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Pentacyclic Triterpene Synthesis. 5. Synthesis of Optically Pure Ring AB Precursors[1]

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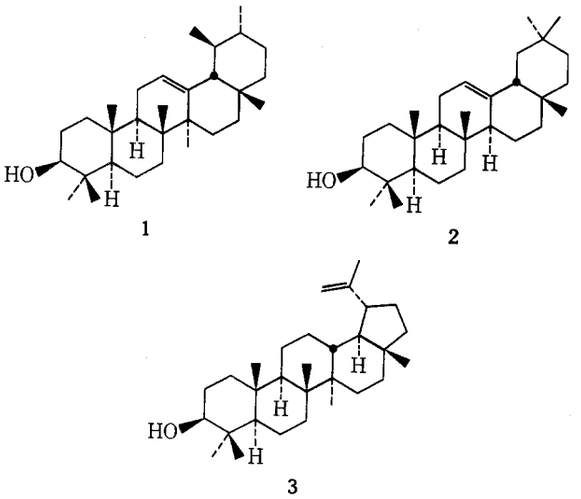
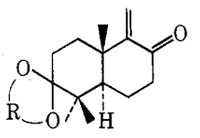
Bicyclic enone **5**, which is a precursor for rings A and B of the pentacyclic triterpenes, has been synthesized in ten steps from enedione **14** in 16% overall yield. Unsaturated keto alcohol **15** has been resolved into its enantiomers and absolute stereostructures assigned. The levorotatory enantiomer of **5** has the absolute configuration corresponding to that of the pentacyclic triterpenes.

In contrast to the massive amount of research which has been directed toward the total synthesis of the lower terpenes and steroids,[2] relatively little attention has been paid to triterpenes.[3] This lack of interest has been due in part to the fact that the triterpenes are relatively devoid of interesting physiological activity, and in part to their greater complexity. Within the triterpene class,[4] the pentacyclic group is the most numerous and represents the greatest structural complexity. The most notable synthetic achievements to date are Stork's synthesis of lupeol,[5] Ireland's syntheses of alnusenone[6] and shionone,[7] Ireland and Johnson's synthesis of germanicol,[8] van Tamelen's synthesis of tetrahymanol,[9] and Prestwick and Labovitz's synthesis of serratenediol.[10] In addition, van Tamelen has reported a biogenetic synthesis involving cyclization of a bicyclic polyolefinic epoxide which affords a mixture of δ-amyrin, β-amyrin, and germanicol.[11]

In most of the pentacyclic triterpenes, rings A and B are the same; the differences occur mainly in rings C, D, and E, as illustrated below with α-amyrin (**1**), β-amyrin (**2**), and lupeol (**3**). We have initiated a convergent synthetic approach in which preformed AB and DE synthons would be coupled together, and then ring C would be closed. In such an approach, the same AB synthon might serve for the synthesis of a variety of the triterpenes. Our candidate for a general AB synthon is the bicyclic enone **5**. In this paper, we report the synthesis, in racemic form, of enones **4** and **5**, and in optically pure form of enone **5**.



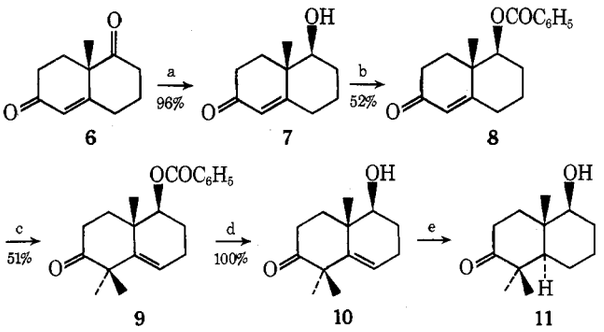
1 **2** **3**



4, R = $-CH_2CH_2-$
5, R = $-CH_2C(CH_3)_2CH_2-$

As a precursor to enones **4** and **5**, we chose keto alcohol **11**, which had previously been prepared by Sondheimer and Elad (Chart I).[12] However, in our hands, this route to **11** proved exceptionally tedious. In particular, the hydrogenation of **10** to **11** is erratic. Unless **10** is scrupulously purified (column chromatography), diol **12** is a major product of the hydroge-

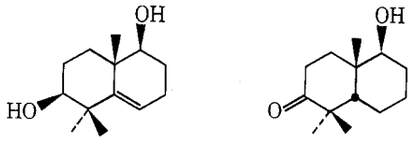
Chart I



6 **7** **8** **9** **10** **11**

a, $NaBH_4$, EtOH; b, C_6H_5COCl, pyridine; c, *t*-BuOK, CH_3I; d, KOH, EtOH; e, H_2, Pd/C, EtOH.

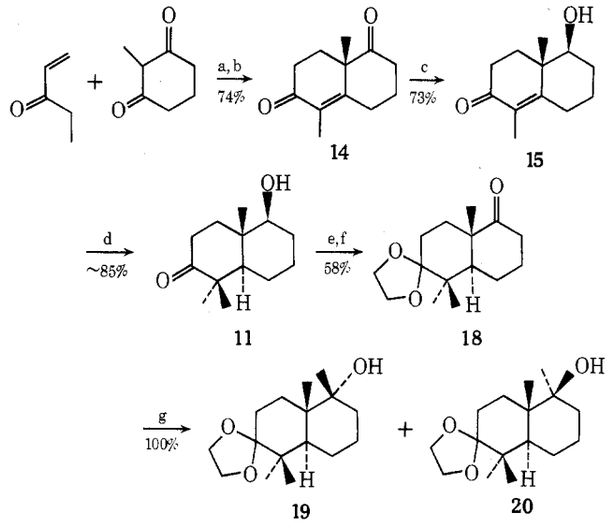
nation. Even when **10** is carefully purified, the reduction is slow and large amounts of catalyst are required (50–100 weight percent), and some cis keto alcohol **13** is often obtained.



12 **13**

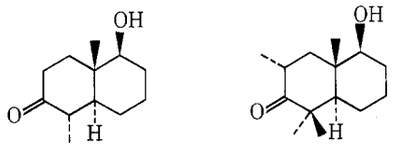
To circumvent these problems, we developed an alternate synthesis of **11**, which is both shorter and more reliable (Chart II).[13] Dimethyloctalindione **14** is produced by Robinson an-

Chart II



a, KOH, CH_3OH; b, pyrrolidine, benzene; c, $NaBH_4$, EtOH; d, Li, NH_3, CH_3I; e, $HOCH_2CH_2OH$, β-$NpSO_3H$, benzene; f, bispyridinechromium(VI) oxide, CH_2Cl_2; g, CH_3Li, ether.

nelation of 2-methyl-1,3-cyclohexanedione with ethyl vinyl ketone. Selective reduction of the saturated carbonyl in **14** affords the crystalline keto alcohol **15** in 73% yield. Reductive methylation of **15** by a modification of Stork's procedure[14] affords keto alcohol **11**, along with about 8% of the reduced, unalkylated keto alcohol **16** and 8% of dialkylated keto alcohol

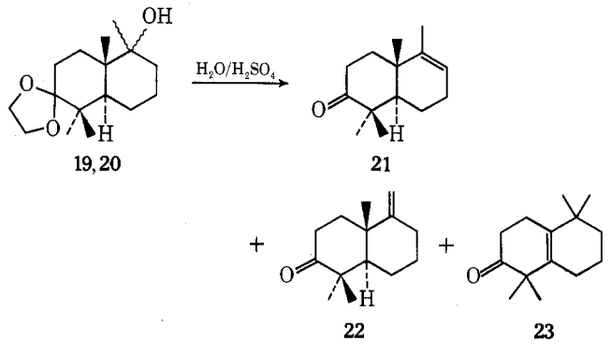


16 **17**

17. Ketalization of the crude product from reductive methylation affords a crystalline hydroxy ketal, which is oxidized to ketone **18**. This ketone reacts with methyllithium in ether at −78 °C to give a 3:2 mixture of tertiary alcohols **19** and **20**.

The stereochemistry of the tertiary carbinol center in alcohols **19** and **20** was assigned using the NMR shift reagent tris(2,2,6,6-tetramethylheptane-3,5-dionato)europium(III).[15] Upon addition of shift reagent, the resonance due to the angular methyl group shifted downfield much more for the minor isomer (**20**) than for the major isomer (**19**).[16]

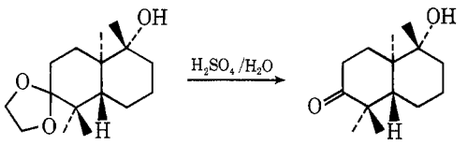
Acid-catalyzed dehydration of the mixture of **19** and **20** (aqueous H_2SO_4/pentane or CCl_4, heterogeneous) affords a mixture of olefins **21**, **22**, and **23**. The amount of exocyclic olefin **22** and rearranged olefin **23** produced was found to be



19,20 **21** **22** **23**

dependent on the concentration of acid used in the dehydration and upon the organic solvent used as second phase. Results are tabulated in Table I. For dehydration of the racemic mixture of **19** and **20**, 25% H_2SO_4/H_2O proved to be optimal. Using stronger acid gave more rearranged product, and also caused subsequent rearrangement of **21** to **22**. For example, after 1 h using 50% H_2SO_4/H_2O, the ratio of **23** to **21** had increased to 73:27. However, with more dilute acid, the initial dehydration product is unchanged even after much longer reaction times.

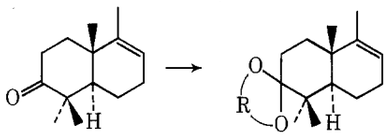
A practical problem arose when we attempted the aqueous H_2SO_4/pentane dehydration of enantiomerically pure samples of **19** and **20** (vide infra). For example, attempted dehydration of the 4a*R* alcohol **20a** in this system resulted in the rapid



20a **24**

precipitation of keto alcohol **24**. Because of its low solubility in pentane, no dehydration occurred. For the optically active series, CCl_4 was found to be a suitable organic phase, the optimum acid strength being 35% (Table I).

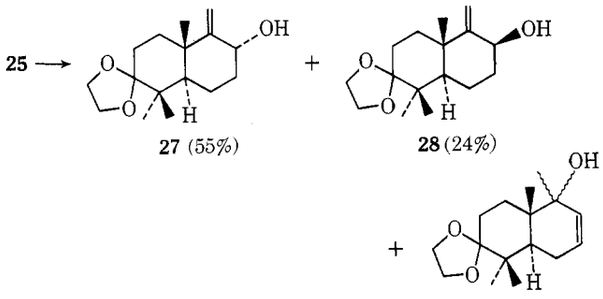
Ketalization of the crude dehydration product, followed by crystallization, gave pure ketals **25** or **26** in 54–58% yield, based on alcohols **19–20**.



21

25, R = $-CH_2CH_2-$
26, R = $-CH_3C(CH_3)_2CH_2-$

We completed the synthesis of enones **4** and **5** by two methods. Initially, we examined the reaction of olefin **25** with singlet oxygen. Oxygenation of **25** using rose bengal as sensitizer gave a mixture of allylic alcohols **27–29** in the ratio indicated. Alcohols **27** and **28** were separated and their stere-

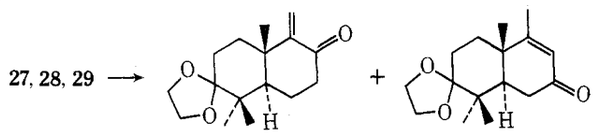


27 (55%) **28** (24%)

29 (21%)

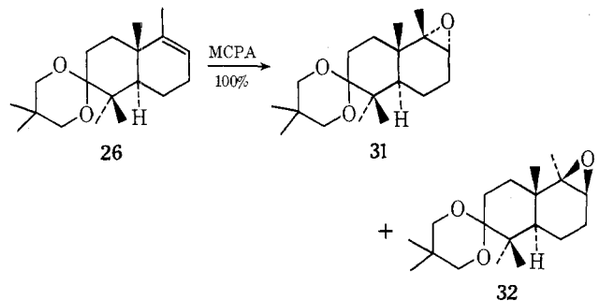
ostructures were assigned on the basis of their NMR spectra. The carbinol proton resonances in **27** and **28** have half-height bandwidths ($W_{1/2}$) of 21 and 5 Hz, respectively. Thus, the hydroxyl group in **27** is equatorial, while that in **28** is axial.[17]

Oxidation of the mixture of **27, 28,** and **29** with bispyridinechromium(VI) oxide in methylene chloride[18] affords a mixture of enones **4** and **30** in a ratio of 3:1. After chromatog-

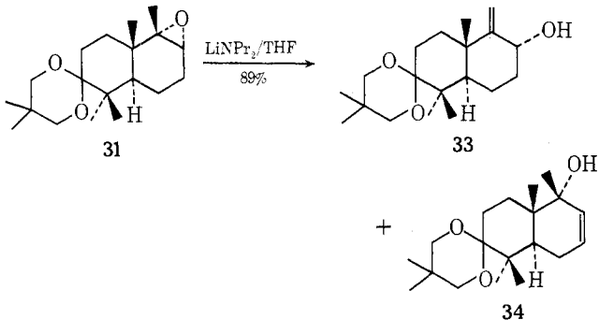


raphy, the enones were isolated in yields of 39 and 13%, respectively, based on olefin **25.** The oxidation of tertiary allylic alcohol **29** to enone **30,** which involves allylic rearrangement of the intermediate chromate ester, is well precedented.[19]

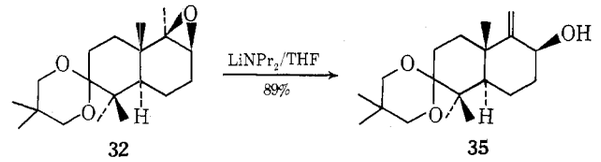
Alternatively, olefin **26** may be epoxidized by *m*-chloroperoxybenzoic acid to an equimolar mixture of epoxides **31**



and **32.** Samples of the two pure epoxides were obtained by fractional crystallization in order to study the base-catalyzed ring-opening reaction. Epoxide **31** reacted with lithium di-*n*-propylamide in refluxing THF[20] for 4 h to give a 3:2 mixture of alcohols **33** and **34** in 94% yield. Epoxide **32** reacted more



slowly under these conditions, requiring 6 h for completion, but gave only isomer **35** in 89% yield. As in the case of alcohols **27** and **28,** stereostructures were assigned to alcohols **33** and



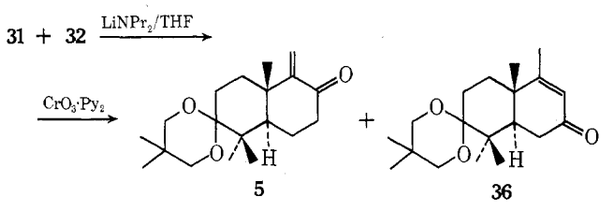
35 on the basis of the half-height bandwidths of the carbinol resonances ($W_{1/2}$ = 21 and 5 Hz, respectively).

When the crude mixture of epoxides **31** and **32** is treated with lithium di-*n*-propylamide, and the resulting mixture of alcohols oxidized with bispyridinechromium(VI) oxide, enones **5** and **36** are obtained in a ratio of 71:29. After chromatography, enone **5** is obtained in 58% yield, based on olefin **26.** Thus,

Table I. Dehydration of Alcohols 19 and 20

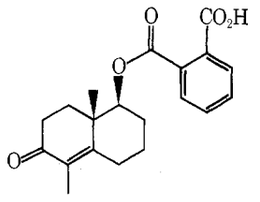
Acid concn,[a] %	Organic phase	Reaction time, min[b]	Product analysis, % 21	22	23
50	Pentane	5	44	0	56
30	Pentane	90	88	4	8
25	Pentane	420	89	6	5
20	Pentane	60	No dehydration		
50	CCl_4	30	76	0	24
40	CCl_4	150	88	3	9
35	CCl_4	450	87	5	8
30	CCl_4	180	No dehydration		

[a] Volume/volume H_2SO_4/H_2O in aqueous phase. [b] Reactions were followed to complete disappearance of starting material by GLC. Time cited is for complete reaction.



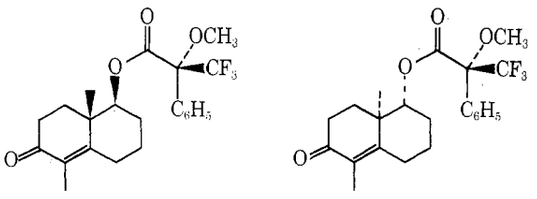
the most efficient route to enone **5** (**14** → **15** → **11** → **18** → **19** + **20** → **21** → **26** → **31** + **32** → **33** + **35** → **5**) requires ten steps and affords **5** in 16% overall yield.

Unsaturated keto alcohol **15** was converted to the hydrogen phthalate **37,** which was resolved via the brucine salt. A pure



dextrorotatory salt was obtained after four recrystallizations from acetone. Careful acidification of this salt afforded (+)-**37** ([α]D 176.2°), which was hydrolyzed with 5 N aqueous KOH (see Experimental Section) to afford (+)-**15** ([α]D +162.7°). The mother liquors from recrystallization of the brucine salt of **37** were acidified to obtain levorotatory **37.** After recrystallization, (−)-**37** ([α]D −171.6°) was obtained. Alkaline hydrolysis of this material afforded (−)-**15** ([α]D −164.4°). Overall yields for the resolution were 31% for (+)-**15** and 28% for (−)-**15.** It is interesting that racemic **15** is a crystalline solid with mp 88–89 °C, and the pure enantiomers are liquids at room temperature.

Optical purities for the resolved alcohols were determined by Mosher's method,[21] using the (+)-α-methoxy-α-trifluoromethylphenylacetyl esters **38** and **39.** Analysis was accom-



plished with the methoxy ^1H NMR resonances (δ 3.44 and 3.37 ppm for isomers **38** and **39,** respectively) and the CF_3 ^{19}F NMR resonances (−7.65 and −7.49 ppm from trifluoroacetic acid for isomers **38** and **39,** respectively. Both enantiomers were found to be ≥94% optically pure.[22]

Absolute stereostructures were assigned to (+)-**15** and (−)-**15** on the basis of their circular dichroism spectra. The dextrorotatory enone shows a strong positive $\pi \rightarrow \pi^*$ Cotton effect and a weak negative $n \rightarrow \pi^*$ Cotton effect.[23] On the basis of analogy to similar enones of known structure,[24] (+)-**15** may therefore be assigned the (4a*S*,5*S*) configuration.

Optically pure (−)-**15** ([α]D −164.4°) has been converted, by the sequence of reactions discussed earlier in the paper, into optically pure enone (+)-**5** ([α]D +66.9°) via (+)-**18** ([α]D +51.8°) and (−)-**26** ([α]D −14.3°). Thus, the levorotatory enantiomer of enone **5** ([α]D −67°) has the absolute configuration corresponding to that of the pentacyclic triterpenes.

Experimental Section

Melting points (Pyrex capillary) are uncorrected. The following instrumentation was used to record spectra: infrared (ir), Perkin-Elmer 137 and 237; ultraviolet (uv), Perkin-Elmer 202; mass spectra, Varian MS-12; high-resolution mass spectra, Consolidated 21-110B; optical rotations, Carl Zeiss polarimeter; circular dichroism (CD), Cary Model 60; proton magnetic resonance (^{1}H NMR), Varian T-60. The line positions for the ^{1}H NMR spectra are given in the δ scale as parts per million downfield from internal trimethylsilane. Significant ^{1}H NMR data are tabulated in the order (number of protons, multiplicity, proton assignments). Gas–liquid partition chromatography (GLC) analyses were performed on a Varian Aerograph 90-P instrument. Brinkmann Silplates (PSF-22, 0.5 mm thickness, 20 × 20 cm) were used for preparative thin layer chromatography (preparative TLC). Elemental analysis were performed by the Microanalytical Laboratory, operated by the College of Chemistry, University of California, Berkeley, Calif.

(±)-1,4a-Dimethyl-4,4a,7,8-tetrahydronaphthalene-2,5-(3*H*,6*H*)-dione (14). A solution of 73.1 g (0.58 mol) of methyldihydroresorcinol,[25] 75.3 g (0.90 mol) of ethyl vinyl ketone, and 225 ml of methanol was made basic with potassium hydroxide pellets and then refluxed for 4 h. The solvent and excess ethyl vinyl ketone were removed on a rotary evaporator at room temperature, using benzene as an azeotroping agent.

The yellow residue was dissolved in 380 ml of benzene, and 5.6 ml (65 mmol) of pyrrolidine was added. After refluxing the solution for 16 h with water separation (Dean-Stark trap), it was cooled, washed with 5% hydrochloric acid, water, and saturated brine, dried ($MgSO_4$), and evaporated. The light-red oil (117 g) was distilled to give 82.3 g (74%) of yellow oil, bp 133–160 °C (0.4 Torr). Crystallization from ethyl acetate/hexane gave the analytical sample: mp 46.0–47.5 °C; ir (CCl_4) 1701, 1650, 1590, 1447, 1437, 1346, 1323, 1304, 1235, 1106, 1007 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.42 ppm (3 H, s, angular CH_3), 1.72 ppm (3 H, s, vinyl CH_3).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.85; H, 8.20.

(±)-1,4aβ-Dimethyl-5β-hydroxy-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (15). A solution of 1.05 g (0.11 equiv) of sodium borohydride in 240 ml of absolute ethanol was added over 3 h to a stirring solution of 20.0 g (0.10 mol) of **14** and 120 ml of absolute ethanol cooled in an ice bath. After an additional 20 min the excess hydride was destroyed by slowly adding 2.2 ml of acetic acid. The solvent was evaporated and the residue was taken up in chloroform. After washing with water and drying over $MgSO_4$, the solvent was evaporated to give 23.8 g of yellow oil which crystallized upon standing. Recrystallization from hexane/acetone gave 14.8 g (73.4%) of white crystals, mp 86–89 °C. A second recrystallization gave the analytical sample: mp 88–89 °C; ir (CCl_4) 3480, 1680, 1600, 1000 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.14 (3 H, s, angular CH_3), 1.70 (3 H, s, vinyl CH_3).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.89; H, 9.31.

(±)-1,4aβ-Dimethyl-5β-hydroxy-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one Hydrogen Phthalate (37). A mixture of 1.00 g (5.15 mmol) of (±)-**15**, 0.79 g (5.30 mmol) of phthalic anhydride, and 1.9 ml of pyridine was stirred under nitrogen for 68 h. The solution was then poured into ice and 10% hydrochloric acid, and the white precipitate removed by filtration and recrystallized from acetone to afford 1.45 g (82.5%) of white solid: mp 186–189 °C; ir ($CDCl_3$) 1706, 1656, 1351, 1299, 943 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.28 (3 H, s, angular CH_3), 1.80 (3 H, s, vinyl CH_3), 4.86 (1 H, m, C-5 H).

Anal. Calcd for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 69.99; H, 6.34.

Resolution of 37. To a solution of 24.0 g (70.2 mmol) of (±)-**37** dissolved in 400 ml of boiling acetone was added 27.6 g (70.0 mmol) of brucine hydrate dissolved in 100 ml of acetone. The solvent volume was reduced to 150 ml and the solution refrigerated to induce crystallization. The solid which formed was isolated and then recrystallized to constant rotation (twice more): [α]^{25}D +18.8° (*c* 4.00, $CHCl_3$).

A solution of 21.0 g (28.6 mmol) of the dextrorotatory brucine salt dissolved in 300 ml of acetone was poured with rapid stirring into 600 ml of ice and water containing 25 ml of 5% hydrochloric acid. After 1 h, the solid was removed by filtration and dried. Crystallization from acetone to constant rotation gave 8.99 g (76% from (±)-**37** based on one enantiomer) of crystals: mp 190–192.5 °C; [α]^{25}D +172.6 ° (*c* 2.01, $CHCl_3$).

To a magnetically stirred suspension of 8.8 g (25.7 mmol) of (+)-**37**, 50 ml of water, and 50 ml of ether cooled to 5 °C was slowly added 50 ml of 40% potassium hydroxide. The reaction flask was fitted with a continuous extractor and magnesium sulfate was added to the receiving flask (to precipitate any base dissolved in the ether during the extraction). The ice bath was removed and the solution was extracted with ether for 24 h. The organic solution was filtered and evaporated to give 5.2 g (100%) of (+)-**15** as a yellow oil: [α]^{25}D +162.6° (*c* 2.17, $CHCl_3$); uv (MeOH) λ_{max} 250 nm (ε 14,740); CD (MeOH) [θ] 37 100 (247 nm), −5500 (319 nm).[23]

The mother liquors from the resolution were combined and stripped of solvent to give a brownish semisolid. A solution of 2.97 g (4.04 mmol) of this salt dissolved in 15 ml of acetone was treated as described for the salt of the dextrorotatory acid to give 1.28 g (68% from (±)-**37**, based on one enantiomer) of white solid: mp 190.5 °C; [α]^{25}D −174.5° (*c* 2.02, $CHCl_3$). This acid (8.1 g, 24.7 mmol) was hydrolyzed as described previously to yield 4.8 g (100%) of (−)-**15** as a yellow oil: [α]^{25}D −164.6° (*c* 2.16, $CHCl_3$); uv (MeOH) λ_{max} 250 nm (ε 12 850), 309 (81); CD (MeOH) [θ] −24 800 (247 nm), +4780 (320 nm).[23]

1,4aβ-Dimethyl-5β-hydroxy-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one α-Methoxy-α-trifluoromethylphenylacetate (38 and 39). Into a 10 × 75 mm oven-dried test tube fitted with a rubber septum were syringed the following compounds: 300 μl of anhydrous pyridine, 45 mg (30 μl, 0.18 mmol) of (+)-α-methoxy-α-trifluoromethylphenylacetyl chloride[21] dissolved in 150 μl of carbon tetrachloride, and 21 mg (0.11 mmol) of (±)-**15** dissolved in 150 μl of carbon tetrachloride. The tube was shaken and allowed to stand at room temperature for 2 h, after which 100 μl of 3-dimethylamino-1-propylamine was added. After 5 min, the solution was diluted with 10 ml of ether, washed with cold 5% hydrochloric acid, cold 5% sodium bicarbonate, and saturated brine, dried ($MgSO_4$), and evaporated. The procedure was repeated using samples of (+)-**15** and (−)-**15**.

The ^{1}H NMR spectra of each of the three ester samples were measured at 60 MHz for ^{1}H and at 56.4 MHz for ^{19}F. The relevant shifts and assignments for compounds **38** (+,+ ester) and **39** (−,+ ester) are summarized in Table II. The ester produced from (±)-**15** was found to be a mixture of 63% **38** and 37% **39**, indicating that (+)-**15** undergoes esterification more rapidly than (−)-**15**. The esters produced from (+)-**15** and (−)-**15** were found to have the following diastereomeric composition (% **38**, % **39**): (+)-**15** (96.2, 3.8); (−)-**15** (12.6, 87.4). These crude values were corrected for the greater reactivity of (+)-**15** to obtain enantiomeric purities of the resolved alcohols of ≥94% each.

5β-Hydroxy-1,1,4aβ-trimethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3H)-one (11). An apparatus consisting of a three-necked flask, a dry ice condenser, and a pressure-equalizing dropping funnel was oven dried and assembled, along with a magnetic stirrer and a nitrogen bubbler. Liquid ammonia (700 ml) was distilled from lithium into the flask immersed in a dry ice/isopropyl alcohol bath. Lithium wire (1.37 g, 196.0 mmol) was added, the bath was removed, and stirring was continued for 0.5 h. A solution of 10.0 g (5.15 mmol) of **15** in 100 ml of anhydrous THF was added dropwise over 0.5 h. After another 0.5 h, 50 ml (540 mmol) of methyl iodide was added as rapidly as possible. Violent reaction was observed until the blue color was discharged. One minute after addition was complete the white heterogeneous mixture turned clear and lithium iodide slowly precipitated. After 15 min, solid ammonium chloride was added, the condenser was replaced with a water-cooled condenser, and 300 ml of ether was added. The ammonia was evaporated, the residue washed with 5% hydrochloric acid, and the acid washings extracted with ether. The combined organic solutions were washed with 5% sodium bicarbonate and saturated brine, dried ($MgSO_4$), and evaporated to give 10.8 g (100%) of yellow, viscous oil: ir (CCl_4) 3356, 1701, 1449, 1385, 1366, 1248, 1149, 1057, 862 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.00 (2 × 3 H, s), 1.03 (3 H, s). Mass spectral analysis indicated that little (less than 10%) reduced or trimethylated ketone was present. Several attempts were made to remove these impurities, but all were unsuccessful.

Recrystallization from hexane afforded a crystalline product (mp 54.5–60 °C) which still contained approximately 8% each of hydroxy ketones **16** and **17**.

5β-Hydroxy-1,1,4aβ(*S*)-trimethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one [(4a*S*)-11]. Keto alcohol (+)-**15** (5.6 g, 28.9 mmol) was reduced as described above to afford 6.1 g (100%) of yellow oil.

5β-Hydroxy-1,1,4aβ(*R*)-trimethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one [(4a*R*)-11]. Keto alcohol (−)-**15** (8.3 g, 42.8 mmol) was reduced as described above to afford 9.1 g (100%) of yellow oil.

1,4aβ-Dimethyl-5β-hydroxy-3,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(1*H*)-one (16). Liquid ammonia (60 ml) was distilled from lithium into a flame-dried apparatus consisting of a 100-ml three-necked flask fitted with a dry ice condenser, a nitrogen bubbler, a magnetic stirrer, and a pressure-equalizing dropping funnel. Lithium wire (77 mg, 2.14 mmol) was added, the blue solution was stirred for 0.5 h, and a solution of 1.0 g (5.2 mmol) of **15** in 10 ml of anhydrous THF was slowly added. Another 41 mg (16.9 mmol total) of lithium wire was needed to maintain the blue color during the addition. Thirty minutes after the addition was complete, excess ammonium chloride was added and the ammonia allowed to evaporate overnight. The residue was partitioned between water and ether, the layers separated, and the aqueous phase extracted with ether. The combined organic solutions were dried ($MgSO_4$) and evaporated to give 0.99 g (98%) of slightly yellow oil which crystallized upon standing. The analytical sample was obtained by recrystallization from hexane: mp 83–84.5 °C; ir (KBr pellet) 3990, 1709, 1447, 1058 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3 H, d, J = 7 Hz, C-1 CH_3), 1.07 (3 H, s, angular CH_3), 3.22 (1 H, m, C-5 H).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.41; H, 10.08.

5β-Hydroxy-1,1,4aβ-trimethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one Ethylene Ketal. A stirring solution of 18.2 g (92.2 mmol) of **11**, 50 ml (895 mmol) of ethylene glycol, 1.0 g of β-naphthalenesulfonic acid, and 500 ml of benzene was refluxed for 68 h with water separation (Soxhlet extractor containing calcium hydride). The yellow solution was washed with 5% sodium bicarbonate, water, and saturated brine, dried ($MgSO_4$), and evaporated to give 23.5 g (99.6%) of white-orange solid. Recrystallization from hexane gave the analytical sample: mp 101.5–102.5 °C; ir (CCl_4) 1247, 1087, 868 cm^{-1}; ^1H NMR (CCl_4) δ 0.77 (3 H, s), 0.87 (3 H, s), 0.90 (3 H, s), 3.06 (1 H, m, C-5 H), 3.83 (4 H, s, ketal H's).

Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 71.02; H, 10.19.

5β-Hydroxy-1,1,4aβ(*S*)-trimethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one Ethylene Ketal. Crude keto alcohol (4a*S*)-**11** (6.42 g, 30.6 mmol) was ketalized as described above. After 36 h of reflux, 7.8 g (100%) of yellow solid was isolated.

5β-Hydroxy-1,1,4aβ(*R*)-trimethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one Ethylene Ketal. Crude keto alcohol (4a*R*)-**11** (5.2 g, 24.8 mmol) was ketalized as described above. After 53 h of reflux, 6.3 g (100%) of yellow solid was isolated.

1,1,4aβ-Trimethyl-1,4,4a,7,8,8aα-hexahydronapthalene-2,5(3*H*,6*H*)-dione 2-Ethylene Ketal (18). To a mechanically stirred solution of 90 ml (1.1 mol) of pyridine (distilled from barium oxide) and 1.4 l. of methylene chloride (distilled from phosphorus pentoxide) cooled in ice was added 56 g (0.56 mol) of chromium trioxide (stored over phosphorus pentoxide). The burgundy solution was stirred for 30 min, and then 23.5 g (92.5 mmol) of ketal alcohol dissolved in 100 ml of methylene chloride was added in one portion. After another 15 min, the dark mixture was vacuum filtered through Woelm alumina (activity 4). A small amount of methylene chloride was used to rinse the flask and the alumina. The clear organic solutions were evaporated to give a greenish solid which was recrystallized from hexane to give 13.5 g (57.9% from **11**) of white crystals: mp 121–122 °C; ir (CCl_4) 1709, 1248, 1112, 1103, 909, 865 cm^{-1}; ^1H NMR (CCl_4) δ 0.83 (3 H, s), 1.00 (3 H, s), 1.50 (3 H, s), 3.92 (4 H, s, ketal H's).

Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.16; H, 9.58.

(−)-1,1,4aβ(*S*)-Trimethyl-1,4,4a,7,8,8aα-hexahydronaphthalene-2,5(3*H*,6*H*)-dione 2-Ethylene Ketal [(−)-18]. Crude (4a*S*)-ketal alcohol (11.0 g, 43.4 mmol) was oxidized as described in the preceding procedure. Recrystallization from hexane to constant rotation gave 6.2 g [57.6% from (+)-**15**] of white needles: mp 108–112 °C; $[\alpha]^{24}D$ −53.9° (*c* 2.08, $CHCl_3$).

(+)-1,1,4aβ(*R*)-Trimethyl-1,4,4a,7,8,8aα-hexahydronaphthalene-2,5(3*H*,6*H*)-dione 2-Ethylene Ketal [(+)-18]. Crude (4a*R*)-ketal alcohol (9.6 g, 37.9 mmol) was oxidized as described in the preceding procedure. Recrystallization from hexane to constant rotation gave 5.7 g [50.6% from (−)-**15**] of white needles: mp 105–114 °C; $[\alpha]^{25}D$ +51.8° (*c* 2.00, $CHCl_3$).

Table II. Chemical Shifts for Compounds 38 and 39

Ester	^1H NMR[a] Angular CH_3	Vinyl CH_3	OCH_3	5α-H	^{19}F NMR,[b] CF_3
38	73	104	212	287	−7.65
39	74	104	208	285	−7.49

[a] ^1H NMR shifts given in hertz downfield from internal Me_4Si at 60 MHz. [b] ^{19}F NMR shifts given in parts per million downfield from external trifluoroacetic acid.

5α-Hydroxy-1,1,4aβ,5β-Tetramethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one Ethylene Ketal (19) and 5β-Hydroxy-1,1,4aβ,5α-tetramethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one Ethylene Ketal (20). Methyllithium (1.5 M in ether, 20 ml, 30 mmol) was added to a dry three-necked flask fitted with a nitrogen bubbler, a pressure-equalizing dropping funnel, and a magnetic stirrer. After the solution was cooled in a dry ice/isopropyl alcohol bath, a solution of 1.96 g (7.8 mmol) of **18** in 100 ml of anhydrous ether was added dropwise over 3 h. After 45 min of stirring at room temperature, 50 ml of 5% ammonium chloride was added, the layers were separated and the aqueous phase was extracted with ether. The combined organic solutions were washed with saturated brine, dried ($MgSO_4$), and evaporated to give 2.1 g (100%) of a light yellow oil which solidified upon standing, mp 72–94 °C.

Anal. Calcd for $C_{16}H_{28}O_3$: C, 71.60; H, 10.52. Found: C, 71.33; H, 10.35.

Addition of $Eu(THD)_3$ shift reagent to the solid split the ketal proton ^1H NMR absorptions into two groups, indicating a 3:2 mixture of the two possible isomeric alcohols. Four recrystallizations of the alcohol mixture from hexane gave white crystals: mp 106–111 °C; ir (CCl_4) 3460, 1198, 1138, 1112, 1093 cm^{-1}; ^1H NMR (CCl_4) δ 0.80 (3 H, s), 0.90 (3 H, s), 0.98 (3 H, s), 1.03 (3 H, s), 3.84 (4 H, s, ketal H's). The mother liquors from the first recrystallization were concentrated and another crop of crystals was obtained. Recrystallization three times from hexane gave white crystals: mp 92–98 °C; ir (CCl_4) 1458, 1387, 1370, 1142, 1093 cm^{-1}; ^1H NMR (CCl_4) δ 0.82 (3 H, s), 0.93 (3 H, s), 1.03 (3 H, s), 1.25 (3 H, s), 3.85 (4 H, s, ketal H's).

Each of the separated alcohols was dissolved in carbon tetrachloride, and ^1H NMR spectra were determined after the addition of varying amounts of $Eu(THD)_3$. The chemical shifts of the four methyl resonances and the ketal resonance of each isomer was plotted against the amount of $Eu(THD)_3$ per milligram of each isomer. As expected, the C-5 methyl shifted substantially in both isomers, and the ketal resonance was relatively unaffected in each isomer. Of the remaining three methyl resonances, two were relatively unaffected in each isomer (probably the C-1 methyls). The chief difference occurred in the methyl resonance at δ 1.25 ppm in the minor isomer. This resonance shifted to δ 6 ppm after the addition of 0.8 mg of $Eu(THD)_3$ per milligram of alcohol. Consequently, we assign structure **20** to this isomer.[16]

The methyllithium addition was repeated on enantiomerically pure (+)-**18** and (−)-**18**, giving quantitative yields of the corresponding alcohols (4a*R*)-**19** + **20** and (4a*S*)-**19** + **20**, respectively.

1,1,4aβ,5-Tetramethyl-1,4,4a,7,8,8aα-hexahydronaphthalen-2(3*H*)-one (21). To a stirring solution of 15.7 g (56.8 mmol) of **19** + **20** and 320 ml of pentane was added 320 ml of 30% (volume/volume) sulfuric acid. After 12 h, the organic layer was washed with 5% sodium bicarbonate and satrated brine, dried ($MgSO_4$), and evaporated to afford 11.0 g (85%) of yellow oil. ^1H NMR and GLC analysis indicated a 88:4:8 mixture of **21**, **22**, and **23**. Preparative GLC gave the analytical samples.

Olefin **21**: ir (neat) 1706, 1458, 1381, 1112 cm^{-1}; ^1H NMR (CCl_4) δ 1.05 (3 H, s), 1.07 (3 H, s), 1.10 (3 H, s), 1.63 (3 H, d, $J \approx 2$ Hz, C-5 CH_3), 5.23 (1 H, m, C-6 H).

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.27; H, 10.72.

Olefin **23**: ir (neat) 1715, 1460, 1374, 1355, 1094, 955 cm^{-1}; ^1H NMR (CCl_4) δ 1.03 (6 H, s), 1.10 (6 H, s).

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.38; H, 10.57.

1,1,4aβ(*S*),5-Tetramethyl-1,4,4a,7,8,8aα-hexahydronaphthalen-2(3*H*)-one [(4a*S*)-21]. The foregoing dehydration procedure was repeated using 8.3 g (31.0 mmol) of (4a*S*)-**19** + **20**, 165 ml of carbon tetrachloride, and 165 ml of 35% (volume/volume) sulfuric acid. After 6.75 h, workup gave 6.8 g (100%) of yellow oil. ^1H NMR and GLC

analysis showed a 84:6:10 mixture of (4a*S*)-**21**, (4a*S*)-**22**, and (4a*S*)-**23**.

1,1,4aβ(*R*),5-Tetramethyl-1,4,4a,7,8,8aα-hexahydronaphthalen-2(3*H*)-one [(4a*R*)-21]. Alcohols (4a*R*)-**19** + **20** (6.2 g, 23.1 mmol) were treated as described above to give 4.7 g (99%) of yellow oil. ^{1}H NMR and GLC analysis showed the product to be a 87:5:8 mixture of (4a*R*)-**21**, (4a*R*)-**22**, and (4a*R*)-**23**.

1,1,4aβ,5-Tetramethyl-1,4,4a,7,8,8aα-hexahydronaphthalen-2(3*H*)-one Ethylene Ketal (25). A solution of 54 mg (2.6 mmol) of crude **21**, 1.5 ml (22 mmol) of ethylene glycol, 50 ml of anhydrous benzene, and a trace of β-naphthalenesulfonic acid was stirred and refluxed for 46 h with water separation (Soxhlet extractor containing calcium hydride). The solution was washed with 5% sodium bicarbonate and water, dried ($MgSO_4$), and evaporated to give 62 mg of slightly yellow solid. Recrystallization from methanol gave 35 mg (54% from **18**) of white crystals: mp 107–108 °C; ir (CCl_4) 2882, 1383, 1106, 1095, 1054 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.82 (3 H, s), 0.92 (3 H, s), 1.02 (3 H, s), 1.48 (3 H, s), 3.87 (4 H, s, ketal H's), 5.01 (1 H, m, C-6 H).

Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.61; H, 10.30.

1,1,4aβ,5-Tetramethyl-1,4,4a,7,8,8aα-hexahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal (26). Crude **21** (11.0 g, 51 mmol) was ketalized as described above, using 27.8 g (267 mmol) of 2,2-dimethyl-1,3-propanediol in place of the ethylene glycol. Workup gave 16.6 g of yellowish solid which was recrystallized from methanol to afford 9.9 g (58% from **18**) of fine, white crystals: mp 112–113 °C; ir (CCl_4) 1244, 1106, 1095, 862, 842 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.65 (3 H, s), 0.77 (3 H, s), 0.95 (6 H, s), 1.10 (3 H, s), 3.33 (4 H, complex m, ketal H's), 4.98 (1 H, m, C-6 H).

Anal. Calcd for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 77.84; H, 10.97.

1,1,4aβ(*R*),5-Tetramethyl-1,4,4a,7,8,8aα-hexahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal [(−)-26]. Crude (4a*R*)-**21** (5.8 g, 26.8 mmol) was ketalized as described above to give 8.2 g of yellow solid. Recrystallization from hexane to constant rotation yielded 4.65 g [56.8% from (+)-**18**] of long needles: mp 124–126 °C; $[\alpha]^{25}D$ −14.3° (*c* 2.12, $CHCl_3$).

(+)-1,1,4aβ(*S*),5-Tetramethyl-1,4,4a,7,8,8aα-hexahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal [(+)-26]. Crude (4a*S*)-**21** (6.8 g, 32.9 mmol) was ketalized as described above to give 8.7 g of yellow solid. Recrystallization from hexane to constant rotation yielded 5.4 g [63.0% from (−)-**18**] of fine, white needles: mp 123–125 °C; $[\alpha]^{25}D$ +14.7° (*c* 4.14, $CHCl_3$).

5-Methylene-1,1,4aβ-trimethyl-1,4,4a,5,8,8aα-hexahydronaphthalene-2,6(3*H*,7*H*)-dione 2-Ethylene Ketal (4) and 1,1,4aβ,5-Tetramethyl-1,4,4a,8aα-tetrahydronaphthalene-2,7(3*H*,8*H*)-dione 2-Ethylene Ketal (30). A solution of 1.7 g (6.7 mmol) of **25**, 100 ml of isopropyl alcohol, and 340 mg of rose bengal was placed in an immersion-type photoreactor. Oxygen was bubbled through the deep-red solution while it was photolyzed with a 450-W Hanovia lamp through a Pyrex filter. Analysis (TLC) of the reaction mixture showed only a small amount of starting material after 7 h. Irradiation was continued for an additional 0.5 h, and the alcohol solution was then stirred overnight with 3 g of potassium iodide. The dark mixture was evaporated and the residue taken up in ether, washed with water and 10% sodium thiosulfate, dried ($MgSO_4$), and evaporated. ^{1}H NMR analysis of the yellow oil (1.6 g, 88.8%) showed the product to be a mixture of 55% of **27**, 24% of **28**, and 21% of **29**.

Anhydrous chromium trioxide (3.6 g, 36 mmol) was added under nitrogen to a magnetically stirred solution of 5.8 ml (72 mmol) of anhydrous pyridine and 90 ml of anhydrous methylene chloride. After 20 min, 1.57 g (5.9 mmol) of the foregoing mixutre of **27**, **28**, and **29** dissolved in methylene chloride was added in one portion. After 20 min, the solution was vacuum filtered through Woelm alumina (activity 4) and the clear solution evaporated to give 1.33 g of oil. Column chromatography (60 g silica gel, 40% ether/hexane) gave two compounds.

The early fractions afforded 690 mg (39.4% from **25**) of enone **4**: ir (CCl_4) 2950, 1669, 1623, 1381, 1105, 907, 863 cm^{-1}; uv (MeOH) λ_{max} 227 nm (ϵ 4100); ^{1}H NMR (CCl_4) δ 0.88 (3 H, s), 1.00 (3 H, s), 1.07 (3 H, s), 3.90 (4 H, broad s, ketal H's), 4.91 (1 H, d, J = 2 Hz, vinyl H), 5.10 (1 H, d, J = 2 Hz, vinyl H).

The later fractions yielded 230 mg of enone **30**: ir (CCl_4) 2967, 1706, 1623, 1381, 1282, 1199, 1107, 911, 865 cm^{-1}; uv (MeOH) λ_{max} 239 nm (ϵ 11 800); ^{1}H NMR (CCl_4) δ 0.85 (3 H, s), 1.02 (3 H, s), 1.15 (3 H, s), 2.22 (3 H, s, vinyl CH_3), 3.92 (4 H, broad s, ketal H's), 3.59 (1 H, broad s, vinyl H).

5β,6β-Oxido-1,1,4aβ,5α-Tetramethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal (32) and 5α,6α-Oxido-1,1,4aβ,5β-tetramethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal (31). To a stirring solution of 5.0 g (17.1 mmol) of **26** and 150 ml of chloroform was added 5.6 g (26.9 mmol) of *m*-chloroperoxybenzoic acid. After 2 h, the solution was washed with 10% potassium hydroxide, dried ($MgSO_4$), and evaporated to give 5.3 g (100%) of white crystals, mp 93–128 °C. ^{1}H NMR analysis showed this product to be a mixture of epoxides, with a slight excess (5%) of the β isomer (**32**). Repeated crystallization from hexane gave β-epoxide **32** as white needles: mp 145.5–146.4 °C; ir (CCl_4) 1129, 1116, 1095, 1037, 1027, 899 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.72 (3 H, s), 0.78 (3 H, s), 0.97 (3 H, s), 1.02 (3 H, s), 1.12 (3 H, s), 1.17 (3 H, s), 2.72 (1 H, broad s, $W_{1/2}$ = 4 Hz), 3.33 (4 H, complex m, ketal H's).

Anal. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 73.93; H, 10.30.

Recrystallization of the mother liquors from above did not give pure α-epoxide **31**. Dissolution in hexane and slow evaporation (over several days) gave two types of crystals: needles (β-epoxide) and rectangles (α-epoxide). These were manually separated and the procedure repeated on the α-epoxide to afford **31** as rectangular crystals: mp 123.5–126 °C; ir (CCl_4) 1129, 1116, 1104, 910, 864 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.72 (3 H, s), 0.78 (3 H, s), 0.93 (3 H, s), 1.05 (3 H, s), 1.12 (3 H, s), 1.15 (3 H, s), 2.66 (1 H, broad s, $W_{1/2}$ = 6 Hz, epoxide H), 3.35 (4 H, complex m, ketal H's).

Anal. Calcd for $C_{19}H_{32}O_3$: mol wt, 308.2352. Found: 308.2339 (high-resolution mass spectrum).

5,6-Oxido-1,1,4aβ(*R*),5-tetramethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal [(4a*R*)-31 and (4a*R*)-32]. Olefin (−)-**26** (4.5 g, 15.4 mmol) was epoxidized as described above to afford 4.7 g (100%) of α- and β-epoxides (4a*R*)-**31** and (4a*R*)-**32**.

6α-Hydroxy-5-methylene-1,1,4aβ-trimethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal (33) and 5α-Hydroxy-1,1,4aβ,5β-tetramethyl-1,4,4a,5,8,8aα-hexahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal (34). To an oven-dried three-necked flask and a reflux condenser fitted with a magnetic stirrer, a rubber septum, and a nitrogen bubbler were added 124 mg (1.2 mmol) of di-*n*-propylamine (distilled from potassium hydroxide), 0.9 ml of anhydrous THF, and 0.83 ml (1.5 M in hexane, 1.2 mmol) of *n*-butyllithium. After 30 min, a solution of 252 mg (0.82 mmol) of epoxide **31** and 1.7 ml of THF were added and the mixture brought to reflux. The disappearance of epoxide was followed by TLC. After 2 h, the solution was partitioned between ether and water and the organic solution washed with water and saturated brine, dried ($MgSO_4$), and evaporated. ^{1}H NMR analysis of the yellow, oily product (243 mg, 96.2%) showed it to be a mixture of 60.5% of **33** and 39.5% of **34**. Careful chromatography of this product (silica gel, 5% ether/hexane) separated the two compounds. The first material eluted from the column was identified as **34**, a white solid: ^{1}H NMR (CCl_4) δ 0.70 (3 H, s), 0.87 (3 H, s), 0.93 (3 H, s), 0.98 (3 H, s), 1.03 (3 H, s), 1.13 (3 H, s), 3.42 (4 H, complex m, ketal H's), 5.35 (2 H, complex m, vinyl H's).

Anal. Calcd for $C_{19}H_{32}O_3$: mol wt, 308.2352. Found: 308.2343 (high-resolution mass spectrum).

The second material eluted was identified as allylic alcohol **33**, which was also obtained as a white solid: mp 128–129 °C; ir (CCl_4) 3636, 2959, 1650, 1383, 1244, 1107, 1045, 1027, 898, 865 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.73 (3 H, s), 0.85 (3 H, s), 0.98 (3 H, s), 1.07 (3 H, s), 1.17 (3 H, s), 3.48 (4 H, complex m, ketal H's), 4.16 (1 H, broad m, $W_{1/2}$ = 21 Hz, C-6 H), 4.62 (1 H, broad s, vinyl H), 4.68 (1 H, broad s, vinyl H).

Anal. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 73.90; H, 10.49.

6β-Hydroxy-5-methylene-1,1,4aβ-trimethyl-1,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(3*H*)-one 2,2-Dimethyltrimethylene Ketal (35). Epoxide **32** (300 mg, 0.97 mmol) was treated for 4.5 h as described for **31** above. The oily product contained 7% of starting material.

Chromatography (14 g of silica gel, 30% ether/hexane) gave 270 mg (96.3% based on recovered starting material) of oil which crystallized upon standing. Recrystallization from hexane gave the analytical sample: mp 103.5–105 °C; ir (CCl_4) 3571, 2941, 1634, 1111, 1033, 1010, 912, 863 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.73 (3 H, s), 0.88 (3 H, s), 0.98 (3 H, s), 1.17 (3 H, s), 1.25 (3 H, s), 3.48 (4 H, complex m, ketal H's), 4.20 (1 H, broad s, $W_{1/2}$ = 6 Hz, C-5 H), 4.66 (1 H, broad s, vinyl H), 4.73 (1 H, broad s, vinyl H).

Anal. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 73.71; H, 10.37.

When the lithium di-*n*-propylamide ring-opening reaction was carried out on an equimolar mixture of α- and β-epoxides **31** and **32**, a mixture of 73% of **33** and **35** and 27% of **34** was obtained.

5-Methylene-1,1,4aβ-trimethyl-1,4,4a,5,8,8aα-hexahydronaphthalene-2,6(3*H*,7*H*)-dione 2-(2,2-Dimethyl)trimethylene Ketal (5) and 1,1,4aβ,5-Tetramethyl-1,4,4a,8aα-tetrahydronaphthalene-2,7(3*H*,8*H*)-dione 2-(2,2-Dimethyl)trimethylene Ketal (36). To a stirring solution of 6.5 ml (81 mmol) of anhydrous pyridine and 80 ml of anhydrous methylene chloride was added 3.2 g (32 mmol) of dry chromium trioxide. After 15 min, 1.7 g (5.5 mmol) of a mixture of **33, 34,** and **35,** obtained from opening of an equimolar mixture of **31** and **32,** dissolved in a small amount of methylene chloride, was added in one portion. After 15 min, the dark solution was vacuum filtered through activity 4 Woelm alumina, and the organic solution was evaporated to afford 1.08 g of yellow solid. ^{1}H NMR analysis indicated a mixture of 71% of **5** and 29% of **36.** Chromatography (40 g of silica gel, 20% ether/hexane) yielded two fractions.

The first fraction (0.99 g, 58% from **26**) was shown to be enone **5.** Recrystallization from hexane gave the analytical sample: mp 118–122 °C; ir ($CDCl_3$) 1692, 1618, 1381, 1285, 1212, 1129, 1106, 1027 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.74 (3 H, s), 0.93 (3 H, s), 1.03 (3 H, s), 1.08 (3 H, s), 1.15 (3 H, s), 3.35 (4 H, complex m, ketal H's), 4.72 (1 H, d, J = 1 Hz, vinyl H), 5.25 (1 H, d, J = 1 Hz, vinyl H).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.38. Found: C, 74.39; H, 9.59.

The second fraction was identified as **36.** Recrystallization from ether gave the analytical sample: mp 189–189.5 °C; ir ($CDCl_3$) 1658, 1626, 1244, 1105 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.73 (3 H, s), 0.98 (3 H, s), 1.05 (3 H, s), 1.15 (3 H, s), 1.20 (3 H, s), 2.34 (3 H, s, vinyl CH_3), 3.50 (4 H, complex m, ketal H's), 5.69 (1 H, broad s, vinyl H).

(+)-5-Methylene-1,1,4aβ(*R*)-trimethyl-1,4,4a,5,8,8aα-hexahydronaphthalene-2,6(3*H*,7*H*)-dione 2-(2,2-Dimethyl)trimethylene Ketal [(+)-5]. The foregoing procedure was repeated with 2.4 g of a mixture of α- and β-epoxides obtained from (−)-**26.** The product allylic alcohol mixture (2.4 g, 7.3 mmol) was oxidized as described above to obtain 1.40 g [59.5% based on (−)-**26**] of (+)-**5** as a white powder, mp 148–152 °C. Recrystallization from hexane to constant rotation gave 0.99 g [42% from (−)-**26**] of fine white crystals: mp 154.5–158 °C; $[\alpha]^{25}$D +66.9° (*c* 8.00, $CHCl_3$).

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Registry No.—**4,** 59270-02-9; **5,** 52782-57-7; (+)-**5,** 59331-17-8; **11,** 52782-49-7; 11 ethylene ketal, 59331-18-9; 4a*S*-**11** ethylene ketal, 25826-86-2; 4a*R*-**11** ethylene ketal, 59331-19-0; **14,** 41019-71-0; **15,** 24138-10-1; (+)-**15,** 38405-15-1; (−)-**15,** 52842-07-6; **16,** 15292-92-9; **17,** 59286-41-8; **18,** 59270-03-0; (+)-**18,** 59331-20-3; (−)-**18,** 59331-21-4; **9,** 59270-04-1; **20,** 59331-22-5; **21,** 59270-05-2; 4a*S*-**21,** 59331-23-6; 4a*R*-**21,** 59331-24-7; **23,** 52782-59-9; **25,** 59270-06-3; **26,** 52782-51-1; (+)-**26,** 59331-25-8; (−)-**26,** 59331-26-9; **30,** 59270-07-4; **31,** 52842-10-1; **32,** 52782-54-4; **33,** 52842-11-2; **34,** 52782-56-6; **35,** 52782-55-5; **36,** 52782-58-8; **37,** 52782-39-5; (+)-**37,** 59270-08-5; (−)-**37,** 52842-06-5; (+)-**37** brucine salt, 59270-09-6; (−)-**37** brucine salt, 59270-10-9; (+,+)-**38,** 52782-40-8; (−,+)-**39,** 52782-41-9; methyldihydroresorcinol, 1193-55-1; ethyl vinyl ketone, 1629-58-9; phthalic anhydride, 85-44-9; (+)-α-methoxy-α-trifluoromethylphenylacetyl chloride, 39637-99-5; ethylene glycol, 107-21-1; 2,2-dimethyl-1,3-propanediol, 126-30-7.

Supplementary Material Available. Circular dichroism curves for (+)-**15** and (−)-**15** and graphs of the chemical shifts of various ^{1}H NMR resonances as a function of added $Eu(THD)_3$ for alcohols **19** and **20** (4 pages). Ordering information is given on any current masthead page.

References and Notes

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