Stereochemistry of the Thermal Isomerizations of (1*R*,2*R*)-1-((*E*)-Styryl)-2-methylcyclopropane to 3-Phenyl-4-methylcyclopentenes

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Abstract: (1*R*,2*R*)-1-((*E*)-Styryl)-2-methylcyclopropane at 250 °C racemizes and isomerizes to 6-phenylhexa-1,4-(*Z*)-diene and to the four isomers of 3-phenyl-4-methylcyclopentene. From the measured rate constants for racemization and for structural isomerizations, and from information on the relative amounts of the four 3-phenyl-4-methylcyclopentenes as a function of time, the relative contributions of the four stereochemically distinct paths for this vinylcyclopropane rearrangement have been found to be 60% *si*, 10% *ar*, 19% *sr*, and 11% *ai*. The substantial contributions from these four kinetically competitive paths, participating to relative extents similar to those experimentally determined for *trans*-1-(2-deuterioethenyl)- and *trans*-1-((*E*)-propenyl)-2-methylcyclopropanes, imply that the rearrangement is neither governed by orbital symmetry constraints nor dominated by moment-of-inertia-dependent rotational propensities.

Introduction

The thermal isomerization of vinylcyclopropane to cyclopentene has been recognized since 1960 as one of the simplest known instances of a [1,3] carbon sigmatropic reaction.[1,2] Whether the isomerization should be understood as an orbital symmetry allowed and concerted process,[3] or as an isomerization not controlled by a need to conserve orbital symmetry and proceeding through diradical transition states, has remained an unresolved question.[4–14] As the fundamental mechanistic issue has remained open, the reaction has been developed and exploited in an ever-widening array of synthetic applications.[15–18]

Kinetic and stereochemical studies for the vinylcyclopropane rearrangements shown by (1*S*,2*S*)-1-((*E*)-2-deuterioethenyl)-2-methylcyclopropane and (1*R*,2*R*)-1-((*Z*)-2-deuterioethenyl)-2-methylcyclopropane,[19] and by (1*S*,2*S*)-1-((*E*)-propenyl)-2-methylcyclopropane,[20] have shown that the reactions take place with substantial contributions from all four possible paths. The orbital symmetry allowed suprafacial, inversion stereochemical mode is the most important for the *trans*-1-vinyl- and *trans*-1-((*E*)-propenyl)-2-methylcyclopropanes, amounting to 55% and 65% of all [1,3] sigmatropic reactions, and yet the two "forbidden" paths contribute 30% and 27% in these two cases of the rearrangement.[19,20]

The present work sought and attained a third complete stereochemical delineation for a vinylcyclopropane rearrangement using (1*R*,2*R*)-1-((*E*)-styryl)-2-methylcyclopropane as the substrate. The relative importance of the four stereochemical paths for isomerization to 3-phenyl-4-methylcyclopentenes, it was hoped, might reveal a mechanistically suggestive pattern of relative rate constants when compared with similar data for the analogous deuteriovinyl[19] and propenyl[20] systems.

The kinetic situation is outlined in Scheme I. The [1,3] sigmatropic reactions leading from (1*R*,2*R*)-1-((*E*)-styryl)-2-methylcyclopropane ((1*R*,2*R*)-**1**) to 3-phenyl-4-methylcyclopentenes (**2**) are in competition with two other reactions: racemization of the cyclopropane through a two-center epimerization and geometrical isomerization of the substrate through one-center epimerizations to one or the other chiral form of *cis*-1-((*E*)-styryl)-2-methylcyclopropane, followed by a rapid [1,5] hydrogen shift from methyl[21] to give 6-phenylhexa-1,4(*Z*)-diene (**3**).

The racemization rate constant is $k_\alpha = 2k_a$; k_b is the sum of four rate constants for [1,3] shifts ($k_{si} + k_{ar} + k_{sr} + k_{ai}$); and the rate constant for structural isomerizations, k_i, is ($k_b + k_c$).

Here, as in the similar deuterioethenyl and propenyl systems studied earlier,[19,20] the experimental challenge is strongly conditioned by the fact that k_b is much smaller than k_α and k_i: while the methyl substituent at C(2) and the rapid [1,5] hydrogen shift from cis isomers to form diene **3** that it dictates simplify the kinetic analysis, because all cyclopentene products stem from *trans*-2-methyl-1-vinylcyclopropanes, the quantitative definitions of all species present in thermal reaction mixtures and determinations of absolute stereochemistry necessitate either work with relatively large amounts of substrates or accurate mea-

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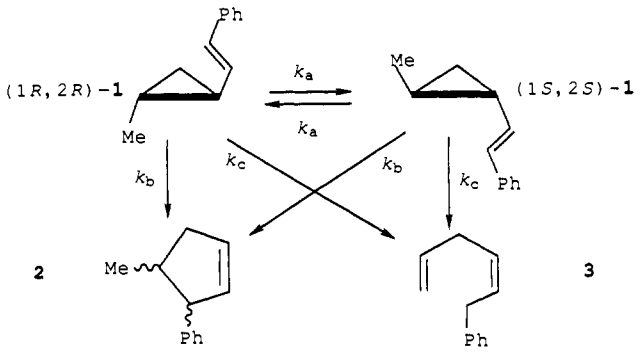
Scheme I

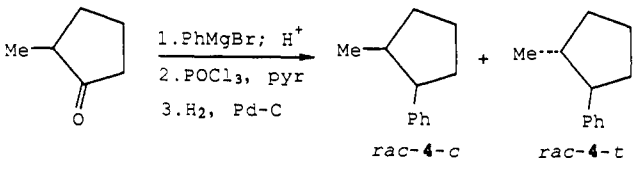


surements of optical purities on very small amounts of cyclopentene products. The essential stereochemical information must be found in the few percent of the 3-phenyl-4-methylcyclopentenes **2** formed before the substrate is substantially racemized or largely isomerized to diene **3**! For the present study, the latter alternative was selected, and analytical gas chromatography using a capillary column having a chiral stationary phase, a Machery-Nagel Lipodex E (octakis(2,6-di-*O*-pentyl-3-*O*-butyryl)-γ-cyclodextrin) column, was adopted as the mainstay analytical tool.

Chiral gas chromatography is by now well established as a powerful method whenever it does indeed resolve the enantiomeric mixture or mixtures which must be quantitated; modified cyclodextrins have been particularly useful as chiral stationary phases.[22] For laboratories lacking a full inventory of different chiral GC columns, the applicability of the method in a given case then involves some uncertainty until the essential resolutions have been demonstrated. The first task addressed was to learn if chiral GC might prove effective for analyses of the four 3-phenyl-4-methylcyclopentanes (**4**).

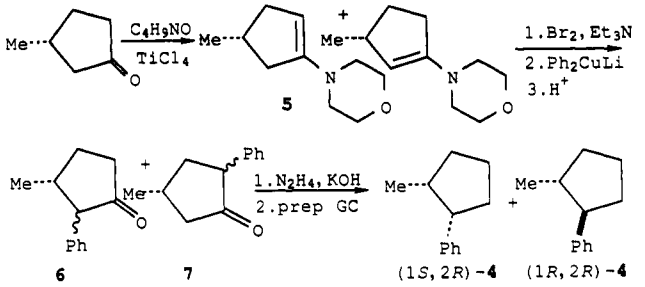
Results

Test of Chiral Gas Chromatographic Method. To check the applicability of a chiral GC based analytical strategy, and anticipating that assignments of absolute stereochemistry might be based on 1-phenyl-2-methylcyclopentanes, the racemic cis and trans isomers of these cyclopentanes (*rac*-**4**-*c* and *rac*-**4**-*t*) were prepared from 2-methylcyclopentanone through reaction with phenylmagnesium bromide followed by dehydration and subsequent catalytic hydrogenation.[23,24]

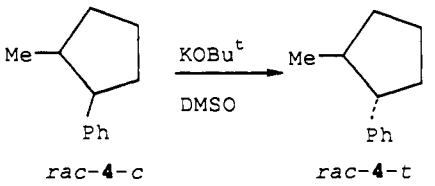


The cis and trans isomers of **4** could be readily separated by analytical and by preparative gas chromatography. Analyses under a variety of conditions with the Lipodex E column showed that the mirror image forms of **4**-*t* could be well separated, but the enantiomers of **4**-*c* were not adequately resolved. This disappointment was ameliorated quickly, though, because the chiral GC unresolvable mixture of **4**-*c* antipodes was converted to the chiral GC separable mixture of **4**-*t* enantiomers by isomerization with potassium *tert*-butoxide in DMSO at 80 °C.[25] If this isomerization does not compromise stereochemistry at the methyl-substituted asymmetric center, the chiral GC analytical tactic will work for determining ee values for both **4**-*t* isomers,

Scheme II

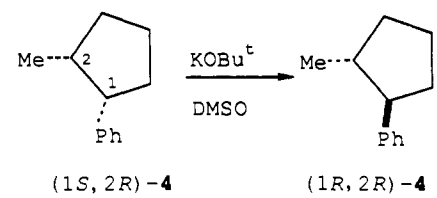


directly, and **4**-*c* isomers, indirectly, after isomerization to the resolvable **4**-*t* enantiomers.



Assignments of Absolute Stereochemistry. The first correlation used to established the absolute stereochemistry of the *trans*-1-phenyl-2-methylcyclopentanes was based on (*R*)-(+)-3-methylcyclopentanone[26] (Scheme II). Adapting the method for introducing a phenyl group α to a ketone carbonyl function reported by Rathke and Vogiazoglou,[27] the chiral ketone was converted[28] to a mixture of enamines (**5**); they were subjected to allylic bromination, and the bromides were replaced by phenyl from (diphenylcuprio)lithium to give after hydrolysis a mixture of ketones **6** and **7**. Wolff–Kishner reduction[29] and preparative GC afforded pure samples of (1*R*,2*R*)-**4** and (1*S*,2*R*)-**4**.

Chiral GC analyses of *rac*-**4**-*t*, of the authentic sample of (1*R*,2*R*)-**4**, and of mixtures of *rac*-**4**-*t* and (1*R*,2*R*)-**4** showed that the enantiomers appear in a chromatograph in the order (1*S*,2*S*)-**4** before (1*R*,2*R*)-**4**. When the authentic sample of the chiral cis isomer (1*S*,2*R*)-**4** was isomerized by KOBu^t in DMSO and the product trans isomer was scrutinized by chiral GC, it was found to be (1*R*,2*R*)-**4**, exclusively (Figure 1). The base-catalyzed isomerization thus does not lead to epimerization at C(2), and the ee of a sample of **4**-*c* may indeed be determined by chiral GC examination of the corresponding mixture of **4**-*t* isomers after this isomerization.



To be doubly sure of the assignment of absolute stereochemistry, a second correlation with a different reference sample was completed. The (1*R*,2*R*) isomer of 1-(methoxycarbonyl)-2-methylcyclopentane ((1*R*,2*R*)-**8**) was prepared both from (1*R*,2*R*)-**4** through oxidative degradation of the phenyl group[30] and esterification of the resulting carboxylic acid with diazomethane and from (*R*)-(+)-3-methylcyclohexanone,[31] following

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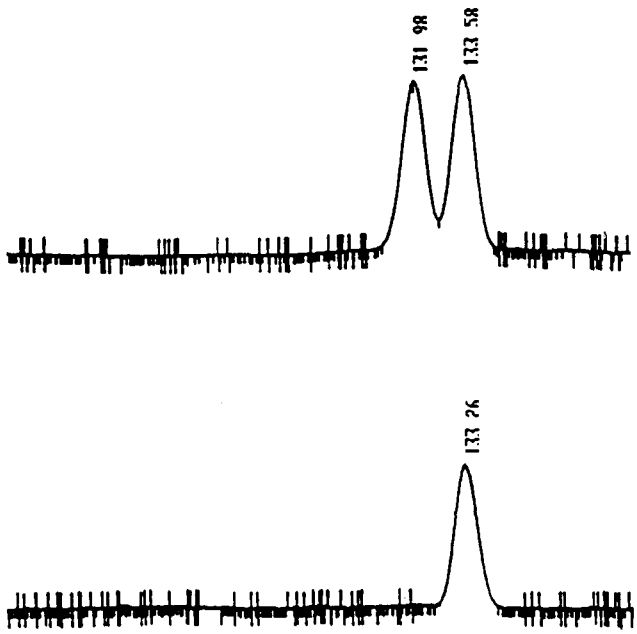


Figure 1. Chiral GC resolution on a Machery-Nagel Lipodex E column of enantiomeric forms of *trans*-1-phenyl-2-methylcyclopentane: (top) *rac*-**4**-*t*; (bottom) (1*R*,2*R*)-**4** from base-catalyzed isomerization of the cis isomer (1*S*,2*R*)-**4** (Scheme II).

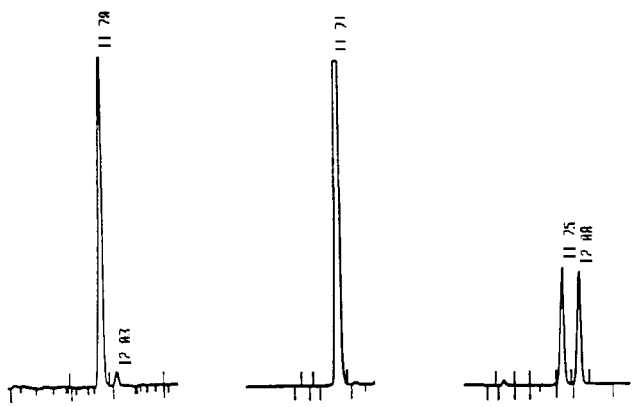
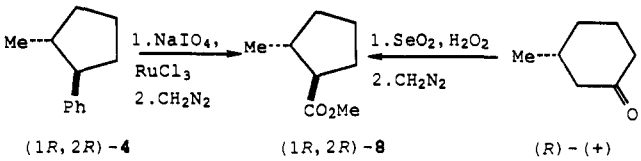


Figure 2. Chiral GC resolution of enantiomeric forms of *trans*-1-(methoxycarbonyl)-2-methylcyclopentane: (left) (1*R*,2*R*)-**8** from (1*R*,2*R*)-**4**, 96% ee; (center) (1*R*,2*R*)-**8** from (*R*)-(+)-3-methylcyclohexanone; (right) *rac*-**8**.

the route described by Hill, Foley, and Gardella.[32] Based on chiral GC analyses (Figure 2), the ester (1*R*,2*R*)-**8** derived from the sample of (1*R*,2*R*)-**4** was of 96% ee, while the sample from (*R*)-(+)-3-methylcyclohexanone was optically pure.



These two independent correlations of absolute stereochemistry, relating (1*R*,2*R*)-**4** with (*R*)-(+)-3-methylcyclopentanone and with (*R*)-(+)-3-methylcyclohexanone, provide a secure basis for interpreting the chiral GC indications of enantiomeric ratios for samples of **4**-*t*. Whether or not the two pairs of enantiomers of 3-phenyl-4-methylcyclopentene may be resolved by chiral GC on the Lipodex E column available, one could be sure at this stage of the investigation that the required analyses by chiral GC could be obtained, if not on the cyclopentenes, then on the isomeric cyclopentanes secured through diimide reductions of the cyclopentenes.

(32) Hill, R. K.; Foley, P. J., Jr.; Gardella, L. A. *J. Org. Chem.* **1967**, *32*, 2330–2335.

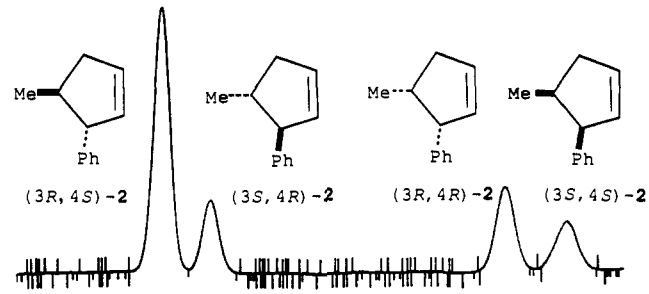
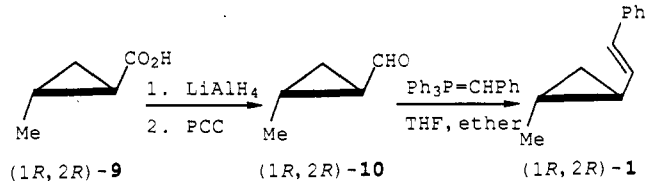
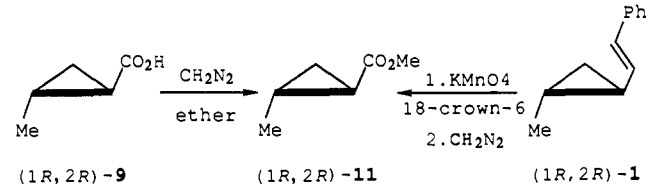


Figure 3. Chiral GC separation of the four 3-phenyl-4-methylcyclopentenes formed from thermolysis of (1*R*,2*R*)-**1** at 250 °C for 90 min. See text for the given assignments of absolute stereochemistry.

Synthesis of (1*R*,2*R*)-1-((*E*)-Styryl)-2-methylcyclopropane. The substrate selected for kinetic and stereochemical investigation was prepared from the well-known and relatively accessible (1*R*,2*R*)-2-methylcyclopropanecarboxylic acid ((1*R*,2*R*)-**9**).[20,33] Reduction of the acid function with lithium aluminum hydride, followed by an oxidation with pyridinium chlorochromate on alumina,[34] gave aldehyde (1*R*,2*R*)-**10**, which was converted to the vinylcyclopropane substrate (1*R*,2*R*)-**1** through a Wittig reaction with benzylidenetriphenylphosphorane in THF–ether.[13]



Chiral GC analysis of the methyl ester (1*R*,2*R*)-**11** obtained from the resolved acid (1*R*,2*R*)-**9** showed that it was optically pure. As a check on the optical purity of (1*R*,2*R*)-**11**, and to demonstrate a method to be used later for determining the ee of partially racemized kinetic samples of **1**, a sample of (1*R*,2*R*)-**1** was oxidized to (1*R*,2*R*)-**9** with $KMnO_4$ and 18-crown-6 in benzene,[35] and that acid was esterified with diazomethane in ether. Racemic ester *rac*-**11** gave well-separated equal intensity chiral GC peaks, at 10.38 and 12.97 min. The samples of (1*R*,2*R*)-**11** from both (1*R*,2*R*)-**9** and (1*R*,2*R*)-**1** were optically pure, by chiral GC analysis; only the early eluting enantiomer could be detected.



Absolute Stereochemistry of 3-Phenyl-4-methylcyclopentenes. The vinylcyclopropane to cyclopentene rearrangement of (1*R*,2*R*)-**1** gives achiral diene **3** and a mixture of the four 3-phenyl-4-methylcyclopentenes **2**. These olefins are readily quantified by analytical GC on methyl silicone and phenyl methyl silicone capillary columns as two diastereomers, and on the chiral GC column as the four distinct stereoisomers (Figure 3).

The assignments of absolute stereochemistry given in Figure 3 are based on correlations with authentic (1*R*,2*R*)-**4**. When the early eluting pair of isomers, enantiomers of **2**-*t*, were isolated by preparative GC and reduced with diimide, there was obtained a sample of **4**-*t* shown by chiral GC to be (1*S*,2*S*)-**4**:(1*R*,2*R*)-**4** enriched in the (1*S*,2*S*)-**4** form. The early eluting trans

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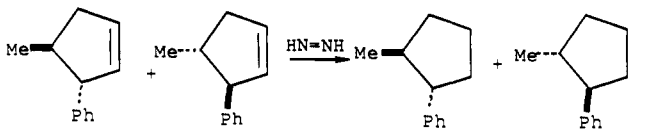
(34) Cheng, Y. S.; Liu, W. C.; Chen, S. *Synthesis* **1980**, 223–224.
(35) Sam, D. J.; Simmons, H. E. *J. Am. Chem. Soc.* **1972**, *94*, 4024–4025.
(36) Baird, W. C.; Franzus, B.; Surridge, J. H. *J. Am. Chem. Soc.* **1967**, *89*, 410–414.

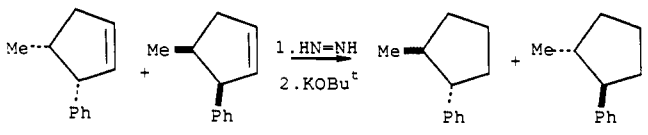
Table I. Product Mixtures from (1*R*,2*R*)-**1** from Thermal Isomerizations at (250.3 ± 0.2) °C

time (min)	**1**	ee (%)	**2**-*t*	**2**-*c*	**3**
0	100	100	0	0	0
90	54.6	57.6	2.2	0.9	42.3
150	36.1	39.6	3.0	1.3	59.6
210	24.1	27.6	3.6	1.6	70.7

cyclopentene enantiomer (3*R*,4*S*)-**2** corresponds stereochemically with the early eluting trans cyclopentane enantiomer (1*S*,2*S*)-**4**.



Preparative GC isolated and purified **2**-*c*, shown by chiral GC to be enriched in the early eluting enantiomer (Figure 3), was reduced with diimide and then isomerized to the corresponding trans cyclopentanes, which were found by chiral GC to be (1*S*,2*S*)-**4**:(1*R*,2*R*)-**4** enriched in the late eluting (1*R*,2*R*)-**4** enantiomer. Thus, the major cis isomer formed from (1*R*,2*R*)-**1** (Figure 3, third peak from the left) is (3*R*,4*R*)-**2**.



Reaction Kinetics and Stereochemistry. To define the relative importance of the four stereochemical paths followed as (1*R*,2*R*)-**1** is heated and converted to the four isomers of **2**, one must measure the rate constant for overall isomerization, $k_i = (k_b + k_c)$ (Scheme I), the rate constant for racemization, $k_\alpha = 2k_a$, and the relative proportions of the four isomers of **2** at several reaction times. The kinetic experiments were conducted in sealed glass ampules submerged in a constant temperature bath at 250 °C. Analysis of reaction mixtures by capillary GC gave mole fraction data for **1**, **2**-*t*, **2**-*c*, and **3** as a function of time (Table I).

The starting material in each kinetic run was optically pure (1*R*,2*R*)-**1** that had been purified by preparative GC; analytical GC confirmed that it was homogeneous. Product mixtures contained, in addition to **1**, **2**, and **3**, small amounts of as many as eight other components of similar retention times, indicative of reactions in addition to those included in Scheme I. For the three kinetic runs from which stereochemical and kinetic information was obtained, all of these additional components together amounted to from 3.7 to 4.1% of all components; the percentages in Table I are calculated with [**1** + **2** + **3**] taken as 100%. Neither the reactions responsible for nor structural identifications of these minor products were pursued. In ampules that had not been rigorously prepared to minimized surface-catalyzed chemistry, these extraneous components were much more prominent in product mixtures.

Recovered starting material **1** from each kinetic run was oxidized to carboxylic acid **9** and converted to methyl ester **11**; each sample of ester was analyzed by chiral GC to establish the ee values also included in Table I. The calculated rate constant values are $k_i = 1.1 \times 10^{-4}$ s^{-1} and $k_\alpha = 1.0 \times 10^{-4}$ s^{-1}. The trans enantiomers constituted (70 ± 1)% of the total (**2**-*t* + **2**-*c*) formed through the vinylcyclopropane rearrangement.

Table II gives the relative proportions of the isomeric 3-phenyl-3-methylcyclopentenes in reaction mixtures as determined by chiral GC.

To convert the data summarized in Table II to values of the relative importance of the rate constants k_{si}, k_{ar}, k_{sr}, and k_{ai}, one may calculate P, the weighted average optical purity of the substrate (1*R*,2*R*)-**1**, from the initial optical purity P_i, the rate constants k_i and k_α, and the reaction time t: $P = [P_i k_i(1 - \exp(-(k_i + k_\alpha)t))]/[(k_i + k_\alpha)(1 - \exp(-k_i t))]$.[19,20] Table III gives calculated values of P and of $k_{si}:(k_{si} + k_{ar})$ and $k_{sr}:(k_{sr} + k_{ai})$ ratios. The rate constant ratios may be readily calculated; the first entry, for example, is found by solving the simple equation $89.5\chi + 10.5(1 - \chi) = 78$; the 89.5:10.5 ratio of enantiomers corresponds to the weighted average P value of 79%, which leads to trans product that is 78% the (3*R*,4*S*) isomer, the isomer formed from (1*R*,2*R*)-**1** through a suprafacial, inversion path.

Table II. Proportions of Enantiomeric 3-Phenyl-4-methylcyclopentenes from Isomerizations of (1*R*,2*R*)-**1**[a] at (250.3 ± 0.2) °C Determined by Chiral Gas Chromatography

time (min)	(3*R*,4*S*)-**2**	(3*S*,4*R*)-**2**	(3*R*,4*R*)-**2**	(3*S*,4*S*)-**2**
90	78[b]	22	62[c]	38
150	75	25	60	40
210	73	27	57	43

[a] Initially, optically pure (1*R*,2*R*)-**1**. [b] Percentage of total **2**-*t* that is (3*R*,4*S*) (see Figure 3). [c] Percentage of total **2**-*c* that is (3*R*,4*R*) (see Figure 3).

Table III. Calculated Weighted Optical Purities of (1*R*,2*R*)-**1** and $k_{si}:(k_{si} + k_{ar})$ and $k_{sr}:(k_{sr} + k_{ai})$ Ratios

time (min)	P (%)	$k_{si}:(k_{si} + k_{ar})$	$k_{sr}:(k_{sr} + k_{ai})$
90	79.0	0.854	0.652
150	70.4	0.855	0.642
210	64.6	0.856	0.608

The final step in deducing the relative importance of each of the four stereochemically distinct paths in this vinylcyclopropane rearrangement involves combining the rate constant ratios of Table III with the finding that trans enantiomers constituted (70 ± 1)% of the cyclopentenes formed. Thus, the relative importance of k_{si} is 0.855 × 70 = 60%, and similarly k_{ar} = 10%, k_{sr} = 19%, and k_{ai} = 11%. The experimental uncertainties in these percentages are estimated to be on the order of 1–2%.

Discussion

An earlier investigation of the vinylcyclopropane rearrangements shown by a chiral *trans*-1-((*E*)-styryl)-2-methylcyclopropane, the (1*R*,2*R*) enantiomer of about 84% optical purity, has been published;[13] in many respects, the two studies are in excellent agreement. Thus, at 249.89 °C, kinetic data from thermal reactions over 74, 147, 207, and 305 min[37] correspond to $k_i = 9.2 \times 10^{-5}$ s^{-1} and $k_\alpha = 8.7 \times 10^{-5}$ s^{-1}; the trans diastereomer **2**-*t* is favored kinetically over **2**-*c* by a 70:30 ratio; and from estimates of the ee of the **2**-*t* products may be calculated a kinetic preference ratio of 0.89. No technique investigated allowed determination of the relative concentrations of the enantiomers of **2**-*c* in product mixtures.[13] The corresponding values determined in the present work at a slightly higher measured temperature are $k_i = 1.2 \times 10^{-4}$ s^{-1} and $k_\alpha = 1.0 \times 10^{-4}$ s^{-1}; **2**-*t*:**2**-*c* = 70:30; and one rate constant leading to an enantiomer of trans product is 0.855 of (k_{si} + k_{ar}). Considering the quite distinct analytical methodologies employed in the two sets of experiments, this very close agreement is noteworthy.

In two important respects, however, the investigations differ: they come to opposite conclusions about the relative importance of *si* and *ar* paths, and the present work defines the partitioning between *sr* and *ai* reactions.

The results reported here show that the major enantiomer of **2**-*t* formed from (1*R*,2*R*)-**1** is (3*R*,4*S*)-**2** and, thus, that the most important path for this vinylcyclopropane to cyclopentene rearrangement is of suprafacial, inversion stereochemistry: k_{si} is 60% of $k_b = (k_{si} + k_{ar} + k_{sr} + k_{ai})$; the earlier report[13,38] concluded that $k_{ar} > k_{si}$. This deduction was based on a three-

(37) Simon, R. J. Ph.D. Dissertation, Cornell University, 1987; p 130.
(38) *Ibid.*, pp 69–70.

Table IV. Relative Contributions from Four Paths for Chiral *trans*-1-(2-Substituted-ethenyl)-2-methylcyclopropanes Rearranging to 3-Substituted-4-methylcyclopentenes

substituent	*si* (%)	*ar* (%)	*sr* (%)	*ai* (%)
E deuterium[a]	55	15		
Z deuterium[a]			18	13
methyl[b]	65	8	22	5
phenyl	60	10	19	11

[a] Reference 19. [b] Reference 20.

step conversion of chiral **2**-*t* from a thermal isomerization of (1*R*,2*R*)-**1** to a chiral sample of *trans*-1-(methoxycarbonyl)-2-methylcyclopentane of negative optical rotation;[13,38] experimentally, however, it appears that the sample had a *positive* rotation at 589 nm,[39] which implies a preponderance of (1*S*,2*S*)-**8**[32] and thus of (3*R*,4*S*)-**2** in the thermal rearrangement product mixture, and this infers that $k_{si} > k_{ar}$. The values now found for the relative importance of all four rate constants for [1,3] carbon shifts converting (1*R*,2*R*)-**1** to 3-phenyl-4-methylcyclopentenes show that all four paths do contribute to significant extents and that the pattern of values is remarkably similar to those observed earlier for the corresponding 2-deuteriovinyl and (*E*)-1-propenyl systems. Table IV summarizes these values.

The similar patterns of relative rate constants for the vinylcyclopropane to cyclopentene rearrangements seen in these three systems make clear that the formal suprafacial, retention and antarafacial, inversion pathways, though not allowed to be concerted by the strictures of orbital symmetry theory,[3] nevertheless contribute significantly to the rearrangement. The two orbital symmetry allowed paths are favored kinetically over the two not allowed paths to such a minor extent that they cannot be said to signal any meaningful energy of concert. The *si* and *ar* paths are kinetically favored, slightly, over the *sr* and *ai* paths for reasons not related to the factors governing orbital symmetry control in concerted reactions.

It has long been known that the activation energy for the vinylcyclopropane to cyclopentene rearrangement does not entail an obvious energy of concert.[3] The results summarized in Table IV simply underscore this point on the basis of stereochemical evidence secured for three different vinylcyclopropane systems and using three different analytical methodologies for sorting out product mixtures: ^{2}H NMR with the aid of chiral lanthanide shift reagents,[19] GC and polarimetry,[20] and here, chiral GC.

There seems to be no simple relationship between the bulk or moment of inertia of a substituent on a cyclopropane and relative rate constants for one-center thermal epimerizations.[33,40] For the vinylcyclopropane to cyclopentene rearrangements of Table IV, one sees very little change in the pattern of rate constants as the substituent on the vinyl group is changed from deuterium to methyl to phenyl. A vision of competitive rotations about C–C single bonds in some long-lived 1-vinyl-1,3-trimethylene diradical intermediates will hardly suffice as a mechanistic model for the stereochemical patterns observed experimentally. Conrotatory formation of such an intermediate and conrotatory progress in the same rotational sense with formation of a cyclopentene will indeed give the formal antarafacial, inversion product, but this mechanistic vision, predicated on an invariant spatially-anchored trimethylene, provides no basis for understanding why the *ai* path does not become less important as the bulk of the substituent on the vinyl function increases.

Complete stereochemical information on the vinylcyclopropane to cyclopentene rearrangements shown by systems having other groups in place of the 2-methyl functionality common to the three cases of Table IV would seem to be the next experimental priority. Computationally based understandings of this rearrangement may also eventually contribute to a more complete appreciation of this and other [1,3] carbon sigmatropic shifts.[14,41]

(39) *Ibid.*, p 116.
(40) Doering, W. von E.; Barsa, E. A. *Tetrahedron Lett.* **1978**, 2495–2498.

Experimental Section

Preparative gas chromatography was performed on a Varian Aerograph A90-P3 using packed 4.83-mm-i.d. aluminum columns and helium as carrier gas. Analytical GC was conducted two-dimensionally on a Hewlett-Packard (HP) 5790 gas chromatograph equipped with one injection port, two flame ionization detectors, two HP 25 m × 2 mm × 0.33 μm ultraperformance capillary columns (cross-linked methyl silicone (A) and cross-linked 5% phenyl methyl silicone (B)), and a dual channel HP 3396 Series II reporting integrator, with helium as carrier gas. These analyses were performed with an initial column temperature of 100 °C using a 10 °C/min ramp, unless otherwise specified; GC retention times on columns A and B are listed in order, the time on B being given in parentheses. Chiral GC analyses were done isothermally using a 50-m 0.25-mm-i.d., 0.4-mm-o.d. fused silica Lipodex E column, with octakis-(2,6-di-*O*-pentyl-3-*O*-butyryl)-γ-cyclodextrin as the stationary phase (Machery-Nagel, Düren, Germany). Analytical HPLC was performed on a Rainin HPLC system, incorporating two Rainin Rabbit HBX pumps, a Gilson 112 UV/vis detector, and an Apple Macintosh Plus computer, using a 4 mm × 20 cm Machery-Nagel Nucleosil 50–5 column. Preparative liquid chromatography was conducted on the Rainin HPLC system using a custom-made 20 mm × 25 cm Machery-Nagel Nucleosil 50–5 column.

Mass spectra were determined with a HP 5970 mass selective detector interfaced with a HP 5890 gas chromatograph using a HP 25 m × 2 mm × 0.33 μm ultraperformance cross-linked methyl silicone column and a HP 59970B workstation. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ solutions on a General Electric QE-300 spectrometer. Chemical shifts are reported in parts per million relative to Me_4Si at 0.0 ppm. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 589 (Na) nm, using a 1-mL 100-mm-path-length glass microcell.

1-Phenyl-2-methylcyclopentanes (*rac*-4-*c* and *rac*-4-*t*) were prepared following the route described by Pines, Sih, and Lewicki:[23] 2-Methylcyclopentanone (5 g) was treated with phenylmagnesium bromide to give after a hydrolytic workup 1-phenyl-2-methylcyclopentanols; dehydration using $POCl_3$ in dry pyridine[24] gave 3.5 g of a mixture of olefins, 1-phenyl-2-methylcyclopentene and 2-phenyl-3-methylcyclopentene, which were hydrogenated in ethyl acetate over palladium on carbon to give *rac*-**4**-*t* and *rac*-**4**-*c* in a 1:10 ratio: analytical GC 6.43 (6.73) and 6.91 (7.25) min. Separation of the isomers by preparative GC on a 3-m 20% SE-30 column afforded pure samples for spectroscopic characterization. For **4**-*t*: ^{1}H NMR δ 0.92 (d, J = 6.22 Hz, 3H), 1.13 (m, 1H), 1.71 (m, 4H), 1.96 (m, 2H), 2.42 (m, 1H), 7.25 (m, 5H); ^{13}C NMR δ 18.6, 34.8, 35.4, 40.9, 43.0, 54.5, 125.8, 127.5, 128.2, 139.4; MS *m*/*e* 160 (M^+, 27), 117 (42), 104 (100), 91 (26), 78 (9). For **4**-*c*: ^{1}H NMR δ 0.58 (d, J = 7 Hz, 3H), 1.41 (m, 1H), 1.72 (m, 1H), 1.93 (m, 4H), 2.29 (m, 1H), 3.14 (m, 1H), 7.23 (m, 5H); ^{13}C NMR δ 16.2, 23.3, 29, 33.4, 38.2, 49.2, 125.5, 127.8, 128.4, 143.5; MS *m*/*e* 160 (M^+, 30), 117 (45), 104 (100), 91 (28), 78 (11).

Chiral GC analysis of *rac*-**4**-*c* was not successful, but *rac*-**4**-*t* was separated into its distinct enantiomeric forms on the Lipodex E column; at 65 °C isothermal, the two enantiomers of **4**-*t* have retention times of 131.98 and 133.58 min (Figure 1).

Isomerization of *cis*-1-Phenyl-2-methylcyclopentane to *trans*-1-Phenyl-2-methylcyclopentane. Approximately 10 mg (0.06 mmol) of *rac*-**4**-*c* was added to 3 mL of dry DMSO. Potassium *tert*-butoxide (337 mg, 3 mmol) was added to this solution to give a 1 M solution of the base. The reaction mixture was stirred and heated at 80 °C under nitrogen for 3 h.[25] The reaction mixture was cooled and diluted with 10 mL of distilled water, added all at once with stirring. The aqueous DMSO solution was extracted with 10 mL of ether, and the ether extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated by distillation. Analytical GC confirmed the complete conversion of *rac*-**4**-*c* to *rac*-**4**-*t*.

2-Phenyl-(*R*)-3-methylcyclopentanones (6) and 2-Phenyl-(*R*)-4-methylcyclopentanones (7). (*R*)-(+)-3-Methylcyclopentanone[26] (2.5 g, 25 mmol; Aldrich) was converted to enamine **5** with excess morpholine and $TiCl_4$ (4.325 g, 23 mmol) in dry hexane at 65 °C for 90 min.[27,28] The reaction mixture was cooled, diluted with ether, and filtered through medium porosity sintered glass; analysis of the filtrate by GC/MS confirmed that all starting material had reacted and that enamine **5** had been formed: MS *m*/*e* 167 (M^+, 30), 166 (27), 152 (100), 67 (18), 41 (18). Concentration and Kugelrohr distillation under vacuum gave 2.82 g (17 mmol; 68%) of enamine **5**. It was dissolved in 40 mL of THF; triethylamine (1.92 g, 19 mmol) was added, the solution was cooled to −78 °C, and 2.76 g (17 mmol) of bromine was added dropwise to the

(41) Houk, K, N.; Li, Y.; Evanseck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682–708.

stirred reaction mixture. After 10 min at −78 °C, the reaction mixture was taken from the cold bath, stirred for another 10 min, and diluted with 50 mL of ether. Filtration through sintered glass gave a clear solution of bromo enamines; it was immediately added dropwise over a 5-min period to 20 mL (36 mmol) of a freshly prepared 1.8 M solution of Ph_2CuLi in THF cooled to −20 °C. The reaction mixture was stirred at −20 °C for 2 h and then warmed to room temperature and strired for 90 min longer. The mixture of intermediate enamines (MS *m/e* 243 (M^+); analytical GC 14.11 (14.96) and 14.48 (15.39)) was hydrolyzed with 50 mL of 2 N HCl; the two-phase system was stirred vigorously for 36 h to complete the hydrolysis and then filtered through sintered glass. The organic layer was extracted with 50 mL of distilled water; the aqueous solutions were combined and extracted with 25 mL of ether. The ethereal solutions were combined, washed with brine, and dried over Na_2SO_4. Filtration concentration by distillation using a 15-cm Vigreux column, flash chromatography of the concentrate using 3:2 hexane/ether as the eluting solvent, concentration of product-containing fractions by distillation, and Kugelrohr distillation under high vacuum gave 2.25 g (57%) of four isomeric products, in 48:34:16:2 proportions, by analytical GC: 8.96 (9.66), 9.20 (9.90), 9.25 (9.96), and 9.71 (10.28) min. For *trans*-(2*R*,3*R*)-**6**, the earliest eluting isomer: MS *m/e* 174 (M^+, 77), 131 (17), 118 (96), 117 (100), 115 (32), 104 (45), 91 (59), 39 (22); ^1H NMR δ 1.13 (d, *J* = 6.0 Hz, 3H), 1.19 (m, 1H), 1.57 (m, 1H), 2.30 (m, 2H), 2.51 (m, 1H), 2.82 (d, *J* = 11.7 Hz, 1H), 7.09 (m, 2H), 7.24 (m, 3H).

(1*S*,2*R*)-1-Phenyl-2-methylcyclopentane ((1*S*,2*R*)-4) and (1*R*,2*R*)-1-Phenyl-2-methylcyclopentane ((1*R*,2*R*)-4). The mixture of four ketones prepared above (1.04 g, 6 mmol) was added to a reaction flash along with 800 mg of KOH, 385 mg (10.2 mmol) of 85% $H_2NNH_2 \cdot H_2O$, and 20 mL of diethylene glycol.[29] The reaction flask was heated to 55 °C, and low-boiling components were distilled. The reaction mixture was stirred and heated to 145 °C for 24 h. Analysis of a small aliquot indicated a 33% conversion to hydrocarbon products. The reaction mixture was cooled and then diluted with 50 mL of 5% HCl and 50 mL of ether. The ethereal phase was separated and washed with 25 mL of brine, dried over Na_2SO_4, filtered, and concentrated by distillation to give 256 mg of a mixture of the cis isomer (1*S*,2*R*)-**4**, the trans isomer (1*R*,2*R*)-**4**, two isomers of 1-phenyl-3-methylcyclopentane, and unreacted ketones. For (1*R*,2*R*)-**4**: $[\alpha]_D$ = −47.7° (*c* = 0.3, CCl_4); analytical GC 6.45 (6.75) min; ^1H NMR identical to that observed for *rac*-**4**-*t*.

The trans isomer (1*R*,2*R*)-**4** was purified by preparative GC on a 3-m 20% SE-30 column and then analyzed by chiral GC. A single enantiomeric form of the molecule having a retention time of 134.98 min at 65 °C was seen; a racemic sample of **4**-*t* was resolved under these conditions with the enantiomers eluting in the order (1*S*,2*S*)-**4** before (1*R*,2*R*)-**4** (Figure 1). Mixing equal amounts of (1*R*,2*R*)-**4** and *rac*-**4**-*t* together, then analyzing by chiral GC, confirmed the stereochemical assignment to the two peaks, for the later eluting enantiomer was dominant.

Base-catalyzed isomerization of the homochiral cis isomer (1*S*,2*R*)-**4** to the trans isomer (1*R*,2*R*)-**4** was achieved as described above for *rac*-**4**-*c* to *rac*-**4**-*t*. Chiral GC analysis of the product (1*R*,2*R*)-**4** indicated it to be of 100% ee (Figure 1).

1-(Methoxy)-2-methylcyclopentanes from 1-Phenyl-2-methylcyclopentanes. A 250-mL round-bottomed flask was charged with 20 mL of CCl_4, 20 mL of CH_3CN, and 800 mg (5 mmol) of a mixture of *rac*-**4**-*t* and *rac*-**4**-*c*. The mixture was stirred, and 35 mL of water followed by 16.04 g (75 mmol) of $NaIO_4$ was added. After several minutes of stirring, 42 mg of $RuCl_3 \cdot 3H_2O$ (36.3% Ru) was added.[30] The reaction mixture was stirred for 24 h at room temperature and then filtered through a sintered glass funnel with the aid of 50 mL of CH_2Cl_2. The filtrate was transferred to a separatory funnel, and 25 mL of H_2O was added. The organic layer was removed and the aqueous layer extracted further with three 25-mL portions of CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated by distillation. The concentrate was then diluted with 100 mL of ether, and the solution was filtered through a pad of Celite. Extraction of this solution with 1 N NaOH, acidification of the basic extracts with 6 N HCl, extraction of this acidic aqueous solution with three 50-mL portions of ether, drying the ethereal solution over Na_2SO_4, filtration, and concentration of the filtrate by distillation gave 242 mg (38%) of *cis*- and *trans*-2-methylcyclopentanecarboxylic acids: analytical GC 4.00 (4.22) and 4.20 (4.45) min. These components were separated by preparative GC using a 10% FFAP on 60/80 mesh NAW Chromosorb W column. For the late eluting component, the cis isomer: ^1H NMR δ 0.99 (d, *J* = 7.26 Hz, 3H), 1.40 (m, 1H), 1.59 (m, 1H), 1.82 (m, 3H), 1.96 (m, 1H), 2.34 (m, 1H), 2.82 (m, 1H).

A mixture of these acids (242 mg, 1.9 mmol) was treated with diazomethane in ether with stirring for 45 min; concentration by distillation gave 243 mg (91%) of two esters; analytical GC 3.53 (3.71) and 3.68 (3.88) min. Chiral GC analysis of this mixture indicated that each diastereomer separated into its distinct enantiomeric forms with retention times at 85 °C of 11.75 and 12.08 min for the *trans* enantiomers and 13.24 and 13.80 min for the *cis* enantiomers.

In a separate conversion, 6 mg of the optically pure trans isomer (1*R*,2*R*)-**4** was oxidized following the protocol detailed above. The resulting acid was treated with diazomethane to give one product with a GC retention time of 3.52 (3.68) min. Chiral GC analysis of the product (1*R*,2*R*)-**8** derived from this conversion showed it to be nearly optically pure (96% ee), the major enantiomer having a retention time of 11.70 min at 85 °C, identical with the time characteristic of the early eluting enantiomer observed for *rac*-**8** (Figure 2).

(1*R*,2*R*)-1-(Methoxycarbonyl)-2-methylcyclopentane ((1*R*,2*R*)-8) from (*R*)-(+)-3-Methylcyclohexanone.[31,32] To 8.1 mL of 30% H_2O_2 was added 270 mg (2.43 mmol) of SeO_2, and the mixture was heated to reflux for 2 h. The reaction mixture was cooled to room temperature, and an additional 8.1 mL of 30% H_2O_2 was added, followed by 0.27 mL of pyridine and 4 g (36 mmol) of (*R*)-(+)-3-methylcyclohexanone (Aldrich) dissolved in 6 mL of *tert*-butyl alcohol. The reaction mixture was heated to reflux for 24 h and then cooled to room temperature. Saturated $NaHCO_3$ (50 mL) was added, and the aqueous solution was extracted with 50 mL of ether; the ethereal phase was extracted with 50 mL of aqueous $NaHCO_3$. The two aqueous solutions were combined and acidified with 75 mL of 4 N HCl saturated with NH_4Cl. The acidic solution was extracted with three 50-mL portions of ether, and the ethereal material was washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated by distillation to give 3.15 g (69%) of isomeric acids, the desired (1*R*,2*R*) acid together with two isomers of 3-methylcyclopentanecarboxylic acid.

An ethereal solution containing 2.91 g (22.8 mmol) of this mixture of methylcyclopentanecarboxylic acids was treated with 120 mL (34.3 mmol) of 0.29 M diazomethane in ether. The reaction mixture was stirred for 30 min. Unreacted acids were removed by extraction of the ethereal solution with saturated $NaHCO_3$. The organic solution was washed with 100 mL of brine, dried over Na_2SO_4, filtered, and concentrated by distillation to give 2.32 g (72%) of methyl ester (1*R*,2*R*)-**8** and methyl 3-methylcyclopentanecarboxylates. These esters were purified on a 1-m 20% Carbowax 20M column but were not separated from one another: analytical GC 3.52 (3.71) and 3.66 (3.86) min. Chiral GC analysis of the early eluting isomer, (1*R*,2*R*)-**8**, showed it to be a single enantiomeric form having a retention time of 11.71 min at 85 °C. Chiral GC comparisons based on a racemic sample demonstrated that the (1*R*,2*R*) isomer (1*R*,2*R*)-**8** is the early eluting form (Figure 2).

***trans*-1-((*E*)-Styryl)-2-methylcyclopropane (*rac*-1).** *trans*-2-Methylcyclopropanemethanol (1.22 g; Aldrich; containing some cis isomer) dissolved in 30 mL of dry hexane was oxidized to *trans*-2-methylcyclopropanecarboxaldehyde through a PCC-on-alumina oxidation.[34] After 30 min, the reaction was judged by GC analysis to be complete. The ethereal solution was filtered through a pad of Florisil covering a sintered glass funnel, and the filter pad was washed with 150 mL of dry ether. The combined ethereal filtrates were dried over Na_2SO_4, filtered, and added dropwise to a solution of benzylidenetriphenylphosphorane at −78 °C prepared in 150 mL of ether and 100 mL of THF from 11 g (28.3 mmol) of benzyltriphenylphosphonium chloride and 28.3 mmol (14.14 mL) of 2.0 M *n*-butyllithium in pentane at 0 °C.[13] The reaction mixture was stirred for 24 h; 5 mL of *tert*-butyl alcohol was added, and after 10 min at room temperature, the quenched reaction solution was filtered through a pad of Celite. The salts were washed further with 200 mL of ether. The ethereal solution was washed with two 1-L portions of distilled water, dried over Na_2SO_4, filtered, and concentrated by distillation. The yellow concentrate was diluted with hexane and purified by flash chromatography using hexane as the eluting solvent. Fractions containing products were combined, dried, filtered, and concentrated by distillation to give 785 mg (36%) of a mixture of four isomeric vinylcyclopropanes: analytical GC 6.68 (7.01), 7.17 (7.55), 7.69 (8.06), 7.85 (8.24) min; intensity ratios 6.6:1:14.9:1.1, respectively. These have been identified as the *trans*-1-((*Z*)-styryl)-2-methyl-, *cis*-1-((*Z*)-styryl)-2-methyl-, *trans*-1-((*E*)-styryl-2-methyl-, and *cis*-1-((*E*)-styryl)-2-methylcyclopropanes.[13] The ^1H NMR spectral characteristics of these isomers match the data reported for them by Newman-Evans, Simon, and Carpenter.[13] For the *trans*-1-((*Z*)-styryl)-2-methyl isomer: MS *m/e* 158 (M^+, 14), 143 (21), 129 (100), 128 (56), 115 (29), 91 (14), 39 (16); ^1H NMR δ 0.62 (m, 2H), 0.87 (m, 1H), 1.10 (d, *J* = 5.95 Hz, 3H), 1.55 (m, 1H), 5.08 (dd, *J* = 10.2, 11.1 Hz, 1H), 6.31 (d, *J* = 11.5 Hz, 1H), 7.31 (m, 5H). For the *trans*-1-((*E*)-styryl)-2-methyl isomer, *rac*-**1**: MS *m/e* 159 (M^+, 21), 143 (24), 129 (100), 128 (58), 115 (31), 91 (16), 39 (15); ^1H NMR

($CDCl_3$) δ 0.57 (m, 1H), 0.66 (m, 1H), 0.89 (m, 1H), 1.11 (d, J = 5.9 Hz, 3H), 1.25 (m, 1H), 5.76 (dd, J = 9, 15.8 Hz, 1H), 6.41 (d, J = 15.8 Hz, 1H), 7.16 (m, 1H), 7.28 (m, 4H).

(1*R*,2*R*)-(−)-2-Methylcyclopropanecarboxylic Acid ((1*R*,2*R*)-9). Racemic *trans*-2-methylcyclopropanecarboxylic acid (10 g) was converted to a mixture of diasteromeric amides derived from (*R*)-(−)-2-phenylglycinol, and the amides were separated by preparative HPLC using 60:40 ethyl acetate/isooctane as the mobile phase.[20,34] A sample of the early eluting, less polar amide (2.06 g) of 100% ee as judged by analytical HPLC was hydrolyzed in 50 mL of THF and 50 mL of 3 N H_2SO_4 at reflux. When the hydrolysis was complete as judged by TLC, the acid was isolated (1*R*,2*R*)-**9** (662 mg) (73%) was obtained as a clear liquid. A small sample was purified by preparative GC using a 1-m 20% Carbowax 20M column: ^{1}H NMR δ 0.75 (m, 1H), 1.12 (d, J = 5.99 Hz, 1H), 1.22 (quintet, J = 4.29 Hz, 1H), 1.32 (quintet, J = 4.14 Hz, 1H), 1.44 (m, 1H), 11.60 (br s, 1H); ^{13}C NMR: δ 17.56, 17.81, 18.28, 21.16, 181.18; $[\alpha]_D^{25}$ = −102° (c = 0.97, 95% EtOH); lit.[19] $[\alpha]_D^{25}$ = +95.8° for the (1*S*,2*S*) enantiomer. Chiral GC analysis of the methyl ester derived from this acid, (1*R*,2*R*)-**8**, showed exclusively one enantiomeric form present, with a retention time of 10.38 min at 65 °C. A sample of *rac*-**8** prepared from racemic *trans*-2-methylcyclopropanecarboxylic acid showed two equal intensity peaks on chiral GC analysis, at 10.38 and 12.97 min.

(1*R*,2*R*)-1-((*E*)-Styryl)-2-methylcyclopropane ((1*R*,2*R*)-1). (1*R*,2*R*)-2-Methylcyclopropanecarboxylic acid (600 mg) was reduced with $LiAlH_4$ and given a conventional workup: the product alcohol (480 mg, 93%) had analytic GC retention times of 5.44 (6.04) min at 40 °C. It was converted to the *trans*-1-styryl-2-methycyclopropanes as described above for the racemic compounds, through PCC oxidation followed by a Witting reaction: there was obtained 592 mg (67% yield from the alcohol) of two products having GC retention times of 6.70 (7.05) and 7.71 (8.09) min and present in a ratio of 1:4, respectively. The early isomer corresponds to (1*R*,2*R*)-1-((*Z*)-styryl)-2-methylcyclopropane and the later to (1*R*,2*R*)-1-((*E*)-styryl)-2-methylcyclopropane, (1*R*,2*R*)-**1**, based on GC and ^{1}H NMR spectral data. These isomers were easily separated by preparative GC using a 3-m 20% SE-30 column. In this manner, sufficient samples could be purified for further study. For (1*R*,2*R*)-**1**: ^{1}H NMR δ 0.57 (m, 1H), 0.65 (m, 1H), 0.88 (m, 1H), 1.11 (d, J = 5.9 Hz, 3H), 1.25 (m, 1H), 5.75 (dd, J = 9, 15.8 Hz, 1H), 6.41 (d, J = 15, 8 Hz, 1H), 7.15 (m, 1H), 7.29 (m, 4H); ^{13}C NMR δ 15.72, 18.52, 23.42, 125.49, 126.41, 126.87, 128.43, 134.62, 137.85. For the 1-((*Z*)-styryl) isomer: ^{1}H NMR δ 0.61 (m, 2H), 0.87 (m, 1H), 1.11 (d, J = 5.9 Hz, 3H), 1.57 (m, 1H), 5.10 (dd, J = 11.3, 10 Hz, 1H), 6.31 (d, J = 11.44 Hz, 1H), 7.31 (m, 5H).

Conversion of (1*R*,2*R*)-1-((*E*)-Styryl)-2-methylcyclopropane to Methyl (1*R*,2*R*)-2-Methylcyclopropanecarboxylate. A 10-mg sample of preparative GC purified (1*R*,2*R*)-**1** was dissolved in 2 mL of dry benzene. In a separate flask, 110 mg of 18-crown-6 and 79 mg of $KMnO_4$ were dissolved in benzene and stirred for 2 h at room temperature.[35] Hydrocarbon (1*R*,2*R*)-**1** in benzene was then added, and the reaction mixture was stirred for 24 h and then diluted with 20 mL of 5% aqueous KOH. Precipitated MnO_2 was removed by filtration through a sintered glass funnel. Sufficient aqueous $NaHSO_3$ was added to the filtrate to destroy excess $KMnO_4$, and the solution became clear. It was made acidic with 6 N HCl and extracted with ether (2 × 40 mL). The ether extracts were combined and extracted with 1 N NaOH (2 × 25 mL). The resulting aqueous solution was made acidic and extracted with ether (2 × 50 mL). The ethereal material was dried over $NaSO_4$, filtered, and concentrated by distillation to give an acid, which was esterified with diazomethane. The product from this sequence, (1*R*,2*R*)-**11**, and *rac*-**11** had identical analytical GC retention times. Chiral GC analysis of (1*R*,2*R*)-**11** showed it to be enantiomerically pure, retention time 10.44 min, and to be the early eluting enantiomer when compared to racemic *rac*-**11**, retention times 10.38 and 12.97 min.

Thermal Reactions of (1*R*,2*R*)-1-((*E*)-Styryl)-2-methylcyclopropane. A single large-scale thermal reaction of (1*R*,2*R*)-**1** was performed to gain a preliminary insight into the stereochemical distribution of cyclopentene products. Kinetic parameters were subsequently determined with smaller samples heated at various time intervals.

The reaction bulbs used in this study were cylindrical Pyrex 35 mm diameter × 90 mm long (about 65 mL) ampules, with a 6-mm tubing stem facilitating attachment to a vacuum line and convenient sealing with a torch. Each bulb was prepared carefully to minimize unwanted wall-catalyzed reactions: they were soaked in concentrated HCl for 24 h, rinsed with water, then soaked in concentrated NH_4OH containing EDTA for 24 h, then rinsed 20 times with distilled water, and finally dried in an oven at 160 °C for 1 week.

Samples of (1*R*,2*R*)-**1** were purified by preparative GC using a 3-m 20% SE-30 column just prior to use.

For the large-scale reaction, 110 mg of (1*R*,2*R*)-**1** was transferred into a reaction bulb with the aid of a microsyringe. The bulb was placed on a vacuum line, frozen in a dry ice–acetone bath, and then evacuated at less than 1 Torr for 15 min. The stopcock to the vacuum line was closed, and the bulb was allowed to warm to room temperature and frozen again; after a second freeze–pump–thaw cycle, the sample was sealed in the bulb under vacuum.

The sealed reaction bulb was completely immersed in a hot oil bath heated to 250.2 °C for a period of 3 h. The oil bath contained poly(phenylsiloxane) heated with a resistance type metal rod attached to a Variac. The temperature was monitored with a calibrated digital platinum resistance thermometer (Hewlett-Packard-2802A with a HP-34740A display) and regulated within ±0.2 °C using a Bayley 253 temperature controller. After the reaction, the bulb was removed from the bath, allowed to cool to room temperature, and opened. The reaction mixture was dissolved in hexane and passed through a column of silica gel, eluting with more hexane as necessary.

Initially, a 20% SE-30 column was used to separate and purify products from this reaction. Several fractions were collected and analyzed by ^{1}H NMR. For the 6.46-min (6.79-min) component, 6-phenylhexa-1,4(*Z*)-diene (**3**): ^{1}H NMR δ 2.92 (t, J = 5.9 Hz, 2H), 3.41 (d, J = 7.1, 2H), 5.06 (m, 2H), 5.61 (m, 2H), 5.85 (m, 1H), 7.24 (m, 5H); ^{13}C NMR δ 31.51, 33.43, 114.91, 125.89, 127.62, 128.35, 128.41, 129.30, 136.69, 140.80.[13] The ^{1}H NMR spectrum for the 7.69-min (8.07-min) component matched that observed for a synthetic sample of (1*R*,2*R*)-**1**. The cis and trans isomers of 3-phenyl-4-methylcyclopentene were assigned from GC retention time characteristics.

Preparative GC on a 3-m 20% SE-30 column gave a sample of the *trans*-cyclopentene product free from other components in the reaction mixture. Chiral GC analysis of the trans isomer of 3-phenyl-4-methylcyclopentene showed complete resolution of the enantiomeric forms of the molecule. The dominant enantiomer was found to be the early eluting form. The *trans*-3-phenyl-4-methylcyclopentenes were reduced with diimide.[36] At 50% conversion, chiral GC analysis of the reaction mixture indicated that in both the pair of olefin enantiomers and the corresponding enantiomeric cyclopentanes the dominant enantiomer present was the early eluting form; thus, the dominant trans cyclopentene enantiomer in the product mixture is (3*R*,4*S*)-**2** (Figure 3).

By employing a 1-m 20% Carbowax 20M column, it was possible to separate the cis and trans olefins **2** from all other reaction products. The cis olefin was then isolated in pure form by preparative GC on the SE-30 column and subjected to chiral GC analysis. Resolution was achieved, and the early eluting isomer was found to be dominant.

Together, the cis and trans olefins were reduced with diimide to the corresponding cyclopentanes. The isomeric cis and trans cycloalkanes were then separated on the Carbowax 20M column. The cis cycloalkane enantiomers were then isomerized with $KOBu^t$ in DMSO to the corresponding trans enantiomers. Chiral GC analysis indicated that the later eluting enantiomeic form was dominant. Thus, the dominant, early eluting cis enantiomer in the thermolysis reaction mixture is (3*R*,4*R*)-**2**, and the dominant trans cyclopentane obtained through diimide reduction and epimerization at the phenyl-substituted carbon is the late eluting enantiomer, (1*R*,2*R*)-**4**.

To characterize thermal reaction mixtures, analytical GC was used to determine mole fractions of starting material and diastereomeric products. The mole fractions of [**1** + **2**-*t* + **2**-*c* + **3**] were from 0.959 to 0.963 in the three kinetic runs; for the tabulations in Table I, the proportions of these four diastereomers were normalized so that [**1** + **2**-*t* + **2**-*c* + **3**] = 100%. Then, using a 1-m 20% Carbowax 20M column, the substituted cyclopentene products were separated from other components and analyzed directly by chiral GC at 65 °C (Figure 3). The unreacted starting vinylcyclopropane, (1*R*,2*R*)-**1**, was collected for each run and converted through oxidation and esterification to (1*R*,2*R*)-**11** for chiral GC determinations of ee.

Three thermal reaction mixtures were fully characterized. For each reaction, 25 mg of (1*R*,2*R*)-**1** was placed in a prepared bulb and the bulb was sealed as described above. When the prescribed reaction times at (250.3 ± 0.2) °C had elapsed, the reaction bulbs were cooled and opened; the product mixtures were dissolved in dry hexane and analyzed at outlined above. No visible decomposition was noted for the 90-, 150-, and 210-min reactions. The results of these analyses are summarized in Tables I and II.

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