# Stereochemical Evidence of Dual Chemoreceptors for an Achiral Sex Pheromone in Lepidoptera[1]

Orville L. Chapman,*[2a,b] Kenneth C. Mattes,[2a,b] Robert S. Sheridan,[2b] and Jerome A. Klun[3]

Contribution from the Department of Chemistry, University of California—Los Angeles, Los Angeles, California 90024, and the Organic Chemical Synthesis Laboratory, Beltsville Agricultural Research Center, U.S. Department of Agriculture, Beltsville, Maryland 20705. Received December 23, 1977

Abstract: The racemate and optically pure enantiomers of 9-(cyclopent-2-en-1-yl)nonyl acetate have been synthesized and found to mimic certain biological properties of a natural sex pheromone, (Z)-11-tetradecenyl acetate. European corn borer and redbanded leaf rollers respond differently to the racemate and to the enantiomers in precopulatory-behavior bioassay. The bioassay results demonstrate the presence of two stereospecific chemoreceptors for the achiral pheromone and the chiral character of these chemoreceptors, and define the conformation of carbon atoms 10-14 of (Z)-11-tetradecenyl acetate in each receptor. Specificity in communication is the adaptive advantage the insect gains by using two stereospecific chemoreceptors with different conformational requirements for the achiral pheromone. The methodology described provides a new tool for neurochemical investigation of chemical sensing. A correlation of specific rotation and molecular weight is demonstrated for 3-substituted cyclopentenes. Optically active aleprolic acid, the parent acid of the chaulmoogric acid series, has been synthesized and fully characterized.

Several insects use (Z)-11-tetradecenyl acetate (**1**) as a pheromone. The European corn borer (*Ostrinia nubilalis*)[4] and the redbanded leaf roller (*Argyrotaenia velutinana*),[5] for example, use **1** both as a sex-attraction pheromone and as a


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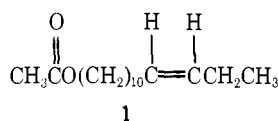
precopulatory-behavior pheromone. The two pheromone receptor systems are clearly differentiated. The sex-attraction system requires specific ratios of (Z)- to (E)- 11-tetradecenyl acetates[5,6] for each insect, and the precopulatory behavior system is relatively insensitive to the presence or absence of (E)-11-tetradecenyl acetate.[7,8]

The conformation of (Z)-11-tetradecenyl acetate in the chemoreceptor is of considerable interest. This problem at first encounter seems inherently impossible because an infinite number of conformations of (Z)-11-tetradecenyl acetate are possible. We wish to describe experiments which illustrate an approach to the solution of this problem and demonstrate that within the precopulatory-behavior pheromone system there exist at least two different chemoreceptors for (Z)-11-tetradecenyl acetate, that the receptors for the achiral pheromone are chiral, and that (Z)-11-tetradecenyl acetate is coiled in a recognizably different manner in the two receptors. Our approach to the problem starts with the observation that the European corn borer can distinguish the presence or absence of the C-14 methyl group in (Z)-11-tetradecenyl acetate.[7,8] Atoms 10-13 are fixed in the same plane by the double bond. The insect is thus able to detect the conformational position of the C-14 methyl group. One conformation (**2**) is particularly


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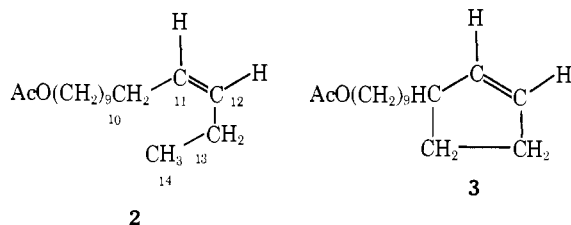
easily fixed and tested. Removal of two hydrogens from atoms 10 and 14 in **2** gives the cyclic analogue **3** in which the conformation of the C-14 methyl group is fixed. In this transfor-

mation, a chiral center is generated at C-10. Compounds related to **3** occur in nature. These compounds are the fatty acids of chaulmoogra oil, chaulmoogric acid (**4**, n = 12). hydnocarpic acid (**4**, n = 10), alepric acid (**4**, n = 8), aleprylic acid (**4**, n = 6), aleprestic acid (**4**, n = 4), and aleprolic acid (**4**, n

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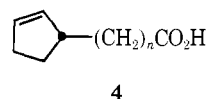
= 0). Chaulmoogra oils from various sources (especially that from seeds of *Hydnocarpus laurifolia* (formerly *wightiana*)) have been used in the treatment of leprosy, and the antimycobacterial activity of hydnocarpic acid has been studied in detail.[10] Syntheses of (R)-(+)-chaulmoogric acid,[11] (±)-chaulmoogric acid,[12] (±)-hydnocarpic acid,[13] (±)-aleprylic acid,[14] (±)-aleprestic acid,[15] and (±)-aleprolic acid[16] have been reported. Our approaches to the synthesis of **3** were based on stereochemical considerations, since we required the optically pure enantiomers. Mislow's synthesis of (R)-(+)-chaulmoogric acid based on (S)-(+)-cyclopent-2-en-1-yl-acetic acid (**5**)[11] suggested that this chiral starting material
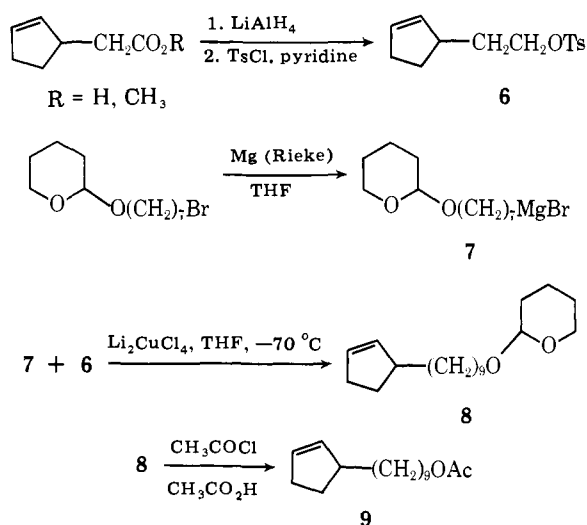

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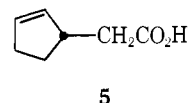
would serve our purposes for the synthesis of (R)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate. Resolution of cyclopent-2-en-1-ylacetic acid was accomplished by recrystallization of the brucine salt.[11] The optically pure enantiomer of **5** is not available by this method, and in the end a different chiral starting material had to be prepared.

Synthesis of (±)-9-(cyclopent-2-en-1-yl)nonyl acetate and (R)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate was accomplished via the reactions outlined in Scheme I. Reduction of methyl (±)-cyclopent-2-en-1-ylacetate followed by tosylation gave **6**. The Grignard reagent (**7**) prepared from the tetrahydropyranyl ether of 7-bromo-1-heptanol and the tosylate (**6**) were coupled using lithium tetrachlorocuprate.[17] Acetylation gave the desired (±)-9-(cyclopent-2-en-1-yl)nonyl acetate (**9**). The same sequence starting with optically pure (S)-(+)-cyclopent-2-en-1-ylacetic acid (**5**) gave (R)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate (**3**) which had [α]²⁵_D +70.8 ± 0.7°.

All attempts to obtain the (R)-(−)-enantiomer of **5** optically

Scheme I

R = H, CH$_3$

6

7

7 + 6 $\xrightarrow{\text{Li}_2\text{CuCl}_4, \text{ THF}, -70 \text{ °C}}$

8

8 $\xrightarrow{\text{CH}_3\text{COCl}}{\text{CH}_3\text{CO}_2\text{H}}$

9

pure have been unsuccessful.[11] Consequently, we turned our attention to the resolution of (±)-cyclopent-2-enecarboxylic

5, (S)-(+)   3, (R)-(+)
                +70.8 ± 0.7°
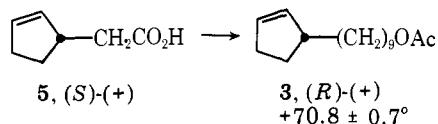
acid (10). Resolution of 10 should be more facile because the carboxyl group is attached to the asymmetric atom. This arrangement, however, opens new possibilities for racemization. Racemic cyclopent-2-enecarboxylic acid (10) was prepared

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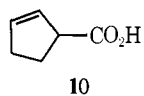
by carboxylation of the Grignard reagent from 3-chlorocyclopentene. Use of magnesium prepared by the Rieke[18] procedure gave significantly better yields than those obtained with ordinary magnesium.[16] Resolution using (−)-α-phenethylamine gave (S)-(−)-cyclopent-2-enecarboxylic acid (11), [α]^{25}D −262.0°. Similar resolution with (+)-α-phenethylamine gave (R)-(+)-cyclopent-2-enecarboxylic acid (12). The absolute configuration of (R)-(+)-cyclopent-2-enecarboxylic acid (12) was established by conversion to the methyl ester of (S)-(+)-cyclopent-2-en-1-ylacetic acid (5)[19] using the Arndt-Eistert procedure. The critical step in this procedure (the Wolff rearrangement) is known to proceed with retention of configuration in secondary alkyl groups.[20]

The transformation of (S)-(−)-cyclopent-2-enecarboxylic acid (11) to the tosylate 15 was accomplished by the reactions shown in Scheme II. Octane-1,8-diol was converted to 8-bromo-1-octanol and protected as the tetrahydropyranyl ether (17). The Grignard reagent (18) coupled with the tosylate 15, giving 19. Removal of the protective group and acetylation gave the desired (S)-(−)-9-(cyclopent-2-en-1-yl)nonyl acetate (20), [α]^{25}D −70.7 ± 0.4° (Scheme III). A similar sequence of reactions starting with the enantiomeric tosylate 16 gave (R)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate (3), [α]^{25}D +70.0 ± 0.6°. The agreement of the specific rotations of the enantiomers and the agreement of the specific rotations of the (R)-(+) enantiomer from two different optical precursors (5 and 12) strongly suggest that the products (3 and 20) are optically pure.

A completely different line of reasoning also leads to the conclusion that 3 and 20 are optically pure. A plot of specific rotation for the well-characterized acids of chaulmoogra oil
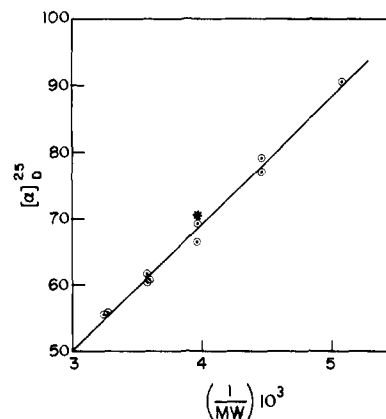

Figure 1. Plot of [α]^{25}D vs. reciprocal of molecular weight for the acids and esters derived from chaulmoogra oil. Data were taken from ref 9. The least-squares line is shown ([α]^{25}D = 19.23 × 10^3(1/MW) − 7.72). The specific rotation of (R)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate (3) is shown by an asterisk.
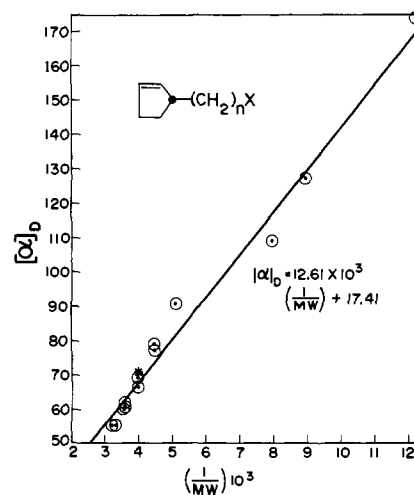

Figure 2. Plot of [α]D vs. reciprocal of molecular weight for chiral 3-substituted cyclopentenes of the type 21 (n ≥ 1). Data were taken from ref 9, 11, and 21. Specific rotations were taken in the 25–30 °C range. The least-squares line is shown ([α]D = 12.61 × 10^3(1/MW) + 17.41). The specific rotation of (R)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate is shown by an asterisk.

and their esters (4)[9] vs. the reciprocal of the molecular weight is linear. Figure 1 shows the plot with the least-squares line

4, R = H, alkyl
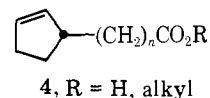
drawn through the data points. The line is described by [α]D = 19.23 × 10^3(1/MW) − 7.72. This equation predicts a specific rotation for the 9-(cyclopent-2-en-1-yl)nonyl acetates of 68.6° in agreement with the observed values (3, +70.8 ± 0.7°, +70.0 ± 0.6°; 20, −70.7 ± 0.4°). It is interesting to compare the plot for the acids and esters derived from chaulmoogra oil with a more extensive plot for chiral 3-substituted cyclopentenes (Figure 2). This line is described by [α]D = 12.61 × 10^3(1/MW) + 17.41, which predicts a slightly lower specific rotation ([α]D 67.5°) for the 9-(cyclopent-2-en-1-yl)nonyl acetates. The plot in Figure 2 seems to be generally useful for predicting the specific rotation of 3-substituted cyclopentenes (21) in which functionality is not directly attached to the chiral

21

Scheme II

[Scheme II: cyclopentenyl-Cl →(1. Mg (Rieke), THF, −60 °C; 2. CO₂; 3. H₃O⁺; 81%)→ cyclopentenyl-CO₂H (10) →(1. (−)-α-Phenethylamine; 2. recryst. from EtOAc; 3. NaOH, H₂O; 4. H₃⁺O)→ cyclopent-2-enyl-CO₂H (11, (S)-(−)) →(CH₂N₂, 88%)→ cyclopent-2-enyl-CO₂CH₃ (13) →(LiAlH₄, 100%)→ cyclopent-2-enyl-CH₂OH (14) →(TsCl, pyridine, 61%)→ cyclopent-2-enyl-CH₂OTs (15)

10 →(1. (+)-α-phenethylamine; 2. recryst. from EtOAc; 3. NaOH, H₂O; 4. H₃⁺O)→ cyclopentenyl-CO₂H (12, (R)-(+))

12 →(1. SOCl₂; 2. CH₂N₂; 3. Ag₂O, CH₃OH)→ cyclopentenyl-CH₂CO₂CH₃

cyclopentenyl-CH₂CO₂H (5) →(CH₂N₂)→ cyclopentenyl-CH₂CO₂CH₃

5 → cyclopentenyl-CH₂OTs (16)]

Table I. Sex Stimulation Assay Results with European Corn Borer and Redbanded Leaf Roller Males[a]

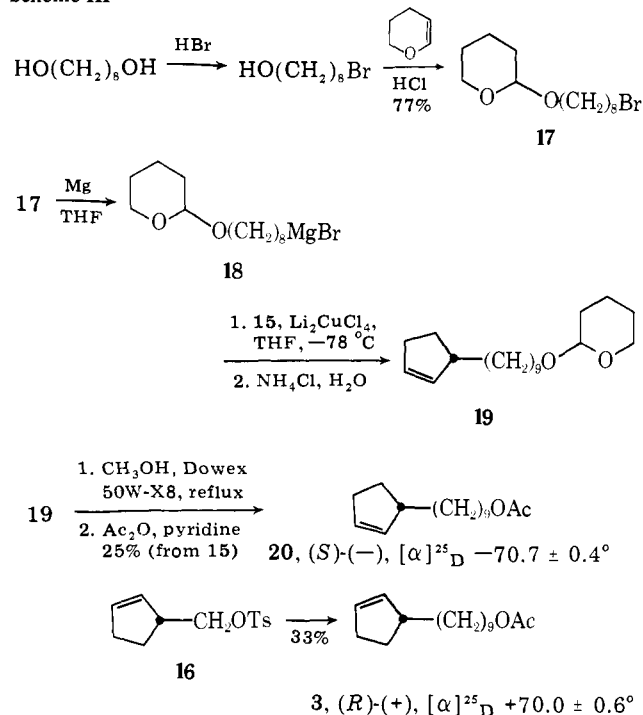|	mean % male response	
stimulus (500 ng)	European corn borer	redbanded leaf roller
(Z)-11-tetradecenyl acetate	64a	90d
(±)-9-(cyclopent-2-en-1-yl)nonyl acetate	44b	93d
(R)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate	16c	67e
(S)-(−)-9-(cyclopent-2-en-1-yl)nonyl acetate	65a	67e

[a] See ref 23 and 24. Numbers followed by the same letter are not statistically different from each other based on contingency table analyses.

center (vide infra). The linearity of the plots in Figures 1 and 2 is an experimental fact. It is due to an essentially constant specific rotation from the chiral center which is being diluted as the mass of R (**21**) increases. The correlation should hold for compounds of type **21** when $n \geq 1$ and in the absence of specific interactions between functionality in R and the double bond.

The synthesis of (R)-(+)-cyclopent-2-enecarboxylic acid (**12**) is the first synthesis of aleprolic acid, the lowest homologue of the acids of chaulmoogra oil. This substance has not been obtained in pure form from natural sources[9] and has not been fully characterized until now. The specific rotation (+262°) of **12** does not fall on the line in Figure 2. This is reasonable since the carboxyl group is now attached directly to the asymmetric center. The literature[9] estimate (+120°) for the specific rotation of **12** is substantially in error.

The biological data presented in Table I show remarkable differences in perception of the enantiomers of 9-(cyclopent-2-en-1-yl)nonyl acetate by the two species of moths. The biological assay with (R)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate from the two different precursors gave similar biological results, thus providing assurance that the bioassay is free from activity due to trace contamination from reactants. The European corn borer responds to (S)-(−)-9-(cyclopent-2-en-1-

Scheme III

[Scheme III: HO(CH₂)₈OH →(HBr)→ HO(CH₂)₈Br →(dihydropyran, HCl, 77%)→ THP-O(CH₂)₈Br (17)

17 →(Mg, THF)→ THP-O(CH₂)₈MgBr (18)

→(1. 15, Li₂CuCl₄, THF, −78 °C; 2. NH₄Cl, H₂O)→ cyclopent-2-enyl-(CH₂)₉O-THP (19)

19 →(1. CH₃OH, Dowex 50W-X8, reflux; 2. Ac₂O, pyridine, 25% (from 15))→ cyclopent-2-enyl-(CH₂)₉OAc (20, (S)-(−), [α]²⁵_D −70.7 ± 0.4°)

cyclopentenyl-CH₂OTs (16) →(33%)→ cyclopentenyl-(CH₂)₉OAc

3, (R)-(+), [α]²⁵_D +70.0 ± 0.6°]

yl)nonyl acetate (**20**) as effectively as it responds to the natural pheromone ((Z)-11-tetradecenyl acetate), but it responds only weakly to the (R)-(+) enantiomer. The response to the racemate is intermediate between the response to the pure enantiomers. The European corn borer data are consistent with the presence of a single, stereoselective chemoreceptor. The redbanded leaf roller shows equal response to the (R)-(+) and (S)-(−) enantiomers, but it exhibits a much stronger response to the racemate than to either enantiomer. The leaf roller data are reminiscent of the data obtained using the enantiomers of the aggregation pheromone of *Gnathotricus sulcatus*.[22] Inhibition by optical antipodes has been observed in the gypsy moth[33] and in the Japanese beetle.[34] The greater activity of the racemate in the redbanded leaf roller requires two stereo-

specific chemoreceptors, one primarily (or exclusively) sensitive to (*R*)-(+)-9-(cyclopent-2-en-1-yl)nonyl acetate and one sensitive to the (*S*)-(−) enantiomer.

The difference in placement of the cyclopentene ring in the two chemoreceptors is limited to two possibilities. Either the double bond is in the same position and the C-10 stereochemistry is different (model I) or the C-10 stereochemistry

model I

model II
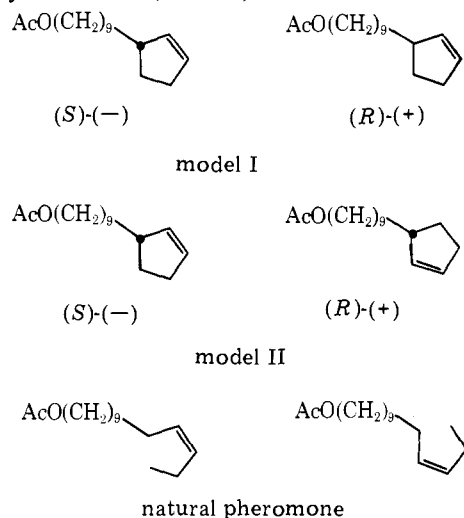
natural pheromone

is the same and the position of the double bond is different (model II). The achiral, natural pheromone coiled as it would be in model I has hydrogens up and down at C-10 and no distinction between the receptors is possible. Model II is sensible in terms of two chemoreceptors for the achiral, natural pheromone (*Z*)-11-tetradecenyl acetate. In model II, the two possible arrangements correspond to reasonable but distinctly different conformations of the natural pheromone. The redbanded leaf roller has thus evolved *at least* two chemoreceptors which sense different conformations of the same achiral (but prochiral) pheromone molecule in the precopulatory-behavior pheromone detection system. This striking result suggests that insect chemoreceptor systems which are known to sense ratios of different geometric isomers[6] also use ratio discrimination based on two or more receptor systems in detecting a single chemical compound. The adaptive advantage for the insect is clearly specificity in detection. Specificity is the most important factor in chemical communication. The greater the number of specific conformations of a single molecule required to satisfy the different chemoreceptors, the lower will be the probability that an incorrect molecule will meet the conformational requirements. It is probable that other highly selective chemoreceptors (such as hormone receptors—the prostaglandins are an intriguing possibility) also use multiple receptors with different conformational requirements to gain specificity. In any chemoreceptor system in which precise chemical information is important, multiple receptors leading to greater specificity in perception hold a strong adaptive advantage for the organism.

It is now clear that these simple moths which use (*Z*)-11-tetradecenyl acetate in both the sex-attraction pheromone system and in the precopulatory-behavior pheromone system, not only have different receptors for sensing (*Z*)-11-tetradecenyl acetate for each purpose, but also have, in the case of the redbanded leaf roller, two chemoreceptors for this substance in the precopulatory-behavior pheromone system. The insect detection system makes very clever use of the prochiral character of the achiral pheromone. This finding provides an insight into the degree of sophistication to be encountered in pheromone perception systems. The utility of stereochemical models as probes of the neurochemical receptors of achiral molecules has now been demonstrated. This methodology provides a new tool for investigation of chemical sensing.

Experimental Section

Proton magnetic resonance spectra were recorded on a Varian Associates A-60, Varian Associates T-60, or Hitachi Perkin-Elmer R-20B spectrometer and are reported in parts per million relative to internal tetramethylsilane. Infrared spectra were recorded on a Beckman IR-12, Beckman IR-9, or Beckman IR-4250 spectrometer. Mass spectra were recorded on an Atlas CH-4, AEI-MS-9, or AEI-MS-902 spectrometer. Optical rotations were obtained on a Perkin-Elmer 141 polarimeter. Concentrations are recorded in grams per 100 mL.

Vapor phase chromatography was performed on a Varian Aerograph 90-P or a Varian Aerograph 920 chromatograph, both equipped with thermal conductivity detectors, using the following columns: column A, 1 m × 6 mm, 20% SE-30 on 60/80 Chromosorb W-AW, 175 °C, 120 mL/min; column B, 5 ft × 0.25 in., SE-30 on 60/80 Chromosorb W; column C, 15 ft × $\frac{3}{8}$ in., 30% SE-30 on Chromosorb W.

All melting points were determined on a Uni-melt, Thomas-Hoover capillary melting point apparatus and are uncorrected. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn., Schwarzkopf Microanalytical Laboratory, Inc., Woodside, N.Y., or Spang Microanalytical Laboratory, Ann Arbor, Mich.

Methyl (±)-2-(Cyclopent-2-en-1-yl)acetate. A methylene chloride solution (120 mL) of 2-(cyclopent-2-en-1-yl)acetic acid (50.4 g, 400 mmol), methanol (48.4 mL, 1.2 mol), and sulfuric acid (1.2 mL) was refluxed ca. 18 h.[25] The layers were separated, and the aqueous layer was extracted with methylene chloride (100 mL). The combined methylene chloride extracts were washed with saturated aqueous sodium carbonate solution (100 mL), water (100 mL), and brine (100 mL), dried (MgSO₄), and filtered and the methylene chloride distilled off at atmospheric pressure to yield a yellow liquid. Distillation gave pure methyl 2-(cyclopent-2-en-1-yl)acetate (48.6 g, 86% yield): bp 65–68 °C (14 mm); NMR (CDCl₃) δ 1.2–2.6 (complex, 6 H, CH_2CH_2, CH_2CO_2), 2.8–3.3 (m, 1 H, CH), 3.7 (s, 3 H, CO_2CH_3), 5.6–5.9 (m, 2 H, CH=CH).

(±)-2-(Cyclopent-2-en-1-yl)ethanol. A flame-dried 500-mL three-necked flask, fitted with a mechanical stirrer and an addition funnel, was charged with dry ether (200 mL) and lithium aluminum hydride (5.6 g, 150 mmol). The flask was immersed in an ice bath and a solution of (±)-methyl 2-(cyclopent-2-en-1-yl)acetate (28 g, 200 mmol) in ether (100 mL) was added dropwise with vigorous stirring under nitrogen. When the addition was complete the ice bath was removed and the solution stirred overnight. The reaction was cautiously quenched with water (6 mL), 15% aqueous sodium hydroxide solution (6 mL), and water (18 mL). After stirring for 5 h, the solid aluminum salts were filtered off and washed with ether. The ether was removed in vacuo and the residue distilled under reduced pressure giving pure (±)-2-(cyclopent-2-en-1-yl)ethanol (19 g, 85% yield): bp 80–83 °C (10 mm); lit.[26] bp 86–87 °C (16 mm); NMR (CDCl₃) δ 1.1–2.5 (complex, 6 H, CH_2CH_2, CH_2CH_2OH), 2.5–3.0 (m, 1 H, CH), 2.9 (s, 1 H, OH), 3.7 (t, 3 H, CH_2O, *J* = 6 Hz), 5.5–5.8 (m, 2 H, CH=CH).

7-Bromo-1-heptanol. 1,7-Heptanediol (50 g, 379 mmol) was stirred with 9 N hydrobromic acid (400 mL) for 5 days at 40 °C while being continuously extracted with hexane. The hexane extract (1 L) was washed with 5% aqueous sodium bicarbonate solution (100 mL), water (100 mL), and brine (2 × 100 mL), dried (MgSO₄), and filtered and the solvent removed in vacuo to give crude product. Distillation through a 6-in. Vigreux column gave pure 7-bromo-1-heptanol (52.7 g, 71% yield): bp 103–105 °C (1.75 mm); lit.[27] bp 108 °C (1 mm).

1-Bromo-7-(tetrahydropyran-2-yloxy)heptane. 7-Bromo-1-heptanol (53 g, 272 mmol) was added to 2,3-dihydropyran (25.2 g, 300 mmol) and the magnetically stirred solution was cooled to 0–2 °C with an ice bath. Addition of concentrated hydrochloric acid (3 drops) resulted in an exothermic reaction. When the temperature dropped, anhydrous potassium carbonate was added and a vacuum was carefully drawn on the reaction mixture. After 30 min, heat was applied and the product distilled (63 g, 90% yield) at 103–115 °C (0.15–0.4 mm). Redistillation of a small sample yielded an analytical sample: bp 102–103 °C (0.08 mm); IR (CCl₄) ν 2940 (s), 2860 (s), 1470 (m), 1460 (m), 1445 (m), 1355 (m), 1205 (m), 1140 (m), 1125 (m), 1080 (m), 1040 (s) cm⁻¹; NMR (CCl₄) δ 1.1–2.1 (m, 16 H, $(CH_2)_5$, $(CH_2)_3$), 3.0–4.0 (m, 6 H, CH_2O, CH_2Br), 4.4 (m, 1 H, OCHO); mass spectrum (70 eV) m/e (relative intensity) 280 (6, M + 2), 278 (6, M⁺), 85 (100). Anal. Calcd for $C_{12}H_{23}O_2Br$: C, 51.62; H, 8.30;

Br, 28.62. Found: C, 51.46; H, 8.17; Br, 28.49.

1-(Tetrahydropyran-2-yloxy)-7-heptylmagnesium Bromide (7).[18] Anhydrous magnesium chloride (2.86 g, 30.3 mmol) and anhydrous tetrahydrofuran (30 mL) were placed in a flame-dried 100-mL three-necked flask, equipped with a magnetic stirring bar and condenser. Freshly cleaned and finely cut potassium (2.16 g, 55 mg-atoms) was added to the flask and the mixture stirred and refluxed for ca. 2.5 h. Vigorous foaming occurred during the first 30 min, once reflux temperature was reached. The suspension of black, finely divided powder was cooled to room temperature over 30 min and the flask immersed in a water bath at room temperature. 7-Bromo-1-(tetrahydropyran-2-yloxy)heptane (3.4 mL, 4.18 g, 15 mmol) was added, via syringe over 5 min, to the vigorously stirred suspension. The mixture was stirred for 10 additional min. Hydrolysis and VPC analysis (column A, 175 °C, 120 mL/min) of a small aliquot showed less than 5% starting bromide.

9-(Cyclopent-2-en-1-yl)-1-(tetrahydropyran-2-yloxy)nonane (8).[17] The 2-(cyclopent-2-en-1-yl)ethyl-4-toluenesulfonate (6) (2.2 mL, 2.6 g, 10 mmol; prepared from the alcohol in 81-97% yield by standard procedures, vide infra, and used without further purification) was syringed into dry tetrahydrofuran (30 mL) and cooled to −70 °C (acetone-dry ice). The Grignard solution 7 was syringed over ca. 20 min into the stirred solution. When the addition was complete, dilithiocopper(II) tetrachloride[28] (2 mL, 0.1 M solution in tetrahydrofuran) was added, via syringe, and the mixture was allowed to warm over 2 h to room temperature and then stirred for 12 h. The solution was poured into ice-cold sulfuric acid (10 mL, 3 M H$_2$SO$_4$ in 200 mL of ice water) and extracted with hexane (3 × 50 mL). The hexane was washed with saturated aqueous ammonium chloride solution (50 mL), saturated aqueous sodium bicarbonate solution (50 mL), and brine (50 mL), dried (MgSO$_4$), and filtered and the solvent was removed in vacuo to yield a brown oil.

(±)-9-(Cyclopent-2-en-1-yl)nonyl Acetate (9). The crude tetrahydropyranyl ether 8 was dissolved in acetic acid (15 mL), acetyl chloride (1 mL) was added, and the solution was warmed on a steam bath overnight. The reaction mixture was poured into ice water (100 mL) and extracted with hexane (4 × 25 mL). The hexane extract was washed with water (25 mL), saturated aqueous sodium carbonate solution (25 mL), water (25 mL), and brine (2 × 25 mL), dried (MgSO$_4$), and filtered, and the solvent was removed to yield a clear brown oil. This material was adsorbed onto 10 g of silica gel and separated by dry column chromatography (40 cm × 2.5 cm column of silica gel, 60-200 mesh, 10% Et$_2$O/hexane as eluent). The column was developed and broken into five equal fractions. Each fraction was eluted with ethyl acetate. TLC analysis (SiO$_2$, 10% Et$_2$O/hexane) showed fractions three and four contained product, but were contaminated with minor impurities. Preparative thick-layer chromatography (10% ether in hexane) gave material that showed one spot by TLC; VPC analysis (column A) showed a volatile impurity, however. Preparative VPC (same conditions) gave analytically pure acetate 9 (0.25 g, 10% yield): IR (CCl$_4$) ν 3060 (w), 2930 (s), 2860 (s), 1745 (s), 1640 (m), 1370 (m), 1240 (s), 1040 (m) cm^{-1}; NMR (CCl$_4$) δ 1.1-1.7 (m, 16 H, (CH$_2$)$_8$), 1.95 (s, 3 H, CH$_3$CO$_2$), 1.7-2.8 (complex, 5 H, CH$_2$CH$_2$CHR), 3.96 (t, 2 H, CH$_2$O, J = 6 Hz), 5.6 (s, 2 H, CH=CH); mass spectrum (70 eV) m/e (relative intensity) 252 (31) M$^+$, 192 (24), 135 (39), 121 (35), 93 (79), 82 (81), 80 (97), 67 (100), 66 (81), 55 (83), 43 (100). Anal. Calcd for C$_{16}$H$_{28}$O$_2$: C, 76.14; H, 11.18. Found: C, 76.08; H, 11.11.

(S)-(+)-(Cyclopent-2-en-1-yl)acetic Acid (5).[11] Racemic cyclopent-2-en-1-ylacetic acid (14.9 g, 118 mmol) was dissolved in acetone/water (100 mL:3.5 mL) and brucine (55 g, 140 mmol) was added with stirring and warming on a hot plate. The mixture was cooled to room temperature and filtered giving crude salt, [α]^{24}$_D$ −16.4° (c 5, H$_2$O). This material was recrystallized from acetone/water (100 mL:4 mL) three times, and one time from acetone (50 mL + 3 drops of water) giving 1.6 g of pure salt: [α]^{24}$_D$ +0.8 ± 0.3° (c 5, H$_2$O); mp 146-147 °C (lit.[11] [α]^{28}$_D$ +1.2 ± 0.3° (water); mp 147.5-148.5 °C). The salt was dissolved in water (20 mL) and made basic with concentrated ammonium hydroxide. The precipitated brucine was filtered off and the aqueous solution acidified with 1 M aqueous hydrochloric acid. The acidified solution was extracted with ether (2 × 35 mL), the ether was dried (Na$_2$SO$_4$) and filtered, and the solvent was removed in vacuo giving ca. 300 mg of crude acid 5.

(S)-(+)-2-(Cyclopent-2-en-1-yl)ethanol. The crude (S)-(+)-cyclopent-2-en-1-ylacetic acid (5) (300 mg, 2.38 mmol) was dissolved in dry tetrahydrofuran (5 mL) and this solution added dropwise to a stirred solution of lithium aluminum hydride (0.18 g, 5 mmol) in dry tetrahydrofuran (5 mL). The solution was stirred overnight and quenched by cautiously adding water (5 drops), 15% aqueous sodium hydroxide solution (5 drops), and water until a white flocculent precipitate formed. The mixture was filtered and the solvent distilled off at atmospheric pressure to give crude alcohol.

(S)-(+)-2-(Cyclopent-2-en-1-yl)ethyl 4-Toluenesulfonate. The crude (S)-(+)-2-(cyclopent-2-en-yl)ethanol was dissolved in pyridine (5 mL) and cooled in an ice-acetone bath (−16 °C) and p-toluenesulfonyl chloride (0.90 g, 4.8 mmol) was added. The solution was swirled until the solid dissolved and was allowed to stand overnight at 0 °C. The solution was poured into ice water and the aqueous layer extracted with ether (4 × 10 mL). The ether extracts were washed with 5% aqueous hydrochloric acid (3 × 15 mL) and water (3 × 15 mL) and dried (K$_2$CO$_3$ and Na$_2$SO$_4$), and the ether was removed in vacuo giving crude tosylate (1 g) that was used directly.

(R)-(+)-9-(Cyclopent-2-en-1-yl)-1-(tetrahydropyran-2-yloxy)nonane. Magnesium chloride (1.72 g, 18 mmol), potassium (1.25 g, 32 mg-atoms), and 7-bromo-1-(tetrahydropyran-2-yloxy)heptane (2.51 g, 9 mmol) were allowed to react following the procedure previously described. The Grignard reagent, the crude (S)-(+)-2-(cyclopent-2-en-1-yl)ethyl 4-toluenesulfonate, and dilithiocopper(II) tetrachloride (1.8 mL of a 0.1 M tetrahydrofuran solution) were allowed to react by the procedure previously described. The reaction mixture was poured into saturated aqueous ammonium chloride solution (100 mL) and extracted with hexane (2 × 50 mL). The combined hexane extracts were washed with water (3 × 50 mL) and brine (50 mL), dried (MgSO$_4$), and filtered, and the solvent was removed in vacuo to give 1.9 g of crude product.

(R)-(+)-9-(Cyclopent-2-en-1-yl)nonyl Acetate (3). The crude coupling product was allowed to react with acetic acid (10 mL) and acetyl chloride (1 mL) and worked up by the procedure described previously. Purification by dry column chromatography, preparative thick-layer chromatography, and preparative VPC as in the racemic compound gave chemically pure acetate 3 (60.7 mg, 12% yield based on resolved acid): [α]^{25}$_D$ +70.8 ± 0.7 ° (c 3.18, CHCl$_3$); NMR (CCl$_4$) δ 1.1-1.7 (m, 16 H, (CH$_2$)$_8$), 1.95 (s, 3 H, CH$_3$CO$_2$), 1.7-2.8 (complex, 5 H, CH$_2$CH$_2$CH), 3.96 (t, 2 H, CH$_2$O, J = 6 Hz), 5.6 (s, 2 H, CH=CH); mass spectrum (70 eV, major fragments) m/e (relative intensity) 252 (21) M$^+$, 80 (45), 67 (68), 28 (100). Anal. Calcd for C$_{16}$H$_{28}$O$_2$: P$^+$, 252.2089; C, 76.14; H, 11.18. Found: P$^+$, 252.2088; C, 75.91; H, 11.05.

3-Chlorocyclopentene. The procedure reported by Moffett[29] was used. Dry hydrogen chloride was bubbled through freshly distilled cyclopentadiene (280 g, 4.2 mol) at −78 °C until weighing indicated an uptake of 132 g of HCl (3.6 mol). Distillation at 27 °C (5 mm) gave pure 3-chlorocyclopentene (218 g, 59% yield): NMR (CDCl$_3$) δ 2.0-2.8 (m, 4 H, CH$_2$CH$_2$), 4.9-5.2 (m, 1 H, CHCl), 5.8-6.2 (m, 2 H, CH=CH).

(±)-Cyclopent-2-en-1-ylcarboxylic Acid (10). Anhydrous magnesium chloride (61.2 g, 0.66 mol) and anhydrous tetrahydrofuran (500 mL) were placed in an oven-dried, 1-L, three-necked flask fitted with mechanical stirrer, reflux condenser, and thermometer. Potassium (45.9 g, 1.2 g-atoms) was added and the mixture was carefully brought to reflux with stirring. After the vigorous foaming ceased, the black suspension was refluxed 1 h. The condenser was replaced by a constant addition funnel, and the suspension was cooled to ca. −60 °C in a dry ice-acetone bath. A solution of 3-chlorocyclopentene (60 g, 0.585 mol) in anhydrous tetrahydrofuran (200 mL) was added dropwise over 4 h with stirring at −60 °C. The solution was stirred for an additional hour and then cannulated under nitrogen pressure into a large excess of dry ice (ca. 700 g). This mixture was stored at −35 °C overnight and then carefully poured into a 2-L separatory funnel half-filled with ice. After the ice melted, water (300 mL) and concentrated hydrochloric acid were added to dissolve the magnesium salts, and the solution was extracted with ether (3 × 300 mL). The combined ether extracts were extracted with 10% aqueous sodium hydroxide solution (3 × 250 mL). The aqueous solution was extracted with ether (300 mL) and acidified to pH 2 with concentrated hydrochloric acid, and the product was extracted into ether (3 × 300 mL). The combined ether layers were washed with water (300 mL) and brine (300 mL) and dried (Na$_2$SO$_4$), and removal of the solvent in vacuo gave crude acid 10 (53 g, 81% yield) which was used directly: bp 65 °C (4 mm); lit.[16] bp 103-104 °C (11 mm); NMR (CDCl$_3$) δ 1.9-2.7 (m, 4 H, CH$_2$CH$_2$), 3.4-3.8 (m, 1 H, CHCO$_2$), 5.7-6.1 (m, 2 H, CH=CH), 10.1 (s, 1 H, CO$_2$H). Repetition of this procedure gave 85 additional

g of **10**.

(S)-(−)-Cyclopent-2-en-1-ylcarboxylic Acid (11). (−)-α-Methylbenzylamine (74 g, 0.61 mol) was added dropwise to a solution which was being stirred of racemic acid **10** (85 g, 0.76 mol) in ether (700 mL). A white precipitate formed which was allowed to sit for 2 h with occasional shaking. The solid was filtered, washed with ether, and dried in vacuo giving crude salt (118 g). The salt was dissolved in boiling ethyl acetate (1 L), filtered, and allowed to cool very gradually to room temperature producing long, colorless, very fine needles. The crystals were filtered, washed with ethyl acetate, and dried in vacuo to give 70 g of salt, $[\alpha]^{25}_{578}$ −84.5° (c 0.4, CH_3OH). Repeating this procedure eight times gave 3.6 g of pure salt whose rotation did not change substantially upon further recrystallization: $[\alpha]^{25}_{578}$ −156.5° (c 0.4, CH_3OH); mp 118.5–119.5 °C.

The pure diastereomeric salt (3.15 g, 13.5 mmol) was dissolved in water (75 mL), and sodium hydroxide (0.59 g, 14.9 mmol) was added. This solution was washed with ether (4 × 50 mL), acidified with concentrated hydrochloric acid (1.56 g, 16.2 mmol), and extracted with ether (4 × 35 mL). The combined ether extracts were washed with brine (50 mL) and dried (Na_2SO_4) and the solvent was removed in vacuo to give crude carboxylic acid **11**: $[\alpha]^{25}_{578}$ −273.9°, $[\alpha]^{25}_{D}$ −262.0° (c 3.53, $CHCl_3$).

Methyl (S)-(−)-Cyclopent-2-en-1-ylcarboxylate (13). The crude acid **11** (3.1 g, 28 mmol) was added dropwise to a solution which was being stirred of diazomethane (ca. 1 g) in ether (100 mL) at 0 °C. The solution was stirred an additional 0.5 h, and glacial acetic acid was added dropwise until the yellow diazo color was destroyed. Drying (K_2CO_3 + Na_2SO_4) and removal of solvent via short-path distillation at atmospheric pressure gave crude ester **13** (1.42 g, 88% yield by NMR) contaminated with small amounts of ether and methyl acetate (by NMR). The ester **13** was used without further purification: NMR ($CDCl_3$) δ 1.9–2.7 (m, 4 H, CH_2CH_2), 3.3–3.7 (m, 1 H, CHCO$_2$), 3.7 (s, 3 H, CO$_2CH_3$), 5.6–6.0 (m, 2 H, CH=CH).

Racemic cyclopent-2-en-1-ylcarboxylic acid (**10**; 0.2 g, 1.8 mmol) was treated with diazomethane (ca. 0.25 g, 6 mmol) in the same manner giving pure (±)-methyl cyclopent-2-en-1-ylcarboxylate (0.19 g, 83% yield) after distillation: bp 50 °C (12 mm); lit.[16] bp 44–45 °C (9 mm); NMR ($CDCl_3$) identical with spectrum of **13** described previously.

(S)-(−)-Cyclopent-2-en-1-ylcarbinol (14). Lithium aluminum hydride (0.48 g, 12.6 mmol), anhydrous ether (25 mL), and a magnetic stirring bar were placed in an oven-dried, 50-mL, three-necked flask fitted with a reflux condenser and an addition funnel. Ester **13** (1.42 g, 11 mmol) in ether (5 mL) was added dropwise to the stirring solution under nitrogen. The mixture was stirred overnight and quenched cautiously with water (0.5 mL), 15% aqueous sodium hydroxide solution (0.5 mL), and water (1.5 mL). The precipitated salts were filtered and washed well with ether, and the combined washings were dried ($MgSO_4$). Removal of the solvent via short-path distillation at atmospheric pressure, followed by brief application of vacuum, gave crude alcohol **14** (1.1 g, 100% yield by NMR) which was used directly: NMR ($CDCl_3$) δ 1.2–3.3 (complex, 6 H, CH_2CH_2CH, OH), 3.5 (d, 2 H, CH_2O, J = 6 Hz), 5.6–6.0 (m, 2 H, HC=CH).

Racemic methyl cyclopent-2-en-1-ylcarboxylate (4.6 g, 37 mmol) was reduced with lithium aluminum hydride (1.4 g, 37 mmol), following the procedure above, to give pure (±)-cyclopent-2-en-1-ylcarbinol (3.2 g, 89% yield) after distillation: bp 79 °C (12 mm); lit.[16] bp 58–59 °C (9 mm); NMR ($CDCl_3$) identical with spectrum described for **14**.

(S)-(−)-Cyclopent-2-en-1-ylmethyl 4-Toluenesulfonate (15). A solution of the (S)-alcohol **14** (1.1 g, 11 mmol) in dry pyridine (35 mL) was cooled to 0 °C, and freshly recrystallized p-toluenesulfonyl chloride (4.2 g, 22 mmol) was added. The solution was stored at 10 °C overnight, then poured into ice water (60 mL) and extracted with ether (3 × 40 mL). The combined extracts were washed with a cold 1:1 mixture of concentrated hydrochloric acid in water (60 mL) and water (2 × 60 mL), and dried (Na_2SO_4 + K_2CO_3), and the solvent was removed in vacuo to give a clear oil. Two recrystallizations from petroleum ether (30–60 °C) at −78 °C gave pure tosylate **15** (1.7 g, 61% yield) as a colorless oil: mp −1–2 °C; lit.[30] mp 1–2 °C (for racemate); NMR ($CDCl_3$) δ 1.2–2.4 (complex, 4 H, CH_2CH_2), 2.5 (s, 3 H, Ph-CH$_3$), 2.8–3.3 (m, 1 H, CH), 3.9 (d, 2 H, CH_2OSO_2, J = 7 Hz), 5.5–6.0 (m, 2 H, HC=CH), 7.3–8.0 (aa'xx', 4 H, C_6H_4).

8-Bromo-1-octanol. A mixture of 1,8-octanediol (100 g, 685 mmol) and 9 M aqueous hydrobromic acid (800 mL) was stirred for 7 days at 50 °C while being continuously extracted with hexane. The hexane

extract (500 mL) was washed with 5% aqueous sodium bicarbonate solution (250 mL), water (250 mL), and brine (250 mL) and dried ($MgSO_4$) and the solvent was removed in vacuo to give crude product. Chromatography (120 g of SiO_2, 20–40% ether in hexane) of a small portion of crude product (20 g) gave pure 8-bromo-1-octane (14 g, 70% yield): bp 79–80 °C (0.07 mm); lit.[31] bp 77–78 °C (0.01 mm) for material ca. 90% pure; NMR ($CDCl_3$) δ 0.9–2.1 (m, 12 H, (CH$_2$)$_6$), 3.0 (s, 1 H, OH), 3.3–3.7 (2 overlapping triplets, 4 H, CH_2O, CH_2Br). Anal. Calcd for $C_8H_{16}Br$ (P − 17 for loss of OH): P − 17, 191.0436. Found: P − 17, 191.0438.

8-Bromo-1-(tetrahydropyran-2-yloxy)octane (17). Concentrated hydrochloric acid (2 drops) was added to a stirring mixture of 8-bromo-1-octanol (14 g, 67 mmol) and 2,3-dihydropyran (6.2 g, 74 mmol) which was cooled to 5 °C in an ice bath. The temperature of the solution immediately rose 5 °C and then returned. After 15 min of stirring, anhydrous potassium carbonate (2 g) was added and the flask was fitted with a short-path distilling head. After a small forerun, the protected bromoalcohol **17** was distilled as a colorless oil (15.1 g, 77% yield): bp 99 °C (0.02 mm); lit.[31] bp 97–100 °C (0.008 mm) for material ca. 95% pure; NMR ($CDCl_3$) δ 1.2–2.2 (complex, 18 H, (CH$_2$)$_6$, (CH$_2$)$_3$), 3.2–4.1 (complex, 6 H, CH_2O, CH_2Br), 4.6 (br s, 1 H, OCHO).

1-(Tetrahydropyran-2-yloxy)-8-octylmagnesium Bromide (18). A 25-mL, three-necked flask was charged with Mg turnings (0.16 g, 6.6 mg-atoms) and a magnetic stirring bar, and dried for several hours in an oven. After cooling under nitrogen, the flask was fitted with an addition funnel and nitrogen inlet. A small amount of a solution of bromo compound **17** (0.57 g, 2 mmol) in anhydrous tetrahydrofuran (20 mL) and a small crystal of iodine were added. After initiation, signified by the discharge of the yellow iodine color, the solution of the bromo compound **17** was added dropwise over 1 h. Hydrolysis and VPC analysis (column **B**, 200 °C, 60 mL/min) of a small aliquot showed complete destruction of starting material.

(S)-9-(Cyclopent-2-en-1-yl)-1-(tetrahydropyran-2-yloxy)nonane (19). The (S)-(−)-tosylate **15** (0.252 g, 1 mmol), anhydrous tetrahydrofuran (ca. 3 mL), and a magnetic stirring bar were placed in a flame-dried, 25-mL, round-bottomed flask which was then sealed with a serum cap under nitrogen. The solution was cooled to −78 °C in a dry ice-acetone bath, and the Grignard reagent **18** was added via syringe. Dilithiocopper(II) tetrachloride (0.1 mL of a 1 M solution in tetrahydrofuran) was added slowly to the stirring solution via syringe. The solution was allowed to warm to room temperature over ca. 2 h and then stirred under nitrogen for 14 h. The reaction mixture was poured into saturated aqueous ammonium chloride solution (100 mL) and extracted with hexane (2 × 50 mL). The combined hexane extracts were washed with water (3 × 50 mL) and brine (50 mL) and dried ($MgSO_4$) and the solvent was removed in vacuo to give crude **19**.

Deprotection of the Alcohol. The crude coupling product **19** was dissolved in absolute methanol (50 mL). Boiling chips and acid-treated Dowex 50W-X8 ion exchange resin[32] (0.3 g) were added, and the mixture was refluxed for 3 h. Filtration and removal of solvent in vacuo gave the crude alcohol as a mixture of oil and white solid. NMR analysis showed 100% removal of the tetrahydropyran group (as judged by disappearance of resonance at δ 4.6).

(S)-(−)-9-(Cyclopent-2-en-1-yl)nonyl Acetate (20). The crude (S)-9-(cyclopent-2-en-1-yl)nonanol was dissolved in acetic anhydride (15 mL), and dry pyridine (30 drops) was added. This solution was stirred at room temperature overnight, poured into water (60 mL), and extracted with hexane (3 × 25 mL). The combined hexane extracts were washed with 5% aqueous hydrochloric acid (2 × 50 mL), 5% aqueous sodium bicarbonate solution (2 × 50 mL), and brine (50 mL), and dried ($MgSO_4$), and removal of the solvent in vacuo gave 0.89 g of a yellow oil. This oil was divided in half and preparatively chromatographed on two commercial thick-layer silica gel plates (10% ether in hexane). The product containing bands, which showed only faintly on the fluorescent adsorbant (R_f 0.31–0.43), were scraped off and the product was eluted with ethyl acetate. Preparative VPC (column **C**, 256 °C, 91 mL/min, 43 min retention time) gave analytically pure acetate **20** (62 mg, 13% yield based on optically pure acid, 25% based on tosylate): $[\alpha]^{25}_{D}$ −70.7 ± 0.4° (c 3.18, $CHCl_3$): NMR ($CDCl_3$) δ 1.1–1.7 (m, 16 H, (CH$_2$)$_8$), 2.05 (s, 3 H, CH_3CO), 1.7–2.9 (complex, 5 H, CH_2CH_2CH), 4.1 (t, 2 H, CH_2O, J = 7 Hz), 5.7 (s, 2 H, HC=CH); mass spectrum (70 eV, major fragments) m/e (relative intensity) 252 (32) M$^+$, 80 (44), 67 (63), 32 (72), 28 (100). Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.12; H,

11.08.

(R)-(+)-Cyclopent-2-en-1-ylcarboxylic Acid (12). Racemic cyclopent-2-en-1-ylcarboxylic acid (**10**, 40 g, 360 mmol) was allowed to react with (+)-α-methylbenzylamine (35 g, 290 mmol), following the procedure described previously, to give crude salt (61.3 g). Resolution required fractional crystallization (13 crops) to give 1.3 g of salt with rotation $[\alpha]^{25}_{578}$ +153.0° (c 0.4, CH$_3$OH). Workup as for the (−) enantiomer gave (R)-(+)-carboxylic acid **12** (0.5 g): NMR (CDCl$_3$) identical with the spectrum described for (−)-acid **11**.

(R)-(+)-Methyl Cyclopent-2-en-1-ylcarboxylate. The crude acid **12** (0.5 g, 4.5 mmol) and diazomethane (ca. 0.5 g) were allowed to react as described previously, to give (R)-(+)-methyl cyclopent-2-en-1-ylcarboxylate (0.57 g, 100% yield by NMR): NMR (CDCl$_3$) identical with the spectrum described for **13**.

(R)-(+)-Cyclopent-2-en-1-ylcarbinol. The crude (R)-(+)-methyl cyclopent-2-en-1-ylcarboxylate (0.57 g, 4.5 mmol) was allowed to react with lithium aluminum hydride (0.3 g, 8 mmol), as described previously, to give crude (R)-(+)-cyclopent-2-en-1-ylcarbinol (0.45 g, 100% yield by NMR): NMR (CDCl$_3$) identical with the spectrum described for **14**.

(R)-(+)-Cyclopent-2-en-1-ylmethyl 4-Toluenesulfonate (16). The crude (R)-(+)-cyclopent-2-en-1-ylcarbinol (0.45 g, 4.5 mmol) was allowed to react with p-toluenesulfonyl chloride (1.7 g, 9 mmol), as described previously, to give pure tosylate **16** (0.62 g, 55% yield): NMR (CDCl$_3$) identical with the spectrum described for **15**.

(R)-(+)-9-(Cyclopent-2-en-1-yl)nonyl Acetate (3). The (R)-(+)-tosylate **16** (0.37 g, 1.5 mmol) was coupled with Grignard reagent **18** (prepared from 0.16 g of Mg and 0.57 g of **17**) following the previously described procedure. The crude product was deprotected, acetylated, and purified as before giving chemically pure acetate **3** (0.12 g, 33% yield based on tosylate, 18% from resolved acid): $[\alpha]^{25}$D 70.0 ± 0.6° (c 3.20, CHCl$_3$); NMR (CDCl$_3$) identical with that previously described for **3**. Anal. Calcd for C$_{16}$H$_{28}$O$_2$: P$^+$, 252.2089. Found: P$^+$, 252.2093.

(R)-(+)-Cyclopent-2-en-1-ylcarbonyl Chloride. Optically active (R)-(+)-cyclopent-2-en-1-ylcarboxylic acid (3 g, 27 mmol) was recovered from the first mother liquor of the purification of the (−)-α-methylbenzylamine salt using the procedure described previously. The acid (1.12 g, 10 mmol, $[\alpha]^{24}_{578}$ +108° (c 1.8, CHCl$_3$)) was stirred for 3 h with freshly distilled thionyl chloride (0.71 mL, 1.2 g, 10 mmol) at room temperature under nitrogen. Distillation via kügelrohr at 50–65 °C (23 mm) gave (R)-(+)-cyclopent-2-en-1-ylcarboxylic acid chloride (0.9 g, 69% yield): lit.[16] bp 59–60 °C (22 mm); IR (film) ν 1795 cm^{-1}; NMR (CCl$_4$) δ 1.9–2.8 (m, 4 H, CH$_2$CH$_2$), 3.9–4.2 (m, 1 H, CHCOCl), 5.8–6.2 (m, 2 H, CH=CH).

(R)-(+)-Cyclopent-2-en-1-yl Diazomethyl Ketone. The (R)-(+)-cyclopent-2-en-1-ylcarboxylic acid chloride was added dropwise to a solution of diazomethane (ca. 1.5 g, 36 mmol) in 150 mL of ether with stirring at 0 °C. After the addition was complete, the mixture was stirred for 2 h at room temperature. The solution was filtered, and the solvent and excess diazomethane were removed in vacuo giving crude diazo ketone as a yellow oil which was used directly: IR (film) ν 2100, 1640 cm^{-1}; NMR (CDCl$_3$) δ 1.9–2.6 (m, 4 H, CH$_2$CH$_2$), 3.4–3.8 (m, 1 H, RCHCO), 5.4 (s, 1 H, CHN$_2$), 5.6–6.1 (m, 2 H, CH=CH).

Methyl (S)-(+)-2-(Cyclopent-2-en-1-yl)acetate. The crude (R)-(+)-cyclopent-2-en-1-yl diazomethyl ketone was dissolved in methanol (15 mL) and heated at 55 °C. Small portions of silver oxide were added with stirring until nitrogen production visibly ceased. The mixture was then maintained at this temperature until small aliquots no longer showed nitrogen production upon addition of concentrated hydrochloric acid. The solution was filtered into water (90 mL) and extracted with methylene chloride (3 × 50 mL). The methylene chloride extracts were washed with water (50 mL) and brine (50 mL) and dried (MgSO$_4$), and the solvent was removed in vacuo giving crude ester. Preparative VPC (column B, 130 °C) gave chemically pure optically enriched methyl (S)-(+)-2-(cyclopent-2-en-1-yl)acetate: $[\alpha]^{25}_{578}$ +45° (c 0.94, CHCl$_3$); NMR (CDCl$_3$) identical with spectrum previously described for racemic ester.

Methyl (R)-(−)-Cyclopent-2-en-1-ylacetate. Optically enriched (R)-(−)-cyclopent-2-en-1-ylacetic acid ($[\alpha]^{24}_{578}$ −66° (c 2, CHCl$_3$)) was recovered from the first mother liquor of the purification of the brucine salt following the procedure described previously. A small portion of this acid (0.31 g, 2.4 mmol) was added dropwise to a slight excess of diazomethane in ether at 0 °C. Removal of the solvent and excess diazomethane in vacuo and preparative VPC (same conditions

as for (+) enantiomer) gave chemically pure methyl (R)-(−)-cyclopent-2-en-1-ylacetate: $[\alpha]^{25}_{578}$ −58.3° (c 1.4, CHCl$_3$); NMR (CDCl$_3$) identical with the spectrum of racemic ester described previously.

References and Notes

(1) Joint contribution of the Agricultural Research Service, U.S. Department of Agriculture, and Journal Paper No. J-9038 of the Iowa Agriculture and Home Economics Experiment Station, Ames, Iowa, Project No. 2183, and the Department of Chemistry, Los Angeles, California, Contribution No. 3945. A preliminary report of this work has been submitted to *Science.* No endorsement of specific commerical products is intended.
(2) (a) Formerly of the Department of Chemistry, Iowa State University, Ames, Iowa 50011. The initial phase of this work was carried out at Iowa State University. (b) Department of Chemistry, University of California—Los Angeles.
(3) Formerly Research Entomologist, Agricultural Research Service, U.S. Department of Agriculture, Ankeny, Iowa 50021, and Associate Professor, Department of Entomology, Iowa State University, Ames, Iowa 50011. Presently at Organic Chemical Synthesis Laboratory, Beltsville Agricultural Research Center.
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