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# Formation and Thermal Rearrangements of Some Dimers of Butadiene and Piperylene. Tests of the Validity of Thermochemical-Kinetic Arguments for Identification of Common Biradical Intermediates[1,2]

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**Abstract:** The mechanisms of the dimerization of butadiene and piperylene and the thermal rearrangements of the corresponding dimers are investigated by kinetic and stereochemical techniques. Particular attention is given to the question whether, in the Diels–Alder dimerization of the dienes **1a** or **1b**, intermediates are involved that are common to the 1,3-sigmatropic rearrangements of the corresponding [2 + 2] dimers **3a** and **3b**. Substituents on the terminal vinyl position of *cis*-1,2-divinylcyclobutane (**5a**) retard the normal stereospecific boat-like Cope rearrangement to 3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene and permit the detection of a new "nonboat" process, which leads to a stereoisomeric product. The boat-like rate constant declines with increasing terminal cis-methyl sustitution in the series **5a** > cTT-**8** > cCT-**8** > cCC-**8**. The total range of the effect amounts to a factor of $1.81 \times 10^5$. The *trans*-1,2-dipropenylcyclobutanes also give Cope rearrangement products, but this reaction occurs exclusively by an indirect mechanism: prior epimerization to the cis isomer followed by Cope rearrangement of the latter. The rearrangement of *trans*-3,4-dimethyl-*cis,trans*-cycloocta-1,5-diene (**16**) to *cis*-3,4-dimethyl *cis,cis*-cycloocta-1,5-diene (**10**), involving overall epimerization at one asymmetric center and geometric isomerization at one olefinic site, proceeds by a two-step mechanism in which *cis*-1,2-*trans,trans*-dipropenylcyclobutane (cTT-**8**) is an intermediate. The 1,3-sigmatropic rearrangement of (1*R*,2*R*)-(+)-*trans*-1,2-divinylcyclobutane (**3a**) gives (*R*)-(+)-4-vinylcyclohexene (**2a**) with 7.7% preservation of enantiomeric purity (corrected for competing racemization of **3a**). This corresponds to 54% inversion and 46% retention of configuration of the migrant carbon. By attaching stereochemical labels to the terminal vinyl positions as in optically active tTT-**9** and tCT-**9**, the stereochemistry of the 1,3-sigmatropic rearrangement can be subdivided into the four possible pathways (Schemes IX and X), suprafacial inversion, antarafacial retention, suprafacial retention, and antarafacial inversion. In this way, it can be shown that relative rates through these four pathways are, respectively, 50.2, 6.0, 41.1, and 2.7 from tTT-**9**, and 49.5, 2.8, 46.8, and 0.9 from tCT-**9**. These results can be fitted by a biradical mechanism, but are more fruitfully interpreted as mainly the outcome of two competing concerted reactions, one allowed (suprafacial inversion) and one forbidden (suprafacial retention). The absence of any substantial antara contribution in the dipropenyl systems rules out a stereorandom biradical intermediate in the tTT-**9** and tCT-**9** rearrangements and makes it unlikely in the divinyl system **3a**. The Diels–Alder dimerization of *trans*-penta-1,3-diene-*trans*-1-*d* (**45**, Scheme XIV) in both the exo and endo orientations gives exclusively the product of reaction cis-on-the-diene,cis-on-the-dienophile. This is consistent with a concerted [4s + 2s]cycloaddition and rules out common intermediates in the formation of product tT-**13** and cT-**12** from the two alternative pathways of Diels–Alder dimerization of piperylene and 1,3-sigmatropic rearrangement of tTT-**9**.

Although historical documentation is sparse and scattered, we suspect that many of the early proposals of biradical intermediates in thermal reactions really were simple bookkeeping schemes devised to permit the authors to identify readily the molecular sites of bond making and bond breaking. In time, however, biradicals took on more clearly defined mechanistic significance, and with the advent of transition-state theory, the investigation of thermal reactions incorporated as one of its objectives the location of such species as intermediates on reaction energy surfaces.

It is obviously required of a biradical intermediate that its heat of formation ($\Delta H_f°$) be lower than that of the highest-energy transition state of the reaction. The heat of formation of the transition state usually is an experimental (or semiexperimental) quantity, being the sum of the measured activation energy ($\Delta H^{\ddagger}$) and the measured (or estimated) $\Delta H_f°$ of the reactant. The biradical $\Delta H_f°$ is nonexperimental and usually is estimated from bond-additivity tables, with certain additional assumptions.

However, to be plausible, any particular biradical intermediate also must be convertible to the rate-determining transition state by processes whose energies and entropies are reasonable and predictable. The development of methods for making such predictions has come from the examination of large collections of data on the rates and activation parameters of many thermal reactions.[6,7] As a result of such studies, biradical intermediates and transition states leading to them have been shown to have heats and entropies of formation that permit them to be placed on reaction energy surfaces. The existence of these correspondences has led to the postulation of biradical mechanisms for a wide variety of thermal reactions.[6,7]

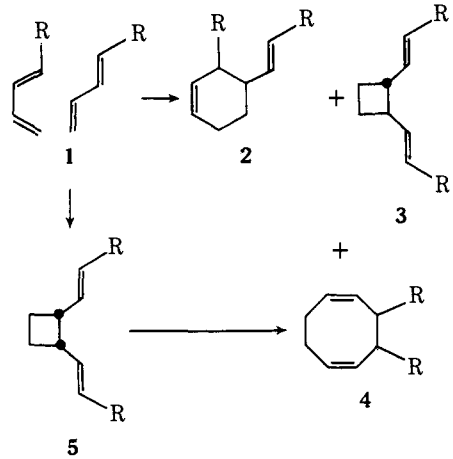
In support of such mechanisms, it has been noted that some hypothetical biradical intermediates might be formed from two or more different reactants or be converted to two or more different products, and that the values of $\Delta H_f°$ of the transition states flanking the biradical all can be derived by the same additivity schemes.[6,7] Within the framework of the thermochemical-kinetic approach, the thermodynamic properties of such biradical *common intermediates* have provided an important check on the internal consistency of the method.

Stereochemical experiments can provide a supplementary

criterion for the validity of the biradical mechanism. The most compelling of such experiments do not depend upon a simplistic dichotomy, concerted/stereospecific vs. biradical/stereorandom, but rather upon a judicious prior evaluation of what the biradical and concerted mechanisms predict about stereochemistry. When the mechanism postulates the derivation of a product from a biradical intermediate *common* to two separate pathways, the stereochemical criterion of mechanism takes a simple form: each pathway must give product of identical stereochemistry. Note that whether biradical ring closure should be fast or slow relative to internal bond rotations, and hence whether the biradical reaction should be stereospecific or not, are questions of only incidental interest in the application of this criterion.

The bisallylic octadienediyl biradicals hypothetically formed by end-to-end junction of two molecules of buta-1,3-diene have been extensively discussed[8,9] and, on the basis of thermochemical-kinetic arguments, have been proposed[8] as common intermediates in the dimerization of butadiene and the thermal rearrangements of the dimers. The present paper investigates the stereochemical aspects of the formation and interconversions of the dimers of butadiene and the dimers of its relative piperylene (penta-1,3-diene). For two pathways, one leading from the dienes by Diels–Alder dimerization and another from the dialkenylcyclobutane dimers by sigmatropic rearrangement, to common 4-alkenylcyclohexene products, the results now clearly exclude common intermediates.

When heated, buta-1,3-diene (**1a**) dimerizes mainly to 4-vinylcyclohexene (**2a**). Small amounts of *trans*-1,2-divinylcyclobutane (**3a**) and *cis,cis*-cycloocta-1,5-diene (**4a**) also are formed.[10] These reactions are formally [4 + 2] (Diels–Alder), [2 + 2], and [4 + 4] cycloadditions, respectively, but the latter may well occur in two discrete steps,[11] a [2 + 2] cycloaddition to *cis*-1,2-divinylcyclobutane (**5a**) followed by a rapid, irreversible Cope rearrangement.



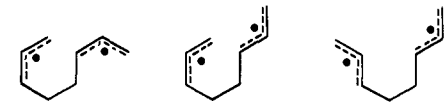

a: R = H
b: R = $CH_3$

Analogously, *trans*-piperylene (**1b**) gives 3-methyl-4-*trans*-propenylcyclohexene (**2b**), a small amount of 3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**4b**), and at most a trace of *trans*-1,2-dipropenylcyclobutane (**3b**).[12,13]

In addition to the facile ($E_a$ = 24.0 kcal/mol[11,14,15]) Cope rearrangement of *cis*-divinylcyclobutane to *cis,cis*-cycloocta-1,5-diene (**5a** → **4a**), several other thermal interconversions of the butadiene dimers are known: a slower ($E_a$ = 35.4 kcal/mol) Cope rearrangement of *trans*-1,2-divinylcyclobutane to *cis,cis*-cycloocta-1,5-diene (**3a** → **4a**),[14,15] a 1,3-sigmatropic rearrangement of *trans*-1,2-divinylcyclobutane to 4-vinylcyclohexene (**3a** → **2a**),[14,15] and a 1,3-sigmatropic rearrangement of *cis,cis*-cycloocta-1,5-diene to 4-vinylcyclohexene (**4a** → **2a**).[16]

A counterpart of each of these reactions now is found in the piperylene dimer series, **2b–5b**. The study of this series, which has additional stereochemical labels, provides detailed information on the steric course of the interconversions that is not available from the butadiene dimers.

If the bisallylic radicals preserve their stereochemical configurations[17] in a biradical mechanism for these reactions,[8] three distinct configurations must be considered: *cis,cis*, *cis,trans*, and *trans,trans*. On the assumption[8] that trans cycloalkenes are not involved, product **4** could be formed only from *cis,cis*, product **2** from *cis,cis* or *cis,trans*, and product **3** from any of the three. In the context of the present work, the key proposal[8] of the biradical mechanism is that the

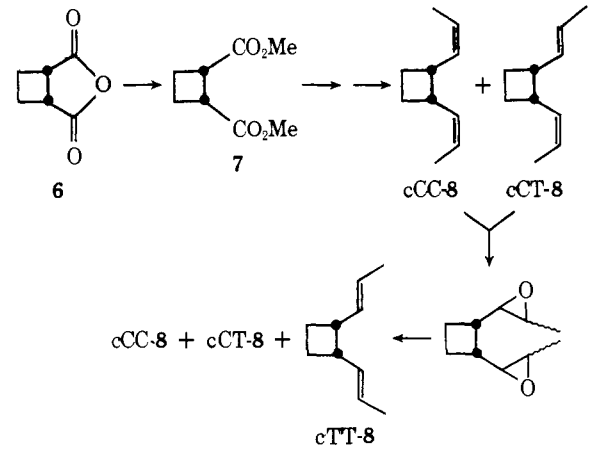



Diels–Alder dimerization of butadiene and the thermal rearrangement of *trans*-divinylcyclobutane both form 4-vinylcyclohexene through the common intermediates *cis,cis* and/or *cis,trans*.

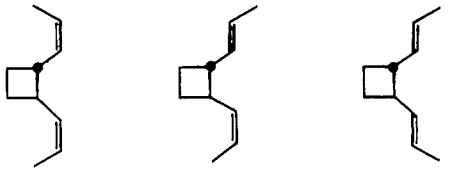
The experiments to be reported here bear on the mechanism of the **3a** → **2a** sigmatropic rearrangement in the butadiene dimer series, the mechanism of the Diels–Alder dimerization of piperylene, and the mechanisms of three rearrangements, **3b** → **2b**, **3b** → **4b**, and **5b** → **4b**, in the piperylene dimer series. A related study concerns the possibility that cycloocta-1,5-dienes with a trans double bond may play a role in these rearrangements.

**Cope Rearrangements of *cis*- and *trans*-1,2-Dipropenylcyclobutanes.** The chair-like geometry normally favored in the acyclic Cope rearrangement[18,19] should be difficult to achieve from *cis*-1,2-divinylcyclobutane because the small ring would resist the internal rotation needed to generate the true chair, and because, even if a quasi-chair conformation could be attained, the product, *cis,trans*-cycloocta-1,5-diene, would be severely strained.[21] Although the transient intermediacy of the latter substance cannot be excluded on purely energetic grounds,[9] the rearrangement of *cis*-1,2-divinylcyclobutane (**5a**) to *cis,cis*-cycloocta-1,5-diene (**4a**) usually is formulated[14,15,18] with a boat-like transition state, the free energy of which in the acyclic system normally lies about 6 kcal/mol above that of the chair.[18,20] Our studies support this formulation and, moreover, they show how *cis*-1,2-dialkenylcyclobutanes can be subjected to incremental steric effects that gradually deny access even to the "second-best" boat-like reaction.

*cis*-Cyclobutane-1,2-dicarboxylic acid anhydride (**6**) serves as the starting material for the syntheses of the three *cis*-1,2-dipropenylcyclobutanes. Dimethyl *cis*-cyclobutane-1,2-



dicarboxylate (**7**) can be reduced with $NaAlH_2(OCH_2CH_2OCH_3)_2$ to the dialdehyde, which upon treatment with ethylidenetriphenyphosphorane gives a 1:2 mixture of *cis*-1,2-*cis,trans*- and *cis*-1,2-*cis,cis*-dipropenylcyclobutane (cCT-**8** and cCC-**8**). Although only 2% of the product is the cis-1,2-trans,trans compound cTT-**8**, this isomer can be obtained readily by application of the elegant Vedejs-Fuchs olefin inversion[22] to the cCT-**8**–cCC-**8** mixture. Thus, treatment of the derived mixture of diepoxides with lithium diphenylphosphide and then with methyl iodide gives a mixture of *cis*-1,2-dipropenylcyclobutanes in which the desired cTT-**8** isomer predominates. Similar procedures effect the syntheses of the *trans*-1,2-dipropenylcyclobutanes tCC-**9**, tCT-**9**, and tTT-**9** from dimethyl *trans*-cyclobutane-1,2-dicarboxylate.



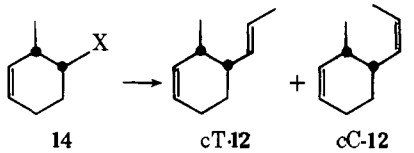
tCC-**9** tCT-**9** tTT-**9**

The Cope rearrangement products, *cis*- and *trans*-3,4-dimethylcycloocta-1,5-diene (**10** and **11**), occur in the pyrolysis

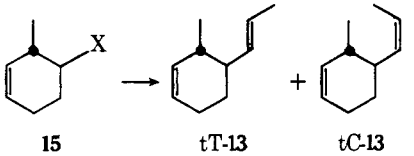
**10** **11**

mixtures from the 1,2-dipropenylcyclobutanes and are identified by spectra and ozonolysis to succinic acid and, respectively, *meso*- and *rac*-2,3-dimethylsuccinic acid.

The four 1,3-sigmatropic rearrangement products, 3-methyl-4-propenylcyclohexenes cT-**12**, cC-**12**, tT-**13**, and tC-**13**, have been identified in the mixtures of dimers of *cis*- and *trans*-piperylene[12] by conversions to aromatic derivatives. The present work independently synthesizes them by Wittig olefination sequences from the known[23] *cis*- and *trans*-3-methylcyclohexene-4-carboxaldehydes **14d** and **15d**.



**14** cT-**12** cC-**12**



**15** tT-**13** tC-**13**

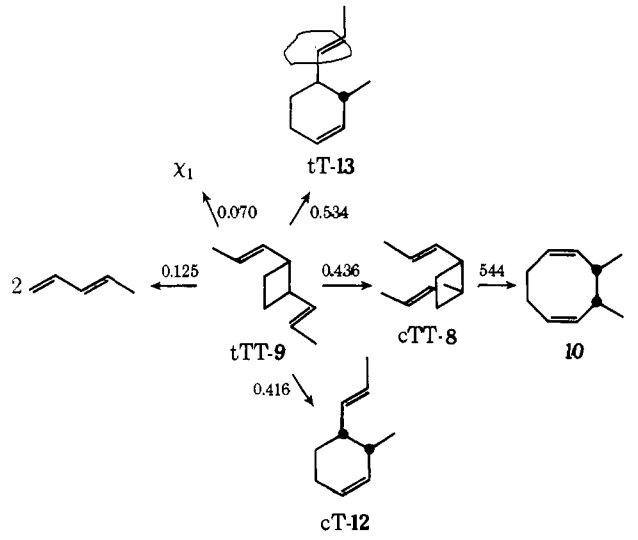
a, X = $CO_2H$
b, X = $CO_2Me$
c, X = $CH_2OH$
d, X = CHO

The pyrolyses of the *cis*- and *trans*-1,2-dipropenylcyclobutane series (**8** and **9**) are carried out at 146.5 °C in sealed ampules with decane as an internal standard. Under these conditions, most of the pyrolysis sample is in the liquid phase. Added surface is without appreciable effect on the overall rate of pyrolysis or the composition of the products.

**1,2-*trans,trans*-Dipropenyl Series (cTT-8 and tTT-9).** The pyrolysis of cTT-**8** gives only the product of Cope rearrangement, *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**). The stereochemistry of the product is that expected if the *trans*-propenyl groups take up the conformation (shown in Scheme I) appropriate to a boat-like transition state. The observed rate constant for the disappearance of starting material is (5.44 ± 0.01) × $10^{-3}$ $s^{-1}$.

In contrast, the trans isomer tTT-**9** gives a mixture of products: 15.8% piperylene (from 7.9% cycloreversion); 26.3% of *cis*- and 33.8% of *trans*-3-methyl-4-*trans*-propenylcyclohexene (cT-**12** and tT-**13**) from 1,3-sigmatropic rearrangement; 27.6% of *cis*-3,4-*cis,cis*-dimethylcycloocta-1,5-diene (**10**) from formal Cope rearrangement; and 4.4% of an unidentified product of short VPC retention time ($X_1$). The pyrolysis obeys first-order kinetics with a rate constant of (1.58 ± 0.04) × $10^{-5}$ $s^{-1}$ and the product composition is independent of the extent of reaction. These observations justify the treatment of the overall rate constant for tTT-**9** as the sum of the rate constants for the competing first-order reactions shown in Scheme I.

**Scheme** I ($k \times 10^5$ s)



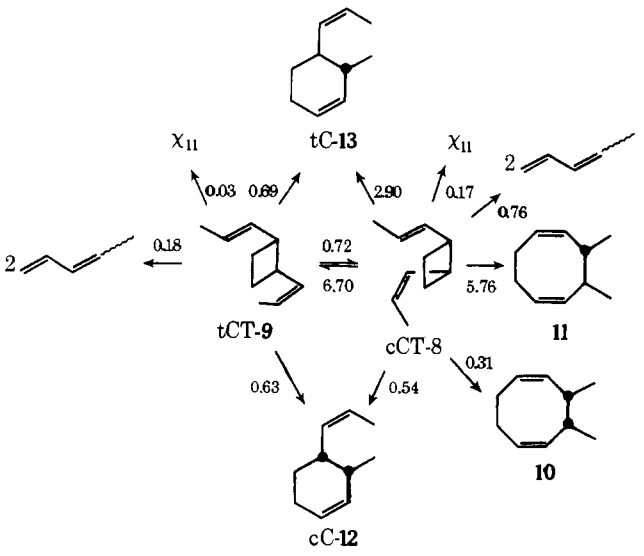

Note that the 1,3-sigmatropic rearrangement products, cT-**12** and tT-**13**, preserve the original *trans*-propenyl configuration, so that if bisallylic biradical intermediates are involv, their stereochemistry must remain fixed throughout the reaction, as would be expected.[17,24]

The only (>99.9%) Cope rearrangement product from tTT-**9** is *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**), the same product that is formed from cTT-**8**. This observation suggests that cTT-**8** may be an intermediate in the formal Cope rearrangement of tTT-**9**, that is that the conversion may take the course tTT-**9** → cTT-**8** → **10**. Direct evidence for this pathway would be difficult to provide, because cTT-**8** rearranges 1250 times as fast as tTT-**9** and hence would not accumulate in more than trace amounts during the pyrolysis of tTT-**9**.

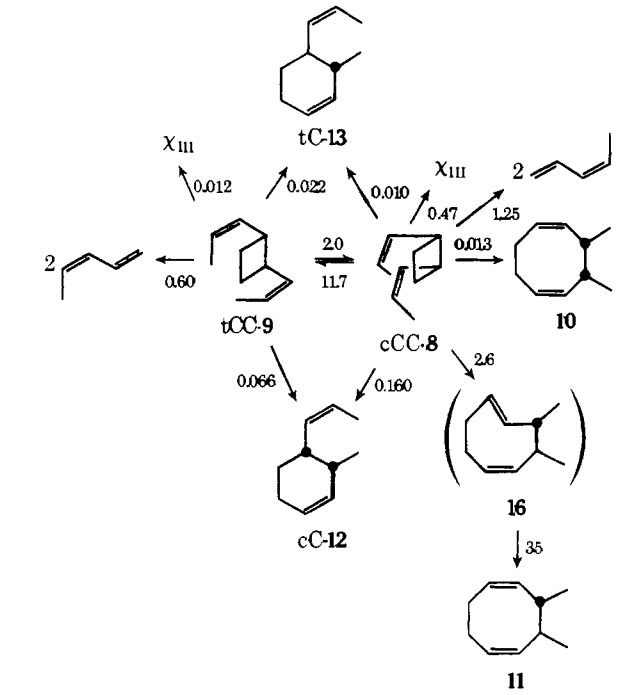
**1,2-*cis,trans*- and 1,2-*cis,cis*-Dipropenyl Series (cCT-8–tCT-9 and cCC-8–tCC-9).** When one or both of the propenyl groups of a *cis*-1,2-dipropenylcyclobutane has a cis configuration (cCT-**8** or cCC-**8**), there is a marked decline in the rate of Cope rearrangement. In these cases, the interconversion of the *trans*-1,2- and *cis*-1,2-dipropenyl isomers (t and c) becomes competitive with the retarded Cope rearrangement, so that the overall kinetics no longer are first order, and although the products themselves are stable under the reaction conditions, their distribution during a pyrolysis changes with time. The complete kinetic descriptions of these systems (Scheme II for cCT-**8**–tCT-**9**, Scheme III for cCC-**8**–tCC-**9**) require 14 rate constants each, since there are two cyclobutanes in each system, and each can give rise to its epimer in addition to six other products. Examination of the product distributions at

early points in the kinetic runs, starting from either component of the epimeric cyclobutane pair, gives rough values of the individual rate constants. These serve as input data for a digitally computed Runge-Kutta numerical integration of the differential rate equations.[25] The trial rate constants are adjusted until a satisfactory fit of the computed and experimental concentration vs. time data is achieved. Schemes II and III give the refined rate constants.

Scheme II ($k \times 10^5$ s)




Scheme III ($k \times 10^5$ s)

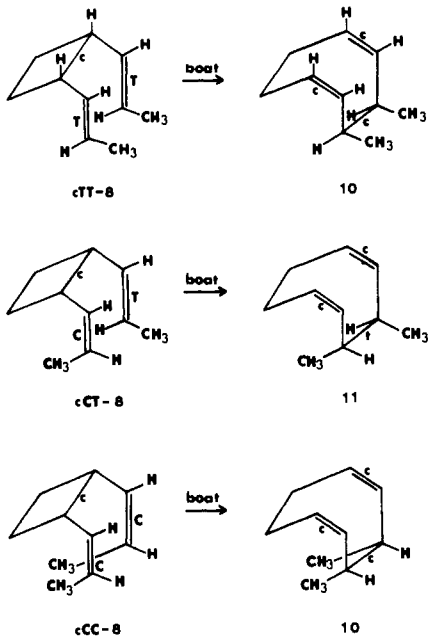



*cis*-Propenyl groups not only depress the rate of the boat-like Cope rearrangement, but by doing so, they permit the observation of a much slower "nonboat" Cope process, which gives a different product. This reaction just begins to emerge in the pyrolysis of cCT-**8** (Scheme II), which gives both the boat and nonboat products, *trans*- and *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11** and **10**), in relive amounts of 95 and 5%, respectively. The new pathway becomes prominent in the case of cCC-**8** (Scheme III), where it accounts for 99.5% of the cyclooctadiene product.

Table I. Rates and Products of Pyrolyses of *cis*-1,2-Dialkenylcyclobutanes at 146.5 °C

| Reactant | Boat | | Nonboat | |
|---|---|---|---|---|
| | Product | $k_b$, rel | Product | $k_c$, rel |
| 5a | 4a | 181 000[a] | | |
| cTT-8 | 10 | 41 800[b] | 11 | |
| cCT-8 | 11 | 435[c] | 10 | 24[c] |
| cCC-8 | 10 | 1[c,d] | 11 | 200[c] |

[a] Calculated from published activation parameters.[14] [b] Measured directly. [c] Calculated as the product of the observed overall first-order rate constant for disappearance of cCT-**8** (or cCC-**8**) and the fraction of the indicated 3,4-dimethylcycloocta-1,5-diene in the product mixture, which also contains *trans*-1,2-*cis,trans*-(resp. *cis,cis*)-dipropenylcyclobutanes from cCT-8 and cCC-8, as well as piperylene and 3-methyl-4-propenylcyclohexenes. [d] $k_b$(abs) = 1.3 $\times 10^{-7}$ s$^{-1}$.




As a basis for a mechanistic discussion of the boat and nonboat Cope rearrangements of the *cis*-dipropenylcyclobutanes **8**, we excerpt the rates and products of these reactions from Schemes I-III and combine them in Table I with those of the rearrangement of *cis*-1,2-divinylcyclobutane (**5a**). The formal Cope rearrangements of the trans series **9** are discussed later.

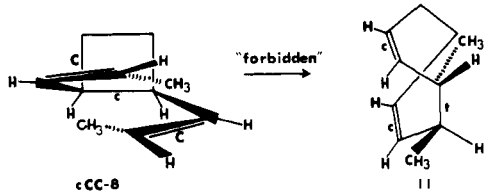
The data show that methyl substitution at the terminal carbons of the vinyl groups of *cis*-1,2-divinylcyclobutane (**5a**) causes a regular decline in the rate of the boat-like rearrangement. In the transition state of cTT-**8** → **10**, the side-by-side arrangement of the terminal methyl groups causes a repulsive steric effect that is not present in the ground state, where the propenyl chains are free to adopt sterically uncongested conformations. The corresponding change from ground- to transition-state conformation in *cis*-1,2-divinylcyclobutane produces only a hydrogen-hydrogen repulsion. The ratio of rates cTT-**8**/**5a** therefore may be expressed as a free energy of activation increment $\Delta\Delta F_{MM}^{\ddagger}$ due to the difference in the methyl-methyl and hydrogen-hydrogen repulsions.

The boat transition state for cCT-**8** produces two methyl-hydrogen repulsions, but also introduces a new steric effect, the repulsion of the cis-terminal methyl group and the four-membered ring, which results from the "tucked under" side-chain conformation. The corresponding energies are $2\Delta\Delta F_{MH}^{\ddagger}$ and $\Delta\Delta F_{MR}^{\ddagger}$. Finally, the boat transition state from cCC-**8** has one methyl-methyl interaction (assumed here to be equal to that in the cTT-**8** boat transition state) and two

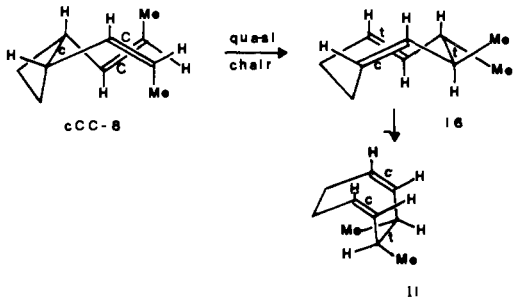
methyl-ring interactions. If the interaction free energies remain constant in the series, the relative rate data of Table I for the boat-like reactions can be expressed in the form of the following parameters (in kcal/mol): $\Delta\Delta F_{MH}^{\ddagger} = 0.29$; $\Delta\Delta F_{MM}^{\ddagger} = 1.22$; $\Delta\Delta F_{MR}^{\ddagger} = 4.43$.

By far the largest steric effect is the methyl-ring interaction, which comes into play in the boat-like transition states from the reactants (cCT-**8** and cCC-**8**) with *cis*-propenyl groups. The sum of two such interactions, with a small additional contribution by one methyl-methyl interaction, retards the boat-like Cope rearrangements by more than five orders of magnitude.

The emergence of the nonboat rearrangement in the lower part of Table I seems to be caused by two reinforcing effects, a relatively gradual increase in absolute rate of the nonboat reaction and the already described sharp decrease in the rate of the boat reaction. We consider two mechanisms for the nonboat reaction. The first is a direct transformation, for example, cCC-**8** → **11**, either via biradical intermediates or

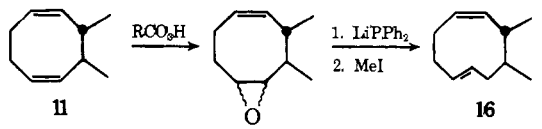



perhaps in a concerted reaction whose transition-state geometry corresponds to that of an orbital symmetry forbidden process ($_2\pi_a + _2\pi_s + _2\sigma_s$).[27,28] The second is a two-step reaction involving a quasi-chair transition state in a preliminary rearrangement, cCC-**8** → *trans*-3,4-dimethyl-*cis,trans*-cycloocta-1,5-diene (**16**), followed by geometric isomerization (by an unspecified mechanism) of the trans double bond of **16** to give *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**).




Although the highly strained cis,trans diene **16** must be thermodynamically unstable with respect to the cis,cis isomer **11**, it is not clear that a readily attainable mechanistic pathway connects them. The only previous *cis,trans*-cycloocta-1,5-diene in the literature is the parent compound, which isomerizes readily to the cis,cis isomer under iodine catalysis,[29] but which apparently has not been studied under pyrolytic conditions. A study of the thermal reactions of **16**, the hypothetical intermediate in the two-step nonboat rearrangement of cCC-**8**, is therefore indicated.

**Preparation and Properties of *trans*-3,4-Dimethyl-*cis,trans*-cycloocta-1,5-diene (16).** Application of the Vedejs-Fuchs olefin inversion[22] to *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**) achieves the synthesis of **16** for this purpose. The monoepoxide, obtained from **11** with *m*-chloroperbenzoic acid upon successive treatments with lithium di-




phenylphosphide and methyl iodide, is converted to the cis,trans diene **16**.

The infrared spectrum of compound **16** shows both trans ($\lambda_{max}$ 990 $cm^{-1}$) and cis ($\lambda_{max}$ 720 $cm^{-1}$) double bonds.[30] The substance is unstable, like the parent *cis,trans*-cycloocta-1,5-diene. It can be purified by VPC on an ammonia-purged column, but only with severe losses. Concentrated solutions or neat samples of **16** deposit a solid (dimer or polymer) upon standing a few hours at room temperature. Treatment with $I_2/CHCl_3$ converts **16** to the cis,cis diene **11**.

Two diastereomers of *trans*-3,4-dimethyl-*cis,trans*-cycloocta-1,5-diene **16** can exist. It is not clear whether one or both of these are present in our preparation of **16**, and consequently, the following observations on the behavior of **16** may be irrelevant to the question of its intermediacy in the cCC-**8** → **11** rearrangement.

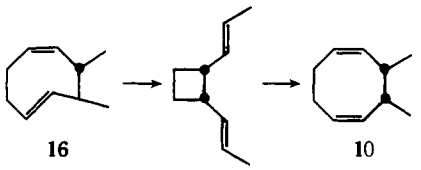
Under the conditions (dibutyl tetrachlorophthalate capillary column, 75 °C) used for analysis of the products from the pyrolysis of cCC-**8**, compound **16** does not survive, but instead gives a complex trace of peaks with retention times inermediate between those of decane (internal standard) and **11**. This behavior would preclude the detection of small amounts of **16** under the analytical conditions, so that **16** cannot be ruled out as a possible intermediate in the Cope rearrangement of cCC-**8**.

Indirect support for an intermediate in the nonboat Cope rearrangement of cCC-**8** to **11** is provided by the detailed kinetic analysis of the pyrolysis (Scheme III). The relative yield of **11** increases with time during the pyrolysis of cCC-**8**, an observation consistent with the initial accumulation of an intermediate and its subsequent transformation to **11**. In fact, the numerical integration of the kinetic equations for Scheme III does not converge upon an internally consistent set of rate constants unless an intermediate is interposed between cCC-**8** and **11**.

In Scheme III, we (somewhat arbitrarily) show this intermediate as **16**. The difficulty of analysis for this substance has just been described, but it is possible to account quantitatively for the observed time dependence of the concentration of **11** by the assignment of a rate constant $2.6 \times 10^{-5}$ $s^{-1}$ to the step generating the intermediate and a rate constant $35 \times 10^{-5}$ $s^{-1}$ to the step in which it is converted to **11** (see Scheme III). The calculated amount of the intermediate never exceeds 4%, so that even a complete failure to detect it in the VPC analysis would not seriously perturb the overall material balance.

There remains, however, a major question about the mechanism of the hypothetical **16** → **11** isomerization, since this reaction does not occur when synthetic **16** is pyrolyzed. In an attempt to simulate the conditions prevailing during the pyrolysis of cCC-**8**, a 0.7 M decane solution of the cis,trans diene **16** (containing about 9% of cis,cis diene **11**) is heated for 1000 s at 146.5 °C. This gives a substantial amount of polymer, but 35% of identifiable products also are obtained. The relative amount of **11** now is 30%, which would correspond to no net formation of **11** by pyrolysis, the original 9% of **11** now having been concentrated by selective removal of some of the **16** as polymer. The remaining 70% of material consists largely of *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**). At first glance, this is a puzzling product, since its formation from **16** requires not only formal geometric isomerization about one double bond, but also formal inversion of configuration at one of the asymmetric carbon atoms of **16**.

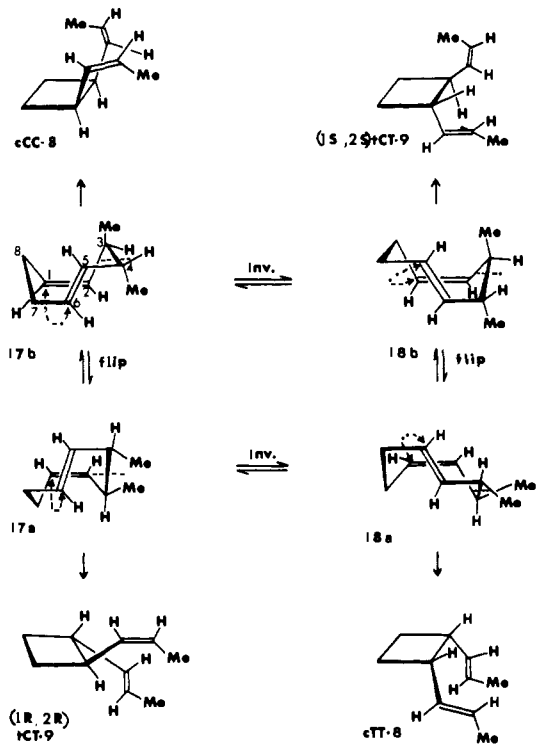
This part of the mechanistic problem is solved by the identification of a minor product (about one part to 12 parts of **10** in the 1000-s pyrolysis) as *cis*-1,2-*trans,trans*-dipropenylcyclobutane (cTT-**8**). Since pyrolysis of this substance gives **10** exclusively (Table I), a sequential mechanism (**16** → cTT-**8** → **10**) for the conversion **16** → **10** becomes likely. In accord with this, we find that the proposed intermediate apparently




cTT-8

builds up during a run, for the proportion of cTT-**8** is greater (one part to three parts of **10**) in a 500-s pyrolysis. Again, polymer formation limits the yield of volatiles to 30%, but no other pyrolysis products appear. The overall process **16** → **10** thus consists of two successive highly stereospecific Cope rearrangements, the first chair-like (**16** → cTT-**8**) and the second boat-like (cTT-**8** → **10**, see Scheme IV).

Scheme IV



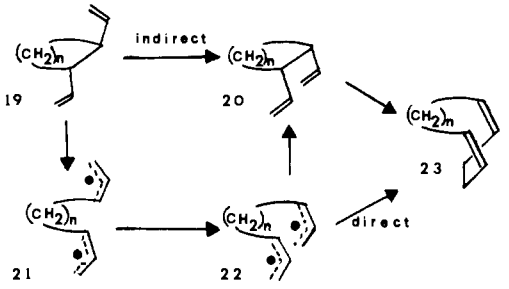

The synthetic sample of **16** thus gives **10** as the only observable cyclooctadiene, whereas the **16** postulated as an intermediate in the nonboat Cope rearrangement in the pyrolysis of cCC-**8** (Scheme III) is required to give **11**. This is not necessarily contradictory, since it is conceivable that different diastereomers of **16** are involved in the two reactions. There is also a possibility that adventitious catalysis in the pyrolysis of cCC-**8** may effect the direct cis-trans olefin geometric isomerization of **16** to **11**, and that such a catalyst happens not be present in the synthetic sample of **16**. Finally, of course, we cannot avoid the admission that the cCC-**8** → **16** → **11** mechanistic proposal for the nonboat Cope rearrangement simply may be incorrect.

The highly stereospecific thermal rearrangement **16** → cTT-**8** can occur by way of a transition state with a chairlike 1,5-hexadiene geometry from one conformation of one diastereomer of *trans*-3,4-dimethyl-*cis,trans*-cycloocta-1,5-diene (**18a**) (Scheme IV). In principle, **18a** and its conformational isomer **18b** differ from their diastereomers **17a** and **17b** in the axial dissymmetry element associated with the ring. Internal rotations about bonds C(6)-C(7) and C(4)-C(5), by analogy to the racemization of *trans*-cyclooctene,[31] would invert the configuration of this element and interconvert the diastereomers. Moreover, just as in the parent *cis,trans*-cycloocta-1,5-diene,[29] ring flips should rapidly interconvert conformational isomers (**18a** ⇌ **18b**, **17a** ⇌ **17b**, Scheme IV).

We do not know which diastereomer, **17a** or **18a** (or both), corresponds to our sample of **16**. However, although the inversion barrier is undoubtedly much higher than the conformational one,[29] it might be surmounted at 146.5 °C. Therefore, even if only diastereomer **17a**–**17b** results from the synthesis, the other, **18a**–**18b**, might be formed under the conditions of pyrolysis and theby provide a source of conformation **18a**, which leads to the observed product cTT-**8**. It is not surprising that in the **18** diastereomer series, reaction from the **18a** conformation should predominate, since in its transition state both methyl groups would occupy equatorial positions, whereas the methyl groups would be axial in the transition state from **18b**.

Scheme IV reversibly converts *trans*- to *cis*-1,2-dipropenylcyclobutanes and therefore might appear to provide a previously overlooked mechanism for the thermal racemizations and trans-cis isomerizations of 1,2-dialkenylcyclobutanes observed in this work and elsewhere.[14,15] In detail, however, this is unlikely. Although the racemization ((*RR*)-tCT-**9** ⇌ (*SS*)-tCT-**9**) cannot be formally excluded, Scheme IV requires that a trans-cis transformation of the relationship of the propenyl groups on the cyclobutane ring be coupled with a T → C inversion of one of the olefinic geometric configurations. It provides no means for achieving the simple epimerizations tCC-**9** ⇌ cCC-**8** and tCT-**9** ⇌ cCT-**8**, and therefore it conflicts with the experimental observations reported in Schemes II and III.

**Mechanisms of the Epimerically Unfavorable Cope Rearrangements of *trans*-1,2-Dialkenylcyclobutanes to Cycloocta-1,5-dienes.** Obviously, it is easier to bring the ends of the bisallyl system of a 1,2-dialkenylcyclopropane or cyclobutane together when the alkenyl groups are in a cis (**20**) rather than a trans (**19**) relationship. The cis and trans configurations, therefore, may be said to be respectively epimerically favorable and epimerically unfavorable to Cope rearrangement.[32] Nevertheless, Cope rearrangements of *trans*-1,2-dialkenylcycloalkanes do occur,[34] and such reactions raise the question whether their mechanism is *indirect*, requiring prior epimerization to the *cis*-1,2-dialkenylcycloalkene, or *direct*, perhaps by ring closure of an intermediate bisallylic biradical with two cis-allylic groups (**22**).




In one previously discussed example of this problem, the thermal rearrangement of *trans*-1,2-divinylcyclobutane (**19**, $n$ = 2) to *cis,cis*-cycloocta-1,5-diene (**23**, $n$ = 2), a clear thermochemical-kinetic evaluation of the indirect mechanism so far is not feasible, because there are two conflicting estimates (~0[8] and ≥7.6[9] kcal/mol) of the activation energy for cyclization of the octa-1,7-diene-3,6-diyl biradical (**22**, $n$ = 2), the hypothetical precursor of **23** ($n$ = 2). Moreover, the question is difficult to test experimentally with *trans*-1,2-divinylcyclobutane (**19**, $n$ = 2) because the epimerically favorable cis isomer (**20**, $n$ = 2) rearranges too rapidly[14] to accumulate during the pyrolysis of **19** ($n$ = 2).

In this respect, the epimeric pair of *trans*-1,2-dipropenyl-

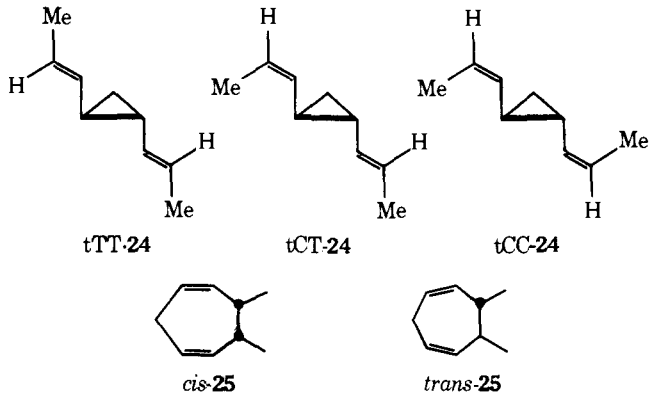
cyclobutanes with two *trans*-propenyl groups, tTT-**9** and cTT-**8**, offer no advantage over the unsubstituted 1,2-divinylcyclobutanes. As Scheme I shows, the rearrangement of cTT-**8** is still too fast to permit ready detection of that substance as an intermediate in the Cope rearrangement of its epimer tTT-**9**. However, the other two pairs of 1,2-dipropenylcyclobutanes are suitable for such an analysis, since the rearrangements of the cis isomers cCT-**8** and cCC-**8** are much slower than those of **19** ($n$ = 2) or cTT-**8** (Table I).

In fact, cCT-**8** andcCC-**8** do accumulate during pyrolyses of tCT-**9** and tCC-**9**, respectively, at 146.5 °C, and both reactions are reversible. Although consistent with the indirect mechanism, these observations alone do not exclude contributions from the direct one. The relative importance of the two paths, however, emerges from the kinetic analysis of Schemes II and III, which show that within the limitations of the numerical integration method, the rate constants for the direct epimerically unfavorable Cope rearrangements of tCT-**9** or tCC-**9** are indistinguishable from zero. The rate constants for the Cope rearrangement of cCC-**8** depend upon measurements of small components of the total reaction and therefore are rather rough, whereas the values for cCT-**8** (and hence, for tCT-**9**) are more reliable. In both the tCC-**9** and tCT-**9** series, however, it is clear that the indirect pathway predominates heavily. The relative rates of boat and nonboat reactions, 94.7/5.3 from tCT-**9** and 0.5/99.5 from tCC-**9**, correspond exactly to those found from cCT-**8** and cCC-**8**, respectively (Table I), and hence also are consistent with the indirect mechanism.

The absence of a direct mechanism leading to the cycloocta-1,5-diene product from the epimerically unfavorable *trans*-1,2-dipropenylcyclobutanes may be associated with a strain barrier to closure of a biradical intermediate, similar to that postulated for the unsubstituted divinylcyclobutane case.[9] However, another factor unique to the propenyl systems operates in the same direction. Formation of a bisallylic biradical with two *cis*-allylic groups is required for the direct pathway to a *cis,cis*-cycloocta-1,5-diene. Such a biradical could only be formed via a transition state in which both propenyl groups were in the "tucked under" conformation (**22**). This would produce one methyl-ring repulsive interaction in the case of tCT-**9** and two in the case of tCC-**9**. These interactions retard the rate of the ordinary boat rearrangement of the epimerically favorable cis isomers by factors of about 200 each (see Table I) and could similarly affect the direct epimerically unfavorable rearrangement from the trans isomers tCT-**9** and tCC-**9**.

This discussion is pertinent to the analogous epimerically unfavorable Cope rearrangements of *trans*-1,2-dipropenylcyclopropanes (**24**) to the 6,7-dimethyl *cis,cis*-cyclohepta-1,4-dienes (**25**). The observations[34b] that tTT-**24** and tCT-**24** rearrange readily to *cis*- and *trans*-**25**, respectively, whereas tCC-**24** rearranges only slowly, are interpreted[34b] as evidence against the direct mechanism on the grounds that "if it were the mechanism, all three substrates would be expected to give Cope products at comparable rates". However, an extension of the argument just given for the dipropenylcyclobutanes suggests that *cis*-methyl substituents would slow down the direct mechanism by interfering with the formation of the doubly cis-allylic biradical. Hence, even in the direct mechanism, the isomers of **24** would be expected to react at different rates, and tCC-**24** should be the least reactive. The *cis*-methyl retardation might not be as great as in the cyclobutane series, but the data reported[34b] do not permit rejection of the direct mechanism for the Cope rearrangements of tTT-**24** and tCT-**24**.

The doubly cis-allylic configuration **22** is not required of a biradical intermediate or transition state for the epimerization of tCT-**9** to cCT-**8** (or of tCC-**9** to cCC-**8**). Epimerization





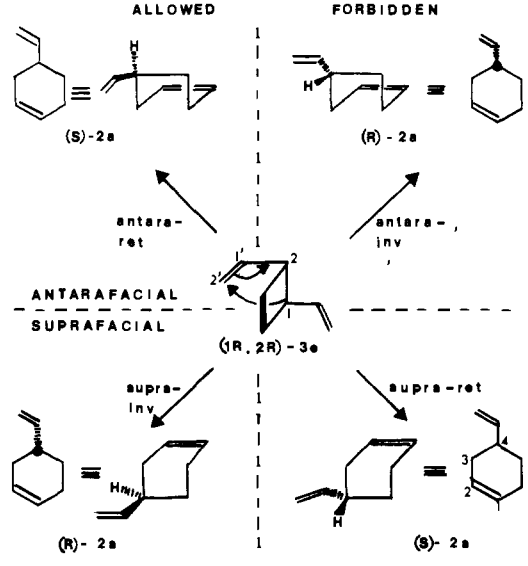

*cis*-**25** *trans*-**25**

therefore could occur more rapidly via a transition-state conformation free of the methyl-ring repulsions and the indirect mechanism could predominate overall if its final step, the Cope rearrangement of the cis isomer, were fast enough. It remains to be seen whether the direct mechanism might be detected in *trans*-1,2-divinylcyclobutane or other systems in which the methyl-ring repulsion is absent.

**1,3-Sigmatropic Rearrangement of *trans*-1,2-Divinylcyclobutane and the *trans*-1,2-Dipropenylcyclobutanes.** The activation energy, $\Delta H^{\ddagger}$ = 34.0 kcal/mol, for the thermal rearrangement of *trans*-1,2-divinylcyclobutane (**3a**) corresponds fairly closely to that calculated for a mechanism in which the formation of a biradical is rate determining and there is a small activation energy for the recyclization of the biradical.[8,14,35] Pyrolysis[14] of optically active **3a**, $[\alpha]_D$ 2.0°, at 176.3 °C causes simultaneous racemization and sigmatropic rearrangement to vinylcyclohexene **2a**, $[\alpha]_D$ 0.12°. The retention of some optical activity in the product is rationalized[14] with a biradical in which the rates of ring closure and internal rotation are comparable. However, in the absence of either the absolute configurations or maximum rotations of the starting material and product, these data do not define either the sense or magnitude of the chirality that is preserved.

In fact, even that information is insufficient to define the stereochemistry fully. Correlation of the chiralities of **3a** and **2a** would permit a determination of the configurational outcome at the migrant carbon (C(1) of **3a** ≡ C(4) of **2a**) as retention (ret) or inversion (inv), but not at the migration terminus (C(2′) of **3a** ≡ C(3) of **2a**). It is the stereochemistry at the latter site that determines whether migration has occurred suprafacially (supra) or antarafacially (antara) on the C(2′) allyl group of **3a**.

Scheme V

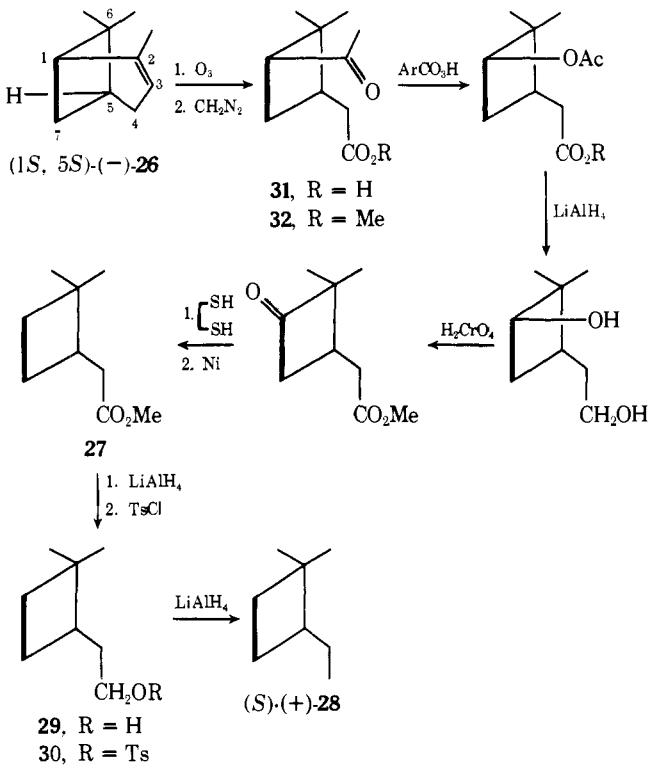


As Scheme V shows, there are four possible combinations of one member of category ret-inv with one of supra-antara. Two of these pathways are orbital symmetry allowed, and two are forbidden.[36,37] The complete analysis into the four pathways requires a stereochemical label at the migration terminus, as in the dipropenyl series to be described later. The incomplete characterization available in the divinyl series, nevertheless, provides some mechanistic clarification in the form of a two-pathway analysis: antara-ret + supra-ret vs. antara-inv + supra-inv, or more simply, ret vs. inv. The experiment rests upon the following configurational correlations. Readers to whom these details are of secondary interest may pick up the thread of the mechanistic argument by skipping to the next bold-face heading (Pyrolysis).

**Configurational Correlation and Thermal Rearrangement of (1*R*,2*R*)-(+)-*trans*-1,2-Divinylcyclobutane 3a.** $\alpha$-Pinene (**26**)[38,39] and 3-methylcyclohexanone (**36**)[40,41] serve as reference substances for the determination of the absolute configurations of *trans*-1,2-divinylcyclobutane (**3a**) and its rearrangement product, 4-vinylcyclohexene (**2a**), respectively.

Schemes VI and VII show the steps that convert both (1*S*,5*S*)-(−)-$\alpha$-pinene (**26**) and (1*S*,2*S*)-(−)-**3a** to the enantiomers of the common relay compound 1,1-dimethyl-2-ethylcyclobutane **28**.[42] The overall strategy of Scheme VI is

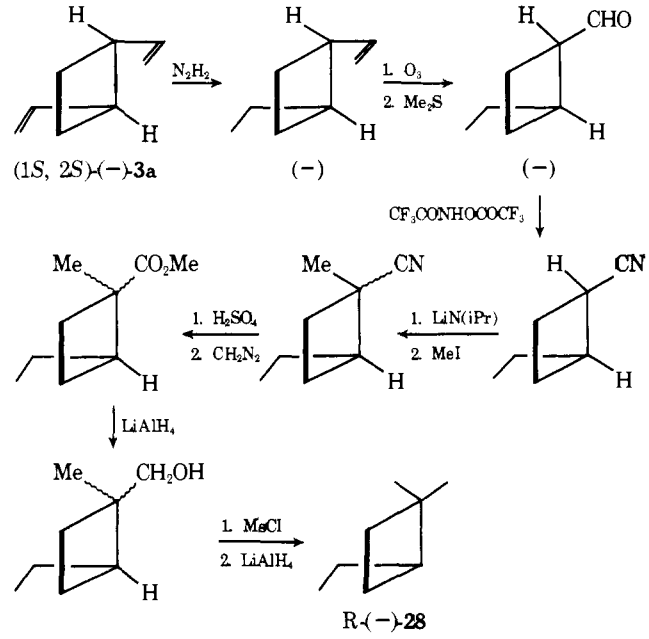
Scheme VI




to delete C(2) and its attached methyl group and convert the C(3)-C(4) unit of $\alpha$-pinene to an ethyl group. This is achieved by cleavage of the unsaturated bridge at C(2)-C(3) to ketoacid **31,** replacement of the acetyl group by H, and reduction of the acetic acid chain. The Experimental Section describes the details of these transformations. The ten-step sequence starting with $\alpha$-pinene (**26**) of $[\alpha]^{21}D$ − 42.06°, 82% enantiomerically pure,[39] gives (*S*)-(+)-1,1-dimethyl-2-ethylcyclobutane (**28**) of $[\alpha]D$ 4.76°. Since fractionations are scrupulously avoided in all the transformations, the latter sample also is 82% enantiomerically pure, so that the maximum rotation of **28** is $[\alpha]D$ 5.80°.

In Scheme VII, one of the vinyl groups of *trans*-1,2-divinylcyclobutane (**3a**) eventually becomes an ethyl group,

Scheme VII



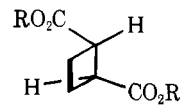

whereas the other is transformed first into a cyano group to permit $\alpha$ methylation. Further unexceptional steps convert the $\alpha$-methyl cyano unit to *gem*-dimethyl. The correlation is carried out with *trans*-1,2-divinylcyclobutane (**3a**) of $[\alpha]D$ −11.3°, prepared by partial asymmetric hydroboration[43] of racemic **3a**. The 1,1-dimethyl-2-ethylcyclobutane (**28**) has $[\alpha]D$ −0.647 ± 0.018°, which corresponds to an enantiomeric purity of 11.1%, based upon the maximum rotation of 5.80° established by Scheme VI. The **3a** starting material of Scheme VII, therefore, also is 11.1% enantiomerically pure, from which a maximum rotation for **3a** of $[\alpha]D$ 101 ± 4° may be calculated.

The synthesis of **3a** from optically active *trans*-cyclobutane-1,2-dicarboxylic acid (**33**) provides a more efficient source of highly resolved material. Moreover, the direct analysis of the enantiomeric composition of the derived methyl ester **34** establishes the maximum rotation of **3a** in an independent manner.

Resolution of the acid **33** via the quinine salt[44] gives material of $[\alpha]^{24}D$ 95.8°, which is 60.5% of 158°, the highest reported rotation.[45] Conversion to the dimethyl ester **34,** $[\alpha]D$ 88.9°, establishes the relative rotations of the acid and ester. A separate sample of the ester, $[\alpha]D$ 56.2°, when treated with the chiral shift reagent tris[3-(heptafluorbutylhydroxymethylene)-*d*-camphorato]europium(III),[46] shows two *O*-methyl NMR signals in the ratio 69.3/30.7, corresponding to an enantiomeric purity of 38.6%. The maximum rotations of the ester **34** and acid **33,** therefore, are 145 ± 5 and 156 ± 5°, respectively, and the resolution[45] of **33** to a rotation of 158°, therefore, is complete.

Reduction of the diester **34,** $[\alpha]D$ 56.2°, 38.6% enantiomerically pure, to the dialdehyde and double Wittig methylenation of the latter give *trans*-1,2-divinylcyclobutane **3a,** $[\alpha]D$ 37.8°, from which the maximum rotation of **3a** is calculated to be 99°. This is within experimental error of the value 101° deduced from the correlation with $\alpha$-pinene (Schemes VI and VII). Moreover, the assignment[47] of absolute configuration to the acid **33,** which is based upon optical rotatory dispersion curves of the thionamide, now is confirmed by the chemical correlation (+)**34** → (+)**3a**.

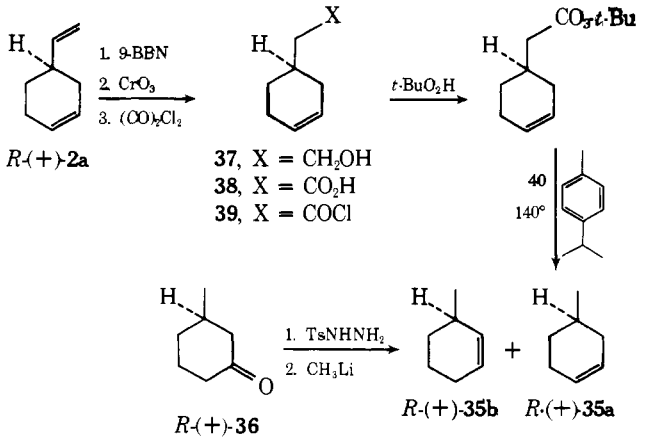
Correlation of the 1,3-sigmatropic rearrangement product (+)-4-vinylcyclohexene (**2a**), obtained by asymmetric hydroboration, with (+)-4-methylcyclohexene (**35a**) is achieved



(1*S*, 2*S*)-(+)-**33**, R = H
(1*S*, 2*S*)-(+)-**34**, R = Me

by the overall strategy of removal of one carbon atom from the side chain of **2a**. The steps are outlined in Scheme VIII. Cor-

**Scheme VIII**



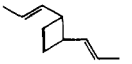
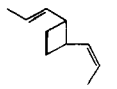
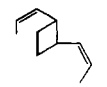
relation of the relay compound **35a** by synthesis from enantiomerically pure[41] 3-methylcyclohexanone (**36**) establishes the absolute configuration and maximum rotation ([α]D 136°) of **35a**, and hence of **2a**. This correlation (**36** → **35a** + **35b**) also establishes the absolute configuration and maximum rotation ([α]D 89.4°) of (+)-3-methylcyclohexene (**35b**), an important relay compound in the 3-methyl-4-propenylcyclohexene series. The maximum rotation of **2a**, [α]D 112° ($CCl_4$), is in good agreement with another recent determination,[9] [α]D 115° ($CCl_4$). The chemical method of absolute configurational assignment used in the present work is confirmed by a recently described physical method,[48] and the maximum rotation of **2a** is confirmed by direct analysis of the enantiomeric composition of the chemically correlated cyclohexenes described later.

**Pyrolysis of racemic *trans*-1,2-divinylcyclobutane (3a)** in the liquid phase at 146.5 °C (a sample of two parts of **3a** and one part of decane) gives 70.4% of 4-vinylcyclohexene (**2a**), 8.0% of butadiene (from 4% of cycloreversion), and 25.6% of cycloocta-1,5-diene (**4a**). The rate constant $k_p$ for the consumption of starting material is $9.8 \times 10^{-6}$ $s^{-1}$, in good agreement with the value $9.0 \times 10^{-6}$ $s^{-1}$ interpolated from data[14] at other temperatures. Note that *cis*-1,2-divinylcyclobutane is a plausible precursor of **4a**, but not of **2a** under these conditions.[14]

A similar pyrolysis of (1*R*,2*R*)-(+)-*trans*-1,2-divinylcyclobutane (**3a**), [α]D 37.8°, 37.4% enantiomerically pure, for 24.5 h (57. 7% total consumption of starting material), gives (*R*)-(+)-4-vinylcyclohexene (**2a**), [α]D 3.16°, 2.8% enantiomerically pure. The **3a** recovered by VPC, [α]D 31.9°, is 16% racemized. A one-point first-order rate constant, $k_\alpha = (1/t) \ln (\alpha_0/\alpha) = 1.96 \times 10^{-6}$ $s^{-1}$, where $\alpha$ is the rotation of pure **3a**, can be calculated from these data.

The enantiomeric purity, $P_t$, of the product **2a** actually isolated at any finite time is lower than it would be if the starting material were not racemizing during the reaction. One can correct for this by calculating the preservation of enantiomeric purity in the product relative to an *effective* enantiomeric purity of the reactant ($\bar{P}$) during the experimental time period. The assumption of a linear decline of enantiomeric purity of the reactant would lead to a crude estimate of $\bar{P}$ as

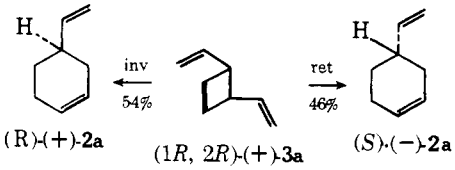
Table II. Absolute Configurations and Maximum Rotations ($CCl_4$) of the *trans*-1,2-Dipropenylcyclobutanes and *trans*-1,2-Divinylcyclobutane

| Compd | Maximum rotation, deg [α]D | Maximum rotation, deg $[\alpha]_{365}$ |
|---|---|---|
|  (1*R*,2*R*)-(+)-3a | 101 | 342 |
|  (1*R*,2*R*)-(+)-tTT-9 | 119 | 388 |
|  (1*R*,2*R*)-(−)-tCT-9 | −51.9 | −270 |
|  (1*R*,2*R*)-(−)-tCC-9 | −251 | −1066 |

the arithmetic mean of the initial and final values, $(P_0 + P_t)/2$. On this basis the value normalized to unity would be $\bar{P} = (P_0 + P_t)/2P_0 = 0.923$. A more rigorous method[49] recognizes the exponential decay of $P$ in

$$\bar{P} = \frac{k_p}{k_\alpha + k_p}\left[\frac{1 - e^{-(k_\alpha + k_p)t}}{1 - e^{-k_p t}}\right] \quad (1)$$

The rate constant $k_\alpha$ is that defined above; $k_p$ is the rate constant for total disappearance of the starting material (not that for formation of **2a**).[50] From eq 1, we calculate $\bar{P} = 0.966$, so that the maximum optical purity that could be expected of product **2a** in this experiment is 0.966 × 37.4% = 36.2%. The observed value corresponds to 7.7% of this. Consequently, the rearrangement of the portion of *trans*-1,2-divinylcyclobutane ((1*R*,2*R*)-(+)-**3a**) that has not suffered prior racemization gives 54% (*R*)-(+)-**2a** and 46% (*S*)-(−)-**2a**, the products, respectively, of rearrangement with inversion and retention of configuration.



This weakly stereospecific result appears superficially to be in accord with the suggestion[14] of competitive ring closure and internal rotation in a biradical intermediate. There should be some concern for the observed slight preference for *inversion* of configuration of the migrant carbon, but this might be plausibly interpreted as a small, stereospecific, orbital symmetry allowed component (supra-inv) superimposed upon a biradical mechanism with a stereorandomized intermediate. As we shall see, this interpretation is unsatisfactory.

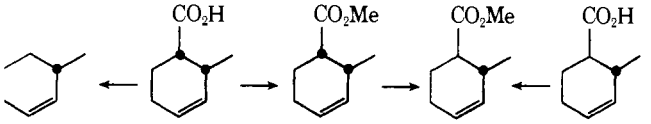
**Mechanistic Analysis of the Four Pathways in the 1,3-Sigmatropic Rearrangements of *trans*-1,2-*trans,trans*- and *trans*-1,2-*cis,trans*-Dipropenylcyclobutane (tTT-9 and tCT-9).** The synthesis of the optically active *trans*-1,2-dipropenylcyclobutanes required for this quadrisection is achieved by application to dimethyl *trans*-1,2-cyclobutanedicarboxylate (**34**) of a reduction alkenylation sequence similar to that used in the racemic series. The Experimental Section describes how the absolute configurations and maximum rotations of Table II are established. The following discussion of stereochemical

details may be omitted by the general reader, who is directed to the section headed "1,3-sigmatropic rearrangements in the racemic series".

There is a change in the sign of rotation of the 1*R*,2*R* configuration in this series. Although both divinylcyclobutane **3a** and *trans*-1,2-*trans*,*trans*-dipropenylcyclobutane (tTT-**9**) are dextrorotatory to about the same extent, tCT-**9** and tCC-**9** are levorotatory, with the magnitude of levorotation increasing with *cis*-propenyl substitution. It is tempting to speculate that these effects may be associated with different distributions of rotational and/or ring-puckered conformations dictated by steric interactions in the *cis*-propenyl compounds. Whether the C(1)-C(2) cyclobutane ring bond permits electronic interaction between the alkenyl groups, perhaps from some conformations more favorably than from others, remains as a theoretical problem.

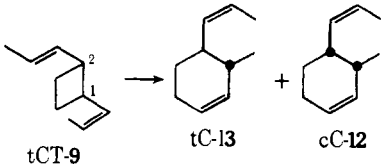
The absolute configurations and maximum rotations of the 1,3-sigmatropic rearrangement products cT-**12**, cC-**12**, tT-**13**, and tC-**13** are established by synthesis from *cis*- and *trans*-3-methylcyclohexene-4-carboxylic acids (**41** and **42**). Dr. L. M. Jordan finds[51] that the cis acid **41**, $[\alpha]D$ −231.5°, can be decarboxylated to (*S*)-(−)-3-methylcyclohexene (**35b**), $[\alpha]D$ −59.6°, 66.7% enantiomerically pure by reference to the maximum rotation of 89.4° established above. The configuration of the levorotatory cis acid, therefore, is 3*R*,4*S*, and its maximum rotation is −347°. The corresponding 3*R*,4*S* methyl ester **43** has $[\alpha]^{max}D$ −297°. This value is confirmed by an independent determination, $[\alpha]^{max}D$ −297 ± 11°, obtained using the chiral NMR shift reagent of Goering.[46]

Correlation of the cis ester (3*R*,4*S*)-(−)-**43** with the trans ester (3*R*,4*R*)-(−)-**44** is achieved by direct epimerization in methanolic sodium methoxide. The value of $[\alpha]^{max}D$ so obtained for **44** is −80.3°.



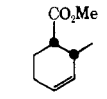
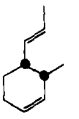
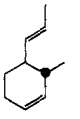

The Experimental Section describes the syntheses of cT-**12**, cC-**12**, tT-**13**, and tC-**13** from **43** and **44**. Table III collects the absolute configurations and values of $[\alpha]^{max}$.

**The 1,3-sigmatropic rearrangements in the racemic series** of Schemes I, II, and III show some noteworthy patterns. In the rearrangement of tCT-**9**, which has one *cis*- and one *trans*-propenyl side chain, only the *trans*-propenyl unit acts as a migration framework. The migrant carbon (C(1) of tCT-**9**) carries the *cis*-propenyl group in both sigmatropic products, tC-**13** and cC-**13**. A plausible attribution of this




specificity is to the requirement that the rearrangement avoid the generation of a trans double bond in the cyclohexene ring of the product. To meet this requirement, the migration framework propenyl group must adopt a conformation syn to the cyclobutane ring, which is very unfavorable for *cis*-propenyl. It follows that, when both propenyl groups of the reactant are cis, as in tCC-**9**, the absolute rate of 1,3-sigmatropic rearrangement should decrease. This effect is observed experimentally, the rates for tCC-**9** being depressed by factors of 10-30 relative to those for tCT-**9** (Schemes II and III).

Table III. Absolute Configurations and Maximum Rotations ($CCl_4$) of Cyclohexenes

| Compd | Maximum rotation, deg $[\alpha]D$ | Maximum rotation, deg $[\alpha]_{365}$ |
|---|---|---|
|  (3*R*,4*S*)-(−)-43 | −297 | |
|  (3*R*,4*R*)-(−)-cT-12 | −210 | −713 |
|  (3*R*,4*R*)-(−)-cC-12 | −138 | −451 |
|  (3*R*,4*R*)-(−)-tT-44 | −80.3 | |
|  (3*R*,4*S*)-(−)-tT-13 | −63.0 | −256 |
|  (3*R*,4*S*)-(−)-tC-13 | −112 | −444 |

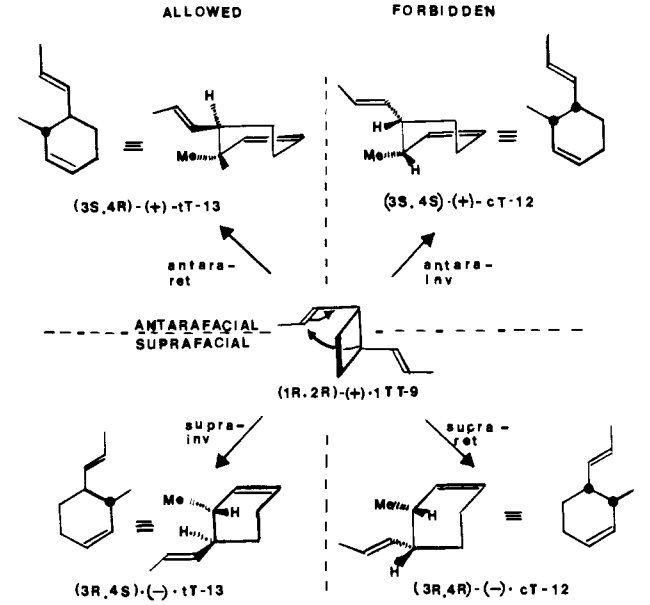
In the rearrangement of tTT-**9**, all of the 1,3-sigmatropic products tT-**13** and cT-**12** arise directly from tTT-**9** (Scheme I). Although some of the tTT-**9** epimerizes to cTT-**8**, the Cope rearrangement drains off the latter material to 3,4-dimethylcycloocta-1,5-diene (**10**) very rapidly, so that cTT-**8** is not a source of the cyclohexene products tT-**13** and cT-**12**.

However, the presence of one *cis*-propenyl group in the cyclobutane, as in the tCT-**9**-cCT-**8** system (Scheme II), retards the Cope rearrangement of the cis isomer cCT-**8** by a factor of 100 relative to that of cTT-**8**. Therefore, the 1,3-sigmatropic rearrangement of the cis isomer competes more successfully and some fraction of the cyclohexene products arise from cCT-**8** in the pyrolysis of tCT-**9**. This complication must be taken into account in the kinetic analysis (see below).

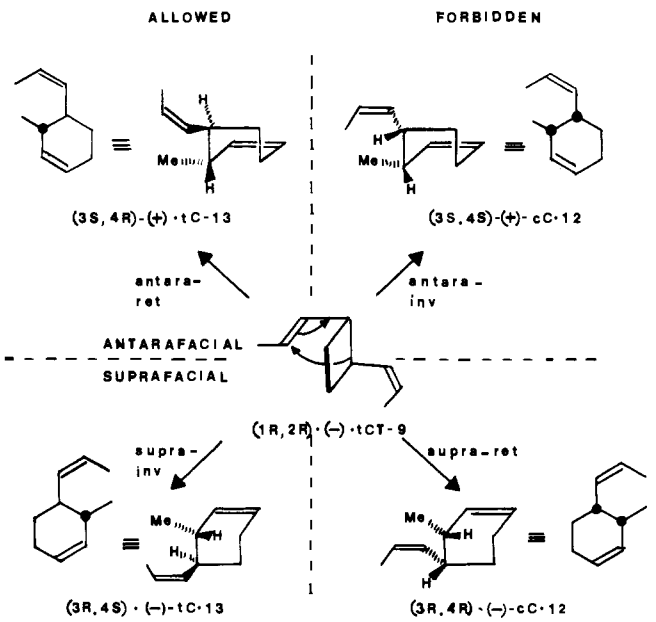
The system with two *cis*-propenyl groups, tCC-**9**-cCC-**8**, gives so little 1,3-sigmatropic rearrangement that it is not practical for studies in the optically active series.

Schemes IX and X show the four-pathway analysis of the 1,3-sigmatropic rearrangements of optically active tTT-**9** and tCT-**9**, respectively. The orbital symmetry[53] allowed and forbidden rearrangements of a *trans*-2-substituted-1-*trans*-propenylcyclobutane (e.g., tTT-**9**, Scheme IX) would give, respectively, a trans- and a cis-3,4-disubstituted cyclohexene (e.g., tT-**13** and cT-**12**). Thus, an evaluation of the relative importance of the two processes would be available merely from a determination of the trans/cis product ratio. Experiments with substrates leading to the two-path dissection of the rearrangement of 2-substituted-1-alkenylcyclopropanes have been reported.[52] However, a more complete mechanistic analysis can be achieved with optically active allylically labeled reactants, which permit further subdivision of the allowed and

Scheme IX




Scheme X




forbidden pathways according to whether the migrant carbon retains (ret) or inverts (inv) its configuration and whether the allylic receptor framework participates in an antarafacial (antara) or suprafacial (supra) way.

The allowed pathways, antara-ret and supra-inv, lead from one enantiomer of *trans*-1,2-*trans,trans*-dipropenylcyclobutane (tTT-**9**) to optical antipodes of *trans*-3-methyl-4-*trans*-propenylcyclohexene (tT-**13**), whereas the forbidden ones, antara-inv and supra-ret, lead to antipodes of the cis compound cT-**12** (Scheme IX). Thus, the relative rates of each of the four processes can be evaluated from the cT-**12**/tT-**13** ratio of the products combined with their chirality relationships to the reactant tTT-**9** given by the observed rotations, absolute configurations, and maximum rotations. A similar analysis for the tCT-**9** system is outlined in Scheme X.

**Experimental Study of Scheme IX.** Pyrolysis of (1*R*,2*R*)-(+)-tTT-**9**, $[\alpha]_D$ 48.1°, 40.3% enantiomerically pure, under the same conditions used in the study of divinylcyclobutane gives, after about 2 half-lives for disappearance of tTT-**9**, (3*R*,4*S*)-(−)-tT-**13** and (3*R*,4*R*)-(−)cT-**12**, 27.2 and 30.2% enantiomerically pure, respectively. The starting material racemizes partially during a run, and the racemization rate constant $k_\alpha$ is used together with $k_p$, the rate constant for total disappearance of tTT-**9**, to calculate by eq 1[49,50] the effective enantiomeric purity, $\bar{P}$ = 0.856, for the reactant. The maximum enantiomeric purity that could survive in the products, therefore, is 0.856 × 40.3 = 34.5%, so that relative to the tTT-**9** that has not suffered prior racemization, tT-**13** and cT-**12** are formed with 78.8 and 87.5% preservation of optical activity, respectively.

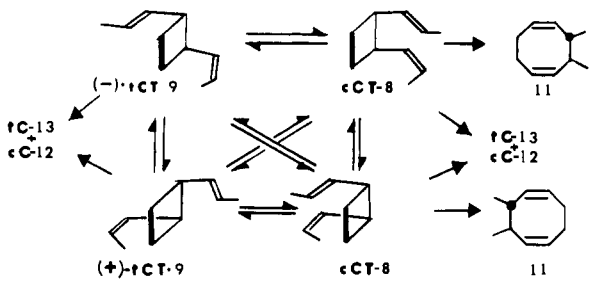
To complete the quadrisection of the 1,3-sigmatropic rearrangement of tTT-**9**, we note that product tT-**13**, which results from the sum of the antara-ret + supra-inv pathways, amounts to 56.2%, whereas product cT-**12**, from antara-inv + supra-ret, amounts to the remaining 43.8%. Because of the simple kinetics in this system, the ratio of products is the same as the ratio of rate constants.

The optical rotations show that the predominant enantiomer of tT-**13** formed is (3*R*,4*S*)-(−), which means (Scheme IX) that the 79% survival of optical activity in its formation, 89.5% (−) and 10.5% (+), corresponds to 0.562 × 89.5 = 50.4% of the 1,3-sigmatropic rearrangement by path supra-inv and 0.562 × 10.5 = 5.9% by path antara-ret. Similarly, the data for cT-**12** can be analyzed as 0.438 × 93.9 = 41.1% supra-ret and 0.438 × 6.1 = 2.6% antara-inv.

**Experimental Study of Scheme X.** Because the *cis*-propenyl group retards the Cope rearrangement of cCT-**8** the pyrolysis of tCT-**9** is kinetically more complex than the tTT-**8** system we have just analyzed. As Scheme II shows, some of the 1,3-sigmatropic rearrangement products cC-**12** and tC-**13** must be formed not only directly from the starting material tCT-**9**, but also indirectly by epimerization to cCT-**8** and rearrangement of the latter. For comparison with the *trans*-divinylcyclobutane and tTT-**9** systems, it is only the direct rearrangement of tCT-**9** that concerns us here. To achieve the quadrisection in Scheme X, we therefore must assign to each mechanism, direct and indirect, not only its fraction of the products tC-**13** and cC-**12**, but also an appropriate stereochemistry.

Moreover, the reversible interconversion of tCT-**9** and cCT-**8** (Scheme II) adds a further complication, since it provides a potential second pathway for racemization of tCT-**9** (Scheme XI). Without an evaluation of the rate constants of

Scheme XI




Scheme XI, explicit determinations of the effective optical purities of tCT-**9** and cCT-**8** are not possible. Such an evaluation would be difficult, because the overall rearrangement of cCT-**8** is much faster than that of tCT-**9** (Scheme II), and therefore the concentration of cCT-**8** always remains so low that its isolation for the necessary measurement of the time dependence of its optical rotation would be infeasible.

Of the three kinetic problems generated by these complications, the first is quite straightforward. The dissection of the 1,3-sigmatropic rearrangements into direct and indirect

pathways merely requires that Scheme II be rewritten so that products tC-**13** and cC-**12** each are divided into two portions, one from each pathway. The Runge-Kutta numerical integration then uses the initial conditions and the refined rate constants of Scheme II to generate a series of concentrations of the direct and indirect products as functions of time. In this way, it can be shown that the total tC-**13** product at 63 800 s, for example, is derived 86 and 14% by the direct and indirect mechanisms, respectively. For the cC-**12** product, these values are 97% direct and 3% indirect.

So far, we cannot provide exact solutions to the other two problems, which pertain to the stereochemistry of the rearrangement in the tCT-**9** case. However, we offer reasonable approximations. If it is assumed that the epimerizations of optically active starting material (−)-tCT-**9** (Scheme XI) to both enantiomers of cCT-**8** occur at equal rates, all of the cCT-**8** and the products formed from it by the indirect mechanism will be racemic. This assumption seems plausible, since presumably the epimerization involves merely rotation of a ring carbon and its attached propenyl group, and it seems likely that any mass or steric effect (especially in anti propenyl-ring conformations) would be approximately the same for a *cis*- as for a *trans*-propenyl group. Some experimental support for this assumption comes from an examination of the *trans*-3,4-dimethylcycloocta-1,5-diene (**11**), which we already have shown to be entirely a product of the indirect mechanism tCT-**9** → cCT-**8** → **11**. Although the 1,3-sigmatropic products tc-**13** and cC-**12** formed by pyrolysis of 40.3% enantiomerically pure tCT-**9** both are active (see below), the **11** formed in this reaction is inactive. We do not know the rotation of enantiomerically pure **11**, so that we cannot estimate quantitatively the completeness of the racemization of **11**, but the observation is nevertheless consistent with an indirect mechanism passing over racemic cCT-**8** as an intermediate. If we therefore assume that the indirect fractions of tC-**13** and cC-**12** also are racemic, it is possible to assign the stereochemistry of the direct rearrangement.

Pyrolysis for 17.7 h of (1*R*,2*R*)-(−)-tCT-**9**, 40.3% enantiomerically pure, gives (3*R*,4*S*)-(−)-tC-**13**, 23.4% enantiomerically pure, and (3*R*,4*R*)-(−)-cC-**12**, 28.5% enantiomerically pure. The enantiomeric purities of those portions, 86 and 97%, respectively, of these products formed by the direct pathway, therefore, are 23.4/0.86 and 28.5/0.97, or 27.2 and 29.4%, respectively.

The optical purity of the reactant tCT-**9** at intermediate points during the run is monitored by isolation and polarimetry. The effective optical purity ($\bar{P}$) is calculated for each time increment by multiplication of the fraction of the direct product formed during that period times the mean optical purity of tCT-**9** during the same period, and the overall $\bar{P}$ is the sum of these products. The results do not differ significantly from those obtained if we calculate $\bar{P}$ as simply the mean of the initial and final values of $P$.

The value of $\bar{P}$ is 0.758, so that the maximum enantiomeric purity that could prevail in this experiment is 0.758 × 40.3% = 30.6%. We deduce, therefore, that the preservation of enantiomeric purity in the tC-**13** and cC-**12** formed by the direct path from prior unracemized tCT-**9** is (27.3/30.6)100 and (29.4/30.6)100, or 89.2 and 96.1%, respectively.

To complete the quadrisection in Scheme X, we divide the total 1,3-sigmatropic rearrangement into two portions in accord with the rate constants of Scheme II, which shows that product tC-**13**, formed by pathways supra-inv + antara-ret, accounts for 52.3% and product cC-**12**, formed by pathways supra-ret + antara-inv, accounts for the remaining 47.7%.

The optical rotations show that the predominant enantiomers of tC-**13** and cC-**12** are (3*R*,4*S*)-(−) and (3*R*,4*R*)-(−), respectively. This means (Scheme X) that the 89.2 and 96.1% survival of enantiomeric purity in these products results from the percentage contributions of the four pathways shown in Table IV, which also summarizes the quadrisection of the tTT-**9** rearrangement. The values there are probably uncertain to about ±2 units, with most of the experimental error being attributed to the estimated uncertainty of about 4% in the values of the maximum rotations.

**Discussion of the 1,3-Sigmatropic Rearrangements of *trans*-1,2-Divinylcyclobutane and the *trans*-1,2-Dipropenylcyclobutanes.** We now can interpret more sharply the stereochemistry of the rearrangement of optically active *trans*-1,2-divinylcyclobutane (**3a**), where the mechanistic quadrisection cannot be achieved for lack of a supra-antara stereochemical label. The gross inversion/retention ratio, 54:46, might suggest a small inversion component superimposed upon a stereorandom, chirality-destroying process passing through planar or rapidly rotating biradical intermediates. However, this interpretation would require that a substantial portion of the product be formed by antarafacial participation of the allylic framework.

In the rearrangements of tTT-**9** and tCT-**9**, the gross inversion/retention ratios consist of (supra-inv + antara-inv)/(supra-ret + antara-ret). The ratios are 53:47 and 50:50, remarkably similar to the 54:46 value for **3a**, but Table IV makes it clear that the rearrangements of tTT-**9** and tCT-**9** contain very little (9 and 4%, respectively) antarafacial component. A stereorandom intermediate from tTT-**9** would be required to cyclize to the enantiomeric rearrangement products (+)- and (−)-tT-**13** at exactly equal rates (Scheme IX). Similar equalities are required for (+)- and (−)-cT-**12** (Scheme IX) and products tC-**13** and cC-**12** from tCT-**9** (Scheme X). Thus, twice the antarafacial component of the product represents the upper limit of any contribution from a mechanism involving a stereorandom intermediate (18% from tTT-**9**, 8% from tCT-**9**). Unless there is an unexpected sharp discontinuity in mechanisms between these reactions and that of **3a**, it seems likely that rearrangements of the latter also are almost exclusively suprafacial.

With a major contribution from a stereorandomized biradical intermediate having been excluded, confidently for **3a** and rigorously for tTT-**9** and tCT-**9**, the explanation of the near balance in the inversion/retention ratio emerges as a near equivalence in rate of two highly stereospecific reactions, supra-inv and supra-ret. It is instructive to formulate a nonrandomized biradical mechanism for these results.

Imagine three extreme conformations of tTT-**9**: syn,syn; syn,anti; and anti,anti. When the cyclobutane ring breaks at the bond between the propenyl groups, these conformations become "frozen" as stable[17,24] configurations of the allylic radical groups: TT*cis,cis*; TT*cis,trans*; and TT*-trans,trans*. In the biradicals, the symbols TT refer to the configurations of the terminal methyl groups relative to the

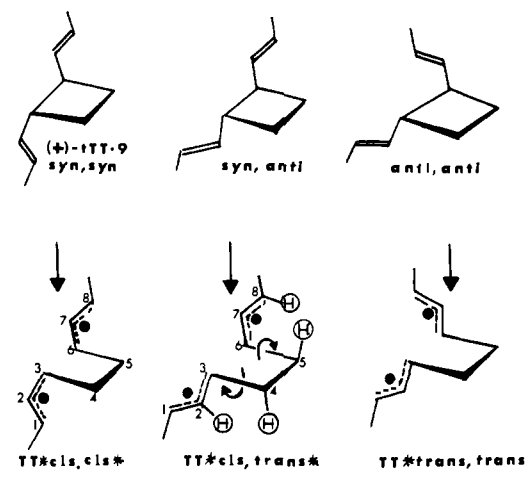


Table IV. Analysis of Pathways in 1,3-Sigmatropic Rearrangements of *trans*-1,2-Dipropenylcyclobutanes

| | Relative rate of product formation | | | |
|---|---|---|---|---|
| | Allowed | | Forbidden | |
| Reactant | Supra-inv | Antara-ret | Supra-ret | Antara-inv |
| tTT-9 (Scheme IX) | 50.2 | 6.0 | 41.1 | 2.7 |
| tCT-9 (Scheme X) | 49.5 | 2.8 | 46.8 | 0.9 |

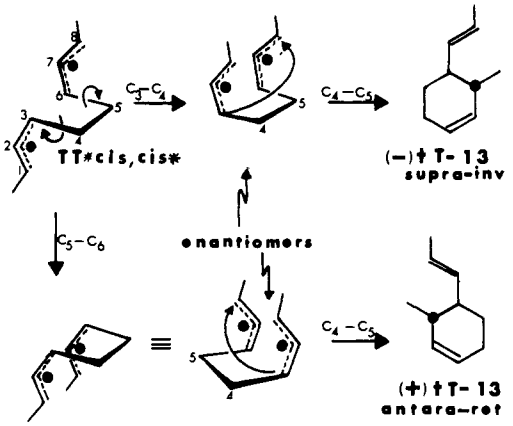
chain beginning with C(2) or C(7), whereas the terms cis and trans refer to the allylic systems.

The formation of a trans double bond in the cyclohexene ring of the 1,3-sigmatropic rearrangement product would be prohibitively unfavorable under these conditions. Therefore, only those biradicals with one or two cis-allylic configurations, TT*cis,trans* and TT*cis,cis*, could cyclize to cyclohexene products.

We consider first the rotations needed for cyclization of TT*cis,cis*. Note that because the configuration of the propenyl group at the migrant carbon, C(3), is immaterial, this part of the analysis applies also to TT*cis,trans*. All four 1,3-sigmatropic products (Scheme IX) require rotation about C(4)-C(5), a shearing motion of the two allylic groups past each other (Scheme XII) to permit juncture of the migrant carbon C(3) and the terminus C(8). Formation of the supra-ret product (−)-cT-**12** (not shown in Scheme XII) requires no additional rotations. Pathways supra-inv to (−)-tT-**13** and antara-ret to (+)-tT-**13** each require one (or an odd number of) additional rotation(s) about one bond and zero (or an even number of) additional rotations about another. For supra-inv, the odd-numbered rotations are about C(3)-C(4) and the even about C(5)-C(6), whereas for antara-ret the number of C(3)-C(4) rotations are even and of C(5)-C(6) odd (Scheme XII). Pathway antara-inv requires an odd number of rotations about each of C(3)-C(4) and C(5)-C(6). The rotations required for each pathway are summarized in Table V.

By symmetry, the C(3)-C(4) and C(5)-C(6) rotations in TT*cis,cis* (but not in TT*cis,trans*) must occur at equal rates, and the enantiomeric biradicals produced by these rotations must cyclize at equal rates (Scheme XII). Therefore,

Scheme XII




the supra-inv and antara-ret pathways must be of equal importance in that portion of the total 1,3-sigmatropic rearrangement which passes through TT*cis,cis*. As Table IV shows, the antara-ret pathway accounts for only 6% of the 1,3-sigmatropic products, which means that no more than 12% of the reaction can involve TT*cis,cis*. The only other permissible biradical, TT*cis,trans*, therefore, must account for the remaining 88%. This rate difference corresponds to a $\Delta\Delta H_f°$ of at least 1.67 kcal/mol between the transition states

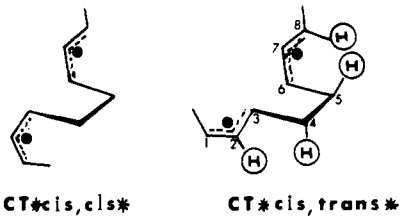
Table V. Rotations Required in Biradicals TT*cis,cis* and TT*cis,trans* for the Four 1,3-Sigmatropic Pathways

| | Rotation | | |
|---|---|---|---|
| Pathway | C(4)–C(5) | C(3)–C(4) | C(5)–C(6) |
| Supra-ret | Odd | Even | Even |
| Supra-inv | Odd | Odd | Even[a] |
| Antara-ret | Odd | Even[a] | Odd |
| Antara-inv | Odd | Odd | Odd |

[a] In TT*cis,cis*, the rates of these rotations are equal by symmetry. The rotations shown in Scheme XII are only *formally* sequential. In fact, some C(4)–C(5) shearing motion must occur simultaneously with C(3)–C(4) or C(5)–C(6) rotation to avoid generation of an achiral intermediate.

connecting tTT-**9** with TT*cis,cis* and TT*cis,trans*. This could reasonably be ascribed to the sum of two of the same unfavorable *cis*-butene-type interactions of about 1 kcal/mol each, which are assumed[8,9] to be the cause of the slight preference for *cis,trans* over *cis,cis* in the parent unsubstituted butadiene dimer system.

When one of the propenyl groups has a cis configuration, as in tCT-**9**, the methyl-ring repulsion energy of 4.4 kcal/mol previously found in the boat-like Cope rearrangements of the *cis*-1,2-dipropenylcyclobutanes should also apply, at least approximately, to the 1,3-sigmatropic transition state. This would preclude any significant reaction through a doubly cis-allylic biradical, CT*cis,cis*, so that the biradical mechanism for the 1,3-sigmatropic rearrangement of tCT-**9** would involve only biradical CT*cis,trans*. The close similarity in



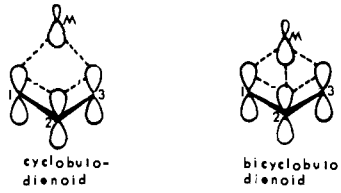

the populations of the four pathways in the 1,3-sigmatropic rearrangements of tTT-**9** and tCT-**9** (Table IV), therefore, confirms the previous conclusion that the overall results for tTT-**9** are but little influenced by any contribution from the TT*cis,cis* route.

One of the major features of the 1,3-sigmatropic rearrangements is the large preference for suprafacial rather than antarafacial reaction. How can this be explained in terms of the biradical TT*cis,trans*? To cyclize, this species must undergo rotations analogous to those described for TT*cis,cis* (Table V). In particular, the supra-inv and antara-ret pathways each require one rotation in addition to that at C(4)-C(5). However, in contrast to TT*cis,cis*, TT*cis,trans* no longer has a symmetry requirement for equivalence of the C(3)-C(4) and C(5)-C(6) rates of rotation. We might, therefore, ascribe the preference for suprafacial over antarafacial rearrangement to an abnormally slow rate of rotation at C(5)-C(6), the rotational site for both antara pathways. Supra-inv is 8.5 and 17.7 times as fast as antara-ret from tTT-**9** and tCT-**9**, respectively, and the question arises whether these are reasonable ratios of rotation rates C(3)-C(4) vs. C(5)-C(6). Although there is no good way to estimate these relative rates quantitatively, one can see from models that steric interference of the circled hydrogens at C(5)-C(8) during rotation at C(5)-C(6) in TT*cis,trans* or CT*cis,trans* is worse than that at C(2)-C(4) during rotation at C(3)-C(4), so that, qualitatively, the preference for C(3)-C(4) rotation seems reasonable.

On this basis, the migration framework of TT*cis,trans* or CT*cis,trans*, C(5)-C(6)-C(7)-C(8), would be imagined to remain rather rigidly fixed because of the restricted rotation,

whereas the chain C(4)-C(3)-C(2)-C(1) which includes the migrant carbon C(3) is free to rotate about C(3)-C(4). It is then not obvious why pathway supra-ret, which requires only C(4)-C(5) rotation, should not be strongly favored over supra-inv, which requires that same rotation *in addition to* rotation at C(3)-C(4) (Table V). The observed preference (Table IV) for supra-inv seems to call for either ascription of special ad hoc properties to the alleged badicals, or more simply, for the postulate that at least some of the 1,3-sigmatropic rearrangement gives the "allowed" supra-inv product by a concerted reaction under orbital symmetry control.[53]

There remains the question of the mechanism of the other major component of the 1,3-sigmatropic rearrangement, supra-ret, which is formally an orbital symmetry "forbidden" reaction. It would be reasonable to interpret this as a "least-motion" ring closure of the biradical intermediate, particularly if the result were considered in isolation from the results of other 1,3-sigmatropic rearrangements. However, arguments given elsewhere[28a,b] suggest that "forbidden" 1,3-sigmatropic rearrangements may occur concertedly in certain systems, especially when steric factors permit bicyclobutadienoid bonding to mitigate the cyclobutadienoid nature of the transition state. In our view,[2d,28b,54] the concerted formulation of




the present supra-ret reactions offers definite explicative and predictive advantages. In particular, it rationalizes the variations in the observed relative importance of the supra-ret and supra-inv pathways for a range of systems.[2d,28b,54] Our attraction to a concerted mechanism for the supra-ret reaction in these cases, therefore, is not based merely upon the observation of high stereospecificity in the dipropenylcyclobutane rearrangements.

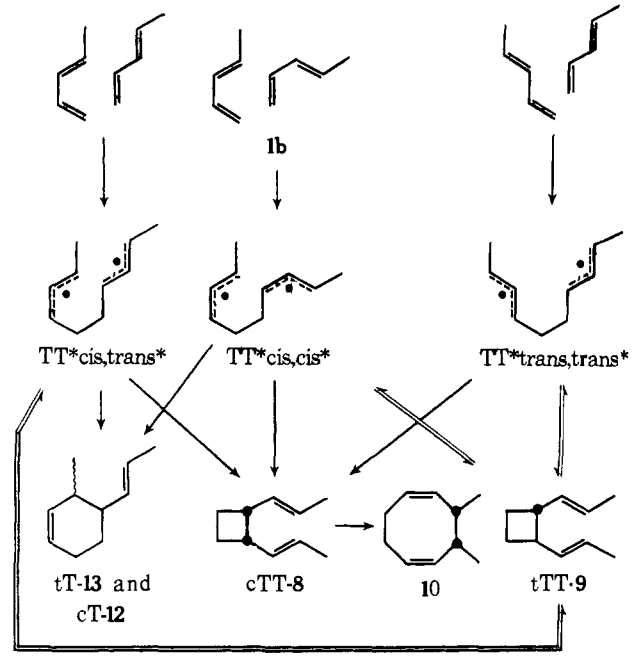
It has been recognized[14,15,37] for some time that the activation energies for many 1,3-sigmatropic rearrangements may be high enough to permit complete cleavage of the allylic framework-migrant carbon bond. The reliability of the bond-energy estimates depend upon the validity of additivity tables,[6] and few if any such estimates can be considered accurate to more than a few kilocalories per mole, even for the hypothetical biradical intermediates themselves. For the transition states leading to or from such biradicals, the estimates necessarily are even less reliable, because the transition-state energies contain bonding and strain energy terms that are not present in the biradicals and are difficult to evaluate for lack of appropriate models. In limiting the term "concerted reaction" to those in which the transition-state energy differs by some arbitrary amount from that estimated for the biradical reaction, one excludes most 1,3-sigmatropic rearrangements. Similarly, by insisting that only orbital symmetry "allowed" reactions are concerted and omitting to provide predictions on the stereochemical behavior to be expected of biradicals, one simply defines the problem of "forbidden" stereochemistry out of existence.

Our approach is not to substitute stereochemistry for energy as a criterion of concert. Rather, we emphasize that bonding of the reactive sites in the transition state, if worth only a few kilocalories per mole, might well escape detection in an energy comparison, but still would be strong enough to have profound stereochemical consequences. The stereochemical results in the series of 1,3-sigmatropic rearrangements described[2d,28b,54] are readily interpreted as signifying stronger bonding in the "forbidden" transition state with stronger overlap of the relevant orbitals. That this bonding is stereochemically palpable but energetically too small to detect by the necessarily insensitive Arrhenius kinetic method seems to us not to disqualify it as a manifestation of concert. In fact, we would define a "concerted reaction" as one in which the reactive sites remain bonded throughout.[28b,37] If it be insisted that the term is already preempted for another purpose, we would relinquish the nomenclature, but retain the concept.

**The Stereochemistry of the Diels–Alder Dimerization of Piperylene.** If there is a biradical intermediate in the rearrangements of the dialkenylcyclobutanes, is the same species involved in the Diels–Alder dimerization of the corresponding acyclic diene? Scheme XIII shows the hypothetical biradical mechanism for the dimerization of *trans*-piperylene (**1b**) and the 1,3-sigmatropic rearrangement of *trans*-1,2-*trans,trans*-dipropenylcyclobutane (tTT-**9**). For steric reasons, the biradical TT*trans,trans* cannot be an intermediate in the formation of the cyclohexene products tT-**13** and cT-**12**, so that only the biradicals TT*cis,cis* and TT*cis,trans* with a cis-allylic structure are shown in that role.

It should be clear from Scheme XIII that mere observation

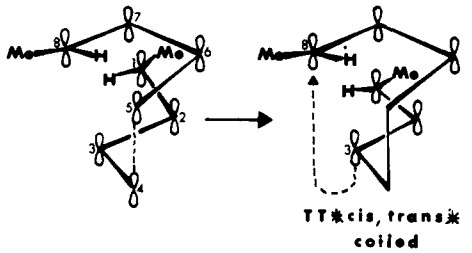
Scheme XIII




that the stoichiometric ratio of cyclohexenes tT-**13** and cT-**12** vs. cyclooctadiene **10** differs in the products from **1b** as compared to those from tTT-**9** does not suffice to exclude a common intermediate for the two pathways. In fact, according to Scheme XIII, different ratios are to be expected, since in general the relative rates of formation of the three configurationally isomeric biradicals generated by the dimerization of piperylene **1b** will not be the same as those generated by pyrolysis of tTT-**9**.

The key to the question is in the behavior of the individual biradicals. As we have previously noted, the observed nonequivalence of the rates of the antara-ret and supra-inv pathways requires that most of the 1,3-sigmatropic rearrangement of tTT-**9** in a hypothetical biradical mechanism pass through TT*cis,trans* and not through TT*cis,cis*. The cyclization of TT*cis,trans* to the cyclohexenes consists of juncture of the *back face* of C(3) to the front face of C(8) to give supra-inv product, and at a slightly slower competitive rate, juncture of the front face of C(3) to the front face of C(8) to give supra-ret product (Tables IV and V).

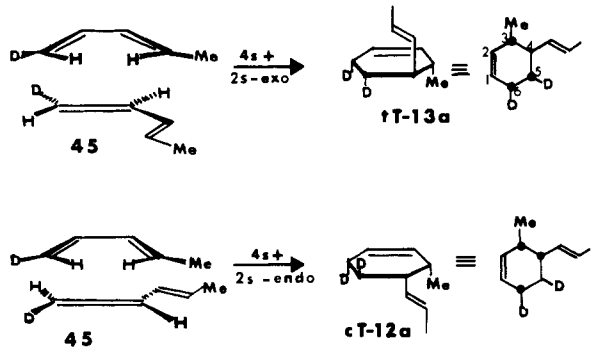
If the same intermediate is involved in the Diels-Alder dimerization, it must behave identically. We are thus led to the peculiar prediction that the dimerization of piperylene must take place cis on the diene (front faces of C(8) and C(5)) and with a slight preference for trans on the dienophile (back face of C(3)). The possibility that the dimerization might pass through a conformational isomer of the coiled TT*cis,trans* shown here does not qualitatively change the argument. One might postulate an extended conformation as the first intermediate in the dimerization from which the coiled biradical would be derived by rotation about C(4)-C(5). Formation of the extended biradical might permit more time for rotation about C(3)-C(4) and hence might lead to more stereorandomization at the dienophilic site, but it is difficult to imagine why this species or any other conformational isomer of TT*cis,trans* should produce the normal cis-on-the-dienophile Diels-Alder stereochemistry with *higher* cis stereospecificity than the coiled one.




The problem of the common intermediate thus reduces to a determination of the stereochemistry at the diene (C(5)-C(8)) and dienophilic (C(3)-C(4)) sites in the dimerization of piperylene. Its solution requires a deuterium as a stereochemical label at the terminal methylene group of the reactant.

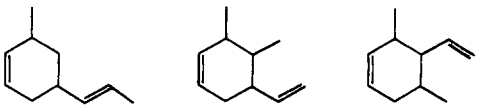
Scheme XIV shows that an exo or an endo relationship between the propenyl substituent on the dienophile and the diene system leads to tT-**13** or cT-**12**, respectively. These products are simple, separable diastereomers, a property that permits the complete analysis of the stereochemistry of the cycloaddition.

Scheme XIV




The stereochemistry of the deuteriums expected in each isomer if the dimerization of *trans,trans*-penta-1,3-diene-*1-d* (**45**) were exclusively suprafacial on the diene (4s) and, respectively, suprafacial-exo (2s-exo) and suprafacial-endo (2s-endo) on the dienophile is shown in Scheme XIV. The [4s + 2s] exo product would be tT-**13a**, with the cis-*5,6-d*$_2$ configuration, both deuteriums being trans to the propenyl group. Loss of stereospecificity by some formally antarafacial process on the dienophile would give C(5) deuterium cis to the propenyl group; antarafacial reaction on the diene would give C(6) deuterium cis to the propenyl group (trans to the methyl group). Similarly, any deviation from suprafaciality on the diene or dienophile would produce partial loss of the deuterium configuration shown in cT-**12a** for the [4s + 2s] endo product.

Heating sealed samples of *trans*-piperylene, either neat or in heptane solution, gives in addition to some polymer a 50-60% yield of dimers, 77% of which consist of the two "ortho" dimers tT-**13** and cT-**12** in a 48:52 ratio. The remainder of the dimer fraction consists of 13% of dimers, probably **46–48** of



**46** **47** **48**

other orientations and unknown stereochemistry, and 10% 3,4-dimethylcycloocta-1,5-dienes. This distribution agrees roughly with that reported in the literature.[12]

It is important to note that when (but only when) the *trans*-piperylene sample contains small amounts of *cis*-piperylene, the product contains approximately proportionate amounts of dimers tC-**13** and cC-**12** with the *cis*-propenyl side

tC-**13** cC-**12**

chain. The absence of these products in the dimerization of pure *trans*-piperylene is mechanistically significant.

Reduction of *trans*-pent-3-en-1-yne[60] with dicyclohexylborane, followed by deuteriolysis with $CH_3CO_2D$ give stereospecifically *trans,trans*-penta-1,3-diene-*1-d* (**45**) containing 90 ± 2% of one deuterium at the trans-1 position ($^1$H NMR analysis). Dimerization and VPC separation give the cyclohexene products tT-**13** and cT-**12**. There is no detectable isotopic fractionation during these operations, since analyses by direct $^2$H NMR ($CDCl_3$ internal standard)[62] and combustion (falling drop)[63] show no decrease in deuterium content: 90 ± 2 and 87.7 ± 1% of two deuteriums, respectively.

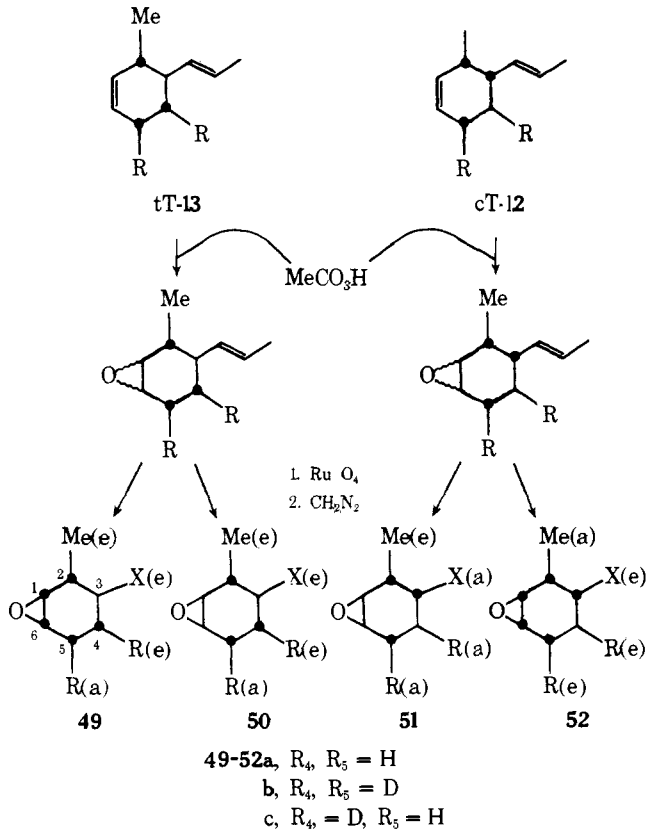
The configurations of the deuteriums in tT-**13** and cT-**12** are difficult to establish by NMR spectroscopy of the hydrocarbons themselves. Scheme XV shows the procedures for conversion of these compounds to four epoxy esters in pairs, **49b–50b** and **51b–52b**, from which **49b**, **50b**, and **52b** are isolated by VPC. The assignments of the proton NMR resonances in these compounds are greatly facilitated by the enhancement of chemical shift differences upon treatment with tris(heptafluorodimethyloctanedione)europium (Eu(fod)$_3$).[59]

Independent stereospecific syntheses (Scheme XVI) of the undeuterated analogues **49a–52a** as model compounds are achieved by epoxidation of the known[2d,51,23a] methyl *trans*- and *cis*-2-methylcyclohex-3-ene-1-carboxylates (**53** and **54**). Similarly, authentic samples of the 4-deuterio-5-protio analogues **55** and **56** result from epoxidation of the exo and endo Diels-Alder adducts of methyl acrylate-*cis-3-d*[60] and *trans*-piperylene.

The assignment of equatorial (e) or axial (a) conformations to the ring protons is achieved by correlation of large (10-11 Hz) and small (2-3 Hz) coupling constants with $H_a$-$H_a$ and $H_a$-$H_e$ (or $H_e$-$H_e$) groups, respectively.[61] Spin decoupling experiments on Eu(fod)$_3$-treated samples confirm the coupling deduced by inspection. It is then easy to recognize deuterium incorporation at specific sites in the deuterated series. The Experimental Section describes these studies.

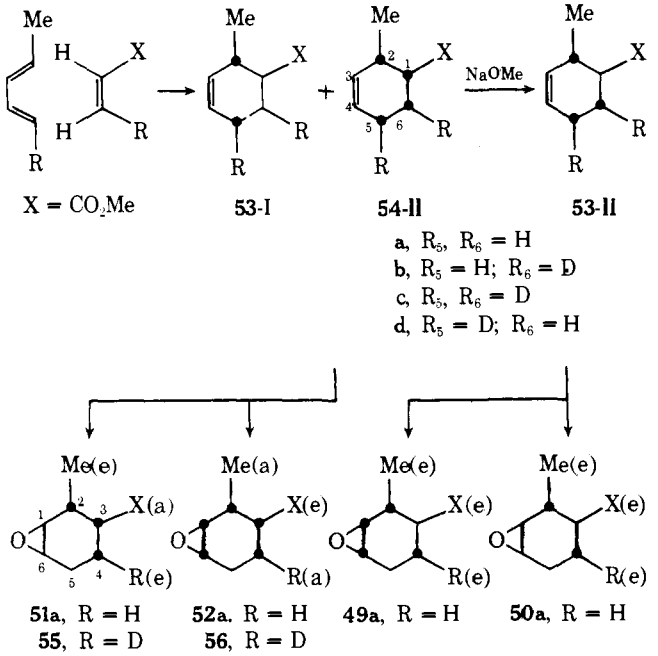
A typical set of data, obtained on the epoxy ester **50b** (Scheme XV) at a Eu(fod)$_3$/substrate concentration ratio of 0.40 in $CCl_4$ solution show (proton, chemical shift in δ units, integrated intensity): H(6), 8.95, 1.04; H(1), 8.47, 1.02; H(2a)

Scheme XV (X = $CO_2Me$)




49-52a, $R_4$, $R_5$ = H
b, $R_4$, $R_5$ = D
c, $R_4$, = D, $R_5$ = H

Scheme XVI



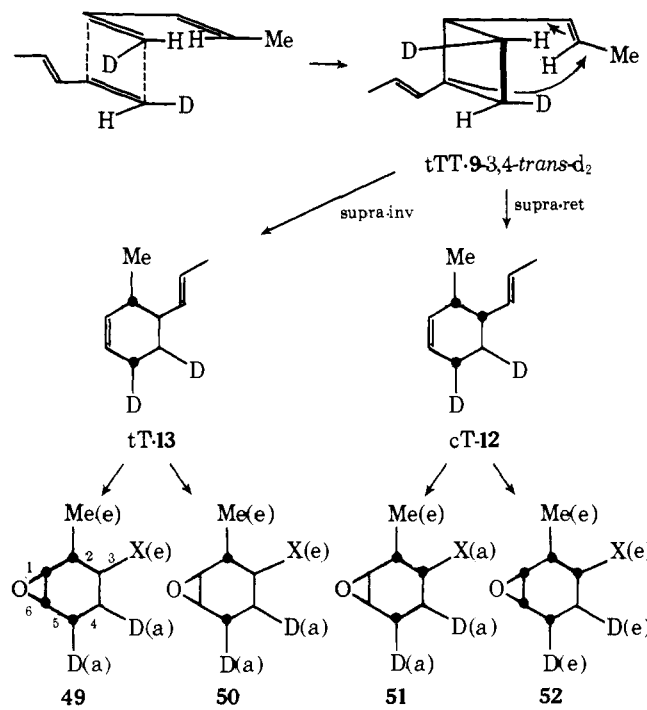

a, $R_5$, $R_6$ = H
b, $R_5$ = H; $R_6$ = D
c, $R_5$, $R_6$ = D
d, $R_5$ = D; $R_6$ = H

+ H(4a), 7.15, 1.98; H(5e), 5.60, 1.00; H(3a) + $CO_2Me$, 5.23, 3.93; H(4e), 4.40, 0.14; H(5a), 3.80, 0.11; Me, 2.66, (3.00). Relative to the signal of the aliphatic methyl group at C(2), defined as three units, all of the protons except H(4e) and H(5a) cause a signal intensity of one unit. The H(4e) and H(5a) intensities, corresponding to 14 and 11% of one proton, respectively, are equal to each other within experimental error and in good agreement with the values expected if these positions are 86 and 89% deuterated. These proton data and similar observations (see Experimental) on **49b** and **52b** establish that in all three compounds, the extents of D labeling in the C(4) position trans to $CO_2Me$ and the C(5) position cis to Me are identical with each other and essentially 100% of the maximum permitted by the total deuterium incorporation.

Both continuous wave[57] and Fourier transform[62] direct deuterium NMR spectroscopy of **49b** and **50b** in Eu(fod)$_3$-treated solutions show two approximately equal resonances at chemical shifts corresponding to positions 4e and 5a, and no detectable (<2%) absorption elsewhere. In particular, signals at chemical shifts corresponding to positions 4a and 5e, which would signify some stereochemical nonspecificity, are absent. These observations fully and independently confirm the proton spectroscopic results.

There is another possible source of nonspecificity that could complicate the interpretation. If any *trans*-1,2-*trans,trans*-dipropenylcyclobutane had been formed by a formal [2 + 2] dimerization of the labeled piperylene, it would rearrange rapidly at the reaction temperature (195 °C) to give tT-**13** and cT-**12**, the same products formed by the direct [4 + 2] dimerization. The labeling pattern to be expected in these products and the epoxy esters derived from them may be deduced from Scheme XVII.

Scheme XVII (X = $CO_2Me$)




Either a concerted (forbidden) [2 + 2] cycloaddition or a stepwise reaction by way of a bisallylic biradical in the dimerization of *trans*-piperylene-*trans*-1-*d* would produce a trans relationship between the two deuteriums in the cyclobutane product tTT-**9**. The suprafacial 1,3-sigmatropic rearrangement of tTT-**9**-3,4-*trans*-$d_2$ with retention of configuration at the migrant carbon would give product cT-**12** and the corresponding epoxy esters **51** and **52** with the same trans-4e,5e and trans-4a,5a deuterium configurations that would result from the direct Diels-Alder dimerization (Scheme XV). Therefore, any contribution to product cT-**12** by an indirect mechanism would not perturb the stereospecificity.

Rearrangement of tTT-**9**-3,4-*trans*-$d_2$ suprafacially with inversion of the migrant carbon would product tT-**13**, also with a trans relationship of the deuteriums, but now this product and its derived epoxy esters **49** and **50** would have a configuration different from the cis-4e,5a configuration that would

result from the direct Diels-Alder dimerization (Scheme XV). Since about 50% of the rearrangement of tTT-**9** is known to be supra-inv (Table IV), the practical consequences of such a contribution to the total product tT-**13** would be to introduce a fraction of protium at the 4e site and deuterium at the 4a site of **49** and **50** equal to about half the fraction of the cyclohexene product (tT-**13** plus cT-**12**) that is formed by the indirect mechanism. The direct deuterium NMR analysis is more sensitive than the proton method in this application. If we take 2% as the limit of detectability of 4a deuterium, the absence of the corresponding signals in the $^2H$ spectrum of **50b** (see Experimental) may be interpreted to mean that less than 4% of the cyclohexene product is formed by the indirect mechanism.

The determination of the deuterium stereochemistry in the epoxy esters **49b, 50b,** and **52b** (Scheme XV) shows that the dimerization of piperylene (Scheme XIV), in both the endo and the exo orientations and on both the diene and dienophile, is ≥ 98% stereospecifically suprafacial. The result may be compared to the observation by Stephenson et al.[63] that the closely related compound butadiene gives Diels-Alder dimer with unknown stereochemistry on the diene and highly (90%), but not completely specific, suprafacial stereochemistry on the dienophile.

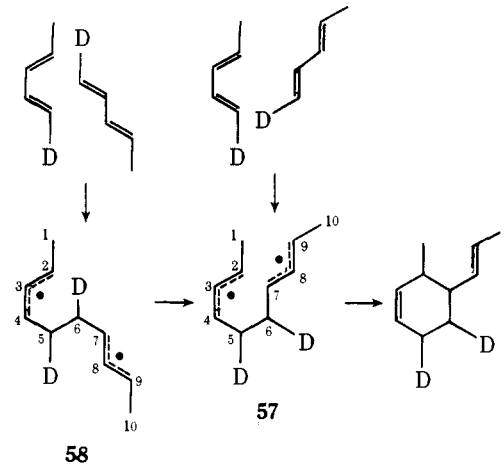
**Mechanism of the Diels-Alder Dimerization of Piperylene and Other Simple Acyclic Dienes.** A mechanistic energy surface based upon the thermochemical and kinetic data for the formation and rearrangement of the dimers of butadiene suggests that the bisallylic biradicals *cis,cis* or *cis,trans* are energetically accessible intermediates Although the necessary thermochemical data for the piperylene dimer system are not available, the kinetic and stereochemical behavior is so similar to that of the butadiene dimer system that it seems reasonable to discuss the two in the same framework.

Advocacy of the biradical mechanism[8] takes its justification largely from the internal consistency of the scheme, a key portion of which is the previously described assumption of the biradical as a common intermediate. A later analysis of the butadiene data, augmented by a new experiment which fixes the height of the transition state for the degenerate stereomutation (racemization) of vinylcyclohexene, leads to the conclusion regarding the dimerization, "It is clear that the magnitude of concert in this Diels-Alder reaction, if it be not zero, is at best small."[9]

Neither analysis predicts the stereochemistry that should prevail in the alkenylcyclohexene Diels-Alder product by the mechanism proposed. It is tautological but didactically useful to state our assumption that a Diels-Alder reaction with a "small" magnitude of concert should be stereospecific, if the most favored concerted transition state is energetically well below the next most favored one. If there are two competing concerted pathways, e.g., supra-diene-supra-dienophile vs. antara-diene-antara-dienophile, the overall reaction could be nonstereospecific.

Similarly, it is argued[64] that a biradical mechanism need not result in any particular stereochemistry, and that the familiar supra-diene-supra-dienophile stereochemistry could be a consequence of a biradical ring-closure rate that is rapid relative to the rates of internal rotation. A closer analysis of this argument helps to clarify the properties that must be ascribed to the hypothetical biradical intermediate.

The precursor of the Diels-Alder product in a biradical dimerization of *trans*-piperylene-*trans*-1-*d* would be a species with a coiled conformation **57** appropriate for bond formation between C(2) and C(7). Those biradicals born in this conformation could cyclize stereospecifically supra-dienophile and supra-diene if rotation about bonds C(5)-C(6) and C(6)-C(7) were slow. Those biradicals born in other conformations, for example, the extended conformation **58,** would be required to achieve the coiled conformation **57** by an internal rotation about the C(5)-C(6) bond before cyclization could occur. Again, one could achieve stereospecific reaction from **58,** but now only with the additional postulate that configuration-destroying rotation about C(6)-C(7) does not occur. Since the necessary C(5)-C(6) rotation and the prohibited C(6)-C(7) rotation are very similar structurally, no reasons for a large difference in rate are apparent. It must be concluded, therefore, that only those biradicals born directly in the coiled conformation **57** can cyclize.




But if the dimerization gives some coiled biradicals **57,** surely it also must give some extended biradicals **58.** If **58** does not cyclize, its only reaction must be reversion to the starting material.

The biradical mechanism then would interpret the stereospecificity of the Diels-Alder dimerization as a consequence of internal rotations which, in the coiled diyl, are too slow to compete with ring closure to product and, in the extended diyl, are too slow to compete with dissociation to reactant. The latter condition is the weak point of this mechanistic proposal.

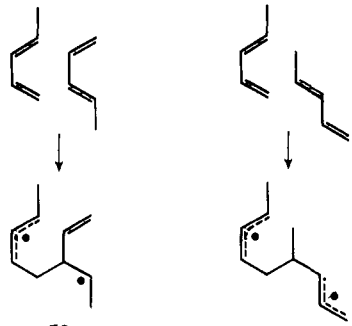
The rate of reversion of the extended diyl to piperylene may be calculated approximately using activation parameters estimated from thermochemical-kinetic data. The activation enthalpy for dissociation of a closely analogous species, the dimeric butadiene biradical *cis,trans*, to two molecules of butadiene may be estimated to be about 14 ± 3 kcal/mol, or about 1 kcal/mol less than that proposed[9] for cleavage of its stereoisomeric *trans,trans* biradical. The activation entropy, by analogy to that for cleavage of the 2,4-hexanediyl biradical, may be estimated as −6.8 eu.[6b] The free energy of activation $\Delta F^{\ddagger}$ at our reaction temperature of 463 K, therefore, would be 17.1 kcal/mol.

If biradicals **57** and **58** were formed at roughly the same rate from piperylene, mixed labeling in the Diels-Alder dimer could be avoided only if the activation free energy for the internal rotation $\Delta F^{\ddagger}_{rot}$ of **58** were greater than 17.1 kcal/mol. Our experimental limit of 2% of antara reaction would be exceeded if any more than 4% of the extended biradicals **58** succeeded in rotating and cyclizing, that is, if the rate of dissociation of **58** were any less than 25 times the rate of rotation. At 463 K, this rate ratio corresponds to 3 kcal/mol, so that it would become necessary to postulate that internal rotations in the extended biradical **58** have $\Delta F^{\ddagger}_{rot} \geq 20$ kcal/mol. This is clearly an unreasonably high value. A lower dissociation barrier would result if the model were taken to be the cleavage of the C(3)-C(4) bond in hexane-2,5-diyl, for which an activation enthalpy of 5 kcal/mol is suggested.[6b] This leads to $\Delta F^{\ddagger}_{rot} \geq$ 11 kcal/mol, still a formidable internal rotational barrier for an unbranched, unsubstituted hydrocarbon chain.

The structural similarity between **58** and *cis,trans* would favor the latter system as a better model than hexane-2,5-diyl.

Therefore, if the activation energies for both model systems were of equal reliability, the value $\Delta F^{\ddagger}_{rot} \geq 20$ kcal/mol for internal rotation in **58** would be more likely to be correct.

A high dissociation barrier in **58** also might permit rotations about the C(4)-C(5) and C(6)-C(7) bonds during its lifetime, thereby causing some loss of the original trans-deuterium configuration in the "unreacted" piperylene[65] and eventually some nonspecificity in the labeling of the dimer. Similarly, internal rotations in **59** and **60,** the extended isomers of the



**59** **60**

biradical precursors of the "meta" adducts **47** and **48,** followed by dissociation, would generate *cis*-piperylene and ultimately Diels-Alder adducts tC-**13** and cC-**12** with *cis*-propenyl groups. Such adducts are not observed (<1%) in the dimer mixture from pure *trans*-piperylene.

The biradical mechanism now is left with only two counterarguments, adoption of either of which severely damages its credibility. The first would be that the estimates of the activation parameters for dissociation of *cis,trans* are seriously in error. Were this the case, the entire biradical mechanism would be in jeopardy, since the internal consistency of the thermochemical-kinetic quantities is its justification.

The second counterargument would be that it is incorrect to assume that dimerization to extended diyl **58** competes with dimerization to coiled diyl **57**. The biradical mechanism then would reduce to the postulate that piperylene dimerizes only to the coiled conformation **57** and that the intermediate cyclizes without internal rotations.

Clearly, a biradical mechanism conforming to this set of restrictions would satisfy both the thermochemical and stereochemical facts as completely as a concerted mechanism. Moreover, the volumes of activation expected for the two mechanisms would be similar, so that the compact transition states for simple diene dimerizations revealed by high-pressure liquid-phase kinetic measurements[66] would not serve as the basis of a distinction.

The second counterargument, however, is completely ad hoc, since there is no independent reason to expect dimerization exclusively to coiled diyl **57**. Therefore, although unable to claim rigorous exclusion of the biradical mechanism, we assert that the weight of evidence in the piperylene dimerization now forces a mechanistic choice that is not a mere matter of taste, but is unequivocally in favor of a concerted process.

Nevertheless, it may well be that the biradical mechanism, as is suggested by the thermochemical-kinetic analysis in the butadiene dimer system,[8,9] is not very unfavorable. Stephenson, Gemmer, and Current[63] find about 10% antara-dienophile reaction in that case, although they prefer to interpret the minor pathway as a competing forbidden concerted [4s + 2a] reaction. Our 2% detection limit would permit the biradical (or competing antara-diene or antara-dienophile concerted) transition state to lie only 3.6 kcal/mol above the one for the concerted supra-diene–supra-dienophile reaction in the piperylene dimerization.

**On the Question of a Common Intermediate.** Even if the preceding arguments against the biradical Diels-Alder dimerization of piperylene be rejected, it is clear that the sigmatropic rearrangement of *trans*-1,2-*trans,trans*-dipropenylcyclobutane (tTT-**9**) and the dimerization cannot involve a common intermediate. That would require diyl **57,** when derived from tTT-**9,** to cyclize at C(2)-C(7) with a slight preference for inversion of configuration at C(7), but when derived by dimerization of piperylene, to cyclize with complete retention at C(7). It is true that practical factors have made it convenient to study the sigmatropic rearrangement at a slightly lower temperature (146.5 °C) than the dimerization (190 °C), but the difference could not reasonably be expected to affect the conclusion.

Similarly, the present observation of a small preference for inversion of the migrant carbon in the rearrangement of *trans*-1,2-divinylcyclobutane (at 146.5 °C), when combined with Stephenson's observation[63] of predominant retention at the same site (the dienophile) in the Diels-Alder dimerization of butadiene (at 130 °C), excludes a common intermediate in those reactions.

The thermochemical-kinetic analysis of mechanism can be valuable in the prediction of potentially accessible biradical pathways. However, a fit of the observed data to the thermochemical-kinetic parameters calculated for a biradical mechanism is always a necessary but insufficient criterion. Moreover, as the present study illustrates, the application of such data to identify supposed common intermediates is hazardous. The thermochemical-kinetic parameters are useful for estimating the energies of intermediates. Other techniques are needed to define their structures.

## Experimental Section

Melting points were obtained using a Thomas-Hoover capillary melting-point apparatus and are uncorrected. Elemental analyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, West Germany, Atlantic Microlab, Inc., Atlanta, Georgia, and Galbraith Laboratories, Inc., Knoxville, Tennessee.

Infrared spectra (ir) were recorded on a Perkin-Elmer Infracord or 237B infrared spectrophotometer.

Nuclear magnetic resonance (NMR) spectra were obtained on a Varian Associates A-60 or A-60A, a Jeolco 100 MHz, or a Bruker-270 Spectrometer, and are uncalibrated. Chemical shifts are given as parts per million (ppm) downfield from $Me_4Si$ in $\delta$ units and coupling constants in cycles per second (Hz). Nuclear magnetic resonance data are reported in the order: chemical shift: multiplicity, s = singlet, d = doublet, t = triplet, m = multiplet; number of protons; coupling constants: assignment.

For analytical vapor-phase chromatography (VPC), a Perkin-Elmer 900 Gas Chromatograph, equipped with flame ionization detector and nitrogen carrier gas, was used. Both capillary columns, stainless steel tubing (0.01-in. inner diameter) coated with the designated substrate, and 0.125-in. packed columns were used in this instrument and are listed in Table VI. The dibutyl tetrachlorophthalate (DBT) capillary column was prepared by passing a solution of 1 g of pure DBT diluted to 10 ml with methylene chloride through new tubing once at 10 psi nitrogen pressure. The nitrogen flow was continued overnight to ensure removal of the solvent. The column was placed in the VPC oven, which was then temperature programmed to the maximum expected operating temperature (75 °C) over 8 h with continued nitrogen flow. Quantitative VPC analysis was accomplished using a Hewlett-Packard 3370A electronic digital integrator.

For preparative VPC, a Varian Aerograph Model A-90-P3 instrument, equipped with thermal conductivity detector and helium carrier gas, was used. The 0.375-in. packed columns used in this instrument are listed in Table VI.

Optical rotations were measured with an O. C. Rudolph and Sons, Inc. Model 80 high precision polarimeter equipped with a Model 200 photometer unit, a Model 340 oscillating polarizer, and a Model 313 tube trough. Rotations were obtained in a 1-dm tube on solutions of samples in reagent-grade chloroform or carbon tetrachloride. An estimate of the error, reported as one standard deviation, is included only in those cases where the rotation was repeated on the same sample. The polarimetric error is not reported, since it is unusually small compared to the 1% volumetric error.

Table VI

| VPC columns | |
|---|---|
| Column designation | Description |
| DBT | 190 ft capillary, dibutyl tetrachlorophthalate. |
| $AgNO_3$/Carbowax 200 | 10 ft × 0.125 m, 10% $AgNO_3$/Carbowax 200 on 100/120 Chromosorb P. |
| $AgNO_3$/Carbowax 200 | 8 ft × 0.375 in., 25% $AgNO_3$/Carbowax 200 on 60/80 Chromosorb A. |
| Carbowax 20M | 10 ft × 0.375 in., 25% Carbowax 20M on 60/80 Chromosorb W. |
| DBT | 10 ft × 0.375 in., 25% dibutyl tetrachlorophthalate on 60/80 Chromosorb A. |
| FFAP | 20 ft × 0.375 in., 20% FFAP on 60/80 Chromosorb W. |
| MNPM | 20 ft × 0.375 in., 25% γ-methyl-γ-nitropimelonitrile on 60/80 Chromosorb A. |
| SE-30 | 20 ft × 0.375 in., 25% SE-30 on 45/60 Chromosorb P. |
| SF-96 | 10 ft × 0.375 in., 25% SF-96 on 60/70 Anakrom AS. |

Most reagent-grade chemicals were used without further purification. Diglyme and tetrahydrofuran were distilled from lithium aluminum hydride, pyridine from barium oxide, and boron trifluoride etherate from calcium hydride.

**Synthesis of the *cis*-1,2-*cis,trans*- and *cis,cis*-Dipropenylcyclobutanes (cCT-8 and cCC-8).** Into a three-neck, 500-ml flask equipped with mechanical stirrer, addition funnel, low-temperature thermometer (−70 °C), and under a nitrogen atmosphere was placed 8.60 g (0.05 mol) of dimethyl *cis*-1,2-cyclobutanedicarboxylate (**7**) in 200 ml of dry ether. This was cooled to −70 °C (dry ice–methoxyethanol bath). Then 15 ml (0.05 mol) of $NaAlH_2(OCH_2CH_2OCH_3)_2$ as a 70% benzene solution (Vitride, Eastman) diluted with 20 ml of dry ether was added dropwise via the addition funnel, maintaining the temperature at −70 °C. The reaction mixture was allowed to stir for 24 h at −70 °C.

To the dialdehyde was added 0.10 mol of ethylidenetriphenylphosphorane in ether at −70 °C. This was allowed to warm to −10 °C (45 min) and 10 ml of water was added. The cream-colored reaction mixture was allowed to stir for 30 min. Then, 100 ml of diluted $H_2SO_4$ (1:5) was added slowly in small portions with cooling. This was allowed to stir for 30 min at room temperature. The reaction mixture was extracted with 200 ml of pentane. The pentane layer was extracted twice with 10% aqueous sodium bicarbonate, three times with water, and once with saturated sodium chloride. This was dried ($MgSO_4$), concentrated, and distilled, giving 3.3 g (48%) of *cis*-1,2-dipropenylcyclobutane (**8**). VPC on an analytical column ($AgNO_3$/Carbowax 200, 50 °C) indicated the ratio of isomers cTT-**8**, cCT-**8**, and cCC-**8** was 2:31:67, respectively. The second eluted isomer, *cis*-1,2-*cis,trans*-dipropenylcyclobutane (cCT-**8**), was isolated by preparative VPC (MNPN, 85 °C): ir (neat) 965 (alkene, disubstituted, trans) and 715 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) δ 5.48 (m, 4, olefin), 3.48–2.80 (m, 2, methine, CH), 2.28–1.40 (m, 4, cyclobutane), 1.66 (d, 3, $J$ = 5 Hz, $CH_3$), and 1.53 (d, 3, $J$ = 5 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.16; H, 11.75.

Similarly, the third eluted isomer, *cis*-1,2-*cis,cis*-dipropenylcyclobutane (cCC-**8**), was isolated: ir (neat) 740 and 695 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) δ 5.48 (m, 4, olefin), 3.36 (m, 2, methine CH), 2.32–1.60 (m, 4, cyclobutane), and 1.50 (d, 6, $J$ = 5 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.08; H, 11.85.

***cis*-1,2-Dipropenylcyclobutane Dioxide.** To 3.3 g (0.024 mol) of *cis*-1,2-dipropenylcyclobutane (**8**) in 50 ml of methylene chloride was added dropwise 16.5 g (0.096 mol) of *m*-chloroperbenzoic acid in 150 ml of methylene chloride at 0 °C. This was allowed to stir for 7 h at room temperature. The reaction mixture was extracted once with saturated aqueous sodium sulfite, twice with saturated aqueous sodium bicarbonate, and once with saturated sodium chloride. This was dried ($Na_2SO_4$), concentrated, and distilled under reduced pressure giving 2 g (49%) of bisepoxide. A pure sample was isolated by preparative VPC (SF-96, 150 °C): ir (neat) 1270, 885, 840, and 800 $cm^{-1}$ (epoxide).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.57. Found: C, 71.22; H, 9.59.

***cis*-1,2-*trans,trans*-Dipropenylcyclobutane (cTT-8).** The olefin inversion procedure of Vedejs and Fuchs[22] was followed. All equipment was flame dried and argon purged. Under a static pressure of argon, 2 g (0.012 mol) of bisepoxide **93** in 4 ml of dry THF was added in one portion to 35 ml (0.024 mol) of 0.70 M lithium diphenylphosphide (LDP) solution at room temperature (exothermic reaction). The brick-red solution decolorized immediately and 1.5 ml (0.024 mol) of methyl iodide was added via a syringe (exothermic reaction). The resulting pale yellow solution was allowed to stir for 2 h at room temperature. The reaction mixture was taken up in 150 ml of pentane and extracted ten times with water to remove the THF and methyldiphenylphosphine oxide. The pentane layer was dried ($MgSO_4$), concentrated, and distilled, giving 250 mg (15%) of inverted olefin. VPC analysis on an analytical column (MNPN, 80 °C) indicated the ratio of isomers cTT-**8**, cCT-**8**, and cCC-**8** was 81:19:0, respectively. The first eluted isomer, *cis*-1,2-*trans,trans*-dipropenylcyclobutane (cTT-**8**) was isolated by preparative VPC (MNPN, 70 °C): ir (neat) 965 $cm^{-1}$ (alkene, disubstituted, trans); NMR ($CDCl_3$) δ 5.42 (m, 4, olefin), 2.96 (m, 2, methine CH), 2.20–1.60 (m, 4, cyclobutane), and 1.66 (d, 6, $J$ = 5 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.89; H, 12.05.

**Synthesis of the *trans*-1,2-Dipropenylcyclobutanes tTT-9, tCT-9, and tCC-9.** *trans*-1,2-Bis(bromomethyl)cyclobutane was synthesized by successive treatment of dimethyl *trans*-1,2-cyclobutanedicarboxylate with lithium aluminum hydride and phosphorous tribromide according to procedures described in the literature[67] (51% overall yield): bp 63 °C (0.8 mm) [lit.[67] bp 54–56 °C (0.45 mm)].

A mixture of 18.6 g (0.077 mol) of the dibromide and 42 g (0.160 mol) of triphenylphosphine in 60 ml of chlorobenzene was heated for 12 h at 130 °C under a nitrogen atmosphere. The cooled white solid was triturated with 100 ml of acetone and dried in a desiccator ($P_2O_5$, 0.2 mm), giving 50 g (84%) of the bisphosphonium salt: mp 325–327 °C; NMR ($CDCl_3$) δ 8.18–7.20 (m, 30, phenyl), 5.03 (m, 2, methine CH), 3.92–2.80 (m, 4, $P^+CH_2$), and 1.43 (m, 4, cyclobutane $CH_2$).

Anal. Calcd for $C_{42}H_{40}Br_2P_2$: C, 65.81; H, 5.26; Br, 20.85. Found: C, 65.63; H, 5.26; Br, 20.94.

To a stirred suspension of 19.2 g (0.025 mol) of the bisphosphonium salt in 150 ml of dry ether under a nitrogen atmosphere was added 70 ml of 1 M *n*-butyllithium (0.070 mol) in hexane. The resulting deep red solution was allowed to stir for 2 h. This was cooled to −70 °C and 5.28 g (0.120 mol) of acetaldehyde in 5 ml of ether was added. The cream-colored suspension was allowed to stir for 30 min at room temperature, and 100 ml of water was added. The layers were separated and the aqueous layer was extracted twice with pentane. The combined organic layers were extracted with water and saturated sodium chloride. This was dried ($Na_2SO_4$), concentrated, and flash distilled, giving 1.5 g of unpurified product. The pure mixture of isomers of **9** was isolated by preparative VPC (Carbowax, 130 °C) giving 0.54 g (16%). The three isomers were then separated (1:2:1 ratio) by preparative VPC ($AgNO_3$/Carbowax 200, 60 °C). The first eluted isomer was *trans*-1,2-*trans,trans*-dipropenylcyclobutane (tTT-**9**): ir (neat) 970 $cm^{-1}$ (alkene, disubstituted, trans); NMR ($CCl_4$) δ 5.50–5.02 (m, 4, olefin), 2.50 (m, 2, methine CH), 2.02–1.42 (m, 4, cyclobutane $CH_2$), and 1.60 (d, 6, $J$ = 5 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.09; H, 11.88.

The second eluted isomer was *trans*-1,2-*cis,trans*-dipropenylcyclobutane (tCT-**9**): ir (neat) 980 (alkene, disubstituted, trans) and 735 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CCl_4$) δ 5.40–5.04 (m, 4, olefin), 2.84 (m, 1, methine CH), 2.48 (m, 1, methine CH), 2.04–1.40 (m, 4, cyclobutane $CH_2$), 1.62 (d, 3, $J$ = 5 Hz, $CH_3$), and 1.54 (d, 3, $J$ = 5 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.87; H, 11.89.

The third eluted component was *trans*-1,2-*cis,cis*-dipropenylcyclobutane (tCC-**9**): ir (neat) 725 and 710 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CCl_4$) δ 5.40–5.00 (m, 4, olefin), 2.88 (m, 2, methine CH), 2.12–1.40 (m, 4, cyclobutane $CH_2$), and 1.52 (d, 6, $J$ = 5 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.92; H, 11.75.

**Synthesis of *trans*- and *cis*-3-Methyl-4-*trans*- and *cis*-propenylcyclohexenes (tT-13, tC-13, cT-12, and cC-12).** In the racemic series, the *trans*- and *cis*-3-methylcyclohex-4-ene-1-carboxaldehydes (**14** and **15**) were prepared by reduction of methyl *trans*- and *cis*-3-methylcyclohex-4-ene-1-carboxylates to the carbinols and oxidation of the latter with $CrO_3$ in pyridine $CH_2Cl_2$.

**Methyl *cis*-3-Methylcyclohexene-4-carboxylate (14a).** Ethereal diazomethane, made from *N*-nitrosomethylurea and aqueous 40% potassium hydroxide, was added to 5.4 g (0.038 mol) of *cis*-3-methylcyclohexene-4-carboxylic acid (**14a**) in ether. This was concentrated and distilled, giving 5.5 g (95%) of methyl ester **14b**. A pure sample was isolated by preparative VPC (UCON, 180 °C): ir (neat) 1735 (ester C=O) and 700 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.65 (m, 2, olefin), 3.68 (s, 3, $OCH_3$), 2.63 (m, 2), 2.25–1.62 (m, 4), and 0.90 (d, 3, $J$ = 7 Hz, $CH_3$).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.81, H, 9.05.

**Methyl *trans*-3-Methylcyclohexene-4-carboxylate (15a).** To 2.3 g (0.10 mol) of sodium was added slowly 100 ml of anhydrous methanol at such a rate as to maintain vigorous reflux. To this was added 16 g (0.10 mol) of a mixture of methyl *cis*- and methyl *trans*-3-methylcyclohexene-4-carboxylate (**14b** and **15b**), respectively (1:1 ratio), in 25 ml of anhydrous methanol. This was allowed to reflux for 1.5 h. Then the reaction mixture was poured onto 20% HCl and cracked ice. Ether was added and the layers were separated. The ethereal layer was extracted twice with 10% aqueous sodium bicarbonate, and saturated sodium chloride. This was concentrated, dried ($MgSO_4$), and distilled, giving 12 g (75%) of methyl ester. VPC analysis (Carbowax 20M, 180 °C) indicated a *trans*-**15b**/*cis*-**14b** ratio of 3:1, respectively. The first eluted component, methyl *trans*-3-methylcyclohexene-4-carboxylate (**15b**), was isolated by preparative VPC (Carbowax 20M, 180 °C): ir (neat) 1735 (ester C=O), and 675 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.55 (m, 2, olefin), 3.68 (s, 3, $OCH_3$), 2.73–1.47 (m, 6), and 0.98 (d, 3, $J$ = 7 Hz, $NH_3$).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.32; H, 9.23.

**cis-3-Methylcyclohexene-4-carbinol (14c) and *trans*-3-Methylcyclohexene-4-carbinol (15c).** To a stirred suspension of 3.0 g (0.08 mol) of lithium aluminum hydride in 100 ml of dry ether was added dropwise 12 g (0.08 mole) of trans and cis methyl esters **15b** and **14b** (3:1 ratio, respectively) in ether. This was allowed to stir for 1 h. Then 3 ml of water, 3 ml of 15% aqueous sodium hydroxide, and 9 ml of water were added dropwise. The white granular precipitate was removed by filtering and the ethereal solution was dried ($MgSO_4$) and concentrated, giving 7.6 g (86%) of alcohols **14c** and **15c**. Pure samples of the isomeric alcohols were isolated by preparative VPC (FFAP, 175 °C). The major and first-eluted isomer was *trans*-3-methylcyclohexene-4-carbinol (**15c**): ir (neat) 3320 (OH), 1075, 1045, 1010 (primary OH), and 680 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.55 (m, 2, olefin), 3.63 (m, 2, $CH_2OH$), 2.18 (s, 1, OH), 2.18–1.22 (m, 6), and 0.87 (d, 3, $J$ = 7 Hz, $CH_3$).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.03; H, 11.05.

The minor and second eluted component, having the identical VPC retention time as the lithium aluminum hydride reduction product of pure **14b**, was *cis*-3-methylcyclohexene-4-carbinol (**14c**): ir (neat) 3340 (OH), 1045, 1015 (primary OH), and 700 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.65 (m, 2, olefin), 3.68–3.48 (m, 2, $CH_2OH$), 2.55–1.07 (m, 6), 1.98 (s, 1, OH), and 0.87 (d, 3, $J$ = 7 Hz, $CH_3$).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: 76.34; H, 11.36.

**cis-3-Methylcyclohexene-4-carboxaldehyde (14d) and *trans*-3-Methylcyclohexene-4-carboxaldehyde (15d).** Chromium trioxide (12 g, 0.120 mol) was added to a magnetically stirred solution of 19 g (0.240 mol) of dry pyridine in 300 ml of methylene chloride. The deep burgundy solution was allowed to stir for 15 min at room temperature. A solution of 2.53 g (0.020 mol) of *cis*- and *trans*-3-methylcyclohexene-4-carbinol (**14c** and **15c**, respectively) in 25 ml of methylene chloride was added in one portion. A black deposit separated immediately. After the mixture had stirred for 15 min at room temperature the solution was decanted from the residue, which was washed with 200 ml of ether.

The combined organic solutions were extracted three times with 5% aqueous sodium hydroxide, once with 10% aqueous HCl, 10% aqueous sodium bicarbonate, and saturated sodium chloride. This was dried ($Na_2SO_4$), concentrated, and flash distilled (0.5 mm), giving 1.91 g (88%) of aldehydes **14d** and **15d**. The isomers were separated and purified by preparative VPC (Carbowax 20M, 160 °C). The major and first eluted isomer was *trans*-3-methylcyclohexene-4-carboxaldehyde (**15d**): ir (neat) 2850, 2830, 2700 (aldehyde CH), 1725 (aldehyde C=O), and 685 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 9.72 (d, 1, $J$ = 2 Hz, CHO), 5.62 (m, 2, olefin), 2.76–1.40 (m, 6), and 1.02 (d, 3, $J$ = 7 Hz, $CH_3$).

Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.12; H, 9.65.

The minor and second eluted isomer, having the same VPC retention time as an authentic sample,[23] was *cis*-3-methylcyclohexene-4-carboxaldehyde (**14d**): ir (neat) 2850, 2830, 2700 (aldehyde CH), 1725 (aldehyde C=O), and 710 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 9.82 (s, 1, CHO), 5.69 (m, 2, olefin), 2.64 (m, 2), 2.28–1.60 (m, 4), and 0.98 (d, 3, $J$ = 7 Hz, $CH_3$).

***cis*-3-Methyl-4-*trans*-propenylcyclohexene (cT-12) and *cis*-3-Methyl-4-*cis*-propenylcyclohexene (cC-12).** Ethylidenetriphenylphosphorane was prepared by adding slowly, via a syringe, 13.3 ml of 1.2 M *n*-butyllithium (0.016 mol) in hexane to a stirred suspension of 6.0 g (0.016 mol) of ethyltriphenylphosphonium bromide in 100 ml of dry ether. The resulting red solution of ylide was allowed to stir for 2 h at room temperature. *cis*-3-Methylcyclohexene-4-carboxaldehyde (**14d**) (1.98 g, 0.016 mol) in ether was added all at once. The reaction mixture was allowed to stir for 10 min at room temperature and 50 ml of water was added. This was extracted twice with pentane. The combined organic layers were extracted with water and saturated sodium chloride. This was dried ($MgSO_4$), concentrated, and flash distilled. The mixture of isomers, *cis*-3-methyl-4-propenylcyclohexene (**12**), was isolated by preparative VPC (Carbowax 20M, 150 °C), giving 920 mg (42%) of cT-**12** and cC-**12**. The isomers were then separated by preparative VPC (MNPN, 85 °C). The minor and first eluted isomer was *cis*-3-methyl-4-*trans*-propenylcyclohexene (cT-**12**): ir (neat) 965 (alkene, disubstituted, trans) and 700 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.68–5.40 (m, 4, olefin), 2.48–1.92 (m, 4, allylic), 1.66 (d, 3, $J$ = 4 Hz, $CH_3$), 1.64–1.46 (m, 2), and 0.85 (d, 3, $J$ = 7Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.98; H, 11.80.

The major and second eluted isomer was *cis*-3-methyl-4-*cis*-propenylcyclohexene (cC-**12**): ir (neat) 735 and 670 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.68–5.36 (m, 4, olefin), 2.72 (m, 1, allylic), 2.28 (m, 1, allylic), 2.03 (m, 2, allylic), 1.61 (d, 3, $J$ = 6 Hz, $CH_3$), 1.53 (m, 2), and 0.85 (d, 3, $J$ = 7 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.95; H, 11.84.

***trans*-3-Methyl-4-*trans*-propenylcyclohexene (tT-13) and *trans*-3-Methyl-4-*cis*-propenylcyclohexene (tC-13).** The Wittig reaction of 2.00 g (0.016 mol) of pure *trans*-3-methylcyclohexene-4-carboxaldehyde (**15d**) and 0.016 mol of ethylidenetriphenylphosphorane was run as described above for the **14d** → **12** conversion.

The mixture of isomers, *trans*-3-methyl-4-propenylcyclohexene (**13**), was isolated by preparative VPC (Carbowax 20M, 150 °C), giving 1.2 g (55%) of tT-**13** and tC-**13**. The isomers were then separated by preparative VPC ($AgNO_3$/Carbowax 200, 65 °C). The minor and first eluted isomer was *trans*-3-methyl-4-*trans*-propenylcyclohexene (tT-**13**): ir (neat) 965 (alkene, disubstituted, trans) and 680 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.68–5.20 (m, 4, olefin), 2.12–1.24 (m, 6), 1.66 (d, 3, $J$ = 5 Hz, $CH_3$), and 0.93 (d, 3, $J$ = 6 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.09; H, 11.74.

The major and second eluted isomer was *trans*-3-methyl-4-*cis*-propenylcyclohexene (tC-**13**): ir (neat) 735, 710, and 680 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.76–5.04 (m, 4, olefin), 2.28–1.72 (m, 4, allylic), 1.72–1.12 (m, 2), 1.62 (d, 3, $J$ = 6 Hz, $CH_3$), and 0.92 (d, 3, $J$ = 7 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.45; H, 11.74.

**Correlation of (1*S*,5*S*)-(−)-α-Pinene (26) to (*S*)-(+)-1,1-Dimethyl-2-ethylcyclobutane (28) (Scheme VI). 2,2-Dimethyl-3-acetylcyclobutylacetic Acid (Pinonic Acid (31)).** Into a 500-ml gas dispersion apparatus equipped with an aqueous KI trap was placed

5.15 g (0.038 mol) of (1*S*,5*S*)-(−)-α-pinene (Fluka), $[\alpha]^{21}D$ −42.06° (1 dm, neat), 82% optically pure, in 35 ml of EtOAc, 35 ml of $CCl_4$, and 2 ml of AcOH. This was cooled to 0 °C. Ozone, generated by a Welsbach ozonator, was bubbled through the reaction mixture until the KI trap turned dark (30 min). The above procedure was repeated eight times and the combined fractions were poured into a 1-l. flask equipped with a reflux condenser. To this was added 300 ml of $H_2O$ and 25 ml of 30% $H_2O_2$. After refluxing with stirring for 8 h on a steam bath, the reaction mixture gave a negative test for active oxygen (KI starch test paper). The solvent was removed under reduced pressure and dilute aqueous sodium hydroxide was added to pH 13. This was extracted twice with ether and the combined organic extracts were concentrated and dried ($MgSO_4$). The NMR spectrum of this crude mixture indicated ethyl 2,2-dimethyl-3-acetylcyclobutylacetate.[42] The aqueous layer was acidified with 2 N HCl to pH 2 and extracted twice with chloroform. The combined organic extracts were washed with saturated sodium chloride, dried ($MgSO_4$), and concentrated under reduced pressure. The NMR and ir spectra of the yellow oil are consistent with pinonic acid[42] (**31**): ir (neat) 3000 (broad) and 1750 $cm^{-1}$ (broad, ketone and acid C=O); NMR ($CDCl_3$) δ 11.50 (s, 1, COOH), 2.92 (t, 1, *J* = 8 Hz, C(3)-H), 1.80–2.67 (m, 4), 2.03 (s, 3, $COCH_3$), and 0.88 (s, 3, $CH_3$).

**Methyl 2,2-Dimethyl-3-acetylcyclobutylacetate.** The pinonic acid (**31**) was taken up in 250 ml of ether. An ethereal solution of diazomethane, made from *N*-nitrosomethylurea and aqueous 40% potassium hydroxide, was added to the mixture until a yellow color persisted. The excess diazomethane was discharged with a few drops of acetic acid. The solution was dried ($MgSO_4$) and concentrated, giving 30.8 g (~50% from α-pinene) of a pale yellow oil which contained mostly methyl pinonate[42] (**32**): ir (neat) 1750–1700 $cm^{-1}$ (ester and ketone C=O); NMR ($CDCl_3$) δ 3.63 (s, 3, $OCH_3$), 2.88 (t, 1, C(3)-H), 1.72–2.42 (m, 5), 2.03 (s, 3, $COCH_3$), 1.33 (s, 3, $CH_3$), and 0.88 (s, 3, $CH_3$).

**Methyl 2,2-Dimethyl-3-acetoxycyclobutylacetate.** The 30.8 g (0.15 mol) of unpurified methyl pinonate (**32**) was taken up in 200 ml of chloroform and allowed to react with 20.7 g (0.12 mol) of *m*-chloroperoxybenzoic acid (Aldrich) with stirring in the dark for 9 days. The potassium iodide starch paper test for active oxygen was negative. The chloroform was removed under reduced pressure and the reaction mixture was taken up in ether, extracted once with 10% aqueous sodium hydroxide, saturated sodium chloride, and dried ($MgSO_4$). The NMR spectrum of the product mixture indicated equal portions of desired acetoxy product and starting ketone. In order to remove the ketone fraction, this mixture was allowed to react with a solution of 13.4 g (0.08 mol) of Girard reagent T and 24 g of acetic acid in 200 ml of absolute ethanol for 1 h on a steam bath. A solution of 7.2 g of sodium hydroxide in 500 ml of water was added, and this was extracted twice with ether. The combined ethereal layers were washed successively with saturated aqueous sodium bicarbonate, water, and saturated sodium chloride. This was dried ($MgSO_4$) and concentrated, giving 15 g (45%) of unpurified acetate product:[42] ir (neat) 1740 (ester C=O) and 1238 $cm^{-1}$ (acetate); NMR ($CDCl_3$) δ 4.62 (t, 1, C(3)-H), 3.65 (s, 3, $OCH_3$), 1.68–2.47 (m, 5), 2.02 (s, 3, $OCOCH_3$), 1.17 (s, 3, $CH_3$), and 0.93 (s, 3, $CH_3$).

**β-2,2-Dimethyl-3-hydroxycyclobutylethanol.** The 15 g (0.07 mol) of the above acetate in dry ether was added dropwise to 6.1 g (0.16 mol) of lithium aluminum hydride in 200 ml of dry ether under nitrogen at 0 °C. This was allowed to stir for 8 h at room temperature. According to the work-up procedure described by Fieser,[68] 6.1 ml of water, 6.1 ml of 15% aqueous sodium hydroxide, and 18.3 ml of water were added. The granular precipitate was removed by filtering and the reaction mixture was concentrated, giving 12.4 g of a pale yellow oil, the desired diol, contaminated with a small amount of ethyl ether: ir (neat) 3400 (broad, OH), no C=O absorption, 1050, and 1125 $cm^{-1}$; NMR ($CDCl_3$) δ 4.07–3.25 (m, 3), 2.43–1.38 (m, 5), 1.03 (s, 3, $CH_3$), and 0.93 (s, 3, $CH_3$).

**Methyl 2,2-Dimethyl-3-ketocyclobutylacetate.** A solution of the 12.4 g of unpurified diol in 200 ml of acetone was cooled to 0 °C and Jones reagent[69] was added dropwise until the solution remained orange. After regenerating the green color with a few milliliters of 10% aqueous sodium bisulfite, 200 ml of ether and 200 ml of saturated sodium chloride were added and the layers were separated. The aqueous layer was extracted twice with ether. The combined ether layers were dried ($MgSO_4$) and concentrated, giving 8.4 g of a yellow oil, 2,2-dimethyl-3-ketocyclobutylacetic acid.

This was taken up in 200 ml of ether and treated with an ethereal solution of diazomethane. Excess diazomethane was discharged with a few drops of acetic acid. The reaction mixture was dried ($MgSO_4$), concentrated, and distilled at 78–100 °C (5 mm), giving 3.5 g of keto ester.[42] ir (neat) 1780 (cyclobutanone) and 1740 $cm^{-1}$ (ester C=O); NMR ($CDCl_3$) δ 3.63 (s, 3, $OCH_3$), 3.02 (m, 2), 2.53 (m, 3), 1.20 (s, 3, $CH_3$), and 1.05 (s, 3, $CH_3$).

**Methyl 2,2-Dimethylcyclobutylacetate (27).** To a solution of 3 g (0.017 mol) of the above keto ester and 6 ml (0.072 mol) of ethanedithiol was added 6 ml of freshly distilled $BF_3$·$Et_2O$ in a well ventilated hood. This was allowed to react for 3 h. The reaction mixture was taken up in 200 ml of ether and extracted three times with 10% aqueous sodium hydroxide and once with saturated sodium chloride. The ethereal extract was dried ($MgSO_4$) and concentrated, giving the ethylene thioketal derivative: ir (neat) 1730 $cm^{-1}$ (ester C=O); ($CDCl_3$) δ 3.63 (s, 3, $OCH_3$), 3.13 (s, 4, $SCH_2CH_2S$), 2.42 (m, 5), and 1.15 (s, 6, $CH_3$).

The above unpurified ethylene thioketal was added to 30 g of Raney nickel, prepared by the method of Burgstahler,[68b] in 300 ml of absolute ethanol. This was allowed to reflux gently on a steam bath for 12 h. After removal of the nickel by filtration, the ethanolic solution was taken up in ether and extracted three times with water and once with saturated sodium chloride. The ethereal solution was dried ($MgSO_4$) and concentrated, and the product was isolated by preparative VPC (Carbowax 20M, 150 °C), giving 0.8 g (30%) of a clear liquid:[42] ir (neat) 1740 $cm^{-1}$ (ester C=O); NMR ($CDCl_3$) δ 3.63 (s, 3, $OCH_3$), 2.13–2.47 (m, 3), 1.50–2.13 (m, 4, ring $CH_2$), 1.07 (s, 3, $CH_3$), and 1.00 (s, 3, $CH_3$).

**β-2,2-Dimethylcyclobutylethanol (29).** The 0.8 g (5 mmol) of ester in dry ether was added dropwise to 0.23 g (6 mmol) of lithium aluminum hydride in 50 ml of ether under nitrogen at 0 °C. This was allowed to stir for 8 h at room temperature. To this was added 0.25 ml of water, 0.25 ml of 15% aqueous sodium hydroxide, and 0.70 ml of water. This was filtered, dried ($MgSO_4$), and concentrated, giving 0.6 g (94%) of the alcohol[42] **29**: ir (neat) 3300 (OH) and 1050 $cm^{-1}$ (primary alcohol); NMR ($CDCl_3$) δ 3.58 (t, 2, *J* = 7 Hz, $CH_2OH$), 2.13–1.43 (m, 7), 1.57 (s, 1, OH), 1.05 (s, 3, $CH_3$), and 1.02 (s, 3, $CH_3$).

**β-2,2-Dimethylcyclobutylethanol *p*-Toluenesulfonate (30).** To a magnetically stirred, cold solution of 0.6 g (4.7 mmol) of the alcohol **29** in 15 ml of dry pyridine was added 2.0 g (10.5 mmol) of *p*-toluenesulfonyl chloride. The light brown reaction mixture was allowed to stand at 5 °C for 20 h. This was poured over crushed ice and extracted three times with ether. The combined ether fractions were extracted four times with cold 1 N HCl, once with water, and once with saturated sodium chloride. This was dried ($MgSO_4$) and concentrated, giving the crude *p*-toluenesulfonate **30**: NMR ($CDCl_3$) δ 7.55 ($A_2B_2$, 4, aromatic), 3.97 (t, 2, *J* = 6 Hz, $CH_2OTs$), 2.45 (s, 3, $CH_3$), 2.17–1.33 (m, 7), 0.98 (s, 3, $CH_3$) and 0.93 (s, 3, $CH_3$).

**(*S*)-(+)-1,1-Dimethyl-2-ethylcyclobutane (28).** A solution of crude **30** (4.7 mmol) in 50 ml of dry THF and 0.45 g (11.8 mmol) of lithium aluminum hydride in THF were allowed to react under nitrogen with stirring for 12 h. Saturated sodium sulfate was added dropwise until a white precipitate appeared. The reaction mixture was taken up in pentane, filtered, and extracted three times with water. This was dried ($MgSO_4$) and concentrated. The product was isolated by preparative VPC (SE-30, 115 °C), giving 70 mg (13% from the alcohol **29**) of the hydrocarbon (*S*)-(+)-**28**: $[\alpha]^{24}D$ 4.76° (*c* 4.93, $CHCl_3$); NMR ($CDCl_3$) δ 1.97–1.12 (m, 7), 1.05 (s, 3, $CH_3$), 0.98 (s, 3, $CH_3$), and 0.78 (t, 3, $CH_2CH_3$). Ir (neat) and correct C,H analysis are recorded for (*R*)-(−)-**30** in the **3a** → **30** correlation.

**Correlation of (1*S*,2*S*)-(−)-*trans*-1,2-Divinylcyclobutane (3a) to (*R*)-(−)-1,1-Dimethyl-2-ethylcyclobutane (28) (Scheme VII). (1*S*,2*S*)-(−)-*trans*-1,2-Divinylcyclobutane (3a).** Following the procedure of Brown[70] for asymmetric hydroboration of olefins, 200 ml of diglyme was distilled from lithium aluminum hydride under reduced pressure at 80 °C into a dry 500-ml flask equipped with a magnetic stirrer, addition funnel, and reflux condenser. The reaction was carried out under a nitrogen atmosphere with an acetone trap to scavenge excess diborane.

To the diglyme was added first 5.68 g (0.15 mol) of sodium borohydride and then 54.5 g (0.40 mol, $[\alpha]D$ −42.1° (1 dm, neat)) of

α-pinene (Fluka) with stirring. The reaction mixture was cooled to 0 °C (ice-methanol bath) and 28.4 g (0.20 mol) of $BF_3$·$Et_2O$, freshly distilled from calcium hydride, was added dropwise with stirring. This was allowed to stir for 5 h at 0 °C.

The white reaction mixture (diisopinocampheylborane) was cooled to −18 °C and 45 g (0.41 mol) of *trans*-1,2-divinylcyclobutane (**3a**)[14] was added all at once with vigorous stirring. This was allowed to stir at −18 °C for 1.5 h and at room temperature for 2 h. Distillation of the reaction mixture at 25–35 °C (1 mm) afforded 125 ml of clear liquid, which was extracted three times with water and twice with saturated sodium chloride. This was dried ($MgSO_4$) and concentrated, giving 28 g (62%) of recovered starting material **3a**. A pure sample of **3a** was isolated by preparative VPC (Carbowax 20M, 80 °C): $[\alpha]^{24}D$ −11.30 ± 0.05° (*c* 30.5, $CCl_4$).

**(1*S*,2*R*)-(−)-*trans*-2-Ethyl-1-vinylcyclobutane.** The 28 g (0.25 mol) of (1*S*,2*S*)-(−)-**3a** ($[\alpha]D$ −11.30°) was taken up in 150 ml of 95% ethanol, 200 ml of hydrazine hydrate (4.0 mol), and a few drops of 1% copper sulfate solution. The diimide was generated by dropwise addition of 100 ml of 30% hydrogen peroxide at 0 °C. The reaction was followed by VPC (Carbowax 20M, 100 °C).

The reaction mixture was extracted once with water and twice with saturated sodium chloride. This was dried ($Na_2SO_4$), concentrated, and distilled at 110–112 °C (760 mm), giving 37 ml of a mixture of products containing 50% (by VPC) of the desired monoreduced olefin. A pure sample was isolated by preparative VPC (Carbowax 20M, 50 °C): $[\alpha]^{24}D$ −6.47° (*c* 19.2, $CCl_4$); ir ($CCl_4$) 3070 (vinyl), 2940 (alkane), 990 (vinyl), and 910 $cm^{-1}$ (vinyl); NMR ($CCl_4$) δ 6.17–5.57 (m, 1, vinyl H), 5.07–4.68 (m, 2, vinyl H), 2.62–1.12 (m, 8), and 0.80 (t, 3, *J* = 7 Hz, $CH_3$).

Anal. Calcd for $C_6H_{14}$: C, 87.19; H, 12.81. Found: C, 87.30; H, 12.85.

**(1*R*,2*R*)-(−)-*trans*-2-Ethylcyclobutanecarboxaldehyde.** A solution of 11.2 g (0.10 mol) of (1*R*,2*S*)-(−)-*trans*-2-ethyl-1-vinylcyclobutane ($[\alpha]D$ −6.47°) in 85 ml of methanol was cooled to −60 °C (dry ice-acetone). Ozone, generated by a Welsbach ozonator, was bubbled through the reaction mixture until the KI trap turned dark (4 h). The solution was flushed with nitrogen and fitted with a reflux condenser in the hood. A reductive workup, according to the method of Pappas and Keaveney,[71] was accomplished by adding 20 ml (0.272 mol) of dimethyl sulfide to the cold reaction mixture and allowing this to warm to room temperature with stirring for 8 h. This was concentrated, taken up in ether, and extracted twice with saturated sodium chloride. The ethereal solution was dried ($MgSO_4$) and concentrated. VPC analysis (Carbowax 20M, 115 °C) indicated two products, whose NMR spectra were consistent with the desired aldehyde and its dimethyl acetal. This crude product mixture was taken up in 40 ml of water and dioxane (1:1) and a trace of sulfuric acid and allowed to reflux for 2.5 h. The reaction mixture was extracted twice with ether and the combined ethereal layers were extracted twice with saturated sodium chloride, dried ($MgSO_4$), and concentrated, giving 13 g of crude product. A pure sample of *trans*-2-ethylcyclobutanecarboxaldehyde was isolated by preparative VPC (Carbowax 20M, 95 °C): $[\alpha]D$ −8.30° (*c* 31.2, $CCl_4$); ir (neat) 2985 (alkane), 2830, 2730 (aldehyde CH), and 1740 $cm^{-1}$ (C=O); NMR ($CDCl_3$) δ 9.67 (d, 1, *J* = 2, CHO), 3.00–1.25 (m, 8), and 0.87 (t, 3, *J* = 7 Hz, $CH_3$).

Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.81; H, 10.60.

***trans*-2-Ethylcyclobutanecarbonitrile.** The ~13 g (~0.1 mol) of the preceding aldehyde ($[\alpha]D$ −8.30°) and 37 g (0.16 mol) of freshly prepared *N,O*-bis(trifluoroacetyl)hydroxylamine[72] were taken up in 70 ml of benzene. The reaction mixture was cooled to 0 °C and 25.6 ml (0.32 mol) of dry pyridine was added (exothermic reaction). This was allowed to stir for 10 h at room temperature. Ether (250 ml) was added and this was extracted with 1 N HCl, saturated aqueous sodium bicarbonate, and saturated sodium chloride. This was dried ($MgSO_4$) and concentrated, giving 6.6 g (60%) of the desired nitrile. A pure sample was isolated by preparative VPC (Carbowax 20M, 130 °C): ir (neat) 2960 (alkane) and 2240 $cm^{-1}$ (C≡N); NMR ($CCl_4$) δ 2.70–1.25 (m, 8) and 0.90 (t, 3, *J* = 7 Hz, $CH_3$).

Anal. Calcd for $C_7H_{11}N$: C, 77.01; H, 10.16; N, 12.83. Found: C, 77.16; H, 10.02; N, 12.66.

***cis*- and *trans*-2-Ethyl-1-methylcyclobutanecarbonitrile.** To 16 g (0.16 mol) of diisopropylamine in 50 ml of dry ether was added 66 ml of 2.25 M (0.15 mol) *n*-butyllithium under a nitrogen atmosphere. This was allowed to stir for 5 min and 6.6 g (0.06 mol) of *trans*-2-ethylcyclobutanecarbonitrile in benzene was added. After the mixture had stirred for 5 min, the reaction mixture was cooled to 0 °C and 100 ml of freshly distilled methyl iodide was added. The yellow reaction mixture was allowed to stir at room temperature for 1 h. This was extracted with water, 1 N HCl, and saturated sodium chloride. This was dried ($Na_2SO_4$) and concentrated, giving 7.4 g of crude product. VPC analysis (Carbowax 20M, 120 °C) indicated two components (2:1 ratio). Pure samples of the alkylated nitriles were isolated by preparative VPC and were not assigned. The major and first eluted isomer had the following NMR spectra: NMR ($CCl_4$) δ 2.48–1.58 (m, 7), 1.47 (s, 3, $CH_3$), and 0.90 (t, 3, *J* = 7 Hz, $CH_3$).

Anal. Calcd for $C_8H_{13}N$: C, 77.99; H, 10.64; N, 11.37. Found: C, 77.86; H, 10.57; N, 11.52.

The minor isomer had the following NMR spectra: NMR ($CCl_4$) δ 2.80–1.45 (m, 7), 1.38 (s, 3, $CH_3$), and 0.90 (t, 3, *J* = 7 Hz, $CH_3$).

Anal. Calcd for $C_8H_{13}N$: C, 77.99; H, 10.64; N, 11.37. Found: C, 77.88, H, 10.51; N, 11.46.

**Methyl *cis*- and *trans*-2-Ethyl-1-methylcyclobutanecarboxylate.** The ~7.4 g (0.06 mol) of unpurified mixture of isomeric nitriles in 100 ml of 50% sulfuric acid was allowed to reflux with stirring for 8 h. The reaction mixture was extracted twice with ether and the combined ethereal layers were extracted with saturated aqueous sodium bicarbonate. The basic aqueous layer was acidified to pH 2 and extracted with ether. The ethereal layer was dried ($MgSO_4$) and concentrated. This was treated with an ethereal solution of diazomethane. The reaction mixture was dried ($Na_2SO_4$) and concentrated, giving 4 g (43%) of unpurified product. Pure samples of the two isomeric methyl esters were isolated by preparative VPC (Carbowax 20M, 130 °C) and were not assigned. The first eluted isomer had the following spectra: ir (neat) 1735 $cm^{-1}$ (ester C=O); NMR ($CCl_4$) δ 3.63 (s, 3, $OCH_3$), 2.58–1.00 (m, 7), 1.33 (s, 3, $CH_3$), and 0.77 (t, 3, *J* = 7 Hz, $CH_3$). The second eluted isomer had the following spectra: ir (neat) 1735 $cm^{-1}$ (ester C=O); NMR ($CCl_4$) δ 3.62 (s, 3, $OCH_3$), 2.67–1.08 (m, 7), 1.23 (s, 3, $CH_3$), and 0.78 (t, 3, *J* = 7 Hz, $CH_3$).

***cis*- and *trans*-2-Ethyl-1-methylcyclobutylcarbinol.** The 4 g (0.026 mol) of unpurified esters in 25 ml of ether was added dropwise to a stirred suspension of 1 g (0.26 mol) of lithium aluminum hydride in ether. This was allowed to stir at room temperature for 1 h. To the reaction mixture was added 1 ml of water, 1 ml of 15% aqueous sodium hydroxide, and 3 ml of water. This was filtered, dried ($Na_2SO_4$), and concentrated, giving ~3 g (90%) of unpurified alcohol **79**. Pure samples of the two isomeric product alcohols were isolated by preparative VPC (Carbowax 20M, 140 °C) and were not assigned. The first eluted isomer had the following spectra: ir ($CCl_4$) 3675 (-OH) and 1030 $cm^{-1}$ (primary OH); NMR ($CCl_4$) δ 3.55 (s, 2 H, $CH_2OH$), 2.13–0.97 (m, 7), 1.20 (s, 1, OH), 1.10 (s, 3, $CH_3$), and 0.78 (t, 3, *J* = 7 Hz, $CH_3$).

The second isomer had the following spectra: ir ($CCl_4$) 3650 (OH), 1025, and 1250 $cm^{-1}$ (primary OH); NMR ($CCl_4$) δ 3.33 (s, 2, $CH_2OH$), 2.08–1.08 (m, 7), 1.17 (s, 1, OH), 1.00 (s, 3, $CH_3$), and 0.80 (t, 3, *J* = 7 Hz, $CH_3$).

**2-Ethyl-1-methylcyclobutylcarbinyl Methanesulfonate.** The 3 g (0.023 mol) of alcohols were allowed to react with 3 g (0.26 mol) of methanesulfonyl chloride, distilled from $P_2O_5$, in 30 ml of dry pyridine at 0 °C for 0.5 h. This was allowed to stand at −18 °C for 24 h. The red reaction mixture was poured over cracked ice and extracted with ether. The ethereal layer was extracted twice with 1 N HCl, twice with 10% aqueous sodium bicarbonate, and once with saturated sodium chloride. This ethereal solution was dried ($MgSO_4$) and used in the next reduction step without further purification.

**(*R*)-(−)-1,1-Dimethyl-2-ethylcyclobutane (28).** The ethereal solution of mesylate (0.023 mol) was added dropwise to a stirred suspension of 3.8 g (0.10 mol) of lithium aluminum hydride in 50 ml of dry ether. This was allowed to stir at room temperature for 16 h. Then, 4 ml of water, 4 ml of 15% aqueous sodium hydroxide, and 12 ml of water were added slowly at 0 °C. The granular salts were removed by filtering and the ethereal filtrate was extracted with 10% aqueous sodium bicarbonate and saturated sodium chloride. This was dried ($Na_2SO_4$) and concentrated. The pure hydrocarbon (*R*)-(−)-**28** was isolated by preparative VPC (SF-96, 75 °C), giv-

ing 0.507 g (19%): $[\alpha]_D$ −0.647 ± 0.018° (*c* 50.7, $CHCl_3$); ir (neat) 2960 (alkane), 1460 (alkane, $CH_2$), 1380, and 1370 $cm^{-1}$ (alkane, *gem*-dimethyl); NMR ($CCl_4$) δ 2.08–1.12 (m, 7), 1.05 (s, 3, $CH_3$), 0.98 (s, 3, $CH_3$), and 0.78 (t, 3, $J$ = 7 Hz, $CH_3$).

Anal. Calcd for $C_8H_{16}$: C, 85.63; H, 14.37. Found: C, 85.78; H, 14.45.

**Correlation of (1*S*,2*S*)-(+)-*trans*-1,2-Cyclobutanedicarboxylic Acid (33) to (1*S*,2*S*)-(+)-Dimethyl *trans*-1,2-Cyclobutanedicarboxylate (34).** (1*S*,2*S*)-(+)-*trans*-1,2-Cyclobutanedicarboxylic acid (**33**), resolved by way of its quinine salt according to the method of Goldsworthy,[44] was recrystallized from benzene and dried ($P_2O_5$) in a desiccator at 0.5 mm for 5 h. The diacid, mp 103–104.5 °C, was diluted to 100 ml with water, giving a specific rotation $[\alpha]^{23.6}_D$ 95.8° (*c* 0.81, $H_2O$). The water was removed under reduced pressure and the contents of the flask were taken up in ether. Ethereal diazomethane was added until a yellow color persisted. This was discharged with a few drops of acetic acid. The ethereal solution was washed once with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated. The pure dimethyl ester **34** was isolated by preparative VPC (Carbowax 20M, 170 °C): $[\alpha]^{240}_D$ 88.9° (*c* 21.1, $CCl_4$), 60.5% optically pure, based on the highest reported rotation[47] for the diacid **80** of $[\alpha]^{18.5}_D$ −158° (*c* 0.75, $H_2O$).

**(1*R*,2*R*)-(+)-*trans*-1,2-Divinylcyclobutane (3a).** Optically active **3a** was prepared from (1*S*,2*S*)-(+)-dimethyl *trans*-1,2-cyclobutanedicarboxylate (**34**), $[\alpha]^{24.1}_D$ 56.2 (*c* 20.3, $CCl_4$), 38.2% optically pure, by reduction to the dialdehyde, which then was treated with methylidenetriphenylphosphorane. The procedure followed that described for the dipropenyl series cTT-**8**, cCT-**8**, and cCC-**8**. Pure (1*R*,2*R*)-(+)-**3a**, 1.03 g (23%), was isolated by VPC (SE 30, 100 °C), $[\alpha]^{23}_D$ 37.8°, $[\alpha]^{23}_{365}$ 128° (*c* 18.2, $CCl_4$).

**Correlation of (1*R*,2*R*)-(+)-*trans*-1,2-Divinylcyclobutane (3a) to (1*S*,2*S*)-(+)-Dimethyl *trans*-1,2-Cyclobutanedicarboxylate (34).** Ozone was passed through 350 mg (0.003 mol) of (1*R*,2*R*)-(+)-**3a** ($[\alpha]^{23}_D$ 37.8°) in 30 ml of methanol at −78 °C, until the KI trap turned dark. The reaction mixture was concentrated at room temperature under reduced pressure and the remaining colorless liquid was taken up in 6 ml of formic acid (90%). Then, 3 ml (0.035 mol) of 30% hydrogen peroxide was added dropwise. The reaction mixture was heated at 55 °C for 4 h. This was concentrated under reduced pressure and 40 ml of ether was added. Ethereal diazomethane was added directly to this flask until a yellow color persisted, which was discharged with a few drops of acetic acid. The ethereal solution was extracted with saturated aqueous sodium bicarbonate and saturated sodium chloride. This was dried ($MgSO_4$) and concentrated. The dimethyl ester, (1*S*,2*S*)-(+)-**34**, was isolated by preparative VPC (Carbowax 20M, 160 °C): $[\alpha]^{23.1}_D$ 54.8°, 37.2% optically pure.

**Direct Determination of the Enantiomeric Composition[46] of (1*S*,2*S*)-(+)-Dimethyl *trans*-1,2-Cyclobutanedicarboxylate.** To a solution of 18 mg (0.10 mmol) of dimethyl ester **34**, $[\alpha]_D$ 56.2°, in ~1 ml of $CCl_4$ was added ~200 mg (0.10 mmol) of chiral NMR shift reagent tris[3-(heptafluorobutylhydroxymethylene)-*d*-camphorato]europium(III).[46] At 679-Hz offset, 54-Hz sweep width, and 250-s sweep time on a Jeolco 100 MHz instrument, two well-defined peaks were recorded for the nonequivalent *R* and *S* *O*-methyl protons. The pseudocontact shift difference for enantiomers (ΔΔδ) was 0.15 ppm. The NMR spectrum was photocopied five times and the peak areas were determined by the cut and weigh method. The ratio of peak areas, corresponding to enantiomeric composition, was 69.3 ± 0.6:30.7 ± 0.6. The optical purity of **34**, $[\alpha]_D$ 56.2°, is 38.6 ± 1.2% and the maximum rotation is 145 ± 5°.

**Correlation of (*R*)-(+)-3-Methylcyclohexanone (36) to (*R*)-(+)-4-Methylcyclohexene (35a) and (*R*)-(+)-3-Methylcyclohexene (35b) (Scheme VIII).** According to the method of Dauben and Shapiro,[73] a solution of 11.2 g (0.10 mol) of (*R*)-(+)-3-methylcyclohexanone (**36**) (Aldrich), $[\alpha]^{24}_D$ 12.5° (1 dm, neat), $[\alpha]^{24}_D$ 14.6° (*c* 14.2, $CHCl_3$), 18.6 g (0.10 mol) of *p*-toluenesulfonylhydrazine and 5 drops of concentrated HCl in 60 ml of dry THF was allowed to reflux for 6 h. Then, 50 ml of benzene was added and the THF and benzene–water azeotrope was removed by distillation at atmospheric pressure. The distillation was continued until the temperature was near 80 °C. The reaction mixture was cooled in an ice bath and 100 ml of 2.2 M methyllithium (0.23 mol) was added dropwise over a 40-min period with stirring. Water was added slowly and the mixture was extracted with pentane. The pentane layer was extracted with water and saturated sodium chloride. This was concentrated, dried ($MgSO_4$), and flash distilled under reduced pressure. The pure isomers 3- and 4-methylcyclohexene were isolated by preparative VPC, first as a mixture (MNPN, 75 °C), then separated from each other (DBT, 90 °C). The first eluted isomer (*R*)-(+)-3-methylcyclohexene (**35b**) had the same retention time and NMR as an authentic sample: $[\alpha]^{25}_D$ 89.4° (*c* 4.1, $CCl_4$), optically pure; ir (neat) 720 and 670 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CCl_4$) δ 5.57 (br s, 2, olefin), 2.40–1.15 (m, 7), and 0.97 (d, 3, $J$ = 6.5 Hz, $CH_3$).

The second eluted isomer, (*R*)-(+)-4-methylcyclohexene (**35a**), had the same retention time and NMR as an authentic sample: $[\alpha]^{24}_D$ 136° (*c* 4.5, $CCl_4$), optically pure; ir (neat) 650 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CCl_4$) δ 5.58 (m, 2, olefin), 2.27–1.10 (m, 7), and 0.95 (d, 3, $J$ = 5 Hz, $CH_3$).

**Correlation of (*R*)-(+)-4-Vinylcyclohexene (2a) to (*R*)-(+)-4-Methylcyclohexene (35a). (*R*)-(+)-4-Vinylcyclohexene (2a).** Following the procedure of Brown[74] for the asymmetric hydroboration of olefins, 250 ml of diglyme was distilled from lithium aluminum hydride under reduced pressure at 80 °C into a dry 500-ml flask equipped with a mechanical stirrer, addition funnel, and reflux condenser. The reaction was run under a nitrogen atmosphere with an acetone trap to scavenge excess diborane.

To the diglyme was added 7.9 g (0.21 mol, 10% excess) of sodium borohydride and 68.1 g (0.50 mol, $[\alpha]_D$ −42.1° (neat)) of α-pinene (Fluka) with stirring. The reaction mixture was cooled to 0 °C, and 35.5 ml (0.28 mol, 10% excess) of $BF_3{\cdot}Et_2O$, freshly distilled from calcium hydride, was added dropwise with stirring. This was allowed to stir for 5 h at 0 °C. The white reaction mixture (diisopinocampheylborane) was cooled to −18 °C and 54 g (0.50 mol) of 4-vinylcyclohexene (**2a**) (Aldrich) was added all at once with vigorous stirring. This was allowed to stir at −18 °C for 1.5 h and at room temperature for 2 h. Distillation of the reaction mixture at 25–40 °C (1 mm) afforded 135 ml of clear liquid, which was extracted three times with water and once with saturated sodium chloride. This was dried ($Na_2SO_4$), giving 28 g (0.26 mol) of (*R*)-(+)-4-vinylcyclohexene (**2a**) (104%), containing a small amount of α-pinene. A pure sample of (*R*)-(+)-**2a** was isolated by preparative VPC (SE-30, 135°): $[\alpha]^{23}_D$ 2.42 ± 0.03°, $[\alpha]^{23}_{365}$ 7.62 ± 0.06° (*c* 14.7, $CCl_4$).

**(*S*)-(+)-2-(4-Cyclohexenyl)ethanol (37).** 9-Borabicyclo[3.3.1]nonane (9-BBN) was prepared by the reaction of 1,5-cyclooctadiene with diborane in dry THF according to the method of Brown.[75]

To a solution of 24.4 g (0.20 mol) of 9-BBN in 200 ml of dry THF was added 24.5 g (0.23 mol) of (*R*)-(+)-4-vinylcyclohexene (**2a**), $[\alpha]_D$ 2.42°, at 0 °C under a nitrogen atmosphere. This was allowed to stir at room temperature for 1 h. Then, 100 ml of 6 M NaOH (0.60 mol) and 80 ml of 30% $H_2O_2$ (0.93 mol) was added and the reaction mixture was heated to 60 °C for 1.5 h. This was cooled and potassium carbonate was added until the aqueous phase was saturated. The organic layer was separated and distilled with the oil bath at 80–90 °C (1 mm), giving 16 g (64%) of the alcohol **37**: [lit.[79] bp 86–87 °C (6 mm)]. A pure sample of **37** was isolated by preparative VPC (FFAP, 180 °C): $[\alpha]^{24}_D$ 2.04°, $[\alpha]^{24}_{365}$ 6.60° (*c* 17.3, $CCl_4$); ir (neat) 3600–3100 (br, OH), 3010 (alkene), 1055 (primary OH), and 650 $cm^{-1}$ (alkene, cis); NMR ($CCl_4$) δ 5.60 (m, 2, olefin), 3.62 (t, 2, $J$ = 6 Hz, $CH_2OH$), and 2.50–1.00 (m, 10).

**2-(4-Cyclohexenyl)acetic Acid (38).** To a stirred solution containing 16 g (0.127 mol) of alcohol **37**, $[\alpha]^{24}_D$ 2.04°, in 200 ml of acetone was added Jones reagent[74] dropwise at 0 °C until the orange-brown color persisted. This was taken up in ether and extracted with water and saturated sodium chloride.

The ethereal layer was extracted with saturated aqueous sodium bicarbonate. The basic aqueous layer was acidified with 1 N HCl to pH 2 and extracted twice with ether. The combined ether extracts were washed once with saturated sodium chloride, dried ($MgSO_4$), and concentrated, giving 9.5 g (53%) of a pale yellow oil, the acid[9] **38**; NMR ($CCl_4$) δ 9.30 (s, 1, COOH), 5.60 (m, 2, olefin), and 2.43–0.85 (m, 9).

**2-(4-Cyclohexenyl)acetyl Chloride (39).** The 9.5 g (0.068 mol) of crude acid **38** was taken up in 60 ml of dry benzene. Then 25 ml of benzene was distilled from the reaction mixture to remove any traces of water. Oxalyl chloride (12.7 g, 0.10 mol) was added dropwise at room temperature under a nitrogen atmosphere. The reac-

tion mixture was allowed to stir for 2 h and the excess oxalyl chloride and benzene were removed under reduced pressure. The acid chloride **39** was distilled, giving 10 g (93%) of a colorless liquid: bp 25–36 °C (0.2 mm) [lit.[9] bp 95–96 °C (20 mm)].

***tert*-Butyl 2-(4-Cyclohexenyl)peroxyacetate.** According to the method of Wiberg,[76] the 10 g (0.063 mol) of acid chloride **39** was added to 8.5 g (0.094 mol) of *tert*-butyl hydroperoxide in 10 ml of dry pyridine and 30 ml of *p*-cymene at 0 °C under a nitrogen atmosphere. This was allowed to stir for 3 h. The reaction mixture was poured into cold, saturated sodium chloride and the layers were separated. The organic layer was extracted with cold 1 N HCl, cold 10% aqueous sodium bicarbonate, and cold saturated sodium chloride. This was dried ($MgSO_4$) and used in the decarboxylation step without isolation or further purification.

**(*R*)-(+)-Methylcyclohexene (35a).** The solution containing the peroxyacetate **40** in *p*-cymene was placed in a 250-ml flask equipped with a short-path condenser and a receiver cooled to −78 °C (dry ice–acetone). The reaction mixture was slowly heated to 140 °C and vigorous bubbling commenced. This temperature was maintained for 1 h and then raised to 180 °C. A sample of pure hydrocarbon **35a** was isolated from the 7.5 ml of distillate by preparative VPC (SE-30, 135 °C), giving 280 mg, which was then purified again by VPC (Carbowax 20M, 100 °C): $[\alpha]^{25}D$ 2.92°, $[\alpha]^{25}_{365}$ 9.40° (*c* 24.5, $CCl_4$). The product **35a** had the same VPC retention time (SE-30 and Carbowax 20M) and NMR spectrum as an authentic sample of 4-methylcyclohexene (Aldrich).

**(1*R*,2*R*)-(−)-*trans*-1,2-*cis*,*cis*-Dipropenylcyclobutane (tCC-9).** Optically active tCC-**9** was prepared from (1*S*,2*S*)-(+)-dimethyl *trans*-1,2-cyclobutanedicarboxylate (**34**), $[\alpha]^{23}D$ 67.8° (*c* 18.8, $CCl_4$), 46.1% optically pure, by reduction to the dialdehyde, which then was treated with ethylidenetriphenylphosphorane in the same manner as described in the cis series cTT-**8**, cCT-**8**, and cCC-**8**. The combined product from five separate runs was distilled (32 °C, (1.5 Torr)) to give 20.5 g (60% yield). VPC analysis on an analytical column (DBT capillary, 75 °C) indicated the ratio of isomers tTT-**9**, tCT-**9**, and tCC-**9** was 2:30:68, respectively. Pure (1*R*,2*R*)-(−)-*trans*-1,2-*cis*,*cis*-dipropenylcyclobutane (tCC-**9**) was isolated by preparative VPC ($AgNO_3$/Carbowax 200, 65 °C) and repassed on a Carbowax 20M column (105 °C): $[\alpha]^{21}D$ −101°, $[\alpha]^{21}_{365}$ −430° (*c* 11.0, $CCl_4$).

***trans*-1,2-Dipropenylcyclobutane diepoxide** was prepared in 86% yield by *m*-chloroperbenzoic acid oxidation of the above sample of **9**. A pure sample isolated by VPC (SF-96, 150 °C) had bp 46–50 °C (0.4 mm); ir (neat) 865, 845, and 795 $cm^{-1}$ (epoxide); NMR ($CDCl_3$) δ 2.92 (m, 4, OCH), 2.00 (m, 6, cyclobutane), and 1.22 (d, 6, $J$ = 5 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.46; H, 9.70.

**(1*R*,2*R*)-(+)-*trans*-1,2-*trans*,*trans*- and (1*R*,2*R*)-(−)-*trans*-1,2-*cis*,*trans*-dipropenylcyclobutane (tTT-9 and tCT-9)** were prepared from the above-described diepoxide by the Vedejs–Fuchs olefin inversion.[22] Distillation of the product gave a 37% yield of inverted olefins **9**. VPC analysis on an analytical column (DBT, capillary, 75 °C) indicated the ratio of isomers tTT-**9**, tCT-**9**, and tCC-**9** was 76:22:2, respectively.

Pure (1*R*,2*R*)-(+)-*trans*-1,2-*trans*,*trans*-dipropenylcyclobutane (tCT-**9**) was isolated by preparative VPC ($AgNO_3$/Carbowax 200, 65 °C) and repassed on a Carbowax 20M column (120 °C): $[\alpha]^{19}D$ 48.1°, $[\alpha]^{19}_{365}$ 156° (*c* 10.1, $CCl_4$).

Pure (1*R*,2*R*)-(−)-*trans*-1,2-*cis*,*trans*-dipropenylcyclobutane (tCT-**9**) was isolated by preparative VPC ($AgNO_3$/Carbowax 200, 65 °C) and repassed on a Carbowax 20M column (105 °C): $[\alpha]^{20}D$ −20.9°, $[\alpha]_{365}$ −109° (*c* 11.0, $CCl_4$).

**Correlation of (1*R*,2*R*)-(−)-tCC-9 to (1*S*,2*S*)-(+)-Dimethyl *trans*-1,2-Cyclobutanedicarboxylate (34).** Ozone was passed through 300 mg (22 mmol) of (1*R*,2*R*)-(−)-tCC-**9** ($[\alpha]^{21}D$ −101°) in 30 ml of methanol at −78 °C until the KI trap turned dark. The reaction mixture was concentrated at room temperature under reduced pressure. The remaining colorless liquid was taken up in 6 ml of formic acid (90%) and 2 ml (0.025 mol) of 30% hydrogen peroxide was added. The reaction mixture was heated at 55 °C for 4 h. This was concentrated under reduced pressure and ether was added. Ethereal diazomethane was added directly to this flask until a yellow color persisted, which was discharged with a few drops of acetic acid. The ethereal solution was extracted with saturated aqueous sodium bicarbonate and saturated sodium chloride. This was dried ($MgSO_4$) and concentrated. The dimethyl ester, (1*S*,2*S*)-(+)-**34**, was isolated by preparative VPC (Carbowax 20M, 165 °C): $[\alpha]^{22}D$ 59.3° (*c* 9.3, $CCl_4$), 40.3% optically pure. This corresponds to 87.5% of the optical purity of the starting diester **34**. The maximum rotations given in Table II are based upon the assumption that the amount of racemization in tTT-**9** and tCT-**9** is the same as that in the precursor tCC-**9** used in the olefin inversion and that the extent of racemization in the latter is represented by the 12.5% loss of optical purity revealed in the ozonolysis. The most likely source of racemization is the cyclobutane dialdehyde used in the Wittig ethylidenation.

**Correlation of (3*R*,4*S*)-(−)-Methyl 3-*cis*-Methylcyclohexene-4-carboxylate (43) and (3*R*,4*R*)-(−)-Methyl 3-*trans*-Methylcyclohexene-4-carboxylate (44).** The quinine salt[77] of *cis*-3-methylcyclohexene-4-carboxylic acid (**41**) was taken up in 300 ml of 3 N HCl and extracted three times with 100 ml of chloroform. The organic layer was separated and extracted three times with saturated aqueous sodium bicarbonate. The aqueous layer was acidified to pH 2 with HCl. This was extracted three times with 100 ml of methylene chloride. The organic layer was separated and extracted with saturated sodium chloride. This was dried ($Na_2SO_4$), concentrated, and distilled at 80–82 °C (0.3 mm), giving 9 g of the carboxylic acid **41**.

Ethereal diazomethane, made from *N*-nitrosomethylurea, was added to the 9 g (0.064 mol) of acid **41** in ether. This was concentrated and flash distilled. VPC analysis (Carbowax 20M, 150 °C) indicated the cis ester **43** was 99% isomerically pure. This was then purified by preparative VPC (Carbowax 20M, 160 °C), giving 4.5 g of isomerically pure (3*R*,4*S*)-(−)-methyl *cis*-3-methylcyclohexene-4-carboxylate (**43**).

Epimerization of 1.1 g (7 mmol) of pure (3*R*,4*S*)-(−)-**43** was accomplished with sodium methoxide in methanol, according to the procedure already described for the racemic modification. VPC analysis (Carbowax 20M, 180 °C) of the epimerized ester, 0.8 g (73%), indicated the *trans*-**44**/*cis*-**43** ratio was 3:1. The isomers were separated and isolated by preparative VPC (Carbowax 20M, 190 °C). The major and first eluted isomer was (3*R*,4*R*)-(−)-methyl *trans*-3-methylcyclohexene-4-carboxylate (**44**): $[\alpha]^{21}D$ −37.3° (*c* 16.6, $CCl_4$), 46.4% optically pure.

The minor and second eluted isomer was (3*R*,4*S*)-(−)-methyl *cis*-3-methylcyclohexene-4-carboxylate (**43**): $[\alpha]^{21}D$ −138° (*c* 16.6, $CCl_4$), 46.4% optically pure.

**Correlation and Synthesis of (3*R*,4*R*)-(−)-*cis*-3-Methyl-4-*trans*-propenylcyclohexene (cT-12) and (3*R*,4*R*)-(−)-*cis*-3-Methyl-4-*cis*-propenylcyclohexene (cC-12).** Into a three-neck, 250-ml flask equipped with mechanical stirrer, addition funnel, low-temperature thermometer (−70 °C), and under nitrogen atmosphere was placed 3.4 g (0.022 mol) of (3*R*,4*S*)-(−)-methyl *cis*-3-methylcyclohexene-4-carboxylate (**43**) ($[\alpha]^{21}D$ −138°, 46.4% optically pure) in 90 ml of dry ether. This was cooled to −70 °C (dry ice–methoxyethanol bath). Then, 3.5 ml (0.011 mol) of $NaAlH_2(OCH_2CH_2OCH_3)_2$ as a 70% benzene solution (Vitride, Eastman) diluted with 20 ml of dry ether was added dropwise via the addition funnel, maintaining the temperature at −70 °C. The reaction mixture was allowed to stir for 19 h at −70 °C.

Ethylidenetriphenylphosphorane (0.022 mol), prepared as described previously, was added directly to the aldehyde **14d** at −70 °C. This was allowed to warm to 10 °C and 9.3 g (0.050 mol) of potassium *tert*-butoxide–*tert*-butyl alcohol complex (1:1) was added. The cream-colored reaction mixture was allowed to stir for 2 h at room temperature and 20 ml of dilute $H_2SO_4$ (1:5) was added slowly. Water was added and the reaction mixture was extracted once with 100 ml of pentane. The pentane layer was extracted with water, dilute aqueous sulfuric acid, 10% aqueous sodium bicarbonate, and saturated sodium chloride. This was dried ($MgSO_4$), concentrated, and distilled at ~70 °C (17 mm). The mixture of *cis*-3-methyl-4-propenylcyclohexenes (**12**) was isolated by preparative VPC (Carbowax 20M, 150 °N), giving 1.3 g (43%) of cT-**12** and cC-**12**. The isomers were separated by VPC ($AgNO_3$/Carbowax 200, 70 °C) and then passed through a Carbowax 20M column (135 °C). The minor and first eluted isomer was (3*R*,4*R*)-(−)-*cis*-3-methyl-4-*trans*-propenylcyclohexene (cT-**12**): $[\alpha]^{20}D$ −97.5°, $[\alpha]^{20}_{365}$ −331° (*c* 11.3, $CCl_4$). 46.4% optically pure.

The major and second eluted isomer was (3*R*,4*R*)-(−)-*cis*-3-methyl-4-*cis*-propenylcyclohexene (cC-**12**): $[\alpha]^{20}D$ −64.2°, $[\alpha]^{20}_{365}$ −210° (*c* 8.9, $CCl_4$), 46.4% optically pure.

**Correlation and Synthesis of (3*S*,4*R*)-(+)-*trans*-3-Methyl-4-*trans*-propenylcyclohexene (tT-13) and (3*S*,4*R*)-(+)-*trans*-3-**

**Methyl-4-*cis*-propenylcyclohexene (tC-13).**

According to procedures already described above, 11 g of *cis*-3-methylcyclohexene-4-carboxylic acid (**41**) was obtained from its quinine salt, esterified with ethereal diazomethane, and epimerized with sodium methoxide in methanol. The major isomer **44** was isolated 100% isomerically pure by preparative VPC (Carbowax 20M, 145 °C) to give 3.4 g (0.022 mol) of (3*S*,4*S*)-(+)-methyl *trans*-3-methylcyclohexene-4-carboxylate (**44**): $[\alpha]^{22}D$ 26.0° (*c* 16.7, $CCl_4$), 32.4% optically pure.

According to procedures already described above, this was reduced to the aldehyde with $NaAlH_2(OCH_2CH_2OCH_3)_2$ at −70 °C and then allowed to react with ethylidentriphenylphosphorane, giving 1 g (32%) of a mixture of (3*S*,4*R*)-(+)-*trans*-3-methyl-4-propenylcyclohexenes (**13**). These were isolated by preparative VPC (Carbowax 20M, 145 °C) and then separated ($AgNO_3$/Carbowax 200, 70 °C).

The minor and first eluted isomer was (3*S*,4*R*)-(+)-*trans*-3-methyl-4-*trans*-propenylcyclohexene (tT-**13**): $[\alpha]^{19}D$ 20.4°, $[\alpha]^{19}_{365}$ 83.0° (*c* 7.1, $CCl_4$), 32.4% optically pure.

The major and second eluted isomer was (3*S*,4*R*)-(+)-*trans*-3-methyl-4-*cis*-propenylcyclohexene (tC-**13**): $[\alpha]^{19}D$ 36.4°, $[\alpha]^{19}_{365}$ 144° (*c* 9.5, $CCl_4$), 32.4% optically pure.

**Direct Determination of the Enantiomeric Composition of (3*R*,4*S*)-(−)-Methyl *cis*-3-Methylcyclohexene-4-carboxylate (43).** Although the maximum rotations of *cis*- (and *trans*-) 3-methyl-4-*cis*-(and *trans*-) propenylcyclohexenes (cT-**12**, cC-**12**, tT-**13**, tC-**13**) seem firm on the basis of a chemical correlation to 3-methylcyclohexanone, it would be helpful to measure *directly* the enantiomeric composition of (3*R*,4*S*)-(−)-methyl *cis*-3-methylcyclohexene-4-carboxylate (**43**), the synthetic precursor to the four isomeric, optically active 3-methyl-4-propenylcyclohexenes **12** and **13**. Using the chiral NMR shift reagent, tris[3-heptafluoropropylhydroxymethylene)-*d*-camphorato)europium(III) (Eu-OPTISHIFT II, WBL),[46] the NMR spectrum of the nonequivalent *R* and *S* *O*-methyl protons of (3*R*,4*S*)-methyl *cis*-3-methylcyclohexene-4-carboxylate (**43**), $[\alpha]D$ −137° in $CCl_4$, was recorded (190-Hz offset, 50-Hz sweep width, and 250-s sweep time on a Varian A-60 instrument). The pseudocontact shift difference for enantiomers ($\Delta\Delta\delta$) was 0.04 ppm. The NMR spectrum was photocopied five times and the peak areas were determined by the cut and weigh method. The ratio of peak areas, corresponding to enantiomeric composition, was 26.8 ± 0.2:73.2 ± 1.6. Therefore, the optical purity of the *cis*-methyl ester **43**, $[\alpha]D$ −137°, is 46.4 ± 1.8% (from 73.2 ± 1.6 − 26.8 ± 0.2 = 46.4 ± 1.8) and the maximum rotation is 297 ± 11° (from 137/0.464), in excellent agreement with the maximum rotation ($[\alpha]D$, $CCl_4$) of 297° determined from the chemical correlations.

**Methyl Succinate.** Ethereal diazomethane was added to 1.18 g (0.01 mol) of succinic acid (Fisher) in ether. This was extracted with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), concentrated, and distilled, giving 1.05 g (72%) of the dimethyl ester: bp 41 °C (0.4 mm) [lit.[78] bp 80 °C (11 mm)].

***meso*-Dimethyl 2,3-Dimethylsuccinate and *dl*-Dimethyl 2,3-Dimethylsuccinate.** Ethereal diazomethane was added to 1.46 g (0.01 mol) of a mixture of *meso*- and *dl*-2,3-dimethylsuccinic acid (Aldrich), mp 192–194 °C, in ether. This was extracted with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), concentrated, and distilled, giving 1.33 g (91%) of the mixture of diesters, bp 42 °C (0.4 mm). VPC analysis (Carbowax 20M, 170 °C) indicated the meso and *dl* isomers in a ratio 95:5 (relative retention times 1.00 and 1.13, respectively). This assignment was made on the basis of the melting point of the mixture of diacids, 192–194 °C, since the *meso*- and *dl*-2,3-dimethylsuccinic acids have reported[79] mp 197–199 and 128–129 °C, respectively.

Dimethyl succinate has the same relative retention time (Carbowax 20M, 170 °N) as the *dl* ester.

***cis*-3,4-Dimethyl-*cis,cis*-cycloocta-1,5-diene (10).** The single, long-retention time product from the pyrolysis of *cis*-1,2-*trans,trans*-dipropenylcyclobutane (cTT-**8**) in a sealed tube at 158 °C for 19 h was isolated pure by VPC (Carbowax 20M, 140 °C) and assigned as *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**): ir (neat) 770, 745, 720, and 645 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.60–5.08 (m, 4, olefin), 3.12–2.44 (m, 4, allylic), 2.20–1.80 (m, 2, allylic), and 0.93 (d, 6, $J$ = 6 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.01; H, 11.91.

This same compound (~100 mg, 0.7 mmol), isolated by preparative VPC (DBT, 110 °C) from the pyrolysis of *trans*-1,2-*trans,trans*-dipropenylcyclobutane (tTT-**9**), was taken up in methanol and cooled to −78 °C. Ozone was passed through this solution until the KI trap turned dark. This was concentrated under reduced pressure. Then, 1 ml of 90% formic acid and 0.5 ml (6 mmol) of 30% hydrogen peroxide were added, and this was allowed to stir for 3 h at 55 °C. The reaction mixture was extracted once with saturated aqueous sodium sulfite and concentrated. Ether was added to the solid residue and this was esterified with ethereal diazomethane. The ethereal layer was extracted with saturated aqueous sodium bicarbonate and saturated sodium chloride, dried ($Na_2SO_4$), and concentrated. VPC analysis (Carbowax 20M, 170 °C) indicated two peaks having the same retention times as *meso*-dimethyl 2,3-dimethylsuccinate and methyl succinate, respectively, confirming the assignment of **51**.

***trans*-3,4-Dimethyl-*cis,cis*-cycloocta-1,5-diene (11).** The major, long-retention time product from the pyrolysis of *cis*-1,2-*cis,trans*-dipropenylcyclobutane (cCT-**8**) in a sealed tube at 173 °C for 24 h was isolated pure by VPC (Carbowax 20M, 130 °C) and assigned as *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**): ir (neat) 740, 720, 700, and 650 $cm^{-1}$ (alkene, disubstituted, cis); NMR ($CDCl_3$) $\delta$ 5.40 (m, 4, olefin), 2.36 (m, 6, allylic), and 1.02 (d, 6, $J$ = 6 Hz, $CH_3$).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.05; H, 11.90.

The major, long-retention time product from the pyrolysis of *cis*-1,2-*cis,cis*-dipropenylcyclobutane (cCC-**8**) in a sealed tube at 175 °C for 24 h was isolated pure by VPC (Carbowax 20M, 130 °C) and had the same NMR spectra and identical VPC retention time (spiking experiment) on two analytical VPC columns (MNPN and Carbowax 400) as compound **11**.

This same compound **11** was isolated by preparative VPC (DBT, 110 °C) from the pyrolysis of *trans*-1,2-*cis,trans*-dipropenylcyclobutane (tCT-**9**). According to procedures already described above, this was ozonized and, after oxidative workup, esterified with ethereal diazomethane. VPC analyis (Carbowax 20M, 170 °C) indicated one peak, having the same retention time as *dl*-dimethyl 2,3-dimethylsuccinate and methyl succinate, confirming the assignment of **11**.

***trans*-3,4-Dimethyl-*cis,trans*-cycloocta-1,5-diene (16).** A solution of 1.3 g (0.0098 mol) of pure *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**) in 15 ml of $CH_2Cl_2$ was cooled to 0 °C and 2.3 g (0.011 mol, 15% excess) of 85% *m*-chloroperbenzoic acid in 30 ml of $CH_2Cl_2$ was added dropwise over a period of 20 min. The suspension was stirred at room temperature for 4 h, extracted with $Na_2CO_3$, water, and brine, dried over $MgSO_4$, and the solution concentrated on a rotatory evaporator. The monoepoxide was isolated by preparative VPC (SF-96, 122 °C, retention time ~12 min) to give 661 mg of pure material: NMR ($CDCl_3$) $\delta$ 1.10 (d × d, 6 H, methyl), 7.60–8.30 (m, 6 H, H(3,4,7,8)), 7.35 (d × d, 1 H, H(5)), 7.05 (m, 1 H, H(6)), and 4.5 (m, 2 H, vinyl).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.86; H, 10.61. Found: C, 78.72; H, 10.58.

Olefin inversion was accomplished by the general method of Vedejs.[22] All equipment was flame dried and argon purged. The reaction was run under a static pressure of argon. A solution of 0.200 g (0.0013 mol) of monoepoxide in 0.4 ml of dry THF was added in one portion to 1.87 ml (0.0013 mol) of 0.70 M LPD solution at room temperature. The solution was stirred at room temperature until the brick red coor was nearly discharged (~10 min). To the tan solution was then added at 0 °C 0.21 g (0.0014 mol) of MeI (exothermic!). The resulting yellow homogeneous solution was stirred at room temperature for 7 h. The solution was diluted with cold pentane, washed with ten portions of ice-cold water to remove THF and methyldiphenylphosphine oxide, dried over $MgSO_4$ in the freezer, filtered, and stored as a dilute pentane solution in the freezer. An aliquot of the solution was stripped of solvent on the rotatory evaporator at room temperature to give a clear, colorless mobile liquid possessing a strong characteristic odor: ir (neat) 990 (trans) and 720 $cm^{-1}$ (cis). Comparison of the ir of **11** and **16** indicated none of the former was present.

A solution of the cis,trans-diene **16** in chloroform was treated with several milligrams of iodine and stored in the dark at room temperature for 30 h. Appearance of a characteristic NMR signal at $\delta$ 5.37 indicated isomerization to *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**) had occurred.

**Pyrolysis of *trans*-3,4-Dimethyl-*cis,trans*-cycloocta-1,5-diene (16). Sample 1.** A solution of 25 mg of decane (internal standard) and 2.5 mg of **16** was prepared. A chromatogram from column DBT (75 °C) showed numerous peaks between the responses for decane and

*trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**) (retention time 2.30 relative to decane). The amount of compound **11** was 8.9%.

The sample was heated at 146 °C for 500 s and the pyrolysis products diluted with pentane. A VPC trace (DBT column) indicated *only* (vide supra) three compounds with retention times longer than decane: *cis*-1,2-*trans,trans*-dipropenylcyclobutane (cTT-**8**), **11**, and *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**), whose retention times relative to decane were 1.17, 2.30, and 2.93, respectively. The corresponding retention times of authentic samples under the same set of conditions were 1.18, 2.34, and 2.99. On Carbowax 20M (80 °C) pyrolyzed sample 1 gave retention times of 1.50 and 2.07 for compounds **11** and **10**, respectively. Authentic samples of each under the same conditions gave respective relative retention times of 1.50 and 2.06. Further verification of the presence of **10** was obtained by an appropriately "spiked" aliquot of sample 1 that had been pyrolyzed for 1000 s (vide infra). Summation of the integrated peaks beyond decane indicated only a 30% mass balance, i.e., 70% of the pyrolyzed sample remained on the column. The normalized yields of **8**, **11**, and **10** were 19, 32, and 49%, respectively.

A duplicate sample 1 was heated at 146 °C for 1000 s. At the end of the heating period the pyrolysate was milky white, indicating the presence of polymer. A VPC trace (DBT, 75 °C) gave similar results: 35% mass balance, of which 6, 30, and 64% were **8**, **11**, and **10**, respectively.

**Sample 2.** A solution of 12 mg of decane, 22 mg of cT-**12**, 24 mg of tT-**13**, and 2.2 mg of **16** was prepared. A VPC trace (DBT) before pyrolysis showed the presence of **11**, but no **8** or **10**. The amount of **11** was 8.2%. Again, numerous responses appeared between the signals for decane and **11**.

Sample 2 was heated at 146 °C for 1000 s. The mass balance was 35.5% (DBT, 75 °C). The absolute amount of **11** was 8.7%, and the normalized amounts of **8**, **11**, and **10** were 1.6, 24, and 74%, respectively. As in sample 1, compounds **8**, **11**, and **10** were the only observable components in the pyrolysis of **16**.

**Thermal Reactions. Apparatus.** The analytical and preparative pyrolyses were carried out in a constant temperature SF-96 (GE Silicone Fluid) bath contained in an 8-l. stainless steel beaker. The temperature was measured with a Hewlett-Packard 2801A quartz thermometer at 146.54 ± 0.03 °C over a 3-h range. All analytical and preparative pyrolyses were run at this temperature, which can probably be stated as 146.5 ± 0.1 °C with confidence. The steel rod used to hold the pyrolysis semples for both the kinetic and preparative runs initially depressed the temperature to 146.3 ± 0.1 °C, which rose to 146.5 ± 0.1 °C over a period of 200 s.

**Analytical Pyrolyses (liquid phase).** Pyrex tubing, 3 × 100 mm, was allowed to stand in cleaning solution for 24 h. This was washed several times with distilled water, allowed to stand in concentrated ammonium hydroxide for 24 h, washed with distilled water, and dried in an air oven (110 °C).

The tubes were sealed at one end and filled by syringe with 5 μl of a solution of pure starting material and internal standard decane (usually ~2:1 ratio, respectively). Each tube was centrifuged, frozen in liquid nitrogen, and sealed on the vacuum line at 0.02 μm, giving a pyrolysis tube 60 mm in length.

These tubes were then bound by wire to a steel rod or placed in a specially constructed steel holder and lowered to a fixed position in the silicone fluid bath. Upon removal from the bath, the tubes were quenched in ice water, centrifuged, opened, and filled with 50 μl of solvent (heptane). This solution of pyrolysate was then syringed out of the tube (to ensure mixing) into a small screw-cap vial and analyzed by VPC.

The VPC columns used for analysis were a DBT capillary column (75 °C) and a 0.125-in. $AgNO_3$/Carbowax 200 column (50 °C). Decane (D) was purified by preparative VPC and used as the internal standard. It was assumed that the detector response for decane and the $C_{10}$ olefins was unity and linear over the entire range involved in the analyses. The relative retention times of starting material and products with respect to decane are given in Table VII. All dipropenylcyclobutane isomers that were separated on a preparative $AgNO_3$/Carbowax 200 column were passed through a 10-ft Carbowax 20M column (110 °C) to remove any possible impurities from column bleed that might affect the kinetics. All kinetic samples were isomerically pure (except where indicated) and were checked on the DBT capillary column before pyrolysis.

**Preparative Pyrolyses (liquid phase).** The preparative pyrolysis tubes, 1 × 6 cm with a 4 mm × 2 cm neck, were cleaned according to the procedure described above. A neat 200–1000 mg sample of pure, optically active starting material was added to this tube with a drawn-out pipet. The contents of the tube were frozen in liquid nitrogen and after one freeze–thaw cycle, the tube was sealed on the vacuum line at 0.05 μm. The pyrolysis tube was bound by wire to a steel rod and lowered to a fixed position in the silicone fluid bath. Upon removal from the bath, the tubes were quenched in cold water, frozen in liquid nitrogen, and opened. After the contents had been analyzed by VPC, the starting material and products were separated by preparative VPC (DBT, 110 °C).

Table VII

| Substrate | VPC relative retention times: DBT | VPC relative retention times: $AgNO_3$/Carbowax 200 |
|---|---|---|
| 1a | 0.12 | |
| 1b | 0.15 | |
| 3a | 0.29 | |
| $X_I$ | 0.39 | |
| 2a | 0.52 | |
| $X_{III}$ | 0.61–0.81 | |
| $X_{II}$ | 0.71–0.81 | |
| Decane | 1.00 | 1.00 |
| 4a | 1.14 | |
| tCT-9 | 1.16 | 3.54 |
| tTT-9 | 1.18 | 2.44 |
| cTT-8 | 1.18 | 3.72 |
| tCC-9 | 1.19 | 5.43 |
| cCT-8 | 1.35 | 6.60 |
| tT-13 | 1.39 | 2.64 |
| tC-13 | 1.41 | 3.98 |
| cCC-8 | 1.50 | 13.1 |
| cT-12 | 1.60 | 3.35 |
| cC-12 | 1.69 | 5.43 |
| 11 | 2.34 | |
| 10 | 3.00 | |

**Treatment of the Data.** The ratio of substrate to internal standard decane was recorded. Most of the VPC injections for each point were repeated at least twice to ensure the reproducibility of the results. Generally, five points were taken for the first-order rate constant, calculated by the method of least squares using a computer program written by Professor K. B. Wiberg[80] for the PDP-8 computer. In the six dipropenyl cases, the kinetic runs were done twice to determine some estimate of the error, expressed as one standard deviation, in the rate constant. In the *trans*-1,2-divinylcyclobutane case only one run was determined as it agreed in rate and product distribution with the work of Hammond and DeBoer.[14]

In the tCT ⇌ cCT and tCC ⇌ cCC systems, the pyrolyses do not follow first-order kinetics because of trans ⇌ cis reversibility. The kinetic scheme was solved numerically by the Runge–Kutta method using a computer program RUNGG written for the PDP-10 computer by Professor M. Saunders.[81] Two short subroutines, DERVA and DERVN, contained the eight differential equations which describe the kinetic schemes in Schemes II and III.

Early points in the kinetic runs provided approximate values of the rate constants. Numerical integration of the differential kinetic equations (14 rate constants) using these trial values then generated a set of reactant and product concentrations as a function of time. The approximate rate constants were adjusted until a satisfactory fit to the experimental data is obtained. Generally, when a change of ±10% in the estimated rate constant did not improve the fit to the experimental data, this was accepted as the refined value.

**Pyrolysis of *trans*-1,2-Divinylcyclobutane (3a).** Pyrolysis of 5-μl samples of *trans*-1,2-divinylcyclobutane (**3a**) and decane (2:1 ratio, respectively) was carried out in the liquid phase at 146.5 °C in the silicone fluid bath. VPC analysis on a DBT capillary column indicated three products, butadiene (**1a**), 4-vinylcyclohexene (**2a**), and *cis,cis*-cycloocta-1,5-diene (**4a**) in a ratio of 4:70.4:25.6, respectively. Least-squares analyses give a first-order rate constant for disappearance of starting material **3a**, $k = 0.98 \times 10^{-5}$ s$^{-1}$.

**Pyrolysis of *cis*-1,2-*trans,trans*-Dipropenylcyclobutane (cTT-8).** Pyrolysis of 5-μl samples of *cis*-1,2-*trans,trans*-dipropenylcyclobutane (cTT-**8**) and decane (0.7:1 ratio, respectively) was carried out in the liquid phase at 146.5 °C. VPC analyses on a 0.125-in. $AgNO_3$/Carbowax 200 and DBT capillary column indicate only one product,

Table VIII. Observed and Calculated (*) Relative Concentrations in the Pyrolysis of cCT-8

| tCT-9 | cCT-8 | tC-13 | cC-12 | $X_{II}$ | 1b | 11 | 10 | Time, s | |
|---|---|---|---|---|---|---|---|---|---|
| | 1.03 | | | | | | | | * |
| | 0.950 | | | | | | | | |
| 0.048 | 0.819 | | | | | 0.033 | | 900 | |
| 0.044 | 0.835 | 0.019 | 0.004 | 0.001 | 0.005 | 0.039 | 0.002 | 1 300 | * |
| 0.095 | 0.722 | | 0.005 | | | 0.074 | | 2 000 | |
| 0.090 | 0.716 | 0.040 | 0.008 | 0.002 | 0.010 | 0.079 | 0.004 | 2 200 | * |
| 0.168 | 0.516 | 0.074 | 0.015 | 0.003 | 0.020 | 0.147 | 0.007 | 4 000 | |
| 0.165 | 0.510 | 0.077 | 0.016 | 0.005 | 0.020 | 0.149 | 0.008 | 4 200 | * |
| 0.202 | 0.411 | | 0.018 | | | 0.172 | | 5 200 | |
| 0.200 | 0.410 | 0.096 | 0.021 | 0.006 | 0.025 | 0.183 | 0.010 | 5 500 | * |
| 0.212 | 0.369 | 0.097 | | | | 0.173 | | 6 000 | |
| 0.211 | 0.377 | 0.103 | 0.023 | 0.006 | 0.027 | 0.194 | 0.011 | 6 000 | * |
| 0.241 | 0.257 | 0.124 | 0.032 | | | 0.230 | 0.013 | 8 000 | |
| 0.244 | 0.256 | 0.125 | 0.029 | 0.007 | 0.033 | 0.233 | 0.013 | 8 000 | * |
| 0.278 | 0.134 | 0.156 | 0.040 | 0.001 | 0.036 | 0.277 | | 12 000 | |
| 0.273 | 0.139 | 0.155 | 0.040 | 0.009 | 0.040 | 0.277 | 0.015 | 12 000 | * |

Table IX. Observed and Calculated (*) Relative Concentrations in the Pyrolysis of tCT-9

| tCT-9 | cCT-8 | tC-13 | cC-12 | $X_{II}$ | 1b | 11 | 10 | Time, s | |
|---|---|---|---|---|---|---|---|---|---|
| 1.000 | | | | | | | | | |
| 0.809 | 0.035 | 0.065 | 0.053 | 0.003 | 0.021 | 0.012 | | 10 280 | |
| 0.813 | 0.030 | 0.067 | 0.057 | 0.003 | 0.018 | 0.012 | | 10 400 | * |
| 0.641 | 0.027 | 0.139 | 0.114 | 0.006 | 0.035 | 0.036 | | 23 534 | |
| 0.630 | 0.029 | 0.143 | 0.118 | 0.007 | 0.037 | 0.034 | 0.002 | 23 400 | * |
| 0.290 | 0.011 | 0.291 | 0.238 | 0.012 | 0.070 | 0.085 | | 63 800 | |
| 0.288 | 0.014 | 0.289 | 0.234 | 0.013 | 0.075 | 0.082 | 0.004 | 63 800 | * |

*cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**). Least-squares analysis of two runs gave a first-order rate constant for disappearance of starting material cTT-**8**, $k = (5.44 \pm 0.01) \times 10^{-3}$ s$^{-1}$.

There was a 6.3% impurity in the starting material cTT-**8** which could be tTT-**9** by the method of synthesis. This impurity had the same relative retention time as tTT-**9** on the DBT capillary and 0.125-in. $AgNO_3$/Carbowax 200 column and remained constant with respect to the internal standard throughout the pyrolysis of cTT-**8**.

**Pyrolysis of *trans*-1,2-*trans,trans*-Dipropenylcyclobutane (tTT-9).** Pyrolysis of 5-μl samples of *trans*-1,2-*trans,trans*-dipropenylcyclobutane (tTT-**9**) and decane (~1.4:1 ratio, respectively) was carried out in the liquid phase at 146.5 °C. VPC analysis on a 0.125-in. $AgNO_3$/Carbowax 200 and DBT capillary column indicated five products: 7.9% of piperylene (**1b**), 4.4% of unidentified product $X_I$, 33.8% of *trans*-3-methyl-4-*trans*-propenylcyclohexene (tT-**13**), 26.3% of *cis*-3-methyl-4-*trans*-propenylcyclohexene (nT-**12**), and 27.6% of *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**). Least-squares analysis of two runs gave a first-order rate constant for the disappearance of starting material tTT-**9**, $k = (1.58 \pm 0.04) \times 10^{-5}$ s$^{-1}$.

**Pyrolysis of *cis*-1,2-*cis,trans*-Dipropenylcyclobutane (cCT-8).** Pyrolysis of 5-μl samples of *cis*-1,2-*cis,trans*-dipropenylcyclobutane (cCT-**8**) and decane (~1:1 ratio, respectively) was carried out in the liquid phase at 146.5 °C. VPC analysis on a 0.125-in. $AgNO_3$/Carbowax 200 and DBT capillary column indicated seven products: piperylene (**1b**), unidentified products $X_{II}$, *trans*-1,2-*cis,trans*-dipropenylcyclobutane (tCT-**9**), *trans*-3-methyl-4-*cis*-propenylcyclohexene (tC-**13**), *cis*-3-methyl-4-*cis*-propenylcyclohexene (cC-**12**), *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**), and *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**). Since there is cCT ⇌ tCT interconversion and both isomers under the pyrolysis conditions give the same set of products, the kinetics are not first order and the product distribution varies with time. Least-squares analysis of two runs gave an observed first-order rate constant for the disappearance of starting material cCt-**8**, $k = (1.61 \pm 0.05) \times 10^{-4}$ s$^{-1}$.

This kinetic scheme was solved numerically using the computer program RUNGG described previously. Table VIII shows the experimental and numerically-generated (*) set of reactant and product concentrations as a function of time from the refined values of the 14 individual rate constants obtained (Scheme II). The refined first-order rate constant for disappearance of starting material cCT-**8** was $1.71 \times 10^{-4}$ s$^{-1}$.

The ratio of **11**/**10** was 94.7:5.3 measured by a large injection of the pyrolysate.

**Pyrolysis of *trans*-1,2-*cis,trans*-Dipropenylcyclobutane (tCT-9).** Pyrolysis of 5-μl samples of *trans*-1,2-*cis,trans*-dipropenylcyclobutane (tCT-**9**) and decane (~2:1 ratio, respectively) was carried out in the liquid phase at 146.5 °C. VPC analysis on a 0.125-in. $AgNO_3$/Carbowax 200 and DBT capillary column indicated the same seven products as found in the pyrolysis of cCT-**8**. Since there is tCT ⇌ cCT interconversion the kinetics are not first order and the product distribution varies with time. Least-squares analysis of two runs gave an observed first-order rate constant for the disappearance of starting material tCT-**9**, $k = (2.17 \pm 0.01) \times 10^{-5}$ s$^{-1}$. This kinetic scheme was solved numerically using the computer program RUNGG. Similarly, pyrolysis of optically active tCT-**9** (described in detail later) gave a set of reactant and product concentrations as a function of time. Table IX shows the experimental and numerically-generated (*) set of concentrations from this pyrolysis, using the refined rate constants of Scheme II. The refined first-order rate constant for disappearance of starting material tCT-**9** was $2.25 \times 10^{-5}$ s$^{-1}$.

The ratio of **11**/**10** was 94.7:5.3 measured by a large injection from the pyrolysis tube of 83% conversion of starting material tCT-**9**.

**Pyrolysis of *cis*-1,2-*cis,cis*-Dipropenylcyclobutane (cCC-8).** Pyrolysis of 5-μl samples of *cis*-1,2-*cis,trans*-dipropenylcyclobutane (cCC-**8**) and decane (~1.8:1 ratio, respectively) was carried out in the liquid phase at 146.5 °C. VPC analysis on a DBT capillary column indicated seven products: piperylene (**1b**), unidentified products ($X_{III}$), *trans*-1,2-*cis,cis*-dipropenylcyclobutane (tCC-**9**) *trans*-3-methyl-4-*cis*-propenylcyclohexene (tC-**13**), *cis*-3-methyl-4-*cis*-propenylcyclohexene (cC-**12**), *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**), and *cis*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**10**). Since there is cCC ⇌ tCC interconversion and both isomers under the pyrolysis conditions give the same set of products, the kinetics are not first order and the product distribution varies with time. Least-squares analysis of two runs gave an observed first-order rate constant for the disappearance of starting material cCC-**8**, $k = (1.56 \pm 0.03) \times 10^{-4}$ s$^{-1}$. This kinetic scheme was solved numerically using the computer program RUNGG. Table X shows the experimental and numerically-generated (*) set of reactant and product concentrations as a function of time from the refined velues of the 14 individual rate constants obtained (Scheme III). The refined first-order rate constant for disappearance of starting material cCC-**8** was $1.62 \times 10^{-4}$ s$^{-1}$.

The ratio of **11**/**10** was 99.4:0.6, measured by a large injection from

Table X. Observed and Calculated (*) Relative Concentrations in the Pyrolysis of cCC-8

| tCC-9 | cCC-8 | tC-12 | cC-12 | $X_{III}$ | 1b | 16 | 11 | Time, s | |
|---|---|---|---|---|---|---|---|---|---|
| | 1.86 | | | | | | | | |
| 0.188 | 1.60 | | | 0.010 | 0.022 | | 0.003 | 1 000 | |
| 0.189 | 1.60 | | 0.003 | 0.008 | 0.021 | 0.036 | 0.007 | 1 500 | * |
| 0.409 | 1.30 | | 0.004 | 0.032 | 0.057 | | 0.028 | 2 300 | |
| 0.398 | 1.30 | | 0.006 | 0.016 | 0.047 | 0.062 | 0.030 | 2 800 | * |
| 0.630 | 0.960 | 0.001 | 0.008 | 0.017 | 0.079 | | 0.088 | 4 400 | |
| 0.632 | 0.959 | 0.001 | 0.010 | 0.027 | 0.081 | 0.072 | 0.079 | 4 800 | * |
| 0.714 | 0.824 | | 0.011 | 0.015 | 0.113 | | 0.110 | 5 500 | |
| 0.718 | 0.828 | 0.001 | 0.012 | 0.031 | 0.096 | 0.070 | 0.103 | 5 800 | * |
| 0.905 | 0.519 | 0.001 | 0.018 | 0.017 | 0.140 | | 0.183 | 9 100 | |
| 0.905 | 0.521 | 0.002 | 0.018 | 0.042 | 0.141 | 0.054 | 0.177 | 9 100 | * |
| 1.00 | 0.297 | 0.004 | 0.025 | 0.005 | | | 0.245 | 14 400 | |
| 1.01 | 0.290 | 0.003 | 0.024 | 0.053 | 0.198 | 0.051 | 0.254 | 14 400 | * |

Table XI

| % conversion of cCC-8 | 13.8 | 28 | 45 | 49 | 54 | 71 | 83 |
|---|---|---|---|---|---|---|---|
| % **11** | 5.4 | 5.6 | 8.5 | 10.2 | 11.6 | 14.2 | 16.5 |

the pyrolysis tubes of 49 and 83% conversion of starting material cCC-**8**. The relative amount of *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**) increases with time. Table XI indicates the percent conversion of starting material cCC-**8** and percent **11** of the total products.

**Pyrolysis of *trans*-1,2-*cis,cis*-Dipropenylcyclobutane (tCC-9).** Pyrolysis of 5-μl samples of *trans*-1,2-*cis,cis*-dipropenylcyclobutane (tCC-**9**) and decane (~2.2:1 ratio, respectively) was carried out in the liquid phase at 146.5 °C. VPC analysis on a DBT capillary column indicated the same seven products as found in the pyrolysis of cCC-**8**. Since there is tCC ⇌ cCC interconversion, the kinetics are not first order and the product distribution varies with time. Least-squares analysis of two runs gave an observed first-order rate constant for the disappearance of starting material tCC-**9**, $k = (1.17 \pm 0.03) \times 10^{-5}$ $s^{-1}$. The kinetic scheme was solved numerically using the computer program RUNGG. Table XII shows the experimental and numerically-generated (*) set of reactant and product concentrations as a function of time from the refined values of the 14 individual rate constants obtained. The refined first-order rate constant for disappearance of starting material tCC-**9** was $2.70 \times 10^{-5}$ $s^{-1}$.

The ratio of **11**/**10** was 99.6:0.4, measured by a large injection from the pyrolysis tube at 41% conversion of starting material tCC-**9**.

There are five unidentified short-retention time products $X_{III}$ that are found in the pyrolysis of both tCC-**9** and cCC-**8**. The largest component appears to arise from cCC-**8** and is not stable under the pyrolysis conditions. These products, possibly acyclic trienes, totaled only ~6% of the product mixture and are treated in the analysis as a whole.

**Preparative Pyrolyses. Pyrolysis of (1*R*,2*R*)-(+)-*trans*-1,2-Divinylcyclobutane (3a).** A 600-mg sample of (1*R*,2*R*)-(+)-*trans*-1,2-divinylcyclobutane (**3a**), $[\alpha]^{23}D$ 37.8°, $[\alpha]^{23}_{365}$ 128° (*c* 18.2, $CCl_4$), 37.4% optically pure, was heated in the liquid phase at 146.5 °C for 24.5 h (57.7% total conversion of **3a**). The starting material, (1*R*,2*R*)-(+)-**3a**, and product, (*R*)-(+)-**2a**, were isolated from the pyrolysate by preparative VPC (Carbowax 20M, 100 °C).

The reisolated (1*R*,2*R*)-(+)-**3a**, $[\alpha]^{19}D$ 31.9°, $[\alpha]^{19}_{365}$ 108° (*c* 18.9, $CCl_4$), was 16% racemized. A one-point first-order rate constant for the loss of optical activity of **3a** was calculated, $k_\alpha = 1.96 \times 10^{-4}$ $s^{-1}$.

The 1,3-shifted product, (*R*)-(+)-4-vinylcyclohexene (**2a**), $[\alpha]^{19}D$ 3.16°, $[\alpha]^{19}_{365}$ 10.3° (*c* 18.8, $CCl_4$), was 2.8% optically pure. The rate of formation of 4-vinylcyclohexene (**2a**) is $(0.98 \times 10^{-5}\ s^{-1}) \times 0.704 = 6.90 \times 10^{-4}\ s^{-1}$.

**Pyrolysis of (1*R*,2*R*)-(+)-*trans*-1,2-*trans,trans*-Dipropenylcyclobutane (tTT-9).** A 1.5-g sample of (1*R*,2*R*)-(+)-*trans*-1,2-*trans,trans*-dipropenylcyclobutane (tTT-**9**), $[\alpha]^{19}D$ 48.1°, $[\alpha]^{19}_{365}$ 156° (*c* 10.1, $CCl_4$), 40.3% optically pure, was flash distilled on the vacuum line to remove any possible trace impurities resulting from isolation on a $AgNO_3$/Carbowax 200 column. The starting material was 100% pure on the DBT capillary column.

**Sample 1.** A 195-mg sample of (1*R*,2*R*)-(+)-tTT-**9** was heated in the liquid phase at 146.5 °C for 18 000 s (23.9% total conversion of tTT-**9**). The starting material was reisolated by preparative VPC (DBT, 110 °C), giving (1*R*,2*R*)-(+)-tTT-**9**, $[\alpha]^{20}D$ 43.6°, $[\alpha]^{20}_{365}$ 141° (*c* 8.5, $CCl_4$).

**Sample 2.** A 266-mg sample of (1*R*,2*R*)-(+)-tTT-**9** was heated in the liquid phase at 146.5 °C for 43 870 s (50.3% total conversion of tTT-**9**). The starting material was reisolated by preparative VPC (DBT, 110 °C), giving (1*R*,2*R*)-(+)-tTT-**9**, $[\alpha]^{19}D$ 38.8°, $[\alpha]^{19}_{365}$ 125° (*c* 8.0, $CCl_4$).

**Sample 3.** A 1.022-g sample of (1*R*,2*R*)-(+)-tTT-**9** was heated in the liquid phase at 146.5 °C for 87 740 s (75.8% total conversion of tTT-**9**). The starting material was re-isolated by preparative vpc (DBT, 110 °C), giving (1*R*,2*R*)-(+)-tTT-**9**, $[\alpha]^{20}D$ 31.3°, $[\alpha]_{365}$ 102°, (*c* 13.4, $CCl_4$).

From these three pyrolyses, the rate of racemization ($k_\alpha$) of (1*R*,2*R*)-(+)-tTT-**9** at 146.5 °C can be calculated. Least-squares analysis gives two first-order rate constants of $4.72 \times 10^{-6}$ and $4.76 \times 10^{-6}$ $s^{-1}$, measured at 365 and 589 mμ, respectively.

The two 1,3-shifted products were isolated by preparative VPC (DBT, 110 °C), giving (3*R*,4*S*)-(−)-*trans*-3-methyl-4-*trans*-propenylcyclohexene (tT-**13**), $[\alpha]^{20}D$ −17.5°, $[\alpha]^{20}_{365}$ −68.4° (*c* 12.8, $CCl_4$), 27.2% optically pure, and (3*R*,4*R*)-(−)-*cis*-3-methyl-4-*trans*-propenylcyclohexene (cT-**12**), $[\alpha]^{21}D$ − 63.4°, $[\alpha]^{21}_{365}$ −215° (*c* 10.7, $CCl_4$), 30.2% optically pure. VPC analysis on the DBT capillary column indicated the (3*R*,4*S*)-(−)-tT-**13** and (3*R*,4*R*)-(−)-cT-**12** were 97.7 and 100% pure, respectively.

**Pyrolysis of (1*R*,2*R*)-(−)-*trans*-1,2-*cis,trans*-Dipropenylcyclobutane (tCT-9).** A 1.2-g sample of (1*R*,2*R*)-(−)-*trans*-1,2-*cis,trans*-dipropenylcyclobutane (tCT-**9**), $[\alpha]^{20}D$ −20.9°, $[\alpha]^{20}_{365}$ −109° (*c* 11.0, $CCl_4$), 40.3% optically pure, was passed through a Carbowax 20M column (110 °C) to remove any possible trace impurities resulting from separation on a $AgNO_3$/Carbowax 200 column. The starting material was 100% pure on the DBT capillary column.

**Sample 1.** A 194-mg sample of (1*R*,2*R*)-(−)-tCT-**9** wa heated in the liquid phase at 146.5 °C for 10 280 s (19.0% total conversion of tCT-**9**). The starting material was reisolated by preparative VPC (DBT, 110 °C), giving (1*R*,2*R*)-(−)-tCT-**9**, $[\alpha]^{19}D$ −18.5°, $[\alpha]^{19}_{365}$ −97.5° (*c* 7.7, $CCl_4$), 35.7% optically pure.

**Sample 2.** A 236-mg sample of (1*R*,2*R*)-(−)-tCT-**9** was heated in the liquid phase at 146.5 °C for 23 534 s (36.4% total conversion of tCT-**9**). The starting material was reisolated by preparative VPC (DBT, 110 °C), $[\alpha]^{19}D$ −16.2°, $[\alpha]^{19}_{365}$ −84.2° (*c* 10.7, $CCl_4$), 31.0% optically pure.

**Sample 3.** A 1.253-g sample of (1*R*,2*R*)-(−)-tCT-**9** was heated in the liquid phase at 146.5 °C for 63 800 s (71.0% total conversion of tCT-**9**). The starting material was reisolated by preparative VPC (DBT, 110 °C, giving (1*R*,2*R*)-)-)-tCT-**9**, $[\alpha]^{20}D$ −10.5°, $[\alpha]^{20}_{365}$ −54.2° (*c* 12.5, $CCl_4$), 20.2% optically pure.

From these three pyrolyses, the rate of racemization ($k_\alpha$) of (1*R*,2*R*)-(−)-tCT-**9** at 146.5 °C can be calculated. Least-squares analysis gives two first-order rate constants of $1.09 \times 10^{-5}$ and $1.07 \times 10^{-5}$ $s^{-1}$, measured at 365 and 589 mμ, respectively.

The two 1,3-shifted products were isolated by preparative VPC (DBT, 110 °C), giving (3*R*,4*S*)-(−)-*trans*-3-methyl-4-*cis*-propenylcyclohexene (tC-**13**), $[\alpha]^{20}D$ −26.4°, $[\alpha]^{20}_{365}$ −104° (*c* 12.1, $CCl_4$), 23.4% optically pure, and (3*R*,4*R*)-(−)-*cis*-3-methyl-4-*cis*-propenylcyclobutane (cC-**12**), $[\alpha]^{20}D$ −39.4°, $[\alpha]^{20}_{365}$ −128° (*c* 11.1, $CCl_4$), 28.5% optically pure. VPC analysis on the DBT capillary column in-

Table XII. Observed and Calculated (*) Relative Concentrations in the Pyrolysis of tCC-9

| tCC-9 | cCC-8 | tC-13 | cC-12 | $X_{III}$ | 1b | 16 | 11 | Time, s | |
|---|---|---|---|---|---|---|---|---|---|
| 2.19 | | | | | | | | | |
| 2.02 | 0.115 | | 0.003 | | 0.048 | | | 4 000 | |
| 2.02 | 0.112 | 0.002 | 0.005 | 0.002 | 0.047 | 0.004 | 0.002 | 4 000 | * |
| 1.81 | 0.183 | 0.003 | 0.001 | 0.012 | 0.114 | | 0.017 | 9 500 | |
| 1.83 | 0.184 | 0.004 | 0.013 | 0.007 | 0.119 | 0.011 | 0.016 | 9 400 | * |
| 1.69 | 0.202 | 0.005 | 0.019 | 0.010 | 0.182 | | 0.038 | 14 700 | |
| 1.70 | 0.203 | 0.006 | 0.021 | 0.013 | 0.187 | 0.014 | 0.040 | 14 600 | * |
| 1.42 | 0.186 | 0.008 | 0.040 | 0.015 | 0.287 | | 0.112 | 29 900 | |
| 1.42 | 0.187 | 0.012 | 0.042 | 0.030 | 0.367 | 0.014 | 0.118 | 29 900 | * |
| 1.17 | 0.157 | 0.017 | 0.059 | 0.014 | 0.417 | | 0.184 | 47 200 | |
| 1.16 | 0.155 | 0.017 | 0.061 | 0.046 | 0.539 | 0.012 | 0.198 | 47 200 | * |

dicated the (3*R*,4*S*)-(−)-tC-**13** and (3*R*,4*R*)-(−)-cC-**12** were 97.7 and 99.6% pure, respectively.

The major long-retention time product, *trans*-3,4-dimethyl-*cis,cis*-cycloocta-1,5-diene (**11**), was also isolated by preparative VPC (DBT, 110°), $[\alpha]^{19}_{365}$ 0.0° (*c* 1.8, $CCl_4$).

The numerical analysis of this pyrolysis, using the computer program RUNGG, allows a dissection of that component of 1,3-shifted product that came from (1*R*,2*R*)-(−)-tCT-**9** by the direct pathway (tCT → tC and cC) and the indirect pathway (tCT → cCT → tC and cC). For the 63 800-s pyrolysis (71.0% total conversion of tCT), 86% of the tC-**13** and 97% of the cC-**12** came via the *direct* pathways, tCT → tC and cC, respectively.

**Controls.** Each of the four 1,3-shifted products (tT-**13**, tC-**13**, cT-**12**, and cC-**12**) and the two 3,4-dimethyl-*cis,cis*-cycloocta-1,5-dienes (**10** and **11**) were heated in the liquid phase at 146.5 °C for 155 h and shown to be stable under the pyrolysis condition by VPC analysis on the DBT capillary column.

A mixture of *cis*- and *trans*-piperylene was heated in decane at 146.5 °C for 48 h. VPC analysis on DBT capillary indicated only trace amounts (~2% of total piperylene) of what could be 3-methyl-4-propenylcyclohexenes.

All kinetic runs were checked for surface catalysis by pyrolyzing a duplicate sample with a plug of glass wool. None was found.

The 5-μl and preparative pyrolyses haved the same, both in rate and product distribution, for the divinyl- and dipropenylcyclobutanes studied.

**Dimerization of Piperylene.** Heating neat piperylene (85% trans and 15% cis) and a few crystals of pyrogallol in a sealed tube at 180–200 °C for 2 h gave 50–60% yields of dimers after distillation (40–45 °C (15 Torr)). Dilution of the piperylene (2 g) with heptane as an inert solvent (1 g) gave a mixture that required 18 h at 190 °C to give 1.004 g of distilled dimers.

The composition of the dimers was determined by VPC on the DBT column at 75 °C: 30% tT-**13**; 32% cT-**12**; 7% cC-**12**; 11% of "meta" dimers **46–48**; 8 and 2% of *cis*- and *trans*-3,4-dimethylcycloocta-dienes (**10** and **11**), respectively; and <7% of an unidentified component. Identification by isolation and NMR spectroscopy was carried out for tT-**13**, cT-**12**, cC-**12**, and **46–48**. The presence of a small amount of tC-**13**, which has (Table VII) a retention time very close to that of tT-**13**, was inferred by a preparative VPC isolation (FFAP, 125 °C or $AgNO_3$/Carbowax, 70 °C) of the tail of the tT-**13** peak and reinjection.

Under the same conditions, pure (>99%) *trans*-piperylene (Aldrich) gave essentially the same product distribution, except for the absence (<1%) of the cC-**12** component.

***trans*-Penta-1,3-diene-*1-d*.** Cyclohexene and tetrahydrofuran (THF) were freshly distilled from $CaH_2$. A solution of 32.4 g of cyclohexene in 30 ml of THF was treated at −10 °C with 208 ml of 0.98 N $BH_3$THF (Ventron). After 1 h at 0 °C, the reaction mixture was treated with 13.2 g of *trans*-pent-3-en-1-yne[55] in 20 ml of THF. The mixture was stirred for an additional 2 h at 0 °C, treated with 60 ml of $CH_3CO_2D$, and then with excess $NaOH/H_2O_2$. The organic layer was washed with 2 N NaOH and brine, dried over $MgSO_4$, and distilled. The enriched fraction so obtained then was carefully fractionated through a spinning-band column to give 11.0 g of a fraction consisting of four parts of *trans*-piperylene to one part of THF. Final purification of the piperylene was effected by preparative VPC ($AgNO_3$/Carbowax, 30–40 °C).

The NMR spectrum of a reference sample of pure *trans*-piperylene-*trans-1-d* showed absorptions at δ 6.5–5.6 (m, 3 H), 5.12 (d, *J* = 17 Hz, 1 H), 5.00 (d, *J* = 5 Hz, 0.1 H), and 1.72 (d, *J* = 6 Hz, 3 H).

**Methyl *cis*-2-Methylcyclohex-3-ene-1-carboxylate (54-IIa) (≡43)** was obtained as the major component (91%) of the $AlCl_3$-catalyzed reaction of methyl acrylate and *trans*-piperylene.[82] It was purified by VPC (FFAP, 190 °C) as the second eluting component of the adduct mixture. Epimerization with NaOMe/MeOH gave a mixture of two parts of **54a** and three parts of the trans isomer **53a**, from which 99% pure **53a** was obtained by preparative VPC. Both **53a** and **54a** also were obtained by esterification of the product from the uncatalyzed Diels–Alder reaction of piperylene and acrylic acid.[23]

Similarly, the C(6)-monodeuterio esters were prepared, **53-Ib** and **54-IIb** from the Diels–Alder reaction of methyl acrylate-*cis-3-d*[60] and piperylene and **53-IIb** by base epimerization of **54-IIb**. The C(5)-deuterated ester **54-IId** was obtained from methyl acrylate and *trans*-piperylene-*trans-d*. The dideuterio esters **54-IIc** and **53-Ic** were obtained by the catalyzed Diels–Alder route as the major and minor products from *trans*-piperylene-*trans-d* and methyl acrylate-*cis-3-d*.

At δ 2.05 the proton NMR spectrum of **54-IId** (C(5) deuterated) showed a signal of intensity 1.1 instead of the value of 2.0 shown by the undeuterated ester **54-IIa**. The NMR spectrum of **54-IIb** (C(6) deuterated) showed 1.0 proton at δ 1.72, while the peaks at 2.05 (H(5a)) and 2.60 (H(1a)) became sharper than those in **54-IIa**. This suggested that in **54-IIb** the $CO_2Me$ substituent was pseudo-equatorial and the C(5) deuterium, therefore, was pseudo-axial, so that the C(5)–C(6) and C(1)–C(6) axial–axial couplings were cancelled.

**54-IIc,** NMR: δ 5.70 (s, 2 H), 3.72 (s, 3 H), 2.64 (m, 2 H), 2.06 (m, 1 H), 1.82 (m, 1 HO), and 0.84 (d, 3 H).

**53-Ic,** NMR: δ 5.6 (m, 2 H), 3.62 (s, 3 H), 2.03 (m, 2 H), 1.88 (m, 1 H), 1.65 (m, 1 H), and 0.90 (d, 3 H).

Treatment of samples of **53-IIa** and **54-IIc** with $Eu(fod)_3$[59a] caused pronounced lanthanide-induced shifts (LIS), but failed to separate the C(5) and C(6) absorptions satisfactorily into identifiable axial and equatorial peaks.

**The Synthetic Epoxy Esters. Unlabeled Series. Cis Isomers 51a and 52a.** To a solution of 2.10 g (12.4 mmol) of *m*-chloroperbenzoic acid in 100 ml of $CHCl_3$ at 0 °C was added slowly 1.54 g (10 mmol) of methyl *cis*-2-methylcyclohex-3-ene-1-carboxylate (**54-IIa**) (≡**43**). After being kept overnight, the solution was washed with 10% $NaHCO_3$ and dried over $MgSO_4$. Evaporation left a crude product which was distilled to give a quantitative yield of material, bp 48–50 °C (1 Torr). VPC analysis (Carbowax, 200 °C) showed two components in a ratio of 80:20. Epoxidation with peracetic acid was less stereospecific; giving the same two products in a ratio of 68:32.

The major product eluted first and was isolated in >99% purity. It was identified as the anti isomer **51a** on the basis of its LIS NMR spectrum (see below) and also on the grounds that its formation should be sterically more favorable than that of the cis isomer. Moreover, this preference should be greater with a bulkier epoxidizing agent, as was observed: ir 2935, 1720, 1178, 1160, and 1098 $cm^{-1}$; NMR δ 3.76 (s, 3 H), 3.13 (m, 1 H), 2.99 (m, 1 H), 2.76 (m, 1 H), 2.65 (m, 1 H), 2.05 (m, 1 H), 1.96 (m, 1 H), 1.8–1.3 (m, 2 H), and 1.01 (d, 3 H).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.52; H, 8.24. Found: C, 63.52; H, 8.29.

The minor product was **52a:** ir 2940, 1725, 1540, 1530, 1442, 1258, 1230, 1190, 1158, and 1143 $cm^{-1}$; NMR δ 3.76 (s, 3 H), 3.2 (m, 2 H), 2.7–2.1 (m, 3 H), 1.8–1.4 (m, 3 H), and 0.98 (s, 3 H).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.52; H, 8.24. Found: C, 63.57; H, 8.31.

**Trans Isomers 49a and 50a.** A mixture of 770 mg (5 mmol) of pure methyl *trans*-2-methylcyclohex-3-ene-1-carboxylate (**53-IIa**) (≡**44**), 5.0 g of anhydrous sodium acetate, and 60 ml of $CHCl_3$ was cooled to 0 °C and treated with 900 mg of 40% peracetic acid. After 15 h, the sodium acetate was dissolved by the addition of 40 ml of water and the organic layer was washed with $NaHCO_3$ and dried over $MgSO_4$. Evaporation left 800 mg of crude product, which consisted of a 1:1 mixture of **49a** and **50a**.

The first eluted component was obtained 98% pure and identified by its LIS spectrum (see below) as the *anti*-3-carbomethoxy-*syn*-2-methyl-7-oxabicyclo[4.1.0]heptane (**49a**): ir 2925, 1730, 1177, 1150, and 1090 $cm^{-1}$; NMR 3.70 (s, 3 H), 3.12 (m, 1 H), 2.98 (m, 1 H), 2.4–1.2 (m, 6 H), 1.10 (d, 3 H).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.52; H, 8.24. Found: C, 63.47; H, 8.30.

The second eluted component was *syn*-3-carbomethoxy-*anti*-2-methyl-7-oxabicyclo[4.1.0]heptane (**50a**): ir 2940, 2920, 1722, 1187, 1141, 1122, and 1092 $cm^{-1}$; NMR $\delta$ 3.62 (s, 3 H), 3.03 (m, 1 H), 2.68 (d, 1 H), 2.4–1.3 (m, 6 H), 1.05 (d, 3 H).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.52; H, 8.24. Found: C, 63.56; H, 8.32.

**The Monodeuterated Series.** The cis isomers **55** and **56** were prepared by application of the above described peracetic acid oxidation to the deuterated ester methyl *cis*-2-methylcyclohex-3-ene-1-carboxylate-*cis*-6-*d* (**54-IIb**). The isomers **55** and **56** were purified in the same way as the undeuterated analogues **51a** and **52a**.

Compound **56** showed a proton NMR spectrum similar in groupings of peaks to that of its undeuterated analogue **52a,** except that the 3 H multiplet at $\delta$ 1.8–1.4 was reduced in intensity to 2 H. This places the chemical shift of H(4a) in **52a** in the $\delta$ 1.8–1.4 region, in rough agreement with the value $\delta$ 1.2 extrapolated from LIS exriments (see below).

Similarly, compound **55** showed a decrease of 1 H in the intensity of the 2 H $\delta$ 1.8–1.3 absorption as compared to its undeuterated analogue **51a,** which fixes the chemical shift of H(4e) of the latter compound in the $\delta$ 1.8–1.3 region. The value extrapolated from LIS measurements on **51a** is $\delta$ 1.8.

**LIS Spectra of the Model Compounds.** The values of the mole ratio $Eu(fod)_3$/substrate (E/s) within one shift experiment are comparable, since the measurements were made upon a stock sample which was treated with increasing amounts of $Eu(fod)_3$. Values of E/s for different samples are only roughly comparable, since the absolute concentrations are only roughly known (ca. 0.4 ml of solvent for each sample). All measurements were in $CCl_4$, unless otherwise stated.

Treatment of the deuterated compound **55** with $Eu(fod)_3$ at E/s = 0.66 gave a sample upon which the following spin decoupling experiments were carried out. Irradiation at the Me doublet caused the signal at $\delta$ 9.55 to sharpen, thereby identifying the absorption of H(2). Irradiation at $\delta$ 5.62, the absorption of H(5a), collapsed the H(4a) absorption at $\delta$ 8.38 from a d × d ($J$ = 15 and 4 Hz) to a doublet ($J$ = 4 Hz). This confirms the equatorial conformation of the deuterium in **55**.

Systematic addition of $Eu(fod)_3$ up to values of E/s ~ 0.8 to samples of the undeuterated compounds **49a, 50a, 51a,** and **52a** caused linear downfield shifts of the proton signals. Higher E/s values caused nonlinearity in some cases, perhaps because of complexing with the $CO_2CH_3$ group. Extrapolation of the linear plots ($\delta$ vs. E/s) for each proton gave the chemical shift for each proton, since in most cases the signals were well separated at high E/s values and could be followed without difficulty. The extrapolated $\delta$ value for each proton then was subtracted from its observed position at each E/s value to give $\Delta\delta$ and a new plot of $\Delta\delta$ vs. E/s gave a series of lines with slopes characteristic of each proton's LIS sensitivity. These data are collected in Table XIII, with the slopes for each compound normalized to that for H(1) or H(6), whichever had the greater slope, defined as 1.00. The distinction between H(1) and H(6) at this point of the argument is arbitrary, but final assignments become possible with the double irradiation experiments to be described on the dideuterated series.

The data suggest that the major complexing with $Eu(fod)_3$ occurs at the epoxy function, as would be expected.[59c] The LIS spectra of **49a** permit the identification of coupling constants of 10, 10, and 3 Hz for H(3), which is in accord with the values expected for an axial proton coupled to two other axial protons and one equatorial proton. In **49a,** H(4a) is anti to the epoxide function and shows only a small slope, but in **50a, 51a,** and **52a** H(4a) is syn to the epoxide and has a large slope, especially in **52a.** The assignment of H(4a) in **52a** is confirmed in the LIS spectrum of the 4-axial monodeuterated analogue **56,** for which all the slopes have values identical with those of **52a,** except that the largest slope (1.45) is missing. Moreover, only **52a** in this series has an axial methyl group syn to the epoxy function, in accord with the observation that only **52a** has a large methyl slope.

At E/s = 0.32, compound **50a** was subjected to spin decoupling. Irradiation at the Me doublet $\delta$ 1.35 caused collapse of the $\delta$ 5.21 (H(2a)) signal from a multiplet to a perturbed doublet, and conversely, irradiation at $\delta$ 5.21 caused collapse of the $\delta$ 1.35 doublet to a sharp singlet. Irradiation at $\delta$ 2.40 assigned to H(5a) produced a sharpened signal at $\delta$ 4.95, which is attributed to H(4a).

**The Labeled Dimers.** The product *trans*-penta-1,3-diene-*1-d* from the reduction of 23.1 g of *trans*-pent-3-en-1-yne was distributed into three Pyrex Carius tubes, each containing 40–50 mg of pyrogallol, and heated at 195–200 °C for 8–20 h. Distillation gave 7.6 g of crude dimers. Separation on an SE-30 VPC column at 120 °C, recycling fractions when necessary, gave two fractions. Fraction I, 1.14 g, consisted of 2% of unidentified compounds, 6.5% of cC-**12,** and 91.5% of cT-**12** as determined by analysis with the DBT capillary column. Fraction II, 1.57 g, consisted of 12% of cT-**12,** 16% of unidentified components, the major one of which had the same retention time as tC-**13,** and 72% of tT-**13.**

In preliminary experiments with unlabeled dimers, it was established that the degradation of the dimers to epoxy esters could be carried out with fractions of composition similar to those above. Most of the impurities were destroyed in the $RuO_4$ step, and the remaining ones did not interfere with the final purification of the epoxy esters.

A known weight (160.73 mg) of tT-**13**-$d_2$ was diluted with a known weight (173.07 mg) of $CDCl_3$, which corresponds to a mole ratio of 0.81 dimer/$CDCl_3$. The deuterium intensity ratio for 2 D was thus 1.62. The deuterium NMR was recorded at three different amplitudes (Bruker 270[57]). The spectrum showed three well-separated absorptions, the two upfield peaks being due to dimer, and the downfield one to $CDCl_3$. The intensities of the two dimer peaks were identical within 2%, and their sum was 90.5 ± 1.7% of 1.62 times the intensity of the $CDCl_3$ peak.

Deuterium analysis of the tT-**13**-$d_2$ sample by the falling drop technique[58] showed 10.95 atom % excess D, corresponding to 87.7 ± 1% 2 D. The mass spectrum showed a base peak at $m/e$ = 69, corresponding to the monomer, but analysis for deuterium content was unreliable by this method because of strong M − 1 and M − 2 peaks in the monomer spectrum.

**Conversion of the Dimers to Epoxy Esters.** To 620 mg (4.5 mmol) of tT-**13**-$d_2$ and 4.0 g of anhydrous sodium acetate in 50 ml of $CH_2Cl_2$ was added at 0 °C 1.0 g of peracetic acid (40% excess). After 24 h, the KI test was weakly positive. Addition of water and separation gave an organic layer, which after having been washed with 5% $NaHSO_3$, 10% $NaHCO_3$, and brine, was dried over $MgSO_4$, filtered, and evaporated to give 612 mg of epoxy olefin. VPC on Carbowax at 80 °C showed 3% of unreacted starting material.

A solution of $RuO_4$[83] was generated by stirring a suspension of 80 mg of $RuO_2$ hydrate with a solution of 700 mg of sodium metaperiodate in 25 ml of water. A solution of 612 mg of the epoxy olefin in 20 ml of acetone was added slowly and the mixture was treated with 450 mg of $NaHCO_3$ as buffer and cooled to 15 °C, at which temperature it was kept while adding during 12 h small portions of a solution of 3.7 g of $NaIO_4$ in 80 ml of acetone–water (40:60 v/v). After having been treated with 5 ml of isopropyl alcohol and filtered through a column of Celite diatomaceous earth, the solution was brought to pH 12 and the nonacidic fraction was extracted with ether to give 383 mg of material.

Acidification of the aqueous phase to pH 3.5 and extraction with ether gave 363 mg of crude acidic material. Treatment with diazomethane gave 325 mg of esters, which VPC analysis (XE60 capillary column, 90 °C) showed to contain small amounts of unidentified material and the epoxy ester **51b** and to consist largely of the two epoxy esters **49b** and **50b** in a ratio of 46:54. Epoxy esters **49b** and **50b** were obtained >98% pure after preparative VPC (Carbowax, 190 °C) and Kugelrohr distillation.

Application of the same degradation conditions to the other dimer cT-**12**-$d_2$ gave some of the "all-cis" ester **52b,** but relatively little of the anti-cis ester **51b.** Apparently, **51b** or a precursor of it epimerizes under the reaction conditions. because substantial amounts of the two trans esters **49b** and **50b** were present in the degradation mixture. It is also possible that the two trans esters were derived from some tC-**13**

which might have been concentrated in the cT-**12** fraction during the VPC purification.

The "all-cis" ester **52b** was obtained >95% pure by preparative VPC (Carbowax, 190 °C). The proton NMR spectra of **49b, 50b,** and **52b** at 270 MHz (Bruker) were well resolved and the chemical shift differences permitted further analysis by spin decoupling. The coupling constants reported below were deduced by inspection when the absorption was first order and confirmed by double irradiation when complex couplings precluded a direct visual analysis. The spectra were taken in the Fourier transform mode (5 pulses each) with a $D_2O$ capillary as a lock reference sample.

**49b** NMR (2.71 mg in $CCl_4$) $\delta$ 3.70 (s, OMe), 3.12 (t, $J_{6,1}$ = 4.4, $J_{6,5e}$ = 4.0 Hz, H(6)), 2.98 (d × d, $J_{1,2a}$ = 2.5, $J_{1,6}$ = 4.5 Hz, H(1)), 2.17 (d + m, $J_{2a,Me}$ = 7.3; $J_{2a,3a}$ = 11; $J_{2a,1}$ = 2.5 Hz, H(2a)), 2.09 (t, $J_{3a,2a}$ = 11; $J_{3a,4a}$ = 10 Hz, H(3a)), 1.93 (br, $J_{5e,6}$ = 4.0 Hz, H(5e)), 1.80 (weak absorption, H(4e)), 1.60 (weak absorption, H(5a)), 1.39 (br d, $J_{4a,3a}$ = 10 Hz, H(4a)), 1.10 (d, $J$ = 7.3 Hz, Me).

**50b** NMR (22.8 mg in $CCl_4$) $\delta$ 3.62 (s, OMe), 3.03 (br s, H(6)), 2.68 (d, $J_{1,6}$ = 3.7 Hz, H(1)), 2.25 (pseudoquintet, $J_{2a,Me}$ = 7.3 Hz, $J_{2a,3a}$ = 10.5, $J_{2a,1} \sim 0$ Hz, H(2a)), 2.12 (br s, $J_{5e,4a}$ = 3 Hz, H(4a)), 1.70 (t, $J_{3a,4a}$ = 11, $J_{3a,2a}$ = 10.5 Hz, H(3a)), 1.53 (br d, $J_{4a,3e}$ = 11, $J_{4a,5e}$ = 3 Hz, H(4a)), 1.05 (d, $J$ = 7.3 Hz, Me).

**52b** NMR (10 mg in $CDCl_3$) $\delta$ 3.70 (s, ome), 3.22 (perturbed s, $J_{6,5a}$ = 2 Hz, H(6)), 3.16 (d × d, $J_{1,2e}$ = 6.5, $J_{1,6}$ = 4.5 Hz, H(1)), 2.53 (sextet, $J_{2e,Me}$ = 7.3, $J_{2e,3a}$ = 7, $J_{2e,1}$ = 6.5 Hz, H(2e)), 2.36 (d × d, $J_{3a,2e}$ = 7, $J_{3a,4a}$ = 12.5 Hz, H(3a)), 1.67 (br d, $J_{5a,4a}$ = 13, $J_{5a,6}$ = 2 Hz, H(5a)), 1.60 (m, $J_{4a,3a}$ = 12.5, $J_{4a,5a}$ = 13 Hz, H(4a)), 0.98 (d, $J$ = 7.3 Hz, Me).

Integrations of the proton signals at the sites geminal to the expected deuterium sites were facilitated by LIS. For example, in compound **49b,** the 4-axial position should be entirely H and the 4-equatorial position should contain only as much protium as is permitted by the total deuterium incorporation. At E/s = 0.30, the spectrum of **49b** showed 1.06 and 1.08 H at H(4a) relative to OMe and the sum of H(3a) + H(6) + H(1), respectively. At E/s = 0.63, H(4a), H(6), H(1), and H(3a) had identical intensities to ±3%. At E/s = 0.82, the H(4a), H(1), H(6), and H(2a) intensities varied by ±2%. We conclude that there is no detectable amount of deuterium at position 4a of **49b.** The amount of protium at positions 4e and 5a was estimated to 10–20% by integration of the weak proton peaks in LI shifted spectra. At E/s = 0.82, the proton NMR of **49b** showed the following absorptions: $\delta$ 17.1 (H(3a)), 13.7 (H(1)), 12.75 (H(6)), 10.85 (H(2a))9.90 (OMe), 9.50 (H(5e)), 9.20 (Me), 6.45 (H(4a)). The weak proton signals of H(5a) and H(4e) were buried under the OMe and Me peaks.

The direct deuterium NMR spectrum was run[62] in the FT mode (9479 scans) on the same LIS sample in Freon 11 solution and showed only two absorptions, for D(5a) at 20.91 ppm (relative intensity 1.00) and D(4e) at 19.59 ppm (relative intensity 0.98). The assumption of proportionality between the H and D chemical-shift differences permits the assignment of 20.16 and 14.41 ppm as the expected deuterium shift positions for D(5e) and D(4a), from the equations

$$\delta D(5e) = \delta D(5a) - [((\delta D(5a) - \delta D(4e))/(\delta H(5a) - \delta H(4e))\,(\delta H(5a) - \delta H(5e))]$$

$$\delta D(4a) = \delta D(5a) - [((\delta D(5a) - \delta D(4e))/(\delta H(5a) - \delta H(4e))\,(\delta H(5a) - \delta H(4a))]$$

The D(5e) absorption should fall close to that of D(4e) and might escape detection, but the D(4a) shift is far removed from any other and should be readily seen. The absence of any absorption at this position and the conservative estimate of a 2% limit of signal detectability based upon a noise level of a few tenths of a percent permit the conclusion that deuterium labeling was >98% stereospecific at D(4e) in **49b.**

Similarly, the LIS proton NMR spectra of **50b** at three E/s values showed two weak absorptions of essentially equal intensity (0.16 H) at positions corresponding to H(4e) and H(5a). The total deuterium content of 87–90% of 2 D would produce signal intensities of 0.10–0.13 H at these sites in the epoxy ester from a stereospecifically labeled dimer formed by supra-diene–supra-dienophile Diels–Alder addition. The slightly higher value observed might be interpreted as evidence for a small amount (3–6%) of nonstereospecificity, but the discrepancy is within experimental error of zero.

Table XIII. LIS Relative Slopes ($\Delta\delta$/E/s) and Extrapolated Chemical Shifts for the Model Compounds

| | Compd | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 49a | | 50a | | 51a | | 52a | |
| Proton | Slope | Ext $\delta$ | Slope | Ext $\delta$ | Slope | Ext $\delta$ | Slope | Ext $\delta$ |
| H(1) | 1.00 | 3.2 | 0.87 | 3.6 | 1.00 | 3.1 | 1.00 | 3.3 |
| H(6) | 0.96 | 3.2 | 1.00 | 4.1 | 0.93 | 3.1 | 0.85 | 3.5 |
| H(3) | 1.16 | 2.1 | 0.72 | 1.8 | 0.85 | 2.8 | 1.02 | 2.1 |
| H(2) | 0.70 | 2.2 | 0.93 | 2.6 | 0.64 | 2.7 | 0.77 | 2.7 |
| OMe | 0.47 | 3.8 | 0.32 | 3.8 | 0.24 | 3.8 | 0.62 | 3.5 |
| H(4a) | 0.35 | 2.2 | 0.96 | 2.1 | 0.60 | 2.1 | 1.45 | 1.2 |
| H(4e) | 0.70 | 1.5 | 0.53 | 1.7 | 0.44 | 1.8 | 0.62 | 2.3 |
| H(5a) | 0.70 | 1.5 | 0.35 | 2.1 | 0.30 | 2.5 | 0.42 | 1.7 |
| H(5e) | 0.70 | 1.5 | 0.55 | 2.7 | 0.44 | 1.8 | 0.74 | 1.6 |
| Me | 0.70 | 1.1 | 0.32 | 1.1 | 0.30 | 1.0 | 1.07 | 1.0 |

That no significant scrambling has occurred is demonstrated again with higher sensitivity by the direct $^2H$ NMR. At E/s = 0.63, the proton NMR of **50b** showed absorptions for H(2a) +H(4a) at $\delta$ 10.72 (intensity 2.09), H(3a) + H(5e) at $\delta$ 7.4 (intensity 2.00), H(4e) at $\delta$ 5.84 (intensity 0.17), and H(5a) at $\delta$ 4.75 (intensity 0.20). The deuterium NMR[62] was run on the same sample in Freon 11 solution in the FT mode (16 384 scans) and showed peaks at 16.22 (intensity 1.00). 15.09 (intensity 0.88), and 23.42 ppm (intensity 0.005). The latter 0.5% impurity peak (probably caused by a trace of diol shifted strongly downfield by $Eu(fod)_3$) was readily visible as an absorption about 3–4 times the noise level. The extrapolated deuterium chemical shifts anticipated for H(4a) and H(5e), the sites that would be labeled by any cycloaddition stereochemistry other than supra-supra, were 21.30 and 17.74 ppm. The spectrum at these positions showed no absorptions above the noise level, either by visual inspection or the FT computer integration. We consider 2% to be a conservative limit of detectability.

The proton LIS spectra of **52b** at three E/s values permitted the integration of the absorptions of H(4a) and, in one case, H(5a). These would be fully protonated in a stereospecifically supra-supra-derived product. The observed intensities relative to that of H(1) as internal standard were 0.98 ± 0.02 for H(4a) and 1.05 for H(5a).

## References and Notes


(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the partial support of this work. The National Science Foundation (GP-33909X and GP-11017X) and thhhhe Hoffman–LaRoche Foundation also provided support, for which we are grateful.

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