# Stabilization of a Putative Cyclohexane-1,4-diyl Intermediate Elicits an Antarafacial Cope Rearrangement via a Stepwise Mechanism. Pyrolysis of (*R*,*E*)-5-Methyl-1,2,6-octatriene to 4-Methyl-3-methylene-1,5-heptadiene

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**Abstract:** The pyrolysis of (*E*)-5-methylocta-1,2,6-triene (**1**) has been designed to bring to light a stepwise Cope rearrangement by stabilization of the putative biradical intermediate. Compound **1** rearranges to (*E*)-4-methyl-3-methylene-1,5-heptadiene ((*E*)-**3**) with the Arrhenius parameters $E_a$ = 31.7 kcal/mol and log *A* 10.6 (*A* in $s^{-1}$). (*R*,*E*)-5-Methylocta-1,2,6-triene ((*R*,*E*)-**1**), 90.8 ± 0.8% enantiomerically pure, upon pyrolysis at 440 K gives (*R*,*E*)-**3** with 62% ee, which corresponds to 68% retention of enantiomeric specificity in the rearrangement to *E*-product. Antarafacial participation of one allylic unit thus accounts for about 16% of the reaction. The simplest mechanistic interpretation involves two competitive chairlike pathways which lead respectively to the axial and equatorial biradicals **4** and **6**. Products are formed by cleavage of the $C_3$–$C_4$ bond of the biradicals, either before or after internal rotations to conformational isomers **5** and **7**.

Although the ordinary Cope rearrangements of many simple 1,5-dienes probably are concerted reactions,[1-3] the energy of the transition state is close to that of a cyclohexane-1,4-diyl.[4] This circumstance has prompted speculation that, in some cases at least, the diyl might be an actual intermediate in a hypothetical nonconcerted, stepwise cyclization-then-cleavage mechanism.[4-10] A previous test in this laboratory[5] excluded a diyl intermediate in the acetylenic Cope rearrangement. That result provides motivation for the present work, in which the objective is to modify the reactant's structure so as to favor a stepwise mechanism. Both studies use a stereochemical probe to follow the faciality of reaction of an allylic unit bearing linked configurational markers at the bond-forming and bond cleavage sites.

It is convenient to classify the relationship of the allylic facialities and the mechanisms of thermal Cope rearrangements of 1,5-dienes as follows: (i) both allylic units participate suprafacially in the orbital symmetry allowed "chair" and "boat" reactions; (ii) both participate antarafacially in the also formally allowed (but so far experimentally unknown) "twist" and "plane" reactions; and (iii) one participates suprafacially and one antarafacially in the orbital symmetry forbidden pathways.[1,11]

A stepwise mechanism through a conformationally mobile diyl intermediate would allow antarafacial participation of one allylic unit and hence would be stereochemically indistinguishable from a formally forbidden mechanism.[5] As mentioned, our earlier examination of the acetylenic Cope rearrangement,[5] as well as other studies[12,13] of dienic Cope rearrangements, found only suprafacial allylic participation, and prior examples of antarafacial participation of one or both allyl units in a Cope rearrangement seem to be unknown.

For the present work, we have designed a new test molecule to stabilize the cyclohexane-1,4-diyl through conjugation, thereby encouraging the stepwise rearrangement mechanism and the consequent antarafacial stereochemical course of reaction. This strategy now has produced what is apparently the first antarafacial Cope rearrangement, which is most simply interpreted as the result of a stepwise mechanism.[14]

**Experimental Design and Synthesis.** The test compound is 5-methylocta-1,2,6-triene (**1**, Scheme 1), in which bond formation between $C_7$ and $C_2$, the center carbon of an allene unit, can generate an allylic radical **2** (Scheme 2). Figure 1 shows the energy diagrams for the unsubstituted parent compound of this case (hepta-1,2,6-triene, Figure 1b) and the paradigmatic Cope system (hexa-1,5-diene, Figure 1a). Although the values of the heats of formation of the biradicals are not known from experiment, they can be calculated by the Benson group additivity method[15a] to allow a comparison of the hypothetical eneallenic and dienic stepwise Cope rearrangements. (Two variations of the Benson method for calculating the heats of formation of these

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(1) Review: (a) Gajewski, J. J. *Hydrocarbon Thermal Isomerizations*; Academic Press: New York, 1981; p 165.

(2) Review: Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1.

(3) Review: Berson, J. A. In *Rearrangements in Ground and Excited States*; de Mayo., P., Ed.; Academic Press: New York, 1980; Vol. I, p 311.

(4) (a) Grob, C. A.; Link, H.; Schiess, P. W. *Helv. Chim. Acta* **1963**, *46*, 483. (b) Doering, W. von E.; Toscano, V. G.; Beasley, G. H. *Tetrahedron* **1971**, *27*, 5299.

(5) (a) Owens, K. A.; Berson, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 627. (b) Owens, K. A.; Berson, J. A. *J. Am. Chem. Soc.* **1990**, *112*, 5973. (c) Berson, J. A. *Chemtracts: Org. Chem.* **1989**, *2*, 213.

(6) (a) Hrovat, D. A.; Borden, W. T.; Vance, R. L.; Rondan, N. G.; Houk, K. N.; Morokuma, K. *J. Am. Chem. Soc.* **1990**, *112*, 2018. (b) Dewar, M. J. S.; Jie, C. *Acc. Chem. Res.* **1992**, *25*, 537 and references cited therein.

(7) Roth, W. R.; Lennartz, H.-W.; Doering, W. von E.; Birladeanu, L.; Guyton, C. A.; Kitagawa, T. *J. Am. Chem. Soc.* **1990**, *112*, 1722.

(8) Padwa, A.; Blacklock, T. J.; Cordova, D. M.; Loza, R. *J. Am. Chem. Soc.* **1981**, *103*, 7202.

(9) (a) Roth, W. R.; Schaffers, T.; Heiber, M. *Chem. Ber.* **1992**, *125*, 739. (b) See also: Bohnen, A. *Diplomarbeit*, Universität Bochum, 1989, as cited in ref 9a.

(10) Biradical intermediates in the Cope rearrangements of other systems have been proposed on criteria other than those used in the present work. See refs 8 and 9.

(11) Goldstein, M. J.; Benzon, M. S. *J. Am. Chem. Soc.* **1972**, *94*, 5119. (b) Goldstein, M. J.; Benzon, M. S. *J. Am. Chem. Soc.* **1972**, *94*, 7147.

(12) Hill, R. K.; Gilman, N. W. *J. Chem. Soc., Chem. Commun.* **1967**, 619.

(13) Gajewski, J. J.; Benner, C. W.; Hawkins, C. M. *J. Org. Chem.* **1987**, *52*, 5198.

(14) (a) The term "antarafacial" as introduced by Woodward and Hoffmann[14b] is a purely geometrical description of a reaction "in which the newly formed or broken bonds lie on opposite faces of the reacting systems." Specifically, it carries no mechanistic implication and should not be interpreted in the present context as suggesting a concerted process. (b) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim, Germany, and Academic Press: New York, 1970; p 65.

(15) (a) Benson, S. W. *Thermochemical Kinetics*; Wiley: New York, 1976. (b) For hexa-1,5-diene, see: Doering, W. von E.; Toscano, V. G.; Beasley, G. H. *Tetrahedron* **1971**, *27*, 5299. For hepta-1,2,6-triene, see ref 21.

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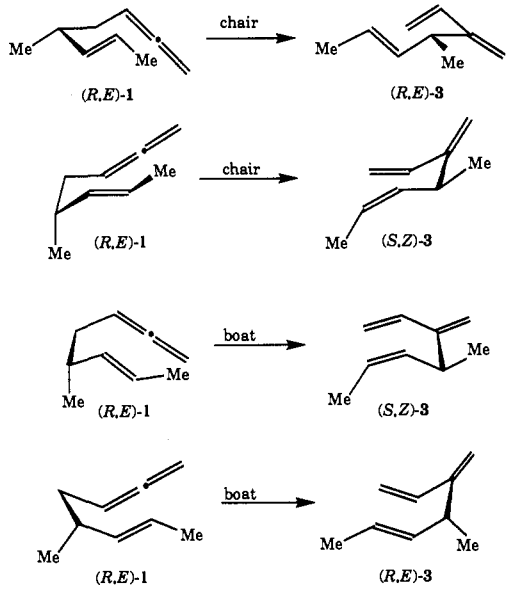
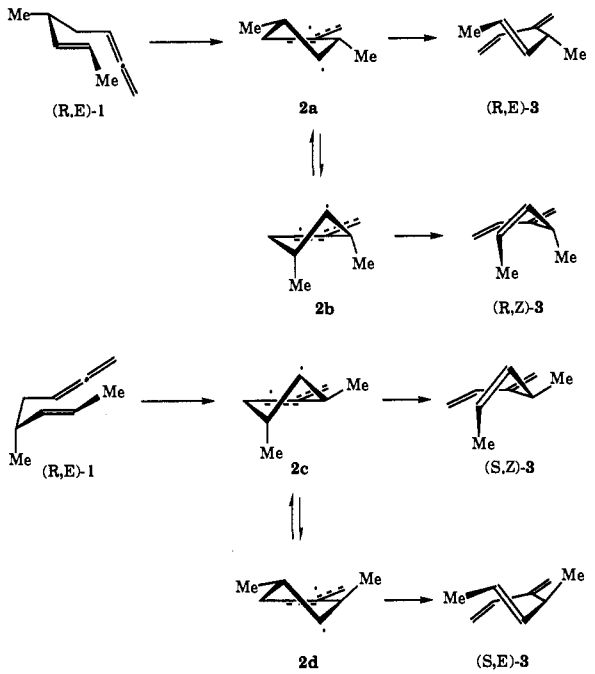
**Scheme 1**




**Scheme 2.** Equatorial (top) and Axial (bottom) Pathways




biradicals are provided in the supplementary material.) It should be emphasized that the method provides only a rough estimate of the heats of formation of free energies of biradicals. The calculations are not capable of accounting for spin-state or through-bond coupling between the radical centers.

There is a striking difference between the two cases. In this crude estimate, the cyclohexane-1,4-diyl from cyclization of hexa-1,5-diene (Figure 1b) can generate a biradical which lies enthalpically 17.6 kcal/mol *below* the transition state (11.5 kcal/mol in free energy). By an argument[5c] derivable from the Hammond postulate, stabilization of the biradical intermediate would correspond to a deeper excavation in the reaction's energy surface. At the same time, the barrier to formation of the intermediate would decrease and the corresponding transition state geometry would move in the direct of the starting material. It follows that the *stabilized* intermediate should have a relatively low barrier to formation and a relatively high barrier for conversion to products. The stepwise pathway might thus represent an energetically accessible alternative to the concerted process, and, if so, the biradical intermediate should have a finite lifetime in the deep energy well. The conformational inversion (stereomutation) of the biradical then would be made more competitive with bond cleavage, thereby enabling the formation of antarafacial products. The energetic relationships in Figure 1 thus justify the expectation that a stepwise mechanism in the hepta-1,2,6-triene system might be observable.

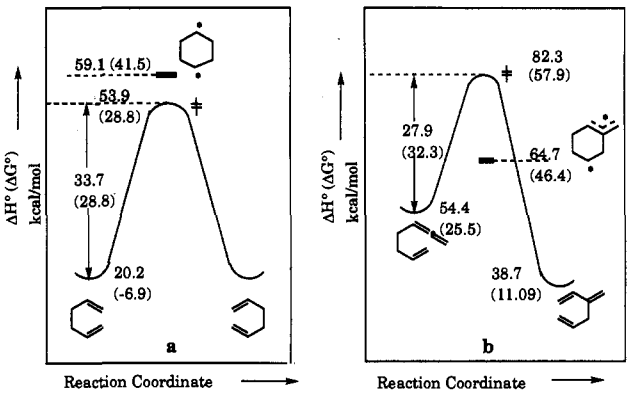


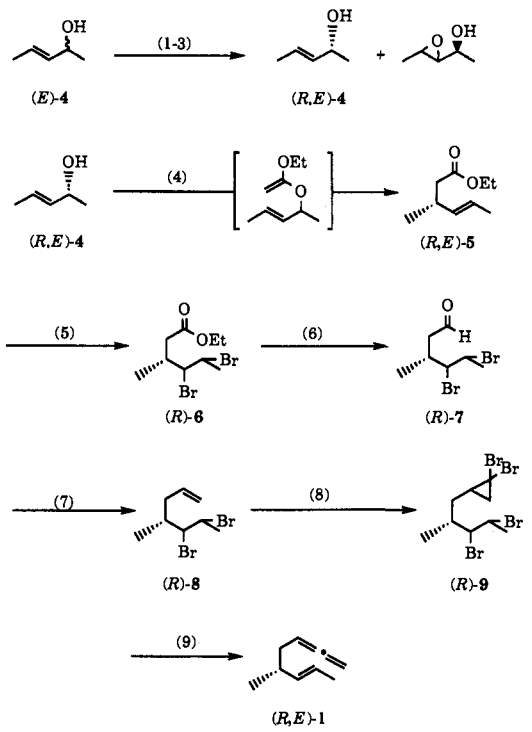

**Figure 1.** Energies of reactants and transition states. Heats of formation (and free energies of formation) of reactants and products were calculated from Benson's group equivalents.[15a] Energies of transition states were calculated by adding the experimental activation energies[15b,c] to the energies of the reactants. Since these are not potential energy diagrams, the reaction coordinate is defined only for the fixed points shown. (a) Rearrangement of 1,5-hexadiene. (b) Rearrangement of 1,2,6-heptatriene.

**Stereochemical Consequences[16] of the Concerted and Stepwise Cope Rearrangement of (*R,E*)-5-Methyl-1,2,6-octatriene ((*R,E*)-1) to 4-Methyl-3-methylene-1,5-heptadiene (3).** Scheme 1 shows the products, (*R,E*)-3 and (*S,Z*)-3, expected from concerted chair or boat Cope rearrangements in the thermolysis of the optically active substrate (*R,E*)-5-methyl-1,2,6-octatriene ((*R,E*)-**1**) to 4-methyl-3-methylene-1,5-heptadiene (**3**). Note that all of these pathways are suprafacial on the allylic unit and that the same two products are generated by either a chair or a boat transition-state conformation.

In contrast, Scheme 2 shows how the incursion of a stepwise pathway with a conformationally mobile biradical intermediate can produce antarafacial participation of the allylic unit and lead to two additional products. Cyclization of (*R,E*)-**1** through a chairlike transition state would lead to biradical conformers **2a** or **2c**, depending upon whether the methyl group is oriented equatorially or axially, respectively. Cleavage from conformers **2a** and **2c**, *before* internal rotation, would yield the supra products (*R,E*)-**3** and (*S,Z*)-**3**, respectively, as in the above (Scheme 1) concerted mechanisms. However, conformational inversion of either of the biradical conformers **2a** or **2c** by internal rotation effectively twists the former allyl unit (Scheme 2); in this way, **2a** gives **2b**, and **2c** gives **2d**. Cleavage of **2b** and **2d** would yield products (*R,Z*)-**3** and (*S,E*)-**3**, respectively, both corresponding to antarafacial participation of the allyl unit. A similar analysis shows that the pathway passing through the corresponding boatlike conformationally mobile intermediates would yield the same products (*R,Z*)-**3** and (*S,E*)-**3**. The predictions of Schemes 1 and 2 thus constitute the proposal of a stereochemically based test for a stepwise mechanism. An exclusively concerted rearrangement (Scheme 1) would preserve the optical purity of the starting eneallene and yield only the supra products (*R,E*)-**3** and (*S,Z*)-**3**, but a stepwise rearrangement (Scheme 2) via a conformationally mobile biradical intermediate would compromise the stereospecificity, and both enantiomers of each of the products (*E*)-**3** and (*Z*)-**3** would be formed.

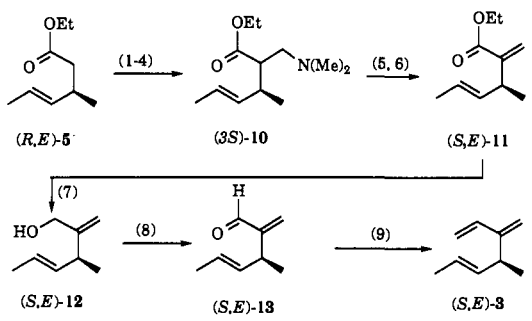
(16) The experimental design does not permit the determination of the stereochemistry at the allenic unit. The antara–antara plane and twist pathways, although orbital symmetry allowed, are sterically difficult. They have been excluded by a deliberate test experiment in another case,[13] and we assume they are not involved here.

**Scheme 3**[a]




[a] Methods: (1) $Ti(OiPr)_4$, L-(+)-DIPT, $CH_2Cl_2$, −30 °C, molecular sieves. (2) $(CH_3)_3CO_2H$. (3) Aqueous $FeSO_4$, tartaric acid. (4) $CH_3CH(OEt)_3$, $H^+$, 180 °C. (5) $Br_2$, $CH_2Cl_2$, NaBr, 15-Cr-5. (6) DIBAL-H, hexanes, −77 °C. (7) $Ph_3P{=}CH_2$, THF. (8) $CHBr_3$, NaOH(aq), $Et_3N$, $CH_2Cl_2$. (9) MeLi, $Et_2O$, −40 °C.

**Scheme 4**[a]




[a] Methods: (1) LDA, THF, hexanes, HMPT, −78 °C to −42 °C. (2) $CH_2{=}N^+(CH_3)_2$ $I^-$, THF, −42 °C to 25 °C. (3) Aqueous HCl. (4) Aqueous NaOH. (5) MeI, 60 °C. (6) Aqueous $NaHCO_3$, $Et_2O$. (7) DIBAL-H, hexanes, −78 °C. (8) $MnO_2$, hexanes. (9) $Ph_3P{=}CH_2$, THF.

**Syntheses of Reactant 1 and Product 3.** The racemic (*R,S,E*)- and enantiomerically enriched (*R,E*)-5-methyl-1,2,6-octatriene (**1**) were synthesized, respectively, from the racemic (*R,S,E*)- and 90.8% enantiomerically enriched (*R,E*)-allylic alcohol 3-penten-2-ol (**4**) in six steps as shown in Scheme 3. The enriched **1** was obtained in 90.8 ± 0.8% enantiomeric excess (ee). The rearrangement product was synthesized (Scheme 4) in racemic and 90.8 ± 0.8% enantiomerically enriched form, (*R,S,E*)- and (*S,E*)-4-methyl-3-methylene-1,5-heptadiene (**3**), respectively. In the case of the *S,E*-form, the starting material was the ester (*R,E*)-**5**, obtained from the *same* enantiomerically enriched allylic alcohol (*R,E*)-**4**.[17]

The commercially available allylic alcohol **4** was enantiomerically enriched using the Sharpless kinetic resolution.[18] The ee of **4** was estimated by polarimetry and by a $^1H$ NMR study of the corresponding acetate in the presence of tris{3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato}europium(III) (Eu(hfpc)$_3$). The sign of the specific rotation, $[\alpha]^{21}_D = +17.62 \pm 0.50°$ (*c* $2.10 \times 10^{-3}$ g/mL, $CDCl_3$), confirmed the assignment of this sample of (*E*)-3-penten-2-ol (**4**) as having the *R*-configuration. The observed rotation corresponds to an ee of 96 ± 5%.[19,20]

The ortho ester–Claisen reaction of (*R,E*)-3-penten-2-ol (**4**) and triethyl orthoacetate yielded (*R,E*)-ethyl 3-methyl-4-hexenoate **5** with virtually complete transfer of chirality.[20] The remaining steps in the syntheses of **1** and **3** did not compromise the optical purity of the samples; the ees of **1** and **3** determined at the end of the syntheses (90.8 ± 0.8%) were in rough agreement with that of the optically enriched starting allylic alcohol **4** (96 ± 5%). The ees of both **1** and **3** were independently evaluated using chiral capillary gas chromatography (CCGC). These analyses are discussed in the Experimental Section. In the absence of a reasonable mechanistic hypothesis for complete inversion of configuration during either of the syntheses, the assignments of the configurations of the synthetic **1** and **3** as *R* and *S*, respectively, seem secure.

**Practical and Stereochemical Issues in the Synthesis of 1 and 3 from the Ester 5 (Schemes 3 and 4).** We planned to construct the allenic moiety of **1** by reductive debromination–rearrangement of a dibromocyclopropane, which in turn could be derived by dibromocarbene addition to a terminal double bond. Selectivity necessitated the reversible protection of the (eventual) $C_6$–$C_7$ *trans* double bond, which is present in the starting material **5**. Protection of the *trans* double bond with molecular bromine exploited a stereospecific (*anti*) addition and, after suitable transformation of the dibromide, enabled a subsequent stereospecific (*anti*) elimination (deprotection) with methyllithium. Methyllithium also was useful in the reductive rearrangement, so that this reagent effected both the deprotection and the rearrangement to the allene in the same step, **9** → **1**. The *trans* stereochemistry in the ester **5** and in the enallene **1** was confirmed by $^1H$ NMR. Both compounds showed coupling constants, $J_{6,7}$ = 15.3 Hz, which were of the magnitude expected for the *trans* configuration.

One difficulty occurred in the addition of bromine to **5**, which gave, in addition to the desired dibromide, substantial quantities of a bromolactone. Presumably, the two products result from partitioning of an intermediate bromonium ion between attack of bromide ion and intramolecular cyclization. To circumvent this problem, an excess of NaBr was added to the reaction mixture to increase the concentration of $Br^-$ and speed up the bimolecular reaction relative to the cyclization. Addition of the $Na^+$-selective crown ether 15-crown-5 improved the limited solubility of NaBr in the $CCl_4$ solvent. Under these conditions, no bromolactone was formed, and relatively pure dibromoester **6** was obtained. The remaining steps in the synthesis of **1** were carried out according to standard literature procedures.

The synthesis of (*S,E*)-**3** from (*R,E*)-**5** (Scheme 4) used steps modeled upon known general procedures. The stereochemistry of the double bond of **3** could not be confirmed directly but could be confidently assigned from the configuration of the starting ester **5**, which was known, and the configuration of the synthetic intermediate dienic alcohol **12**, which could be identified as *trans* from the observed $J_{4,5}$ = 15.3 Hz.

**Pyrolysis of Racemic (*E*)-5-Methyl-1,2,6-octatriene (1). Determination of Arrhenius Parameters.** Samples of racemic en allene **1**, analytically pure by GC, were obtained by preparative

(17) (a) We thank V. Griffin for a fruitful suggestion that facilitated the synthesis of the rearrangement product **3**. (b) The predominant *S,E*-enantiomer of **3** independently synthesized from (*R,E*)-3-penten-2-ol (**4**) is opposite in configuration to (*R,E*)-**3**, the major product of the pyrolysis of (*R,E*)-**1**.

(18) This procedure is based on that reported by: Gao, Y.; Hanson, R. E.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765

(19) The basis for the assignment of the *R*-configuration to the recovered (+)-alcohol **4** is discussed in ref 5a and 20.

(20) Hill, R. K.; Soman, R.; Sawada, S. *J. Org. Chem.* **1972**, *37*, 3737.

GC. Gas-phase pyrolyses were carried out in sealed silanized Pyrex glass tubes immersed in a molten salt bath. The bath temperature was varied between 214 °C and 255 °C, and pyrolysis times ranged from 32 to 260 min. Internal surface area was in the range 10–20 cm$^2$, and internal pressure was in the range 16–20 Torr. Product composition was monitored by capillary GC analysis of the crude pyrolysate in pentane. The major rearrangement product **3** initially constituted about 75% of the total product; it was isolated by preparative GC. Capillary GC–MS analysis of the crude pyrolysate revealed that except for dimeric material, which was distinguishable by its exceptionally long GC retention time, all of the pyrolysis products were isomeric with the starting eneallene. That several of the minor products resulted from secondary rearrangements of the triene **3** was evidenced by time–composition profiles. The minor components of the pyrolysate could not be isolated, although there is evidence (see the Experimental Section) that the *Z*-isomer of **3** is present to the extent of 5–6%.

A kinetic investigation of the thermal rearrangement of racemic eneallene **1** was carried out as described in the previous paragraph with the following exceptions: the temperature range was 142–177 °C, the internal surface area was in the range 20–90 cm$^2$, and the internal pressure was in the range 4–16 Torr. Under these conditions, no dimeric material was observed. The total material balance was 92–104%, as determined by comparison to toluene internal standard. Differential volatility of **1** and the internal standard probably caused the slight deviation from 100%.

Rate constants for the disappearance of **1** were evaluated at five different temperatures ranging from 142 °C to 177 °C. At each temperature, between four and six tubes were pyrolyzed for different lengths of time (usually $t/16$, $t/8$, $t/4$, $t/2$, and $t$, where $t$ is the half-life of the substrate **1** at the given temperature). In all cases, **1** exhibited first-order kinetics with no dependence on internal pressure nor on internal surface area. The rate constants obtained corresponded to the formation of all primary pyrolysis products; therefore, they were corrected to reflect only the formation of **3**. Samples of the kinetic data are presented in the Experimental Section, and all of the runs are reported in the supplementary material.

An Arrhenius plot of the rate data for the rearrangement of **1** to **3** yielded an activation energy of 31.7 ± 1.6 (or 0.8) kcal/mol and a log $A$ value of 10.6 ± 0.8 (or 0.4) ($A$ in s$^{-1}$). At 432 K, the corresponding activation enthalpy is 30.9 ± 1.6 (or 0.8) kcal/mol and the activation entropy is −12.7 ± 3.7 (or 1.8) eu. The significance of the two values each for the error limits is given in the Experimental Section.

The present values are comparable to those obtained by Frey and Lister[21] for the analogous rearrangement of the parent unsubstituted compound 1,2,6-heptatriene ($E_a$ = 30.47 kcal/mol, log $A$ = 9.97, $\Delta H^{\ddagger}$(432 K) = 29.62 kcal/mol, $\Delta S^{\ddagger}$(432 K) = −15.63 eu). Those authors interpreted the relatively low activation energy and the large negative activation entropy for the rearrangement of 1,2,6-heptatriene as consistent with a concerted [3,3]-sigmatropic process by way of a cyclic transition state.

**Pyrolysis of Enantiomerically Enriched (*R*,*E*)-5-Methyl-1,2,6-octatriene (1).** GC analytically pure samples of enantiomerically enriched eneallene **1** were pyrolyzed in the gas phase under the conditions described for the kinetic analyses. The degree of chirality transfer was evaluated for the rearrangement at three different temperatures between 142 °C and 194 °C. The ee of the starting eneallene was 90.8 ± 0.8%. In each investigation, the eneallene **1** and the product **3** were recovered from the crude pyrolysate by preparative GC. Enantiomeric excess evaluations of the (capillary) GC analytically pure samples were made using chiral capillary GC (CCGC). In this technique, accurate enantiomer ratios are obtained when the enantiomeric peaks do not overlap those of other components in the sample. Isomeric contaminants can be especially troublesome since these are likely to elute from the GC column in the same general region as the enantiomers of interest. In the present ee determinations, the purity of each sample was established by capillary GC prior to analysis. Details of purification procedures and purity assessments are described in the Experimental Section.

(21) Frey, H. M.; Lister, D. H. *J. Chem. Soc. A* **1967**, *26*.

**Table 1.** Percent Enantiomeric Excess (ee) of **1** and **3** Recovered from Pyrolysis of Enantiomerically Enriched (*R*,*E*)-**1** (90.8 ± 0.8% ee)

| pyrolysis temperature (°C) | pyrolysis time ($\times t_{1/2}$)[a] | % ee of recovered **1** | % ee of recovered **3** |
|---|---|---|---|
| 142 | 1 | 90.9 ± 0.8 | 63.4 ± 0.8 |
| 172 | 4.5 | 91.4 ± 0.8 | 61.9 ± 0.8 |
| 194 | 1.5 | 90.5 ± 0.8 | 62.4 ± 0.8 |

[a] $t_{1/2}$ is the half-life of **1** at the given temperature.

The data of Table 1 indicate that eneallene (*R*,*E*)-**1** recovered from the pyrolyses had an ee that was essentially undiminished from its starting ee. Similarly, triene product (*S*,*E*)-**3** was recovered with undiminished ee from a separate pyrolysis of the analytically pure enantiomerically enriched (90.8 ± 0.8% ee) and independently synthesized product (*S*,*E*)-**3**. Also, the ee of the rearrangement product **3** isolated from the pyrolysate was independent within experimental error of the pyrolysis temperature and time in the range investigated. These experiments demonstrate that the partial racemization of the rearrangement product (*R*,*E*)-**3** from pyrolysis of (*R*,*E*)-**1** is not a consequence of prior racemization of **1** or of secondary racemization of **3**.

The major component of the *E*-product, which emerged first in CCGC analysis of GC analytically pure pyrolysis product, was (*R*,*E*)-**3**, as established by the already described independent synthesis of the minor enantiomer (*S*,*E*)-**3**. The average ee of material recovered from three separate runs was 62.6 ± 0.8% (Table 1). This corresponds to a 68.9% retention of ee in the Cope rearrangement.[22] Less than 6% of the total pyrolysate mixture corresponded to the *Z*-isomer of **3** (see below). So far, the presence of other minor pyrolysis products in the reaction mixture has prevented us from isolating (*Z*)-**3** or determining its ee. CCGC traces of the starting eneallene (*R*,*E*)-**1** and purified pyrolysis product (*E*)-**3** are shown in the supplementary material.

**Mechanistic Implications (Scheme 2).** The minor enantiomer of the pyrolysis product, (*S*,*E*)-**3**, results from a contribution of 15.5% (half of the observed loss of ee) from a process that is antarafacial with respect to the allyl unit.[23] It should be clear that these results cannot be explained in the framework of a conventional concerted Cope rearrangement. The simplest mechanistic interpretation of the results (Scheme 2) invokes conformationally mobile biradical intermediates in the eneallenic Cope rearrangement. Our experimental design does not shed light on the exact conformation of these biradicals (see below), but for the present argument it is convenient to describe them as half-chairs. Two competitive chairlike pathways lead respectively to the equatorial and axial biradicals **2a** and **2c**. These are isomeric, although not directly interconvertible by internal rotations. Products are formed by cleavage of the $C_3$–$C_4$ bond of the biradicals, either before or after internal rotations to conformational isomers **2b** and **2d**.

The two major products resulting from the thermolysis of (*R*,*E*)-**1** are (*R*,*E*)-**3** and (*S*,*E*)-**3**, in a roughly 4:1 ratio. In the stepwise rearrangement they result from cleavage of the biradicals **2a** and **2d**, respectively. Of these two, only **2a** is formed directly from the starting material **1**, by cyclization of (*R*,*E*)-**1** via a

(22) Percent retention of ee was calculated as follows: 100(ee observed/ee initial) = ee retained; 100(62.6%/90.8%) = 68.9%.

(23) Although the labeling scheme in the rearrangement studied is only capable of detecting the faciality of the allyl unit's participation and not that of the allenic unit, the products formed from the "ring-flip" biradical conformers **2b** and **2d** formally arise from antara–antara processes.

chairlike transition state with an equatorially oriented $C_5$ methyl group. In contrast, according to Scheme 2, the biradical **2d** can only be formed from conformational inversion of the biradical **2c**, which, like **2a**, is formed directly from the starting material **1**, again by cyclization of (*R*,*E*)-**1** via a chairlike transition state, but now with an *axially* oriented $C_5$ methyl group. Internal rotation in **2c** leads to the "ring-flip" conformer **2d**, which undergoes cleavage to the formally antara-antara product (*S*,*E*)-**3**.[23]

Note that the specific postulation of a half-chair conformation for the hypothetical biradical intermediates of Scheme 2 is not a crucial feature of the mechanistic analysis, since the same products, in different proportions, would be expected from a biradical mechanism with boatlike transition states. The possibility of competing concerted and stepwise rearrangements of (*R*,*E*)-**1**, as proposed on other grounds for a different system,[9] cannot be excluded at present.

The fact that the *Z*-olefinic isomer accounts for not more than 6% of the total pyrolysis product mixture is not surprising. The *Z*-isomer is higher in energy than the *E*-isomer, and the transition states preceding these products, to the extent that they resemble the products, should also retain this energetic preference. Similar considerations apply in the case of the acetylenic Cope rearrangement of (*R*)-4-methyl-2-hepten-6-yne, in which the same 2-penten-4-yl (1,3-dimethylallyl) unit was used as a stereochemical probe and in which only 5% of the *Z*-product (*Z*)-4-methyl-1,2,5-heptatriene was formed.[5] Another point of analogy with the enynic system[5] is the (relatively) sterically undemanding second $\pi$ moiety (monosubstituted acetylene in the enynic case and monosubstituted allene in the present case).

That Scheme 2 is compatibile with the properties expected of the putative biradicals is demonstrated by two arguments that lead to plausible approximate predictions of the relative distribution of the stereoisomeric rearrangement products **3**.

The first is based upon the relative steric energies of the biradicals and the assumption, for the sake of argument, that the product composition is controlled by transition-state energies that parallel the biradical energies. The assumption probably is not totally unreasonable, since the conversion of the biradical intermediate **2** to product **3** should be exothermic by 26 kcal/mol (see Figure 1), and the Hammond postulate[24] would predict that the transition state for the cleavage process should closely resemble the biradical species.

A rough qualitative estimate of the relative energies of the four biradicals based upon an examination of molecular models[25] is **2a** < **2d** < **2c** < **2b**. If the triene product distribution reflects the relative energies of the biradicals, one then might predict that the order of contribution to total product would be (*R*,*E*)-**3** > (*S*,*E*)-**3** > (*S*,*Z*)-**3** > (*R*,*Z*)-**3**. Although the enantiomeric ratio of the *Z*-olefinic isomers is unknown, the observed product proportions tend to support the prediction.

A more quantitative way to estimate the rate preference[26] for the equatorial pathway in Scheme 2, and ultimately the product distribution, is by analogy to the Cope rearrangement of 3-methyl-1,5-hexadiene studied by Frey and Solly.[27] In that system, the ratio of (*E*)- to (*Z*)-1,5-heptadiene products formed was 80.3:19.7 at 440 K. The Arrhenius parameters for the rearrangements were $E_a$ = 34.2 kcal/mol, log *A* = 10.55 and *E*a = 35.7 kcal/mol, log *A* = 10.54, respectively; they are consistent with a concerted pericyclic mechanism involving a cyclic transition state.

The (*E*)- and (*Z*)-1,5-heptadiene products from 3-methyl-1,5-hexadiene presumably are formed by way of chair transition states[27,28] with respectively equatorial and axial methyl groups. In the rearrangement of the eneallene **1**, cyclization to the biradicals **2a** and **2c** via the corresponding chairlike equatorial and axial pathways, respectively, would be expected to occur in about the same 80.3:19.7 ratio.

Formation of (*R*,*Z*)-**3** via the equatorial pathway in this scheme is unfavorable because of the severe steric repulsion of the 1,3-diaxial methyl groups in the precursor biradical **2b**. Thus, the most likely source of the 5–6% of (*Z*)-**3** formed in the reaction is the (*S*,*Z*)-**3** formed from the biradical **2c** in the axial pathway.

The remaining contribution to the rearrangement product then would have the *E*-configuration. It would consist of a contribution of (*S*,*E*)-**3** from the biradical **2d** in the axial pathway in the amount of (19.7 – 5)% = 14.7% (or (19.7 – 6)% = 13.7%) of the total product and a contribution of (*R*,*E*)-**3** of 80.3% from the equatorial pathway. The expected ratio (*R*,*E*)-**3**/(*S*,*E*)-**3** then would be between 80.3:14.7 (=84.5:15.5) and 80.3:13.7 (=85.5:14.5), corresponding to 69–71% retention of ee. This matches the observed value of 68%.

Our present inability to determine the sense and magnitude of the ee of the minor product (*Z*)-**3** deprives us of an additional check on the plausibility of the mechanistic scheme proposed. Therefore, the close match of the observed and predicted retention of ee in the (*E*)-**3** product may be partly fortuitous. Nevertheless, the conformity of the available data to the mechanism is reassuring.

## Discussion

Since little or no temperature dependence on the ee of recovered (*E*)-**3** is observed, the competing processes responsible for the partial racemization of rearrangement product evidently have nearly equal activation energies. This is reasonable for partitioning of a reactive intermediate between two pathways each passing over a low barrier, for example, internal rotation and bond cleavage in a biradical as shown in Scheme 2.

Alternatives to account for the racemization may be imagined, but such interpretations also must provide an alternative explanation for the temperature-independence. This requirement leads to difficulties. For example, one might hypothesize that a concerted Cope rearrangement competes with a dissociation of the $C_4$–$C_5$ bond of the reactant **1** to give two allylic radicals. However, model reactions[29] suggest that the activation energy $E_a$ for the latter process should be 55–60 kcal/mol, which is much higher than the observed value of 31 kcal/mol for the present rearrangement.

Moreover, the rate constant for the dissociation at 467 K (the highest temperature used in the evaluation of the percent chirality transfer in the present study) can be estimated[29] to be about $1.8 \times 10^{-10}$ s$^{-1}$, which is to be compared with the rate constant of $5.8 \times 10^{-5}$ s$^{-1}$ at the same temperature obtained from the Arrhenius plot in the present work. Thus, the hypothetical dissociative process would be $10^4$–$10^5$ too slow to compete with the intramolecular Cope rearrangement.

## Conclusion

The stereochemical analysis of the product **3** resulting from gas-phase pyrolysis of the optically active substrate (*R*,*E*)-**1** has

(24) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

(25) (a) Wessel, T. E. Ph.D. Dissertation, Yale University, New Haven, CT, 1994. (b) This analysis could be made more quantitative by molecular mechanics calculations, but it is not clear that reliable estimates of steric energies of biradicals can be made by this method.

(26) The analysis that follows does not require (or assume) that equilibrium is achieved between the members of the biradical pairs **2a**–**2b** and **2c**–**2d**.

(27) Frey, H. M.; Solly, R. K. *Trans. Faraday Soc.* **1968**, *64*, 1858.

(28) Doering, W. von E.; Roth, W. R. *Tetrahedron* **1962**, *18*, 67.

(29) (a) As models, we note the Arrhenius parameters reported for the dissociation of 1,5-hexadiene: (b) Golden, D. M.; Rossi, M.; King, K. D. J. *J. Am. Chem. Soc.* **1979**, *101*, 1223. (c) Tsang, W. *Int. J. Chem. Kinet.* **1969**, *1*, 245. (d) In ref. 13, the free energy of activation for the dissociation of the tetramethyl-substituted 1,5-hexadiene, *threo*-4,5-dimethyl-(*Z*,*Z*)-1,1,1,8,8,8-hexadeuterio-2,6-octadiene was reported as 47.0 kcal/mol at 300 °C. The values given in the present paper for the Arrhenius activation energy and corresponding rate constant for the dissociation of the *threo*-4,5-dimethyl-(*Z*,*Z*)-1,1,1,8,8,8-hexadeuterio-2,6-octadiene at our highest reaction temperature, 467 K, were calculated using either of the *A* values[29b,c] in the literature for the dissociation of unsubstituted 1,5-hexadiene. Since *threo*-4,5-dimethyl-(*Z*,*Z*)-1,1,1,8,8,8-hexadeuterio-2,6-octadiene has a methyl unit on *both* ends of the breaking bond and forming bond, it probably undergoes dissociation more readily than the eneallene **1**.

indicated that the eneallenic Cope rearrangement proceeds with 68.9% retention of ee. This corresponds to a contribution of 15.5% from a process that is antarafacial with respect to the allyl subunit. The simplest mechanistic interpretation of this result is that the present experimental design, as we had hoped it would, does confer stabilization upon the intermediate sufficient to divert the Cope rearrangement from its normally concerted pathway into a stepwise mechanism passing over a conformationally mobile biradical species (Scheme 2).

## Experimental Section

**Spectrometers.** Proton and carbon NMR spectra were recorded either on a Bruker WM 250 or on a Bruker AM 500 (250 or 500 MHz for proton spectra and 62.5 or 125.7 MHz for carbon spectra, respectively). Couplings in the carbon spectra were determined by off-resonance decoupling experiments. All spectra were taken in $CDCl_3$ unless otherwise specified. The shifts are reported in parts per million using the $CHCl_3$ peak at 7.24 ppm as reference for the proton spectra and the central peak of $^{13}CDCl_3$ at 77.0 ppm as reference for the carbon spectra. The proton spectra are reported in the following manner: chemical shift (multiplicity [s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad], coupling constants, number of nuclei, assignment). When possible, the major and minor diastereomer resonances were identified.

Low-resolution mass spectrograms were obtained using a Hewlett-Packard 5971A GC/MSD. The gas chromatograph was fitted with a 30-m fused silica capillary column. The capillary inner diameter was 0.25 mm, and the stationary phase SE-30 had a film thickness of 0.25 $\mu$m. The carrier gas was helium. Mass spectra were obtained at 70 eV. Mass spectral data are reported in the following manner: $m/e$ fragment (relative abundance as a percent of the parent). High-resolution mass spectra were obtained by Mr. D. Pentek of Yale Univesity Chemical Instrumentation Center using a Kratos MS80 RFA.

Infrared (IR) spectra were recorded on a Nicolet 5-SX FT-IR spectrometer. All spectra were recorded in $CDCl_3$ solution.

**Polarimetric Analyses of 3-Penten-2-ol (4).** All measurements were obtained on a Perkin-Elmer 241 polarimeter at room temperature (21 °C) in $CDCl_3$ solution using the sodium D lines at 5890 and 5896 Å. Samples of the allylic alcohol were obtained by preparative gas chromatography, and, prior to polarimetric analysis, their analytical purity was confirmed by capillary gas chromatography. The allylic alcohol was typically transferred to a preweighed 2-mL volumetric flask and weighed on an analytical balance (precision ±0.0001 g); measurements were performed quickly to minimize evaporation of the sample and absorption of moisture. $CDCl_3$ was then added to a total volume of 2 mL. In all analyses, roughly the same concentration of allylic alcohol was used, and polarimetric readings of blank samples of pure $CDCl_3$ were taken. Measured rotations were typically in the range +0.035° to +0.053° and had an uncertainty of ±0.002°. The uncertainty in the reported rotation was calculated to be ±0.5°.

**$^1$H NMR Eu(hfpc)$_3$ Shift Study of (*R,E*)-3-Penten-2-yl Acetate.** Approximately 5 mg (0.03 mmol) of the acetate, purified by preparative GC, was placed in a 5-mm NMR tube along with 1.5 mL of dry $C_6D_6$. In a separate dry vial, 52.8 mg of Eu(hfpc)$_3$ was dissolved in 1.25 mL of $CCl_4/C_6D_6$ (4:1) solution. The resulting reagent solution was 0.035 mM in Eu(hfpc)$_3$. $^1$H NMR (500 MHz) spectra were recorded for the initial solution and after each 10-$\mu$L (0.35 $\mu$mol) aliquot addition of the chiral shift reagent mixture. After a total of 90 $\mu$L (approximately 10 mol %) had been added, the $^1$H NMR signal associated with the acetate methyl group split into two signals corresponding to the major and minor enantiomers,[30] and both moved downfield to approximately 4.2 ppm. Integration of the two signals provided a rough value of the percent ee, 96%.

**Syntheses.** General methodology is described in the supplementary material.

**Scheme 3. Kinetic Resolution[31] of (±)-(*E*)-3-Penten-2-ol (4).**[32] A dry 1-L round-bottomed flask was charged with 6 g of powdered 3-Å molecular sieves. The sieves were flame activated under a stream of nitrogen for 30 min. The flask was cooled to room temperature, and 700 mL of dry, freshly distilled $CH_2Cl_2$ and 15.00 g (174.2 mmol) of **4** (Aldrich Chemical Co.) were added. The solution was stirred under a nitrogen atmosphere and cooled to approximately –40 °C. Next, 5.50 mL (26.2 mmol) of L-(+)-diisopropyl tartrate was added dropwise to the stirring solution, followed by 5.20 mL (17.4 mmol) of titanium tetraisopropoxide. The reaction solution was stirred at –40 °C for 1 h. Next, 25.80 mL (122.0 mmol) of anhydrous *tert*-butyl hydroperoxide solution[33] (4.72 M in $CH_2Cl_2$) was added dropwise to the stirring solution over a period of 2 h using a gas-tight syringe and a syringe pump. The reaction was allowed to proceed at –40 °C for approximately 30 h.

After the solution was warmed to 0 °C, the reaction was quenched with 300 mL of a prechilled (0 °C) aqueous solution of $FeSO_4$ and tartaric acid (made by dissolving 100 g of $FeSO_4$ and 30 g of tartaric acid in 300 mL of distilled water). After the solution was stirred vigorously for 1 h, two fairly clear phases were observed. The phases were separated, and the aqueous layer was extracted with three 200-mL portions of $CH_2Cl_2$. The combined organic extracts were stirred with 50 mL of 30% NaOH in brine[34] for 1 h at 0 °C. After warming to room temperature, the mixture was diluted with 50 mL of distilled water, and the two phases were separated. The aqueous layer was extracted three times with 100 mL of $CH_2Cl_2$. The combined organic extracts were washed with brine, dried ($MgSO_4$), and vacuum filtered.

Capillary GC analysis of the crude solution revealed primarily two components, the allylic alcohol **4** and the epoxy alcohol [cap column A: programmed column temperature, 35 °C (10 min) to 240 °C at 15 °C/min; retention times, 3.5 min (**4**), 5.7 min (epoxy alcohol)]. The crude solution was concentrated; the $CH_2Cl_2$ and 2-propanol were removed by careful distillation through an 8-in. vacuum-jacketed Vigreux column fitted with a water-cooled condenser and receiving flask. The same apparatus enabled distillation of the allylic alcohol (vapor temperature, 119–120 °C) and the epoxy alcohol (vapor temperature, 156 °C) at ambient pressure. Milligram quantities of capillary GC analytically pure **4** and the epoxy alcohol were obtained by preparative gas chromatography [prep column A: column temperature, 50 °C; flow (He), 38 mL/min; retention times, 4 min (**4**), 8 min (epoxy alcohol)].

The ee of the resolved allylic alcohol was estimated by polarimetry and by a $^1$H NMR study on the corresponding acetate in the presence of tris{3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato}europium-(III) (Eu(hfpc)$_3$). The sign of the specific rotation, $[a]^{21}_D = +17.62$ ($c$ $2.10 \times 10^{-3}$ g/mL, $CDCl_3$), confirmed the assignment of (*E*)-3-penten-2-ol (**4**) as having the *R*-configuration.[5] The ee was estimated to be 96%.

**Epoxy Alcohol.** $^1$H NMR ($CDCl_3$, 250 MHz): δ 3.93 (multiplet, 1 H, methine proton), 3.05 (multiplet, 1 H, methine proton), 2.72 (multiplet, 1 H, methine proton), 1.84 (broad singlet, 1 H, hydroxyl proton), 1.32 (doublet, $J$ = 6.4 Hz, 3 H, methyl group protons), 1.23 (doublet, $J$ = 6.5 Hz, 3 H, methyl group protons).

**(*R,E*)-3-Penten-2-yl Acetate.** (*R,E*)-3-Penten-2-yl acetate was prepared from (*R,E*)-3-penten-2-ol (**4**) according to the procedure outlined by Owens and Berson.[5] A capillary GC analytically pure sample of the acetate was obtained by preparative GC [prep column A: column temperature, 60 °C; flow (He), 38 mL/min; retention time, 12 min].

**(*R,E*)-Ethyl 3-Methyl-4-hexenoate (5).** The Claisen reaction of (2*R*,3*E*)-3-penten-2-ol (**4**) and triethyl orthoacetate yielded **5**. The method of Hill and Gilman[12] was employed, incorporating the slight modification of the workup reported by Owens and Berson.[5] The purity of **5** was usually assessed by capillary GC analysis [cap column A: programmed column temperature, 60 °C (5 min) to 240 °C at 5 °C/min; retention time, 9.8 min.].

**(3*R*,4*S*,5*R*)- and (3*R*,4*R*,5*S*)-Ethyl 4,5-Dibromo-3-methylhexanoate (6).** A 500-mL round-bottom flask was charged with 3.89 g (24.9 mmol) of **5** and 360 mL of $CH_2Cl_2$ (distilled or from a fresh bottle). To the solution was added 55.5 mL of NaBr/15-crown-5/$CH_2Cl_2$ stock solution (1.08 M in NaBr and 1.30 M in 15-crown-5). The mixture was stirred under a nitrogen atmosphere. Next, 30 mL of $Br_2$ solution (1.0 M in $CCl_4$) was added dropwise using a syringe pump. When the addition was complete, the reaction was monitored by TLC to confirm that all of the starting material had been consumed ($CH_2Cl_2$ eluent, $KMnO_4$ stain, $R_f$(**5**) = 0.5, $R_f$(**6**) = 0.6; **5** stains immediately under these conditions,

(30) The NMR signals were assigned on the basis of a control experiment wherein racemic acetate was treated with approximately 10 mol % of Eu(hfpc)$_3$. This procedure is based on that reported by Sharpless *et al.*; Gao, Y.; Hanson, R. E.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

(32) The commercially available (*E*)-**4** contains about 1% of the *Z*-isomer. The configuration of the double bond was also confirmed in the target molecule **1** (see above).

(33) The anhydrous *tert*-butyl hydroperoxide solution was prepared and its titer evaluated according to the procedure of Sharpless (ref 18). The solution's titer was determined just prior to use.

(34) The stock solution of 30% NaOH in brine was made by dissolving 60 g of NaOH and 10 g of NaCl in 180 mL of distilled water.

while **6** requires heating on a hot plate for at least 3 min). In the event that all of **5** is not consumed, additional $Br_2$ solution can be added at this point.

When the reaction was complete, a workup was conducted as follows. The reaction solution was extracted with two 300-mL portions (more if the organic phase was not clear) of a saturated aqueous solution of $Na_2S_2O_3$. Next, the reaction solution was extracted with three 300-mL portions of distilled water to remove most of the 15-crown-5. After drying ($MgSO_4$) and vacuum filtration, the crude solution was concentrated in vacuo. Capillary GC and $^1H$ NMR analysis of the crude product revealed **6** to be the major product. Chromatographic purification of the crude oil (silica gel, $CH_2Cl_2$) yielded 6.45 g (20.4 mmol, 82%) of relatively pure **6**. When the reaction was carried out in the absence of NaBr (and 15-crown-5), an additional product, a bromolactone, was formed in roughly 40% yield (see the discussion of Scheme 3 above).

A mixture of two diastereomers of **6** was obtained. The diastereomers were present in a ratio of approximately 1.7:1.0, as evaluated by $^1H$ NMR and capillary GC analysis [cap column A; programmed column temperature, 100 °C (5 min) to 240 °C at 5 °C/min; retention times, 16.5 min (major), 16.7 min (minor)]. The diastereomers were not separated, and their relative configurations were not determined. Physical characteristics of **6** follow.

$^1H$ NMR ($CDCl_3$, 250 MHz): $\delta$ 4.26–3.95 (m, 4 H, ester methylene protons and $\alpha$-bromo protons), 2.90–2.70 (m, 1 H, methine proton), 2.50–2.05 (m, 2 H, methylene protons), 1.90–1.70 (m, 3 H, terminal methyl protons), 1.22 (bt, $J$ = 7.1 Hz, 3 H, ester methyl protons), 1.06 (minor diastereomer), and 0.90 (major diastereomer) (d, $J$ = 6.4 Hz, 3 H, methyl protons).

GC–MS (70 eV): $m/z$ 273 ($-OCH_2CH_3$, 3), 271 ($-OCH_2CH_3$, 6), 269 ($-OCH_2CH_3$, 3), 237 (–Br, 13), 235 (–Br, 14), 191 (10), 189 (10), 163 (12), 161 (12), 155 ($-HBr_2$, 100), 127 (24), 109 (34), 85 (41), 81 (35).

The physical characteristics of the lactone side product follow.

$^1H$ NMR ($CDCl_3$, 250 MHz): $\delta$ 4.33 (d of d, 1 H), 3.94 (d of q, 1 H), 2.80 (m, 2 H), 2.24 (d, 1 H), 1.82 (d, 3 H), 1.06 (d, 3 H).

GC–MS (70 eV): $m/z$ 139 (4), 137 (4), 100 (6), 99 (100), 83, (4), 71, (20), 55 (15).

FT-IR ($CDCl_3$): 1773 $cm^{-1}$.

**(3*R*,4*S*,5*R*)- and (3*R*,4*R*,5*S*)-4,5-Dibromo-3-methylhexanal (7).** A dry 1-L round-bottom flask was charged with 11.77 g (37.25 mmol) of **6** and 370 mL of freshly distilled hexanes. The flask was fitted with an addition funnel, and the reaction was set stirring under a nitrogen atmosphere. After the reaction mixture was cooled to approximately –50 °C (ethanol constant temperature bath), 45.0 mL of diisobutylaluminum hydride (DIBAL-H) solution (1.0 M in hexanes from Aldrich Chemical Co., 45.0 mmol) was added dropwise over a period of 3 h, using the additional funnel. The reaction solution was allowed to stir overnight at –50 °C.

The reaction was monitored by TLC to confirm that all of the starting material had been consumed [$CH_2Cl_2$ eluent, $KMnO_4$ stain for **6**, vanillin stain followed by heating for **7**, $R_f$(**6**) = 0.6, $R_f$(**7**) = 0.5; vanillin barely stains **6**, whereas it readily stains **7** purple; overreduced product 4,5-dibromo-3-methyl-1-hexanol, present in a small amount, stains dark aqua blue using vanillin, $R_f$ = 0.13; alternatively $KMnO_4$ stain may be used to monitor both **6** and **7**; **7** stains immediately under these conditions, while **6** requires heating on a hot plate for at least 3 min].

When all of the starting material had been consumed, the reaction mixture was allowed to warm to approximately –15 °C. At this point, any remaining DIBAL-H was quenched by adding 30 mL of absolute methanol, dropwise. Upon continued warming to approximately 5 °C, the aluminum salts began to precipitate, forming a thick gelatinous material. At this point, approximately 300 mL of a saturated solution of potassium sodium tartrate was added. The reaction flask was warmed to room temperature, and the clumpy reaction mixture was stirred overnight. The following morning, two reasonably clear phases were observed.

The two phases were separated, and the aqueous phase was extracted with three 200-mL portions of ether. The combined organic extracts were washed with three 300-mL portions of distilled water and one 500-mL portion of brine. After being dried ($MgSO_4$) and vacuum filtered, the crude solution was concentrated in vacuo. Capillary GC and $^1H$ NMR analysis of the crude product revealed **7** to be the major product; 9.96 g (36.6 mmol, 98%) of crude **7** (two diastereomers) was obtained.

A $^1H$ NMR analytically pure sample of **7** was obtained by column chromatography (silica gel, $CH_2Cl_2$, $KMnO_4$, $R_f$(**7**) = 0.65). Under these conditions, **7** separates nicely from the overreduced product but not from **6**, the starting material. (This is why a slight excess of DIBAL-H is used.) Alternatively, crude **7** was often carried on in the synthesis without any problems.

The diastereomers of **7** were present in a ratio of approximately 2:1, as evaluated by $^1H$ NMR and capillary GC analysis [cap column A: programmed column temperature, 100 °C (5 min) to 240 °C at 5 °C/min; retention times, 11.8 min (major), 11.9 min (minor)]. The diastereomers were not separated, and their relative configurations were not determined. The physical characteristics of **7** follow.

$^1H$ NMR ($CDCl_3$, 250 MHz): $\delta$ 9.82 and 9.78 (br s, 1 H, aldehyde protons), 4.32–4.00 (m, 2 H, $\alpha$-bromo protons), 3.07–2.90 (m, 1 H, methine proton), 2.72–2.30 (m, 2 H, methylene protons), 2.00–1.88 (m, 3 H, terminal methyl protons), 1.11 (minor diastereomer) and 0.95 (major diastereomer) (d, $J$ = 6.5 Hz, 3 H, methyl protons).

$^{13}C$ NMR ($CDCl_3$, 62.5 MHz): $\delta$ 200.3 ($C_1$, both), 67.7 ($C_4$, minor), 66.9 ($C_4$, major), 50.5 ($C_5$, minor), 49.5 ($C_5$, major), 45.7 ($C_2$, both), 32.3 ($C_3$, minor), 31.7 ($C_3$, major), 26.6 ($C_6$, major), 25.9 ($C_6$, minor), 19.9 ($C_7$, minor), 13.6 ($C_7$, major).

GC–MS (70 eV): $m/z$ 193 (–Br, 4), 191 (–Br, 4), 149 ($-C_2H_4OBr$, 19), 147 ($-C_2H_4OBr$, 19), 111 ($-HBr_2$, 19), 83 (69), 69 (21), 55 (33).

**(4*R*,5*S*,6*R*)- and (4*R*,5*R*,6*S*)-Dibromo-4-methyl-1-heptene (8).** A dry 50-mL round-bottomed flask was charged with 2.29 g (8.43 mmol) of **7** and 15 mL of dry, distilled THF. The solution was stirred under a nitrogen atmosphere. Next, 15 mL of methylidenetriphenylphosphorane solution (approximately 0.6 M in THF) was added dropwise using a syringe pump to the stirring solution over a period of 1 h. The reaction was monitored independently for the loss of **7** and for the formation of **8** by TLC. The disappearance of **7** was monitored using $CH_2Cl_2$ as eluent and $KMnO_4$ stain; $R_f$(**7**) = 0.62 (under these conditions **8** is not distinguishable from high-$R_f$ contaminants in the ylide stock solution). The appearance of **8** was monitored using hexane as eluent and $KMnO_4$ stain; $R_f$(**8**) = 0.48 (under these conditions **7** is not distinguishable from low-$R_f$ contaminants in the ylide stock solution). When no more **7** was detected, the reaction was worked up.

The solution was quenched with 10 mL of distilled water. The aqueous layer was extracted with three 10-mL portions of THF. The combined organic extracts were washed with 30 mL of brine, dried ($MgSO_4$), vacuum filtered, and concentrated in vacuo. The crude oil obtained was chromatographed (silica gel, hexanes) to give 0.745 g (2.76 mmol, 33%) of relatively pure **8** (two diastereomers).

The diastereomers of **8** were present in a ratio of approximately 1.2:1, as evaluated by $^1H$ NMR and capillary GC analysis [cap column A: programmed column temperature, 100 °C (5 min) to 240 °C at 5 °C/min; retention times, 8.6 min (major), 8.9 min (minor)]. The diastereomers were not separated and their relative configurations were not determined. Physical characteristics of **8** follow.

$^1H$ NMR ($CDCl_3$, 250 MHz): $\delta$ 5.90–5.58 (m, 1 H, internal vinylic proton), 5.19–4.92 (m, 2 H, terminal vinylic protons), 4.43–4.00 (m, 2 H, $\alpha$-bromo protons), 2.44–2.05 (m, 3 H, methine proton and methylene protons), 2.00–1.85 (overlapping d, 3 H, terminal methyl protons, both diastereomers), 1.02 (minor diastereomer) and 0.92 (major diastereomer) (d, $J$ = 6.4 Hz, 3 H, methyl protons).

$^{13}C$ NMR ($CDCl_3$, 62.5 MHz): $\delta$ 136.1 (d, $C_2$, minor), 135.8 (d, $C_2$, major), 117.2 (d of d, $C_1$, major), 116.9, (d of d, $C_1$, minor), 69.1 (d, $C_5$, minor), 67.3 (d, $C_5$, major), 50.3 (d, $C_6$, major), 50.2 (d, $C_6$, minor), 40.5 (t, $C_3$, major), 37.0 (t, $C_3$, minor), 36.6 (d, $C_4$, major), 35.6 (d, $C_4$, minor), 26.7 (q, $C_7$, major), 26.0 (q, $C_7$, minor), 19.0 (q, $C_8$, minor), 13.7 (q, $C_8$, major).

GC–MS (70 eV): $m/z$ 191 (–Br, 1), 189 (–Br, 1), 163 ($-C_2H_4Br$, 1), 161 ($-C_2H_4Br$, 1), 149 ($-C_3H_6Br$, 9), 147 ($-C_3H_6Br$, 9), 109 ($-HBr_2$, 100), 81 (10), 69 (35), 67 (34).

**1-[(2*R*,3*S*,4*R*)- and (2*R*,3*R*,4*S*)-2-Methyl-3,4-dibromopentyl]-2,2-dibromocyclopropane (9).** To a solution of 1.93 g (7.15 mmol) of **8** in 13 mL of $CH_2Cl_2$ was added 6.25 mL (28.6 mmol) of $CHBr_3$, two drops of triethylamine, and 13 mL of 50% aqueous NaOH solution. The flask was fitted with a water-cooled reflux condenser capped with a septum, fitted with a needle vent, and placed under a nitrogen atmosphere. The biphasic solution was stirred and gently heated to approximately 45 °C (refluxing $CH_2Cl_2$). The reaction was monitored by TLC for the loss of **8** and the formation of **9** (hexane eluent, $KMnO_4$ or PMA stain, $R_f$(**8**) = 0.45, $R_f$(**9**) = 0.35). After 48 h, the reaction was complete; the organic layer was black, and the aqueous layer was cloudy.

The biphasic solution was poured into a separatory funnel, and the layers were separated. The aqueous layer was extracted with three 30-mL portions of $CH_2Cl_2$. The combined organic extracts were washed

with 50 mL of 5% aqueous HCl and then with an equal volume of brine. After being dried ($MgSO_4$) and vacuum filtered, the crude solution was concentrated in vacuo. Column chromatography (silica gel, hexanes) afforded 2.70 g (6.11 mmol, 85%) of relatively pure **9** (four diastereomers).

Capillary GC (and GC–MS) analysis revealed the four diastereomers of **9** [cap column A: programmed column temperature, 100 °C (5 min) to 240 °C at 5 °C/min; retention times, 24.2, 24.5, 24.7, 24.8 min]. The diastereomers were not separated, and their relative configurations were not determined. Physical characteristics of **9** follow.

$^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ 4.33–3.98 (m, 2 H, $\alpha$-bromo protons), 2.65–2.35 (m, 1 H, methine proton), 2.30–1.86 (m, 3 H, methyl protons), 1.86–1.40 (m, 3 H, cyclopropyl proton and methylene protons), 1.86–1.40 (m, 3 H, cyclopropyl proton and methylene protons), 1.39–1.16 (m, 2 H, cyclopropyl protons), 1.99 (br d, $J$ = 6.4 Hz, 3 H, methyl protons).

GC–MS (70 eV): $m/z$ 365 (–Br, 4), 363 (–Br, 12), 361 (–Br, 13), 359 (–Br, 4), 283 (–$HBr_2$, 12), 281 (–$HBr_2$, 28), 279 (–$HBr_2$, 14), 202 (–$HBr_3$, 11), 201 (50), 200 (–$HBr_3$, 12), 199 (62), 197 (16), 177 (22), 175 (34), 173 (24), 161 (13), 159 (14), 149 (19), 147 (22), 135 (30), 133 (35), 121 (33), 120 (48), 119 (75), 109 (15), 107 (11), 95 (100), 69 (69).

**(*R*,*E*)-5-Methyl-1,2,6-octatriene (1).** A dry 25-mL round-bottomed flask was charged with 0.649 g (1.47 mmol) of **9** and 3.0 mL of dry, freshly distilled ether. The flask was placed under a nitrogen atmosphere and capped with a septum. The stirring solution was cooled to approximately –45 °C (dry ice/acetonitrile), and 5.0 mL (7.0 mmol) of methyllithium (1.4 M in ether, Aldrich Chemical Co.) was added dropwise over a period of 30 min using a gas-tight syringe and syringe pump. The reaction was monitored for the loss of **9** and the formation of **1** by TLC (hexane eluent, $KMnO_4$ stain, $R_f$(**9**) = 0.35, $R_f$(**1**) = 0.52). After 4 h, the reaction was complete.

The reaction solution was warmed to approximately 0 °C, and any remaining methyllithium was quenched by dropwise addition of distilled water. The two resulting layers were separated, and the aqueous phase was extracted with three 15-mL portions of pentane. The combined organic extracts were washed with an equal volume of distilled water and then with brine. Following drying ($MgSO_4$) and vacuum filtration, the sample was concentrated by careful distillation of the ether and pentane through an 8-in. Vigreux column fitted with a water-cooled short-path distillation apparatus. The final crude solution of **1** was approximately 0.1 M in the ether and pentane solvents. The concentration of the crude solution of **1** was estimated by the amount of material collected in purification by preparative gas chromatography; approximately 100 $\mu$L of crude solution yields 1 mg of **1**. However, no percent yield of **1** was determined. The dilute crude solution was stored in the freezer until needed. (Concentrated solutions of **1** soon form dimeric material, presumably allene [2 + 2] cycloaddition products.)

Capillary GC analysis of the crude product revealed **1** as the major component [cap column A: programmed column temperature, conditions I, 60 °C (5 min) to 240 °C at 5 °C/min; retention time, 5.4 min; conditions II, 35 °C (13 min) to 240 °C at 15 °C/min; retention time, 10.9 min].

Samples of **1**, >99% homogeneous by capillary GC analysis, were then obtained by preparative gas chromatography [column, 2-m × $^1/_4$-in., 10% OV101 on Anakrom AS 60/80; $T_{inj}$ = 190 °C, $T_{det}$ = 200 °C, $T_{col}$ = 65 °C; flow (He), 38 mL/min; retention time, 10 min]. Capillary GC analysis of purified **1** reveals a <1% contaminant, presumed to be the *Z*-isomer [cap column A: programmed column temperatures, 35 °C (13 min) to 240 °C at 15 °C/min; retention time, (*Z*)-**1**, 10.1 min, (*E*)-**1**, 10.9 min]. Physical characteristics of (*E*)-**1** follow.

$^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 5.40 (left portion of $ABX_3Y$ pattern, $J$ = 15.3, 6.0, 0.9 Hz, 1 H, vinylic proton), 5.32 (right portion of $ABX_3Y$ pattern, $J$ = 15.4, 7.3, 1.2 Hz, 1 H, vinylic proton), 5.02 (apparent quintet, $J$ = 7.0 Hz, 1 H, internal allenic proton), 4.62 (left portion of ABX pattern, $J$ = 2.9, 2.8 Hz, 1 H, terminal allenic proton), 4.60 (right portion of ABX pattern, $J$ = 2.9, 2.8 Hz, 1 H, terminal allenic proton), 2.26–2.08 (m, 1 H, methine proton), 2.09–1.84 (m, 2 H, methylene protons), 1.63 (d, $J$ = 5.4 Hz, 3 H, terminal methyl protons), 0.97 (d, $J$ = 6.7 Hz, 3 H, methyl protons).

$^{13}$C NMR ($CDCl_3$, 125.7 MHz): $\delta$ 209.0 (s, $C_2$, central allenic carbon), 136.5 (d, $J$ = 149 Hz, $C_5$, vinylic carbon), 123.5 (d, $J$ = 142 Hz, $C_6$, vinylic carbon), 88.3 (d, $J$ = 158 Hz, $C_3$, allenic carbon), 74.0 (t, $J$ = 149 Hz, $C_1$, allenic carbon), 36.8 (d, $J$ = 108 Hz, $C_5$, methine carbon), 36.1 (t, $J$ = 109 Hz, $C_4$, methylene carbon), 20.0 (q, $J$ = 100 Hz, $C_8$, terminal methyl carbon), 17.9 (q, $J$ = 105.4 Hz, $C_9$, methyl carbon).

GC–MS (70 eV): $m/z$ 122 (0.3), 121 (–H, 1.2), 107 (–$CH_3$, 76), 93 (64), 79 (40), 69 (–$C_4H_5$, 100). HRMS (CI, methane): $m/z$ 123.1164 (+H, calcd 123.1174).

Dimeric material, GC–MS (20 eV): $m/z$ 245 (7), 244 (35), 229 (–$CH_3$, 21), 201 (36), 175 (30), 159 (32), 145 (50), 133 (100), 122 (4), 121 (10), 119 (34), 107 (34), 105 (55), 91 (50), 69 (58).

**Synthesis of the Triene Rearrangement Product 3 (Scheme 4). (3*S*)-Ethyl 2-((*N*,*N*-Dimethylamino)methyl)-3-methyl-4-Hexenoate (10).**[35] A dry 100 mL round bottomed flask was charged with 20 mL of dry, freshly distilled THF and 3.00 mL (21.4 mmol) of diisopropylamine. The solution was stirred under a nitrogen atmosphere and cooled to approximately –78 °C (dry ice/acetone). Over a period of 30 min, 8.57 mL (21.5 mmol) of *n*-butyllithium was added slowly dropwise to the stirring solution using a gas-tight syringe and a syringe pump. After the mixture was stirred for an additional hour at –78 °C, a solution of 2.231 g (14.28 mmol) of **5** in 20 mL of THF was added dropwise using a cannula. Stirring proceeded for an additional hour at –78 °C, and then the reaction was warmed to approximately –40 °C. Next, 9.1 g (49 mmol) of *N*,*N*-dimethylmethyleneammonium iodide (Eschenmoser's salt, Aldrich Chemical Co.) was added through a powder funnel. The resulting reaction solution was allowed to stir for several hours with gradual warming to room temperature.

The crude solution was extracted with four 50-mL portions of 5% aqueous HCl and then set aside. The combined acidic aqueous extracts, which were orange in color, were made slightly basic (pH = 10) with 50% aqueous NaOH. The resulting biphasic solution was extracted with four 150-mL portions of ether. The remaining basic aqueous solution was clear. The combined clear organic extracts were washed with 400 mL of distilled water and 400 mL of brine. The crude solution was dried ($MgSO_4$), vacuum filtered, and concentrated in vacuo to afford 2.503 g (11.81 mmol, 83%) of **10**. An analytically pure sample was not obtained, and the material was carried on in the synthesis without further purification.

The initial crude solution, containing unreacted starting material, was washed with 100 mL of distilled water and 100 mL of brine. After drying ($MgSO_4$) and vacuum filtration of the solution, a capillary GC analysis of the solution revealed the presence of **5**. This sample was combined with other similar solutions of **5**, and the solvents were removed by careful distillation through a 6-in. vacuum-jacketed Vigreux column. **5** was further purified by distillation as described previously.

**(*S*,*E*)-Ethyl 3-Methyl-2-methylene-4-hexenoate (11).** In a dry 100-mL round-bottomed flask fitted with a water-cooled reflux condenser, a solution of 2.503 g (11.81 mmol) of **10** and 50 mL of $CH_3I$ was warmed to approximately 45 °C. The yellow solution was heated at reflux while stirring for 4 days; the resulting crude solution was cloudy orange. The $CH_3I$ then was carefully removed (and recycled) by distillation through an 8-in. vacuum-jacketed Vigreux column. The cloudy dark orange residue was then charged with 30 mL of ether and 30 mL of an aqueous $NaHCO_3$ solution (2.5 g in 30 mL). Before stirring commenced, three layers were observed: the bottom layer was the deep orange ammonium salt solution, the next higher layer was cloudy and yellow, and the top layer was cream colored. Upon stirring, two layers formed: the bottom layer was cloudy and orange, and the top layer was cream colored. After the solution was stirred for 24 h, the top organic layer was removed and stored temporarily in the freezer. A fresh 30-mL portion of ether was then added, and the day-long elimination/extraction was repeated two more times. Finally, the combined ether extracts were washed with three 100-mL portions of 5% aqueous HCl, 100 mL of distilled water, and 100 mL of brine. After being dried ($MgSO_4$) and vacuum filtered, the crude solution of **11** was concentrated by carefully distilling off the ether through a 6-in. vacuum-jacketed Vigreux column. Capillary GC analysis of the crude solution revealed primarily one component, **11** [cap column A: programmed column temperature, 60 °C (5 min) to 240 °C at 5 °C/min; retention time, 12.4 min (**11**)]. Leftover **10** was recovered from the aqueous acid solution as in the workup described for the synthesis of **10**.

The crude solution of **11** was taken on in the synthesis without any further purification; no percent yield was determined. For spectroscopic analysis, a sample of **11**, analytically pure by capillary GC, was obtained by preparative gas chromatography [prep column A, column temperature, 90 °C; flow (He), 38 mL/min; retention time, 26 min (**11**)]. The physical characteristics of **11** follow. $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ 6.10 (br s, 1 H, vinylic proton), 5.60–5.30 (m, 3 H, vinylic protons), 4.18 (q, $J$ = 7.1 Hz, 2 H, ester methylene protons), 3.40–3.24 (m, 1 H, methine proton), 1.63 (d, $J$ = 4.6 Hz, 3 H, terminal methyl protons), 1.27 (t, $J$ = 7.1 Hz, 3 H, ester methyl protons), 1.13 (d, $J$ = 6.9 Hz, 3 H, methyl protons). $^{13}$C NMR ($CDCl_3$, 62.5 MHz): $\delta$ 167.2 (s, carbonyl C), 145.4 (s, vinylic 4° C), 134.0 (d, vinylic CH), 124.6 (d, vinylic CH), 122.7 (t, vinylic $CH_2$), 60.5 (t, ester $CH_2$), 37.5 (d, CH), 19.5 (q, $CH_3$), 17.9 (q,

$CH_3$), 14.2 (q, $CH_3$). GC–MS (70 eV): $m/z$ 169 (2), 168 (21), 153 ($-CH_3$, 33), 125 ($-C_2H_5O$, 100), 95 (43), 93 (42), 79 (61), 67 (36).

**(*S,E*)-3-Methyl-2-methylene-4-hexen-1-ol (12).** A crude solution of **11** (11.81 mmol, assuming complete conversion in the synthesis of **11**) in 20 mL of ether was stirred under a nitrogen atmosphere and cooled to approximately –40 °C (acetonitrile/dry ice). The reaction solution was charged with 47.0 mL (47.0 mmol) of diisobutylaluminum hydride (DIBAL-H) solution (1.0 M in hexanes from Aldrich Chemical Co.). The reaction was monitored for the loss of **11** and the formation of **12** by TLC (2:1 hexane/ether as eluent, $KMnO_4$ stain or UV for **11**, and $KMnO_4$ or PMA for **12**, $R_f$(**11**) = 0.7, $R_f$(**12**) = 0.3). After approximately 30 min, the reaction was complete. The workup described in the synthesis of **7** was performed to yield a crude ether and hexane solution of **12**. Capillary GC analysis of the crude solution revealed primarily one component, **12** [cap column A: programmed column temperature, 60 °C (5 min) to 240 °C at 5 °C/min; retention time, 8.5 min (**12**)]. The solution was concentrated by careful distillation of the ether and some of the hexane through a 6-in. vacuum-jacketed Vigreux column.

The crude concentrated solution of **12** was taken on in the synthesis without any further purification; no percent yield was determined. For spectroscopic analysis, a sample of **12**, analytically pure by capillary GC, was obtained by preparative gas chromatography [prep column A: Column temperature 90 °C; flow (He), 38 mL/min; retention time, 13 min (**11**)]. The physical characteristics of **12** follow. $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ 5.45 (left portion of $ABX_3Y$ pattern, $J$ = 15.3, 5.9 Hz, 1 H, vinylic proton), 5.33 (right portion of $ABX_3Y$ pattern, $J$ = 15.4, 7.3 Hz, 1 H, vinylic proton), 5.03 (singlet, 1 H, terminal vinylic proton), 4.90 (singlet, 1 H, terminal vinylic proton), 4.07 (br d, $J$ = 4.5 Hz, 2 H, methylene protons), 2.82 (m, 1 H, methine proton), 1.64 (d, $J$ = 5.8 Hz, 3 H, terminal methyl protons), 1.38 (br t, 1 H, hydroxyl proton), 1.12 (d, $J$ = 7.0 Hz, 3 H, methyl protons). GC–MS (70 eV): $m/z$ 125 (0.3), 111 ($-CH_3$, 3), 108 (10), 93 (100), 91 (30), 77 (31), 67 (27), 55 (21), 41 (39), 39 (39).

**(*S,E*)-3-Methyl-2-methylene-4-hexenal (13).** A crude, stirring solution of **12** (11.81 mmol, assuming complete conversion in the synthesis of **12**) in hexane (approximately 0.5 M) was charged with 2.05 g (23.6 mmol) of $MnO_2$ powder (Aldrich Chemical Co.). The mixture was stirred overnight at room temperature. In the morning, TLC analysis revealed that all of the **12** had been consumed and a single product **13** had formed [2:1 hexane/ether as eluent, $KMnO_4$ or PMA stain (or UV for **13**), $R_f$(**12**) = 0.3, $R_f$(**13**) = 0.6]. The solution was gravity filtered through a fluted filter paper, and the $MnO_2$ powder was rinsed repeatedly with pentane. The filtrate was washed with 30 mL of distilled water and then 30 mL of brine. After being dried ($MgSO_4$) and vacuum filtered, the solution was concentrated by careful distillation of the pentane through a 6-in. vacuum-jacketed Vigreux column. Capillary GC analysis of the crude solution revealed primarily one component, **13** [cap column A: programmed column temperature, 60 °C (5 min) to 240 °C at 5 °C/min; retention time, 6.1 min (**13**)].

The crude concentrated solution of **13** was taken on in the synthesis without any further purification; no percent yield was determined. For spectroscopic analysis, a capillary GC analytically pure sample of **13** was obtained by preparative gas chromatography [prep column A: column temperature, 90 °C; flow (He), 38 mL/min; retention time, 8 min (**13**)]. The physical characteristics of **13** follow. $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ 9.50 (s, 1 H, aldehyde proton), 6.20 (s, 1 H, vinylic proton), 5.95 (s, 1 H, vinylic proton), 5.54–5.18 (m, 2 H, vinylic protons), 3.33 (m, 1 H, methine proton), 1.62 (d, $J$ = 5.5 Hz, 3 H, terminal methyl protons), 1.11 (d, $J$ = 6.9 Hz, 3 H, methyl protons). GC–MS (70 eV): $m/z$ 124 (1.5), 123 (–H, 2), 109 ($-CH_3$, 100), 81 (89), 79 (49), 67 (26), 53 (34), 41 (33), 39 (52).

**(*S,E*)-4-Methyl-3-methylene-1,5-heptadiene (3).** A crude, stirring solution of **13** (11.81 mmol, assuming complete conversion in the synthesis of **13**) in hexane and pentane was treated with methylidenetriphenylphosphorane solution (approximately 0.6 M in THF) as described for the synthesis of **8**. The reaction was monitored for the loss of **13** and the formation of **3** by TLC [2:1 hexane/ether, UV, $KMnO_4$, or PMA, $R_f$(**13**) = 0.6, $R_f$(**3**) = 0.7)]. The crude solution of **3** was concentrated by careful distillation of the pentane and ether through an 8-in. vacuum-jacketed Vigreux column. Capillary GC analysis of the crude solution revealed primarily one component, **3** [cap column A; programmed column temperature, conditions I, 60 °C (5 min) to 240 °C at 5 °C/min; retention time (**3**), 4.4 min; conditions II, 35 °C (13 min) to 240 °C at 15 °C/min, retention time (**3**), 8.1 min].

Analytically pure (>99% homogeneous by capillary GC analysis) samples of **3** (approximately 1% *cis*) were obtained by preparative gas chromatography [prep column A: column temperature, 65 °C; flow (He), 38 mL/min; retention time, 8 min]. Pure *trans* was obtained by additional preparative gas chromatography using a $AgBF_4$/Carbowax column [prep column B: 2-m × $^1/_4$-in., 7.5% $AgBF_4$, 10% Carbowax-600M on Chromosorb PAWDMCS 60/80; $T_{inj}$ = 190 °C, $T_{det}$ = 200 °C, $T_{col}$ = 65 °C; flow (He), 38 mL/min; retention time (**3**), 8 min]. The $AgBF_4$ column was prepared as follows: 1.5 g of $AgBF_4$ was dissolved in 20 mL of reagent grade acetone. The solution was vacuum filtered and then added to a foil-wrapped flask containing 20 g of Chromosorb PAWDMCS 60/80. Next, 2.0 g of Carbowax-600M was dissolved in 40 mL of distilled $CH_2Cl_2$, and the resulting solution was added to the $AgBF_4$/Chromosorb mixture. After 5 min of vigorous mixing, the solvents were removed in vacuo, and the remaining column packing materials was dried on a high-vacuum line for several hours. All of the manipulations were carefully performed to exclude light. A 2-m length of $^1/_4$-in. aluminum tubing was packed, and the column was conditioned overnight at 100 °C, with a helium flow rate of 40 mL/min. When not in use, the column was stored in a desiccator.

Physical characteristics of **3** follow. $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ 6.31 (d of d, $J$ = 17.8, 10.8 Hz, 1 H, $C_2$ vinylic proton), 5.50–5.40 (m, 2 H, $C_5$ and $C_6$ vinylic protons), 5.29 (d, $J$ = 17.8 Hz, 1 H, $C_1$ *cis* vinylic proton), 5.03 (d, $J$ = 10.8 Hz, 1 H, $C_1$ *trans* vinylic proton), 5.03 (br s, 1 H, $C_8$ vinylic proton), 4.96 (br s, 1 H, $C_8$ vinylic proton), 3.04–3.18 (m, 1 H, methine proton), 1.64 (d, $J$ = 3.8 Hz, 3 H, methyl protons), 1.15 (d, $J$ = 6.9 Hz, 3 H, methyl protons). $^{13}$C NMR ($CDCl_3$, 125.7 MHz): $\delta$ 158.8 ($C_3$), 138.4 ($C_2$), 135.2 ($C_5$), 123.8 ($C_6$), 113.7 ($C_1$), 113.3 ($C_8$), 37.5 ($C_4$), 19.8 ($C_7$), 17.9 ($C_9$). GC–MS (70 eV): $m/z$ 122 (0.3), 121 (–H, 1.2), 107 ($-CH_3$, 76), 93 (64), 79 (40), 69 ($-C_4H_5$, 100). HRMS (CI, methane): $m/z$ 123.1175 (+H, calcd 123.1174).

**Preparative and Capillary Gas Chromatographic Analyses. Purifications, Purity Assessments, and Enantiomeric Excess Evaluations.** Preparative gas chromatography was performed using a Varian Aerograph Model 920 equipped with a thermal conductivity detector. Helium was the carrier gas in all cases.

Analytical gas chromatography was performed using either a Hewlett-Packard 5890 or a Varian 3700 chromatograph. Each was equipped with a split/splitless injector and a flame ionization detector. Integration of the chromatograms was accomplished using a Hewlett-Packard 3393A integrator. Programmed column temperatures and retention times for preparative and capillary GC analyses of synthetic intermediates are reported with the synthetic procedures.

**Purification of (*R,E*)-5-Methyl-1,2,6-octatriene (1).** Capillary GC and $^1$H NMR analytically pure samples of **1** were obtained by preparative gas chromatography. The preparative GC method employed depended on the source of the sample. Eneallene generated from the reductive elimination of the dibromocyclopropane **9** was purified using a 2-m × $^1/_4$-in. column packed with 10% OV101 on Anakrom AS 60/80 (prep column A). Eneallene recovered from the crude pyrolysate required an additional (subsequent) preparative GC purification using a 2-m × $^1/_4$-in. column packed with 7.5% $AgBF_4$ and 10% Carbowax-600M on Chromosorb PAWDMCS 60/80 (prep column B). The purity of the samples obtained by either of these methods was equivalent (within experimental error) when evaluated by capillary GC analysis using a 25-m × 0.32-mm 5% phenylmethylsilicone fused silica capillary column. Occasionally the final samples of purified **1**, recovered from the *crude pyrolysate*, contained not more than 2% **3**. This did not effect the ee analyses as **1** and **3** are well resolved by the chiral capillary GC column.

The pertinent details of these methods and analyses are reviewed in Table 2 and 3.

**Purification of (*E*)-4-Methyl-3-methylene-1,5-heptadiene (3).** Capillary GC and $^1$H NMR analytically pure samples of **3** were obtained by preparative gas chromatography. Samples generated via independent synthesis were purified using prep column A. Subsequent capillary GC (and GC–MS) analysis using cap column A revealed two isomers in a 98.5:1.5 ratio, having retention times 8.0 and 7.6 min, respectively. The minor component was eliminated from the sample by a second preparative GC purification using prep column B; the major component was identified as *trans*-**3**.

Samples of **3** generated via pyrolysis of the eneallene **1** were purified in the same manner (details are provided in Table 4). After the first preparative GC purification, **3** was 79–84% pure. A contaminant that constituted 5–6% of the initial crude pyrolysate, having a capillary GC (cap column A) retention time of 7.6 min, remained after the first preparative GC purification. It and the other contaminants were eliminated in the second preparative GC purification using prep column

**Table 2.** Preparative and Capillary GC Columns Used

| column designation | physical dimensions (He flow or pressure) | stationary phase | programmed temperature |
|---|---|---|---|
| prep column A | 2-m × 1/4-in. (40 mL/min) | 10% OV101 | 60 °C (isothermal) |
| prep column B | 2-m × 1/4-in. (40 mL/min) | 7.5% $AgBF_4$/10% Carbowax-600M | 1:75°C 3:65 °C (isothermal) |
| cap column A | 25-m × 0.32-mm × 0.17-μm (7 psi) | 5% phenylmethylsilicone | 35 °C (13 min) to 240 °C, 15 °C/min |
| cap column B | 25-m × 0.25-mm × 0.25-μm (11 psi) | CHIRASIL-DEX | 35 °C (isothermal) |

**Table 3.** Recovery of Eneallene **1** from Crude Pyrolysate

| | prep column A | prep column B[a] |
|---|---|---|
| column temperature[b] | 60 °C | 75 °C |
| retention time[c] | 23 min | 10 min |
| subsequent purity[d] | 92–94% | 98–100% |
| nature of contaminants | isomeric, all <2% | **3** |

[a] Samples are submitted to prep column B only after purification using prep column A. [b] Column temperatures are maintained within 3 °C of reported temperatures. [c] Retention times vary from run to run by not more than 1 min. [d] Purities reported were determined by capillary GC analysis using cap column A.

**Table 4.** Recovery of Triene **3** from Crude Pyrolysate

| | prep column A | prep column B[a] |
|---|---|---|
| column temperature[b] | 60 °C | 65 °C |
| retention time[c] | 17 min | 10 min |
| subsequent purity[d] | 79–84% | 100% |
| nature of contaminants | 8–10% *cis*-**3** (rest <5%, unidentified) | (none) |

[a] Samples are submitted to prep column B only after purification using prep column A. [b] Column temperatures are maintained within 3 °C of reported temperature. [c] Retention times vary from run to run by not more than 1 min. [d] Purities reported were determined by capillary GC analysis using cap column A.

B. The triene **3** recovered from the crude pyrolysate was identified as the *E*-isomer by comparison to a synthetic sample using GC analysis on two capillary columns and two preparative scale columns, $^1H$ and $^{13}C$ NMR spectroscopy, and GC–MS analysis.

The species responsible for this 5–6% contamination of the crude pyrolysate has the same retention time and presumably is the same as the minor component of once-chromatographed synthetic **3**. Unfortunately, the contaminant could not be discerned in the *preparative* GC analyses of the various samples of **3**, and attempts at isolating the material were fruitless. However, in all likelihood the species corresponds to *cis*-**3**; a rationale follows.

In the synthetic route to **3**, the Claisen reaction of (*R*,*E*)-3-penten-2-ol (**4**) and triethyl orthoacetate is known to yield predominantly the *trans* olefinic ester, (*R*,*E*)-ethyl 3-methyl-4-hexenoate (**5**) (approximately 95%). Indeed, the sample of **5** used in the synthesis of **3** was roughly 98% *E* and 2% *Z*. It follows that the synthetically generated triene should have roughly the same ratio of *E* to *Z* since the synthesis does not compromise the stereochemistry of the double bond, and no substantial difference in reactivity of the stereoisomers is expected. Thus, it is probable that the isomeric contaminant described is the *Z*-isomer. The *Z*-isomer of **3** would also be expected from the pyrolysis of (*R*,*E*)-**1**, by analogy to the thermal interconversion of 4-methyl-5-hepten-1-yne and 4-methyl-1,2,5-heptatriene.[5] It should be noted that the component presumed to be (*Z*)-**3** is eliminated from the sample of **3** by the second chromatography, and its identity does not affect the major experimental results.

**Enantiomeric Excess Evaluations of 1 and 3.** In the present ee determinations, the purity of each sample was established by capillary GC prior to analysis. The ee of **1** and that of **3** were evaluated using chiral capillary GC (Table 5).[2] The method employed a 25-m × 0.25-mm CHIRASIL-DEX column (cap column B) developed by V. Schurig.[36] The stationary phase in the column is cyclodextrin, chemically bound to polysiloxane. In addition, the stationary phase is immobilized (thermally or radically) on the glass capillary wall. Optimum purification procedures and GC conditions for enantiomer resolution were determined using the corresponding racemic samples; the final methods employed gave an enantiomeric ratio within 0.5% of 50.00%:50.00%, reproducibly.

**Table 5.** Chiral Capillary GC (Cap Column B) Retention Times for the Enantiomers of (*E*)-1 and (*E*)-3

| compd | retention time[a] (min) |
|---|---|
| (*S*,*E*)-**1** | 28.2 |
| (*R*,*E*)-**1** | 28.8 |
| (*S*,*E*)-**3** | 19.1 |
| (*R*,*E*)-**3** | 20.2 |

[a] Retention times varied by no more than 0.5 min.

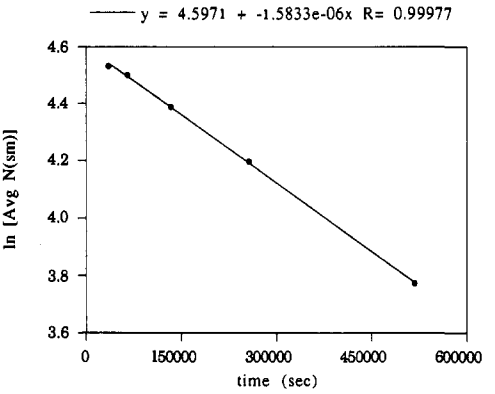



**Figure 2.** First-order plot of kinetic data for the pyrolysis of (*E*)-**1** at 142.1 °C.

**Table 6.** Kinetic Data for the Pyrolysis of (*E*)-1 at 142.1 °C

| time (s) | av *N*(sm) (%) | ln[av *N*(sm)] | mass balance (%) |
|---|---|---|---|
| 34 816 | 92.952 | 4.5321 | 99.554 |
| 64 845 | 90.088 | 4.5008 | 100.965 |
| 133 509 | 80.406 | 4.3871 | 101.107 |
| 256 924 | 66.408 | 4.1958 | 100.579 |
| 518 116 | 43.538 | 3.7736 | 100.615 |

$k = (1.583 \pm 0.041) \times 10^{-6}\ s^{-1}$
$k$(corrected) $= (8.630 \pm 0.041) \times 10^{-7}\ s^{-1}$

Samples to be analyzed by chiral capillary GC were purified as described and dissolved in high-grade pentane. Prior to analysis, the purity of each sample was checked by achiral capillary GC (cap column A). For ee evaluations only, capillary GC analytically pure samples were used. In addition, the number of purifications required to obtain a reliable estimate of the enantiomeric ratio was determined by repeated preparative GC purification and subsequent chiral GC analysis; additional preparative GC purification using the $AgBF_4$/Carbowax column, beyond that detailed above, did not lead to any change in the enantiomeric ratios observed. For each ee evaluation three determinations were made. The average of the three is reported in the text with its corresponding error limits.

**Pyrolyses and Kinetic Studies.** The techniques used were similar to those described elsewhere[5,37] and are given in the supplementary material to this paper. Crude pyrolysate was retrieved from the tubes as follows: each tube was scored with a file to facilitate breakage, and then one end

of the tube was cooled in a liquid nitrogen bath while the other end was warmed in hand; once all the material had condensed at the bottom of the tube, the tube was cracked open at the scored site. Finally, 200–300 μL of HPLC grade pentane (Aldrich Chemical Co.) was dispensed into the tube (care was taken to rinse the walls of the pyrolysis tube). Pyrolysis tube contents were then analyzed by capillary GC using cap column A (see above).

**Study of Surface Effects on the Rearrangement.** Pyrolyses carried out in base-washed ($NH_4OH$) or base-washed and silanized tubes gave identical product distributions as determined by capillary GC analysis. In addition, pyrolyses carried out with increased available surface area, in tubes filled with tiny glass balls, showed identical results. No surface effects on the rates or products of the rearrangement were discerned. Rate constants for overall disappearance of **1** were multiplied by the fraction of **3** in the product to give corrected rate constants.

**Error Analysis of the Kinetic Data.** Error ranges for the derived rate constants were estimated using the analysis outlined by Benson and O'Neal.[38] The uncertainty in the time was ±10 s, and the uncertainty in the temperature was ±0.5 °C for the salt bath and ±1.5 °C for the oil bath. The uncertainty in the concentration measurements was conservatively estimated to be ±1% of the GC peak area.

As prescribed by Benson and O'Neal,[38] only the errors associated with the lowest and highest temperature pyrolyses were used to calculate the uncertainties in the Arrhenius parameters. Since the lowest temperature pyrolysis was carried out in the oil bath, the larger temperature uncertainty (±1.5 °C) was used. The corresponding uncertainties in the Arrhenius parameters were ±1.6 and ±0.8 for $E_a$ and log $A$, respectively. When the error is calculated without the lowest temperature (oil bath) kinetic data, the uncertainties in the (unchanged) Arrhenius parameters were ±0.8 and ±0.4 for $E_a$ and log A, respectively. For both the 5-data point and 4-data point Arrhenius plots, the correlation constant was 0.999 99.

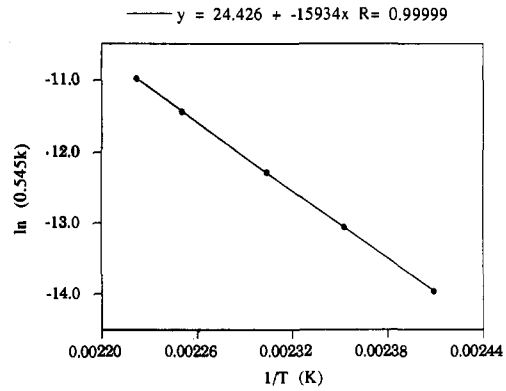



**Figure 3.** Arrhenius plot for the pyrolysis of (*E*)-**1**. Corrected rate constants were used (see text).

**Table 7.** Arrhenius Data for the Pyrolysis of (*E*)-1

| $t$ (°C) | $T$ (K) | $k$ ($s^{-1}$) | $0.545k$ ($s^{-1}$) | $\ln(0.545k)$ |
|---|---|---|---|---|
| 142.1 | 415.1 | $1.583 \times 10^{-6}$ | $8.630 \times 10^{-7}$ | −13.96 |
| 152.0 | 425.0 | $3.896 \times 10^{-6}$ | $2.123 \times 10^{-6}$ | −13.06 |
| 161.0 | 434.0 | $8.513 \times 10^{-6}$ | $4.640 \times 10^{-6}$ | −12.28 |
| 171.4 | 444.4 | $1.978 \times 10^{-5}$ | $1.078 \times 10^{-5}$ | −11.44 |
| 177.0 | 450.0 | $3.129 \times 10^{-5}$ | $1.705 \times 10^{-5}$ | −10.98 |

$E_a = 31.7 \pm 1.6$ kcal/mol
$\log A = 10.6 \pm 0.8$
$\Delta H^{\ddagger}(430\text{ K}) = 30.9 \pm 1.6$ kcal/mol
$\Delta S^{\ddagger}(430\text{ K}) = -12.7 \pm 3.7$ eu

A sample kinetic run is shown in Table 6 and Figure 2, and the complete data set for all the runs is given in the supplementary material.

The temperature dependence of the rate constants is shown in Table 7 and plotted in Figure 3.

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**Supplementary Material Available:** Details of kinetic measurements and bond additivity calculations (19 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(35) This procedure is based on that reported by Danishefsky *et al.*: Danishefsky, S.; Schuda, P. F.; Kitahara, T.; Etheredge, S. J. *J. Am. Chem. Soc.* **1977**, *99*, 6066.

(36) The CHIRASIL-DEX capillary GC column was purchased from V. Schurig, University of Tübingen. The column is described in a recent report by Schurig *et al.*: Schurig, V.; Schmalzing, D.; Schleimer, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 987.

(37) (a) Parziale, P. A.; Berson, J. A. *J. Am. Chem. Soc.* **1991**, *113*, 4595. (b) Getty, S. J.; Berson, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 433.

(38) Benson, S. W.; O'Neal, H. E. *Kinetic Data on Gas Phase Unimolecular Reactions*; National Standard Reference Data Series 21; U.S. National Bureau of Standards; U.S. Government Printing Office: Washington, DC, 1970; pp 8–9.