Stereochemistry of the Thermal Isomerizations of (1*S*,2*R*)-1-(*E*-Styryl)-2-phenylcyclopropane to 3,4-Diphenylcyclopentenes

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Abstract: One stereoisomer of 1-(*E*-styryl)-2-phenylcyclopropane undergoes reversible thermal stereomutations to equilibrate with three other stereoisomers and gives more slowly the four isomers of 3,4-diphenylcyclopentene. Appropriate kinetic data and analyses have provided rate constants for the four stereochemically distinct paths leading from one enantiomer of *trans*-1-(*E*-styryl)-2-phenylcyclopropane to 3,4-diphenylcyclopentenes: at 160 °C the relative significances of the four distinct paths followed in these vinylcyclopropane to cyclopentene rearrangements are (67 ± 3)% *si*, (12 ± 3)% *ar*, (17 ± 1)% *sr*, and (4 ± 1)% *ai*. The orbital symmetry "allowed" *si* and *ar* paths are favored over the "forbidden" alternatives but only by a relatively modest radio, 83:17. *cis*-1-(*E*-Styryl)-2-phenylcyclopropane isomerizes to 3,4-diphenylcyclopropanes at comparable rates, with the "forbidden" paths favored over the "allowed" routes, 91:9. The rearrangements may be considered to be processes mediated by kinetically competitive diradical transition structures rather than controlled by orbital symmetry considerations.

Introduction

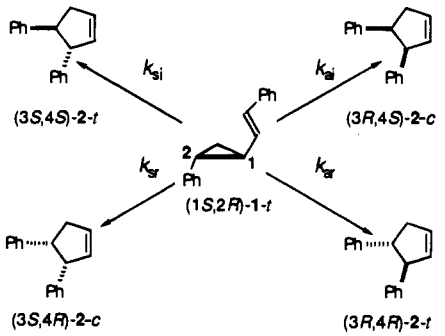
The thermal rearrangements of vinylcyclopropanes to cyclopentenes[1] involve 1,3 carbon shifts which may in principle take place in four stereochemically distinct modes,[2] as exemplified in Scheme 1 for the reactant (1*S*,2*R*)-*trans*-1-(*E*-styryl)-2-phenylcyclopropane ((1*S*,2*R*)-**1**-*t*). There is no difficulty in associating the four isomeric rearrangement products with suprafacial or antarafacial (*s* or *a*) utilization of the allylic unit and retention or inversion (*r* or *i*) at the migrating carbon, C2. The individual rate constants for vinylcyclopropane rearrangements shown in Scheme 1 are labeled with subscripts *s* or *a*, and *r* or *i*, in accord with these stereochemical characteristics.

An experimental determination of the four rate constants for thermal rearrangements of (1*S*,2*R*)-**1**-*t* to the 3,4-diphenylcyclopentenes (3*S*,4*S*)-**2**-*t*, (3*R*,4*R*)-**2**-*t*, (3*S*,4*R*)-**2**-*c*, and (3*R*,4*S*)-**2**-*c* is complicated and made reasonably challenging by the stereomutations summarized in Scheme 2. Enantiomerization and cis,trans isomerization reactions are likely to occur much faster than formation of cyclopentene products.[3,4] The rate constants for one-center (k_1, k_2) and two-center epimerizations (k_{12}, k_{12}') in Scheme 2 are labeled with subscripts utilizing a common convention; primed rate constants are used for reactions starting with a cis isomer of 1-(*E*-styryl)-2-phenylcyclopropane.

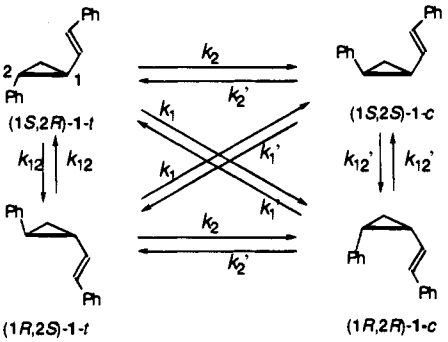
A further complication may be anticipated: the four cyclopentenes may be formed from the *cis*-1-(*E*-styryl)-2-phenylcyclopropanes, (1*S*,2*S*)-**1**-*c* and (1*R*,2*R*)-**1**-*c*, which will inevitably arise in the reaction mixture as well as from the enantiomers of the trans diastereomer (Scheme 3).[4]

The kinetic situation thus involves eight isomers; the time dependent relative concentrations of these isomers are governed by 28 rate constants: the 12 shown in Scheme 2, and four leading from each of the four 1-(*E*-styryl)-2-phenylcyclopropanes to the four 3,4-diphenylcyclopentenes. Yet there are only 13 independent kinetic parameters. The stereomutations of Scheme 2 are dependent on k_1, k_2, k_{12}, k_{12}', and an equilibrium constant, $K_{eq} = (k_1' + k_2')/(k_1 + k_2)$ (Scheme 2); microscopic

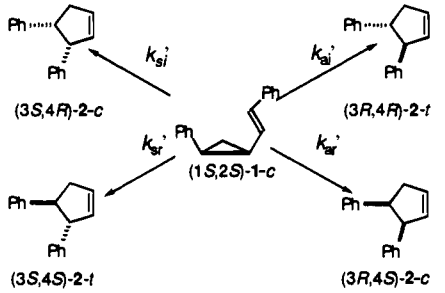
Scheme 1. 3,4-Diphenylcyclopentenes from (1*S*,2*R*)-**1**-*t*



Scheme 2. Stereomutations of 1-(*E*-Styryl)-2-phenylcyclopropanes



Scheme 3. 3,4-Diphenylcyclopentenes from (1*S*,2*S*)-**1**-c



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reversibility implies that $k_1(K_{eq}) = k_1'$ and $k_2(K_{eq}) = k_2'$. The rate constants for formation of cyclopentene isomers from one enantiomer of **1**-*t* are k_{sr}, k_{ar}, k_{sr}, and k_{ai} (Scheme 1), and, when one enantiomer of **1**-*c* is the immediate percursor, the vinylcyclopropane rearrangement rate constants are k_{sr}', k_{ai}', k_{si}', and k_{ar}' (Scheme 3). The sums of all four rate constants for vinylcyclopropane rearrangements from a given isomer are given by $k = (k_{sr} + k_{ai} + k_{si} + k_{ar})$ and $k' = (k_{sr}' + k_{ai}' + k_{si}' + k_{ar}')$. Although the whole kinetic situation appears formidable, 10 of the 13 independent kinetic parameters were measured in the present study, and the essential stereochemical data sought, values of k_{sr}, k_{ar}, k_{sr}, and k_{ai} (Scheme 1), were secured.

Such kinetic complexities have tended to limit stereochemical studies of vinylcyclopropane to cyclopentene rearrangements, yet there have been some successes. Following pioneering experimental demonstrations that such rearrangements do not occur in a completely stereochemically random manner,[5] the first complete mapping of all four stereochemical modes for a vinylcyclopropane rearrangement was attained in 1976 for a simple dimethyl-substituted system, a chiral *trans*-1-(*E*-propenyl)-2-methylcyclopropane.[6] Subsequent experimental[7,8] and theoretical[9] work has begun to clarify the relationships between stereochemical patterns, kinetic trends, and mechanistic alternatives.

Results

Reactants, Products, and Analytical Methods. Racemic *trans*-1-(*E*-styryl)-2-phenylcyclopropane (*rac*-**1**-*t*)[10] and (1*S*,2*R*)-*trans*-1-(*E*-styryl)-2-phenylcyclopropane ((1*S*,2*R*)-**1**-*t*) of 87% enantiomeric excess (ee) were prepared from the corresponding *trans*-2-phenylcyclopropanecarboxylic acids[11] using conventional methods.[12]

Enantiomeric excess values for the (1*S*,2*R*)-**1**-*t* used as a kinetic substrate, and for samples of **1**-*t* and **1**-*c* isolated after a kinetic run, were obtained by oxidizing the styrylcyclopropanes with $KMnO_4$ and 18-crown-6 in benzene[13] and then converting the acids obtained to the corresponding methyl esters with diazomethane. Chiral GC analyses[14] of the methyl esters on a Lipodex E column gave baseline separation for both pairs of enantiomers;[4] the relative intensities of the peaks then were used to calculate ee values.

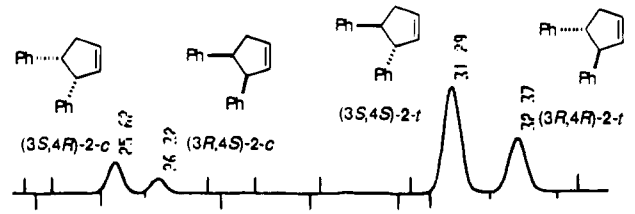
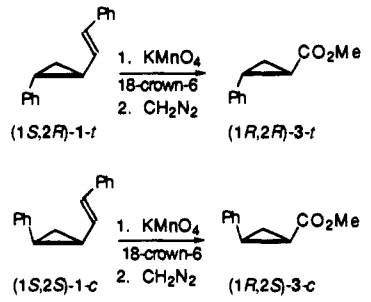
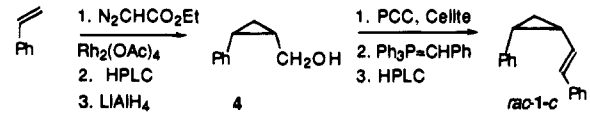


Figure 1. Chiral GC analysis of 3,4-diphenylcyclopentenes from thermal isomerizations of (1*S*,2*R*)-**1**-*t* of 87% ee at 160.2 °C for 90 min.



Racemic *cis*-1-(*E*-styryl)-2-phenylcyclopropane (*rac*-**1**-*c*) was prepared through the rhodium acetate dimer catalyzed addition of ethyl diazoacetate to styrene;[15] the cis isomer of ethyl 2-phenylcyclopropanecarboxylate was separated and purified by preparative HPLC. Reduction of this ester with $LiAlH_4$, oxidation of *cis*-2-phenylcyclopropanemethanol (**4**) with pyridinium chlorochromate in the presence of Celite,[16] followed by a Wittig condensation with benzylidenetriphenylphosphorane[17] and separation of isomers by HPLC, provided *rac*-**1**-*c* as an analytically pure and homogeneous colorless liquid.



Capillary gas chromatography proved well suited to quantitative analyses of mixtures of **1**-*t*, **1**-*c*, **2**-*t*, and **2**-*c*; on a 12-m Hewlett Packard cross-linked methyl silicone fused silica capillary GC column, all four compounds were well resolved.

Chiral gas chromatography using a Cyclodex B column separated all four isomers of 3,4-diphenylcyclopentene, as demonstrated in Figure 1.[12] The correlations of retention times with absolute stereochemistry, as given in Figure 1, are based on chemical correlations with compounds of known absolute stereochemistry.[12]

These analytical methods used together permit a full characterization of a reaction mixture. Analyses by capillary GC provide relative concentration data for **1**-*t*, **1**-*c*, **2**-*t* and **2**-*c*, and chiral GC gives relative concentrations of (3*S*,4*S*)-**2**-*t*, (3*R*,4*R*)-**2**-*t*, (3*S*,4*R*)-**2**-*c*, and (3*R*,4*S*)-**2**-*c* (Figure 1). Preparative GC affords styrylcyclopropanes **1**-*t* and **1**-*c* from a thermal reaction mixture; each diastereomer may then be subjected to the two-step styryl-to-methoxycarbonyl functional group conversion. The methyl esters **3**-*t* and **3**-*c* may be analyzed by chiral GC to

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Table 1. Observed Relative Concentrations for Vinylcyclopropanes **1**-*c* and **1**-*t* and Cyclopentenes **2**-*c* and **2**-*t* from **1**-*c* at 160 °C

time (min)	**1**-*c* (%)	**1**-*t* (%)	**2**-*c* (%)	**2**-*t* (%)
0	100	0	0	0
15	64.1	34.8	0.1	1.0
30	42.5	55.7	0.2	1.6
45	26.1	71.3	0.3	2.3
70	17.7	78.7	0.4	3.2
90	13.6	82.5	0.4	3.5
120	11.9	83.1	0.6	4.4
180	9.8	83.6	0.8	5.8

Table 2. Observed Relative Concentrations for Vinylcyclopropanes **1**-*c* and **1**-*t* and Cyclopentenes **2**-*c* and **2**-*t* from (1*S*,2*R*)-**1**-*t* at 160 °C

time (min)	**1**-*c* (%)	**1**-*t* (%)	**2**-*c* (%)	**2**-*t* (%)
0	2.0	98.0	0	0
15	5.4	94.5	0	0.1
30	7.1	92.3	0.1	0.5
45	7.7	91.6	0.1	0.6
57	8.5	90.5	0.1	0.9
60	8.9	90.0	0.2	0.9
90	10.5	87.2	0.5	1.8
120	9.8	87.5	0.4	2.3

determine ee values and thus provide relative concentrations for (1*S*,2*R*)-**1**-*t*, (1*R*,2*S*)-**1**-*t*, (1*S*,2*S*)-**1**-*c*, and (1*R*,2*R*)-**1**-*c*. Given time-dependent relative concentrations of the eight isomers at such short reaction times that the time-weighted ee of **1**-*t* remains substantial, the rate constants k_{sr}, k_{ar}, k_{sr}, and k_{ai} may be obtained.

Stereomutations. The thermal reactions of vinylcyclopropane **1**-*t* one may follow by capillary GC are a reversible geometric isomerization leading to **1**-*c* and vinylcyclopropane rearrangements to give the 3,4-diphenylcyclopentenes **2**-*c* and **2**-*t* (Schemes 1−3). The rate expressions for this kinetic situation are given in eqs 1 and 2.

$$d[\mathbf{1}\text{-}t]/dt = -(k + k_1 + k_2)[\mathbf{1}\text{-}t] + (k_1' + k_2')[\mathbf{1}\text{-}c] \quad (1)$$

$$d[\mathbf{1}\text{-}c]/dt = (k_1 + k_2)[\mathbf{1}\text{-}t] - (k' + k_1' + k_2')[\mathbf{1}\text{-}c] \quad (2)$$

General solutions for such pairs of differential equations are well-known[18] and may be expressed as in eqs 3 and 4, where $(A_1 + A_2) = [\mathbf{1}\text{-}t]$ at $t = 0$ and $(B_1 + B_2) = [\mathbf{1}\text{-}c]$ at $t = 0$.

$$[\mathbf{1}\text{-}t] = A_1 \exp(-\lambda_1 t) + A_2 \exp(-\lambda_2 t) \quad (3)$$

$$[\mathbf{1}\text{-}c] = B_1 \exp(-\lambda_1 t) + B_2 \exp(-\lambda_2 t) \quad (4)$$

Samples of *cis*-1-(*E*-styryl)-2-phenylcyclopropanes (**1**-*c*) and of (1*S*,2*R*)-**1**-*t* in sealed ampoules were heated for defined periods at 160.2 ± 0.5 °C. Analyses of the thermal reaction mixtures by capillary GC gave the relative concentration data summarized in Tables 1 and 2.

The least-squares best parameters in eqs 1 and 2 may be found by modeling the time-dependent relative concentrations of [**1**-*c*] and [**1**-*t*] with the aid of suitable software, such as Deltagraph Pro 3.[19] The data from Table 1 presented graphically in Figure 2 were fit by the exponential parameters $\lambda_1 = 5.72 \times 10^{-4}$ s^{-1} and $\lambda_2 = 7.0 \times 10^{-6}$ s^{-1}; $[\mathbf{1}\text{-}t] = -89.9 * e^{-\lambda_1 t} + 89.9 * e^{-\lambda_2 t}$ ($R^2 = 0.999$) and $[\mathbf{1}\text{-}c] = 90.2 * e^{-\lambda_1 t} + 9.8 * e^{-\lambda_2 t}$ ($R^2 = 0.999$).

The data from Table 2 for [**1**-*t*] in Figure 3 were modeled using the same λ_1 and λ_2 parameters, and a reasonably good agreement between the theoretical plot and the experimental data points was realized; the two parameter best-fit equations were found to be $[\mathbf{1}\text{-}t] = 6.5 * e^{-\lambda_1 t} + 91.4 * e^{-\lambda_2 t}$ ($R^2 = 0.978$) and $[\mathbf{1}\text{-}c] = -8.4 * e^{-\lambda_1 t} + 10.3 * e^{-\lambda_2 t}$ ($R^2 = 0.971$).

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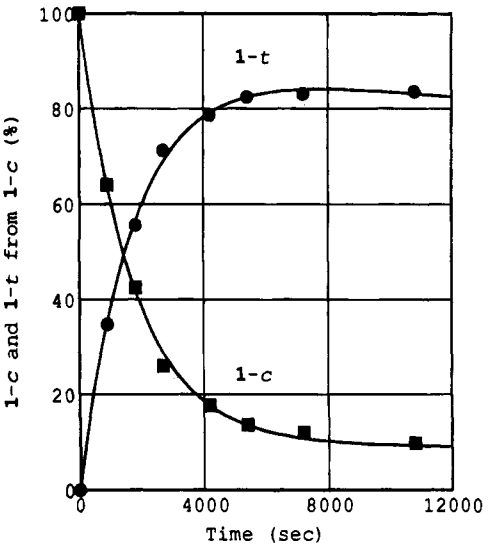

Figure 2. Plots of the [**1**-*c*] and [**1**-*t*] from the rearrangement of *cis*-1-(*E*-styryl)-2-phenylcyclopropane (**1**-*c*) as functions of time using the data of Table 1.

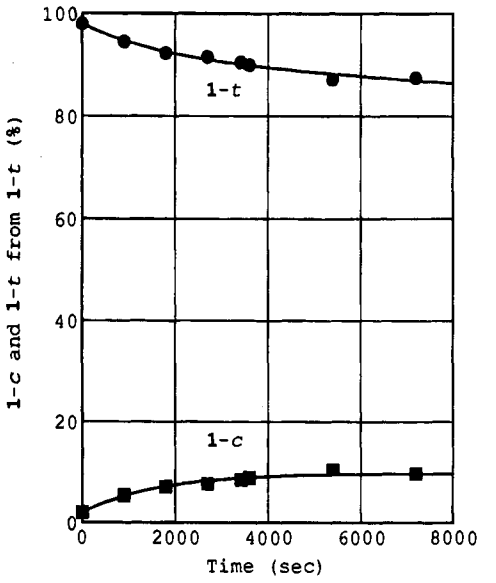

Figure 3. Plots of [**1**-*t*] and [**1**-*c*] as functions of time using the data of Table 2.

Rearrangements to Cyclopentenes. With the explicit and easily integrable functions for [**1**-*t*] and [**1**-*c*] established above one may model the time dependence of the concentrations of the *cis*- and *trans*-cyclopentene products using eqs 5 and 6.

$$d[\mathbf{2}\text{-}t]/dt = (k_{si} + k_{ar})[\mathbf{1}\text{-}t] + (k_{sr}' + k_{ai}')[\mathbf{1}\text{-}c] \quad (5)$$

$$d[\mathbf{2}\text{-}c]/dt = (k_{sr} + k_{ai})[\mathbf{1}\text{-}t] + (k_{si}' + k_{ar}')[\mathbf{1}\text{-}c] \quad (6)$$

Integration of these expressions leads to eqs 7 and 8.

$$[\mathbf{2}\text{-}t](t) = (k_{si} + k_{ar})\int_0^t [\mathbf{1}\text{-}t]dt + (k_{sr}' + k_{ai}')\int_0^t [\mathbf{1}\text{-}c]dt \quad (7)$$

$$[\mathbf{2}\text{-}c](t) = (k_{sr} + k_{ai})\int_0^t [\mathbf{1}\text{-}t]dt + (k_{si}' + k_{ar}')\int_0^t [\mathbf{1}\text{-}c]dt \quad (8)$$

The integrations called for in eqs 7 and 8 and some simplifications give eqs 9 and 10, which express the relative concentrations of cyclopentenes **2**-*t* and **2**-*c* at any given time *t*. The A_i and B_i parameters are those appropriate to the starting material, either 100% **1**-*c* (Table 1) or 98% (1*S*,2*R*)-**1**-*t* and 2% **1**-*c* (Table 2).

$$[\mathbf{2}\text{-}t](t) = (k_{si} + k_{ar})\{(A_1/\lambda_1)(1 - \exp(-\lambda_1 t)) + (A_2/\lambda_2)(1 - \exp(-\lambda_2 t))\} + (k_{sr}' + k_{ai}')\{(B_1/\lambda_1)(1 - \exp(-\lambda_1 t)) + (B_2/\lambda_2)(1 - \exp(-\lambda_2 t))\} \quad (9)$$

$$[\mathbf{2}\text{-}c](t) = (k_{sr} + k_{ai})\{(A_1/\lambda_1)(1 - \exp(-\lambda_1 t)) + (A_2/\lambda_2)(1 - \exp(-\lambda_2 t))\} + (k_{si}' + k_{ar}')\{(B_1/\lambda_1)(1 - \exp(-\lambda_1 t)) + (B_2/\lambda_2)(1 - \exp(-\lambda_2 t))\} \quad (10)$$

The experimental data points from Tables 1 and 2 were modeled using eqs 9 and 10 and the previously determined parameters λ_1, λ_2, A_i, and B_i. The rate constants found through the best-fit calculations and used for the theoretical plots of Figure 4 are summarized in Table 3.

One-Center Epimerizations. The rate constant $(k_1' + k_2')$ may be estimated by evaluating the derivative of eq 3 at $t = 0$, using the best-fit parameters obtained above, and then referring to eq 1, with [**1**-*c*] = 100% at $t = 0$. The rate constant found in this manner is $(k_1' + k_2') = 5.08 \times 10^{-4}$ s^{-1}. From the two determinations of A_2/B_2 (eqs 3 and 4), 9.2 and 8.9, $K_{eq} = (k_1' + k_2')/(k_1 + k_2) \approx 9$; then $(k_1 + k_2) = 5.64 \times 10^{-5}$ s^{-1}. While these estimates cannot be very precise, they may serve nevertheless as reasonable working approximations.

Chiral Analyses of 1 and 2 from Reaction Mixtures. The enantiomer excess characteristics of samples of **1**-*t* and **1**-*c* recovered from the kinetic runs were determined by chiral CG as described above: the styrylcyclopropanes were isolated from reaction mixtures by preparative GC, oxidized to give cyclopropanecarboxylic acids, and esterified with diazomethane to afford **3**-*t* and **3**-*c*, which were then analyzed by GC on a Lipodex E column. The analytical results are provided in Table 4.

The data of Table 4 indicate that the **1**-*c* formed from (1*S*,2*R*)-**1**-*t* is essentially racemic; thus k_1 is about equal to k_2, or k_{12}' is very much larger than $(k_1 + k_2)$, or both. In any event, if the **1**-*c* formed from (1*S*,2*R*)-**1**-*t* is racemic, then [((1*S*,2*R*)-**1**-*t*) − ((1*R*,2*S*)-**1**-*t*)] as a function of time should follow a single exponential decay, which does prove to be the case (Figure 5); [((1*S*,2*R*)-**1**-*t*) − ((1*R*,2*S*)-**1**-*t*)](t) = C*exp(-η*t) with $C = 85.5$ and, when the suspect 15-min data point is excluded from the one-parameter least-squares calculation, $\eta = 1.28 \times 10^{-4}$ s^{-1} ($R^2 = 0.986$). When it is included, $\eta = 1.31 \times 10^{-4}$ s^{-1} ($R^2 = 0.929$). The parameter η is equivalent to the combination of rate constants $(2k_{12} + k_1 + k_2)$; with $(k_1 + k_2) = 5.64 \times 10^{-5}$ s^{-1}, k_{12} is estimated to be 3.6×10^{-5} s^{-1}, and $(k_1 + k_2)/k_{12} \approx 1.6$, an unexceptional ratio.[20]

The time-weighted enantiomeric excess of (1*S*,2*R*)-**1**-*t* as the thermal reactions take place, $P(t)$, is given by eqs 11 or 12,[6] and it too is plotted in Figure 5.

$$P(t) = \int_0^t ((Ce^{-\eta t})*([\mathbf{1}\text{-}t])dt / \int_0^t ([\mathbf{1}\text{-}t]))dt \quad (11)$$

$$P(t) = C*\{(A_1/(\eta + \lambda_1))*(1 - \exp(-(\eta + \lambda_1)t)) + (A_2/(\eta + \lambda_2))*(1 - \exp(-(\eta + \lambda_2)t))\}/\{(A_1/\lambda_1)(1 - \exp(-\lambda_1 t)) + (A_2/\lambda_2)(1 - \exp(-\lambda_2 t))\} \quad (12)$$

The weighted $P(t)$ values decrease less rapidly with time than [((1*S*,2*R*)-**1**-*t*) - ((1*R*,2*S*)-**1**-*t*)] values. At 120 min, for instance, the calculated $P(t)$ value is 56.3%, while [((1*S*,2*R*)-**1**-*t*) − ((1*R*,2*S*)-**1**-*t*)] is only 34.2%.

The isomeric 3,4-diphenylcyclopentene products obtained from the kinetic runs reported in Table 2 were analyzed by chiral GC: the enantiomer distribution values are summarized in Table 5. The sum of both enantiomers for each cyclopentene product was taken to be equal to 100%.

(20) Baldwin, J. E., in *The Chemistry of the Cyclopropyl Group*; Zvi Rappoport, Ed.; John Wiley & Sons, Chichester, 1995, in press.

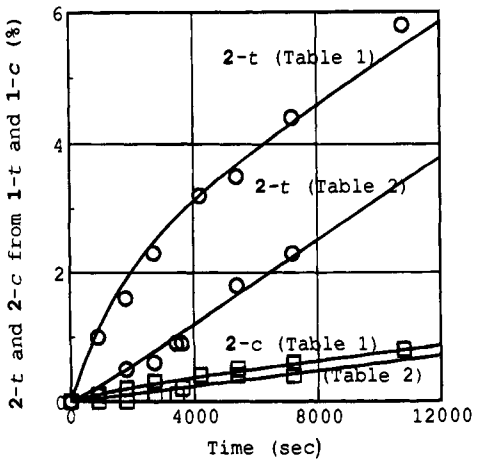

Figure 4. Plots of the formation of [**2**-*t*] and [**2**-*c*] as functions of time using the data of Tables 1 and 2. The theoretical plots were based on eqs 9 and 10; the best parameters found are given in Table 5.

Table 3. Vinylcyclopropane Rearrangement Rate Constants from Best-Fit Plots of Figure 4 (x 10^6 s)

$(k_{si} + k_{ar})$	$(k_{sr} + k_{ai})$	k	$(k_{si'} + k_{ar'})$	$(k_{sr'} + k_{ai'})$	k'
2.1	0.56	2.66	1.4	14.9	16.3

Table 4. Observed Enantiomer Distributions of Methyl 2-Phenylcyclopropanecarboxylates **3**-*t* and **3**-*c* Obtained from **1**-*t* and **1**-*c* Samples from Thermal Reaction Mixtures

time (min)	(1*R*,2*R*)-**1**-*t* (% ee)	((1*R*,2*R*)-**1**-*t*-(1*S*,2*S*)-**1**-*t*)[a]	*P*(*t*) (%)	(1*S*,2*R*)-**1**-*c* (% ee)
0	87.2	85.5	85.5	2.2
15	68.8	65.2[c]	80.8	−0.4
30	77.1	71.4	76.4	−0.5
45	69.2	63.0	72.4	*d*
57	58.5	52.7	69.4	*d*
60	58.2	52.4	68.7	−0.8
90	48.3	42.7	62.1	0.9
120	39.3	34.2	56.3	*d*

[a] (ee(%)/100)*[**1**-t]; [**1**-*t*] = 6.5*e$^{-\lambda_1 t}$ + 91.4 * e$^{-\lambda_2 t}$. [b] Calculated; see text and eq 12. [c] Well below value consistent with other data; see text. [d] Not determined.

The rate constants for isomerizations of the *cis*- and *trans*-1-(*E*-styryl)-2-phenylcyclopropanes to the *cis*- and *trans*-3,4-diphenylcyclopentenes (Table 5) and expressions for the concentrations of the two cyclopropane isomers as functions of time during the kinetic runs of Table 2 allow one to calculate the amounts of the cyclopentene products formed over any time period from racemic cis and chiral trans isomers of the vinylcyclopropane reactants.

For the 45-min point, for example, the **2**-*t* formed from **1**-*c* may be calculated from Eq 8: **2**-*t* from **1**-*c* (%) = $(k_{sr}' + k_{ai}')$*{(B_1/λ_1)*(1 − e$^{-\lambda_1 t}$) + (B_2/λ_2)*(1 − e$^{-\lambda_2 t}$)}, where $(k_{sr}' + k_{ai}') = 1.49 \times 10^{-5}$ s^{-1}, $B_1 = -8.4$, and $B_2 = 10.3$, or 0.238. The results from such calculations for all seven kinetic runs provide the proportions of **2**-*t* and **2**-*c* formed over each reaction period from chiral trans and racemic cis reactants in percentage terms; the sum of the contributions of (1*S*,2*R*)-**1**-*t* (of varying ee) and *rac*-**1**-*c* as direct precursors for each cyclopentene product here is equal to 100% (Table 6).

The observed distributions of enantiomers for **2**-*t* and **2**-*c* in product mixtures (Table 5) reflect the net preferences for (1*S*,2*R*)-**1**-*t* to give one antipode over the other and equal

(21) (a) Burger, A.; Yost, W. L. *J. Am. Chem. Soc.* **1948**, *70*, 2198−2201. (b)DePuy, C. H.; Dappen, G. M.; Eilers, K. L.; Klein, R. A. *J. Org. Chem.* **1964**, *29*, 2813−2815.(c) Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3443−3448. (d) Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M. *J. Am. Chem. Soc.* **1978**, *100*, 3449−3461. (e) Aratani, T. *Pure and Appl. Chem.* **1985**, *57*, 1839−1844.

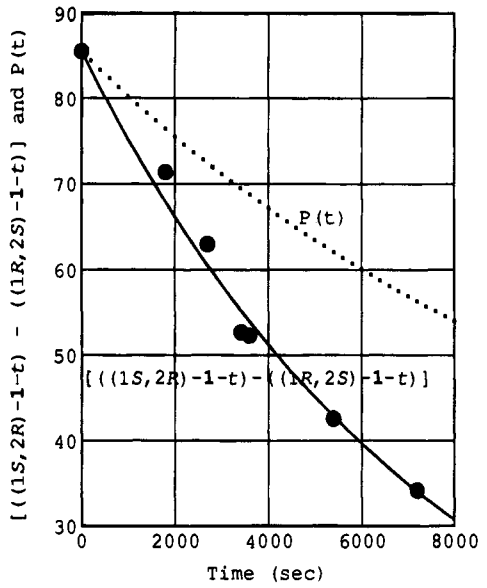

Figure 5. Plots of $[((1S,2R)\text{-}\mathbf{1}\text{-}t) - ((1R,2S)\text{-}\mathbf{1}\text{-}t)] = 85.5 * \exp(-\eta * t)$, with $\eta = 1.28 \times 10^{-4}$ s^{-1}, and $P(t)$ as given in eq 12, using the data of Table 4.

Table 5. Observed Enantiomer Distributions for 3,4-Diphenylcyclopentenes **2**-*t* and **2**-*c* from Thermal Stereomutations of (1*S*,2*R*)-**1**-*t* at 160 °C

time (min)	(3*S*,4*S*)-**2**-*t*	(3*R*,4*R*)-**2**-*t*	(3*S*,4*R*)-**2**-*c*	(3*R*,4*S*)-**2**-*c*
15	70.3	29.7	73.4	26.6
30	66.4	33.6	69.2	30.8
45	68.7	31.3	69.7	30.3
57	67.9	32.1	68.4	31.6
60	65.4	34.6	66.0	34.0
90	64.4	35.6	64.6	35.4
120	65.1	34.9	63.2	36.8

Table 6. Calculated Relative Amounts of **2**-*t* and **2**-*c* Formed from (1*S*,2*R*)-**1**-*t* (of Varying ee) and *rac*-**1**-*c* at 160 °C in Mixtures Starting from (1*S*,2*R*)-**1**-*t*

time (min)	**2**-*t* from **1**-*t*	**2**-*t* from **1**-*c*	**2**-*c* from **1**-*t*	**2**-*c* from **1**-*c*
15	78.6	21.4	91.2	8.8
30	72.8	27.2	88.4	11.6
45	69.1	30.9	86.4	13.6
57	66.9	33.1	85.2	14.8
60	66.5	33.5	84.9	15.1
90	63.2	36.8	83.0	17.0
120	61.4	38.6	81.9	18.1

Table 7. Calculated Enantiomer Excess Values for *trans*- and *cis*-3,4-Diphenylcyclopentenes **2**-*t* and **2**-*c* Derived Directly from (1*S*,2*R*)-**1**-*t* (of Varying ee)

time (min)	(3*S*,4*S*)-**2**-*t* from (1*S*,2*R*)-**1**-*t* (% ee)	(3*S*,4*R*)-**2**-*c* from (1*S*,2*R*)-**1**-*t* (% ee)
15	51.7	51.3
30	45.0	43.4
45	54.2	45.6
57	53.5	43.2
60	46.3	37.7
90	45.5	35.2
120	49.2	32.3

contributions to both enantiomers from racemic **1**-*c*. Thus an arithmetical correction is needed to deduce the net preference for one antipode of a product over the other shown by the isomerizations of chiral trans reactant alone. The corrected ee values for trans and cis products, given by 100*(ee(%) of **2**-*t*)/(**2**-*t* from **1**-*t* (%)) and 100*(ee(%) of **2**-*c*)/(**2**-*c* from **1**-*t* (%)), are provided in Table 7.

The relative magnitudes of the four rate constants leading from (1*S*,2*R*)-**1**-*t* to 3,4-diphenylcyclopentenes may be calculated

Table 8. Relative Magnitudes of the Four Rate Constants for Rearrangements of (1*S*,2*R*)-**1**-*t* to **2**-*t* and **2**-*c* Enantiomers at 160 °C

time (min)	k_{si} (%)	k_{ar} (%)	k_{sr} (%)	k_{ai} (%)
15	64.7	14.2	17.2	3.9
30	62.7	16.2	16.5	4.6
45	69.0	9.9	17.2	3.9
57	69.9	9.0	17.1	4.0
60	66.1	12.8	16.3	4.8
90	68.4	10.5	16.5	4.6
120	73.9[a]	5.0[a]	16.6	4.5
average	66.8 ± 2.8	12.1 ± 2.8	16.8 ± 0.4	4.3 ± 0.4

[a] Not included in average; see text.

Table 9. Summary of Relative Rate Constants for Thermal Rearrangements of Chiral *trans*-2,*E*-2′-(Disubstituted)-1-Ethenylcyclopropanes to 3,4-(Disubstituted)cyclopentenes

R-C2	R-C2′	*T* (°C)	ref	year	k_{si}(%)	k_{ar}(%)	k_{sr}(%)	k_{ai}(%)
D	D	300	7c	1994	40	13	23	24
Me	D	285	7a	1991	55	15	18	13
Me	Me	297	6	1976	65	8	22	5
Me	Ph	250	7b	1993	60	10	19	11
Ph	Me	234	4	1994	44	20	25	11
Ph	Ph	160		1995	67	12	17	4

simply from ($k_{si} + k_{ra}$), ($k_{sr} + k_{ai}$), and k rate constants (Table 3), $P(t)$ values (Table 4), and the ee(t) values of Table 7. When $k = 100\%$, the relative magnitudes of k_{si}, for instance, are given by (100*($k_{si} + k_{ra}$)/k)*(ee(t)of **2**-*t* + $P(t)$)/(2*$P(t)$), with similar and equally simple expressions providing the others.[4] The results of these calculations are summarized in Table 8.

The only experimental point that seems to be irregular is the observed ee value for trans product at 120 min; it leads to values for the relative magnitudes of the k_{si} and k_{ar} paths beyond the estimated probable error limits based on the other analyses of **2**-*t* products in thermal reaction mixtures. If the 120-min estimates for k_{si} and k_{ar} are included, the average values would be (67.8 ± 3.7)% and (11.1 ± 3.7)%—not very significantly different. For purposes of discussion, the relative rate constant values are taken to be 67% and 12% (± 3%) for k_{si} and k_{ar}, and 17% and 4% (±1%) for k_{sr} and k_{ai}.

Discussion

The kinetic situation shown in Schemes 1−3, though complicated, has been unraveled up to a point: estimates for 10 of the 13 independent kinetic parameters have been obtained. These last three could be secured through kinetic studies starting with one enantiomer of **1**-*c*, but they have no bearing on the vinylcyclopropane rearrangement stereochemical preferences for an enantiomer of **1**-*t*.

The stereochemistry of the vinylcyclopropane rearrangement of (1*S*,2*R*)-**1**-*t* shows a pattern similar to those seen in previous studies, as exemplified in the six cases summarized in Table 9.

Comparable rates of isomerization to cyclopentenes for the substituted vinylcyclopropanes of Table 9 are observed at different temperatures, consistent with the relative strengths of the cyclopropyl bonds cleaved and, in turn, on the relative capacities of substituents to lend stability to diradical structures.[20] The *si* path is in every case the most important; the products from the "allowed" k_{si} and k_{ar} pathways invariably comprise the major part of the cyclopentene products formed.

All four possible paths are used when an enantiomer of **1**-*t* rearranges to 3,4-diphenylcyclopentenes, with the two orbital symmetry "allowed" modes (rate constants k_{si} and k_{ar}) favored over the two "forbidden" or "disallowed" paths (rate constants k_{sr} and k_{ai}) 79:21. At 160 °C, this kinetic preference corresponds to a $\Delta\Delta G^{\ddagger}$ of only some 1.1 kcal/mol, too small an energy difference to be viewed confidently as an energy of concert. The fact that the thermochemically favored products, the trans isomers of 3,4-diphenylcyclopentene, are reached by the "al-

lowed" modes, provides additional grounds for being reluctant to ascribe the 79:21 kinetic preference to a manifestation of orbital symmetry control: other sorts of geometrical and thermodynamic factors in the relevant transition structures could contribute to the stereochemical preferences observed.

The vinylcyclopropane to cyclopentene rearrangements of **1**-*c* take place with the two "forbidden" or "disallowed" paths (rate constants k_{sr}' and k_{ai}') favored over the orbital symmetry "allowed" modes (rate constants k_{si}' and k_{ar}') 91:9. Further, (k_{sr}' and k_{ai}') is larger than (k_{si} and k_{ar}) by a factor of 7, a figure very close to $K_{eq} \approx 9$. Most of the difference between ($k_{sr}' + k_{ai}'$) and ($k_{si} + k_{ar}$) may be associated with differences in ground state free energies, leaving only a negligible energetic difference between the relevant transition state structures for the respective "allowed" from **1**-*t* and "forbidden" from **1**-*c* rearrangement paths leading to **2**-*t*. One can hardly postulate that the allowed products are formed from **1**-*t* with benefit of orbital symmetry control, while the forbidden products from **1**-*c* are associated with diradical transition structures. It seems rather more plausible to view these vinylcyclopropane to cyclopentene rearrangements as processes passing through alternative kinetically competitive diradical transition structures, all without benefit of an energy of concert of the sort presupposed by orbital symmetry theory.

Experimental Section

Preparative gas chromatographic (GC) purifications were done using a Varian Aerograph A90-P3 gas chromatograph. Preparative HPLC purifications were done on a Macherey-Nagel Nucleosil 50-5 preparative column using a Gilson 112 UV detector monitoring at 254 nm. Elemental analyses were done by E + R Microanalytical Laboratory, Inc., Corona, NY 11368.

Analyses by GC for thermal reaction product mixtures were done using a Hewlett Packard 5890 A instrument equipped with a Hewlett Packard cross-linked methyl silicone fused silica capillary GC column (12 m × 0.20 mm i.d. × 0.33 μm film thickness) attached to an injection port maintained at 160 °C. The FID detector maintained at 300 °C was connected to a HP 3396 Series II dual channel integrator. Enantiomer excess values were determined by chiral GC, using a Hewlett Packard 5890 A gas chromatograph equipped with a fused silica Cyclodex B capillary GC column (J & W Scientific, 30 m × 0.26 mm i.d.) or a fused silica Lipodex E capillary GC column (Macherey-Nagel, 50 m × 0.25 mm i.d.). The injection port and detector temperatures were maintained at 150 and 300 °C, respectively. Preparations and characterizations of *rac*-**1**-*t* and (1*S*,2*R*)-**1**-*t* of 87% ee have been described elsewhere.[12]

Ethyl *cis*-2-Phenylcyclopropanecarboxylate. Rhodium acetate catalyst ($Rh_2(OAc)_4$, 37.9 mg, 0.09 mmol, 1.0 equiv) was added to 10 mL of dry CH_2Cl_2 in a flame-dried three-necked flask equipped with a reflux condenser. To the green solution was added styrene (3.30 mL, 3.00 g, 28.8 mmol) followed by the dropwise addition of ethyl diazoacetate (Aldrich, 3.03 mL, 3.28 g, 28.8 mmol, 1.0 equiv) over a period of 4 h. The resulting dark green reaction mixture was stirred for an additional 12 h and then passed through a plug of Celite to remove the rhodium catalyst. After the column was washed several times with dry CH_2Cl_2, the yellow filtrate was dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation to give a dark yellow liquid. Analytical GC indicated the presence of 15% of unreacted styrene which was effectively removed by Kugelrohr distillation at 80 °C under aspirator vacuum. The trans and cis ethyl esters were further purified by Kugelrohr distillation at a maximum pot temperature of 100 °C (0.125 mm) to give a clear colorless distillate (4.48 g, 92% esters by GC, 88% yield). Preparative GC purification on a 3-m 20% Carbowax 20 M on 60−80 Chromosorb P-NAW column (200 °C, 10 mL/min) gave a pure sample of the desired cis ester: GC-MS *m/e* 190 (M^+, 23.2%), 145 (M − 45, 17.4), 144 (20.4), 135 (13.6), 133 (12.5), 117 (M − 73, 100.0), 116 (34.2), 115 (79.2), 91 ($C_6H_5CH_2^+$, 27.9), 39 (15.2); ^{1}H NMR δ 7.27−7.19 (m, 5H), 3.85 (q, *J* = 14.10 Hz, 2H), 2.55 (q, *J* = 7.85 Hz, 1H), 2.10 (m, 1H), 1.70 (m, 1H), 1.45 (m, 1H), 1.0 (t, *J* = 7.00 Hz, 3H) (compare ref 21c); ^{13}C NMR δ 170.97, 136.53, 129.27, 127.85, 126.60, 60.15, 25.44, 21.78, 13.99, 11.09. Large scale separation of the esters was accomplished by preparative HPLC (10% EtOAc−hexanes or 10% EtOAc−pentane, 2.0 mL/min).

***cis*-2-Phenylcyclopropanemethanol (4).** A standard lithium aluminum hydride reduction of ethyl *cis*-2-phenylcyclopropanecarboxylate in dry ether gave the corresponding cis alcohol **4** as a colorless liquid. Preparative GC purification on a 1-m 15% SE-30 on 60−80 Chromosorb W column (90 °C, 10 mL/min) afforded pure material: GC-MS *m/e* 148 (M^+, 17.5%), 130 (M − 18, 25.3), 129 (22.3), 118 (27.0), 117 (M − 31, 100.0), 115 (66.7), 104 (52.9), 103 (18.9), 91 ($C_6H_5CH_2^+$, 43.8), 78 ($C_6H_6^+$, 23.6), 77 ($C_6H_5^+$, 18.1), 39 (19.2); ^{1}H NMR δ 7.30 (m, 5H), 3.50 (m, 2H), 3.30 (m, 1H), 2.30 (m, 1H), 1.65 (br s, OH), 1.50 (m, 1H), 1.10−0.9 (m, 1H) (compare ref 47); ^{13}C NMR δ 148.46, 128.80, 128.28, 126.20, 62.88, 20.90, 20.67, 7.64.

***cis*-1-(*E*-Styryl)-2-phenylcyclopropane (*1*-c).** Pyridinium chlorochromate oxidation of a solution of alcohol **4** (323 mg, 2.32 mmol, 1.0 equiv) in 2 mL of dry CH_2Cl_2 led to the formation of the corresponding aldehyde. The ethereal solution of the aldehyde was concentrated by simple distillation and subjected without further purification to a Wittig olefination procedure with benzylidenetriphenylphosphorane. Preparative scale HPLC purification (98:2 hexanes−CH_2Cl_2, 2.0 mL/min) gave the desired E olefin **1**-*c* as a colorless liquid (63 mg, 12% yield): GC-MS *m/e* 220 (M^+, 27.2%), 142 (16.9), 141 (12.0), 129 (M-91, 100.0), 128 (43.3), 116 (12.9), 115 (32.6), 92 (38.7), 91 ($C_6H_5CH_2^+$, 75.2), 77 ($C_6H_5^+$, 11.5), 51 (11.9), 39 (11.1); ^{1}H NMR δ 7.39−7.08 (m, 10 H), 6.50 (d, *J* = 15.78 Hz, 1H), 5.55 (dd, *J* = 9.48 and 6.24 Hz, 1H), 2.45 (q, *J* = 15.17 Hz, 1H), 2.00 (m, 1H), 1.45 (q, *J* = 15.21 Hz, 1H), 1.15 (q, *J* = 11.66 Hz, 1H); ^{13}C NMR δ 138.67, 137.70, 130.55, 128.49, 128.33, 128.06, 126.52, 126.02, 23.86, 22.66, 12.55. Anal. Calcd for $C_{17}H_{16}$: C, 92.68; H 7.32. Found: C, 92.77; H 7.16.

Thermal Reactions of 1-(*E*-Styryl)-2-phenylcyclopropanes (1*S*, 2*R*)-1-*t* and 1-*c*. Thermal isomerizations of 1-(*E*-styryl)-2-phenylcyclopropanes were carried out in kinetic bulbs previously soaked in concentrated HCl overnight followed by NH_4OH/EDTA for at least 2 days. Each bulb was washed copiously with water after each soaking. The bulbs were then dried in a 140 °C oven for at least 2 days. The thermal reactions of racemic **1**-*c* utilized 2-mg samples of 100% purity by GC. For the chiral trans isomer (1*S*,2*R*)-**1**-*t*, 10-mg samples containing 97.8% of trans cyclopropane isomer (1*S*,2*R*)-**17** (87% ee), 1.9% of isomer **1**-*c* (2.2% ee), and 0.3% stilbene were utilized. Each bulb was subjected to three freeze−pump−thaw cycles, and a few milligrams of hydroquinone was added prior to sealing. The thermal reactions were conducted in a mechanically stirred, well-insulated oil bath maintained at 160.2 ± 0.5 °C. After a run, each kinetic bulb was first cooled to room temperature; then cooled to −78 °C, and opened. The thermal reaction mixture diluted with cyclohexane was then analyzed by capillary GC at least twice. The relative concentration data for **1**-*t*, **1**-*c*, **2**-*t*, and **2**-*c* reported in Tables 1 and 2 were the averages for two analyses.

Each chiral product mixture was subjected to preparative GC purification on a 31-cm 20% SE-30 on 60−80 Chromosorb W-AW DMCS-HP column (100 °C, 10 mL/min). The fraction collected after 56 min contained both **1**-*t* and **1**-*c* but no cyclopentene products: it was then dissolved in ~3 mL of dry benzene and placed in a 5-mL round-bottomed flask. Potassium permanganate ($KMnO_4$, Mallinckrodt, 92.7 mg, 0.59 mmol) and 18-crown-6 (Aldrich, 99%, 128.8 mg, 0.49 mmol) were then added to the solution. After 20 h at room temperature, 20 mL of 5% KOH was added. The mixture was filtered and acidified with 10% H_2SO_4. The acidified aqueous layer was extracted with two 25-mL portions of ether. The combined organic material was dried, filtered, and concentrated by rotary evaporation. The corresponding trans and cis methyl esters **3**-*t* and **3**-*c* were prepared by treatment with ethereal CH_2N_2. Their ee values were determined by chiral GC and are summarized in Table 4.

Analyses of cyclopentenes **2**-*t* and **2**-*c* by chiral GC (Figure 1) gave the enantiomer distributions summarized in Table 5.

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