was removed by distillation in vacuo at 18–20 °C to leave the sulfinamide anhydride **11** as a pale yellow syrup, to which was added a solution of 400 mg of 3,4-dihydro-β-carboline (**4**) in 10 ml of dry benzene. The mixture was allowed to stand for 1 h at room temperature. After evaporation of benzene, the residue was dissolved in chloroform, which was washed with 10% sodium hydroxide, water, and dried over sodium sulfate. Evaporation of the solvent gave 465 mg (65%) of evodiamine as pale yellow crystals after recrystallization from ethanol: mp 268–270 °C (lit.[12] mp 270–272 °C); ir ($CHCl_3$) 3475 (NH) and 1640 cm^{-1} (C=O); uv (MeOH) 292, 283, 273, and 268 nm; mass *m/e* 303 (M^+), 288, 170, 160, 143, and 133; NMR ($CDCl_3$) δ 2.53 (3 H, s, NCH_3), 5.90 (1 H, s, C3–H), 7.3–7.8 (8 H, m, ArH), and 8.2 (1 H, s, NH).

Anal. ($C_{19}H_{17}N_3O \cdot H_2O$) C, H, N.

Rutecarpine (3). A solution of 260 mg of 3,4-dihydro-β-carboline (**4**) in 15 ml of dry benzene was added to the sulfinamide anhydride **10** [prepared from 230 mg of anthranilic acid (**7**)] and the mixture was worked up as above to give 345 mg (80%) of rutecarpine (**3**) as pale yellow needles after recrystallization from ethyl acetate: mp 259 °C [lit.[13] mp 258 °C]; ir (KBr) 3325 (NH) and 1655 cm^{-1} (C=O); uv (MeOH) 360, 344, 330, 288, and 276 nm; mass *m/e* 287 (M^+), 259, 243, and 144; NMR ($CDCl_3$) δ 3.23 (2 H, t, J = 7 Hz, $ArCH_2$), 4.60 (2 H, t, J = 7 Hz, CH_2N), 7.3–7.8 (8 H, m, ArH), and 8.3 (1 H, s, NH).

Anal. ($C_{18}H_{13}N_3O$) C, H, N.

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Biomimetic Polyene Cyclizations.[1a,b,c] Asymmetric Induction in the Cyclization of a Dienic Acetal[1d]

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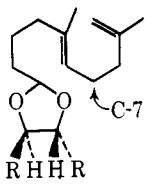
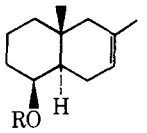
Abstract: Cyclization of the optically active acetal **1**, derived from the aldehyde **14** and (−)-2,3-butanediol, was studied to determine if the reaction proceeds with asymmetric induction. The aldehyde **14** was synthesized from the *trans*-bromodiene **9** by the sequence: **9** → **10** → **11** → **13** → **14.** Cyclization of acetal **1** with stannic chloride in benzene gave the axial hydroxy ether **15a,15b** and the epimeric equatorial hydroxy ether **16a,16b** as the major products. Cleavage of the side chain from each epimer (e.g., **15a,15b** → **17a,17b** → **5a,5b**) followed by oxidation gave the octalone **7a,7b.** The axially derived octalone **7a,7b** was converted to the hydrindanone **22** (i.e., **5a,5b** → **7a,7b** → **19** → **21** → **22**) and its ORD curve compared with the ORD curve from a sample of enantiomerically pure (+)-hydrindanone **22** of known absolute configuration. It was thus determined that the axially derived octalone consisted of 8% **7a** and 92% **7b,** and the equatorially derived octalone consisted of 92% **7a** and 8% of **7b.** An ORD value of $[\Phi]_{222}$ +11 180° was established for the pure octalone **7b,** which was used to calculate the enantiomeric ratios of various octalone specimens produced under different cyclization conditions. When the cyclization of **1** was conducted with stannic chloride in ultradry pentane or in nitromethane, the major products **15a,15b** and **16a,16b** were also formed with a high but lesser degree of asymmetric induction.

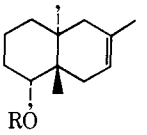
For several years our laboratories have been engaged in a study to test the hypothesis that the stereochemical course of squalene biocyclization may be controlled, at least in part, by stereoelectronic factors rather than by enzymic conformational influences.[3] We have, for example, demonstrated that appropriately constructed polyolefinic acetals undergo nonenzymic, acid-catalyzed cyclizations to give polycyclic substances possessing "natural" configuration.[1a,b,c,4] These cyclizations were stereospecific with respect to the relative configurations of the chiral centers produced at the bridgeheads; however, the products were racemic. In view of the fact that the enzymatic cyclization of squalene proceeds with total asymmetric induction to produce enantiomerically pure products, it has been our aim to simulate this process, at least qualitatively, in nonenzymic systems. To this end we decided to examine the cyclization of the optically active dienic acetal **1,** and we were gratified to find that the reaction did indeed proceed with a remarkably high degree of asymmetric induction without the agency of an enzyme. The present paper constitutes a detailed account of this study.

Previous work has shown that the cyclization of the *trans*-dienic acetal **2** proceeds in high yield and essentially stereospecifically with respect to the ring fusion.[1b] Thus when acetal **2** was treated with 5.0 molar equiv of stannic chloride in nitromethane at 0 °C for 3 min, an 80% yield of the racemic mixture **3a,3b** having an axial side chain at C-5 was obtained, along with 10% of the racemic mixture **4a,4b** having the epimeric equatorial side chain. Degradation of the side chain to

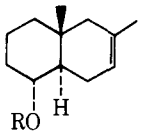


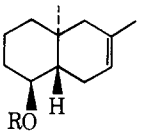
1, R = Me
2, R = H





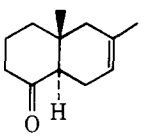
3a, R = CH_2CH_2OH — **3b**
5a, R = H — **5b**
15a, R = CHMeCH(OH)Me — **15b**
17a, R = CHMeCOMe — **17b**



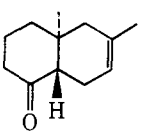


4a, R = CH_2CH_2OH — **4b**
6a, R = H — **6b**
16a, R = CHMeCH(OH)Me — **16b**
18a, R = CHMeCOMe — **18b**

the hydroxyl group by conversion to the tosylate followed by cleavage with sodium iodide and zinc dust gave the epimeric alcohols **5a,5b** and **6a,6b**. Oxidation of both alcohols with Jones reagent yielded a single racemic octalone **7a,7b**. This result



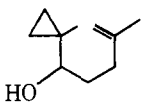
7a



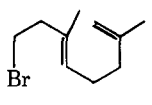
7b

prompted us to investigate the cyclization of the optically active acetal **1** derived from (−)-2,3-butanediol (*R,R* configuration), with the plan of detecting any asymmetric induction by observing, after side chain degradation and oxidation, whether the ketone was enriched in either enantiomer **7a** or **7b**.

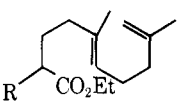
Synthesis of the Optically Active Acetal 1. Since only the *trans*-dienic acetal **1** was required for the present study, we envisaged a synthetic route employing stereoselective introduction of the trisubstituted olefinic linkage.[5] Thus the known *trans*-bromodiene **9**, which is readily available from the carbinol **8** via the modified Julia olefin synthesis,[6] was employed



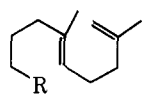
8



9



10, R = CO_2Et
11, R = H
12, R = Ac



13, R = CH_2OH
14, R = CHO

in a condensation with sodiomalonic ester to give the dienic malonic ester **10** in 72% yield. Decarbethoxylation was effected by heating in dimethylsulfoxide, either with sodium cyanide[7] (71% yield) or with tetramethylammonium acetate[8] (95% yield) to afford the monoester **11**. Alkylation of sodio ethyl acetoacetate with the bromodiene **9** gave the keto ester **12**; however, attempts to effect deacylation resulted in only modest yields of the desired monoester.

The pure *trans*-monoester **11** was reduced with lithium aluminum hydride to give a quantitative yield of the alcohol **13** which was oxidized in 94% yield to the corresponding aldehyde **14** by treatment with 6 mol equiv of Collins reagent[9] for 15 min at room temperature. Treatment of the aldehyde with excess (−)-2,3-butanediol[10] and 35 mol % boron trifluoride etherate for 24 h at 0 °C followed by chromatography on alumina gave the optically active acetal **1** in 89% yield. A sample of the acetal **1**, $[\alpha]^{20}_{300}$ −83.9° (*c* 0.721),[11b] was treated under the conditions of the original acetalization for 120 h at 0 °C to determine whether any racemization had occurred during its formation. The reaction mixture afforded a 97% recovery of acetal **1**, $[\alpha]^{20}_{300}$ −87.3° (*c* 0.688). This experiment was repeated on a second sample of the authentic acetal and gave a 99% recovery of acetal **1**, $[\alpha]^{20}_{300}$ −88.1° (*c* 0.772). It can therefore be concluded that no appreciable racemization occurred during formation of the acetal. It is also noteworthy that no detectable cyclization occurred under these conditions.

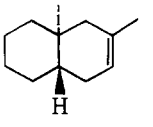
Cyclization Studies. The stannic chloride catalyzed cyclization of the optically active acetal **1** was studied in nitromethane, benzene, and pentane, and the amount of asymmetric induction was determined in each case. Since the amount of asymmetric induction was highest when the cyclization was carried out in benzene, a detailed discussion of the methodology is given for this case only.

A solution of the acetal **1** (0.02 M) and stannic chloride (0.04 M) in benzene was stirred for 7 min at room temperature. At the end of this period cyclization was complete as shown by observing the disappearance of acetal by VPC analysis of aliquots. When nitromethane was used as the solvent, cyclization was complete in 3 min at 0 °C, In pentane the reaction took 4 h at room temperature, and in ultradry pentane 9 days were required for completion.[12]

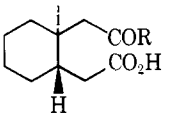
The product from the cyclization in benzene solution was distilled and then chromatographed on Florisil to give two major components, namely the axial hydroxy ether **15a,15b** (52% yield) and the epimeric equatorial hydroxy ether **16a,16b** (21% yield). The two epimers were easily distinguished, as in the case of **3a,3b** and **4a,4b**,[1b] by the relative positions of the NMR signals for the angular methyl groups which appeared at δ 0.92 and 0.80 ppm for **15a,15b** and **16a,16b**, respectively.[13] Attempts to remove the side chain via the tosylate, as in the case of **3a,3b** and **4a,4b** (see above), failed. However the side-chain degradation could be efficiently executed as follows. Oxidation with Collins reagent gave the corresponding keto ethers **17a,17b** and **18a,18b** in nearly quantitative yields. These substances, on treatment with lithium and ethylamine, underwent cleavage affording the octalols **5a,5b** and **6a,6b**, which were separated from by-products by preparative TLC and VPC. Cleavage of the axial keto ether **17a,17b** was accompanied by partial epimerization at C-5, and the product contained 12–19% of the equatorial octalol **6a,6b** which was removed by preparative TLC.

The octalol **5a,5b**, upon oxidation with Jones reagent,[14] yielded a specimen of octalone **7a,7b**, ORD[11a] (*c* 0.261) $[\Phi]_{589}$ +118°, $[\Phi]_{315}$ +594°, $[\Phi]_{222}$ +9278°, which, as shown below, corresponds to a composition of 8.5% **7a** and 91.5% **7b**. The octalone derived from the equatorial octalol **6a,6b** proved to be the enantiomeric counterpart (see Table I for ORD data), corresponding to 92% **7a** and 8% **7b**.

The above enantiomeric ratios were determined as follows. A sample of the axially derived octalone was reduced using the Huang-Minlon modification[15] of the Wolff-Kishner reaction, and the *trans*-octalin **19**,[16] obtained in 67% yield, was sepa-



19



20, R = Me
21, R = OH

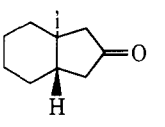


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Table I. ORD Data and Calculated Enantiomeric Ratios

		ORD data for derived octalones								
		$[\Phi]_{xA}$		$[\Phi]_{yB}$		$[\Phi]_{zC}$			Enantiomeric composition	
Cyclization solvent	Product	x, mμ	A, deg	y, mμ	B, deg	z, mμ	C, deg	c[a]	**7a**[f]	**7b**[f]
Benzene	Axial[d]	589	+118	315	+594	222	+9278	0.261	8[b] (7)[c]	92 (93)
	Equatorial[d]	589	−126	313	−577	221	−9379	0.318	92 (94)	8 (6)
Pentane	Axial[e]	589	+126	316	+549	224	+8147	0.261	14 (12)	86 (88)
	Equatorial[e]	589	−119	316	−581	220	−8975	0.278	90 (92)	10 (8)
Nitromethane	Axial[d]	589	+75	314	+365	220	+5580	0.338	25 (24)	75 (76)

[a] Concentration in g/100 ml of dioxane solution. [b] Calculated from the value for pure **7b** $[\Phi]_{222}$ +11 180. [c] Enantiomeric ratios in parentheses were calculated from the value for pure **7b** $[\Phi]_{222}$ +10 750. [d] The ORD measurements are an average of three determinations. [e] The ORD measurements are an average of two determinations. [f] The ratio of **7a:7b** also reflects the ratios for **5a:5b, 17a:17b,** and **15a:15b** in the axial series, and **6a:6b, 18a:18b,** and **16a:16b** in the equatorial series. The values have been rounded off to the nearest whole %.

rated from the cis isomer[17] by preparative VPC. Ozonolysis of octalin **19** in methanol at −78 °C followed by treatment with hydrogen peroxide in aqueous acetic acid afforded the keto acid **20.**[16] Further oxidation with sodium hypobromite[18] gave the diacid **21**[16] which, upon pyrolysis with lead carbonate[19] at 305 °C, underwent ring closure to give the hydrindanone **22,**[16] ORD[11b] (c 0.175) $[\Phi]_{589}$ +396°, $[\Phi]_{325}$ +10 208°, $[\Phi]_{313}$ +8824°, $[\Phi]_{303}$ +1464°, $[\Phi]_{295}$ −4987°, $[\Phi]_{286}$ −7755°, $[\Phi]_{279}$ −8111°. The absolute configuration of the (+) enantiomer is known to be that depicted by formula **22.**[20] In our hands a sample of the pure (+) enantiomer[21] exhibited ORD (c 0.270) $[\Phi]_{589}$ +450°, $[\Phi]_{325}$ +12 350°, $[\Phi]_{314}$ +10 700°, $[\Phi]_{303}$ +1920°, $[\Phi]_{296}$ −5910°, $[\Phi]_{286}$ −9350°, $[\Phi]_{278}$ −9700°. Thus the molecular amplitude[22] (a = +183.2)[11b] of the hydrindanone derived from octalone **7a,7b** was 83.0% of the molecular amplitude (a = +220.5)[23] of the pure (+) enantiomer, corresponding to a composition of 91.5% of **22** and 8.5% of its optical antipode, which, in turn, represents the composition of the octalones **7b** and **7a,** respectively. From these data a value of $[\Phi]_{222}$ +11 180° was calculated for the pure octalone **7b.** This established value was used to calculate the enantiomeric ratios of various octalone specimens from their ORD curves (see Table I).

When the cyclization of acetal **1** was conducted in ultradry pentane, the octalones derived therefrom (see above) consisted of 14% **7a** and 86% **7b** from the axial octalol **5a,5b,** and 90% **7a** and 10% **7b** from the equatorial octalol **6a,6b,** as determined from the ORD data as shown in Table I. In the case of the cyclization in nitromethane, the total cyclization product was submitted to side-chain degradation, and the C-5 epimers were separated at the octalol stage. Since it was subsequently discovered that significant (6–10%) epimerization at C-5 occurs during cleavage of the side chain from the axial keto ether **17a,17b** (see above), the ORD curve for the octalone derived from the equatorial octalol **6a,6b** is probably meaningless (i.e., the equatorial octalol was contaminated with axially derived product). Fortunately no epimerization was observed during cleavage of the equatorial keto ether **18a,18b,** thereby insuring the reliability of the ORD data for the axially derived octalone, which corresponded to a composition of 75% **7b** and 25% **7a.** A sample of this axially derived octalone **7a,7b** was converted to the hydrindanone **22.** The ORD data from this material were used to calculate a second, independent value of $[\Phi]_{220}$ +10 750° for the pure enantiomer **7b,** which, in turn, was used to calculate a comparable set of enantiomeric compositions as shown in parentheses in Table I.

We have not yet been able to envision a completely satisfactory model of the transition state, which accounts for the very high degree of asymmetric induction observed in the cyclization of the substrate **1.** Seemingly there must be considerable rigidity of the acetal moiety in the transition state, i.e., it does not assume an open, extended form. Molecular models of the substrate **1,** in the conformation required for ring closure and with the acetal function intact, suggest that chiral recognition could occur through nonbonded interactions between the substituents on a chiral center and at least one of the hydrogen atoms attached to C-7. This conjecture might be tested by observing how appropriate substitutions at C-7 affect the degree of asymmetric induction.

Experimental Section[24]

General Considerations. Microanalyses were performed by E. H. Meier and J. Consul, Department of Chemistry, Stanford University. Melting points were determined on a Kofler hot-stage microscope calibrated against totally immersed Anschutz thermometers.

Vapor-phase chromatographic (VPC) analyses were performed on a Wilkens Aerograph Hi-Fy Model 600 C instrument using Carbowax columns. Preparative vapor-phase chromatography was performed on a Varian Aerograph Model 202 B instrument using a 20 ft Carbowax column.

Nuclear magnetic resonance (NMR) spectra were determined under the supervision of Dr. L. J. Durham on Varian Associates Model A-60 or HA-100 spectrometers. Carbon tetrachloride was used as solvent unless otherwise specified, and tetramethylsilane (Me_4Si) was employed as the internal reference. Chemical shifts are reported as δ values in parts per million relative to Me_4Si (δ_{Me_4Si} 0.0 ppm).

Infrared (ir) spectra were recorded on a Perkin Elmer Model 137-B spectrophotometer in chloroform solution or as a neat film. Optical rotatory dispersion (ORD) spectra were recorded on a Jasco Model ORD/UV-5 automatic scanning spectropolarimeter. All ORD spectra were recorded as dioxane solutions.

Silica gel G or GF_{254} (E. Merck A.G.) was used as the absorbent for thin-layer chromatography (TLC). Analytical TLC plates were visualized by spraying with a 2% solution of ceric sulfate in 2 N sulfuric acid, followed by heating at 150 °C for 10 min.

Ethyl 2-Carboethoxy-*trans*-5,9-dimethyldeca-5,9-dienoate (10). To a suspension of 36.5 g of sodium hydride (0.81 mol as a 53.4% dispersion in mineral oil, washed with several portions of pentane) in 500 ml of dry dimethylformamide and 120 ml of dry benzene was slowly added 130 ml (137 g, 0.86 mol) of diethyl malonate over a period of 45 min. The resulting yellow solution was stirred for 30 min under nitrogen, and a solution of 17.6 g (0.081 mol) of crude bromodiene **9**[6] in 20 ml of benzene was added over a 30-min period. The resulting solution was heated at 46–50 °C for 21 h, cooled, and poured into 800 ml of ice–water. The pale-yellow, oily product, isolated by pentane extraction,[24] was combined with the crude product from another run in which 15.2 g of sodium hydride (0.34 mol as a 53.4% dispersion in mineral oil), 58 g (0.37 mol) of diethyl malonate, and 7.4 g (0.034 mol) of bromodiene **9** were used. The combined oils were distilled through a 2-ft spinning band column to give 24.5 g (72% yield) of a colorless liquid: bp 94–96 °C (0.025 mm); $n^{20}D$ 1.4587; λ_{max}^{film} 3.21, 5.70 (C=O), 5.75 (C=O), and 11.23 μ (C=CH_2); NMR 1.25 (t, J = 7 Hz, 6 H, carboethoxy CH_3), 1.61 (d, J = 1 Hz, 3 H, CH_3 at C-5),[25] 1.70 (t, J = 1 Hz, 3 H, CH_3 at C-9), 1.8–2.2 (m, 8 H, CH_2's at C-3, C-4, C-7, and C-8), 3.18 (m, 1 H at C-2), 4.15 (q, J = 7 Hz, 4 H, carboethoxy CH_2), 4.57 (broad s, 2 H, –C=CH_2), and 5.13 ppm (s, 1 H at C-6).

Anal. ($C_{17}H_{28}O_4$) C, H.

Ethyl *trans*-5,9-Dimethyldeca-5,9-dienoate (11). A. Decarbethoxylation with Sodium Cyanide. The method of Krapcho[7] was adopted. A mixture of 11.5 g (0.039 mol) of the dienic diestr **10**, 5.74 g (0.117 mol) of sodium cyanide, and 155 ml of freshly distilled dimethylsulfoxide (Me_2SO) was heated under nitrogen for 16 h at 155 °C. The dark reaction mixture was concentrated to approximately 50 ml by distillation (1.5 mm) and poured into 500 ml of water overlaid with 200 ml of pentane. Extraction with pentane[24] followed by short-path distillation at 95–110 °C (0.5 mm) afforded 3.70 g of a colorless oil. An additional 2.50 g (71% total yield) of the monoester **11** was obtained from the Me_2SO distillate after similar extraction and distillation. Analytical VPC (170 °C) showed the product to consist of 92.8% of the desired *trans*-monoester **11**, 1.8% of the corresponding cis isomer, and ca. 5% of compounds presumed to be bond-migrated isomers.

B. Decarbethoxylation with Tetramethylammonium Acetate.[8] A mixture of 5.1 g (17 mmol) of diester **10** and 8.5 g (64 mmol) of tetramethylammonium acetate in 20 ml of dry Me_2SO was heated at 130 °C under nitrogen for 10 h. The resulting light-brown solution was cooled, poured into 250 ml of ice–water, and extracted with pentane.[24] The solvent was removed first by atmospheric distillation and finally under reduced pressure to give a yellow oil which was subjected to short-path distillation at 95–105 °C (0.5 mm) to afford 3.58 g of monoester **11** as a colorless oil and 400 mg of residue composed of the desired monoester and unreacted diester. An additional 70 mg of monoester (total yield 3.65 g; 95%) was obtained from the residue by preparative TLC (1:3 ether–pentane). Analysis by VPC (170 °C) showed the *trans*-monoester **11** (96.5% of the total area) to be contaminated with 2.5% of the cis isomer and ca. 1% of a compound presumed to be the bond-migrated isomer.

The ester mixture was purified by preparative VPC (190 °C) to afford 3.23 g of the *trans*-monoester **11** uncontaminated by *cis*-monoester, as shown by analytical VPC: n^{20}D 1.4564; λ_{max}^{film} 3.22, 5.74 (C=O), 6.05, 8.03 (C–O), and 11.25 μ (C=CH_2); NMR 1.22 (t, J = 7 Hz, 3 H, carboethoxy CH_3), 1.60 (broad s, 3 H, CH_3 at C-5),[25] 1.69 (t, J = 1 Hz, 3 H, CH_3 at C-9), 1.8–2.4 (broad m, 10 H, CH_2's at C-2, C-3, C-4, C-7, and C-8), 4.06 (q, J = 7 Hz, 2 H, carboethoxy CH_2), 4.67 (s, 2 H, C=CH_2), and 5.12 ppm (s, 1 H at C-6).

Anal. ($C_{14}H_{24}O_2$) C, H.

A pure sample of the *cis*-monoester, obtained as the leading peak during the VPC purification of **11**, possessed the following properties: n^{20}D 1.4574; NMR 1.23 (t, J = 7 Hz, 3 H, carboethoxy CH_3), 1.68 (d, J = 1 Hz, 3 H, CH_3 at C-5),[25] 1.69 (unresolved t, 3 H, CH_3 at C-9), 1.8–2.4 (m, 10 H, CH_2's at C-2, C-3, C-4, C-7, and C-8), 4.08 (q, J = 7 Hz, 2 H, carboethoxy CH_2), 4.57 (s, 2 H, C=CH_2), and 5.13 ppm (broad s, 1 H at C-6).

Anal. ($C_{1424}O_2$) C, H.

***trans*-5,9-Dimethyldeca-5,9-dienol (13).** To a mixture of 1.92 g (50.6 mmol) of lithium aluminum hydride and 300 ml of freshly distilled THF was added 3.23 g (14.4 mmol) of the aforementioned pure *trans*-dienic ester **11** in 20 ml of THF. The resulting mixture was stirred under reflux for 2 h, cooled (ice bath), and the reaction quenched by careful addition of saturated sodium sulfate solution. The mixture was stirred for 2 h at room temperature and dried by addition of 60 g of anhydrous sodium sulfate. The mixture was filtered and the solvent removed at reduced pressure to give an oil which was evaporatively distilled at 85–90 °C (0.025 mm) to afford 2.61 g (100% yield) of a colorless oil: λ_{max}^{film} 2.98 (OH), 3.21, 6.05, 9.43 (C–O), and 11.25 μ (C=CH_2); NMR 1.60 (s, 3 H, CH_3 at C-5), 1.68 (s, 3 H, CH_3 at C-9), 3.20 (s, 1 H, hydroxyl), 3.50 (t, 2 H, CH_2 at C-1), 4.50 (s, 2 H, C=CH_2), and 5.1 ppm (broad t, 1 H at C-6).

Anal. ($C_{12}H_{22}O$) C, H.

***trans*-5,9-Dimethyldeca-5,9-dienal (14).** The method of Collins[9] was employed. A solution of 20.4 g (79.0 mmol) of dipyridine–chromium(VI) oxide in 140 ml of dry dichloromethane was rapidly added to a solution of 2.35 g (12.9 mmol) of dienol **13**. The resulting mixture, which turned black immediately, was swirled frequently for 15 min at room temperature and then filtered and rinsed with dichloromethane through a column of Merck acid-washed alumina. The solvent was removed by rotary evaporation to give a pale-yellow oil which was subjected to short-path distillation at 75–85 °C (0.10 mm) to afford 2.18 g (94% yield) of the dienal **14** which appeared to be 99% pure by VPC (165 °C): n^{20}D 1.4654; λ_{max}^{film} 3.20, 3.65 (CHO), 5.78 (C=O), 6.05, and 11.25 μ (C=CH_2); NMR 1.60 (d, J = 1 Hz, 3 H, CH_3 at C-5),[25] 1.70 (t, J = 1 Hz, 3 H, CH_3 at C-9), 1.8–2.5 (m, 10 H, CH_2's at C-2, C-3, C-4, C-7, and C-8), 4.57 (broad s, 2 H, C=CH_2), 5.12 (unresolved t, 1 H at C-6), and 9.58 ppm (t, J = 1 Hz, 1 H at C-1).

Anal. ($C_{12}H_{20}O$) C, H.

(−)-4,5-Dimethyl-2-(*trans*-4,8-dimethyl-4,8-nonadienyl)-1,3-dioxolane (1). A mixture of 2.16 g (12.0 mmol) of the dienal **14**, 11.3 g (125 mmol) of (−)-2,3-butanediol,[10] 37 g of Drierite, and 130 ml of freshly distilled THF was cooled in a dry ice–acetone bath, and 0.53 ml (596 mg, 4.2 mmol) of boron trifluoride etherate was added. The resultant mixture was swirled and allowed to stand at 0 °C for 23 h, then 150 ml of cold, 5% sodium bicarbonate solution was added. Pentane extraction[24] followed by short-path distillation at 85–95 °C (0.10 mm) afforded 3.5 g of a colorless oil. Chromatography of this material on 150 g of a 1:1 mixture of neutral and basic alumina (elution with 1:9 ether–pentane) followed by short-path distillation at 85–95 °C (0.10 mm) afforded 2.69 g (89% yield) of acetal **1**, >99% pure by VPC (175° C): λ_{max}^{film} 6.02 (C=C), 8.70, 8.90, 9.25 (C–O), and 11.21 μ (C=CH_2); NMR 1.14 (s, 3 H, dioxolane CH_3), 1.23 (s, 3 H, dioxolane CH_3), 1.48 (m, 4 H), 1.60 (s, 3 H, CH_3 at C-4),[25] 1.70 (s, 3 H, CH_3 at C-8), 2.00 (broad s, 6 H), 3.50 (m, 2 H, dioxolane methines), 4.62 (s, 2 H, C=CH_2), 4.98 (m, 1 H, O–CH–O), and 5.15 ppm (broad m, 1 H at C-5).

Anal. ($C_{16}H_{28}O_2$) C, H.

A mixture of 100 mg (0.397 mmol) of the above acetal **1**, $[\alpha]^{20}_{400}$ −24.2°, $[\alpha]^{20}_{350}$ −42.3°, $[\alpha]^{20}_{300}$ −83.9°, $[\alpha]^{20}_{250}$ −223°,[11b] 0.375 ml (370 mg, 0.410 mmol) of (−)-2,3-butanediol, 1.21 g of Drierite, and 4.3 ml of freshly distilled THF was cooled in a dry ice–acetone bath while 17.5 μl (19.6 mg, 0.139 mmol) of boron trifluoride etherate was added. The mixture was then swirled and allowed to stand at 0 °C for 120 h. Isolation and purification (by chromatography and distillation) as described above gave 97 mg (97% recovery) of acetal **1** as a colorless oil, $[\alpha]^{20}_{400}$ −26.0°, $[\alpha]^{20}_{350}$ −43.6°, $[\alpha]^{20}_{300}$ −87.3°, $[\alpha]^{20}_{250}$ −222°. The ir and VPC retention times were essentially identical with those of the original sample of acetal.

The experiment described directly above was repeated with a 75-mg sample of acetal. The product amounted to 74 mg (99% recovery) of acetal **1**, $[\alpha]^{20}_{400}$ −28.4°, $[\alpha]^{20}_{350}$ −46.6°, $[\alpha]^{20}_{300}$ −88.1°, $[\alpha]^{20}_{250}$ −233°. The ir and VPC retention time of this material were essentially identical with those of the original sample of acetal.

Cyclization of the Optically Active Acetal 1 in Benzene. Conditions developed for cyclization of the acetal **2**[1b] were employed. A solution of 2.25 g (8.93 mmol) of the acetal **1** in 223 ml of dry benzene (under nitrogen) was added to a solution of 2.09 ml (4.65 g, 17.8 mmol) of stannic chloride in 223 ml of dry benzene (under nitrogen) at room temperature. The resulting solution was stirred for 7 min at room temperature, then 225 ml of 1 N hydrochloric acid was added. Extraction with ether, using acid and base washes,[24] followed by short-path distillation at 90–105 °C (0.025 mm) gave 2.17 g (96% yield) of a colorless oil: λ_{max}^{film} 2.90 (OH), and 9.25 μ (C–O). Chromatography on 200 g of Florisil followed by short-path distillation (0.025 mm) afforded 1.18 g (52% yield) of fraction A (eluent 9:1 pentane–ether; bp 90–100 °C), 477 mg (21% yield) of fraction B (eluent 4:1 pentane–ether; bp 95–105 °C), and 420 mg of fraction C. Fraction A proved to be the axial hydroxy ether **15a,15b** and appeared to be 95% pure by VPC: λ_{max}^{film} 2.5 (OH), and 9.20 μ (C–O); NMR 0.92 (s, 3 H, CH_3 at C-9), 1.01 (d, J = 6 Hz, 3 H, CH–CH_3), 1.08 (d, J = 6 Hz, 3 H, CH–CH_3), 1.2–2.3 (m, 14 H), 2.20 (broad s, 1 H, OH), 2.8–3.7 (m, 3 H, three OCH), and 5.33 ppm (broad s, 1 H at C-3).

Anal. ($C_{16}H_{28}O_2$) C, H.

Fraction B proved to be the equatorial hydroxy ether **16a,16b** and appeared to be 90% pure by vpc: λ_{max}^{film} 2.85 (OH) and 9.25 μ (C–O). The NMR spectrum was very similar to that of the axial isomer described above except that the C-9 methyl group appeared as a 3-proton singlet at 0.80 ppm[13] and the 3-proton multiplet at 2.9–3.5 ppm was considerably more complex.

Anal. ($C_{16}H_{28}O_2$) C, H.

Fraction C consisted of a mixture of the above hydroxy ethers and unidentified compounds.

2,9-Dimethyl-Δ^2-*syn*-5-(3-oxo-2(*R*)-butoxy)-*trans*-octalin[26] (17a,17b). A solution of 9.75 g (37.8 mmol) of dipyridine–chromium(VI) oxide[9] in 68 ml of dry dichloromethane was added rapidly to a solution of 1.15 g (4.56 mmol) of the axial hydroxy ether **15a,15b** from the previous experiment in 68 ml of dry dichloromethane at room temperature. The mixture was occasionally swirled over a 15-min period, then filtered through 50 g of Merck acid-washed alumina and

rinsed with an additional 100 ml of dichloromethane. Short-path distillation of the product at 85–95 °C (0.025 mm) afforded 1.14 g (100% yield) of the axial keto ether **17a,17b** as a colorless oil: λ_{max}^{film} 5.80 (C=O), and 8.95 μ (C-O); NMR 0.99 (s, 3 H, CH_3 at C-9),[13] 1.19 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 1.25–2.05 (m, 13 H), 2.15 (s, 3 H, $COCH_3$), 3.46 (m, 1 H at C-5), 3.62 (q, J = 6.5 Hz, 1 H, $OCHCH_3$), and 5.31 ppm (broad s, 1 H at C-3).

Anal. ($C_{16}H_{26}O_2$) C, H.

2,9-Dimethyl-Δ^2-*anti*-5-(3-oxo-2(*R*)-butoxy)-*trans*-octalin[26] (18a,18b). The oxidation of the equatorial hydroxy ether **16a,16b** was carried out in the same manner as described above for the corresponding axial isomer. Accordingly, 450 mg of the equatorial hydroxy ether gave 440 mg (99% yield) of the corresponding keto ether **18a,18b** which was subjected to short-path distillation at 85–95 °C (0.025 mm): λ_{max}^{film} 5.80 (C=O), and 9.05 μ (C-O); NMR 0.80 (s, 3 H, CH_3 at C-9),[13] 1.18 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 1.1–2.0 (m, 14 H), 2.08 (s, 3 H, $COCH_3$), 2.8–3.3 (broad m, 1 H at C-5), 3.71 (q, J = 7 Hz, 1 H, $OCHCH_3$), and 5.35 ppm (broad s, 1 H at C-3).

Anal. ($C_{16}H_{26}O_2$) C, H.

2,9-Dimethyl-Δ^2-*syn*-5-*trans*-octalol[26] (5a,5b). A mixture of 1.13 g (4.52 mmol) of the axial keto ether **17a,17b**, 3.06 g (0.44 g-atom) of lithium wire, and 550 ml of distilled ethylamine was heated at reflux for 2.5 h at room temperature. Solid ammonium chloride was cautiously added to the resulting solution until the blue color disappeared, and the ethylamine was evaporated under a stream of nitrogen. The white residue was taken up in 150 ml of water and 150 ml of ether. Extraction with ether, including a cold acid wash,[24] followed by short-path distillation at 70–90 °C (0.05 mm) afforded 749 mg of colorless oil. Analytical VPC showed the presence of considerable unreacted keto ether. This mixture was separated by preparative TLC (3:1 pentane–ether) to give 454 mg of axial octalol **5a,5b,** 60 mg of equatorial octalol **6a,6b,** and 215 mg of unreacted keto ether. Short-path distillation of the axial alcohol **5a,5b** at 70–80 °C (0.05 mm) afforded 445 mg of colorless oil which appeared to be 90% pure by VPC. The unreacted keto ether was retreated with lithium and ethylamine as described above to afford 123 mg of the axial octalol **5a,5b** after short-path distillation at 70–80 °C (0.025 mm), 20 mg of the equatorial octalol **6a,6b,** and 64 mg of unchanged keto ether. The total yield of octalols (axial and equatorial) amounted to 648 mg, which represents an 84% yield based on recovered keto ether (64 mg). It is reasonable to assume that little if any enantiomeric enrichment occurred during this incomplete reaction.

The above axial octalol (568 mg) was further purified by preparative VPC (210 °C) followed by short-path distillation at 70–80 °C (0.05 mm) to give 369 mg of the octalol **5a,5b:** λ_{max}^{film} 2.87 μ (OH); NMR 0.98 (s, 3 H, CH_3 at C-9),[13] 1.1–2.2 (m, 12 H), 1.60 (broad s, 3 H, CH_3 at C-2), 3.77 (m, 1 H at C-5), and 5.32 ppm (broad s, 1 H at C-3).

Anal. ($C_{12}H_{20}O$) C, H.

2,9-Dimethyl-Δ^2-*anti*-5-*trans*-octalol[26] (6a,6b). The method described above for the preparation of the axial octalol **5a,5b** was used. Thus cleavage of the side chain of 410 mg (1.64 mmol) of the equatorial keto ether **18a,18b** with lithium and ethylamine gave a mixture of 162 mg (64% yield based on 60 mg of recovered keto ether) of the equatorial octalol (90% pure by VPC) and 60 mg of unreacted keto ether after separation by preparative TLC. Further purification of the octalol by preparative VPC (210 °C) followed by short-path distillation at 75–85 °C (0.05 mm) afforded 95 mg of pure equatorial octalol **6a,6b** as a colorless oil: λ_{max}^{film} 2.95 (OH), and 9.70 μ (C-O); NMR 0.79 (s, 3 H, CH_3 at C-9),[13] 1.0–2.5 (m, 11 H), 1.60 (s, 3 H, CH_3 at C-2), 3.29 (sextet, J_A = 5 Hz, J_B = 2 Hz, 1 H at C-5), and 5.33 ppm (broad s, 1 H at C-3).

Anal. ($C_{12}H_{20}O$) C, H.

2,9-Dimethyl-Δ^2-5-*trans*-octalone[27] (7a,7b). A. From the Axial Octalol 5a,5b. A solution of 360 mg (2.00 mmol) of the pure axial octalol **5a,5b** in 21 ml of acetone under nitrogen was cooled to 0 °C while 0.60 ml (2.40 mmol) of Jones reagent[14,28] was added over a period of 2 min. The mixture was stirred at 0 °C for 5 min, then isopropyl alcohol followed by water was added. Ether extraction[24] followed by short-path distillation at 60–70 °C (0.05 mm) afforded 313 mg (88% yield) of octalone **7a,7b** as a colorless oil: λ_{max}^{film} 5.85 μ (C=O); NMR 0.74 (s, 3 H, CH_3 at C-9), 1.62 (broad s, 3 H, CH_3 at C-2), 1.65–2.35 (m, 11 H), and 5.34 ppm (broad s, 1 H at C-3); ORD, see Table I.

Anal. ($C_{12}H_{18}O$) C, H.

B. From the Equatorial Octalol 6a,6b. Utilizing the procedure described above for the oxidation of the axial octalol **5a,5b,** 55 mg of the pure equatorial octalol **6a,6b** was converted by oxidation with Jones reagent and purified by short-path distillation at 55–65 °C (0.025 mm) to afford 49 mg (90% yield) of the octalone **7a,7b.** The ir and NMR spectra of this material were identical with those of the axially derived octalone described above. The ORD data are reported in Table I.

2,9-Dimethyl-Δ^2-*trans*-octalin (19). The Huang-Minlon modification[15] of the Wolff–Kishner reaction was employed. This procedure was further modified by first conducting the hydrazone formation at 0 °C for 12 h in the absence of base.[17] A solution of 285 mg (1.60 mmol) of the aforementioned axially derived octalone **7a,7b** in 18 ml of triethylene glycol (under nitrogen) was cooled in an ice bath while 2.77 ml (2.80 g, 85 mmol) of 97% hydrazine was added. The solution was swirled and allowed to stand at 0 °C for 12 h. To this solution was then added 285 mg (4.3 mmol) of 85% potassium hydroxide, and the flask was fitted with a micro-distilling head and receiver. The mixture was heated under nitrogen for 1 h at 100–110 °C, 3 h at 200–210 °C, then cooled. The combined residue and distillate were partitioned between 75 ml of pentane and 75 ml of water. The aqueous phase was acidified with hydrochloric acid and extracted with several portions of pentane. The combined organic layers were washed with water, dried, and concentrated by distillation through a Vigreux column at atmospheric pressure. The remaining traces of pentane were removed by rotary evaporation (150 mm), thereby yielding 254 mg (97% yield) of a colorless oil consisting of 81% of the *trans*-octalin **19** and 19% of the cis isomer as determined by analytical VPC. Separation of this mixture by preparative VPC followed by short-path distillation at 95–105 °C (25 mm) afforded 176 mg (67% yield) of pure *trans*-octalin **19**: NMR 0.78 (s, 3 H, CH_3 at C-9), 1.0–2.0 (broad m, 13 H), 1.60 (broad s, 3 H, CH_3 at C-2), and 5.25 ppm (broad s, 1 H at C-3).

Anal. ($C_{12}H_{20}$) C, H.

Conversion of the *trans*-Octalin 19 into *trans*-8-Methylhydrindan-2-one (22). A. Ozonolysis.[29] A solution of 166 mg (1.01 mmol) of pure octalin **19** from the previous experiment in 16 ml of absolute methanol was treated with excess ozone at −78 °C. The methanol was removed at reduced pressure to give a viscous oil which was heated under reflux for 1 h with 15 ml of a 3:2:1 mixture of acetic acid, water, and 30% hydrogen peroxide.[30] An additional 5 ml of 30% hydrogen peroxide was added and refluxing continued for an additional 1 h. The resulting clear solution was concentrated to ca. 2 ml under reduced pressure, taken up in 75 ml of freshly distilled ethyl acetate, washed twice with brine, and dried over anhydrous magnesium sulfate. The solvent was removed by rotary evaporation to give 235 mg of a colorless oil which was dissolved in 50 ml of ether and extracted with several 5-ml portions of sodium bicarbonate solution. The combined basic extracts were acidified with hydrochloric acid and extracted with ethyl acetate[24] to afford 204 mg (95% yield) of the keto acid **20** as a colorless oil: λ_{max}^{film} 2.8–3.2, 3.6–3.9 (OH), 5.85 (C=O), and 7.10 μ (CO_2H).

B. Hypobromite Oxidation.[18] A sodium hypobromite solution was prepared by adding 1.10 g (6.89 mmol) of bromine dropwise to a solution of 0.92 g (23 mmol) of sodium hydroxide in 13.5 ml of water at −10 °C and stirring the resulting solution for 10 min at −10 °C. A solution of 188 mg (0.89 mmol) of the crude keto acid **20** in 22 ml of water was titrated to neutrality with 10% aqueous sodium hydroxide. The resulting solution was cooled to 0 °C while 10 ml (9.9 mmol) of the sodium hypobromite solution was added dropwise. The solution was stirred at 0 °C for 6 h, then 3 g of sodium sulfite was added, and the solution was heated at reflux for 45 min. The yellow solution was concentrated to ca. 15 ml by distillation at atmospheric pressure, acidified with hydrochloric acid, and extracted with freshly distilled ethyl acetate[24] to give 150 mg of a colorless, viscous oil. Preparative TLC (1:12 acetic acid–chloroform, R_f 0.39) gave 40 mg (21% yield) of the diacid **21** as a white, waxy solid: mp 174–194 °C; λ_{max}^{KBr} 2.8–3.3, 3.7–3.9 (OH), 7.10 (CO_2H), and 7.68 μ (CO_2H). The infrared spectrum and R_f of this material were nearly identical with those of an authentic sample.[31]

C. Cyclization of the Diacid 21.[19] A mixture of 30 mg (0.14 mmol) of the diacid **21** and 55 mg (0.21 mmol) of lead carbonate was sealed in a piece of 7-mm Pyrex tubing and then pyrolyzed for 30 min at 305 °C. The yellow pyrolysate was twice submitted to short-path distillation at 95–105 °C (15 mm) to afford 10 mg (47% yield) of hydrindanone **22** as a colorless oil: ORD[11b] $[\Phi]_{589}$ +396°, $[\Phi]_{325}$ +10 208°, $[\Phi]_{313}$ +8824°, $[\Phi]_{303}$ +1464°, $[\Phi]_{295}$ −4987°, $[\Phi]_{286}$

$-7755°$, $[\Phi]_{279}$ $-8111°$ (*c* 0.175). The shape of the ORD curve, the ir spectrum, and the VPC retention time of this product were essentially identical with the corresponding properties of an authentic sample of (+)-*trans*-8-methylhydrindan-2-one:[21] ORD $[\Phi]_{589}$ +450°, $[\Phi]_{325}$ +12 350°, $[\Phi]_{314}$ +10 700°, $[\Phi]_{303}$ +1920°, $[\Phi]_{296}$ −5910°, $[\Phi]_{286}$ −9350°, $[\Phi]_{278}$ −9700° (*c* 0.270).

Cyclization of Acetal 1 in Ultradry Pentane. A solution of 2.07 g (7.94 mmol) of stannic chloride in 98 ml of ultradry pentane (distilled from sodium and stored over clean sodium) was cooled to 0 °C and stirred while a solution of 1.00 g (3.97 mmol) of acetal **1** in 98 ml of ultradry pentane was added. The mixture was allowed to warm to room temperature and stirring was continued until aliquots showed complete disappearance of acetal (215 h). After addition of 150 ml of 1 N hydrochloric acid, the product was isolated as described above for the cyclization in benzene to give 830 mg (83% yield) of a colorless oil after short-path distillation at 80–110 °C (0.025 mm). This material was chromatographed on 85 g of Florisil to afford 381 mg (38% yield) of the axial hydroxy ether **15a,15b** and 200 mg (20% yield) of the equatorial hydroxy ether **16a,16b.**

The axial hydroxy ether **15a,15b** was subjected to side-chain degradation and Jones oxidation as described above to afford octalone **7a,7b;** ORD[11b] (see Table I). Similarly, the equatorial hydroxy ether **16a,16b** was converted to octalone **7a,7b;** ORD[11b] (see Table I).

Cyclization of Acetal 1 in Nitromethane. A solution of 1.89 ml (4.21 g, 16.2 mmol) of stannic chloride in 200 ml of nitromethane was cooled to 0 °C and stirred under nitrogen while a solution of 2.04 g (8.10 mmol) of acetal **1** in 200 ml of nitromethane was added. The resulting solution was stirred for 3 min at 0 °C, then 200 ml of 1 N hydrochloric acid was added and the product isolated as described above for the cyclization in benzene. Short-path distillation at 90–105 °C (0.05 mm) gave 1.93 g of hydroxy ether mixture which was subjected to side-chain cleavage without purification.

Oxidation of 1.90 g of this material with Jones reagent as described above afforded 1.74 g (92% yield) of a colorless oil after short-path distillation at 50–100 °C (0.05 mm). VPC analysis (190 °C) indicated this material to be composed of 79% of the axial keto ether **17a,17b,** 9% of the equatorial keto ether **18a,18b,** and 11.5% of octalone **7a,7b.** Redistillation at 50–65 °C (0.05 mm) gave 121 mg of an oil consisting primarily of the octalone **7a,7b.** Further distillation at 65–100 °C (0.05 mm) gave 1.58 g of a mixture of keto ethers. Reduction of 1.55 g of this keto ether mixture with lithium and ethylamine as described above afforded 1.14 g of a colorless oil after short-path distillation at 80–110 °C (0.05 mm). Preparative TLC (3:1 pentane–ether) followed by preparative VPC yielded 215 mg of the equatorial octalol **6a,6b** (99% pure by VPC) and 415 mg of axial octalol **5a,5b** (99% pure by VPC). Oxidation of 294 mg of the latter octalolwith Jones reagent gave 261 mg (90% yield) of purified (see above) octalone **7a,7b** after short-path distillation at 55–65 °C (0.05 mm); ORD (see Table I). A sample of this octalone was converted, according to the procedure described above, into the hydrindanone **22:** ORD $[\Phi]_{589}$ +403°, $[\Phi]_{325}$ +6604°, $[\Phi]_{314}$ +5776°, $[\Phi]_{303}$ +1076°, $[\Phi]_{296}$ −2903°, $[\Phi]_{286}$ −4572°, $[\Phi]_{278}$ −4847° (*c* 0.113). The ORD molecular amplitude (a = +114.5) was 52.0% of the amplitude (a = +220.5) of the ORD curve from the pure (+) enantiomer of hydrindanone **22,** corresponding to a composition of 76% **12** and 24% of its optical antipode.

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References and Notes

(1) For recent papers in this series, see (a) G. D. Abrams, W. R. Bartlett, V. A. Fung, and W. S. Johnson, *Bioorg. Chem.,* **1**, 243 (1971); (b) A. van der Gen, K. Wiedhaup, J. J. Swoboda, H. C. Dunathan, and W. S. Johnson, *J. Am. Chem. Soc.,* **95**, 2656 (1973); (c) W. S. Johnson, K. Wiedhaup, S. F. Brady, and G. L. Olson, *Ibid.,* **96**, 3979 (1974). (d) A preliminary account of the present work has appeared: W. S. Johnson, C. A. Harbert, and R. D. Stipanovic, *Ibid.,* **90**, 5279 (1968).

(2) National Institutes of Health Postdoctoral Fellow, 1967–1969.

(3) W. S. Johnson, *Acc. Chem. Res.,* **1**, 1 (1968).

(4) W. S. Johnson and R. B. Kinnel, *J. Am. Chem. Soc.,* **88**, 3861 (1966).

(5) The previous synthesis of *trans*-dienic acetal **2** was accomplished by employing the nonstereoselective Wittig reaction. For details see ref 1b.

(6) S. F. Brady, M. A. Ilton, and W. S. Johnson, *J. Am. Chem. Soc.,* **90**, 2882 (1968).

(7) Cf. A. P. Krapcho, G. A. Glynn, and B. J. Grenon, *Tetrahedron Lett.,* 215 (1967).

(8) These decarbethoxylations appear to be analogous to the cleavage of esters by halide ion in which nucleophilic attack of the ester alkyl group followed by decarboxylation has been invoked. See inter alia F. Elsinger, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta,* **43**, 113 (1960); D. Y. Chang, C.-F. Yam, S.-Y. Chan, S. H. Lee, and H.-C. Lee, *J. Org. Chem.,* **31**, 3267 (1966); D. Y. Chang, S.-H. Lee, and H.-C. Lee, *ibid.,* **32**, 3716 (1967). The rationale for developing the use of tetramethylammonium acetate, which was first studied in our laboratory by W. Stern, involved the concept of a system with a highly symmetrical transition state in which the entering and leaving nucleophiles (carboxylate anions in the present case) possess a similar degree of "hardness". Cf. R. G. Pearson and J. Songstad, *J. Am. Chem. Soc.,* **89**, 1827 (1967).

(9) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.,* 3363 (1968).

(10) A generous sample of (−)-2,3-butanediol was donated by Dr. Karl L. Smiley, U.S. Dept. of Agriculture, Peoria, Ill. The absolute configuration of this diol is known to be *R,R:* see inter alia L. J. Rubin, H. A. Lardy, and H. O. L. Fischer, *J. Am. Chem. Soc.,* **74**, 425 (1952).

(11) All ORD measurements were determined as dioxane solutions. Average of (a) three determinations, (b) two determinations.

(12) Rate enhancement of reactions involving Lewis acid catalysts due to the presence of traces of water has been well documented: G. A. Olah, "Friedel–Crafts and Related Reactions", Vol. I, Interscience, New York, N.Y., 1963, pp 205–215.

(13) The position of the NMR signal for an angular methyl group at C-9 in compounds having an axial substituent at C-5 is shifted downfield relative to the equatorial isomers as a result of 1,3-diaxial interactions; see R. F. Zurcher, *Helv. Chim. Acta,* **46**, 2054 (1963).

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(16) As shown below this substance contained ca. 92% of that enantiomeric form depicted by the formula.

(17) The amount of cis isomer formed during the Wolff–Kishner reaction (see ref 1b) can be suppressed to about 20% by first conducting the hydrazone formation at 0 °C for 12 h in the absence of base.

(18) According to a modification of the procedure of C. Djerassi and J. Staunton, *J. Am. Chem. Soc.,* **83**, 736 (1961), in which the dioxane was omitted.

(19) Cf. W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg, and L. J. Chinn, *J. Am. Chem. Soc.,* **74**, 2832 (1952).

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(21) An authentic sample of (+)-*trans*-8-methylhydrindan-2-one was generously provided by Professor Carl Djerassi, Stanford University.

(22) For a definition of molecular amplitude, see C. Djerassi and W. Klyne, *J. Chem. Soc.,* 4929 (1962).

(23) The reported value (methanol solvent) is +216 (ref 20).

(24) In cases where products were isolated by solvent extraction, the procedure generally followed was to extract the aqueous layer with several portions of the indicated solvent; then the organic layers were combined and washed with water followed by saturated brine. The organic layer was dried over anhydrous sodium sulfate or magnesium sulfate and filtered, and the solvent was evaporated under reduced pressure (water aspirator) using a rotary evaporator. The use of the term "base wash" or "acid wash" indicates washing the combined organic layers with saturated aqueous sodium bicarbonate solution or with dilute aqueous hydrochloric acid, respectively, prior to the aforementioned washing with water.

(25) It has been shown that the NMR signal for the methyl group in substances $R_1CH{=}CR_2Me$ appears in the range δ 1.58–1.60 for the trans isomers and δ 1.64–1.68 for the cis isomers: R. B. Bates and D. M. Gale, *J. Am. Chem. Soc.,* **82**, 5749 (1960).

(26) The terms syn and anti refer to the relationship of the substituent on the nearer bridgehead (angular) position with that of the hydrogen atom on the position bearing the substituent in question.

(27) During the course of this study, a considerable quantity of the racemic octalone **7a,7b** was required to develop the degradative route to the hydrindanone **22.** Cyclization of the dienal **14** with stannic chloride in nitromethane at 0 °C proved quite suitable for this purpose. In this manner a 5:1 mixture of **5a,5b** and **6a,6b,** respectively, was obtained in 84% yield. Oxidation of this mixture gave octalone **7a,7b** by a simple and efficient route. For another example of a polyolefinic aldehyde cyclization, see R. E. Ireland, M. I. Dawson, J. Bordner, and R. E. Dickerson, *J. Am. Chem. Soc.,* **92**, 2568 (1970).

(28) Cf. C. Djerassi, R. P. Engle, and A. Bowers, *J. Org. Chem.,* **21**, 1547 (1956).

(29) P. S. Bailey, *J. Org. Chem.,* **22**, 1548 (1957).

(30) According to the post-ozonolysis procedure of F. Holloway, H. J. Anderson, and W. Rodin, *Ind. Eng. Chem.,* **47**, 2111 (1955).

(31) An authentic sample of this compound was generously provided by Professor Carl Djerassi, Stanford University.