(Figure 4). We conclude that the destabilization of **1** by methylation of the oxygen ring substituent causes a large decrease in the chemical selectivity of the electrophile for reaction with halide ions and solvent.

There are many examples of carbocation addition reactions in which nucleophile selectivity is independent of electrophile reactivity.[11a,b] Data from these reactions were used to develop the N_+ scale for the reactivity of nucleophiles toward carbocations and related electrophiles. By contrast, methylation of the carbonyl oxygen of **1** causes a significant decrease in the selectivity of the electrophile toward reaction with halide ions. The change in substituent at **1** from 4-$^-$O to 4-MeO particularly favors the observation of a decrease in selectivity, because the difference in the reactivity of **1** and 4-MeOArC$(CF_3)_2^+$ is extremely large (10^{11}-fold). Further, there is only a small chemical barrier to the capture of 4-MeOArC$(CF_3)_2^+$, and the following recent studies suggest that Hammond effects begin to become significant when the carbocation lifetime is decreased to 10^{-5} s or shorter. (1) β_{nuc} for the reaction of ring-substituted 1-phenylethyl carbocations with alcohols decreases from 0.50 (4-N$(CH_3)_2$) to 0.22 (4-OPh) for an increase in k_s for carbocation capture by 50:50 (v/v) trifluoroethanol/water from $\leq 2000\ s^{-1}$ to $3 \times 10^8\ s^{-1}$.[35a] (2) A large number of substituted triarylmethyl carbocations obey the N_+ equation; however, a breakdown of the N_+ scale has been noted for the triphenylmethyl cation, which is captured by water with a rate constant of $1.5 \times 10^5\ s^{-1}$.[11c,36] By contrast, there are a number of reactions of cations with nucleophiles in which nucleophile selectivities remain constant as the rate constants for nucleophile addition increase up to the diffusion limit.[11b] I can offer no simple explanation to reconcile the differences in these results. This laboratory is in the process of collecting more extensive data for the addition of anionic and neutral nucleophiles to benzyl carbocations in order to determine whether the N_+ scale is generally applicable to the reactions of these highly unstable carbocations.

Biological Relevance. The results of these chemical studies on a simple quinone methide lead to the following generalizations about the biological activity of more elaborate quinone methides.[1-4]

(1) The efficiency with which an electrophilic reagent will label a nucleophilic site in a cell depends on the rate constant ratio k_{Nu}/k_s (M^{-1}) for reaction of the electrophile with the nucleophile and solvent. Efficient labeling is favored by a large value of k_{Nu} and a small value of k_s, so that the electrophile will have a long lifetime in which to encounter and react with the nucleophilic reagent. By this criteria, quinone methides are very well suited to the role of electrophilic labels of biological molecules. The selectivities of **1** for reaction with azide ion ($k_{az}/k_s > 4 \times 10^8$ M^{-1})[37] and bromide ion ($k_{Br}/k_s = 12000\ M^{-1}$) are far larger than the values of 10^6 and 33 M^{-1},[36,38] respectively, for the capture of the more reactive substituted triarylmethyl carbocations.

(2) The results reported in this work show that the addition of nucleophiles to **1** is catalyzed by protonation of the quinone oxygen. Similarly, biologically important quinone methides may react preferentially with "hot" spots along the DNA chain[39] where a general acid is properly aligned to catalyze the nucleophilic addition reaction.

Acknowledgement is made to National Institutes of Health, Grant GM39754, for support of this work. I thank Dr. William Jencks and Dr. Christopher Murray for helpful comments on an early draft of this paper.

(37) Calculated by using a limit of $k_{az} > 10^4\ M^{-1}\ s^{-1}$.[8]
(38) Bunton, C. A.; Huang, S. K. *J. Am. Chem. Soc.* **1972**, *94*, 3536-3544. Ritchie, C. D.; Virtanen, P. O. I. *Ibid.* **1972**, *94*, 4966-4971.
(39) Li, V. S.; Kohn, H. *J. Am. Chem. Soc.* **1991**, *113*, 275-283.
(40) (a) Commission on Physical Organic Chemistry, IUPAC. *J. Pure Appl. Chem.* **1989**, *61*, 23-56. Guthrie, R. D.; Jencks, W. P. *Acc. Chem. Res.* **1989**, *22*, 343-349. (b) These names may be expanded to indicate the relative positions of the atoms that undergo reaction. For instance, $A_N^* + A_HD_{xh}$ could be renamed $1/A_N^* + 6/A_HD_{xh}$, if it were necessary to distinguish this 1,6-addition reaction from the more common 1,2-addition reaction.

Remote Control of Stereogenicity Transfer by Ring-Generated Anisotropic Orbital Overlap. Stereochemistry of Hydrogen Shift in the Intramolecular Reverse Ene Reaction of a *cis*-2-Alkyl-1-alkenylcyclopropane

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Contribution from the Department of Chemistry, Yale University, New Haven, Connecticut 06511.
Received November 7, 1990

Abstract: The thermal rearrangement of *cis*-2-(2-propyl)-1(*E*)-propenylcyclopropane at temperatures near 230 °C in the gas phase occurs with activation parameters of $E_a = 35.5 \pm 0.6$ kcal/mol and $\log A = 12.05 \pm 0.5$ (A, s^{-1}). The optically active isotopically doubly labeled analogue (*cis*-2(*S*)-(2(*S*)-propyl-*1*-d_3)-1(*S*)-(1(*E*)-propenyl-*2*-*d*)cyclopropane **5** was synthesized in 12 steps from dicyclopentadiene. Pyrolysis of **5** gave only 2-methyl-octa-2(*Z*),5(*Z*)-diene-*1*-d_3-*7*(*S*)-*d*, with high stereospecificity at each of the three sites of stereogenicity. This result is the one predicted if the reaction is controlled by optimal overlap of the reacting C-H and π bond orbitals with the C_s symmetric component of the degenerate $3E'$ highest occupied orbital of the cyclopropane ring.

Introduction

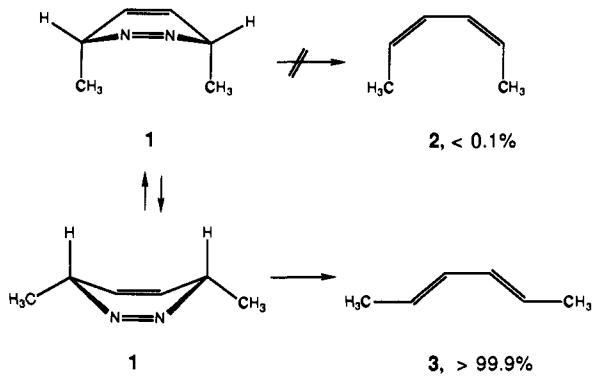
The orbital symmetry rules[1] designate the stereochemical course of pericyclic reactions as allowed or forbidden from the properties of *orbital phases*. Relatively little attention has been directed to the more subtle factor of *orbital overlap*, whose requirements can determine which of several formally allowed pathways will be preferred. We suggest that the structural replacement of a double bond by an alicyclic ring will cause one of two orbital-symmetry-allowed reaction pathways of the derived homologue to enjoy better orbital overlap. The present group of papers[2,3]

(1) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Academic Press: New York, 1970; see also references cited therein.

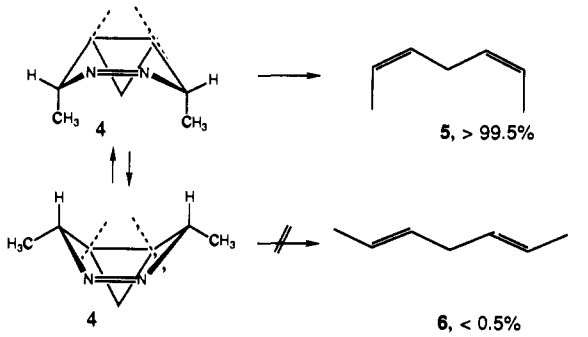
(2) Preliminary communications: (a) Parziale, P. A.; Berson, J. A. *J. Am. Chem. Soc.* **1990**, *112*, 1650. (b) Getty, S. P.; Berson, J. A. *Ibid.* **1990**, *112*, 1652.
(3) (a) Getty, S. P.; Berson, J. A. Companion paper in this issue. (b) Stark, E. J. Ph.D. Dissertation (with Berson, J. A.), Yale University, New Haven, CT, 1990.

0002-7863/91/1513-4595$02.50/0

Scheme I



Scheme II

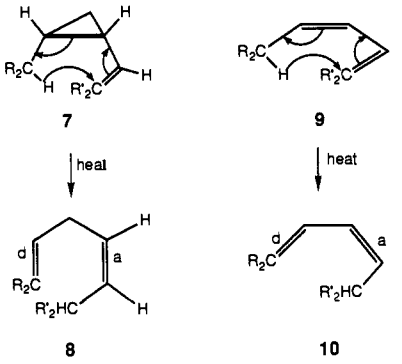


continues an earlier study[4] aimed at testing this prediction and determining its range of applicability.

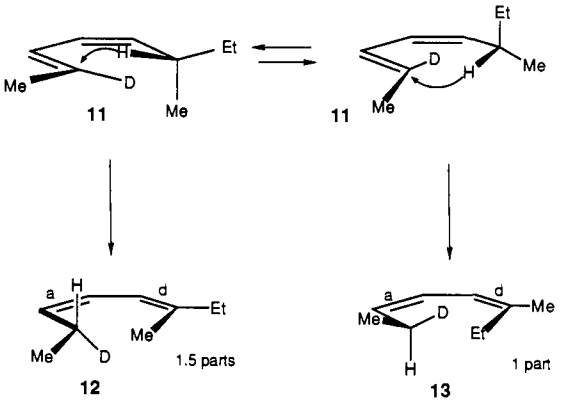
That the stereoelectronic effect can be strong enough to overcome major opposing steric biases can be seen in a comparison of the thermal Diels–Alder cycloreversions (solution phase, <0 °C) of 1,2-dihydropyridazine derivatives.[4] Thus, the preference for the sterically uncongested pathway[5] (**1** → *E,E* diene **3** preferred over *Z,Z* diene **2** with a specificity >1000, Scheme I) is cleanly inverted when the C=C double bond of **1** is replaced by a cyclopropane ring (**4** → *Z,Z* diene **5** rather than *E,E* isomer **6**, Scheme II).

The powerful steric effect seen in the case of **1** surely must be present in the transition state for the cycloreversion of **4** and actually should be enhanced because of the new gauche repulsive interaction with the cyclopropylmethylene group. Thus, on purely steric grounds, the *E,E* diene **6** also should predominate over the *Z,Z* diene **5** by a factor of 1000. In fact, however, the *Z,Z* diene **5** is the exclusive product (>99.5%).[4] The steric preference has been overwhelmed by a countervailing force whose magnitude must correspond to a factor of at least 2×10^5 ($\Delta\Delta G^{\ddagger} > 6$ kcal/mol at 250 K). Inspection of the geometric relationship of the axes of the breaking cyclopropane C–C bond orbitals (symbolized by the dashed lines of Scheme II) to those of the breaking C–N bond orbitals[5] reveals the nature of this stereoelectronic factor. In the transition state leading to the *Z,Z* diene **5**, these axes are in a favorable near-parallel mutual orientation, but in the pro-*E,E* transition state leading to **6** they are virtually orthogonal. The energetic benefit of concert[5,6] therefore must be small in the case of **6** but large in the case of **5**, and the pro-*Z,Z* transition state is much preferred, despite the far greater steric destabilization caused by its two clashing methyl groups.

Scheme III



Scheme IV



Discussion

Orbital Symmetry and Orbital Overlap in the Intramolecular Reverse Ene Reaction (Sigmatropic Homo Hydrogen 1,5-Shifts). The stereoelectronic selection of one orbital-symmetry-allowed pathway seen in the above Diels–Alder cycloreversions should apply to pericyclic reactions generally. On this hypothesis, we have begun a search for such selectivity in sigmatropic rearrangements. The first cases[2] we have studied are the intramolecular reverse ene reactions (homodienyl hydrogen shifts) in *cis*-2-alkyl-1-alkenylcyclopropanes (the present paper) and the analogous *cis*-2-alkyl-1-alkenylcyclobutanes[3a] and *cis*-2-alkyl-1-alkynylcyclopropanes.[3b]

The homodienyl hydrogen shift of *cis*-2-alkyl-1-alkenylcyclopropanes is a general transformation of the type **7** → **8**.[7-11] It is related to the dienyl sigmatropic hydrogen 1,5-shift[12] **9** → **10**. One of the double bonds (d) in the diene products **8** and **10** contains the carbon that has donated the migrant hydrogen, whereas the other (a) contains a carbon that was at the proximal end of the acceptor alkenyl group (Scheme III). For convenience, we refer to these as the "donor-derived" and "acceptor-derived" double bonds. Scheme III indicates what has been known about

(4) (a) Berson, J. A.; Olin, S. S. *J. Am. Chem. Soc.* **1969**, *91*, 777. (b) Petrillo, E. W., Jr.; Ph.D. Dissertation, Yale University, New Haven, CT, 1973. (c) Berson, J. A.; Petrillo, E. W., Jr.; Bickart, P. *J. Am. Chem. Soc.* **1974**, *96*, 636. (d) Berson, J. A.; Olin, S. S.; Petrillo, E. W., Jr.; Bickart, P. *Tetrahedron* **1974**, *30*, 1639.

(5) The diazene structures shown in Schemes I and II are intended to represent conformations resembling the structures of the transition states. The global ground-state conformations may well differ.

(6) For kinetic observations in some related cases, see: (a) Allred, E. L.; Hinshaw, J. C. *J. Chem. Soc., Chem. Commun.* **1969**, 1021. (b) Allred, E. L.; Hinshaw, J. C. *Tetrahedron Lett.* **1972**, 387. (c) Allred, E. L.; Hinshaw, J. C.; Johnson, A. L. *J. Am. Chem. Soc.* **1969**, *91*, 3383. (d) Allred, E. L.; Voorhees, K. J. *Ibid.* **1973**, *95*, 620. (e) Boger, D. L.; Brotherton, C. E. *Tetrahedron* **1986**, *42*, 2777.

(7) (a) Ellis, R. J.; Frey, H. M. *J. Chem. Soc.* **1964**, 4770. (b) Frey, H. M.; Pope, B. M. *J. Chem. Soc. A* **1966**, 1701. (c) Ellis, R. J.; Frey, H. M. *Proc. Chem. Soc.* **1964**, 221. (d) Ellis, R. J.; Frey, H. M. *J. Chem. Soc.* **1964**, 5578.

(8) (a) Roth, W. R.; König, J. *Justus Liebigs Ann. Chem.* **1965**, *688*, 28. (b) Roth, W. R.; König, J. *Justus Liebigs Ann. Chem.* **1966**, *699*, 24.

(9) Glass, D. S.; Boikess, R. S.; Winstein, S. *Tetrahedron Lett.* **1966**, 999.

(10) (a) Daub, J. P.; Berson, J. A. *Tetrahedron Lett.* **1984**, *25*, 4463. (b) Parziale, P. A. Ph.D. Dissertation, Yale University, New Haven, CT, 1990. (c) For recent related work, see: Hansson, T.; Bergman, R.; Sterner, O.; Wickberg, B. *J. Chem. Soc., Chem. Commun.* **1990**, 1260.

(11) Review: Gajewski, J. J. *Hydrocarbon Thermal Isomerizations*; Academic Press: New York, 1981; p 186.

(12) (a) Wolinsky, J.; Chollar, B.; Baird, M. B. *J. Am. Chem. Soc.* **1962**, *84*, 2775. (b) For a review, see ref. 11, p 106.

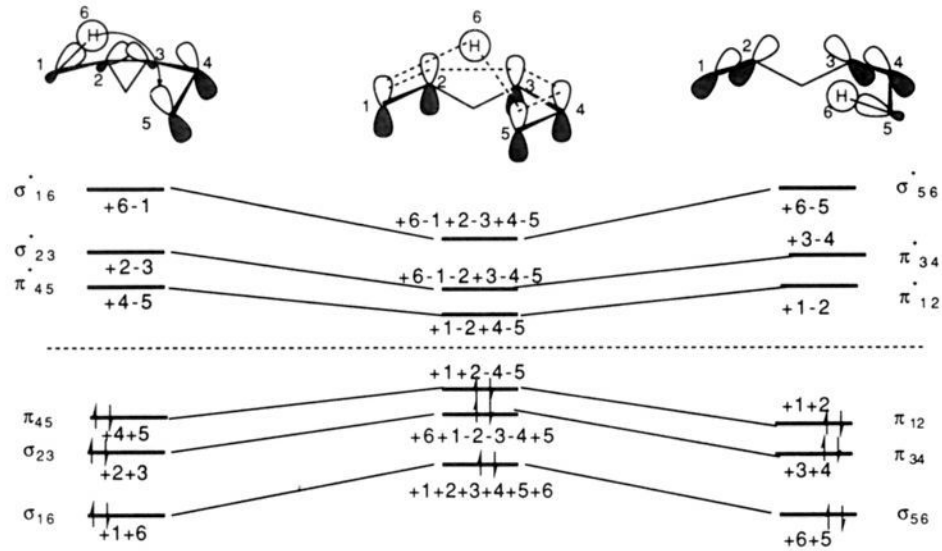


Figure 1. "MO following"[18] correlation diagram for the thermal homodienyl hydrogen shift. For simplicity, the C_2–C_3 localized bond orbital is used to represent the C_s symmetric component **18** of the cyclopropane degenerate canonical $3E'$ HOMO set.

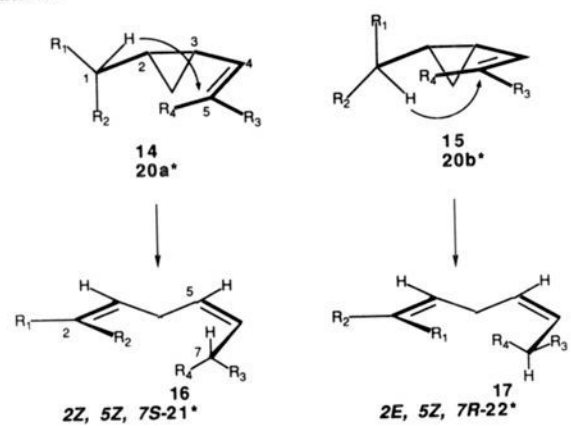
the stereochemistry of the homodienyl shift reaction, namely, that the substituents must be cis for the concerted process to occur and that the new acceptor-derived double bond is always formed cis.[7,8] The latter preference has been estimated experimentally[10] to be at least 12 kcal/mol and calculated by ab initio theoretical methods[13] to be 17 kcal/mol.

As a model for a stereoelectronically unbiased case, the stereochemistry of the thermal dienyl sigmatropic hydrogen 1,5-shift of (*S*)-(2*E*,4*Z*)-6-methyl-2,4-octadiene-*2-d* (**11**; Scheme IV) is instructive. As predicted by orbital symmetry, the reaction is suprafacial, giving only two products: (*R*)-(3*E*,5*Z*)- and (*S*)-3*Z*,5*Z*)-octa-3,5-dienes-*7-d* **12** and **13**, respectively.[14] The electron distribution above and below the plane of the reactant diene **11** diene is essentially isotropic (it would be exactly so were it not for the stereogenic center). If the substituents were free of differential steric demands, one therefore would expect that **12** and **13** would be formed in equal amounts. Actually, product **12** is slightly favored (by 1.5:1), probably because of the slightly smaller steric demand of methyl vs ethyl.

Replacement of the central double bond of a 1,3-diene with a cyclopropane ring, while modifying the dienyl shift to homodienyl, does not change the number of pathways expected. As Scheme V shows, two allowed suprafacial reactions (**14** → **16** and **15** → **17**) again are possible, both of which produce the necessary cis configuration of the acceptor-derived double bond. However, a new stereoelectronic factor is introduced because, with respect to the space above and below the mean plane of the reacting carbon atoms (C_1–C_5, sigmatropic numbering), the electron distribution now is *anisotropic*, for reasons similar to those brought out in the homo-Diels–Alder cycloreversions of Scheme II. Analogously, orbital overlap in a transition state derived from **14** should be better than in one from **15**. Glass, Boikess, and Winstein[9] seem to have been the first to recognize this stereoelectronic requirement of the homodienyl hydrogen shift, which they formulated in the comment "models indicate that this conformation (*i.e.* **14**) is the most favorable for overlap of the developing p-orbitals derived from the cyclopropane ring bond with the olefinic group and also the developing p-orbital derived from the C-H bond".

The idea of overlap outlined in the early research[9] relied merely upon the presumed directions of the cyclopropane orbital axes, but an analysis of the actual orbital shapes and phase properties offers some new explicative and predictive advantages. Perhaps the simplest approach to this is through correlation diagrams.[16-18] A graphic way to present the argument applies Zimmerman's

Scheme V[a]



[a] For compounds marked with an asterisk, $R_1 = CH_3$, $R_2 = CD_3$, $R_3 = CH_3$, and $R_4 = D$.

"MO following" procedure.[18] For the reactant, in addition to the localized σ and σ^* C—H and π and π^* C=C orbitals, we use the localized C_2—C_3 ring bond σ and σ^* orbitals. Figure 1 shows an allowed correlation; that is, all of the reactant's participating ground-state orbitals correlate with ground-state product orbitals through transition-state bonding orbitals. In particular, note that the product's C_3=C_4 π orbital evolves from the reactant C_2—C_3 σ ring bond orbital.

The actual canonical orbital whose phase property of being bonding at C_2–C_3 matches that of the C_2–C_3 σ orbital of Figure 1 is the nominally symmetric component of the degenerate $3E'$ highest occupied molecular orbitals (HOMOs) of cyclopropane,[15]

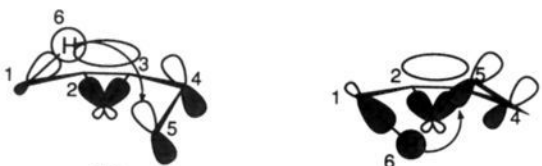
(13) Loncharich, R. J.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 2089.
(14) Roth, W. R.; König, J.; Stein, K. *Chem. Ber.* **1970**, *103*, 426.

(15) See (a) Jorgensen, W. L.; Salem, L. *The Organic Chemist's Book of Orbitals*; Academic Press: New York, 1973; p 154. (b) Honegger, E.; Heilbronner, E.; Schmelzer, A. *Nouv. J. Chim.* **1982**, *6*, 519.
(16) (a) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Academic Press: New York, 1970; p 10.
(17) Longuet-Higgins, H. C.; Abrahamson, E. W. *J. Am. Chem. Soc.* **1965**, *87*, 2045.
(18) (a) Zimmerman, H. E. *Acc. Chem. Res.* **1972**, *5*, 393. (b) The MO following diagrams in Figures 1 and 2 are based upon the simplest procedure recommended[18a] in the model, which assumes directly the transition-state (TS) orbitals with benzene-like symmetry shown. A more refined procedure[18a] would take into account the partial cancellations at atomic sites that are introduced when the TS orbitals are constructed by actual perturbations from the reactant and product orbitals. This leads to TS orbitals of different overall symmetry but leaves the correlations unchanged. An extensive discussion of the perturbations is given in ref 3b. (c) Zimmerman, H. E. *J. Am. Chem. Soc.* **1966**, *88*, 1564.

schematically shown as **18**. The antisymmetric HOMO is **19**, which correlates with a σ C–C bonding product orbital. These phase properties imply that *overlap* of the other reacting orbitals with the symmetric component **18** will be an important influence on the geometry of the transition state.

18 **19**

Structure **14**-o shows that the C–H bond orbital is aligned for good overlap with the symmetric ring orbital when the migrant hydrogen is pointed toward the outside of the ring. Likewise, the best overlap of the acceptor double bond π orbital (made up of the p orbitals shown) with the ring orbital occurs in **14**-o, where the double bond adopts a position that makes its π-orbital nodal plane fit into the nodal notch between the lobes of the ring orbital.



On the other hand, overlap of the relevant orbitals in structure **15**-o is unsatisfactory, since the C–H σ orbital lies in the nodal notch and the double bond π orbital presents its nodal plane to the outside lobe of the ring orbital. Note that both geometries correspond to formally allowed pathways. It is true, of course, that, in the transition state, the geometries **14** and **15** and the orbitals involved will be distorted from those of the ground state, but we follow the usual assumption[16-18] that orbital phase properties tend to persist along the reaction coordinate of a symmetry-allowed reaction.

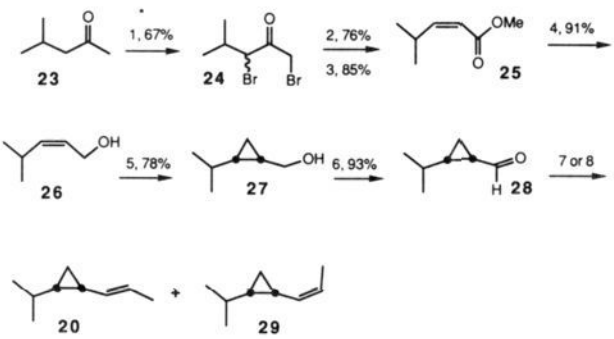
Thus, pathway **14** → **16** should be favored over pathway **15** → **17**, even though both are allowed by orbital symmetry. The analysis predicts the same stereospecificity as the earlier one[9] and differs from it mainly in the identification of the actual orbital correlations. Thus, in the correlation diagram model, the π-like ring orbital **18** and the π orbital of the double bond each correlate with π orbitals of the product, whereas the C–H σ orbital of the reactant correlates with a C–H σ orbital of the product.

Experimental Design. The rearrangement of *cis*-2(*S*)-(2-(*S*)-propyl-*1*-d_3)-1(*S*)-(1(*E*)-propenyl-*2*-*d*)cyclopropane (**20**; Scheme V) provides a test of this analysis. The molecule has the cis configuration of the side-chain substituents necessary for the concerted reverse ene reaction. Making the two substituents at the donor site differ only in isotopic content minimizes any steric bias to the configuration of the donor-derived double bond in the product. Similarly, the product owes its chirality to an isotopic distinction so that the configuration at the newly created stereogenic center cannot be appreciably influenced by a simple steric preference at that site. For most of this research, we chose to use the *E* configuration of the double bond of the reactant **20** to avoid the steric clash of the ring and the inside methyl group that retards[10a] the rearrangement of the *Z* isomer **29**, although we also carried out some studies of the latter.[10b]

If the rearrangement occurred from conformation **20a** of the *E* isomer **20**, analogous to the predicted pathway **14** of Scheme V, the product would be 2-methylocta-2(*Z*),5(*Z*)-diene-*1*-d_3-*7*(*S*)-*d* (**21**), whereas if it occurred from **20b**, analogous to the supposedly less favorable pathway **15**, the diastereisomeric 2*E*,5*Z*-7*R* species **22** would be formed. Which pathway predominates would be revealed by determinations of the configurations of the product's double bonds and by correlation of the configurations of the stereogenic centers of the reactant and product.

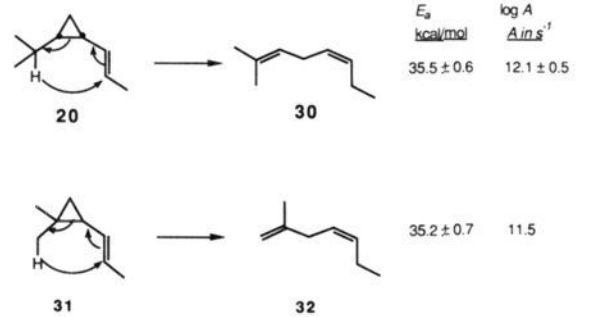
Synthesis of the Racemic, Isotopically Normal Substrate 20 (Scheme VI). For preliminary studies of products and kinetics, racemic unlabeled **20** was prepared by a seven-step synthesis, which is outlined in Scheme VI. The reactions of the sequence are stereospecific up to the aldehyde **28**, which serves as a precursor of **20** when ethylidenated by the Schlosser–Wittig conditions[19] (method 7, Scheme VI) or the ethylidenation of Takai and co-workers[20] (method 8, Scheme VI). The two methods furnish the desired *E* isomer **20** in a 2–3:1 or >10:1 preference to the *Z* isomer **29**, respectively. Separation of the stereoisomeric hydrocarbons is effected by preparative gas chromatography (GC).

Scheme VI[a]



[a] Methods: 1, Br_2, 48% HBr; 2, 1M $KHCO_3$; 3, CH_2N_2; 4, $(i\text{-}Bu)_2AlH$; 5, CH_2I_2, Et_2Zn; 6, $(COCl)_2$, $(CH_3)_2SO$, Et_3N; 7, Ph_3PEtBr, 2 BuLi, 2:1 *E*/*Z*; 8, $CrCl_2$, CH_3CHI_2, >10:1 *E*/*Z*. Steps indicated with an asterisk were used to prepare known compounds by literature procedures. References are given in the Experimental Section.

Scheme VII



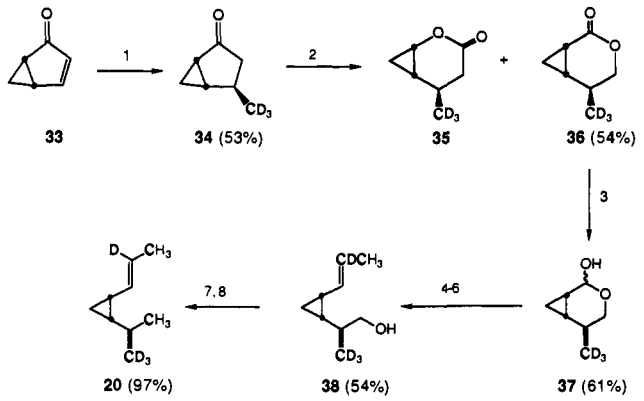
	E_a kcal/mol	log *A* *A* in s^{-1}
	35.5 ± 0.6	12.1 ± 0.5
	35.2 ± 0.7	11.5

Products and Kinetics of Pyrolysis of 20. Samples of **20** and internal standard cyclooctane sealed in base-washed silanized Pyrex tubes were heated at temperatures through the range 183.0–247.9 °C, under which conditions the pressure in the reaction vessels was ≤0.5 atm. The only product observed (0.1% detection limit) was the *Z* diene **30** (Scheme VII), as expected by analogy with the earlier research[7,8,10a]. As comparison standards, the *Z* diene **30** and its *E* isomer were independently synthesized in a Wittig reaction between propanal and the ylide from (4-methyl-3-penten-1-yl)triphenylphosphonium bromide. The configurations were assigned by NMR spectroscopic analysis, which yielded the vicinal vinyl coupling constants 10.7 Hz for the *Z* isomer and 15.4 Hz for the *E* isomer.

The mass balance in all of the rearrangement runs was at least 90% and in most cases >95%. The product **30** was stable at 260.5 °C for a time equivalent to 101 half-lives of rearrangement under these conditions. No new products appeared (GC analysis), and the mass balance was >90%. Of course, in the unlabeled series, it was not possible to test for stereochemical stability of the trisubstituted double bond or the prochiral methylene carbon of the ethyl group of **30**. These issues would become troublesome if the rearrangement in the labeled series were to occur with less than complete stereospecificity so that the decision not to address them at this point amounted to a calculated risk.

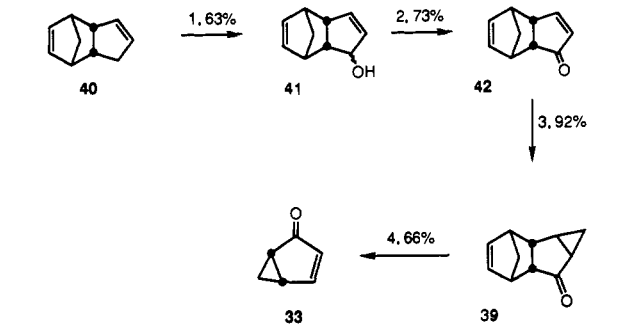
(19) Schlosser, M.; Christmann, K. F. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 126.
(20) Okazoe, T.; Takai, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 951.

Scheme VIII[a]



[a] Methods: 1, $(CD_3)_2CuLi$; 2, *m*-chloroperbenzoic acid; 3, $(i\text{-}Bu)_2AlH$; 4, $CH_3CD{=}PPh_3$; 5, MeOD; 6, D_2O; 7, MsCl; 8, LAH; 9, GC separation. Yields represent isolated chromatographed product in the optically active series.

Scheme IX[a]



[a] Methods: 1, SeO_2; 2, pyridinium dichromate, 3, Me_3SOI, NaH; 4, flash vacuum pyrolysis.

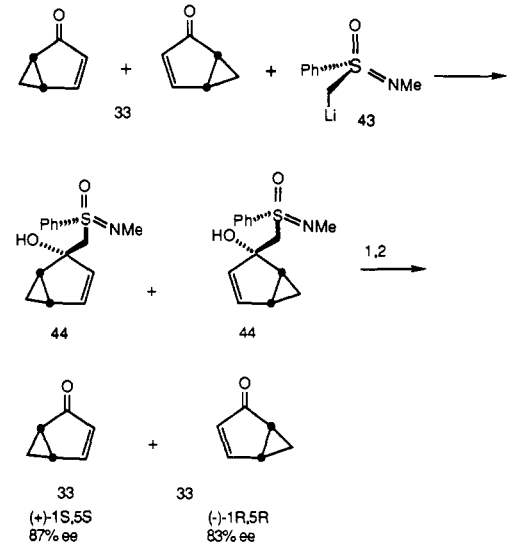
The kinetic activation parameters E_a = 35.5 kcal/mol and log A = 12.1 (A, s^{-1}) were determined by measurements of the rates of disappearance of **20** over the temperature range 183.0–247.9 °C. The reactions followed first-order kinetics for several half-lives, and the activation parameters agreed well with those for pyrolysis of the closely related substance 1-propenyl-2,2-dimethylcyclopropane (**31**) determined[10a] in earlier research (Scheme VII).

Synthesis (Schemes VIII–X) and Assignment of Absolute Configuration (Scheme XI) of the Optically Active Labeled Substrate 20. The key step in the planned construction of the chiral isopropyl group of **20** and the establishment of its configuration was to be the introduction of a trideuteriated methyl group by a conjugate addition to the optically active bicyclic enone **33** (Scheme VIII). We expected that the addition would occur with high stereospecificity anti to the cyclopropane ring to give the adduct **34** and, in any case, that the syn or anti configuration of the product(s) **34** obtained would be readily determinable. The unlabeled second methyl group of the isopropyl unit was to be derived by stereochemically innocuous steps from the CH_2 group of the cyclopentane ring of **34**. This device would fix the relative configurations of the stereogenic center of the chiral isopropyl group and the cyclopropane ring carbons. The absolute configurations of all three stereogenic carbons of **20** then could be established by stereochemical correlation of the bicyclic enone **33** to a known configurational reference or by other means.

The bicyclic enone **33** was prepared from dicyclopentadiene in four steps by a modification of the method of Cox and Rivera[21] (Scheme IX). We found that the reported procedure, which called for the final reverse Diels–Alder pyrolysis of the tetracyclic ketone **39** in mineral oil solution, gave, in addition to the enone **33**, substantial quantities of phenol as an undesirable side product.

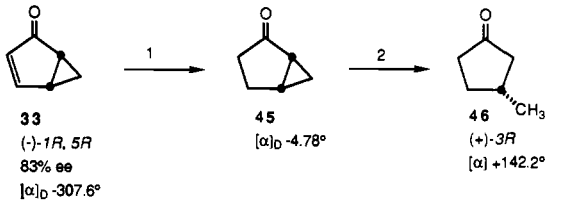
(21) Cox, O.; Rivera, L. *Synth. Commun.* **1978**, *8*, 261.

Scheme X[a]



[a] Methods: 1, HPLC separation; 2, heat at 120 °C (0.02 Torr).

Scheme XI[a]



[a] Methods: 1, H_2, Pd/C; 2, Li, NH_3.

Flash vacuum pyrolysis of **39** proved more convenient for the synthesis of multigram quantities (up to 0.3 mol/day) of **33**, which could be obtained in 66% yield along with 27% of recovered **39** and only a trace of phenol.

Optical resolution of **33** (Scheme X) was achieved by the sulfoximine method of Johnson and Zeller.[22] Treatment of the racemic enone **33** with the lithium salt of *S*-phenyl-*N*-methylsulfoximine (**43**), followed by protic workup, gave a mixture of the diastereomeric adducts **44** resulting from addition anti to the cyclopropane ring. After separation by high-pressure liquid chromatography (HPLC), the individual adducts were pyrolyzed in a bulb to bulb apparatus at 120 °C and 0.02 Torr to yield the corresponding enantiomerically enriched enones **33**. The values of enantiomeric excess (ee) for the two enone samples **33** (Scheme X) were determined by reduction to the corresponding exo allylic alcohols. Enantiospecific analysis was achieved by capillary GC of the exo methyl ethers derived from these alcohols on a Ni-*R*-Cam wall-coated open tubular (WCOT) column.[23] The ratio of the ee values of the (+) and (−) isomers so obtained (87:83 = 1.05) agreed well with the ratio of the absolute specific rotations (284:263 = 1.08).

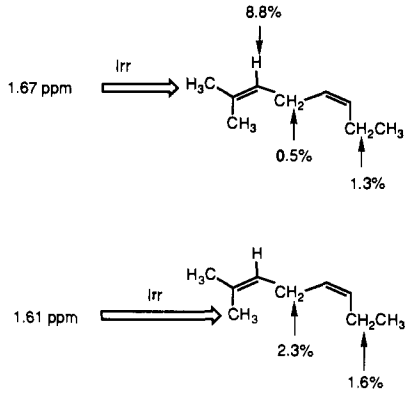
Chemical correlation of the configurations of (−)-(1*R*,5*R*)-**33** and (+)-(3*R*)-3-methylcyclopentanone (**46**; Scheme XI) was achieved when hydrogenation of another sample of (−)-**33** (97% ee) gave (−)-**45** ($[\alpha]_d$ −4.78° (ether)),[24] which in turn was converted with lithium in ammonia to (+)-3(*R*)-methylcyclopentanone (**46**; $[\alpha]_D$ +142.2° ($CHCl_3$)). The absolute configuration of **46** had been established by Eisenbraun and McElvain.[25] The rotation

(22) Johnson, C. R.; Zeller, J. R. *Tetrahedron* **1984**, *40*, 1225.

(23) (a) Schurig, V.; Weber, R. *J. Chromatogr.* **1981**, *217*, 51. (b) Owens, K. A.; Berson, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 627.

(24) (a) Lightner and Jackman[24b] reported a positive rotation (wavelength and solvent not mentioned) for *cis*-(1*R*,5*R*)-bicyclo[3.1.0]hexan-2-one (**45**). Since our sample of **45** was only 97% chemically homogeneous and since the observed rotation was low, we do not feel confident that our observation of a negative rotation for the same substance **45** should replace the earlier one. (b) Lightner, D. A.; Jackman, D. E. *Tetrahedron Lett.* **1975**, 3051.

Scheme XII. Nuclear Overhauser Enhancements



of **46** derived by the steps of Scheme XI is 92% of the highest value reported in this solvent[25] and probably differs from the expected 97% by no more than the combined experimental errors. The correlation of Scheme XI establishes the 1*R*,5*R* configuration of (−)-**33**.

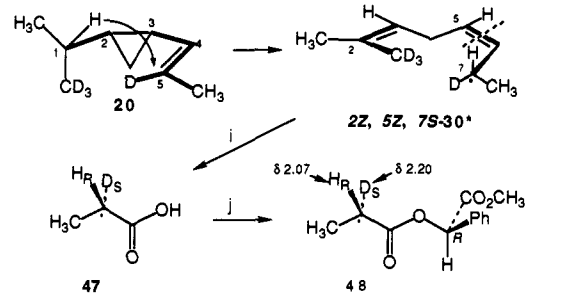
Returning to the main synthetic track (Scheme VIII), we worked out conditions for the early steps of the scheme on unlabeled racemic material, but the formulas shown depict the course of the synthesis in the labeled enantiomerically enriched series. Lithium dimethylcuprate-d_6 converted (1*S*,5*S*)-**33** (ee 86.7%) to the trideuteriomethyl-labeled ketone **34**. Although Baeyer–Villiger oxidation of **34** with peroxytrifluoroacetic acid gave predominantly the lactone **35** instead of the desired regioisomer **36** (see supplementary material), *m*-chloroperbenzoic acid (*m*CPBA) in refluxing 1,2-dichloroethane slowly converted ketone **34** to a 4:1 mixture of lactones **36** and **35** (Scheme VIII).[26] To minimize the thermal decomposition of the peracid, we added 4,4′-thiobis(2-*tert*-butyl-6-methylphenol), a reagent recommended by Kishi[27] for such a purpose.

The reduction of the lactone **36** with diisobutylaluminum hydride, although beset with difficulties,[10b] ultimately afforded the lactol **37**. The remainder of the synthesis proceeded uneventfully. Schlosser–Wittig[19] reaction of the lactol **37** with the ylide formed from ethyl-1,1-d_2-triphenylphosphonium bromide[28] and BuLi gave a mixture of the *E* and *Z* alcohols **38**. Deuterium incorporation was optimized by procedures described in the Experimental Section, and acceptable levels (97 and 94%, respectively) were achieved. Mesylation, reduction, and preparative GC separation gave the desired *E* hydrocarbon **20** and its *Z* isomer **29**.

The starting material **20** obtained in this way was 99.1 ± 0.1% chemically pure by capillary GC analysis. None of the *Z* isomer **29** was observed among the small impurity peaks. Compound **20** was assumed to have the same ee (87%) as its synthetic precursor bicyclic enone **33**, since no plausible racemization pathway is evident in the course of the synthesis of Scheme VIII. The deuterium content in the labeled methyl group of **20**, determined by analysis of the mass spectrum, was 99.5 ± 0.5%, and the deuterium content at the propenyl double bond position, determined by ^{1}H NMR integration, was 97 ± 0.5%.

Stereochemical Analysis of the Product Diene 30. The mechanistic test requires the determination of the configurations of three different stereogenic units of **30**. One is the acceptor-derived double bond, at which configurational isomerism leads to actual separability by GC analysis. The experiments already described in the unlabeled series establish that only the *Z* alkene is formed at this site, the amount of *E* isomer being too small to measure at the 0.1% detection limit.

Table I. Percent Stereospecificity in the Transformation **20** → **30**



method	reactant (**20**)	product (**30**)	stereospecificity
^{2}H NMR	ee 86.7 ± 1.8,[a] 87.3 ± 2.4[b]	ee 86.1 ± 3.7,[c,g] 83.8 ± 5.2[d,g]	ee 99 ± 5[e]
^{1}H NMR	ee 82.0 ± 1.8,[a] 82.5 ± 2.4[b]	ee 80.9 ± 0.7[h]	ee 99 ± 4[f]
^{1}H NMR	(2*S*)-2-propyl-1-d_3 99.5 ± 0.5	2*Z* 99.2 ± 0.3	2*Z* 99.7 ± 0.6
GC		5*Z* >99.9	5*Z* >99.9

[a] Effective ee uncorrected for systematic error in enantiospecific GC analysis of racemate **33**. [b] Effective ee corrected for systematic error in enantiospecific GC analysis of racemate **33**. Values of ee for **20** and **33** assumed equal. [c] Line-broadening parameter 0.3 Hz. [d] Line-broadening parameter 1.0 Hz. [e] 100(average of the four ratios of ee_{30}:ee_{20}). [f] 100(Average of the two ratios of ee_{30}:ee_{20}). [g] ee of **30** obtained from ^{2}H NMR analysis of the derived methyl mandelate propanoate **48**. [h] ee of **30** obtained from ^{1}H NMR analysis of the derived methyl mandelate propanoate **48**. [i] RuO_4. [j] (*R*)-PhCH(OH)CO_2CH_3 (DCC).

The configuration of the donor-derived double bond rests upon the assignment by nuclear Overhauser experiments of the two distinct NMR signals of the allylic methyl groups of **30**, which occur at δ 1.61 and 1.67 ppm. The results of these studies are summarized in Scheme XII, which displays the significant enhancements. The nearly equal enhancements of the CH_2 proton signals of the ethyl group observed upon irradiation of either allylic methyl resonance are not diagnostic, but otherwise the results permit the confident assignments of the δ 1.67 and 1.61 signals to the methyl groups trans and cis, respectively, to the doubly allylic CH_2 group.

To define the configuration of the stereogenic carbon of the deuteriated product **30** (Table I), we oxidized the product diene **30** with ruthenium tetroxide to propanoic acid-2-*d* (**47**). The pro-*R* and pro-*S* protons of propanoic acid, according to Parker,[29] could be distinguished by NMR spectroscopy of the ester **48** obtained from the acid and enantiomerically pure methyl (*R*)-mandelate in the presence of dicyclohexylcarbodiimide. We confirmed this observation by 500-MHz ^{1}H NMR measurements, which showed signals for H_R and H_S of isotopically unlabeled **48** in C_6D_6 solvent at δ 2.07 and 2.20, respectively.

We also carried out control experiments[10b] to show that **30**-7,7-d_2 could be subjected to the oxidation and esterification steps without loss of deuterium. The absence of H–D exchange gave assurance that neither dedeuteriation nor epimerization at the crucial stereogenic center would occur.

Pyrolysis of Optically Active Isotopically Labeled 20 (Table I). In accord with the *Z* stereochemistry observed at the acceptor-derived double bond in the unlabeled series, the NMR spectrum of the pyrolysate (230 ± 0.5 °C for 4.75 h, ~50 half-lives) in the labeled series showed essentially one product (the 5*Z* diene **30**) and GC analysis showed 98.1% **30** and miniscule amounts of unidentified products, the most abundant of which amounted to 1% of the total chromatographic area.

The configuration of the donor-derived double bond of product **30** was determined by ^{1}H NMR spectroscopy to be 2*Z*, which corresponds to that of **21** (see Scheme V), the product expected

(25) Eisenbraun, E. J.; McElvain, S. M. *J. Am. Chem. Soc.* **1955**, *77*, 3383.

(26) Oxidation of bicyclo[3.1.0]hexan-2-one with CF_3CO_3H gives a much higher preference for CH_2 vs cyclopropyl migration. Daub, J. P.; Berson, J. A. Unpublished work.

(27) Kishi, Y. *J. Chem. Soc., Chem. Commun.* **1972**, 64.

(28) Heimgartner, H.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1972**, *55*, 1385.

(29) (a) Parker, D. *J. Chem. Soc., Perkin Trans. 2* **1983**, 83. (b) The chemical shifts originally reported[29a] for **48** are incorrect. The spectrum determined by Parker is in fact the same as the one we measured for **48**. We thank Dr. Parker for confirming this point.

from the overlap-favored pathway (Scheme V, **20a** → **21**). The stereospecificity at this site is very high, the signal at δ 1.67 in the ^{1}H NMR spectrum (see Table I) accounting for >99.2 ± 0.3% of the intensity in the allylic methyl region.

The strong implication from these results that the overlap-favored pathway dominates (Scheme V, **20a** → **21**) was confirmed by oxidative degradation of the product diene **30**-*7-d*. Since **21** has the 7*S* configuration, to the extent that the hydrogen shift is stereospecific, the derived methyl mandelate propanoate **48** should have deuterium in place of the H_S hydrogen. Corrected (see Experimental Section) for the presence of the small amount of enantiomeric and undeuteriated (at the propenyl position) starting material, the methylene regions of the ^{2}H and ^{1}H NMR spectra of the degradation product **48** showed resonances at the D_S and H_R chemical shift positions δ 2.20 and 2.07, respectively (Table I), corresponding to 99 ± 5% and 99 ± 4% of those maximally available from the reactant hydrocarbon **20**.

Table I collects the data on the stereospecificity of the reaction pathway as monitored at three independent sites. The analytical methods and hence the experimental errors differ (see Experimental Section), but in each case the stereospecificity is "complete", that is, too large to measure by currently available techniques. If the preference for the overlap-favored pathway here is the same as the factor of >2 × 10^5 seen in the reverse Diels–Alder reactions,[4] the efficiency of transfer of ee to the product diene **30** may be >99.998%. In future research, a strategy similar to the one used in the Diels–Alder studies,[4] namely, forcing the steroelectronically preferred process to surmount a steric impediment, may permit us at least to raise the lower limit of the stereoelectronic preference and perhaps actually to measure it.

Conclusions

In contrast to the ordinary thermal dienyl hydrogen shift, which in an appropriately labeled case gives a mixture of two suprafacial products,[14] the thermal homodienyl hydrogen shift gives only one. The sense of the stereospecificity in the homodienyl case is that predicted from two postulates: First, the C_S symmetric component of the degenerate pair of canonical cyclopropane HOMOs, which is bonding at the site of ring cleavage, is the only one that can correlate with product bonding π orbitals; second, optimal overlap of that orbital with the reacting σ C—H and π C=C orbitals is maintained.[30]

The anisotropic influence of a cyclopropane ring thus controls the chirality in the creation of a remote stereocenter. In an accompanying paper,[3a] we report the results of a study of such control by a cyclobutane ring.

Experimental Section

Details of standard procedures are given in the supplementary material. Proton NMR spectra were obtained on either a Jeol FX 90-Q (90 MHz), a Bruker WM-250 (250 MHz), a Bruker WM-500 (500 MHz), or Yale's 490 (490 MHz). Proton spectra are recorded in the following manner: chemical shift δ (ppm) relative to tetramethylsilane (TMS) (multiplicity, number of nuclei, coupling constants (Hz), assignments where known). Spectra were obtained in $CDCl_3$ (δ 7.24) and where specified in benzene-d_6 (δ 7.15).

Nuclear Overhauser Effect (NOE). NOE experiments were conducted on the Bruker WM-250 with use of the program listed in the supplementary material.

Carbon spectra were obtained on a Bruker WM-250 (62.5 MHz), a Bruker WM-500 (125.7 MHz), or Yale's 490 (122.5 MHz). All carbon spectra were recorded in $CDCl_3$ (δ 77.0). Carbon spectral data are reported in the following manner: chemical shift relative to TMS (multiplicity).

Deuterium NMR spectra were obtained by Mr. Peter Demou on the Bruker WM-500 (76.8 MHz) instrument and recorded in benzene-h_6.

Low-resolution mass spectrograms were obtained with use of a Hewlett-Packard 5985 GC/MS. All mass spectral data reported were obtained at 20 or at 70 eV where noted. GC/MS spectra were obtained with a $^1/_8$ in. × 3 ft × 2% OV-101 on an Anakrom ABS (110–120 mesh) column. Samples were also introduced for mass spectrometric analysis by the direct insertion probe technique. Mass spectrograms obtained in this manner are noted. High-resolution mass spectra were obtained by Mr. D. Pentek with a Kratos MS80 RFA. All high-resolution mass spectra were by GC/MS. Mass spectral data are reported in the following manner: *m/e* fragment (relative abundance as a percent of the parent).

Synthesis of Racemic Isotopically Unlabeled 20 and 29 (Scheme VI). 1,3-Dibromo-4-methyl-2-pentanone (**24**; Scheme VI) and (*Z*)-4-methyl-2-pentenoic acid (**25**, OH instead of OMe) were prepared by the method of Rappe.[36] 4-Methyl-(*Z*)-2-pentenoic acid, methyl ester (**25**) [20515-16-6], was prepared by addition of a solution of CH_2N_2 (11.3 g, 0.268 mol) in 400 mL of ether to a solution of (*Z*)-4-methyl-2-pentenoic acid (29.1 g, 0.255 mol) in 150 mL of ether. The mixing was accompanied by rapid N_2 evolution. After the solution was stirred for 15 min, 100 mL of a 50% aqueous glacial acetic acid solution was added. The ethereal layer was then washed with saturated $NaHCO_3$ solution and dried over $MgSO_4$. Rotary evaporation of the solvent yielded a colorless liquid (29.1 g, 0.228 mol, 85%).

(*Z*)-4-Methyl-2-penten-1-ol (26). Diisobutylaluminum hydride (DIBAL; 0.279 mol, 279 mL of 1 M solution in hexanes) was added dropwise to a precooled (−78 °C) solution of methyl (*Z*)-4-methyl-2-pentenoate (**25**) (17.0 g, 0.133 mol) in 75 mL of ether. The reaction was stirred for 1 h at −78 °C and then warmed to 0 °C. Methanol (1 mL) was added slowly to quench the unreacted DIBAL. An orange gel resulted, which was treated with 50 mL of 40% sodium potassium tartrate solution. The aqueous solution was subjected to continuous extraction with ether for 18 h. The ethereal layer was dried over $MgSO_4$. Removal of the solvent by rotary evaporation yielded a colorless liquid (12.1 g, 0.121 mol, 91%). ^{1}H NMR (500 MHz): δ 5.45 (dt, 1 H, *J* = 11.0, 6.7 Hz, H_2), 5.35 (dd, 1 H, *J* = 11.0, 11.0 Hz, H_3), 4.14 (br d, 2 H, H_1), 2.58 (m, 1 H, H_4), 1.3 (br s, 1 H, exchanges in D_2O, OH), 0.94 (d, 6 H, *J* = 6.6 Hz, H_5 and H_6. ^{13}C NMR: δ 140 (d, C_2), 126.2 (d, C_3), 58.2 (t, C_1), 26.6 (d, C_4), 22.9 (q, C_5 and C_6). GC/MS: *m/e* 82.1 (30.5, M − H_2O), 69.1 (53.8), 67 (64.6), 59.1 (43.6), 57.1 (92.9), 41 (100). FT-IR: 3613 (m), 3610 (m), 2965 (s), 2934 (m), 2908 (m), 2889 (m), 2871 (m), 1717 (w), 1465 (s), 1382 (s), 1363 (m), 1205 (m) cm^{-1}.

***cis*-2-(2-Propyl)cyclopropanemethanol (27).** The cyclopropanation was accomplished via the general procedure of Furukawa.[38] (Note: The order of addition of reagents should be as described. Explosions have been reported with other orders of addition.) A 15% solution of diethylzinc (167 mL, 175 mmol) in toluene was added to a solution of (*Z*)-4-methyl-2-penten-1-ol (**26**) (8.75 g, 87.5 mmol) in 75 mL of ether that had been precooled to 0 °C. A cloudy white mixture resulted. The first addition funnel was replaced with another containing CH_2I_2 (23.7 mL, 291.6 mmol). The CH_2I_2 was added dropwise, the addition funnel was replaced by a condenser, and the reaction was refluxed for 8 h. After the solution was cooled to room temperature, 100 mL of saturated NH_4Cl solution was added dropwise. The mixture was continuously extracted with ether for 24 h. The ethereal layer was then applied to 50 g of dry silica gel. The silica gel was washed with 500 mL of pentane, which was discarded, and then eluted with pentane/ether (7:3). Rotary evaporation of the organic solution yielded a colorless liquid (7.78 g, 68.2 mmol, 78% yield). ^{1}H NMR: δ 3.69 (dd, 1 H, *J* = 11.2, 7.4 Hz), 3.54 (dd, 1 H, *J* = 11.2, 7.6 Hz), 1.09 (m, 2 H), 0.99 (d, 3 H, *J* = 5.9 Hz), 0.99 (d, 3 H, *J* = 6.0 Hz), 0.64 (m, 2 H), −0.05 (m, 1 H). ^{13}C NMR: δ 63.0 (t), 28.4 (d), 25.0 (d), 23.2 (q), 23.0 (q), 18.8 (d), 8.6 (t). GC/MS: *m/e* 96.1 (10.9, M − H_2O), 81.2 (43.6), 73.1 (37.7), 57.1 (34.8), 56.1 (100), 54.2 (14.7). FT-IR: 3616 (m), 2965 (s), 2960 (s), 2955 (s), 2870 (m), 2245 (m) cm^{-1}.

(30) This analysis, which is expressed in orbital symmetry formalism, necessarily contains the implicit assumption that the reaction is concerted. Conventional arguments in the literature[31] support the concerted pathway by noting that the experimental activation energies for homodienyl hydrogen shifts are at least 10–12 kcal/mol below the value expected for a stepwise mechanism proceeding over a 1,3-biradical intermediate. Although we do not challenge this argument in a qualitative sense, it is not clear how much of the facilitation should be ascribed to the actual energetic advantage of concert and how much to the circumstance that hydrogen tunneling, perhaps "vibrationally assisted,"[32] may cause a decreased temperature dependence of the rate and hence an abnormally low apparent activation energy.

(31) Cf. refs 7–11 and references cited therein.

(32) (a) Dewar, M. J. S.; Merz, K. M., Jr.; Stewart, J. J. P. *J. Chem. Soc., Chem. Commun.* **1985**, 166. (b) Dewar, M. J. S.; Healy, E. F.; Ruiz, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 2666.

(33) Hess, B. A., Jr.; Schaad, L. J.; Pancir, J. *J. Am. Chem. Soc.* **1985**, *107*, 149.

(34) Dormans, G. J. M.; Buck, H. M. *J. Am. Chem. Soc.* **1986**, *108*, 3253.

(35) Jensen, F.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 3139.

(36) Rappe, C. *Org. Synth.* **1973**, *53*, 123.

(37) Arndt, F. *Org. Synth.* **1943**, *2*, 166 (Note 5).

(38) (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1968**, 3495. (b) Simmons, H. E. et al. *Org. React. (N.Y.)* **1973**, *20*, Chapter 1.

cis-2-(2-Propyl)-cyclopropanecarboxaldehyde (28). The oxidation was carried out under Swern[39] conditions. Predistilled oxalyl chloride (6.9 mL, 76.7 mmol) was dissolved in 75 mL of CH_2Cl_2. The reaction mixture was cooled to −60 °C in a dry ice/$CHCl_3$ bath. After the solution was stirred for 2–3 min, dimethyl sulfoxide (10.6 mL, 150 mmol) was added dropwise. The reaction was stirred for 5 min. A solution of *cis*-2-(2-propyl)cyclopropanemethanol (**27**) (7.0 g, 61.4 mmol) in 25 mL of CH_2Cl_2 was added dropwise via syringe. A white cloudy suspension resulted, and 120 mL of CH_2Cl_2 was added. After 10 min, Et_3N (47.3 mL, 341 mmol; distilled from phthalic anhydride and then redistilled from KOH) was added dropwise via syringe. The reaction was stirred for 1 h at −55 °C, warmed to ambient temperature, and stirred for another 2 h. H_2O (100 mL) was added to the brown cloudy solution that resulted. The organic layer was washed several times with H_2O. The CH_2Cl_2 layer was dried over Na_2SO_4; distillation (bp 58 °C (20 Torr)) yielded a pale yellow liquid (6.4 g, 57 mmol, 93%). ^1H NMR: δ 9.32 (d, 1 H, J = 5.6 Hz), 1.86 (m, 1 H), 1.41 (m, 1 H), 1.21 (m, 3 H), 1.04 (d, 3 H, J = 6.6 Hz), 0.91 (d, 3 H, J = 6.6 Hz). ^{13}C NMR: δ 201.4 (d), 33.1 (d), 28.2 (d), 27.9 (d), 22.7 (q), 22.4 (q), 14.2 (t). GC/MS (70 eV): m/e 111 (0.2, M − H), 97 (10.9), 83 (13.9), 69 (26.6), 68 (14.3), 57 (36.4), 56 (100).

cis-2-(2-Propyl)-1-(1(*E*)-propenyl)cyclopropane (20). Method A. This reaction was carried out under Schlosser–Wittig conditions.[19] To a stirring suspension of ethyltriphenylphosphonium bromide (2.1 g, 5.7 mmol) in THF (20 mL) at −78 °C was added BuLi (2.3 mL, 5.7 mmol, 2.5 M solution in hexanes) via syringe. An orange solution resulted after about 30 min. To this solution was added *cis*-2-(2-propyl)cyclopropanecarboxaldehyde (**28**) (507 mg, 4.5 mmol in 10 mL of ether) over a 15-min period. The reaction was stirred for 1.5 h at −78 °C. BuLi (2.3 mL, 5.7 mmol, 2.5 M solution in hexanes) was added. After it was stirred for an additional 1.5 h at −78 °C, the reaction was warmed to 0 °C and potassium *tert*-butoxide (683 mg, 5.7 mmol; KOtBu) and *tert*-butyl alcohol (1.5 mL) were added. The reaction was stirred for an additional 30 min and then slowly quenched with water. The resulting solution was poured into a pentane/water bilayer. The pentane was washed twice with water and three times with brine. Most of the pentane was then removed by distillation through a Vigreux column. A preliminary purification of the resulting THF solution was accomplished by gas chromatography (column E, 75 °C), and a fraction (241 mg, 1.91 mmol, 42.4%) at t_r = 8.5–13 min was collected. The preliminary purification was required to protect the integrity of the $AgNO_3$ column (column H) used in the subsequent separation of the geometric (*E* and *Z*) isomers. This fraction was further chromatographed (column H, 50 °C), and two fractions were isolated. The first fraction (84.0 mg, 0.66 mmol, 14.7%; t_r = 6 min) was identified as the *E* olefin **20** and the longer retained fraction (95.6 mg, 0.76 mmol, 16.9%; t_r = 10 min) as the *Z* olefin **29**.

Data for cis-2-(2-Propyl)-1-(1(*E*)-propenyl)cyclopropane (20). ^1H NMR (500 MHz, $CDCl_3$): δ 5.51 (dq, 1 H, J = 15.2, 6.3 Hz), 5.19 (ddq, J = 15.2, 5.3, 1.5 Hz), 1.65 (dd, 3 H, J = 6.3, 1.5 Hz), 1.40 (m, 1 H), 1.09 (m, 1 H), 0.98 (d, 3 H, J = 6.6 Hz), 0.90 (d, 3 H, J = 6.5 Hz), 0.74 (ddd, 1 H, J = 8.3, 8.3, 4.4 Hz), 0.59 (m, 1 H), 0.10 (dd, 1 H, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 130.7 (d), 124.6 (d), 28.9 (d), 26.7 (q), 22.8 (d), 22.3 (d), 18.9 (q), 18.0 (q), 11.6 (t). GC/MS: m/e 124 (3, M^+), 109 (3), 95 (2), 81 (22), 68 (100), 67 (39). High-resolution GC/MS: m/e 124.1253 (calcd), 124.1264 (obsd). FT-IR: 3064 (w), 2959 (m), 2868 (m), 1663 (vw), 1458 (s), 1437 (m), 1382 (s), 1363 (m) cm^{-1}.

Data for cis-2-(2-Propyl)-1-(1(*Z*)-propenyl)cyclopropane (29). ^1H NMR: δ 5.43 (ddq, 1 H, J = 10.8, 1.0, 6.7 Hz), 5.05 (ddq, 1 H, J = 10.8, 9.3, 1.7 Hz), 1.70 (dd, 3 H, J = 6.7, 1.7 Hz), 1.60 (m, 1 H), 1.10 (m, 1 H), 0.99 (d, 3 H, J = 6.0 Hz), 0.90 (d, 3 H, J = 6.1 Hz), 0.88 (m, 1 H), 0.80 (m, 1 H), 0.12 (pseudo q, 1 H, J_{pseudo} = 5 Hz). ^{13}C NMR: δ 130.5, 124.0, 29.2, 26.9, 22.9, 22.1, 14.4, 13.2, 13.0. GC/MS: 124 (3, M^+), 109 (1), 95 (2), 86 (3), 81 (14), 68 (100), 67 (41). FT-IR: 3070 (w), 2957 (m), 1471 (s), 1380 (s) cm^{-1}.

Method B. This olefination was carried out via the method of Takai.[20] In a drybox and under an atmosphere of N_2, $CrCl_2$ (0.98 g, 8.0 mmol) was weighed into the reaction vessel. THF (20 mL) was added, and a dark green suspension resulted. To this was added dropwise a solution of *cis*-2-(2-propyl)cyclopropanecarboxaldehyde (**28**) (112 mg, 1.0 mmol) and 1,1-diiodoethane (564 mg, 2.0 mmol) in 3 mL of THF. The reaction vessel was wrapped in aluminum foil to protect from stray light and then stirred for 20 h. (After about 2 h, a dark orange suspension had formed.) This suspension was diluted with pentane, and the organic layer was washed several times with water. The organic layer was dried over $MgSO_4$, and most of the solvent was removed by distillation through a Vigreux column. The crude solution showed better than a 10:1 *E*:*Z* ratio by capillary gas chromatography (column C, conditions g). Preparative gas chromatography (column E, 75 °C) yielded one major fraction (25 mg, 20% yield; t_r = 26 min) flanked by two minor impurities. Residual 1,1-diiodoethane had a longer retention time (t_r = 36 min) and could easily be separated from the compound of interest. The isolated compound matched in all properties the *E* isomer isolated in the previous reaction.

Table II. Arrhenius Data for the Pyrolysis of *cis*-1-(1(*E*)-Propenyl)-2-(2-propyl)cyclopropane (**20**)[a]

temp (°C)	temp (K)	10^5k (s^{-1})	ln k
183.0	456.0	1.02	−11.5
192.4	465.4	2.33	−10.7
202.3	475.3	4.92	−9.92
215.6	488.6	14.2	−8.86
225.0	498.0	25.7	−8.27
234.1	507.1	57.5	−7.46
247.9	520.9	133	−6.62

[a] E_a = 35.5 ± 0.6 kcal/mol, log A = 12.05 (A, s^{-1}), ΔS^* = −6.5 ± 1.2 eu, r = 0.996.

Table III. Kinetic Data for the Pyrolysis of *cis*-1-(1(*E*)-Propenyl)-2-(2-propyl)cyclopropane (**20**) at 202.3 °C[a]

t (s)	area (%)	ln area	mass balance (%)
1762	40.41	3.70	95.7 (2)
3847	36.99	3.61	98.9 (2)
4772	34.54	3.54	95.2 (2)
6604	31.78	3.46	96.8 (2)
8843	28.65	3.35	98.9 (2)

[a] k = (4.92 ± 0.23) × 10^{-5} s^{-1}, r = 0.998.

Pyrolysis of cis-1-(1(*E*)-Propenyl)-2-(2-propyl)cyclopropane (20). Samples were prepared for pyrolysis as described in the supplementary material. The mass balance was assessed for every pyrolysis tube. Of the five or six tubes prepared for each pyrolysis, one was opened that had had no exposure to pyrolytic conditions. This sample was treated for analysis in the same way as all pyrolyzed samples (vide infra). In all cases, only one product from the pyrolysis was observed. It corresponded in all chromatographic and spectral properties to an independently prepared sample of (*Z*)-2-methyl-2,5-octadiene (**30**). The temperature dependence of the first-order rate constant is shown in Table II, and a sample kinetic run is shown in Table III. Control experiments showed that the product is stable under the pyrolysis conditions, the effect of surface is negligible, and the mass balance is >95% in most cases (see supplementary material).

Error Analysis of Kinetic Data. Error ranges for the derived rate constants were estimated by the method of Benson and O'Neal.[41] The time error was estimated at 3 s for every sample. Errors in concentration measurements were conservatively estimated as ±1% of the area for each gas chromatography analysis. The largest contributor to the error limits in a rate constant (as is pointed out by Benson) is imprecision or inaccuracy in temperature measurement. Variation in the salt bath itself was about 0.4 °C. The error was estimated as 0.5 °C in any temperature measurement. The final errors in the activation parameters (Table II) were calculated with use of the Benson–O'Neal protcol.[41]

Bicyclo[3,1,0]hex-3-en-2-one (33) (Scheme IX).[21] Bicyclo[3.1.0]hex-3-en-2-one (**33**) was prepared by flash vacuum pyrolysis[42] of 1aα,1bβ,2α,5α,5aβ,6aα-hexahydro-2,5-methanocycloprop[*a*]inden-6-(1*H*)-one (**39**) (18 g, 112 mmol) at 423–425 °C (0.02 Torr). Higher pyrolysis temperatures resulted in higher yields of phenol, and lower temperatures gave lower conversions of starting material. Upon completion of the pyrolysis, the trap was rinsed with ether. Cyclopentadiene and ether were removed by distillation. Further distillation (bp 73–74 °C (15 Torr)) yielded a colorless liquid (7.0 g, 74 mmol, 66%). A yellow viscous liquid (6.13 g) remained in the pot, which was shown by NMR analysis to contain 80% starting tetracyclic ketone **39**, 11% phenol, and 8.8% bicyclo[3.1.0]hex-3-en-2-one (**33**). The material balance for the process was 105%. Yield summary of bicyclo[3.1.0]hex-3-en-2-one (**33**): 66% isolated yield, 71% overall yield, 91% yield based on recovered starting material. ^1H NMR (500 MHz, benzene-d_6): δ 6.72 (ddd, 1 H,

(39) Mancuso, A. J.; Huang, S.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.
(40) Parziale, P. A. Ph.D. Dissertation, Yale University, New Haven, CT, 1990.
(41) Benson, S. W.; O'Neal, H. E. *Kinetic Data on Gas Phase Unimolecular Reactions*; NSRDS-NBS 21; Nat. Bur. Stand., U.S. Dept. of Commerce: Washington, DC, 1970; p 8.
(42) For a good general reference, see: Brown, R. C. *Pyrolytic Methods in Organic Chemistry*; Academic Press: New York, 1980.

J = 5.7, 2.5, 0.6 Hz), 5.32 (d, 1 H, J = 5.7 Hz), 1.67 (m, 1 H), 1.52 (m, 1 H), 0.64 (ddd, pseudo q, 1 H, J = 3.5, 3.5, 3.5 Hz), 0.60 (ddd, 1 H, J = 8.5, 6.7, 3.4 Hz). ^{1}H NMR ($CDCl_3$): δ 7.62 (ddd, 1 H, J = 5.6, 2.5, 0.5 Hz, H_4), 5.60 (d, 1 H, J = 5.6 Hz, H_3), 2.51 (m, 1 H, H_5), 2.17 (m, 1 H, H_1), 1.44 (ddd, 1 H, J = 8.5, 6.8, 3.5 Hz, H_6 (exo)), 1.28 (ddd, pseudo q, 1 H, J = 3.5, 3.5, 3.5 Hz, H_6 (endo)). ^{13}C NMR: δ 206.7 (s, C_2), 163.2 (d, C_4), 127.8 (d, C_3), 35.4 (t, C_6), 24.1 (d, C_1 or C_5), 22.9 (d, C_1 or C_5). GC/MS: m/e 94 (13, M^+), 66 (100), 65 (33), 40 (29), 39 (21). FT-IR: 2248 (s), 1715 (s), 1696 (s), 1570 (w), 1475 (w), 1472 (w) cm^{-1}.

Optical Resolution of Bicyclo[3.1.0]hex-3-en-2-one (33). (1*R*,2*R*,5*R*)-[(*S*)-(*N*-Methyl-*S*-phenylsulfonimidoyl)methyl]bicyclo-[3.1.0]hex-3-en-2-ol and (1*S*,2*S*,5*S*)-[(*S*)-(*N*-Methyl-*S*-phenylsulfonimidoyl)methyl]bicyclo[3.1.0]hex-3-en-2-ol (Enantiomers of 44 (Scheme X). (*S*)-(+)-*N*,*S*-dimethyl-*S*-phenylsulfoximine[22] (43.21 g, 0.255 mol, 92.2% ee) was dissolved in 600 mL of THF. The solution was cooled to 0 °C, and BuLi (0.255 mol, 102 mL of a 2.5 M solution in hexanes) was added dropwise via syringe. The solution was then stirred at ambient temperature for 15 min and recooled to −78 °C. A yellow suspension formed. To this was added bicyclo[3.1.0]hex-3-en-2-one (**33**) (23.94 g, 0.255 mol) as a solution in 125 mL of THF. Upon completion of the enone addition, the reaction was stirred for 2 h at −78 °C. The cold solution was then poured into a bilayer of ether and saturated aqueous NH_4Cl. The aqueous layer was extracted with three portions of ether. The combined ethereal extracts were dried over $MgSO_4$ and filtered, and the solvent was distilled away under a slight positive N_2 pressure. The residue was then applied to a 150-g silica column and flash chromatographed with use of a pentane/ether gradient (from 9:1 to 4:6). The fractions containing the two diastereomers were concentrated in vacuo. The solution was purified by preparative HPLC with one Prep-pak silica cartridge (purchased from Waters, Inc.), which was eluted with hexane/ethyl acetate (3:1) at a rate of 200 mL/min. On the first pass, the earlier eluting ($t_r \approx 3.5$ min) and the later eluting ($t_r \approx 4.5$ min) peaks were shaved, while the remainder was recycled. On the recycled pass, the two diastereomers were nearly completely resolved. Removal of solvents from the fractions gave 28.9 g (0.110 mol, 86.2%) of the earlier eluting diastereomer **44a** and 27.0 g (0.103 mol, 80.7%) of the later eluting diastereomer **44b**. Spectroscopic data for these compounds are given in the supplementary material.

Pyrolysis of the Sulfoximine Adducts. (1*R*,5*R*)-(−)-Bicyclo[3.1.0]-hex-3-en-2-one ((1*R*,5*R*)-(−)-33). A sample (28.91 g, 0.110 mol) of the slightly yellowed earlier eluting diastereomer **44a** was submitted to high vacuum (0.02 Torr) to remove all residual solvent. The sulfoximine adducts were quite viscous, and several hours of pumping were required for all the residual solvent to be removed. The adduct was then heated to 120 °C at 0.02 Torr in a bulb to bulb apparatus. The viscous liquid was stirred as rapidly as possible to minimize bumping. A colorless liquid was collected in a tapered graduated centrifuge tube. Trace amounts of sulfoximine and ethyl acetate (from the HPLC separation) were observed in the NMR of the distillate. Column chromatography (silica, pentane/ether (8:2)) easily separated the unwanted byproducts from the colorless liquid (8.4 g, 89 mmol, 81% yield), which was identical in all spectral properties with racemic bicyclo[3.1.0]hex-3-en-2-one (**33**). A small sample was purified by gas chromatography (column E, 100 °C, t_r = 4–10 min). This sample (98% chemical purity, column C, conditions h) had an optical rotation of $[\alpha]_D$ −263.0° (c 2.424 (EtOH)).

(1*S*,5*S*)-(+)-Bicyclo[3.1.0]hex-3-en-2-one ((1*S*,5*S*)-(+)-33). The later eluting diastereomer (**44b**) (27.0 g, 0.103 mol) was treated in an identical manner. After pyrolysis and purification, a 6.0-g (63.8-mmol, 62.0%) sample of a colorless liquid was obtained. This sample (100% chemical purity, column C) was identical in all spectral properties with racemic bicyclo[3.1.0]hex-3-en-2-one (**33**) and had an optical rotation $[\alpha]_D$ +284.1° (c 2.075 (EtOH)).

Correlation of Configuration of (−)-Bicyclo[3.1.0]hex-3-en-2-one ((−)-33) (Scheme XI). Bicyclo[3.1.0]hexan-2-one (45). A sample of (−)-bicyclohex-3-en-2-one ((−)-**33**) (196 mg, 2.08 mmol; $[\alpha]_D$ −307.6° (c 1.956 (EtOH))) was reduced in 20 mL of absolute EtOH with 10 mg of 10% Pd on carbon under a slight positive pressure of H_2. Over a 1-h period, a H_2 uptake of 30 mL (1.3 mmol) was observed. The catalyst was immediately filtered away, and the reaction was checked by capillary GC (column C, conditions c). The chromatogram showed 49% phenol and 42% bicyclo[3.1.0]hexan-2-one. No starting material was observed. Ether and H_2O were added to the filtrate, and the ethereal layer was washed several times with saturated K_2CO_3 solution. The ethereal layer was dried over $MgSO_4$, and the solvent was removed by distillation. The residue was purified by preparative gas chromatography (column E, 80 °C, t_r = 9 min). ^{1}H NMR: δ 2.05 (m, 5 H), 1.73 (m, 1 H), 1.16 (m, 1 H), 0.90 (m, 1 H).

Reduction of Bicyclo[3.1.0]hexan-2-one (45) to 3-Methylcyclopentanone (46). A sample of (−)-bicyclo[3.1.0]hexan-2-one (**45**) (42.67 mg, 0.444 mmol; $[\alpha]_D$ −4.78° (c 2.113 (ether)); 97.2% chemical purity by capillary gas chromatography, column C, conditions c) was reduced with Li and NH_3. NH_3 (150 mL) was condensed into the distillation chamber, Na was added, and the resulting deep blue solution was refluxed for 1 h. The valve from the distillation chamber to the reaction flask was opened, and approximately 50 mL of NH_3 was condensed in the reaction flask. Li wire (140 mg, 3.2-mm diameter), which had been washed in pentane and weighed in a stoppered flask containing pentane, was added in four small pieces. The deep blue solution was mechanically stirred for 10 min to dissolve all of the Li. (−)-Bicyclo[3.1.0]hexan-2-one (**45**) (42.67 mg) in 5 mL of ether was added. The reaction was refluxed for 1 h, and then sodium benzoate (639 mg, 4.44 mmol; predried at 0.02 Torr for 12 h) was added.[43] The deep blue color disappeared, and a yellow-brown color became apparent. Ether was added, and the reaction was stirred at ambient temperature to allow the residual NH_3 to evaporate. Excess base was neutralized by very slow addition of a saturated NH_4Cl solution to the ethereal solution. The ethereal layer was then washed with aqueous $NaHCO_3$ and brine and dried over $MgSO_4$. Capillary gas chromatography (column C, conditions c) showed 64% 3-methylcyclopentanone (**46**). A colorless liquid (11.28 mg, 0.115 mmol, 26%) was isolated by preparative gas chromatography (column F, 70 °C). The ^{1}H NMR spectrum was identical with that of authentic 3-methylcyclopentanone (Aldrich). Capillary gas chromatography (column C, conditions c) showed a single peak (100%) at t_r = 10 min. The rotation of the entire sample was measured by polarimetry ($[\alpha]_D$ +142.2° (c 0.564 ($CHCl_3$))).[44] The configuration of (−)-bicyclo[3.1.0]hex-3-en-2-one ((−)-**33**) was therefore established: 1*R*,5*R*.

Analysis of Enantiomeric Excess of Bicyclo[3.1.0]hex-3-en-2-one (33). The enantiomeric excess (ee) of optically active bicyclo[3.1.0]hex-3-en-2-one (**33**) was analyzed by conversion of the sample to *exo*-bicyclo-[3.1.0]hex-3-en-2-ol and subsequent methylation with NaH and MeI. The enantiomers of the exo methyl ether could be separated on capillary column B at 80 °C. The column was installed in the Varian capillary gas chromatograph. The injector end of the column was attached as per the instructions in the instrument manual. The detector end was connected to a 20-cm length of uncoated capillary tubing (0.25 mm i.d.) with use of a butt to butt union. The union (catalog number ZU.5FS.4) was obtained from Quadrex Corp. A vent for the effluent was formed by inverting a small funnel over the detector and connecting this to an exhaust vent. All samples were diluted in pentane. (Ethereal solvents had a deleterious effect on the performance of this column.) The head pressure was set at 10 psi, which gave a linear flow velocity of 32.1 cm/s. A calibration analysis of racemic 4-methoxybicyclo[3.1.0]hex-2-ene gave a ratio of enantiomer peak areas (1*R*,5*R*:1*S*,5*S*) of 1.022. The ee value of each enantiomerically enriched sample (see below) was determined by integration of the respective enantiomer peaks and is reported both with and without this correction.

1α,2α,5α- and 1α,2β,5α-Bicyclo[3.1.0]hex-3-en-2-ol (exo) and (endo). Bicyclo[3.1.0]hex-3-en-2-one (**33**) was reduced to the corresponding endo and exo allylic alcohols via the procedure described by Luche.[45] To a stirred solution of the enone **33** (940 mg, 10 mmol) and $CeCl_3 \cdot 7H_2O$ (3.91 g, 10.5 mmol) in 25 mL of MeOH was added $NaBH_4$ (400 mg, 10.5 mmol) in approximately 50-mg portions. Rapid H_2 evolution was observed, and the addition was stopped until the reaction became less vigorous. The reaction was stirred for 15 min and then quenched slowly with H_2O. The aqueous solution was extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. The pale yellow liquid had an odor similar to pyridine. The crude reaction mixture showed a 2:1 ratio of products by capillary gas chromatography on column A (conditions h). This solution was saved and purified by preparative gas chromatography (column F, 80 °C) as needed. Two fractions were collected. The first (t_r = 15 min) and larger of the two was assigned as *exo*-bicyclo[3.1.0]hex-3-en-2-ol by comparison of the ^{1}H NMR to literature spectra.[46–48] These data are reported elsewhere.[40]

Preparation of Methyllithium-d_3 (CD_3Li). The procedure of Schöllkopf et al. for the preparation of methyl lithium was used.[50] Iodomethane-d_3 (Aldrich, 99+ atom % D) was substituted for iodomethane.

(43) We thank Prof. F. E. Ziegler for suggesting this method of quenching excess Li.

(44) Eisenbraun and McElvain (ref 25) report $[\alpha]_D$ +154.8° (c 0.73 ($CHCl_3$)) for (+)-(3*R*)-3-methylcyclopentanone.

(45) Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.

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(47) Farenhorst, E.; Bickel, A. F. *Tetrahedron Lett.* **1966**, 5911.

(48) Hasty, N. Ph.D. Dissertation, Yale University, New Haven, CT, 1971, p 103 and references cited therein.

(49) Proton assignment by E. J. Stark.

Iodomethane-d_3 (105 g, 0.724 mol) was added with rapid stirring via an addition funnel to Li wire (11.8 g, 1.69 g-atoms) in 600 mL of ether under an N_2 atmosphere. Initially, a small amount of iodomethane was added, and the reaction was warmed slightly with a water bath until the ether refluxed gently. Then the iodomethane-d_3 was added at a rate to maintain the ether reflux. The reaction was stirred for several hours and allowed to sit overnight. The cloudy ethereal solution was cannulated into a dry bottle and stored at −10 °C. A white precipitate collected at the bottom of the bottle. The concentration (0.88 M) of CD_3Li was determined by quenching a known volume with water and titrating this solution with 0.1 N HCl.

(1*S*,5*S*)-(+)-*exo*-4-Methylbicyclo[3.1.0]hexan-2-one-7-d_3 ((1*S*,5*S*)-(+)-34) (Scheme VIII). This compound was prepared in the same manner described for (±)-*exo*-4-methylbicyclo[3.1.0]hexan-2-one ((±)-**34** with the substitution of CD_3Li for CH_3Li and of (+)-**33** for (±)-**33**. The cuprate reagent $(CD_3)_2CuLi$ was generated at 0 °C in ether (600 mL) with use of CuI (33.0 g, 173 mmol) and CD_3Li (394 mL of a 0.88 M solution in ether, 347 mmol). (1*S*,5*S*)-(+)-bicyclo[3.1.0]hex-3-en-2-one ((1*S*,5*S*)-(+)-**33** (8.15 g, 86.7 mmol, 86.7% ee) was added dropwise as a solution in 200 mL of ether over about a 1-h period. After the solution was stirred for 1 h at 0 °C, a saturated aqueous NH_4Cl solution was added dropwise. The product was extracted with ether, and the ethereal layer was washed with NH_4Cl solution until the washes were colorless. The ethereal layer was filtered and dried over $MgSO_4$, and the solvent was removed under reduced pressure. A yellow oil (5.15 g, 45.6 mmol, 52.6% yield: $[\alpha]_D$ +51.2° (*c* 0.658 (EtOH))) was obtained. ^1H NMR: δ 2.33 (br d, 1 H, *J* = 7.6 Hz), 2.24 (ddq, 1 H, *J* = 17.5, 7.6, 0.6 Hz), 1.82 (ddd, 1 H, *J* = 7.4, 4.8, 4.8 Hz), 1.73 (m, 1 H), 1.55 (dd, 1 H, *J* = 17.5, 1.2 Hz), 1.13 (m, 1 H), 0.91 (ddd, 1 H, *J* = 4.8, 4.8, 3.1 Hz). ^{13}C NMR: δ 214.5 (C_2), 39.9 (C_3), 29.7 (C_1 or C_5), 29.1 (C_1 or C_5), 26.7 (C_4), 21.3 (septet, *J*(CD) = 18.9 Hz, C_7), 14.1 (C_6). GC/MS: *m/e* (113 (67, M^+), 112 (1.5), 111 (0.1), 85 (22), 71 (29), 70 (42), 69 (21), 68 (76), 67 (62), 55 (100).

(1*R*,5*R*)-(−)-*exo*-4-Methylbicyclo[3.1.0]hexan-2-one-7-d_3 ((1*R*,5*R*)-(−)-34). This compound was prepared from (1*R*,5*R*)-(−)-bicyclo[3.1.0]hex-3-en-2-one ((1*R*,5*R*)-(−)-**33**) (83.0% ee) in the same manner described for (1*S*,5*S*)-(+)-*exo*-4-methylbicyclo[3.1.0]hexan-2-one-7-d_3 ((1*S*,5*S*)-(+)-**34**. This compound exhibited spectral properties identical with those of the 1*S*,5*S* compound (1*S*,5*S*)-(+)-**34** except $[\alpha]_D$ −43.2° (*c* 0.803 (EtOH)).

Racemic *exo*-5-Methyl-3-oxabicyclo[4.1.0]heptan-2-one (36). A solution of racemic 4-methylbicyclo[3.1.0]hexan-2-one (**34**) (1.0 g, 9.1 mmol), 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide[27] (tbp; 20 mg, 0.056 mmol), and *m*-chloroperoxybenzoic acid (2.0 g, 11.6 mmol) in 5 mL of 1,2-dichloroethane was heated to reflux for 15 h. The reaction was checked by gas chromatography on either column A (conditions f) or column C (conditions b) and showed approximately 2% starting ketone **34** remaining. The white crystals that had formed on cooling were dissolved in a mixture of H_2O, saturated $NaHSO_3$ solution, ether, and CH_2Cl_2. The ether layer was washed twice with saturated $NaHSO_3$ solution and twice with saturated K_2CO_3 solution. After the solution was dried over Na_2SO_4, the solvent was removed by rotary evaporation. The yellow oil was flash chromatographed on silica gel with use of a pentane/ether gradient (from 9:1 to 4:6) elution. Approximately 50 mg (5% recovery) of the starting ketone **34** was isolated as the first eluting compound. The next compound to elute was identified as *exo*-5-methyl-2-oxabicyclo[4.1.0]heptan-3-one (**35**) (approximately 60 mg, 5%). The latest eluting material was 5-methyl-3-oxabicyclo[4.1.0]heptan-2-one (612 mg, 4.8 mmol, 53.4%) (**36**).

Data for *exo*-5-Methyl-2-oxabicyclo[4.1.0]heptan-3-one (35). ^1H NMR: δ 3.94 (td, 1 H, *J* = 6.7, 2.8 Hz), 2.27 (dd, 1 H, *J* = 15.9, 4.4 Hz), 2.07 (dd, 1 H, *J* = 15.9, 9.1 Hz), 1.90 (m, 1 H), 1.14 (d, 3 H, *J* = 6.7 Hz), 0.90 (m, 2 H), 0.68 (m, 1 H). ^{13}C NMR: δ 171.5, 54.8, 36.3, 29.3, 21.3, 16.4, 13.3. GC/MS: *m/e* 111 (0.6, M − 15), 98 (5.4), 84 (79), 69 (20), 55 (100). FT-IR: 3085 (w), 3048 (w), 2964 (w), 2875 (w), 1741 (s), 1275 (m), 1247 (m), 1241 (m) cm^{-1}.

Data for *exo*-5-Methyl-3-oxabicyclo[4.1.0]heptan-2-one (36). ^1H NMR: δ 4.06 (dd, 1 H, *J* = 11.9, 3.4 Hz), 3.84 (ddd, 1 H, *J* = 11.9, 1.2, 1.2 Hz), 2.12 (m, 1 H), 1.75 (m, 1 H), 1.53 (m, 1 H), 1.31 (ddd, 1 H, *J* = 5.3 Hz), 1.09 (d, 3 H, *J* = 7.0 Hz), 1.06 (m, 1 H). ^{13}C NMR: δ 171.2 (s), 69.0 (t), 25.1 (d), 21.5 (d), 17.9 (q), 14.8 (d), 8.9 (t). GC/MS: *m/e* 126 (9.6, M), 96 (74), 81 (100), 68 (74), 67 (79). FT-IR: 3026 (w), 2971 (w), 2917 (w), 2880 (w), 1721 (s), 1489 (w), 1407 (w), 1308 (w), 1258 (w), 1234 (w), 1146 (w), 1077 (m) cm^{-1}.

(1*S*,5*S*,6*S*)-*exo*-5-Methyl-3-oxabicyclo[4.1.0]heptan-2-one-8-d_3 ((1*S*,6*S*)-36). This compound was synthesized from the optically active ketone (+)-(1*S*,5*S*)-**34** (5.15 g, 45.6 mmol) in a manner similar to the synthesis of the unlabeled racemic analogue. It was shown by capillary gas chromatography that the basic washes contained some of the desired product so the workup was modified. Upon completion of the reaction, the entire reaction mixture was applied to a silica column and gradient eluted with pentane/ether. The desired product could not be visualized with anisaldehyde, vanillin, or phosphomolybdic acid stains or by UV. I_2 was the only useful visualization method for this compound. The fractions containing the desired product were rechromatographed under identical conditions to remove residual *m*CPBA. The product (3.21 g, 24.9 mmol, 54.6% yield; $[\alpha]_D$ −11.1° (*c* 1.785 (EtOH)); 99.5% by capillary GC, column A, conditions f) existed as a pale yellow semisolid at room tempertaure. ^1H NMR[51] (∼1 mg/mL): δ 4.12 (dd, 1 H, *J* = 11.9, 3.4 Hz), 3.93 (d of pseudo t, 1 H, *J* = 11.9, 1.4 Hz), 2.16 (br s, 1 H), 1.83 (d of pseudo t, 1 H, *J* = 9.3, 4.3 Hz), 1.57 (pseudo q of m, J_q = 7.6 Hz), 1.37 (pseudo q of d, 1 H, J_q = 4.3 Hz, J_d = 1.4 Hz), 1.15 (m, 1 H). ^1H NMR (∼50 mg/mL): δ 3.94 (dd, 1 H, *J* = 11.9, 3.4 Hz), 3.69 (d of pseudo t, 1 H, *J* = 11.9, 1.4 Hz), 1.97 (br s, 1 H), 1.58 (d of pseudo t, 1 H, *J* = 9.3, 4.3 Hz), 1.40 (pseudo q of pseudo t, 1 H, J_q = 7.6 Hz, J_t = 1.9 Hz), 1.20 (pseudo q of d, 1 H, *J* = 4.3, 1.4 Hz), 0.93 (m, 1 H). ^{13}C NMR:[52] δ 171.1 (C_2), 68.7 (C_4), 24.4 (C_1), 21.2 (C_5 or C_6), 16.7 (septet, *J*(CD) = 19.3 Hz, C_8), 14.4 (C_6 or C_5), 8.6 (C_7). GC/MS: *m/e* 129 (23, M^+), 99 (100), 98 (7.9), 97 (1.9), 81 (91), 71 (36), 70 (31).

Determination of the Deuterium Content in the Methyl Position of *exo*-5-Methyl-3-oxabicyclo[4.1.0]heptan-2-one-8-d_3 (36). The deuterium incorporation into the methyl group in each enantiomer of the lactones (1*S*,5*S*,6*S*)-**36** and (1*R*,5*R*,6*R*)-**36** was determined by GC/MS. The molecular ion was not very useful as its intensity was rather low, but the parent ion (96 in the unlabeled compound and 99 for the labeled d_3 compounds) was useful. This ion represented the molecular ion minus a CH_2O fragment. It was assumed that there was no isotope effect in the fragmentation of this molecule; i.e., the fragmentation pattern of the unlabeled compound (d_0) is reflected exactly in the deuteriated compounds (d_3, d_2, d_1). A computer program was used to mimic the observed distribution of masses, given a particular distribution of masses for the unlabeled compound. We are grateful to Mr. Robert Rosenberg, who wrote the program and ran it on a VAX station II/GPX computer. We thank Professor K. B. Wiberg for access to the computer. The program and calculational results are given elsewhere.[40] The analysis indicated at least 99% d_3.

***exo*-5-Methyl-3-oxabicyclo[4.1.0]heptan-2-ol (37).** DIBAL (150 μL, 1 M solution in hexanes, 0.15 mmol) was added via syringe to a precooled (−78 °C) solution of *exo*-5-methyl-3-oxa-bicyclo[4.1.0]heptan-2-one (**36**) (12.6 mg, 0.1 mmol) in 0.5 mL of ether. After it was stirred for 3 h at −78 °C, the reaction was quenched with 10 μL of CH_3OH. The cold solution was applied to an 8-g silica column and eluted with pentane/ether (gradient elution from 9:1 to 1:1). The material ($R_f \approx 0.3$ in pentane/ether (1:1)) that gave green spots when developed with anisaldehyde stain was combined and concentrated in vacuo. The colorless liquid was dissolved in benzene-d_6 for spectral analysis. As this compound exists as a mixture of three distinct isomers (one monocyclic aldehyde and two epimeric bicyclic lactols), the NMR spectrum in benzene-d_6 is shown elsewhere[40] rather than reported in tabular form here.

In $CDCl_3$, the desired lactol was converted to a dimeric lactol, presumably under the influence of traces of acid in the $CDCl_3$. The NMR spectrum of this compound is shown elsewhere.[40] Hydrolysis of this dimeric lactol was effected by dissolving the material from reduction of *exo*-5-methyl-3-oxabicyclo[4.1.0]heptan-2-one (**36**) (1.49 g, 11.5 mmol) in 250 mL of THF and adding H_2O to the saturation point. Then 5 drops of concentrated sulfuric acid was added, and the solution was stirred for 12 h at ambient temperature. The solution was poured into a bilayer of ether and a saturated aqueous $NaHCO_3$ solution. The ethereal layer was washed twice with the bicarbonate solution, once with water, and once with brine. After the solution was dried over $MgSO_4$, the solvent was removed under reduced pressure to give a colorless liquid whose spectral properties were identical with *exo*-5-methyl-3-oxabicyclo[4.1.0]heptan-2-ol (**37**).

Optically Active Labeled 37. The procedure for the reduction of the unlabeled material was generally followed. To a stirring solution of (1*S*,6*S*)-*exo*-5-methyl-3-oxabicyclo[4.1.0]heptan-2-one-8-d_3 ((1*S*,6*S*)-**36**) (2.37 g, 18.4 mmol) in 100 mL of ether, which had been precooled to −78 °C, was added DIBAL (20.2 mL, 1 M solution in hexanes, 20.2 mmol) dropwise via syringe. The reaction was stirred for 3 h at −78 °C and then quenched with 2 mL of MeOH. After it was stirred for 15 min at −78

(50) Schöllkopf, U.; Paust, J.; Patsch, M. R. *Org. Synth.* **1973**, 860 (Note 4).

(51) The chemical shifts for this compound (and presumably for the unlabeled compound) are concentration-dependent.

(52) For a description of the isotope effect of D on ^{13}C chemical shifts, see: Wesener, J. R.; Moskau, D.; Günther, H. *J. Am. Chem. Soc.* **1985**, *107*, 7307.

°C, the entire mixture was filtered through a 50-g silica column and the silica was washed with ether. The filtrate was concentrated in vacuo and carefully chromatographed on a 50-g silica column with a gradient elution of pentane/ether (from 9:1 to 6:4). The appropriate column fractions (R_f = 0.3, pentane/ether (1:1), green spots under anisaldehyde stain) were concentrated in vacuo to give a colorless liquid (1.49 g, 11.3 mmol, 61%). The ^{1}H NMR spectrum is shown elsewhere.[40]

1(*R*)-[2(*S*)-(1-Hydroxypropyl-*3*-d_3)]-2(*R*)-(1(*E*)- and -(*Z*)-propenyl-*2*-*d*)cyclopropane (38). BuLi (11.4 mL of a 2.5 M solution in hexanes, 28.5 mmol) was added dropwise to a stirring suspension of ethyl-*1*-d_2-triphenylphosphonium bromide[53] in 250 mL of THF. The ylide was stirred at room temperature for 2 h until all the solid had dissolved. The bright orange-red solution was then cooled to −78 °C, and a solution of (1*S*,6*S*)-*exo*-5-methyl-3-oxabicyclo[4.1.0]heptan-2-ol-*8*-d_3 ((1*S*,6*S*)-**37**) (1.49 g, 11.4 mmol) in 10 mL of THF was added over a 1-h period. The solution was stirred for 5 h and then warmed to −50 °C. BuLi (5.7 mL of a 2.5 M solution in hexanes, 14.2 mmol) was added, and the reaction was stirred for another 3 h. The reaction was warmed to −30 °C, and 4 mL of MeOD was added to quench. The suspension was stirred for 3 h, D_2O (5 mL) was added, and the reaction was allowed to warm to ambient temperature. The solution was poured into an ether/water bilayer, and the product was extracted with ether. The ethereal extracts were washed with water. After they were dried ($MgSO_4$), the ethereal extracts were concentrated in vacuo and the residue was chromatographed on a 50-g silica column with a gradient pentane/ether elution (from 9:1 to 4:6). A colorless liquid (883 mg, 6.13 mmol, 54%) resulted. Capillary GC analysis showed a 65:35 mixture of two products presumed to be the *E* and *Z* isomers, respectively. Because this mixture was carried forward, the NMR of the mixture is shown elsewhere. When this reaction was carried out with unlabeled ethyltriphenylphosphonium bromide and a D_2O quench at −30 °C, only 82% deuterium incorporation was observed at the vinyl position.

1(*R*)-[2(*S*)-(1-Hydroxypropyl-*3*-d_3)]-2(*R*)-(1(*E*)- and -(*Z*)-propenyl-*2*-*d*)cyclopropyl Methanesulfonate. To a solution of 1(*R*)-[2-(*S*)-(1-hydroxypropyl-*3*-d_3)]-2(*R*)-(1(*E*)- and -(*Z*)-propenyl-*2*-*d*)-cyclopropane (**38**) (883 mg, 6.13 mmol) and triethylamine (929 mg, 9.19 mmol, distilled from phthalic anhydride and stored over KOH) in CH_2Cl_2 (50 mL), which had been cooled to −5 °C, was added methanesulfonyl chloride (913 mg, 7.97 mmol) dropwise. The solution was stirred for 30 min and then warmed to room temperature. The solution was washed with H_2O, saturated $NaHCO_3$ solution, and brine and then dried over $MgSO_4$. The pale yellow liquid (1.32 g, 5.95 mmol, 97%) was used without further purification. The NMR for the *E* and *Z* mixture is shown elsewhere.[40]

***cis*-2(*S*)-(2(*S*)-Propyl-*1*-d_3)-1(*S*)-(1(*E*) and -(*Z*)-propenyl-*2*-*d*)-cyclopropane (20a and 29-d_4) (Scheme VIII).** To an ice-bath-cooled stirred solution of the above mixture of methanesulfonates (1.32 g, 5.94 mmol) in 50 mL of THF was added $LiAlH_4$ (226 mg, 5.94 mmol) in several portions. The reaction was warmed to room temperature and stirred for 12 h. During the 12-h period, the progress of the reaction was monitored by capillary GC (column A, conditions i) and an additional 226 mg $LiAlH_4$ was added. The suspension was added to a pentane/H_2O bilayer in small portions to control the rate of H_2 evolution. The pentane layer was washed with 0.1 N HCl, saturated $NaHCO_3$, H_2O, and brine. After the pentane layer was dried over $MgSO_4$, 500 mL of the pentane was removed by fractional distillation. The remaining pentane solution was passed through a 25-g silica column, and the column was washed with 250 mL of pentane. The pentane was removed by fractional distillation. The residue was subjected to a preliminary purification by gas chromatography with use of column E (75 °C). Capillary gas chromatographic analysis (column A, conditions e) showed an *E*:*Z* ratio of 60.0:38.7. The isolated geometric isomers were separated on column H (room temperature, about 18 °C).

The deuterium incorporation at the vinyl position in each isomer was determined by NMR integration of the two vinyl resonances in each compound. The deuterium incorporation in the vinyl position of the *E* isomer **20** was 97.0 ± 0.5%. The deuterium incorporation of the *Z* isomer **29** was 94.0 ± 0.5%.

Data for *cis*-2(*S*)-(2(*S*)-Propyl-*1*-d_3)-1(*S*)-(1(*E*)-propenyl-*2*-*d*)-cyclopropane (20a). ^{1}H NMR: δ 5.5 (m, 0.03 H), 5.18 (dq, 1 H, *J* = 8.5, 1.9 Hz), 1.64 (br s, 3 H), 1.40 (dddd, 1 H, *J* = 8.4, 8.4, 8.4, 5.4 Hz), 1.09 (m, 1 H), 0.91 (d, 3 H, *J* = 6.4 Hz), 0.74 (ddd, 1 H, *J* = 4.4, 8.2, 8.2 Hz), 0.59 (dddd, 1 H, *J* = 5.7, 8.5, 8.5, 8.5 Hz), 0.09 (ddd, pseudo q, *J* = 5.4 Hz). ^{13}C NMR:[54] δ130.6, 124.3 (CD, t), 28.6, 26.6, 22.2, 18.8, 17.9, 11.6. GC/MS: *m/e* 128 (14, M^+), 113 (10), 110 (5), 82 (52), 69 (100), 68 (43).

Data for *cis*-2(*S*)-(2(*S*)-Propyl-*1*-d_3)-1(*S*)-1(*Z*)-propenyl-*2*-*d*)-cyclopropane (29-d_4). ^{1}H NMR: δ 5.45 (m, 0.06 H), 5.05 (br d, 1 H, *J* = 9.6 Hz), 1.70 (s, 3 H), 1.59 (m, 1 H), 1.08 (m, 1 H), 0.90 (d, 3 H, *J* = 6.4 Hz), 0.86 (m, 1 H), 0.67 (m, 1 H), 0.10 (ddd, pseudo q, 1 H, *J* = 5 Hz). GC/MS: *m/e* 128 (6, M^+), 113 (1), 82 (16), 69 (100).

Oxidative Degradation of (*Z*)- and (*E*)-2-Methyl-2,5-octadiene-*7*-d_2. The oxidative cleavage of (*Z*)- and (*E*)-2-methyl-2,5-octadiene-*7*-d_2 ((*Z*)- and (*E*)-**30**-d_2) was carried out under the conditions described by Sharpless and co-workers.[55] $RuO_2 \cdot H_2O$ (5 mg) was added to a stirring biphasic solution of $NaIO_4$ (171.2 mg, 0.8 mmol) in 0.2 mL of CCl_4, 0.2 mL of CH_3CN, and 0.3 mL of H_2O. The black powdery RuO_2 yielded a yellow-green suspension (RuO_4) after a few seconds. To this were added (*Z*)- and (*E*)-2-methyl-2,5-octadiene-*7*-d_2 (12.6 mg, 0.1 mmol, 92% *Z*, 7% *E*, 96% d_2, 4% d_1, 0% d_0) via syringe. The black suspension reformed immediately upon addition of the diene. The reaction was stirred for 3 h at ambient temperature under a dry N_2 atmosphere. The black suspension was then diluted with 10 mL of CH_2Cl_2 and 10 mL of H_2O. Concentrated HCl (1 drop) was added to the aqueous layer, and the acidic (pH 1–2) aqueous layer was extracted with 30 mL of CH_2Cl_2. The extracts were dried over $NaSO_4$. Capillary GC analysis (column A, conditions j) of the organic extracts showed no diene remaining and a characteristic broad peak (t_r = 14–15 min) for propanoic acid. The solvent volume was reduced to 4 mL by simple distillation. (The distillate was checked by capillary GC and contained no products or starting materials.) The 4-mL solution was distilled bulb to bulb at 0.05 Torr to separate it from the remaining ruthenium oxides. The distillate showed the characteristic broad propanoic acid peak in the capillary GC analysis and was carried on without further purification.

(*R*)-Methyl 2-Propionyloxy-2-phenylethanoate (48). This compound was prepared by the method of Parker.[29] To a solution of 4-(dimethylamino)pyridine (one crystal; DMAP) and propanoic acid (74 mg, 74 μL, 1.0 mmol) in CH_2Cl_2 at −15 °C (ethylene glycol/dry ice) was added (*R*)-(−)-methyl 2-hydroxy-2-phenylethanoate (166 mg, 1.0 mmol) and dicyclohexylcarbodiimide (206 mg, 1.0 mmol; DCC). A white suspension soon formed, and the reaction was stirred for 3 h. The white precipitate was removed by filtration, and the resulting solution was concentrated in vacuo. The residue was chromatographed (silica gel, pentane/ether (9:1), $R_f \approx 0.3$) on silica eluted with pentane/ether (95:5 and then 9:1). ^{1}H NMR ($CDCl_3$): δ 7.43 (m, 2 H), 7.33 (m, 3 H), 5.91 (s, 1 H), 3.64 (s, 3 H), 2.44 (dq, 1 H, J_q = 7.5 Hz, J_d = 15.8 Hz), 2.42 (dq, 1 H, J_d = 15.8 Hz, J_q = 7.5 Hz), 1.15 (t, 3 H, *J* = 7.5 Hz). ^{1}H NMR[56] (C_6D_6): δ 7.43 (m, 2 H, aromatic H), 7.03 (m, 3 H, aromatic H), 6.07 (s, 1 H, benzylic H), 3.17 (s, 3 H, OMe), 2.17 (dq, 1 H, J_d = 16.6 Hz, J_q = 7.5 Hz, H_S), 2.10 (dq, 1 H, J_d = 16.6 Hz, J_q = 7.5 Hz, H_R), 0.94 (t, 3 H, *J* = 7.5 Hz, CH_3). ^{1}H NMR (C_6D_6, 500 MHz): δ 7.44 (m, 2 H), 7.06 (m, 3 H), 6.07 (s, 1 H), 3.17 (s, 3 H), 2.20 (dq, 1 H, J_d = 16.6 Hz, J_q = 7.5 Hz), 2.07 (dq, 1 H, J_d = 16.6 Hz, J_q = 7.5 Hz), 0.95 (t, 3 H, *J* = 7.5 Hz). ^{13}C NMR ($CDCl_3$): δ 173.5 (s), 169.2 (s), 133.8 (s), 129.0 (d), 128.6 (d), 127.4 (d), 74.1 (d), 52.3 (q), 27.1 (t), 8.7 (q). GC/MS: *m/e* 222 (8.9, M^+), 190 (64.8), 166 (96.3), 163 (100), 121 (38.2), 107 (29.8), 105 (64.3), 57 (68.6). FT-IR: 3037 (w), 2987 (w), 2955 (w), 2946 (w), 1744 (s), 1456 (w), 1437 (w), 1220 (m), 1170 (m).

(*R*)-Methyl 2-Propionyloxy-*2'*-d_2-2-phenylethanoate (48-d_2). The bulb to bulb distillate obtained from oxidative degradation of (*Z*)- and (*E*)-2-methyl-2,5-octadiene-*7*-d_2 was submitted to the same conditions described for the labeled propanoic acid with DMAP (one crystal), (*R*)-(−)-methyl 2-hydroxy-2-phenylethanoate (16.6 mg, 0.1 mmol) and DCC (20.6 mg, 0.1 mmol). After chromatography, a white solid (4.0 mg, 0.018 mmol, 18% overall yield from the diene) was isolated. The isotopic distribution (93% d_2, 6.5% d_1, 0.5% d_0) was determined by GC/MS. ^{1}H NMR (C_6D_6): δ 7.44 (dd, 2 H, *J* = 7.7, 1.6 Hz), 7.03 (m, 3 H), 6.07 (s, 1 H), 3.17 (s, 3 H), 0.94 (br s, 3 H). No detectable signals at 2.20 or 2.07 ^{13}C NMR (C_6D_6):[56] δ 173.3, 169.4, 134.8, 129.2, 128.9, 74.8, 51.9, 25.7 (CD coupled), 8.79. GC/MS: *m/e* 224 (7, M^+), 192 (62.3), 191 (4.5), 190 (0.4), 167 (67), 165 (100), 108 (27), 105 (43).

Preparative Pyrolysis of *cis*-2(*S*)-(2(*S*)-Propyl-*1*-d_3)-1(*S*)-(1(*E*)-propenyl-*2*-*d*)cyclopropane (20). Twenty-six base-washed silanized Pyrex tubes each containing 2 mg of *cis*-2(*S*)-(2(*S*)-propyl-*1*-d_3)-1(*S*)-(1-(*E*)-propenyl-*2*-*d*)cyclopropane (**20**) were sealed at (1–5) × 10^{-6} Torr after 3 freeze/pump/thaw cycles. The tubes were pyrolyzed in a salt bath (see supplementary material) at 230 ± 0.05 °C for 4.75 h and removed to an ice bath. Eighteen of the tubes were opened, and all but one tube were rinsed with pentane. One tube was rinsed with $CDCl_3$ for NMR study. The pentane washes were combined, and capillary GC analysis (column A, conditions e) showed 98.1% diene product (t_r = 31.6

(53) Heimgartner, H.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1972**, *55*, 1385.

(54) The deuteriated methyl C was not observed.

(55) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(56) One of the aromatic carbon signals seems to be obscured by the benzene-d_6 peak.

min) and a 1% impurity (t_r = 22.2 min),[57] which was not isolated from the pyrolysate. Most of the pentane was removed from the solution by fractional distillation. The remainder of the solvent was removed, and the major product diene **30** was isolated by preparative GC (column E, 80 °C). The configuration of the 5,6-double bond (*Z*) was established by comparison of the ^{1}H NMR spectrum and the GC retention time with those of the unlabeled compound.

Analysis of the Labeled Enantiomerically Enriched Starting Material 20. The enantiomeric excess (ee) (86.7 ± 1.8%) of **20** was assigned by comparison to that of its precursor ketone (1*S*,5*S*)-**33**, which in turn was established by capillary GC analysis of the 1*S*,5*S* methyl ether of the derived exo alcohol. As has been reported above, the GC analysis of ee showed a slight systematic bias in favor of the 1*R*,5*R* over the 1*S*,5*S* enantiomer (peak ratio 1.022 instead of 1.00), which corresponds to an ee of 0.7% for actually racemic material. Strictly, then, the ee of the enantiomerically enriched sample of **20** should be corrected to 87.3 ± 2.4%. This produces barely significant changes in the overall results, but we list both the corrected and uncorrected values in the sequel.

The deuterium content (99.5 ± 0.5%) at the methyl position of the isopropyl group was determined by computer simulation of the GC/MS of the lactone **36** as described above. The deuterium incorporation in **20** was determined as 97.2 ± 0.2% at the 2-position of the propenyl substituent by integration of the two vinyl proton signals in the ^{1}H NMR.

Determination of Configuration of the Trisubstituted (C_2=C_3) Double Bond in the Diene Product (7*S*)-2-Methyl-2(*Z*),5(*Z*)-octadiene-*1*-d_3-*7*-d_1 ((7*S*)-30-*7*-d_1). The deuterium incorporation at each allylic methyl position was determined by integration of the ^{1}H NMR signals at 1.61 and 1.67 ppm. With use of this method, the deuterium incorporation at 1.61 ppm was 99.2 ± 0.4% and the deuterium incorporation at 1.67 ppm was 0.7 ± 0.4%. Hence, the configuration of the 2,3-double bond could be assigned as *Z*.

Determination of Configuration of the Chiral Center in the Diene Product (7*S*)-2-Methyl-2(*Z*),5(*Z*)-octadiene-*1*-d_3-*7*-d_1 ((7*S*)-30). The isolated tetradeuterio diene (7*S*)-2-methyl-2(*Z*),5(*Z*)-octadiene-*1*-d_3-*7*-d_1 ((7*S*)-**30**-d_4) was then subjected to oxidative degradation with RuO_4 as previously described for the dideuterio compound **30**-d_2. After bulb to bulb distillation, the distillate was condensed with (*R*)-(−)-methyl 2-hydroxy-2-phenylethanoate (49.5 mg, 0.3 mmol) with use of DCC (62 mg, 0.3 mmol) and DMAP (one crystal). Although the unlabeled and dideuteriated methyl 2-propionyloxy-2-phenylethanoates could be visualized on TLC by anisaldehyde stain, the monodeuteriated compound could not be developed in this manner. Consequently, the flash column fractions were monitored for the desired product by capillary GC (column A, conditions k). Less than 1 mg of product **48** was isolated. The configuration of the chiral center (*S*) could be established by comparison to the ^{1}H NMR of the unlabeled compound.

Analysis of the Enantiomeric Purity of the Product 30 as Determined from That of Its Degradation Product 48 (Table I). The esterification product **48** of Table I was analyzed by both ^{1}H and ^{2}H NMR. From five separate electronic integrations of the pertinent region of the ^{1}H NMR spectrum, the signals due to H_R and H_S were found to be in the ratio 9.47 ± 0.38. Here and in the following, the experimental error is reported as twice the standard deviation. The ^{1}H NMR ratio corresponds to a diastereomeric proportion (*S*,*R*):(*S*,*S*)-**48** of (90.45 ± 1.6):(9.55 ± 1.6). The ee of the pyrolysis product **30** thus is 81 ± 4%. However, the deuterium incorporation at the propenyl receptor site of the starting material **20** is only 97.2%, and therefore 2.8% of the reactant molecules will lead to 7-undeuteriated product **30**, which will give undeuteriated ester **48**. In other words, this amounts to a lower effective ee of the starting **20**. Therefore, the observed ee of the pyrolysis product will give too low an estimate of the actual stereospecificity. To correct for this, 2.8% must be subtracted from the percent of each diastereomer of **48**. Thus, (90.45 − 2.8)/(9.55 − 2.8) = 86.5 ± 4% ee of **30** is the proper value to compare with the ee of the starting **20**. Note that this procedure assumes a remote secondary deuterium isotope effect of unity. The ee of **20** is assumed to be the same as that of the precursor **33**, which was established by enantiospecific GC analysis of the derived methyl ether to be 86.7 ± 1.8% (87.3 ± 2.4% corrected for a small systematic error in the GC analysis). Thus, the actual transfer of stereogenicity is 100(86.5/86.7) = 100 ± 4% (99 ± 4% corrected).

In the ^{2}H NMR, the ratio of the signals due to D_S and D_R was not obtainable by electronic means. Rather, it was determined by the cut and weigh technique from repeated plots of the spectral region of interest by use of two different line-broadening (LB) settings: For LB = 0.3, the ratio was 13.5 ± 0.4; for LB = 1, the ratio was 11.5 ± 0.5. These correspond to ee values of 86.1 ± 3.7 and 83.8 ± 5.2%, respectively. This analysis "sees" only deuterium and therefore does not require adjustment for the amount of undeuteriated reactant **20**. The actual transfer of stereogenicity therefore is 98 ± 5% (mean of the four ratios).

The agreement of the ^{1}H and ^{2}H NMR analyses justifies the use of their mean (99 ± 5%) as the experimental value of the transfer of stereogenicity.

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Supplementary Material Available: Details of kinetic experiments, independent synthesis of product **30**, and control experiments (12 pages). Ordering information is given on any current masthead page.

(57) For a discussion of the possible identity of this impurity, see ref 40.