated by distillation. Epoxide *c*-**3**-d_0 was purified on a 15% SE-30 on Chromosorb W column for analysis: GC−MS, *m*/*z* (relative abundance) 160 (22, M^+), 117 (40), 116 (24), 115 (26), 104 (17), 40 (100); ^{1}H NMR δ 7.21 (m, 5H), 3.56 (s, 2H), 3.47 (tt, J = 3.1 and 10.3 Hz, 1H), 2.32 (dd, J = 10.3 and 14.9 Hz, 2H), 2.13 (dd, J = 3.1 and 14.9 Hz, 2H).

(3*R*)-(+)-Phenylcyclopentanone ((3*R*)-4-d_0), prepared following a published route,[11] was purified on a 20% Carbowax 20M on Chromosorb W column; analytical GC showed but a single component: $[\alpha]_D$ = + 51.2° (*c* 0.205, $CDCl_3$);[32] ^{1}H NMR δ 7.3 (m, 5H), 3.43 (m, 1H), 2.68 (dd, 7.7 and 18.3 Hz, 1H), 2.4 (m, 4H), 2.0 (m, 1H); ^{13}C NMR δ 218.4, 143.0, 128.6, 126.7 (2 signals), 45.8, 42.2, 38.8, 31.2.[33]

(3*R*)-Phenylcyclopentanone-2,2,5,5-d_4 ((3*R*)-4-d_4). To a solution of ketone (3*R*)-**4**-d_0 (60 mg, 0.38 mmol) in 10 mL of dry benzene were added 5 mL of D_2O, 20 mg of K_2CO_3, and 5 mg of cetyltrimethylammonium bromide. The biphasic mixture was magnetically stirred and heated to reflux under a N_2 atmosphere for 24 h. The reaction mixture was then cooled to rt and extracted with several portions of benzene. The combined extracts were dried, filtered, and concentrated. Analysis of a small sample of the product by ^{1}H NMR showed the presence of only two upfield hydrogens relative to the integrated absorption of the benzylic hydrogen, indicative of nearly 100% deuterium labeling α to the carbonyl group. The GC retention time of the d_4 product was identical with that of (3*R*)-**4**-d_0. (Preparative GC of this ketone using a Carbowax 20M on Chromosorb W column resulted in some loss of deuterium and the appearance of ^{1}H NMR absorptions at δ 2.68 and 2.4 ppm.)

(4*R*)-Phenylcyclopentene-1,3,3-d_3 ((4*R*)-2-d_3). A 60-mg (0.37 mmol) sample of ketone (3*R*)-**4**-d_4 in 10 mL of dry benzene was cooled to 0 °C under N_2, and 0.11 mL of 3.4 M sodium bis(2-methoxyethoxy)-aluminum hydride (Red-Al) in toluene was added. The cold bath was removed, and the reaction mixture was stirred for 1 h. It was then quenched with 5 mL of water, and the products were extracted with three 15-mL portions of ether. The ether extracts were combined, dried over Na_2SO_4, filtered, and concentrated. The two diastereomeric products were purified together on a 20% Carbowax 20M column. ^{1}H NMR for the mixture: δ 7.26 (m, 10H), 4.54 (s, 1H), 4.46 (s, 1H), 3.41 (t, J = 9 Hz, 1H), 3.1 (t, 9 Hz, 1H), 2.26 (dd, J = 8 and 12.7 Hz, 1H), 2.1 (dd, J = 7.5 and 12.5 Hz, 1H), 1.9 (t, J = 11.5 Hz, 1H), 1.64 (t, J = 12 Hz, 1H), 1.56 (br s, 2H). The later eluting diastereomer was resolved into separate enantiomers by chiral GC on a Lipodex E column: it had an ee of 75%, the dominant (3*R*) enantiomer eluting first. The mixture of crude d_4 alcohols was converted into the corresponding xanthate esters, and they were pyrolyzed at 175 °C to provide a mixture of cyclopentenes (4*R*)-**2**-d_3 and (3*R*)-phenylcyclopentene-2,5,5-d_3. These olefins were separated and purified on a 20% Carbowax 20M on Chromosorb W column. Data for (4*R*)-**2**-d_3: ^{1}H NMR δ 7.26 (m, 5H), 5.77 (s, 1H), 3.45 (t, J = 8 Hz, 1H), 2.82 (ddd, J = 1.9, 9, 16.4 Hz, 1H), 2.44 (ddd, J = 2.3, 7, 16.4 Hz, 1H). Data for the (3*R*) isomer: ^{1}H NMR δ 7.23 (m, 5H), 5.93 (d, J = 2 Hz, 1H), 3.89 (d of t, J = 2.1 and 7.7 Hz, 1H), 2.39 (dd, J = 9, 12.8 Hz, 1H), 1.71 (dd, J = 6.6 and 13 Hz, 1H); ^{13}C NMR δ 142.8, 133.3, 130.9, 127.4, 126.2, 125, 50.3, 32.8, 31.5.

***trans*-(4*R*)-Phenylcyclopentene-1,3,3-d_3 Oxide ((4*R*)-3-d_3).** Following the procedure used to synthesize epoxide *t*-**3**-d_0, (4*R*)-**2**-d_3 was converted to (4*R*)-**3**-d_3, which was purified on a 15% SE-30 column; GC-MS: 169 (M^+, 1), 158 (20), 157 (20), 156 (55), 141 (32) 139 (100), 111 (49). ^{1}H NMR δ 7.27 (m, 5H), 2.98 (t, J = 9 Hz, 1H), 2.45 (dd, J = 7.8 and 14 Hz, 1H), 1.75 (dd, J = 10.31 and 14 Hz).

Resolution of Enantiotopic Proton NMR Absorptions of (4*R*)-3-d_3 With Eu(hfc)$_3$. The ^{1}H NMR spectrum of a GC purified sample of (4*R*)-**3**-d_3 in $CDCl_3$ was recorded, and then small amounts of dry tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]-europium(III) (Eu(hfc)$_3$) were added, recording the NMR spectrum after each addition. After several additions of Eu(hfc)$_3$ the ^{1}H NMR signals for C2 and both C5 hydrogens of (4*R*)-**3**-d_3 and of (4*S*)-**3**-d_3 became apparent. The dominant signals for the (4*R*) isomer could be seen at δ 13.5 and 6.7 ppm. The resolved signals for the minor (4*S*) enantiomer were seen at δ 14.0 and slightly downfield from δ 6.7.

(1*R*,2*R*)-*trans*-2-(Phenyl-d_5)cyclopropanecarboxaldehyde-2,3,3-d_3. Condensation of 10 g of styrene-d_8 (Aldrich) with (±)-menthyl diazoacetate in the presence of a chiral copper catalyst derived from L-alanine was accomplished following a well-established precedent. [17] Reduction of the ester or the corresponding carboxylic acid with $LiAlH_4$ and then oxidation using PCC afforded the trans (1*R*,2*R*) aldehyde: GC−MS, *m*/*z* (relative abundance) 154 (19), 152 (18), 126 (12), 125 (100), 124 (29), 123 (12), 122 (24), 121 (43), 98 (12), 97 (28), 54 (13), 42 (12), 40 (25).

***trans*-1-(2′,2′-Dibromoethenyl)-2-(Phenyl-d_5)cyclopropane-2,3,3-d_3-((1*S*,2*R*)-8).** The aldehyde prepared immediately above (6.9 g, 44.8 mmol) dissolved in 500 mL of dry benzene was added to 62.1 g (237 mmol) of PPh_3 and 39.8 g (120 mmol) of CBr_4. The reaction mixture was heated to reflux for 24 h under N_2, cooled to rt, and filtered through

(32) From this rotation, one may conclude that the ee of the ketone is at least 56−58%; see: (a) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* **1983**, *105*, 5935−5937, note 13. (b) Taura, Y.; Tanaka, M.; Wu, X.-M.; Funakoshi, K.; Sakai, K. *Tetrahedron* **1991**, *47*, 4879−4888.

(33) Fairlie, D. P.; Bosnich, B. *Organometallics* **1988**, *7*, 936−945.

a sintered glass funnel. Concentration of the filtrate gave a red oil which was triturated with pentane; the resulting PPh_3 was removed by filteration. Several repetitions of this procedure served to remove most of the PPh_3. Final purification was achieved by Kugelrohr distillation (0.5 mmHg) to yield 10 g (70%) of a mixture of dibromide (1*S*,2*R*)-**8** along with some cis isomer. Data for (1*S*,2*R*)-**8**: GC−MS, *m*/*z* (relative abundance) 312:310:308 (M^+ for $C_{11}H_2Br_2D_8$, 0.2:0.4:0.2), 231 (15), 229 (15), 150 (100), 149 (21), 148 (28), 121 (12).

(1*R*,2*S*)-*trans*-1-Ethynyl-2-(phenyl-d_5)cyclopropane-2,3,3-d_3 ((1*R*,2*S*)-9). To 5 g (16 mmol) of dibromide (1*S*,2*S*)-**8** in 100 mL of dry pentane under N_2 at −78 °C was added with rapid stirring 20.2 mL (40.4 mmol) of 2.0 M *n*-BuLi in pentane. The reaction mixture was stirred at −78 °C for 1 h and then warmed to rt and stirred for an additional 1 h. It was then cooled to 0 °C, and 25 mL of water was added cautiously. After 30 min at rt, the mixture was acidified with 10% HCl and the products were extracted with three 50-mL portions of pentane. These extracts were combined, dried, filtered, and concentrated. Further purification was achieved by Kugelrohr distillation (0.5 mmHg, bp 60−80 °C) to give 966 mg (40%) of crude alkyne. Data for (1*R*,2*R*)-**9**: GC−MS, *m*/*z* (relative abundance) 150 (58, M^+), 149 (56), 148 (100), 122 (12), 121 (36), 120 (27), 54 (13); ^{1}H NMR δ 1.89 (d, J = 2 Hz, 1H),1.48 (s, 1H); ^{13}C NMR δ 64.7, 10.6.

(1*S*,2*R*)-*trans*-(2′-(*E*)-Deuterioethenyl)-2-(phenyl-d_5)cyclopropane-2,3,3-d_3 ((1*S*,2*R*)-1-*E*). The 966-mg sample (6.44 mmol) of alkyne (1*R*,2*S*)-**9** dissolved in 100 mL of dry pentane in a flame-dried flask was cooled to 0 °C, and 6.66 mL (6.44 mmol) of 1.0 DIBAL in hexanes was added slowly over 15 min. The reaction mixture was stirred rapidly and allowed to warm to rt. Stirring was continued for 18 h, and the reaction was again cooled to 0 °C. Slowly, 10 mL of D_2O was added to the cooled reaction solution. The mixture was stirred rapidly for 3 h at rt, and then enough 10% HCl was added to the mixture to dissolve the gelantinous mass that had formed. The contents of the reaction flask were transferred to a separatory funnel, and the aqueous layer was extracted with three 25-mL portions of pentane. The combined organic extracts were washed with saturated $NaHCO_3$, dried, filtered, concentrated, and Kugelrohr distilled to yield 734 mg (75%) of olefin (1*S*,2*R*)-**1**-*E* along with some unreacted alkyne and some overreduced products. Preparative GC using first a 20% TCEPE and then a 14% Apiezon L column gave the olefin (1*S*,2*R*)-**1**-*E* as a homogeneous sample (analytical GC): GC−MS, *m*/*z* (realtive abundance) 153 (M^+, 38), 152 (20), 151 (18), 137 (52), 136 (100), 135 (78), 134 (50), 133 (26), 122 (17), 121 (27), 97 (17), 82 (18), 70 (28), 69 (28), 54 (23), 42 (19); ^{1}H NMR δ 5.52 (dd, J = 8.5 and 17 Hz, 1H), 5.09 (d, J = 17 Hz), 1.68 (d, J = 8.5 Hz).

(1*S*,2*R*)-*trans*-(2′-(*Z*)-Deuterioethenyl)-2-(phenyl-d_5)cyclopropane-2,3,3-d_3 ((1*S*,2*R*)-1-*Z*). A GC-purified sample of alkyne (1*R*,2*R*)-**9** (206 mg,1.37 mmol) was dissolved in dry pentane and reacted with 1.03 mL (2.06 mmol) of 2.0 M *n*-BuLi in pentane at −78 °C. The flask was warmed briefly to rt and then cooled again. To the cooled solution was added 1 mL of D_2O (99.9% D), and the reaction mixture was stirred rapidly for 30 min while being warmed to rt. The reaction solution was extracted with pentane, and the pentane extracts were dried, filtered, and concentrated to yield 185 mg (1.23 mmol) of alkyne (1*R*,2*R*)-**10**. After a second exchange reaction, ^{1}H NMR analysis of the alkyne indicated greater then 99% deuterium incorporation at the terminal alkynyl position. The labeled alkyne was placed in a reaction flask under a N_2 atmosphere and cooled to 0 °C; it was treated with 2.06 mL (2.06 mmol) of 1.0 M DIBAL in hexanes. The reaction mixture was warmed to room temperature and stirred for 18 h. The reaction flask was then cooled to 0 °C, and 3 mL of 99.9% D_2O was added with rapid stirring. The aqueous solution was extracted with two 25-mL portions of pentane. The pentane extracts were dried over Na_2SO_4, filtered, and concentrated; purification of the concentrate on a 20% TCEPE on Chromosorb P column gave 75 mg of the pure alkene (1*S*,2*R*)-**1**-*Z*): ^{1}H NMR δ 5.53 (ddd, J = 2.3, 8.4, 10.5 Hz, 1H), 4.91 (d, J = 10.3 Hz, 1H), 1.68 (d, J = 8.4 Hz, 1H).

Thermal Isomerizations. Kinetic bulbs were prepared and soaked in 12 M HCl for 24 h, rinsed with distilled water, soaked for 2 days in concentrated NH_4OH saturated with EDTA, and then rinsed 20 times each with distilled water. All bulbs were dried immediately before use in an oven heated to 160 °C. About 65 mg of a GC-purified olefin ((1*S*,2*R*)-**1**-*E* (85% or 96% D at C2′) or (1*S*,2*R*)-**1**-*Z* (99% D at C2′)) and 5 mg of hydroquinone were placed in each of a set of 90 cm^3 reaction bulbs; the bulbs were subjected to three freeze−pump−thaw cycles, and then sealed under vacuum.

All thermal reactions were conducted in a thermally regulated oil bath heated to 216.4 °C; the temperature was monitored with a calibrated digital platinum resistance thermometer (Hewlett-Packard 2802A with a HP 34740A display) and regulated to ±0.2 °C using a Bayley 253 temperature controller. Following each run, the bulb was removed from the oil bath and allowed to cool to rt; it was then cooled to −78 °C, opened, and rinsed out with dry pentane. Capillary GC analyses of the product mixtures were performed on a HP 5% phenyl methyl silicone 25 m × 0.20 mm × 0.33 mm film thickness ultra-high-performance capillary column. The GC analyses of the product mixtures from the thermal reactions of (1*S*,2*R*)-**1**-*E* are summarized in Table 2.

After capillary GC analysis of the thermolysis products, the mixture of components was subjected to preparative GC on a 14% Apiezon L column. Samples of (1*S*,2R)-**1**-*E* and *c*-**1**-*E* were recovered together and oxidized with $KMnO_4$ in benzene containing the crown ether 18-C-6.[3,4] The resulting acids were treated with CH_2N_2, and the methyl esters formed were analyzed by chiral GC on a Cyclodex B chiral GC column. The enantiomeric excesses of the recovered vinylcyclopropanes found in this indirect manner are reported in Table 4.

The cyclopentene products **2** from the thermal reactions of (1*S*,2*R*)-**1**-*E* and (1*S*,2*R*)-**1**-*Z* were isolated by preparative GC. Samples of the cyclopentenes as small as 0.5 mg were first analyzed by ^{1}H NMR to secure the information summarized in Table 5. Data for **2**: GC−MS, *m*/*z* (relative abundance) 153 (M^+, 68), 152 (33), 151 (21), 137 (49), 136 (100), 135 (77), 134 (77), 133 (23), 121 (26), 70 (26), 69 (30), 54 (19); ^{1}H NMR δ 5.8 (s), 2.45 (s), 2.8 (s). The cyclopentenes were then dissolved in CH_2Cl_2 and epoxidized with an excess of MCPBA. The resulting epoxides were isolated by extracting the CH_2Cl_2 solution with pentane and washing the organic phase with aqueous Na_2CO_3. Pure samples of the epoxides **3** were secured by preparative GC on a 15% SE-30 on Chromosorb W column. Data for the epoxides **3**: ^{1}H NMR δ 3.59 (s), 2.43 (s), 1.73 (s). The $CDCl_3$ solutions of the epoxides from each run were treated with enough Eu(hfc)$_3$ to shift the ^{1}H NMR signals originally at δ 2.47 and 1.73 downfield to approximately δ 14.0 and 9.3. The ^{1}H NMR signals for the separate enantiotopic hydrogens were well resolved in these regions of the spectrum and uncomplicated from nearby impurities (Figure 3). The relative integrated absorption intensities are summarized in Table 6.

Samples of *c*-**1**-*E* recovered from thermal isomerizations of (1*S*,2*R*)-**1**-*E* were GC purified to 90:10% cis/trans (capillary GC). Approximately 5 mg of *c*-**1**-*E* was dissolved in 50 μL of pentane to provide a stock solution; small samples of the stock solution, approximately 10 μL, were sealed in 65-mL cleaned reaction bulbs. At the completion of each reaction the cooled reaction bulbs were scored, broken open, and rinsed out with a minimum amount of solvent. The GC analyses of the thermolysis mixtures are summarized in Table 1.

A larger scale thermolysis of *c*-**1**-*E* was conducted using 20 mg of the GC-purified olefin (90:10% cis/trans by analytical GC). The bulb containing the olefin was treated in the same manner as described above. The bulb was placed in an oil bath heated to 216.5 °C for 75 min. The bulb was allowed to cool to rt and was broken open. The contents of the bulb were dissolved in pentane, analyzed by GC, and then purified by GC. The ^{1}H NMR analysis of the cyclopentene products revealed that the downfield signal at δ 2.82 was larger than the signal at δ 2.45, the relative absorption intensities being 56:44 (Table 5).

Acknowledgment. This paper is dedicated to Professor Nelson J. Leonard on the occasion of his 80th birthday. We thank the National Science Foundation for support of this work through Grant CHE 91-00246.

JA9613771