Syntheses of Chiral Cyclohexylidenepropenes and Cyclohexylideneacetaldehydes

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Abstract: Chiral dienes of known absolute configurations and optical purities have been prepared from α,β-unsaturated aldehydes, which in turn have been synthesized from simple starting materials. (*aR*)-(+)-(4-Methylcyclohexylidene)propene (**5**), (*aR*)-(+)-(4-*tert*-butylcyclohexylidene)propene (**10**), (*E*,3*R*)-(−)-(3-methylcyclohexylidene)propene (**23**), (*Z*,3*R*),-(−)-(3-methylcyclohexylidene)propene (**27**), (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)propene (**34**), (*E*,2*S*)-(+)-(2-methylcyclohexylidene)propene (**39**), (*Z*,2*S*,4*R*)-(+)-(2-methyl-4-*tert*-butylcyclohexylidene)propene (**50**), (*E*,2*S*,4*R*)-(+)-(2-methyl-4-*tert*-butylcyclohexylidene)propene (**54**), (*E*,2*R*,4*R*)-(−)-(2-methyl-4-*tert*-butylcyclohexylidene)propene (**58**), and (*E*,2*S*,5*R*)-(−)-(2-isopropyl-5-methylcyclohexylidene)propene (**62**) have been prepared from the corresponding alkylcyclohexylideneacetaldehydes. All these compounds have been characterized by ^{1}H NMR, ^{13}C NMR, UV, and CD spectra.

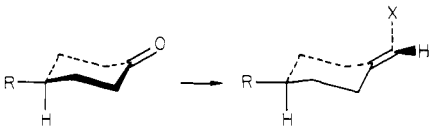
Chiroptical properties of molecules containing cisoid 1,3-dienes have been studied extensively, and their long wavelength $\pi-\pi^*$ Cotton effects in optical rotary dispersion (ORD)/circular dichroism (CD) spectra have been correlated with molecular structure.[1] Although such studies were concerned mainly with nonplanar cisoid dienes, nonplanar transoid dienes and α,β-unsaturated carbonyl compounds have also been studied to some extent.[2] 1,3-Dienes of transoidal planar conformation have been prepared,[3] but their chiroptical properties were not interpreted. In order to evaluate the chiroptical properties of long wavelength $\pi-\pi^*$ transitions of planar 1,3-dienes and α,β-unsaturated carbonyl compounds, a number of 1,3-dienes and α,β-unsaturated aldehydes that have transoidal planar conformation were synthesized and characterized. The synthesis of these compounds is the subject of this article.

Syntheses

The systems were designed in such a way that in each case an α,β-unsaturated carbonyl compound would be precursor to the 1,3-diene. The other requirements were (1) that an intermediate in the synthesis be amenable to the determination of the absolute configuration and optical purity of the system and (2) that an intermediate have a functional group that could be used either to resolve the racemates or to separate the diastereomers as solid derivatives.

(*aR*)-(+)-(4-Methylcyclohexylidene)propene and (4-*tert*-Butylcyclohexylidene)propene. (*aR*)-(+)-(4-Methylcyclohexylidene)propene (**5**) was synthesized according to the outline in Scheme I. A Wittig–Horner reaction involving condensation of 4-methylcyclohexanone (**1**) and triethyl phosphonoacetate gave ethyl (4-methylcyclohexylidene)acetate. Hydrolysis of the ester with alcoholic KOH afforded the racemic (4-methylcyclohexylidene)acetic acid in 90% yield. The racemic acid was resolved[4,5] with (+)-α-phenylethylamine to obtain (*aR*)-(−)-**2**.

Scheme I. Syntheses of (*aR*)-(+)-(4 Methylcyclohexylidene)propene and (*aR*)-(+)-(4-*tert*-Butylcyclohexylidene)propene



1, R = CH_3 — 2, *aR*-(−), R = CH_3; X = COOH
6, R = $C(CH_3)_3$ — 3, *aR*-(−), R = CH_3; X = CH_2OH
4, *aR*-(−), R = CH_3; X = CHO
5, *aR*-(+), R = CH_3; X = $CH{=}CH_2$

7, *aR*-(−), R = $C(CH_3)_3$; X = COOH
8, *aR*-(−), R = $C(CH_3)_3$; X = CH_2OH
9, *aR*-(−), R = $C(CH_3)_3$; X = CHO
10, *aR*-(+), R = $C(CH_3)_3$; X = $CH{=}CH_2$

Reduction of the acid **2** via its acid chloride with lithium tri-*tert*-butoxyaluminum hydride[6] was found to give ~25% of the allylic alcohol **3** and 75% of the α,β-unsaturated aldehyde **4**. Reduction of the acid **2** with LAH or AlH_3[7] yielded mainly the alcohol **3** and varying amounts of the dihydro isomer of **3** and some hydrocarbon impurities. Reduction of the acid **2** via its methyl ester[8] produced the allylic alcohol **3**, free of any dihydro isomers, in 90% yield. Oxidation of **3** with MnO_2 gave a good yield of (*aR*)-(−)-(4-methylcyclohexylidene)acetaldehyde (**4**). Condensation of methylenetriphenylphosphorane with **4** afforded (*aR*)-(+)-(4-methylcyclohexylidene)propene (**5**) in a moderate yield (50%). In an analogous manner, (*aS*)-(−)-(4-methylcyclohexylidene)propene was also prepared.

The absolute configuration of **5** is based on the established absolute configuration of **2**. Gerlach[4] has assigned the *aS* configuration to the (+)-enantiomer of **2**. There was some question concerning Gerlach's assignment because it was based on a mechanistic correlation with (1*R*,2*R*,4*R*)-isoborneol and small rotations due to deuterium asymmetry were involved.

Independent of Gerlach's assignment, the absolute configuration of *2* and **3** have also been correlated (Scheme II) with (1*R*,2*S*,5*R*)-(−)-menthol (**11**), whose absolute configuration has been determined by X-ray analysis.[9] Oxidation of **11** gives

(1) (a) A. W. Burgstahler, R. C. Barkhurst, and J. K. Gawronski in "Modern Methods of Steroid Analysis", E. Heftmann, Ed., Academic Press, New York, 1973; (b) "The Molecular Basis of Optical Activity: Optical Rotary Dispersion and Circular Dichroism", E. Charney, Ed., Wiley, New York, 1979; (c) "Stereochemistry: Fundamentals and Methods", Vol. 2, H. B. Kagan, Ed., George Thieme, Stuttgart, 1977; (d) D. A. Lightner, T. D. Bouman, J. K. Gawronski, K. Gawronska, J. L. Chappuis, B. V. Crist, and A. E. Hansen, *J. Am. Chem. Soc.*, **103**, 5314 (1981), and references cited therein.

(2) (a) E. Charney, H. Ziffer, and U. Weiss, *Tetrahedron*, **21**, 3121 (1965); (b) C. Djerassi, R. Reccords, E. Bunnenberg, K. Mislow, and A. Moscowitz, *J. Am. Chem. Soc.*, **84**, 870 (1962); (c) G. Snatzke, *Tetrahedron*, **21**, 413, 421, 439 (1965); (d) L. Velluz, M. Legrand, and R. Viennet, *C. R. Hebd. Seances Acad. Sci.*, **261**, 1687 (1965); (e) H. Ziffer and C. H. Robinson, *Tetrahedron*, **24**, 5803 (1968).

(3) (a) A. DiCorato, *Gazz. Chim. Ital.*, **98**, 810 (1968); (b) L. Lardicci et al., *Tetrahedron*, **34**, 2015 (1978); (c) R. Bruce Banks and H. M. Walborsky, *J. Am. Chem. Soc.*, **98**, 3732 (1976).

(4) H. Gerlach, *Helv. Chim. Acta*, **49**, 1291 (1966).

(5) (a) R. B. Banks, Ph.D. Thesis, Florida State University, 1976; (b) H. M. Walborsky and R. B. Banks, *Bull. Soc. Chim. Belg.*, **89**, 849 (1980); (c) M. L. A. Banks, Ph.D. Thesis, Florida State University, 1976; (d) W. H. Perkin and W. J. Pope, *J. Chem. Soc.*, **99**, 1511 (1911).

(6) H. C. Brown and S. Rao, *J. Am. Chem. Soc.*, **80**, 5377 (1958).

(7) (a) M. Jorgenson, *Tetrahedron Lett.*, 559 (1962); (b) E. J. Corey and E. Hamanaka, *J. Am. Chem. Soc.*, **89**, 2758 (1967).

(8) M. Brink, *Synthesis*, **4**, 253 (1975).

(9) (a) J. M. Ohrt and R. Parthasarathy, *Acta Crystallogr.*, **S198** (1969); (b) Klyne and Buckingham in "Atlas of Stereo-chemistry: Absolute Configurations of Organic Molecules", Oxford University Press: New York, 1974.

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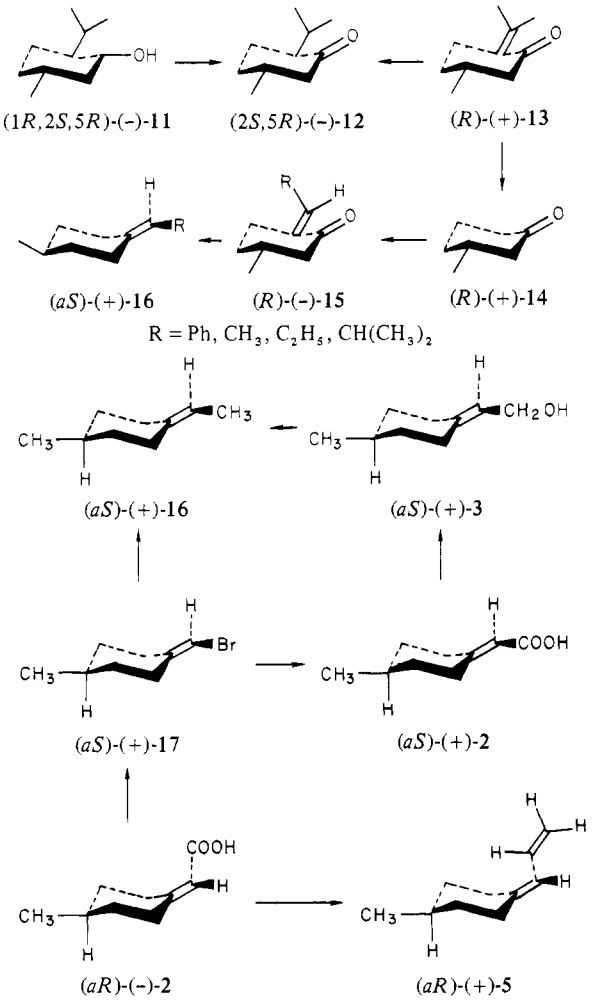
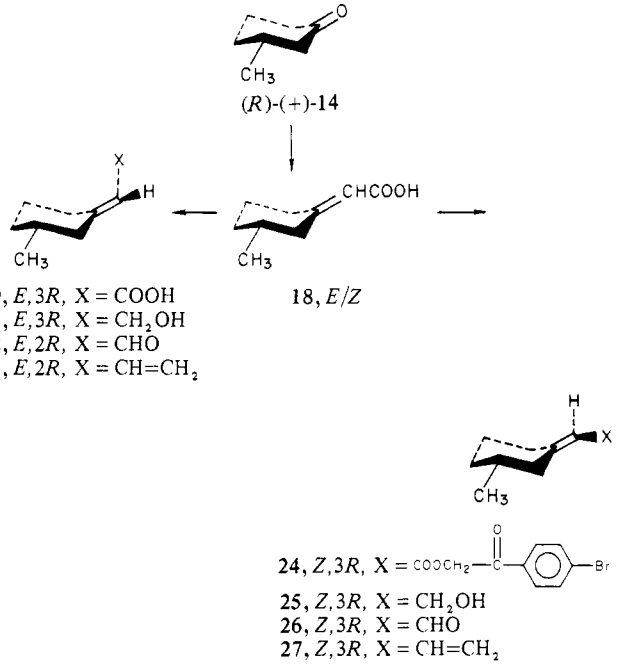
Scheme II. Stereochemical Correlations of (*aR*)-(+)-**5** with (1*R*,2*S*,5*R*)-(−)-Menthol (**11**)



(2*S*,5*R*)-(−)-menthone (**12**), whose absolute configuration has also been deduced by ORD.[10] Since one of the hydrogenation products[11] of (*R*)-(+)-pulegone (**13**) is **12**, the *R* configuration for **13** is correct. (*R*)-(+)-3-Methylcyclohexanone (**14**) is a product[12] derived from **13**. The enone **15** (R = C_6H_5) is a condensation product from **14**, which upon reduction of the carbonyl group yields (*aS*)-(+)-**16** (R = C_6H_5).[13] The olefins **16** [R = C_6H_5, CH_3, C_2H_5, $CH(CH_3)_2$] have been correlated with (*aR*)-(−)-**2** as follows: Decarboxylative bromination[5,13] of (*aR*)-(−)-**2** gave (*aS*)-(+)-**26**. The vinyllithium and copper reagents[14] derived from **17** were alkylated to obtain (*aS*)-(+)-**16** [R = C_6H_5, CH_3, C_2H_5, $CH(CH_3)_2$]. These correlations have proved that Gerlach's original assignment is correct.

Since there is no inversion of configuration or racemization in the transformations leading to **5**, we have assumed that the optical purity of **5** is the same as that of **2**. The maximum rotation of **2** that has been obtained[4,5] is considered to be that of the optically pure sample, and therefore the optical purities in the series **2**–**5** are established indirectly. However, one could not directly assess the optical purity of any one member in the series. ^1H NMR spectrum of **2** in chiral solvent or ^{13}C NMR spectrum of **3** with a chiral shift reagent failed to show signals due to diastereomers,[15] indicating the inapplicability of these methods to such axially dissymmetric molecules.

Scheme III. Syntheses of (*E*,3*R*)-(−)- and (*Z*,3*R*)-(−)-(3-Methylcyclohexylidene)propene



Assuming that the rotation of (*aR*)-(−)-(4-methylcyclohexylidene)acetic acid (**2**), $[\alpha]_{Hg}$ −95.9°, represents an optically pure sample, the aldehyde **4** and the diene **5** are 84.7% optically pure.

In a manner analogous to the 4-methylcyclohexylidene series, compounds in the 4-*tert*-butylcyclohexylidene series were synthesized. (−)-(4-*tert*-Butylcyclohexylidene)acetic acid (**7**) was obtained by resolution of the racemic acid[16] with dehydroabietylamine and assigned the *aR* absolute configuration. The configuration assigned to **7** is supported by the results of an asymmetric synthesis[17] in which (*aR*)-(−)-**2** and (−)-**7** were obtained from **1** and **6**, respectively. On mechanistic considerations the acids **2** and **7** would be expected to have the same absolute configuration, which is *aR*.

We consider that the rotation, $[\alpha]^{22}_{Hg}$ −94.87 ± 0.51°, of (*aR*)-(−)-**7** is maximum based on the observation that in the resolution the salt was crystallized to constant melting point and the melting point was not affected by further crystallization from a different solvent system. Consistent with this conclusion is the observation that the molecular rotation (186°) of **7** is higher than that (148°) of (*aR*)-(−)-(4-methylcyclohexylidene)acetic acid (**2**). Therefore we assume that $[\alpha]_{Hg}$ −94.87° represents the optically pure **7**. On the basis of this assumption the aldehyde **9** and the diene **10** are 91% optically pure.

***E* and *Z* (3*R*)-(3-Methylcyclohexylidene)propenes.** (*E*,3*R*)-(−)-(3-Methylcyclohexylidene)propene (**23**) and (*Z*,3*R*)-(−)-(3-methylcyclohexylidene)propene (**27**) were synthesized from optically pure (*R*)-(+)-3-methylcyclohexanone (**14**) as outlined in Scheme III. A Wittig–Horner reaction involving the condensation of **14** and triethyl phosphonoacetate gave a roughly 1:1 mixture of ethyl (*E*,- and *Z*,3*R*)-(3-methylcyclohexylidene)acetates. Saponification of the ester gave the 1:1 mixture of the carboxylic acids **18** in 87% yield. By salt formation with (−)-α-phenylethylamine and fractional crystallization, one obtained the acid **19**, which was isomerically pure.

(10) C. Djerassi, R. Rinker, and B. Rinker, *J. Am. Chem. Soc.*, **78**, 6377 (1956).
(11) A. J. Birch, *Annu. Rep. Prog. Chem.*, **47**, 190 (1950).
(12) O. Wallach, *Justus Liebigs Ann. Chem.*, **289**, 337 (1896).
(13) (a) J. H. Brewster and J. E. Privett, *J. Am. Chem. Soc.*, **88**, 1419 (1966); (b) A. T. Worm Ph.D. Thesis with J. H. Brewster, Purdue University, 1970.
(14) The vinyllithium derived from (*aS*)-(+)-**26** was carbonated to obtain the optically pure (*aS*)-(+)-**2**. Therefore, the transformations from (*aR*)-(−)-**2** to (*aS*)-(+)-**2** are 100% stereospecific and the configuration of **26** is opposite to that of (*aR*)-(−)-**2**.[5]
(15) M. Raban and K. Mislow in "Topics in Stereochemistry", Vol. 2, N. L. Allinger and E. L. Eliel, Eds., Wiley-Interscience, New York, 1967.
(16) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966).
(17) (a) J. H. Bestmann and L. Juergen, *Chem.-Ztg.*, **94**, 487 (1970); (b) J. H. Bestmann and J. Lienert, *Angew. Chem., Int. Ed. Engl.* **8**, 763 (1969).

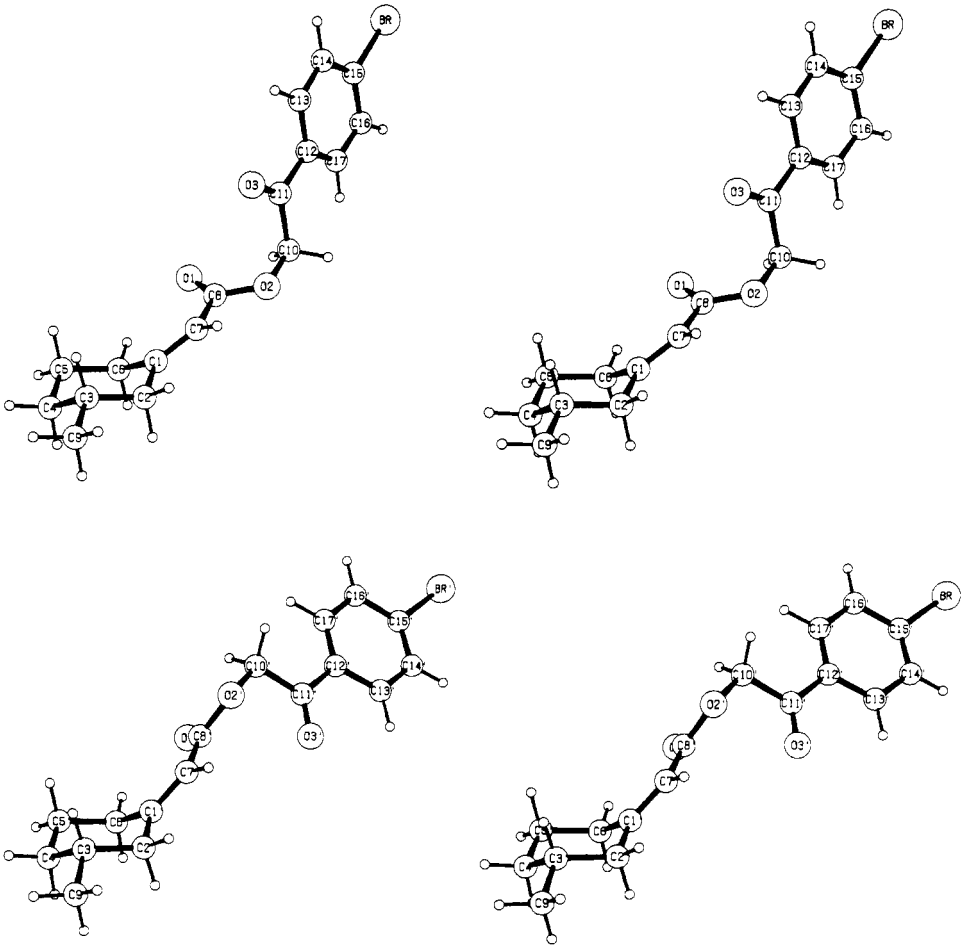


Figure 1. X-ray structure of (*E*,3*R*)-(−)-**20**. (The X-ray analysis was kindly provided by Dr. John F. Blount, Hoffmann-La Roche.)

In the 270-MHz ^{1}NMR spectrum of **19** as well as of the mixture **18** the equatorial hydrogen deshielded by the carboxyl group[16] was found at 3.67 ppm as a broad doublet well separated from the rest of the signals. The large splitting (J = 12 Hz) is due to geminal proton. The other splittings that would be expected are $J_{H_eH_a} \simeq 2.5$ Hz and $J_{H_eH_e} \simeq 2.5$ Hz in the *E* isomer and $J_{H_eH_a} \simeq 2.5$ Hz in the *Z* isomer. It was anticipated that this difference between the two isomers could be used in assigning geometry to **19**. However the doublet in the spectrum of **19** run at 25 °C revealed no fine structure characteristic of either the *E* or the *Z* isomer. On the other hand, ^{13}C NMR spectra revealed large differences between the two isomers. It was deduced that the allylic methylenes resonated at 46.35 and 29.52 ppm in **19** and at 37.80 and 38.00 ppm in the other isomer. If one assigned *E* geometry to **19** then the chemical shifts are consistent with an 8-ppm upfield shift of the allylic methylenes cis to the carboxyl. Without precedent, in the cyclohexylidene system we could not unambiguously use ^{13}C NMR to establish geometry, and therefore X-ray analysis was used. The *p*-bromophenacyl ester derivative **20** gave single crystals suitable for X-ray analysis. The crystals contained two independent molecules (unprimed and primed, Figure 1) in the unit cell. Both molecules had *E* geometry around the double bond, and they contained a planar cisoid C=C—C=O chromophore (for bond angles, bond lengths, and torsion angles see Experimental Section).

The acid **19**, whose configuration has thus been established as *E*,3*R*, was reduced with aluminum hydride to obtain (*E*,3*R*)-(−)-(3-methylcyclohexylidene)ethanol (**21**), contaminated with 9–10% of an inseparable dihydro alcohol, in 87% yield. Oxidation of the allylic alcohol **21** using pyridinium dichromate[18] in DMF resulted in epimerized (mixture of geometric isomers) aldehyde **22**. The epimerization was detected by an unexpected CD spectrum of **22** as well as an inhomogeneous ^{13}C NMR spectrum. MnO_2 oxidation of **21** gave the unepimerized (*E*,3*R*)-(−)-**22** whose ^{13}C NMR spectrum was homogeneous. Methylenetriphenylphosphorane was condensed with **22** to obtain (*E*,3*R*)-(−)-(3-methylcyclohexylidene)propene (**23**).

Conceivably the condensation step may lead to isomerized aldehyde **22**, which can react with the reagent to yield partially epimerized product **23**. Homogenity of the ^{13}C NMR spectrum of **23** established that the condensation step did not lead to any epimerization of **23**.

One could isolate (*Z*,3*R*)-(3-methylcyclohexylidene)acetic acid in pure form as crystalline *p*-bromohenacyl ester **24** from the residue obtained in the isolation of **19**. Aluminum hydride reduction of **24** gave (*Z*,3*R*)-(−)-(3-methylcyclohexylidene)ethanol (**25**) in 87% yield. Oxidation of **25** with MnO_2 gave (*Z*,3*R*)-(−)-(3-methylcyclohexylidene)acetaldehyde **26** in 74% yield. Condensation of (**26**) with methylenetriphenylphosphorane afforded (*Z*,3*R*)-(−)-(3-methylcyclohexylidene)propene (**27**) in 35% yield. All the compounds in the series **24–27** were found by ^{13}C NMR to be pure geometric isomers.

Since one started with optically pure (*R*)-(+)-3-methylcyclohexanone, the α,β-unsaturated aldehydes **22** and **26** and the dienes **23** and **22** are optically pure samples.

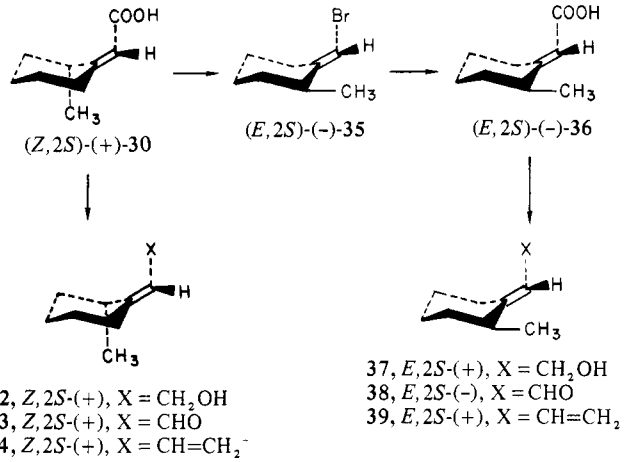
***E* and *Z* (2*S*)-(2-Methylcyclohexylidene)propenes.** (*Z*,2*S*)-(+)-(2-Methylcyclohexylidene)propene (**34**) and (*E*,2*S*)-(+)-(2-methylcyclohexylidene)propene (**39**) were synthesized from racemic 2-methylcyclohexanone as shown in Scheme IV.

Racemic 2-methylcyclohexanone (**28**) was condensed with *tert*-butyl α-lithio(trimethylsilyl)acetate)[19] at −78 °C to obtain *tert*-butyl (2-methylcyclohexylidene)acetate (**29a**) as a mixture

(18) E. J. Corey and G. Schmidt, *Tetrahedron Lett.*, 399 (1979).

(19) (a) S. L. Hartzell, D. F. Sullivan, and M. W. Rathke, *Tetrahedron Lett.*, 1403 (1974); (b) K. Shimoji, H. Taguchi, K. Oshima, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **96**, 1620 (1974).

Scheme IV. Syntheses of (*Z*,2*S*)-(+)- and (*E*,2*S*)-(+)-(2-Methylcyclohexylidene)propene

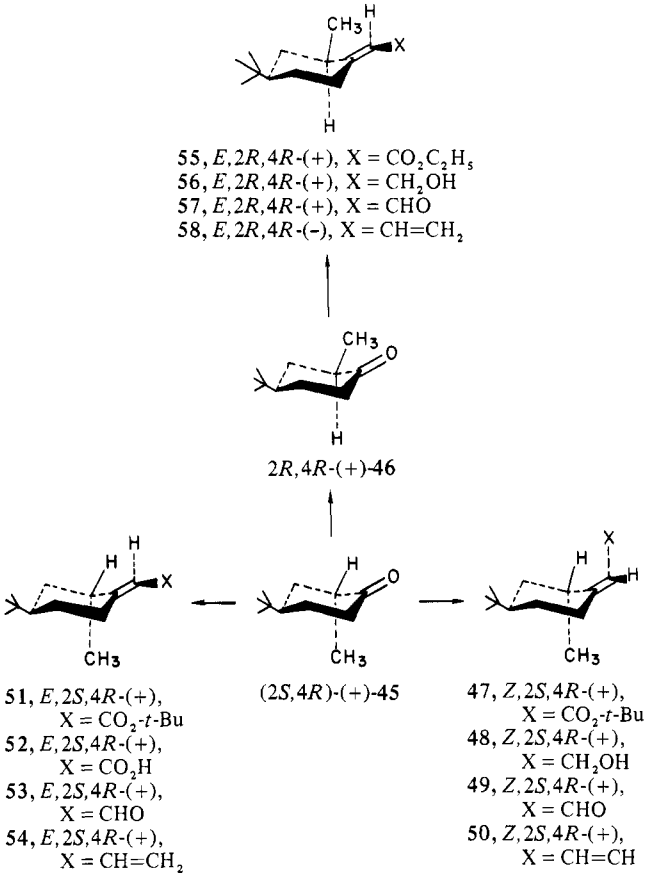


of *E* and *Z* isomers in a 1:4 ratio.[20] The condensation of **28** with triethyl phosphonoacetate, on the other hand, gave *E* and *Z* isomers of (2-methylcyclohexylidene)acetates in a 3:1 ratio in addition to some isomerized products of the ester. Since the former reaction is much cleaner and more selective than the latter, it was utilized in the synthesis.

The *E* and *Z* mixture (1:4) of *tert*-butyl (2-methylcyclohexylidene)acetates was hydrolyzed to obtain a mixture of (2-methylcyclohexylidene)acetic acids (1:4) in 86% yield based on **28**. The mixture was fractionally crystallized to obtain the *Z* isomer **30**. The appearance in the ^1H NMR spectrum of the C_2 proton as a multiplet at 4.25 ppm established[16,21] that the proton was cis to the carboxyl group and equatorial and thereby placing the methyl group on C_2 in an axial position. Also, ^{13}C NMR signal of the C_2 doublet was found 8 ppm upfield of the C_2 doublet in the other isomer. These data established the *Z* configuration of the carbon–carbon double bond as well as the predominantly axial methyl conformation of the six-membered ring.

Upon resolution of the racemic acid **30**, either with (−)-α-phenylethylamine or dehydroabietylamine, (*Z*,2*S*)-(+)-**30** was obtained. The 2*S* absolute configuration was related to (*S*)-(+)-2-methylcyclohexanone[22] by ozonolysis. In our hands the ozonolysis reaction[23] of the acid or its methyl ester was accompanied by loss of optical purity of 2-methylcyclohexanone. Epimerization may have taken place during the decomposition of the ozonide. However, ozonolysis of the methyl ester has been reported[23] to give 2-methylcyclohexanone without loss of optical purity. Therefore a direct estimation of the optical purity of **30** was undertaken. The amide derived from racemic **30** and (−)-α-phenylethylamine showed ^1H NMR signals due to the presence of a set of diastereomers[15,21b] whereas the amide **31** derived from the resolved (*Z*,2*S*)-(+)-**33** showed signals due only to one diastereomer, care being taken to avoid accidental resolution of the amide. Thus it established that the resolved (*Z*,2*S*)-(+)-**30** represented an optically pure sample.

Scheme V. Syntheses of (2-Methyl-4-*tert*-butylcyclohexylidene)-propene



Methyl (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)acetate prepared from **30** was reduced with aluminum hydride to obtain (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)ethanol (**32**) in 94% yield. MnO_2 oxidation of **32** yielded (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)acetaldehyde (**33**) in 70% yield. Condensation of **33** with methylenetriphenylphosphorane gave (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)propene **34** in 32% yield.

(*E*)-(2-Methylcyclohexylidene)acetic acid needed for the synthesis of compounds in the *E* series was found difficult to resolve. Therefore the resolved (*Z*)-(2-methylcyclohexylidene)acetic acid (**30**) was converted into optically active (*E*)-(2-methylcyclohexylidene)acetic acid by an alternative approach. The carboxylic acid **30** was subjected to a decarboxylative bromination reaction. This reaction is known to invert the configuration at the vinyl carbon with 100% stereospecificity.[5a] Indeed, the (*E*,2*S*)-(−)-(2-methylcyclohexylidene)bromomethane (**35**), obtained in 50% yield, was found to be free of the *Z* bromide. Since the asymmetric carbon in **30** does not take part in the reaction, the original optical purity in **35** is preserved. Treatment of the vinyl bromide **35** with *tert*-butyllithium[5a,24] and carbonation of the vinyllithium intermediate[5a] gave (*E*,2*S*)-(−)-(2-methylcyclohexylidene)acetic acid (**36**) with 100% stereospecificity. Reduction of **36** via its methyl ester with aluminum hydride yielded (*E*,2*S*)-(+)-(2-methylcyclohexylidene)ethanol (**37**) in 91% yield. Oxidation of **37** with MnO_2 afforded (*E*,2*S*)-(−)-(2-methylcyclohexylidene)acetaldehyde (**38**) in 80% yield. Methylenetriphenylphosphorane was condensed with **38** to obtain (34%) (*E*,2*S*)-(+)-(2-methylcyclohexylidene)propene (*39*).

Since all compounds in the 2-methylcyclohexylidene series were prepared from optically pure **30**; the α,β-unsaturated aldehydes **33** and **38** and the dienes **34** and **39** are all optically pure samples.

(4-*tert*-Butyl-2-methylcyclohexylidene)propenes. To study allylic (axial) methyl effects, conformationally homogeneous

(20) Predominant formation of the energetically unfavorable *Z* isomer was unexpected. Condensation of *tert*-butyl α-lithio(trimethylsilyl)acetate with benzaldehyde was noted to give predominantly the *E* ester (*E*:*Z* = 4:1).[19b] Under identical conditions we tested this condensation reaction with menthone (2-equatorial isopropyl group in a conformationally rigid cyclohexanone) and found *E* and *Z* isomers in an approximately 4:1 ratio, thus confirming the previous findings.[19b] However, the same condensation with *cis*-2-methyl-4-*tert*-butylcyclohexanone (2-equatorial methyl group) gave *E* and *Z* isomers in an approximately 1:1 ratio. The last reaction gave us access to a sterically crowded cyclohexylideneacetate system. The condensation reactions will be discussed in detail in a future publication.

(21) (a) H. Hauth, D. Stauffacher, P. Niklaus, and A. Melera, *Helv. Chim. Acta*, **48**, 1087 (1965); (b) L. Mamlok and L. LaCombe, *Bull. Soc. Chim. Fr.*, 1524 (1973); (c) E. H. Ken and T. Chung-Ye, *J. Org. Chem.*, **40**, 929 (1975).

(22) (a) C. Beard, C. Djerassi, T. Elliot, and R. C. C. Tao, *J. Am. Chem. Soc.*, **84**, 874 (1962); (b) C. Beard, C. Djerassi, J. Sicher, F. Sipo's, and M. Tichy, *Tetrahedron*, **19**, 919 (1963).

(23) S. Musierowicz, A. Wro'blewski, and H. Krawczyk, *Tetrahedron Lett.*, 437 (1975).

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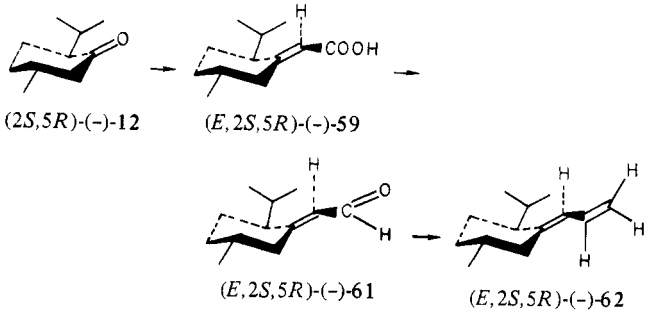
Scheme VI. Syntheses of (*E*,2*S*,5*R*)-(−)-(2-Isopropyl-5-methylcyclohexylidene)propene



(2-methylcyclohexylidene)propenes, in which the methyl group is constrained in an equatorial or axial configuration, was needed. This could be achieved by introducing a *tert*-butyl group to anchor the conformation of the six-membered ring and then selectively introducing the 2-methyl substituent in axial and equatorial orientations (Scheme V).

Thus, 4-*tert*-butylcyclohexanone was converted to its hydrazone **40**[25] and selectively alkylated[26] to obtain the axial methylhydrazone **41**. The hydrazone was cleaved without epimerization[26] to obtain *trans*-2-methyl-4-*tert*-butylcyclohexanone (**42**). Reduction of **42** with lithium aluminum hydride selectively yielded the racemic alcohol **43**,[22b] which was resolved via its succinic acid half-ester **44** into (1*R*,2*S*,4*R*)-(+)-**43**. Oxidation of the optically active alcohol with pyridinium dichromate[18] under neutral conditions yielded (2*S*,4*R*)-(+)-2-methyl-4-*tert*-butylcyclohexanone (**45**), which has also been synthesized starting from chiral naturally occurring precursors.[27]

Condensation of *tert*-butyl α-lithio(trimethylsilyl)acetate[19] with **45** yielded a 1:1 mixture of esters **47** and **51**. The mixture was separated by preparative gas chromatography to obtain pure (*Z*,2*S*,4*R*)-(+)-**47** and (*E*,2*S*,4*R*)-(+)-**51**. The geometric isomers could clearly be distinguished by ^{1}H NMR chemical shifts and multiplicities of the equatorial allylic protons[16] as well as ^{13}C NMR chemical shifts of the allylic carbons.

The ester **47** was reduced with aluminum hydride to obtain (*Z*,2*R*,4*R*)-(+)-**48**. Oxidation of the allylic alcohol **48** with MnO_2 yielded the α,β-unsaturated aldehyde (*Z*,2*S*,4*R*)-(+)-**49**. Methylenetriphenylphosphorane was condensed with **49** to obtain the diene (*Z*,2*S*,4*R*)-(+)-**50**.

The ester **51** was hydrolyzed to obtain the acid (*E*,2*S*,4*R*)-(+)-**52**. Reduction of the acid via its acid chloride with lithium tri-*tert*-butyoxyaluminum hydride[6] gave the α,β-unsaturated aldehyde (*E*,2*S*,4*R*)-(+)-**53**. Condensation of **53** with methylenetriphenylphosphorane yielded the diene (*E*,2*S*,4*R*)-(+)-**54**.

Epimerization of the ketone[27] (2*S*,4*R*)-(+)-**45** with alcoholic potassium hydroxide gave (2*R*,4*R*)-(+)-**46** with the methyl group in an equatorial orientation. Condensation of lithium ethoxyacetylide with **46** and rearrangement of the intermediate acetylene alcohol[28] yielded, selectively, the α,β-unsaturated ester (*E*,2*R*,4*R*)-**55**. The ester was reduced with aluminum hydride to obtain the allylic alcohol (*E*,2*R*,4*R*)-(+)-**56**, which was oxidized with MnO_2 to obtain the α,β-unsaturated aldehyde (*E*,2*R*,4*R*)-(+)-**57**. Methylenetriphenylphosphorane was condensed with **57** to obtain the diene (*E*,2*R*,4*R*)-(−)-**58**.

The optical purity of the compounds in the 2-methyl-4-*tert*-butylcyclohexylidene series is the same as that of (2*S*,4*R*)-(+)-**45** (89.9%), the optical purity of which has previously been established.[27]

(*E*,2*S*,5*R*)-(−)-(2-Isopropyl-5-methylcyclohexylidene)propene. To study the affect of an isopropyl group in an allylic equatorial position, we synthesized a diene from menthone (Scheme VI). (2*S*,5*R*)-(−)-Menthone (**12**) was obtained by oxidation[29] of (1*R*,2*S*,5*R*)-(−)-menthol. Condensation of lithium ethoxyacetylide with **12** and rearrangement[28] of the acetylenic alcohol with H_2SO_4 gave mainly ethyl (*E*,2*S*,5*R*)-(2-isopropyl-5-methylcyclohexylidene)acetate. Saponification of the ester and crystallization of the carboxylic acid gave pure (*E*,2*S*,5*R*)-(−)-**59**. The assignment of *E* configuration was based on the ^{1}H NMR signal (dd, J = 13, 4 Hz) at 3.10 ppm of the equatorial proton on C_6, which is deshielded by the carboxyl group.[16]

The acid **59** was reduced via its methyl ester to (*E*,2*S*,5*R*)-(−)-α-2-isopropyl-5-methylcyclohexylidene)ethanol (**60**) in 92% yield. Oxidation of **60** with MnO_2 provided (*E*,2*S*,5*R*)-(−)-(2-isopropyl-5-methylcyclohexylidene)acetaldehyde (**61**) in 84% yield. Condensation of methylenetriphenylphosphorane with **61** afforded (E,2*S*,5*R*)-(−)-(2-isopropyl-5-methylcyclohexylidene)propene (**62**) in 61% yield. Compounds **59–62** are optically pure samples since we started with optically pure menthol.

Although these α,β-unsaturated aldehydes and dienes are sensitive to air and light, they could be stored without decomposition for prolonged periods of time in sealed tubes in the refrigerator.

Experimental Section

Melting points were determined with a Mel-Temp apparatus. All melting points and boiling points are uncorrected. Infrared (IR) spectra were measured with Perkin-Elmer Model 257 grating spectrophotometer. The 1601-cm^{-1} absorption band of polystyrene film was used to calibrate the chart paper. Nuclear magnetic resonance (NMR) spectra were recorded on a JOEL C-60 or a Brucker 270-MHz spectrometer. The solvent used was $CDCl_3$ unless noted otherwise. Tetramethylsilane (Me_4Si) was used as internal standard. The chemical shifts are given in δ (ppm) downfield from Me_4Si and the coupling constants are in hertz. Mass spectra (MS) were obtained with an AEIMS902 instrument. The microanalyses were performed by Beller Laboratories, Göttigen, Germany.

Optical rotations were measured at either the 546.1-nm mercury line or the 589.3-nm sodium linne on a Bendix-Ericson Model 987 ETL/NPL polarimeter equipped with a Bendix Model DR-1 digital display. The cell length was 0.4 dm, and all solvents used were spectrometric grade. An error limit of ±0.002° was applied to the observed rotations.

Ultraviolet (UV) spectra were recorded with a Cary 219 spectrophotometer and the peak maxima are reported in nm. Circular dichroism (CD) spectra were recorded with a JASCO Model J-500 or J-500C spectrophotometer. The reported values of molecular amplitudes have been corrected for the optical purities of the samples. The cell path lengths used in UV and CD measurements were 1 cm and 0.1 cm, respectively, and the solvent was cyclohexane.

Thin-layer chromatography (TLC) was performed on glass plates coated with Merck silica gel 60 PF-254+366. Column chromatography was carried out by using silica gel 60 F254 (70–230 mesh, E. Merck). Flash chromatography[30] was performed by using silica gel 60 (230–400 mesh, E. Merck). High-pressure liquid chromatography (HPLC) was performed on a Waters Associate Model ALC-202 liquid chromatograph employing a column (8 ft × $^3/_8$ in.) packed with Porasil B. Qualitative G LPC analyses were performed on a Hewlett-Packard Model 5710 A gas chromatograph (thermal conductivity detector with helium as carrier gas) using packed columns (15% Lexan on acid-washed 60/80 Chromosorb P, 4 ft × $^1/_8$ in.; 15% SE-30 on acid-washed 80/100 Chromosorb P, 10 ft × $^1/_8$ in.; 10% UCW 982 on 80/10 Chromosorb W-HP, 20 ft × $^1/_8$ in.; 15% Carbowax 20M on acid-washed 80/100 Chromosorb P, 10 ft × $^1/_8$ in.).

All bulk solvents[31] were distilled before use. Diethyl ether, dimethoxyethane, and THF were dried by refluxing and distilling from sodium benzophenone dianion. DMF was dried by refluxing and distilling from barium oxide. Cyclohexane for spectra was purified by passing through 25% $AgNO_3$ on silica gel and distilling.

4-*tert*-Butylcyclohexanone (Aldrich), ethoxyacetylene (Story Chemical Co., distilled before use), 4-methylcyclohexanone (Aldrich), (*R*)-(+)-3-methylcyclohexanone (Aldrich, $[\alpha]^{24}_D$ +13.5°), 2-methylcyclo-

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hexanone (Aldrich), 1-menthol (Aldrich, mp 44–46 °C), methyltriphenylphosphonium bromide (Aldrich, dried in vacuum oven prior to use), (+)-α-phenylethylamine (Aldrich $[\alpha]^{23}_D$ +38°), (−)-α-phenylethylamine (Aldrich, $[\alpha]^{23}_D$ −39°), sodium hydride (J. T. Baker Co.), and triethyl phosphonoacetate (Aldrich) were obtained commercially.

Concentrations of butyllithium reagents (Alfa) were determined[32] prior to use. Dehydroabietylamine was obtained by purification of technical grade Amine-D following a reported procedure.[33] Diisopropylamine was purified by refluxing and distilling from barium oxide. Trimethylsilyl chloride (Aldrich) was purified by distilling from calcium hydride before use.

tert-Butyl acetate was prepared by using a reported procedure.[34] Active MnO_2 (Attenburrow Oxide) was prepared according to the procedure of Attanburrow et al.[35] Pyridinium dichromate was prepared according to the procedure of Corey.[18]

***tert*-Butyl (Trimethylsilyl)acetate.** By use of a modified procedure of Rathke and Sullivan,[36] *tert*-butyl (trimethylsilyl)acetate was prepared in a molar quantity. A dry three-necked flask equpped with a mechanical stirrer, nitrogen inlet, and a rubber septum was charged with 105 g (1.04 mol) of diisopropylamine. The flask was maintained under a nitrogen atmosphere and cooled in an ice bath. With the aid of a syringe, 435 mL of 2.30 M BuLi (1.00 mol) was slowly added while the solution was being stirred. After the addition was completed, a rapid stirring was continued for 5 min to ensure thorough mixing. The LDA thus prepared was dissolved in 1.8 L of dry THF, and the mechanical stirrer was quickly replaced by a magnetic stirrer. The solution was cooled in a dry ice/acetone bath and maintained at −78 °C. *tert*-Butyl acetate (116 g, 1.0 mol) was injected, and the solution was stirred for 15–20 min. Trimethylsilyl chloride (108.6 g, 1.0 mol), freshly distilled from CaH_2, was then slowly injected and the stirring was continued at −78 °C for 30 min. The cooling bath was removed, and the flask was allowed to warm to 0 °C. The reaction mixture was quenched with ice-cold 1 N HCl, diluted with more water, and extracted with hexane. The organic layer was washed once with HCl and then with water. Drying the solution with Na_2SO_4 and evaporation of the solvent provided the crude product. Distillation yielded 125 g (66%) of a fraction boiling at 172–173 °C. IR and NMR of this fraction were consistent with the proposed structure.

(4-Methlcyclohexylidene)acetic Acid (2). A dry 2-L, three-necked flask was loaded with 37.5 g (0.78 mol) of 50% sodium hydride as a dispersion in mineral oil. The oil was removed by washing three times with pentane. Dry dimethoxyethane (1.1 L) was added and the suspension, maintained under nitrogen atmosphere, was mechanically stirred. After cooling the flask to 0 °C in an ice bath, 176 g (0.785 mol) of triethyl phosphonoacetate was slowly added. After the evolution of H_2 ceased, stirring was continued for 1 h. 4-Methylcyclohexanone (88 g, 0.785 mol) was then added, and the temperature was kept at 25–30 °C. The reaction mixture was stirred for another 45 min, during which time a gelatinous precipitate appeared. Wet ether (500 mL) was added to hydrolyze the reaction. The mixture was transferred to a separatory funnel and washed twice with water and then with saturated NaCl. The organic solution was dried over Na_2SO_4 and the solvent removed under reduced pressure to get the crude ester.

The ester was placed in a 2-L round-bottom flask and refluxed with 600 mL of 2 N KOH in 50% CH_3OH for 30 min. After cooling to room temperature, the mixture was diluted with 500 mL of water and extracted three times with ether to remove all the neutral minerals. The aqueous solution was added to ice/concentrated HCl with stirring. The precipitated carboxylic acid was filtered and washed with water. The acid was crystallized from formic acid to obtain 109 g (90%) of the dry acid, mp 60–62 °C. IR and NMR spectra were identical with those reported.[5]

(*aR*)-(−)-(4-Methylcyclohexylidene)acetic Acid (2). To a solution of 95 g of racemic (4-methylcyclohexylidene)acetic acid in 700 mL of ethyl acetate was added 40 g (0.5 equiv) of (+)-α-phenylethylamine ($[\alpha]^{20}_D$ +38°, neat), and the mixture was heated to ≃60 °C. On standing at room temperature the salt crystallized. After three recrystallization from ethyl acetate the melting point was constant at 122 °C. The salt (17 g, mp 122 °C) was decomposed with 1 N NaOH and the amine that was liberated was extracted with ether. The aqueous solution was poured into ice-cold HCl, with stirring. The carboxylic acid that appeared as an oil was extracted with ether. The ether solution was washed twice with water, dried over Na_2SO_4, filtered to remove suspended impurities, and carefully evaporated to obtain an oil, which slowly solidified. The solid was pulverized and dried under vacuum; mp 48–49 °C; $[\alpha]^{25}_{Hg}$ −92.18 ± 0.49° (*c* 1.02, C_2H_5OH); 96.1% optically pure [lit.[4,5] $[\alpha]_{Hg}$ −95.9° (*c* 0.87, C_2H_5OH)].

(*aR*)-(4-Methylcyclohexylidene)ethanol (3). (*aR*)-(−)-(4-Methylcyclohexylidene)acetic acid (**2**) was esterified by following a literature procedure.[5] Six grams of the acid ($[\alpha]^{25}_{Hg}$ −81.18 ± 0.49°; 84.7% optically pure) was neutralized with 2 N NaOH solution and added to 150 mL of HMPA. To this mixture was added 24 g of CH_3I, and the solution was stirred for 0.5 h at room temperature. The reaction mixture was poured into excess water and extracted with hexane. The hexane solution was washed with NaOH solution, $Na_2S_2O_3$ solution, and water. Stripping the solvent provided the pure ester in quantitative yield, bp 50 °C (1 mm), $[\alpha]^{25.5}_{Hg}$ −86.83 ± 0.58° (*c* 0.86, absolute C_2H_5OH); this corresponds to the corrected rotation of −102.51 ± 0.58° for the optically pure compound (lit.[5a] $[\alpha]^{27}_{Hg}$ −102.90°). IR and NMR spectra were identical with those reported.

The ester was reduced with AlH_3 by following a modified procedure of Jorgenson.[7a] To a stirred slurry of 5.0 g (0.132 mol) of LAH in 100 mL of dry ether at 0 °C, under nitrogen atmosphere was added dropwise a solution of 5.85 g (0.044 mol) of anhydrous $AlCl_3$ in 75 mL of ether. After stirring for 1 h, a solution of 6.0 g of the ester in 25 mL of ether was added dropwise. After stirring for 3 h, the reaction mixture was hydrolyzed with a careful addition of 2 N NaOH solution. The resulting salts were filtered off and washed several times with ether. The combined washings were dried and the solvent was removed in vacuo to give 4.5 g (90%) of (*aR*)-(−)-(4-methylcyclohexylidene)ethanol (**3**), bp 83 °C (1.5 mm), $[\alpha]^{25.5}_{Hg}$ −9.84 ± 0.16° (*c* 3.18, $CHCl_3$); this corresponds to the corrected rotation of −11.62 ± 16° for the optically pure compound. IR (film) 3600, 2940, 2915, 2860, 2840, 1660, and 1500–625 cm^{-1}; ^1H NMR 0.9 (d, J = 5.5 Hz, 3 H), 0.9–2.7 (m, 9 H), 2.9 (OH), 4.13 (d, J = 7 Hz, 2 H), and 5.39 (t, J = 7 Hz, 1 H) ppm.

(*aR*)-(−)-(4-Methylcyclohexylidene)acetaldehyde (4). To a solution of 3.5 g of (*aR*)-(−)-(4-methylcyclohexylidene)ethanol (**3**) (84.7% optically pure), in 250 mL of low-boiling petroleum ether, was added 35 g of active MnO_2, and the mixture was stirred. The progress of the oxidation was monitored by TLC. When all the alcohol disappeared (2 h), the reaction mixture was diluted with ether and stirred for 5 min. The MnO_2 was filtered off and washed with ether. The combined ether solution was evaporated to get the crude product. A column chromatographic separation (silica gel, 5% ether in hexane) and a bulb-to-bulb distillation afforded the pure aldehyde (**4**), bp (pot temperature) 60–65 °C (0.6 mm), $[\alpha]^{25.5}_{Hg}$ −45.19 ± 0.48° (*c* 1.04, CH_3OH); this corresponds to the corrected rotation of −53.35 ± 48° for the optically pure compound. IR (film) 2940, 2910, 2840, 1675, 1630, 1460–1360, 1200–1100, and 1000–820 cm^{-1}; ^1H NMR ($CDCl_3$) 0.97 (d, J = 6 Hz, 3 H), 0.97–2.45 (m, 8 H), 3.33 (br d, J = 12 Hz, 1 H), 5.83 (d, J = 8 Hz, 1 H), and 10.06 (d, J = 8 Hz, 1 H) ppm; UV (*c* 3.12 × 10^{-2}, 7.48 × 10^{-5}) λ_{381} (ε 18), λ_{362} (ε 42), λ_{346}, (ε 54), λ_{333} (ε 51), λ_{321} (ε 41), λ_{230} (ε 19, 500); CD (*c* 3.12 × 10^{-2}, 7.48 × 10^{-4}) $[\theta]_{382}$ −787, $[\theta]_{363}$ −1800, $[\theta]_{347}$ −2020, $[\theta]_{333}$ −1610, $[\theta]_{321}$ −937, $[\theta]_{230}$ +6870.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.17; H, 10.14.

(*aR*)-(+)-(4-Methylcyclohexylidene)propene (5). To a stirred suspension of 2.62 g (7 mmol) of anhydrous methyltriphenylphosphonium bromide in 25 mL of dry ether cooled to −23 °C (dry ice/CCl_4) under nitrogen atmosphere was added 3.15 mL of 2.35 M (7 mmol) *n*-BuLi in hexane. The resulting yellow solution was stirred for 10 min. A solution of 1.0 g (7.2 mmol) of (*aR*)-(−)-(4-methylcyclohexylidene)acetaldehyde (**4**) ($[\alpha]^{25.5}_{Hg}$ −45.19 ± 0.48°, 84.7% optically pure) in 5 mL of ether was slowly added. The yellow color disappeared to give a white precipitate. The cooling bath was removed and the precipitate stirred for 10 min. Wet ether (25 mL) was added to hydrolyze the reaction. Filtration and concentration of the ether solution gave a mixture containing a solid and a liquid. The mixture was chromatographed on silica gel, eluting with pentane. The fractions containing the pure diene were collected, and the solvent was removed under reduced pressure. A bulb-to-bulb distillation yielded 0.49 g (50%) of (*aR*)-(+)-(4-methylcyclohexylidene)propene (**5**) as a colorless liquid, bp (pot temperature) 25–30 °C (0.25 mm), $[\alpha]^{25}_{Hg}$ +25.04 ± 0.71 (*c* 0.7, cyclohexane); this corresponds to the corrected rotation of +29.56 ± 0.71 for the optically pure compound. IR (film) 3050 (w), 3020 (w), 2940, 2910, 2850, 1840, 1800 (sh), 1645, 1595 (w), 1450–1100, 1000, and 900 cm^{-1}; ^1H NMR 0.96 (d, J = 7 Hz, 3 H), 0.96–2.33 (m, 8 H), 2.78 (broad d, J = 12 Hz, 1 H), 4.97 (dd, J = 11, 2 Hz, 1 H), 5.10 (dd, J = 16.5, 2 Hz, 1 H), 5.81 (d, J = 11 Hz, 1 H), and 6.61 (sextet, J = 16.5, 11, 11 Hz, 1 H) ppm; ^{13}C NMR 21.95 (q), 28.52 (t), 32.80 (d), 35.90 (t), 36.58 (t), 36.64 (t), 114.47 (t), 122.91 (d), 132.80 (d), and 143.54 (s) ppm; MS (EI), *m/e* 136 ($M^{+\cdot}$), 121, 95, 94, 93, 91, 81, 80, 79 (100%), and 67; UV (*c* 5.15 × 10^{-5}) λ_{246} (ε 16 400),

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$\lambda_{237.5}$ (ϵ 24 300), and λ_{231} (ϵ 22 000); CD (c 5.15 × 10^{-4}) $[\theta]_{246}$ +7720, $[\theta]_{238}$ +12 300, and $[\theta]_{230}$ +10 900.

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.18; H, 11.71.

(4-*tert*-Butylcyclohexylidene)acetic Acid (7). Following the procedure for (4-methylcyclohexylidene)acetic acid, 118.5 g (0.53 mol) of triethyl phosphonoacetate was condensed with 81 g (0.53 mol) of 4-*tert*-butylcyclohexanone to obtain 115 g of ethyl (4-*tert*-butylcyclohexylidene)-acetate. The IR and NMR of the ester were identical with those reported.[16]

The ester was saponified with alcoholic potassium hydroxide, and (4-*tert*-butylcyclohexylidene)acetic acid was isolated: yield 91 g (89.5%). A crystallization from hexane gave the acid as needles, mp 85 °C [lit. mp 92 °C]. The IR and NMR were identical with those reported.[16]

(*aR*)-(−)-(4-*tert*-Butylcyclohexylidene)acetic acid (7). The racemic (4-*tert*-butylcyclohexylidene)acetic acid was resolved with dehydroabietylamine. To a solution of 80 g of the acid (0.408 mol) in 1.2 L of ethyl acetate was added a solution of 116 g (0.406 mol) of the amine in 400 mL of benzene. The salt that formed was filtered and crystallized three times from ethyl acetate to yield 18 g of a constant melting crystalline solid (mp 162 °C). This was dissolved in 200 mL of warm methanol, and an excess of 1 N NaOH solution was added to free the acid from the amine. The amine was removed by extracting three times with benzene and once with ether. When the aqueous solution was poured into ice-cold 2 N HCl, the carboxylic acid separated as an oil. The oil was extracted with ether, and the ether solution washed with water, dried, filtered, and carefully evaporated to yield an oil, which slowly crystallized. The crystalline material was dried under vacuum to obtain 7.3 g of (*aR*)-(−)-(4-*tert*-butylcyclohexylidene)acetic acid, mp 57.5 °C; $[\alpha]^{25}_{Hg}$ −93.75 ± 0.51° (c 0.98, C_2H_5OH). The maximum rotation obtained from another trial of the same resolution was $[\alpha]^{22}_{Hg}$ −94.87 ± 0.51° (c 0.98, C_2H_2OH). The IR and NMR spectra of this sample were identical with those of a racemic sample.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.48; H, 10.21.

(*aR*)-(−)-(4-*tert*-Butylcyclohexylidene)ethanol (8). (*aR*)-(−)-(4-*tert*-Butylcyclohexylidene)acetic acid (7) ($[\alpha]^{26}_{Hg}$ −86.36 ± 0.48°, 91% optically pure) was esterified with CH_3I in NaOH/HMPA according to an earlier procedure. The product was distilled to give a quantitative yield of the methyl ester of the acid, bp (pot temperature) 80–85 °C (0.25 mm), $[\alpha]^{25.5}_{Hg}$ −84.15 ± 0.72° (c 0.7, $CHCl_3$); this corresponds to the corrected rotation of −92.47 ± 0.72° for the optically pure compound. IR (film) 2940, 2860, 2835, 1720, 1655, and 1500–860 cm^{-1}; ^1H NMR 0.9 (s, 9 H), 0.9–2.50 (m, 8 H), 3.70 (s, 3 H), 3.97 (broad d, 1 H), and 5.68 (s, 1 H) ppm.

The ester (4.0 g, 91% optically pure) was reduced with AlH_3 as described previously to give (*aR*)-(−)-(4-*tert*-butylcyclohexylidene)ethanol (**8**) in 93% yield, bp 80 °C (0.25 mm), $[\alpha]^{25}_{Hg}$ −8.02 ± 0.34° (c 1.45, C_2H_5OH); this corresponds to the corrected rotation of −8.81 ± 0.34° for the optically pure compound. IR (film) 3300 (bonded OH), 2940, 2850, 2825, 1670 (w), 1480–1365, 1230, and 1000 cm^{-1}; ^1H NMR 0.85 (s, 9 H), 1.0–2.95 (m, 9 H), 4.15 (d, J = 7 Hz, 2 H), and 5.43 (t, J = 7 Hz, 1 H) ppm; MS (EI), m/e 182 ($M^{+\cdot}$), 166, 164, 151, 95, 93, 81, 80, 79, 67, and 57 (100%).

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.03; H, 12.04.

(*aR*)-(−)-(4-*tert*-Butylcyclohexylidene)acetaldehyde (9). Following an earlier procedure, 3.5 g of (*aR*)-(−)-(4-*tert*-butylcyclohexylidene)-ethanol (**8**) ($[\alpha]^{25}_{Hg}$ −8.02 ± 0.34°, 91% optically pure) was oxidized with MnO_2. The aldehyde was purified by column chromatography and distilled under vacuum to obtain 3.0 g (86%) of the title compound (**9**), $[\alpha]^{25}_{Hg}$ −45.04 ± 0.36° (c 1.38, $CHCl_3$); this corresponds to the corrected rotation of −49.49 ± 0.36° for the optically pure compound: IR (film) 2940, 2860, 1675, 1640, 1480–1370, and 1240–760 cm^{-1}; ^1H NMR 0.90 (s, 9 H), 0.9–2.5 (m, 8 H), 3.45 (broad d, J = 13 Hz, 1 H), 5.87 (d, J = 8 Hz, 1 H), and 10.02 (d, J = 8 Hz, 1 H) ppm; UV (c 3.24 × 10^{-2} M, 6.48 × 10^{-5} M) λ_{381} (ϵ 16), λ_{363} (ϵ 37), λ_{347} (ϵ 48), λ_{333} (ϵ 47), λ_{321} (ϵ 44), and λ_{231} (ϵ 15 600); CD (c 3.24 × 10^{-2} M, 6.48 × 10^{-4} M) $[\theta]_{382}$ −910, $[\theta]_{363}$ −2070, $[\theta]_{347}$ −2370, $[\theta]_{333}$ −1850, $[\theta]_{321}$ −1170, and $[\theta]_{231}$ +8750.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.97; H, 11.13.

(*aR*)-(+)-(4-*tert*-Butylcyclohexylidene)propene (10). Following an earlier procedure, methylenetriphenylphosphorane (12.2 mmol) was condensed with 2.20 g (12.2 mmol) of (*aR*)-(−)-(4-*tert*-butylcyclohexylidene)acetaldehyde (**9**) ($[\alpha]^{25}_{Hg}$ −45.04 ± 0.36°, 91% optically pure). The diene was isolated, purified, and distilled to obtain 1.35 g (62%) of the title compound (**10**) as a colorless liquid, bp (pot temperature) 55–60 °C (0.25 mm), $[\alpha]^{24}_{Hg}$ +31.13 ± 0.50 °C (c 1.0, cyclohexane); this corresponds to the corrected rotation of +34.21 ± 0.50° for the optically pure compound. IR (film) 3065 (w), 3025 (w), 2940, 2860, 2825, 1800 (sh), 1645, 1595 (w), 1480–1220, 985, and 895 cm^{-1}; ^1H NMR 0.85 (s, 9 H), 0.85–2.5 (m, 8 H), 2.84 (broad d, J = 13 Hz, 1 H), 4.95 (dd, J = 10.5, 2 Hz, 1 H), 5.06 (dd, J = 16.5, 2 Hz, 1 H), 5.78 (d, J = 11 Hz, 1 H), and 6.64 (sextet, J = 16.5, 11, 10.5 Hz, 1 H) ppm; ^{13}C NMR 27.61 (q), 28.39 (t), 29.09 (t, 2 C), 32.47 (s), 37.10 (t), 48.38 (d), 114.37 (t), 124.40 (d), 132.70 (d), and 143.82 (s) ppm; UV (c 4.25 × 10^{-5} M) λ_{246} (ϵ 20 900), λ_{238} (ϵ 31 900), and λ_{231} (ϵ 29 000); CD (c 5.66 × 10^{-4} M) $[\theta]_{246}$ +10 400, $[\theta]_{238}$ +16 900, $[\theta]_{230}$ +16 500, and $[\theta]_{205}$ −15 700.

Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.60; H, 12.58.

***E,Z* Mixture of (3*R*)-(3-Methylcyclohexylidene)acetic Acid (18).** Following the procedure described for (4-methylcyclohexylidene)acetic acid, 100 g (0.446 mol) of triethyl phosphonoacetate was condensed with 50 g (0.445 mol) of (3*R*)-(+)-3-methylcyclohexanone ($[\alpha]^{24}_{D}$ +13.5°, neat; optically pure). An *E,Z* mixture of ethyl (3*R*)-(3-methylcyclohexylidene)acetate (85 g) was obtained. Saponification gave 60 g (87%) of roughly a 1:1 mixture of *E* and *Z* (3*R*)-(3-methylcyclohexylidene)-acetic acids, mp 33 °C, $[\alpha]^{25}_{Hg}$ −73.2 ± 0.3 (c 1.6, CH_3OH).

(*E*,3*R*)-(−)-(3-Methylcyclohexylidene)acetic Acid (19). To 60 g of an *E,Z* mixture of (3*R*)-(−)-(3-methylcyclohexylidene)acetic acid in 700 mL of ethyl acetate was added 47 g of (−)-α-phenylethylamine ($[\alpha]^{25}_{D}$ −40.3°, neat). The salt that formed was crystallized from ethyl acetate several times until the melting point was constant at 122 °C. The salt was decomposed with 1 N NaOH and the solution was extracted with ether to remove the amine. Acification of the aqueous solution with ice cold 2 N HCl precipitated the acid. The solid was filtered, washed with water, and dissolved in CH_3OH. The methanol solution was filtered and saturated by the addition of water. On standing, the acid slowly crystallized as flakes. It was filtered and dried under vacuum to yield 13 g of (*E*,3*R*)-(−)-(3-methlcyclohexylidene)acetic acid: mp 81 °C; $[\alpha]^{25}_{Hg}$ −145.51 ± 0.89° (c 0.51, CH_3OH); IR (KBr pellet) 3400–2200, 1680, 1630, 1450, 1430, 1325–1190, 1050, and 970–820 cm^{-1}; 270-MHz ^1H NMR 0.99 (d, J = 6 Hz, 3 H), 1.18 (q, 1 H), 1.43 (q, 1 H), 1.56–2.1 (m, 5 H), 2.31 (broad d, J = 12 Hz, 1 H), 3.67 (broad d, J = 12 Hz, 1 H), 5.64 (s, 1 H), and 11.78 (OH) ppm; ^{13}C NMR 22.08 (q), 26.67 (t), 29.52 (t), 34.52 (t), 35.00 (d), 46.35 (t), 112.98 (d), 165.74 (s), and 172.72 (s) ppm.

Anal. Calcd for $C_9H_{14}O_2$: C, 70.11; H, 9.15. Found: C, 70.32; H, 9.02.

***p*-Bromophenacyl (*E*,3*R*)-(3-Methylcyclohexylidene)acetate (20).** (*E*,3*R*)-(3-Methylcyclohexylidene)acetic acid (0.3 g) ($[\alpha]^{25}_{Hg}$ −145.51 ± 0.98°) was neutralized with 1.95 mL of 1 N NaOH solution. *p*-Bromophenacyl bromide (0.54 g) in 5 mL of ethyl alcohol was added and the solution refluxed for 1 h. Upon pouring this mixture onto ice, a solid precipitated, which was collected and dried. A crystallization from low-boiling petroleum ether gave single crystals: mp 67 °C; IR ($CHCl_3$) 3020, 2920, 2400 (sh), 1720, 1700, 1640, 1590, 1400, and 1300–925 cm^{-1}. X-ray analysis was obtained for these crystals.

(*E*,3*R*)-(−)-(3-Methylcyclohexylidene)ethanol (21). To a stirred slurry of 12.0 g (0.316 mol) of LAH in 250 mL of dry ether at 0 °C under nitrogen atmosphere was added dropwise a solution of 14.2 g (0.106 mol) of anhydrous $AlCl_3$ in 175 mL of ether. After stirring for 1 h, a solution of 12.0 g (0.078 mol) of (*E*,3*R*)-(−)-(3-methylcyclohexylidene)acetic acid (**19**) ($[\alpha]^{25}_{Hg}$ −145.51 ± 0.98°) in 100 mL of ether was slowly added. The mixture was stirred for 3 h and then hydrolyzed by carefully adding 2 N NaOH solution. The precipitated salts were filtered and washed several times with ether. The combined ether solution was dried with Na_2SO_4. Solvent removal gave the crude product, which was chromatographed on alumina by eluting with hexane and subsequently with hexane–ether. The fractions containing a mixture of hydrocarbon impurities were discarded. The fractions containing the allylic alcohol were collected, and the solvent was removed under reduced pressure. Distillation of the product gave 9.5 g of the alcohol (**21**) (87%): bp 56 °C (1 mm); $[\alpha]^{24}_{Hg}$ −57.41 ± 0.49° (c 1.03, C_2H_5OH); IR (film) 3300 (bonded OH), 2940, 2910, 2830, 1665, 1450, and 1010 cm^{-1}; ^1H NMR 0.9 (d, J = 7 Hz, 3 H), 0.9–2.65 (m, 9 H), 3.0 (OH), 4.08 (d, J = 7 Hz, 2 H), and 5.32 (t, J = 7 Hz, 1 H) ppm; ^{13}C NMR 22.20 (q), 26.78 (t), 28.28 (t), 34.38 (d), 35.04 (t), 45.33 (t), 58.48 (t), 120.73 (d), and 143.38 (s) ppm, MS (EI), m/e 140 ($M^{+\cdot}$), 122 (100%), 107, 97, 96, 95, 93, 81, 79, and 55.

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.13; H, 11.44.

Oxidation of (*E*,3*R*)-(3-Methylcyclohexylidene)ethanol with Pyridinium Dichromate. The allylic alcohol **21** containing 9–10% of its dihydro isomers was oxidized to an α,β-unsaturated aldehyde by the procedure of Corey.[18]

To a solution of 12.0 g (8.6 mmol) of the alcohol in 10 mL of dry DMF cooled to −10 °C was added 4 g (10.6 mmol) of pyridinium di-

chromate, and the solution was stirred for 4 h. The reaction mixture was poured onto water and extracted with low-boiling petroleum ether. The organic solution was washed with $NaHCO_3$ and water and dried, and the solvent was removed under reduced pressure to give a colorless liquid. A bulb-to-bulb distillation, bp (pot temperature) 60 °C (0.2 mm), yielded 1.1 g of an aldehyde, $[\alpha]^{25}_{Hg}$ −90.63 ± 0.95° (*c* 0.53, CH_3OH).

CD (cyclohexane or methanol, $[\theta]_{230}$ (−) and ^{13}C NMR ($CDCl_3$) showed that this sample was a mixture of the *E* and *Z* isomers of (3*R*)-(3-methylcyclohexylidene)acetaldehyde.

(*E*,3*R*)-(−)-(3-Methylcyclohexylidene)acetaldehyde (22). As described above for (4-methylcyclohexylidene)acetaldehyde, 4.0 g of (*E*,3*R*)-(−)-(3-methylcyclohexylidene)ethanol (**21**) containing 9–10% of its dihydro isomers was oxidized with MnO_2. A column chromatographic separation on silica gel and distillation (bulb to bulb) gave 2.9 g of (**22**) as a colorless liquid, bp (pot temperature) 60 °C (0.25 mm), $[\alpha]^{23}_{Hg}$ −136.60 ± 0.82° (*c* 0.61, $CHCl_3$). ^{13}C NMR before and after distillation showed that no isomerization occurred around the carbon–carbon double bond during the reaction and under the conditions of distillation. IR (film) 2940, 2910, 2850, 2830, 2750 (sh), 1675, 1630, 1460–1210, 1190, 1125, 1105, and 1090–820 cm^{-1}; ^1H NMR 1.00 (d, *J* = 6 Hz, 3 H), 1.00–2.4 (m, 8 H), 3.22 (broad d, *J* = 12 Hz), 5.84 (d, *J* = 8 Hz, 1 H), and 9.98 (d, *J* = 8 Hz, 1 H); ^{13}C NMR 22.09 (q), 26.93 (t), 29.03 (t), 34.39 (t), 34.86 (d), 46.11 (t), 125.46 (d), 167.19 (s), and 190.47 (d); MS (EI), *m/e* 138 ($M^{+\cdot}$), 123, 109, 107, 95, 94, 81, 79, 67, 55, 53, and 41 (100%); UV (*c* 1.95 × 10^{-2}, 6.24 × 10^{-5}) λ_{381} (ε 17), λ_{363} (ε 41), λ_{347} (ε 54), λ_{333} (ε 51), λ_{322} (ε 42), and λ_{231} (ε 16 700); CD (*c* 6.90 × 10^{-2}, 5.52 × 10^{-4}) $[\theta]_{381}$ −830, $[\theta]_{363}$ −1990, $[\theta]_{347}$ −2300, $[\theta]_{333}$ −1860, $[\theta]_{321}$ −1200, and $[\theta]_{230}$ +2690.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.15; H, 10.19.

(*E*,3*R*)-(−)-(3-Methylcyclohexylidene)propene (23). As described above for (4-methylcyclohexylidene)propene, 2.0 g (14 mmol) of (*E*,3*R*)-(−)-(3-methylcyclohexylidene)acetaldehyde (**22**) ($[\alpha]^{23}_{Hg}$ −136.60 ± 0.82°) was condensed with methylenetriphenylphosphorane (14 mmol) and the diene was isolated by following the earlier procedure. A bulb-to-bulb distillation afforded 1.2 g of the pure diene (**23**): bp (pot temperature) 25–30 °C (0.25 mm); $[\alpha]^{23}_{Hg}$ −38.84 ● 0.75 (*c* 0.66, cyclohexane); IR (film) 3065, 3025, 2940, 2910, 2860, 2830, 1800 (sh), 1650, 1595, and 1460–850 cm^{-1}; ^1H NMR 0.91 (d, *J* = 5 Hz, 3 H), 0.91–2.33 (m, 8 H), 2.65 (br d, *J* = 12 Hz, 1 H), 4.94 (dd, *J* = 10, 2.5 Hz, 1 H), 5.02 (dd, *J* = 16.5, 2.5 Hz, 1 H), 5.71 (d, *J* = 11 Hz, 1 H), and 6.60 (sextet, *J* = 16.5, 11, 10 Hz, 1 H) ppm; ^{13}C NMR 22.23 (q), 26.66 (t), 28.68 (t), 34.48 (d), 35.14 (t), 45.57 (t), 114.40 (t), 123.08 (d), 132.73 (d), and 143.15 (s) ppm. UV (*c* 4.39 × 10^{-5}) $\lambda_{246.5}$ (ε 20 100), λ_{238} (ε 30 300), and λ_{231} (ε 27 600); CD (*c* 6.37 × 10^{-4}) $[\theta]_{247}$ +6530, $[\theta]_{238}$ +8860, and $[\theta]_{230}$ +8400.

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.24; H, 11.84.

***p*-Bromophenacyl (*Z*,3*R*)-(+)-(3-Methylcyclohexylidene)acetate (24).** A mixture (~25% *E*, ~75% *Z*) of (3*R*)-(3-methylcyclohexylidene)acetic acid (45 g, 0.292 mol) was neutralized with 146 mL of 2 N NaOH solution. *p*-Bromphenacyl bromide (81 g, 0.29 mol) in 800 mL of 95% ethyl alcohol was added. The mixture was refluxed for 1.5 h and poured onto ice, and the solid that separated was filtered and dried (yield 95 g, 93%). Recrystalization from hexane four times yielded **24** as constant melting crystalline needles, mp 95 °C, $[\alpha]^{24.5}_{Hg}$ +8.55 ± 0.53° (*c* 0.95, $CHCl_3$). This material was found by ^{13}C NMR to be isomerically pure. IR ($CHCl_3$) 3020, 2920, 2400 (sh), 1720, 1700, 1640, 1590, 1400, and 1300–925 cm^{-1}; ^1H NMR 0.97 (d, *J* = 5 Hz, 3 H), 0.97–2.5 (m, 8 H), 3.67 (d, *J* = 10 Hz, 1 H), 5.30 (s, 2 H), 5.80 (s, 1 H), and 7.57–7.93 (m, 4 H) ppm; ^{13}C NMR 22.15 (q), 27.21 (t), 34.08 (t), 34.40 (d), 37.48 (t), 37.81 (t), 65.13 (t), 112.92 (d), 128.70 (s), 129.22 (d), 131.97 (d), 133.00 (s), 165.07 (s), 165.42 (s), and 191.73 (s) ppm.

Anal. Calcd for $C_{17}H_{19}BrO_3$: C, 58.13; H, 5.45; Br, 22.75. Found: C, 58.26; H, 5.47; Br, 22.66.

(*Z*,3*R*)-(−)-(3-Methylcyclohexylidene)ethanol (25). To a suspension of 5.25 g (0.138 mol) of LAH in 100 mL of ether at 0 °C under nitrogen atmosphere was added 6.18 g (0.046 mol) of anhydrous $AlCl_3$ in 50 mL of ether. The resulting slurry was stirred for 1 h. *p*-Bromophenacyl (*Z*,3*R*)-(+)-(3-methylcyclohexylidene)acetate ($[\alpha]^{24.5}_{Hg}$ +8.55 ± 0.53°) (14 g) in 225 mL of ether was slowly added. After stirring for 3 h, the mixture was hydrolyzed by a careful addition of 2 N NaOH solution. The precipitated aluminum salts were filtered off and washed with ether. The combined ether solution was washed with H_2O, dried, filtered, and evaporated. The crude product showed two spots in TLC. The product was chromatographed on 250 g of alumina. The column was eluted with 10% ether in hexane, and then the ether content was increased to 50%. The ether–hexane fractions yielded 5.0 g of the pure (*Z*,3*R*)-(−)-(3-methylcyclohexylidene)ethanol (**25**): bp 74 °C (0.5 mm); $[\alpha]^{24}_{Hg}$ −52.38 ± 0.48° (*c* 1.05, CH_3OH); IR 3300 (bonded OH), 2940, 2910, 2860, 2825, 1665, 1460, and 1000 cm^{-1}; ^1H NMR 0.93 (d, *J* = 5 Hz, 3 H), 0.93–2.33 (m, 8 H), 2.50 (d, *J* = 9 Hz, 1 H), 2.00 (OH), 4.03 (d, *J* = 7 Hz, 2 H), and 5.28 (t, *J* = 7 Hz, 1 H) ppm; ^{13}C NMR 22.31 (q), 27.21 (t), 33.72 (d), 35.11 (t), 36.53 (t), 37.08 (t), 58.10 (t), 120.99 (d), and 142.57 (s) ppm; MS (EI), *m/e* 140 ($M^{+\cdot}$), 122 (100%), 107, 95, 93, 81, 79, 67, and 55.

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.16; H, 11.31.

(*Z*,3*R*)-(−)-(3-Methylcyclohexylidene)acetaldehyde (26). By use of a previous procedure, 3.0 g of (*Z*,3*R*)-(−)-(3-methylcyclohexylidene)-ethanol ($[\alpha]^{24}_{Hg}$ −52.38 ± 0.48°) was oxidized with 25 g of MnO_2 in 200 mL of low-boiling petroleum ether. Workup in the usual manner and distillation gave 2.2 g (74%) of (**26**) as a colorless liquid: bp (pot temperature) 55–60 °C (0.25 mm); $[\alpha]^{24}_{Hg}$ −44.03 ± 0.81 (*c* 0.62, $CHCl_3$); IR (film) 2940, 2910, 2850, 2830, 1675, 1630, 1460–1330, and 1200–840 cm^{-1}; ^1H NMR 1.02 (d, *J* = 5 Hz, 3 H), 1.02–2.45 (m, 8 H), 3.20 (d, *J* = 10Hz, 1 H), 5.82 (d, *J* = 8 Hz, 1 H), and 10.02 (d, *J* = 8 Hz, 1 H) ppm; ^{13}C NMR 21.96 (q), 26.99 (t), 34.38 (t), 34.51 (d), 37.53 (t, 2 C), 125.48 (dd), 166.91 (s), and 190.18 (d) ppm; MS (EI), *m/e* 138 ($M^{+\cdot}$), 123 (100%), 109, 105, 95, 94, 93, 81, 79, 77, 67, and 55; UV (*c* 2.16 × 10^{-2}, 6.90 × 10^{-5}) λ_{381} (ε 17), λ_{363} (ε 42), λ_{347} (ε 57), λ_{322} (ε 41), and λ_{232} (ε 17 800); CD (*c* 4.34 × 10^{-2}, 4.34 × 10^{-5}) $[\theta]_{381}$ +774, $[\theta]_{363}$ +1800, $[\theta]_{348}$ +2030, $[\theta]_{333}$ +1570, $[\theta]_{321}$ +956, and $[\theta]_{232}$ −15 000.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.13; H, 10.26.

(*Z*,3*R*)-(−)-(3-Methylcyclohexylidene)propene (27). By use of the procedure for (4-methylcyclohexylidene)propene, 1.60 g of (*Z*,3*R*)-(−)-(3-methylcyclohexylidene)acetaldehyde (**26**) ($[\alpha]^{24}_{Hg}$ −44.03 ± 0.81) was condensed with methylenetriphenylphosphorane. The usual isolation and distillation procedure yielded 0.55 g of pure (*Z*,3*R*)-(−)-(3-methylcyclohexylidene)propene (**27**) as a colorless liquid: bp (pot temperature) 40 °C (1.7 mm); $[\alpha]^{24}_{Hg}$ −119.61 ± 0.65° (*c* 0.78, cyclohexane); IR (film) 3070, 3030, 2940, 2910, 2860, 2820, 1800 (sh), 1645, 1595, 1470–1225 (m), and 1100–850 (m) cm^{-1}; ^1H NMR 0.96 (d, *J* = 5 Hz, 3 H), 0.96–2.23 (m, 8 H), 2.67 (d, *J* = 9.5 Hz, 1 H), 4.92 (dd, *J* = 11, 2 Hz, 1 H), 5.03 (dd, *J* = 16.5, 2 Hz), 5.77 (d, *J* = 11 Hz, 1 H), and 6.62 (sextet, *J* = 16.5, 11, 11 Hz, 1 H) ppm; ^{13}C NMR 22.31 (q), 27.32 (t), 33.75 (d), 35.16 (t), 36.74 (t), 37.51 (t), 114.40 (t), 123.06 (d), 132.65 (d), and 143.00 (s) ppm; MS (EI), *m/e* 136 ($M^{+\cdot}$), 121, 107, 95, 93, 91, 80, 79 (100%), and 67; UV (*c* 4.22 × 10^{-5}) λ_{246} (ε 20 800), λ_{238} (ε 31 300), and λ_{231} (ε 28 600); CD (*c* 6.69 × 10^{-4}) $[\theta]_{246}$ −11 900, $[\theta]_{238}$ −17 800, and $[\theta]_{230}$ −16 300.

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.31; H, 11.81.

***tert*-Butyl (2-Methylcyclohexylidene)acetate (29).** A dry, 3-L, three-necked flask equipped with a mechanical stirrer was charged with 75.0 g (0.741 mol) of diisopropylamine and flushed with nitrogen. The flask was cooled in an ice bath to 0 °C and 310 mL of 2.30 M BuLi in hexane (0.713 mol) was added, with stirring, over a period of 30 min. After the addition was completed, rapid stirring was continued for 10 min. Dry THF (1600 mL) was added, and the solution was cooled in a dry ice/acetone bath to −78 °C. *tert*-Butyl (trimethylsilyl)acetate (134 g, 0.713 mol) was added slowly to obtain a white precipitate. After stirring this precipitate for 30 min, 80.0 g (0.713 mol) of 2-methylcyclohexanone was added over a period of 15 min. The cooling bath was removed and the temperature was raised to 0 °C over 45 min. The reaction mixture was hydrolyzed with water, poured into a large separatory funnel containing ice cold 2 N HCl, and extracted twice with hexane. The hexane extract was washed with 2 N HCl and water and dried over Na_2SO_4. Evaporation of the solvent gave the crude ester (**29a**). A small amount of the ester (≃1 g) was distilled under vacuum: IR (film) 2960, 2920, 2840, 1705, 1640, and 1460–1477 cm^{-1}; ^1H NMR 0.93 (d, *J* = 6 Hz), 1.02 (d, *J* = 7 Hz), 1.02–2.40 (m, including a singlet at 1.35), 3.57 (broad d), 3.90 (m), and 5.32 (d, *J* = 1 Hz) ppm. Integration of the signal at 3.90 vs. 3.37 ppm gave a *Z*:*E* ratio of 77:23.

(*Z*)-(2-Methylcyclohexylidene)acetic Acid (30). *tert*-Butyl (2-methylcyclohexylidene)acetate (*Z*:*E* = 77:23) prepared above was refluxed with 1 L of CH_3OH and 300 mL of 1 N H_2SO_4 for 2 h. The mixture was cooled to room temperature and poured into a separatory funnel containing 600 mL of ice cold 2 N NaOH. The neutral materials were extracted with ether and the aqueous solution was saved.

The ether solution was washed with water, dried, and evaporated to yield 15–20 g of methyl (2-methylcyclohexylidene)acetate. The methyl ester was saponified with 200 mL of 1 N KOH (50% CH_3OH). The saponification mixture was extracted with ether to remove all the neutral materials, and the extract was discarded.

The two aqueous solutions were combined and added to concentrated HCl over ice. The carboxylic acid that separated as an oil was extracted with ether and the ether solution was washed with water, dried over

Na_2SO_4, and evaporated to get 95 g (86% based on 2-methylcyclohexanone) of the acid (*Z*:*E* = 77:23). The acid was dissolved in 500 mL of CH_3OH and enough water was added to saturate the solution. The solution was left at room temperature to crystallize. After 24 h, the crystals were collected, recrystallized from the same solvent system, and dried to obtain 45 g of (*Z*)-(2-methylcyclohexylidene)acetic acid, mp 73–76 °C. Melting point and IR and NMR spectra were identical with those reported.[21a]

(*Z*,2*S*)-(+)-(2-Methylcyclohexylidene)acetic Acid (30). Racemic (*Z*)-(2-methylcyclohexylidene)acetic acid was resolved with (−)-α-phenylethylamine.

When a solution of 80 g of (*Z*)-(2-methylcyclohexylidene)acetic acid in 1 L of ethyl acetate was mixed with 63 g (1 equiv) of (−)-α-phenylethylamine in 250 mL of ethyl acetate, a spontaneous crystallization occurred. The mixture was heated on a steam bath until the solid went into solution. The hot solution was left undisturbed at room temperature. Within hours, a crystalline material was deposited, filtered, and dried to yield 75 g of material, mp 120–123 °C (the melting point did not change with further recrystallizations from ethyl acetate). A small amount of the carboxylic acid was recovered from this salt, mp 66–70 °C, $[\alpha]^{25}_{Hg}$ +31° (*c* 1.1, C_2H_5OH). The salt was recrystallized from a solvent mixture of 1 L of ethyl acetate and 100 mL of methanol to give mp 137–139 °C. In two further recrystallizations the melting point was constant at 142 °C; yield 20.5 g. The carboxylic acid was isolated from the amine salt and crystallized from hot methanol–water solution to yield 11 g of crystalline needles: mp 74 °C (sharp); $[\alpha]^{26}_{Hg}$ +161.86 ± 0.63° (*c* 0.8, C_2H_5OH).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.11; H, 9.15. Found: C, 70.26; H, 9.02.

Ozonolysis of (*Z*,2*S*)-(+)-(2-Methylcyclohexylidene)acetic Acid. Ozone was bubbled through a solution of 1.5 g (9.7 mmol) of (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)acetic acid ($[\alpha]^{26}_{Hg}$ +161.86 ± 0.63° (*c* 0.8, C_2H_5OH)) in 75 mL of CH_2Cl_2 at −78 °C until the reaction was complete. The reaction vessel was removed from the cooling bath and the ozonide was decomposed by adding 0.9 g (14.5 mmol) of dimethyl sulfide and allowing the mixture to remain at room temperature overnight. The solution was washed with water and dried, and the solvent was removed to obtain the crude product. A column chromatographic separation (silica gel, hexane–ether) and a bulb-to-bulb distillation under aspirator pressure gave 0.75 g of pure (2*S*)-(+)-2-methylcyclohexanone: $[\alpha]^{26.5}_{Hg}$ ± 2.45 + 0.38° (*c* 1.3, CH_3OH); CD (CH_3OH) $[\theta]_{286}$ +24.7 [lit.[22] ORD (*c* 0.23, CH_3OH): $[\alpha]_{589}$ +14°, $[\alpha]_{305}$ +515°, $[\alpha]_{265}$ −565°]. IR and NMR spectra were identical with those of authentic racemic 2-methylcyclohexanone.

Optical Purity of (*Z*,2*S*)-(+)-(2-Methylcyclohexylidene)acetic Acid. A diastereomeric mixture of amides were prepared from racemic (*Z*)-(2-methylcyclohexylidene)acetic acid and optically pure (*S*)-(−)-1-phenylethylamine. To a mixture of 2.0 g (13 mmol) of the acid and a drop of DMF in 10 mL of anhydrous ether in a flask fitted with a $CaCl_2$ drying tube was added 2 mL of purified $SOCl_2$. The mixture was stirred at 25 °C for 1 h. All volatile materials were removed from the flask and the acid chloride was redissolved in 50 mL of anhydrous ether. Upon the addition of 4.0 g (33 mmol) of the amine a white precipitate was formed. The mixture was refluxed for 15 min, poured into water, and washed successively with 1 N NaOH, 1 N HCl, and water. The ether solution was dried over Na_2SO_4, filtered, evaporated, and vacuum-dried to obtain a glassy solid, yield 3.2 g: 270-MHz ^1H NMR (C_6D_6) 1.13, 1.19 (d, *J* = 7 Hz, 3 H), 1.19–1.88 (m, 10 H including a CH_3 doublet at 1.37, *J* = 7 Hz), 1.88 (d, *J* = 13 Hz, 1 H), 2.22 (m, 1 H), 4.56 (br s, 1 H), 5.32 (quintet, *J* = 7 Hz, 1 H), 5.64 (d, *J* = 3 Hz, 1 H), 7.07, 7.16, and 7.35 (m, 5 H) ppm.

Following the same procedure, the acid chloride was prepared from (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)acetic acid (**30**) ($[\alpha]^{26}_{Hg}$ +161.86 ± 0.63° (*c* 0.8, C_2H_5OH)) and condensed with optically pure (S)-(−)-1-phenylethylamine. The above isolation procedure yielded (*Z*,1′*S*,2*S*)-*N*-(1′-phenylethyl)-2-methylcyclohexylideneacetamide (**31**) as a crystalline solid in quantitative yield, mp 136 °C, found by ^1H NMR to be free of the (*Z*,1′*S*,2*R*)-diasteriomer. 270-MHz ^1H NMR (C_6D_6) 1.17 (d, *J* = 7 Hz, 3 H), 1.17–1.72 (m, 10 H including a CH_3 doublet at 1.23, *J* = 7 Hz), 1.82 (d, *J* = 13 Hz, 1 H), 2.22 (td, *J* = 12, 2 Hz, 1 H), 4.59 (br s, 1 H), 5.33 (quintet, *J* = 7 Hz, 1 H), 5.78 (d, *J* = 3 Hz, 1 H), and 7.14 (m, 5 H) ppm.

Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.00; N, 5.44. Found: C, 79.26; H, 9.00; N, 5.33.

(*Z*,2*S*)-(+)-(2-Methylcyclohexylidene)ethanol (32). Following an earlier procedure, 8.5 g of (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)acetic acid (**30**) (optically pure) was esterified to yield 8.8 g (95%) of pure methyl (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)acetate: $[\alpha]^{25}_{Hg}$ +156.20 ± 0.54° (*c* 0.92, CH_3OH); IR (film) 2920, 2850, 1715, 1640, and 1470–810 cm^{-1}; ^1H NMR 1.15 (d, *J* = 7 Hz, 3 H), 1.15–2.73 (m, 8 H), 3.67 (s, 3 H), 4.08 (m, 1 H), and 5.58 (d, *J* = 1.5 Hz, 1 H) ppm.

Reduction of 8.2 g of the methyl ester with AlH_3 and the usual workup provided 6.4 g (94%) of (*Z*,2*S*)-(+)-(2-methylcyclohexlidene)ethanol (**32**) as a colorless liquid: bp 74 °C (0.75 mm); $[\alpha]^{25.5}_{Hg}$ +142.58 ± 0.49° (*c* 1.0, CH_3OH); IR (film) 3300 (br, OH), 2950, 2910, 2840, 1665, and 1470–810 cm^{-1}; ^1H NMR 1.08 (d, *J* = 7.5 Hz, 3 H), 1.08–2.42 (m, 8 H), 2.87 (m, 1 H and OH), 4.15 (d, *J* = 7.5 Hz, 2 H), and 5.30 (td, *J* = 7.5, 1.5 Hz, 1 H) ppm.

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.92; H, 11.44.

(*Z*,2*S*)-(+)-(2-Methylcyclohexylidene)acetaldehyde (33). By use of a previous procedure, (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)ethanol (**32**) ($[\alpha]^{25.5}_{Hg}$ +142.58 ± 0.49°) (6.0 g) was oxidized with MnO_2. A column chromatographic separation and distillation of the product gave 4.2 g of (**33**) as a colorless liquid: bp 65 °C (0.8 mm); $[\alpha]^{25}_{Hg}$ +136.50 ± 0.80° (*c* 0.63, cyclohexane); IR (film) 2920, 2840, 1675, 1625, 1460–1320, and 1205–735 cm^{-1}; ^1H NMR 1.26 (d, *J* = 7 Hz, 3 H), 1.26–2.9 (m, 8 H), 3.72 (m, 1 H), 5.80 (dd, *J* = 8, 1.5 Hz, 1 H), and 10.03 (d, *J* = 8 Hz, 1 H) ppm; ^{13}C NMR 19.18 (q), 20.37 (t), 28.28 (t), 31.27 (d), 33.26 (t), 33.45 (t), 125.31 (dd), 171.30 (s), and 189.69 (d) ppm; UV (*c* 2.23 × 10^{-2}, 7.14 × 10^{-5}) λ_{381} (ε 11), λ_{363} (ε 25), λ_{348} (ε 33), λ_{334} (ε 31), λ_{322} (ε 26), and λ_{231} (λ 13 200); CD (*c* 4.64 × 10^{-2}, 7.42 × 10^{-4}) $[\theta]_{381}$ −1070, $[\theta]_{363}$ −2480, $[\theta]_{348}$ −2860, $[\theta]_{334}$ −2220, $[\theta]_{322}$ −1320, $[\theta]_{232}$ +16 275, and $[\theta]_{198}$ +18 400.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.17; H, 10.17.

(*Z*,2*S*)-(+)-(2-Methylcyclohexylidene)propene (34). As in an earlier procedure, condensation of methylenetriphenylphosphorane (16 mmol) with 2.2 g (16 mmol) of (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)acetaldehyde (**33**) ($[\alpha]^{25}_{Hg}$ +136.50 ± 0.80°) produced the diene. A chromatographic separation and distillation provided the pure (*Z*,2*S*)-(+)-(2-methylcyclohexylidene)propene (**34**) (0.7 g): bp ≃ 25–30 °C (0.2 mm); $[\alpha]^{25}_{Hg}$ +152.82 ± 0.52 (*c* 0.96, cyclohexane); IR (film): 3060 (w), 3020 (w), 2950, 2920, 2845, 1800 (sh), 1640, 1590 (w), 1470–980, and 900 cm^{-1}; ^1H NMR 1.10 (d, *J* = 7 Hz, 3 H), 1.10–2.66 (m, 8 H), 3.10 (m, 1 H), 5.00 (dd, *J* = 11, 2 Hz, 1 H), 5.13 (dd, *J* = 16.5, 2 Hz, 1 H), 5.80 (dd, *J* = 11, 1.5 Hz, 1 H), and 6.73 (sextet, *J* = 16.5, 11, 11 Hz, 1 H) ppm; ^{13}C NMR 18.37 (q), 20.95 (t), 28.39 (t), 30.86 (d), 32.66 (t), 33.18 (t), 114.60 (t), 122.80 (d), 132.33 (d), and 147.44 (s) ppm; UV (*c* 6.37 × 10^{-5}) λ_{246} (ε 19 100), λ_{238} (ε 28 700), and λ_{231} (λ 26 200); CD (*c* 6.37 × 10^{-4}) $[\theta]_{246}$ + 9580, $[\theta]_{238}$ +13 100, $[\theta]_{231}$ +12 800, and $[\theta]_{214}$ −5430.

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.20; H, 11.81.

(*E*,2*S*)-(−)-(2-Methylcyclohexylidene)bromomethane (35). To a solution of 11.5 g (0.075 mol) of the acid (**30**) ($[\alpha]^{26.5}_{Hg}$ +163.11 ± 0.61°, optically pure) in 50 mL of dry $CHCl_3$ at −23 °C (dry ice/CCl_4) was added 11.8 g (0.074 mol) of Br_2 in 40 mL of $CHCl_3$. The mixture was stirred at −23 °C for 15 min and then the temperature was raised to 25 °C. The solution was then added dropwise to a steam distilling solution of saturated Na_2CO_3. The distillate was extracted twice with ether. The ether solution was dried over Na_2SO_4 and the solvent removed under reduced pressure to obtain a liquid, which was chromatographed (silica gel, pentane) to remove carbonyl impurities and distilled to yield 6.9 g (49%) of **35** as a colorless liquid: bp 59 °C (1.5 mm); $[\alpha]^{26}_{Hg}$ −13.82 ± 0.30° (*c* 0.83, cyclohexane); IR (film) 3080 (w), 2940, 2910, 2840, 1620, and 1460–700 cm^{-1}; ^1H NMR 1.08 (d, *J* = 6.5 Hz, 3 H), 1.08–2.50 (m, 8 H), 2.84 (br d, *J* = 13 Hz, 1 H), and 6.00 (s, 1 H) ppm; ^{13}C NMR 18.36 (q), 25.00 (t), 27.07 (t), 30.92 (t), 36.20 (t), 38.98 (d), 97.64 (d), and 148.99 (s) ppm.

Anal. Calcd for $C_8H_{13}Br$: C, 50.81; H, 6.93; Br, 42.26. Found: C, 50.95; H, 6.99; Br, 42.11.

(*E*,2*S*)-(−)-(2-Methylcyclohexylidene)acetic Acid (36). To a solution of 5.8 g (31 mmol) of (*E*,2*S*)-(−)-(2-methylcyclohexylidene)bromomethane (**35**) ($[\alpha]^{26}_{Hg}$ −13.82 ± 0.30°, optically pure) in 75 mL of dry THF under a nitrogen atmosphere at −78 °C (dry ice/acetone) was added dropwise a solution (20 mL, 38 mmol) of *tert*-butyllithium in pentane. After the complete addition, the yellow solution was stirred for 5 min and then poured onto dry ice covered with dry THF. The THF solution was warmed up to 0 °C and diluted with water. Hydrochloric acid (1 N) was added to free the carboxylic acid and the mixture was extracted three times with ether. The combined ether solution was extracted with 1 N NaOH. On acidification of the extract with dilute HCl, the carboxylic acid separated, was recrystallized from CH_3OH/H_2O, and was dried to yield 2.3 g (48%) of (*E*,2*S*)-(−)-(2-methylcyclohexylidene)acetic acid (**36**) as crystalline needles: mp 69 °C; $[\alpha]^{25}_{Hg}$ −40.21 ± 0.57° (*c* 0.88, CH_3OH, optically pure); IR (KBr pellet) 3300–2300 (br), 1685, 1630, 1460–1160, 980–760, and 700 cm^{-1}; ^1H NMR was identical with that of racemic (*E*)-(2-methylcyclohexylidene)acetic acid; ^{13}C NMR 18.38 (q), 25.12 (t), 28.55 (t), 29.64

(t), 37.13 (t), 40.32 (d), 110.58 (d), 170.19 (s), and 173.26 (s) ppm.

Anal. Calcd for $C_9H_{14}O_2$: C, 70.11; H, 9.15. Found: C, 70.29; H, 9.08.

The starting bromide (1.1 g) was recovered from the ether solution.

(*E*,2*S*)-(+)-(2-Methylcyclohexylidene)ethanol (37). As in a previous procedure, 2.1 g of (*E*,2*S*)-(−)-(2-methylcyclohexylidene)acetic acid (**36**) ($[\alpha]^{25}_{Hg}$ −40.21 ± 0.57°, optically pure) was esterified to produce 2.1 g of the methyl ester. The usual reduction and isolation procedure yielded 1.6 g of the pure (*E*,2*S*)-(+)-(2-methylcyclohexylidene)ethanol (**37**) as a colorless liquid: bp (pot temperature) 70 °C (0.35 mm); $[\alpha]^{25}_{Hg}$ +15.93 ± 0.54° (*c* 0.93, $CHCl_3$); IR (film) 3300 (bonded OH), 2940, 2910, 2840, 1660, 1450, and 1400–800 cm^{-1}; ^1H NMR 1.03 (d, *J* = 6.5 Hz, 3 H), 1.03–2.50 (m, 8 H), 2.50 (br d, *J* = 12 Hz, 1 H), 3.40 (OH), 4.13 (d, *J* = 7 Hz, 2 H), and 5.28 (t, *J* = 7 Hz, 1 H) ppm; ^{13}C NMR 18.58 (q), 25.55 (t), 28.2 (t), 28.58 (t), 36.72 (t), 38.51 (d), 58.38 (t), 118.42 (d), and 146.97 (s) ppm.

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.17; H, 11.44.

(*E*,2*S*)-(−)-(2-Methylcyclohexylidene)acetaldehyde (38). By use of a previous procedure, 1.5 g of (*E*,2*S*)-(+)-(2-methylcyclohexylidene)-ethanol (**37**) ($[\alpha]^{26}_{Hg}$ +15.93 ± 0.5°, optically pure) was oxidized with MnO_2. A column chromatographic separation and distillation of the product yielded 1.2 g of the pure (*E*,2*S*)-(−)-(2-methylcyclohexylidene)acetaldehyde (**38**) as a colorless liquid: bp (pot temperature) 55 °C (0.5 mm); $[\alpha]^{25}_{Hg}$ −4.87 ± 0.53° (*c* 0.95, cyclohexane); IR (film) 2950, 2910, 2840, 1670, 1620, and 1460–760 cm^{-1}; ^1H NMR 1.08 (d, *J* = 6.5 Hz, 3 H), 1.08–2.15 (m, 8 H), 3.26 (br d, *J* = 12 Hz, 1 H), 5.83 (d, *J* = 8 Hz, 1 H), and 10.06 (d, *J* = 8 Hz, 1 H) ppm; ^{13}C NMR 18.00 (q), 25.09. (t), 28.74 (t), 29.26 (t), 36.86 (t), 39.97 (d), 122.78 (dd), 171.58 (s), and 190.67 (d) ppm. UV (*c* 1.87×10^{-2}, 6.87×10^{-5}) λ_{380} (ε 17), λ_{373} (ε 40), λ_{347} (ε 51), λ_{333} (ε 47), λ_{322} (ε 37), and λ_{232} (ε 17, 700); CD (*c* 1.37×10^{-2}, 6.87×10^{-4}) $[\theta]_{381}$ −793, $[\theta]_{363}$ −1880, $[\theta]_{346}$ −2160, $[\theta]_{332}$ −1690, $[\theta]_{321}$ −1080, and $[\theta]_{231}$ +11 800.

Anal. Calcd for $C_9H_{14}O$: C, 78.21, H, 10.21. Found: C, 78.21; H, 10.33.

(*E*,2*S*)-(+)-(2-Methylcyclohexylidene)propene (39). By use of an earlier procedure, 0.90 g (6.5 mmol) of (*E*,2*S*)-(−)-(2-methylcyclohexylidene)acetaldehyde (**38**) ($[\alpha]^{25}_{Hg}$ −4.87 ± 0.53°, optically pure) was condensed with methylenetriphenylphosphorane (6.5 mmol). The crude product was chromatographed and distilled to obtain 0.31 g of (*E*,2*S*)-(+)-(2-methylcyclohexylidene)propene (**39**) as a colorless liquid: bp (pot temperature) ≃30 °C (0.5 mm); $[\alpha]^{26}_{Hg}$ +75.46 ± 0.51° (*c* 0.98, cyclohexane); IR (film) 3060 (w), 3025 (w), 2990 (w), 2940, 2910, 2840, 1800 (sh), 1645, 1595 (w), and 1460–1350 cm^{-1}; ^1H NMR 1.07 (d, *J* = 7 Hz, 3 H), 1.07–2.33 (m, 8 H), 2.67 (br d, *J* = 12 Hz, 1 H), 4.95 (dd, *J* = 11, 2 Hz, 1 H), 5.06 (dd, *J* = 16.5, 2 Hz, 1 H), 5.75 (d, *J* = 11 Hz, 1 H), and 6.64 (sextet, *J* = 16.5, 11, 11 Hz, 1 H) ppm; ^{13}C NMR 18.55 (q), 25.47 (t), 28.17 (t), 28.82 (t), 36.77 (t), 38.76 (d), 114.74 (t), 120.27 (d), 132.88 (d), and 147.75 (s) ppm; UV (*c* 6.12×10^{-5}) λ_{247} (ε 17 000), λ_{239} (ε 25 650), and λ_{233} (ε 23 400); CD (*c* 6.12×10^{-4}) $[\theta]_{248}$ +8740, $[\theta]_{239}$ +14 200, $[\theta]_{233}$ + 14 900, and $[\theta]_{203}$ −9380.

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.10; H, 11.86.

2-Methyl-4-*tert*-butylcyclohexanone (42). The dimethylhydrazone of 4-*tert*-butylcyclohexanone was prepared according to the procedure of Newcome et al.[25] The hydrazone (**40**) was methylated in a molar quantity by using the procedure of Corey et al.[26] The methylated hydrazone was cleaved to *trans*-2-methyl-4-*tert*-butylcyclohexanone (**42**) by using $NaIO_4$ in aqueous methanolic solution at pH 7.[26] However, this procedure was found to be tedious for large scale reactions.

An alternate procedure was designed, which was found useful for small as well as large scale reactions. According to our procedure, the dimethylhydrazone of *trans*-2-methyl-4-*tert*-butylcyclohexane (60 g, 0.285 mol) was dissolved in 1.0 L of dry DMF and the solution was cooled to −63 °C (dry ice/$CHCl_3$). *m*-Chloroperbenzoic acid (98.0 g, 0.57 mol of 80–90%) was slowly added while the solution was being stirred. After 0.5 h, the solution was poured into $NaHCO_3$ solution and extracted twice with hexane. The hexane extract was washed with sodium bisulfite, $NaHCO_3$, and water. The solution was filtered through Na_2SO_4 and evaporated, and the residue was distilled under vacuum, b 75 °C (1.25 mm), to yield 45.5 g (95%) of *trans*-2-methyl-4-*tert*-butylcyclohexanone (**42**): ^1H NMR 0.90 (s, 9 H), 1.15 (d, *J* = 7 Hz, 3 H), and 1.15–2.8 (m, 8 H) ppm; ^{13}C NMR 16.84 (q), 26.18 (t), 27.40 (q), 32.44 (s), 32.99 (t), 38.03 (t), 41.35 (d), 42.96 (d), and 216.11 (s) ppm.

***cis*-2-Methyl-*trans*-4-*tert*-butylcyclohexanol (43a).** To a slurry of 13.5 g (0.36 mol) of LAH in 1.0 L of dry ether at 0 °C was slowly added 60 g (0.36 mol) of *trans*-2-methyl-4-*tert*-butylcyclohexanone (**42**) in 250 mL of dry ether. After the addition was complete, the reaction mixture was stirred for 45 min. The mixture was hydrolyzed by dropwise addition of 2 N NaOH solution. The aluminum salts were filtered and washed with ether. The combined ether solution was dried over Na_2SO_4 and evaporated to obtain 60 g (99%) of (**43a**) as a solid: ^1H NMR ($CDCl_3$) 0.84 (s, 9 H), 0.94 (d, *J* = 7.5 Hz, 3H), 0.95–2.15 (m, 8 H), 3.16 (OH), and 3.66 (m, 1 H) ppm.

(1*R*,2*S*,4*R*)-(+)-2-Methyl-4-*tert*-butylcyclohexanol (43b). *cis*-2-Methyl-*trans*-4-*tert*-butylcyclohexanol (**43a**) (95 g, 0.56 mol) and succinic anhydride (56 g, 0.56 mol) were refluxed in 100 mL of dry pyridine for 2 h. The mixture was poured into ice cold HCl solution and extracted twice with ether. The ether extract was washed with dilute HCl and water, dried over Na_2SO_4, and evaporated to obtain 150 g of the succinic acid half ester (**44**) as a solid. The crude product was dissolved in 1.3 L of ethyl acetate and a solution of 68 g (0.56 mol) of (−)-α-phenylethylamine in 150 mL of methanol was added. The mixture was warmed and left at room temperature to crystallize. The crystalline material was filtered off and recrystallized from an ethyl acetate–methanol mixture until the melting point was constant (150–151 °C).

The salt (19.5 g) was decomposed by heating with 2 N NaOH solution for 15 min and the mixture was extracted twice with ether. The ether solution was washed with 2 N HCl and water, dried over Na_2SO_4, and evaporated to obtain 8.5 g of (1*R*,2*S*,4*R*)-(+)-(**43b**) as a solid. The solid was recrystallized from pentane: mp 71–72 °C; $[\alpha]^{27}_{Hg}$ +45.49 ± 0.25° (*c* 2.03, $CHCl_3$).

(2*S*,4*R*)-(+)-2-Methyl-4-*tert*-butylcyclohexanone (45). To a solution of 8.5 g (0.05 mol) of (1*R*,2*S*,4*R*)-(+)-2-methyl-4-*tert*-butylcyclohexanol (**43b**) ($[\alpha]^{27}_{Hg}$ +45.49 ± 0.25°) in 200 mL of dry DMF was added 29.8 g (0.11 mol) of pyridinium dichromate and 4.1 g (0.02 mol) of pyridinium trifluoroacetate. The mixture was stirred for 3 h, poured onto water, and extracted with hexane. The hexane extract was washed with water, dried, and evaporated to get 8.5 g (100%) of a liquid. The crude product was chromatographed on silica gel by eluting with hexane–ether mixture. Fractions corresponding to the pure ketone were collected and evaporated to obtain 7.9 g (94%) of (2*S*,4*R*)-(+)-(**45**) as a liquid, which was distilled, $[\alpha]^{27}_{D}$ +125.83 ± 1.1° (*c* 0.45, $CHCl_3$, 89.9% optically pure) (lit.[27] $[\alpha]^{20}_{D}$ +140°; *c* 0.38, $CHCl_3$, for optically pure sample).

***tert*-Butyl (*E*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)-acetate (51)** and ***tert*-Butyl (*Z*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)acetate (47).** A dry three-necked flask was charged with 3.31 g (0.033 mol) of dry diisopropylamine and the flask was maintained at 0 °C under a N_2 atmosphere. With the aid of a syringe, 13.1 mL of 2.50 M (0.033 mol) *n*-butyllithium was slowly added and stirred. The LDA thus prepared was dissolved in 150 mL of dry THF and the solution was cooled to −78 °C (dry ice/acetone). *tert*-Butyl (trimethylsilyl)-acetate (6.15 g, 0.033 mol) was slowly added with stirring. After 20 min, 5.50 g (0.033 mol) of (2*S*,4*R*)-(+)-2-methyl-4-*tert*-butylcyclohexanone (**45**) (89.9% optically pure) in 25 mL of dry THF was added. The cooling bath was removed and the temperature allowed to reach 0 °C. The reaction mixture was quenched with water and extracted twice with hexane. The hexane extract was washed with 2 N HCl and water, dried, and evaporated to obtain a liquid (8.4 g, 95%).

VPC Analysis. The crude product was analyzed by vpc (15% Carbowax 20 M on Chromosorb P, 80/100 acid washed, 10 ft × $^1/_8$ in., column 180 °C, carrier gas flow 17 mL/min). Two peaks of equal intensity with retention times 16.5 and 19.9 min, corresponding to esters **47** and **51**, were found.

The two compounds were separated by preparative VPC (10% Carbowax 20 M on Chromosorb P, 80/100 acid washed, 6 ft × $^3/_8$ in., column 165–170 °C, carrier gas flow 200 mL/min) by injecting 20 μL at a time.

The peak with the retention time of 16.5 min was found to be (*Z*,2*S*,4*R*)-(+)-**47**: $[\alpha]^{26}_{Hg}$ +61.02 ± 0.94° (*c* 0.53, $CHCl_3$, 89.9% optically pure); ^1H NMR ($CDCl_3$) 0.85 (s, 9 H), 1.16 (d, *J* = 7 Hz, 3 H), 1.2–2.8 (m, 16 H, including a singlet at 1.48 for the ester *tert*-butyl group), 3.73–4.33 (m, 1 H), and 5.48 (br s, 1 H) ppm; IR (film) 3000–2820, 1710, 1640, and 1480–860 cm^{-1}; ^{13}C NMR ($CDCl_3$) 18.99 (q), 27.51 (q), 28.31 (q), 29.06 (d), 30.67 (t), 32.12 (s), 33.37 (t), 34.05 (t), 41.25 (d), 79.33 (s), 114.50 (d), 165.17 (s), and 166.02 (s) ppm.

Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.61; H, 11.26.

The peak with the retention time of 19.9 min was found to be (*E*,2*S*,4*R*)-(+)-**51**: low melting solid; $[\alpha]^{26.5}_{Hg}$ +106.78 ± 0.97° (*c* 0.51, $CHCl_3$, 89.9% optically pure); IR (film) 3000–2800, 1710, 1640, and 1480–860 cm^{-1}; ^1H NMR 0.87 (s, 9 H), 1.13 (d, *J* = 7 Hz, 3 H), 1.1–2.8 (m, 16 H including a singlet at 1.47 for the ester *tert*-butyl group), 3.67 (br d, *J* = 13 Hz, 1 H), and 5.56 (s, 1 H) ppm; ^{13}C NMR 19.70 (q), 25.02 (t), 27.47 (q), 28.23 (t), 28.31 (q), 32.15 (s), 34.74 (t), 39.70 (d), 41.33 (d), 79.23 (s), 114.23 (d), 165.62 (s), and 166.38 (s) ppm.

Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.64; H, 11.40.

(*Z*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)ethanol (48). To a slurry of 0.25 g (6.6 mmol) of LAH in 20 mL of ether at 0 °C was added 0.30 g (2.3 mmol) of anhydrous $AlCl_3$ in 5 mL of ether. The mixture was stirred for 15 min, and a solution of 0.32 g (1.2 mmol) of (*Z*,2*S*,4*R*)-(+)-**47** in 5 mL of ether was slowly added. The mixture was stirred for 2 h at 0 °C and hydrolyzed by adding 2 N NaOH solution. The aluminum salts were filtered off and washed with ether. The combined ether solution was dried and evaporated to yield an oil. The crude product was chromatographed on silica gel by eluting with hexane–ether mixture to obtain (*Z*,2*S*,4*R*)-(+)-**48**: $[\alpha]^{27}_{Hg}$ +68.12 ● 1.05° (*c* 0.48, $CHCl_3$); IR (film) 3300 (br OH), 3000–2820, and 1660 cm^{-1}; ^1H NMR 0.82 (s, 9 H), 1.06 (d, *J* = 7 Hz, 3 H), 1.06–2.45 (m, 7 H), 2.56 (s, OH), 2.83–3.20 (m, 1 H), 4.13 (d, *J* = 7 Hz, 2 H), and 5.30 (t, *J* = 7 Hz, 1 H) ppm; ^{13}C NMR 19.26 (q), 27.52 (q), 29.15 (t), 30.54 (d), 32.09 (s), 32.56 (t), 34.25 (t), 41.57 (d), 58.08 (t), 120.30 (d), and 147.03 (s) ppm.

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.45; H, 12.32.

(*Z*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)acetaldehyde (49). (*Z*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)ethanol (**48**) (0.24 g) was stirred with 2.5 g of MnO_2 in 25 mL of pentane for 1.5 h. The product was worked up as before to obtain (*Z*,2*S*,4*R*)-(+)-**49** as an oil (0.20 g): $[\alpha]^{26.5}_{Hg}$ +60.44 ± 0.72° (*c* 0.70, cyclohexane, 89.9% optically pure); IR (film) 3000–2800, 1675, 1630, and 1500–850 cm^{-1}; ^1H NMR 0.87 (s, 9 H), 1.27 (d, *J* = 7 Hz, 3 H), 1.27–2.70 (m, 7 H), 3.50–4.00 (m, 1 H), 5.75 (d, *J* = 8 Hz, 1 H), and 9.98 (d, *J* = 8 Hz, 1 H) ppm; ^{13}C NMR 19.89 (q), 27.45 (q), 29.12 (t), 31.19 (d), 32.14 (s), 33.47 (t), 34.46 (t), 41.10 (d), 124.85 (dd), 171.49 (s), and 189.94 (d) ppm; UV (*c* 1.79 × 10^{-3}, 5.38 × 10^{-5}) λ_{382} (ε 20), λ_{363} (ε 45), λ_{347} (ε 56), λ_{333} (ε 50), λ_{322} (ε 39), and λ_{232} (ε 18 200); CD (*c* 1.79 × 10^{-3}, 5.38 × 10^{-4}) $[\theta]_{382}$ −860, $[\theta]_{363}$ −2210, $[\theta]_{347}$ −2460, $[\theta]_{333}$ −1840, $[\theta]_{322}$ −1100, and $[\theta]_{233}$ +11 500.

MS (high resolution) calcd for $C_{13}H_{22}O$, 194.1670; found, 194.1707.

(*Z*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)propene (50). (*Z*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)acetaldehyde (**49**) (0.12 g, 0.6 mmol) was condensed with methylenetriphenylphosphorane (0.6 mmol) in ether by following a procedure described before. The product was isolated and purified the usual way to obtain (*Z*,2*S*,4*R*)-(+)-**50** as a liquid (0.025 g) 89.9% optically pure: $[\alpha]^{26.5}_{Hg}$ +119.09 ± 4.5° (*c* 0.11, cyclohexane); IR (film) 3060 (w), 3020 (w), 3000–2800, 1800 (w), 1645, 1595 (w), 1500–1000, and 900 cm^{-1}; 270-MHz ^1H NMR 0.86 (s, 9 H), 1.10 (d, *J* = 7 Hz, 3 H), 1.19–2.40 (m, 7 H), 3.14 (m, 1 H), 5.05 (br d, *J* = 10 Hz, 1 H), 5.11 (br d, *J* = 16 Hz, 1 H), 5.76 (d, *J* = 11 Hz, 1 H), and 6.65 (sextet, *J* = 16, 11, 10 Hz, 1 H) ppm; UV (*c* 5.72 × 10^{-5}) λ_{246} (ε 18 700), λ_{239} (ε 26 900), and λ_{232} (λ 24 700); CD (*c* 5.72 × 10^{-4}) $[\theta]_{246}$ +7320, $[\theta]_{239}$ +10 000, and $[\theta]_{232}$ +8860. MS (high resolution) calcd for $C_{14}H_{24}$, 192.1877; found, 192.1862.

(*E*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)acetic Acid (52). (*E*,2*S*,4*R*)-(+)-*tert*-Butyl (2-methyl-4-*tert*-butylcyclohexylidene)acetate (**51**) (0.32 g), 89.9% optically pure, was refluxed with 2 drops of concentrated H_2SO_4 in 25 mL of methanol–water solution. After 2 h the mixture was poured into a 2 N NaOH solution and washed several times with ether. The aquous solution was acidified with 2 N HCl and extracted twice with ether. The ether solution was washed with water, dried over Na_2SO_4, and evaporated to give **52** as an oil (0.27 g): $[\alpha]^{26.5}_{Hg}$ +117.82 ± 1.19° (*c* 0.42, C_2H_5OH, 89.9% optically pure); IR (film) 3500–2200 (br), 1750–1600 (br), and 1500–700 cm^{-1}; ^1H NMR 0.83 (s, 9 H), 1.15 (d, *J* = 7 Hz, 3 H), 1.15–2.78 (m, 7 H), 3.68 (br d, *J* = 14 Hz, 1 H), 5.65 (s, 1 H), and 11.96 (s, CO_2H) ppm; ^{13}C NMR 19.69 (q), 25.57 (t), 27.45 (q), 28.25 (t), 32.14 (s), 34.73 (t), 39.96 (d), 41.24 (d), 112.21 (d), 170.51 (s), and 172.85 (s) ppm.

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.24. Found: C, 74.40; H, 10.28.

(*E*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexyliene)acetaldehyde (53). To a solution of 0.26 g (1.2 mmol) of (*E*,2*S*,4*R*)-(+)-(2-methyl-4-*tert*-butylcyclohexylidene)acetic acid (**52**) in 10 mL of dry ether was added a few drops of freshly distilled $SOCl_2$ and the mixture was stirred for 15 min. The ether and excess $SOCl_2$ were removed in vacuo. The acid chloride was dissolved in 10 mL of dry THF and cooled to −78 °C. To this solution was slowly added a solution of 0.31 g (1.2 mmol) of tri-*tert*-butoxylithium aluminum hydride in 10 mL of dry THF. After stirring for a few min, the mixture was allowed to reach room temperature and stirred for an additional 45 min. The mixture was hydrolyzed with water, poured into dilute HCl, and extracted with hexane. The hexane solution was evaporated and the crude product was chromatographed on silica gel by eluting with hexane–ether. Fractions corresponding to the aldehyde were collected, and solvent was removed to obtain (*E*,2*S*,4*R*)-(+)-**53** as an oil (0.15 g): $[\alpha]^{27}_{Hg}$ +60.56 ± 2.78° (*c* 0.44, cyclohexane, 89.9% optically pure); IR (film) 2980–2820, 1675, and 1625 cm^{-1}; ^1H NMR 0.87 (s, 9 H), 1.08 (d, *J* = 7 Hz, 3 H), 1.08–2.5 (m, 7 H), 3.40 (br d, *J* = 13 Hz, 1 H), 5.70 (d, *J* = 8 Hz, 1 H), and 9.90 (d, *J* = 8 Hz, 1 H) ppm; UV (*c* 9.26 × 10^{-3}, 4.63 × 10^{-5}) λ_{391} (ε 8), λ_{380} (ε 18), λ_{362} (ε 46), λ_{346} (ε 70), λ_{332} (ε 88), and λ_{233} (ε 15 100); CD (*c* 9.26 × 10^{-3}, 4.63 × 10^{-4}) $[\theta]_{382}$ +650, $[\theta]_{363}$ +1370, $[\theta]_{347}$ +1550, $[\theta]_{333}$ +1190, $[\theta]_{323}$ +830, and $[\theta]_{233}$ −7140. MS (high resolution) calcd for $C_{13}H_{22}O$, 194.1670; Found, 194.1646.

(*E*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)propene (54). (*E*,2*S*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)acetaldehyde (**53**), 89.9% optically pure, 0.135 g (0.7 mmol), was condensed with methylenetriphenylphosphorane (0.7 mmol) following a procedure described earlier. The reaction was worked up and the product purified to obtain (*E*,2*S*,4*R*)-(+)-**54** as a liquid: 89.9% optically pure, $[\alpha]^{27}_{Hg}$ +80.20 ± 1.25° (*c* 0.40, cyclohexane); IR (film) 3060 (w), 3020 (w), 2980–2820, 1800 (w), 1645, 1595 (w), 1480–1350, 980, and 900 cm^{-1}; ^1H NMR 0.84 (s, 9 H) 1.08 (d, *J* = 6.5 Hz, 3 H), 1.08–2.85 (m, 8 H), 4.92 (dd, *J* = 10, 2 Hz, 1 H), 5.00 (dd, *J* = 16, 2 Hz, 1 H), 5.73 (d, *J* = 11 Hz, 1 H), and 6.52 (sextet, *J* = 16, 11, 10 Hz, 1 H) ppm; UV (*c* 5.18 × 10^{-5}) λ_{246} (ε 17 400), λ_{239} (ε 26 300), and λ_{232} (ε 24 300); CD (*c* 5.18 × 10^{-4}) $[\theta]_{246}$ −3830, $[\theta]_{239}$ −5530, $[\theta]_{232}$ −6800, and $[\theta]_{218}$ −10 200. MS (high resolution) calcd for $C_{14}H_{24}$, 192.1877: found, 192.1838.

(2*R*,4*R*)-(+)-2-Methyl-4-*tert*-butylcyclohexanone (46). (2*S*,4*R*)-(+)-2-Methyl-4-*tert*-butylcyclohexanone (**45**) ($[\alpha]^{27}_{D}$ +125.83 ± 1.1°, 89.9% optically pure), 2.5 g, was treated with 250 mL of 5% KOH in methanol–water overnight. The mixture was poured into water and extracted with hexane. The crude product was chromatographed on silica gel, eluting with hexane–ether mixture. Fractions corresponding to the pure ketone were collected and evaporated to obtain (2*R*,4*R*)-(+)-**46** as a liquid, which was distilled: bp 80 °C (0.75 mm); $[\alpha]_D^{27.5}$ +11.93 ± 0.95 (*c* 0.52, $CHCl_3$, 89.9% optically pure) (lit.[27] $[\alpha]^{20}_{D}$ +12.2°); ^{13}C NMR 14.71 (q), 27.65 (q), 28.64 (t), 32.31 (s), 37.29 (t), 41.25 (t), 44.36 (d), 47.13 (d), and 213.50 (s) ppm.

***Condensation of Lithium Ethoxyacetylide with* (2*R*,4*R*)-(+)-2-Methyl-4-*tert*-butylcyclohexanone (46).** To a solution of 0.50 g (7.1 mmol) of freshly distilled ethoxyacetylene in 15 mL of dry ether at −78 °C under nitrogen atmosphere was added 3.5 mL of 2.0 M (7.0 mmol) *n*-butyllithium over a period of 5 min. The mixture was stirred for 10 min and 1.20 g (7.1 mmol) of (2*R*,4*R*)-(+)-**46** (89.9% optically pure) in 5 mL of ether was added. The reaction mixture was allowed to reach room temperature, quenched with water, and extracted twice with hexane. Evaporation of the hexane solution provided 1.7 g of a liquid: IR (film) 3400 (br) and 2250 cm^{-1}.

The crude product was taken up in 25 mL of THF at 0 °C and 10 drops of concentrated H_2SO_4 were added. In 1 h all the acetylene disappeared (monitored by IR). The reaction mixture was poured into water and extracted twice with hexane. The solution was evaporated to get **55** as a liquid (1.7 g): IR (film) 3000–2800, 1710, 1640, and 1480–850 cm^{-1}.

(*E*,2*R*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)ethanol (56). Ethyl (*E*,2*R*,4*R*)-(+)-(2-methyl-4-*tert*-butylcyclohexylidene)acetate, 1.0 g (4.2 mmol), 89.9% optically pure, was reduced with aluminum hydride (8.4 mmol) following a procedure described earlier. The crude product was chromatographed to obtain (*E*,2*R*,4*R*)-(+)-**56** as a liquid (0.78 g): $[\alpha]^{27}_{Hg}$ +1.17 ± 0.76° (*c* 0.66, $CHCl_3$); IR (film) 3350 (br, OH), 3000–2800, 1660, and 1500–900 cm^{-1}; ^1H NMR 0.84 (s, 9 H), 1.02 (d, *J* = 7 Hz, 3 H), 1.02–2.85 (m, 8 H), 4.13 (d, *J* = 7 Hz, 2 H and OH), and 5.20 (t, *J* = 7 H, 1 H) ppm; ^{13}C NMR 18.34 (q), 27.47 (q), 28.74 (d), 29.27 (t), 32.16 (s), 37.71 (t), 38.09 (t), 48.03 (d), 58.50 (t), 117.07 (d), and 147.31 (s) ppm.

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.63; H, 12.24.

(*E*,2*R*,4*R*)-(+)-(2-Methyl-4-*tert*-Butylcyclohexylidene)acetaldehyde (57). (*E*,2*R*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)ethanol (**56**), 89.9% optically pure, 0.7 g, was oxidized with 7 g of MnO_2 according to a procedure described before. The usual isolation and purification procedure yielded 0.52 g of (*E*,2*R*,4*R*)-(+)-**57** as a low melting solid: $[\alpha]^{27}_{Hg}$ +16.40 ± 0.83° (*c* 0.60, cyclohexane); IR (film) 3000–2750, 1670, 1625, 1500–1360, 1250–1060, and 950–750 cm^{-1}; ^1H NMR 0.85 (s, 9 H), 1.05 (d, *J* = 6.5 Hz, 3 H), 1.05–2.6 (m, 7 H), 3.43 (td, J = 3, 13 Hz, 1 H), 5.70 (d, *J* = 8 Hz, 1 H), and 9.90 (d, *J* = 8 Hz, 1 H) ppm; ^{13}C NMR 17.70 (q), 27.31 (q), 29.28, and 29.65 (d + t), 32.11 (s), 38.21 (t), 39.30 (t), 47.44 (d), 121.79 (dd), 171.04 (s), and 190.45 (d) ppm; UV (*c* 4.96 × 10^{-3}, 4.96 × 10^{-5}) λ_{390} (ε 16), λ_{380} (ε 20), λ_{362} (ε 44), λ_{346} (ε 56), λ_{332} (ε 52), and λ_{232} (ε 17 900); CD (*c* 4.96 × 10^{-3}; 4.96 × 10^{-4}) $[\theta]_{381}$ +780, $[\theta]_{363}$ +1690, $[\theta]_{347}$ +1910, $[\theta]_{333}$ +1550, $[\theta]_{321}$ +980, and $[\theta]_{232}$ −11 100.

Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.08; H, 11.20.

(*E*,2*R*,4*R*)-(−)-(2-Methyl-4-*tert*-butylcyclohexylidene)propene (58). (*E*,2*R*,4*R*)-(+)-(2-Methyl-4-*tert*-butylcyclohexylidene)acetaldehyde

(**57**), 89.9% optically pure, 0.35 g (1.8 mmol), was condensed with methylenetriphenylphosphorane (1.8 mmol) following a procedure described previously. The usual isolation and purification procedure gave (*E*,2*R*,4*R*)-(−)-**58** as a liquid (0.25 g): $[\alpha]^{27}_{Hg}$ −33.39 ± 0.71° (*c* 0.70, cyclohexane); IR (film) 3060 (w), 3020 (w), 3000–2800, 1800 (w), 1645, 1595 (w), and 1480–900 cm^{-1}; ^{1}H NMR 0.84 (s, 9 H), 1.05 (d, *J* = 6.5 Hz, 3 H), 1.05–2.5 (m, 7 H), 2.84 (br, *J* = 13 Hz, 1 H), 4.90 (dd, *J* = 10, 2 Hz, 1 H), 5.04 (dd, *J* = 16, 2 Hz, 1 H), 5.62 (d, *J* = 11 Hz, 1 H), and 6.56 (sextet, *J* = 16, 11, 10 Hz, 1 H) ppm; ^{13}C NMR 18.45 (q), 27.64 (q), 28.83 (d), 29.81 (t), 32.37 (s), 38.09 (t), 38.39 (t), 48.26 (d), 114.83 (t), 119.22 (d), 132.93 (d), and 147.67 (s) ppm; UV (*c* 5.09 × 10^{-5}) λ_{247} (ε 18 300), λ_{239} (ε 26 700), and λ_{232} (ε 24 200); CD (*c* 5.09 × 10^{-4}) $[\theta]_{247}$ −9520, $[\theta]_{239}$ −15 600, and $[\theta]_{232}$ −16 400.

Anal. Calcd for $C_{14}H_{24}$: C, 87.42; H, 12.58. Found: C, 87.11; H, 12.48.

(2*S*,5*R*)-(−)-Menthone (12). *l*-Menthol was oxidized according to the procedure of H. C. Brown et al.[29] The crude product was purified by flash column chromatography (ether–hexane) and distilled, bp 65 °C (4 mm), $[\alpha]^{25}_{D}$ −27.8° (neat) [lit.[29] $[\alpha]_D$ −29.9° (neat)].

Condensation of Lithium Ethoxyacetylide with (2*S*,5*R*)-(−)-Menthone. To 7.75 g (0.111 mol) of ethoxyacetylene in 350 mL of dry ether under nitrogen atmosphere maintained at −78 °C (dry ice/acetone) was slowly delivered 44 mL of 2.50 M *n*-butyllithium (0.110 mol) in hexane. The resulting white precipitate was stirred for 10–15 min. A solution of 16.0 g (0.104 mol) of the (2*S*,5*R*)-(−)-menthone **12** ($[\alpha]^{25}_{D}$ −27.8) in 25 mL of ether was added and the cooling bath removed. When the flask warmed up sufficiently (≃ −40 °C), the precipitate disappeared. The stirring was continued until it reached room temperature and water was added to hydrolyze the reaction. The mixture was washed with water, the ether solution was dried, and the solvent was removed under reduced pressure to obtain 23.5 g of (2*R*,5*S*)-1-(2-ethoxyacetylenyl)-2-isopropyl-5-methylcyclohexanol as a liquid: IR (film) 3470 (broad, bonded OH), 2940, 2860, 2250, and 1470–780 cm^{-1}; ^{1}H NMR 0.78–2.5 (m including OH at 1.67, a CH_3 triplet at 1.33, and other CH_3 multiplets), and 3.97 (q) ppm.

Rearrangement of (2*R*,5*S*)-1-(2-Ethoxyacetylenyl)-2-isopropyl-5-methylcyclohexanol. By use of a modified procedure of Arth et al.,[28] the acetylene alcohol was completely rearranged to the α,β-unsaturated ester. To a solution of 23.5 g of the alcohol in 350 mL of THF at 0 °C was added dropwise 1 mL of 97% H_2SO_4, and the mixture was stirred for 1 h. At the end of this period, the mixture was poured into $NaHCO_3$ solution and extracted with hexane. The hexane extract was washed with water and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave (*E*,2*S*,5*R*)-(2-isopropyl-5-methylcyclohexylidene)acetic acid ethyl ester in quantitative yield (impurities were found in TLC analysis): IR (film) 2940, 2910, 2860, 1715, 1640, and 1460–820 cm^{-1}; ^{1}H NMR 0.9–2.53 (m including CH_3 multiplets at ≃0.9 and a CH_3 triplet at 1.27), 3.15 (dd, *J* = 13, 4 Hz, 1 H), and 5.67 (s, 1 H) ppm.

(*E*,2*S*,5*R*)-(−)-(2-Isopropyl-5-methylcyclohexylidene)acetic Acid (59). Following an earlier procedure, 20 g of the crude (*E*,2*S*,5*R*)-ethyl (2-isopropyl-5-methylcyclohexylidene)acetate was saponified and 17.0 g of a carboxylic acid was isolated, mp 63–65 °C. This on crystallization twice from methanol–water (3:2) gave 13.0 g of the title compound as crystalline thick needles: mp (constant) 79–80 °C; $[\alpha]^{25.5}_{Hg}$ −59.18 ± 0.44° (*c* 1.15, C_2H_5OH); IR (KBr pellet) 3350–2100 (carboxylic OH), 1685, 1630, 1450–860, and 710 cm^{-1}; ^{1}H NMR 0.89–2.7 (m, 17 H including three CH_3 doublets at 0.89, 0.95, and 0.98), 3.10 (dd, *J* = 13, 4 Hz, 1 H), 5.67 (s, 1 H) ppm; ^{13}C NMR 19.64 (q), 20.33 (q), 21.77 (q), 26.94 (d), 27.55 (t), 31.33 (t), 33.70 (d), 36.07 (t), 53.09 (d), 113.21 (d), 167.79 (s), and 172.83 (s); MS (EI), *m/e* 196 ($M^{+\cdot}$), 181, 163, 154, 153, 139, 137, 136, 135, 121, 111, 109, 107, and 95 (100%).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.63; H, 10.17.

(*E*,2*S*,5*R*)-(−)-(2-Isopropyl-5-methylcyclohexylidene)ethanol (60). Following a previous procedure, 8.5 g of (*E*,2*S*,5*R*)-(−)-(2-isopropyl-5-methylcyclohexylidene)acetic acid (**59**) ($[\alpha]^{25.5}_{Hg}$ −59.18 ± 0.44° (*c* 1.15, C_2H_5OH)) was esterified to yield 8.75 g (96%) of its methyl ester. The ester (6.5 g) was reduced with AlH_3 and worked up as before. Distillation of this material yielded 5.2 g (92%) of pure (*E*,2*S*,5*R*)-(−)-(2-isopropyl-5-methylcyclohexylidene)ethanol (**60**) as a colorless liquid: bp 97 °C (0.7 mm); $[\alpha]^{25.5}_{Hg}$ −65.27 ± 0.47° (*c* 1.06, $CHCl_3$); IR (film) 3300 (bonded OH), 2950 (multiplets), 1660, 1460, 1380, and 1020 cm^{-1}; ^{1}H NMR 0.84–2.5 (m, 18 H including a broad doublet for the CH_3 groups at 0.84), 2.67 (OH), 4.23 (d, *J* = 7 Hz, 2 H), and 5.47 (t, *J* = 7 Hz, 1 H) ppm; MS (EI), *m/e* 182 ($M^{+\cdot}$), 164, 149, 138, 122, 121, 95 (100%), 93, 81, 79, and 77.

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.24; H, 12.20.

(*E*,2*S*,5*R*)-(−)-(2-Isopropyl-5-methylcyclohexylidene)acetaldehyde (61). MnO_2 oxidation of (*E*,2*S*,5*R*)-(−)-(2-isopropyl-5-menthylcyclohexylidene)ethanol (**60**) ($[\alpha]^{25.5}_{Hg}$ −65.25 ± 0.47° (*c* 1.06, $CHCl_3$)) (4.2 g) gave the aldehyde **61**. A column chromatographic separation gave 3.5 g of the pure (*E*,2*S*,5*R*)-(−)-(2-isopropyl-5-methylcyclohexylidene)-acetaldehyde (**61**). Trace amounts of solvents were removed by subjecting the sample to low pressure (0.1 mm) for 1 h: $[\alpha]^{25}_{Hg}$ −77.52 ± 0.50 (*c* 1.0, cyclohexane); IR (film) 2950, 2920, 2860, 2740 (sh), 1670, 1625, 1450, 1400, 1200–1000, and 860 cm^{-1}; ^{1}H NMR 0.8–2.34 (m, 17 H), 2.98 (dd, *J* = 10, 4 Hz, 1 H), 5.86 (d, *J* = 8 Hz, 1 H), and 9.96 (d, *J* = 8 Hz, 1 H) ppm; ^{13}C NMR 19.24 (q), 20.36 (q), 21.67 (q), 26.71 (d), 27.27 (t), 31.38 (t), 33.99 (d), 35.86 (t), 52.30 (d), 125.52 (dd), 169.23 (s), and 190.52 (d) ppm; UV (*c* 2.78 × 10^{-2}, 6.66 × 10^{-5}) λ_{400} (ε 3), λ_{380} (ε 17), λ_{363} (ε 37), λ_{347} (ε 44), λ_{333} (ε 41), λ_{321} (ε 33), and λ_{236} (ε 12 500); CD (*c* 2.78 × 10^{-2}; 6.66 × 10^{-4}) $[\theta]_{382}$ +480, $[\theta]_{364}$ +1250, $[\theta]_{348}$ +1460, $[\theta]_{333}$ +1140, $[\theta]_{322}$ +640, $[\theta]_{236}$ −8920, and $[\theta]_{203}$ −19 300.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.85; H, 11.18.

(*E*,2*S*,5*R*)-(−)-(2-Isopropyl-5-methylcyclohexylidene)propene (62). By use of an earlier procedure, condensation of methylenetriphenylphosphorane (11 mmol) with 2.0 g (11 mmol) of (*E*,2*S*,5*R*)-(−)-(2-isopropyl-5-methylcyclohexylidene)acetaldehyde (**61**) and purification of the crude product by column chromatography provided 1.2 g (61%) of the pure diene **62**: bp (pot temperature) 60 °C (0.5 mm); $[\alpha]^{25}_{Hg}$ −102.47 ± 0.84° (*c* 0.6, cyclohexane); IR (film) 3160 (w), 3125 (w), 2940, 2910, 2855, 1800 (sh), 1640, 1595 (w), 1460–1330, 985, and 900 cm^{-1}; ^{1}H NMR 0.84–2.7 (m, 18 H), 4.92 (dd, *J* = 11, 2 Hz, 1 H), 5.05 (dd, *J* = 16.5, 2 Hz, 1 H), 5.79 (d, *J* = 11 Hz, 1 H), and 6.63 (sextet, *J* = 16.5, 11, 11 Hz, 1 H) ppm; ^{13}C NMR 19.78 (q), 20.53 (q), 22.03 (q), 26.80 (d), 27.02 (t), 31.92 (t), 32.75 (d), 35.79 (t), 51.65 (d), 114.48 (t), 123.30 (d), 133.00 (d), and 144.61 (s) ppm; UV (*c* 5.36 × 10^{-5}) λ_{248} (ε 18 700), λ_{239} (ε 28 200), and λ_{233} (ε 25 800); CD (*c* 6.70 × 10^{-4}) $[\theta]_{248}$ −4950, $[\theta]_{238}$ −9100, and $[\theta]_{233}$ −7950.

Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.68; H, 12.43.

X-ray Analysis of 20. The crystals contained two independent molecules in the unit cell. The two molecules have been designated unprimed and primed. The crystals were orthorhombic, space group $P2_12_12_1$, with *a* = 7.137 (2) Å, *b* = 9.361 (1) Å, *c* = 50.041 (8) Å, and d_{calcd} = 1.395 g cm^{-3} for *Z* = 8 ($C_{17}H_{19}BrO_3$, M_r = 351.24). The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse height discrimination). A crystal measuring approximately 0.10 × 0.20 × 0.5 mm was used for data collection. The data were corrected for absorption (μ = 37.6 cm^{-1}). A total of 2649 reflections were measured for θ < 57°, of which 1932 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by heavy atom method and was refined by full-matrix least squares. In the final refinement anisotropic thermal parameters were used for the heavier atoms, and the isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices are *R* = 0.042 and *wR* = 0.044 for the 1932 observed reflections. The final difference map has not peaks greater than ±0.1 e Å^{-3}.

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Registry No. 1, 589-92-4; (±)-**2**, 77842-31-0; (±)-**2** (ethyl ester), 85048-17-5; **2**, 28835-95-2; **2** (methyl ester), 77764-42-2; **2**·(+)-α-phenylethylamine, 85066-69-9; **3**, 85048-13-1; **4**, 85048-14-2; **5**, 85048-15-3; **6**, 98-53-3; (±)-**7**, 85048-16-4; (±)-**7** (ethyl ester), 85048-18-6; **7**, 28835-98-5; **7** (methyl ester), 85048-20-0; **7**·dehydroabietylamine, 85164-98-3; **8**, 85048-19-7; **9**, 85048-21-1; **10**, 85048-22-2; **12**, 14073-97-3; **14**, 13368-65-5; (*E*)-**18**, 85114-21-2; (*Z*)-**18**, 85114-22-3; (*E*)-**18** (ethyl ester), 85048-23-3; (*Z*)-**18** (ethyl ester), 85048-24-4; **19**·(−)-α-phenylethylamine, 85114-67-6; **20**, 85048-25-5; **21**, 85048-26-6; **22**, 85048-27-7; **23**, 85048-28-8; **24**, 85048-29-9; **25**, 85048-30-2; **26**, 85048-31-3; **27**, 85048-32-4; (*Z*)-(±)-**29**, 85048-33-5; (*E*)-(±)-**29**, 85066-65-5; (±)-**30**, 85048-34-6; (±)-**30** (methyl ester), 85114-23-4; (±)-**30** (acid chloride), 85048-35-7; **30**, 85114-25-6; **30** (methyl ester), 55700-95-3; **30** (acid chloride), 85114-26-7; **30**·(−)-α-phenylethylamine, 85114-68-7; **30** (α-phenylethylamide), 85048-36-8; **31**, 85048-37-9; **32**, 85048-38-0; **33**, 85048-39-1; **34**, 85048-40-4; **35**, 85114-27-8; (±)-**36**, 85048-34-6; (±)-**36** (methyl ester), 85114-24-5; **36**, 85114-28-9; **37**, 85048-41-5; **38**, 85048-42-6; **39**, 85048-43-7; (±)-*trans*-**42**, 85114-29-0; (±)-*trans*-**42** (dimethylhydrazone), 85114-30-3; (±)-**43a**, 85114-31-4; **43b**, 85114-32-5; (±)-**44**, 85048-44-8; (1*R*,2*S*,4*R*)-**44**·(−)-α-phenylethylamine, 85114-34-7; **45**, 74365-82-5; **46**, 74365-81-4; **47**, 85048-46-0; **48**, 85048-47-1; **49**, 85048-48-2; **50**, 85048-49-3; **51**, 85048-45-9; **52**, 85048-50-6; **52** (acid chloride), 85048-52-8; **53**, 85048-51-7; **54**, 85066-66-6; **55**, 85114-35-8; **56**, 85048-53-9; **57**, 85048-54-0; **58**, 85048-55-1;

59, 85048-58-4; **59** (ethyl ester), 85048-57-3; **59** (methyl ester), 85048-60-8; **60**, 85048-59-5; **61**, 85048-61-9; **62**, 85048-62-0; *tert*-butyl (trimethylsilyl)acetate, 41108-81-0; *tert*-butyl acetate, 540-88-5; trimethylsilyl chloride, 75-77-4; triethyl phosphonoacetate, 867-13-0; methyltriphenylphosphonium bromide, 1779-49-3; methylenetriphenylphosphorane, 3487-44-3; *p*-bromophenacyl bromide, 99-73-0; (±)-2-methylcyclohexanone, 24965-84-2; (2*S*)-(+)-2-methylcyclohexanone, 22554-27-4; (*S*)-(−)-1-phenylethylamine, 2627-86-3; succinic anhydride, 108-30-5; ethoxyacetylene, 927-80-0; *l*-menthol, 2216-51-5; 1-(2-ethoxyacetylenyl)-2-isopropyl-5-methylcyclohexanol, 85048-56-2.

Supplementary Material Available: Tables IA–C listing bond angles, bond lengths, and torsion angles for compound **20** (3 pages). Ordering information is given on any current masthead page.

Chiroptical Properties of Planar Acyclic 1,3-Dienes and α,β-Unsaturated Aldehydes: A Planar Diene Rule

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Abstract: Cotton effects in circular dichroism (CD) and optical rotatory dispersion (ORD) spectra of 1,3-dienes and α,β-unsaturated carbonyl compounds, for their $\pi-\pi^*$ transitions, are believed to arise from inherent dissymmetry of the chromophore as well as dissymmetric substituents. A selected number of chiral acyclic 1,3-dienes and α,β-unsaturated aldehydes whose chromophores are transoidal and planar have been studied. Ultraviolet (UV) and CD spectra were measured for these molecules and their long wavelength $\pi-\pi^*$ Cotton effects interpreted in terms of a "planar diene rule".

Chiroptical properties of 1,3-dienes and their molecular origin have been interesting modern stereochemical problems.[1] A relationship between the long wavelength $\pi-\pi^*$ Cotton effect in optical rotatory dispersion (ORD) and circular dichroism (CD) spectra of homoannular cisoid 1,3-dienes and the helicity of the diene chromophore was proposed as the "diene chirality rule".[2] According to this rule (Figure 1a) a homoannular cisoid diene skewed in a right-handed sense will give a positive Cotton effect and in a left-handed sense will give a negative Cotton effect for the long wavelength $\pi-\pi^*$ transition. Such a rule was also supported[3] by the Hückel molecular orbital (HMO) calculation[4] of butadiene as an inherently dissymmetric chromophore. For heteroannular cisoid dienes, an inverse rule was proposed;[5a] the inversion of sign is attributable to changes in electronic properties of the diene when the dihedral angle about the central bond is very large compared with that of homoannular dienes.

The HMO theoretical treatment was also extended to skewed transoid dienes and a rule was proposed[5b] (Figure 1b). This rule states that if the diene is oriented in such a way that its carbon atoms 1, 2, and 3 define a plane in a right-handed coordinate system as shown, the sign of the Cotton effect is determined by the position of the carbon atom 4: the sign will be positive or negative respectively if the coordinate of carbon atom 4 is positive or negative.

The various diene chirality rules were also tested on α,β-unsaturated carbonyl compounds for their long wavelength $\pi-\pi^*$ transition Cotton effects.[6,7] Originally it was argued that the contribution from the twist of the chromophore will outweigh the effects due to asymmetric substituents.[2] Exceptions to this theory were noted,[8-11] and it was observed that substituents, by interacting with the chromophore, play a major role. Allylic oxygenated systems were interpreted in terms of a helical chromophore containing the allylic oxygen.[12]

In order to explain the exceptions[9] to the diene chirality rule Burgstahler has introduced the concept known as "allylic axial chirality" to the 1,3-diene chromophore[9] especially in homoannular cisoid dienes[13a] (Figure 1c). The allylic axial bond is thought to

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