of *cis*-diplodialide A (**22**), respectively. Recrystallization of *cis*-diplodialide A (5 mg) from *n*-hexane–ether gave pure **22**: mp 58 °C; IR (film) ν_{max} 1740, 1700, 1640, 1260 cm^{-1}; NMR (acetone-d_6) δ 1.23 (d, 3 H, J = 6.8 Hz), 3.32 (d, 1 H, J = 14.7 Hz), 3.50 (d, 1 H, J = 14.7 Hz), 5.07 (m, 1 H), 5.71 (ddd, 1 H, J = 4.5, 10, and 12 Hz), 6.18 (dd, 1 H, J = 1.9 and 12 Hz); UV (EtOH) λ_{max} 225 nm; MS *m/e* 182 (M$^+$), 164, 154, 122, 95.

(c) Hydrolysis of 21a with 10% Hydrochloric Acid. A solution of 22 mg (0.11 mmol) of **21a** in 5 mL of chloroform containing 1 drop of 10% hydrochloric acid was stirred at room temperature overnight. After removal of the solvent under reduced pressure, the crude product was purified by preparative thin-layer chromatography on silica gel impregnated with silver nitrate using *n*-hexane–ethyl acetate (5:1) to afford 15 mg (73%) of *cis*-diplodialide A (**22**) as colorless needles.

Acknowledgments. We express our thanks to Dr. K. Wada, Nagoya University, for suppling spectra of the natural diplodialides A and C and Dr. B. P. Moore, Division of Entomology, CSIRO, for making the comparison of our synthetic sample of **5** with natural decan-9-olide. This work was supported by Grants-in-Aid for Scientific Researches on Environment (No. 203014) and on Cancer (No. 201017) from the Ministry of Education, Science and Culture, Japan, and by an award from the Mitsubishi Foundation, all of which are gratefully acknowledged.

Registry No.—**1**, 68296-70-8; **3**, 65450-86-4; **5**, 67400-99-1; **7**, 6838-67-1; **9**, 13030-90-5; **10**, 65371-25-7; **11**, 65371-26-8; **12**, 65371-27-9; **13a**, 65371-28-0; **13b**, 65391-45-9; **14**, 65450-87-5; **15**, 64681-03-4; **16**, 69653-43-6; **17**, 69653-44-7; **18**, 69653-45-8; **19a**, 69653-46-9; **19b**, 69744-58-7; **20a**, 69653-47-0; **20b**, 69685-69-4; **21a**, 69653-48-1; **21b**, 69653-49-2; **22**, 69685-70-7; 3-hydroxy-1-iodobutane, 6089-15-2.

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(13) K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, **95**, 2697 (1973).
(14) An NMR spectrum of **21a** in deuteriochloroform after 30 min at room temperature exhibited in addition to a singlet at δ 4.89 (C-2 H) originating from **21a** a singlet at δ 5.08 (C-2 H) resulting from **21b**. After the sample had stood overnight, an NMR spectrum revealed none of **21a** and **21b** and showed signals owing to *cis*-diplodialide A (**22**).

East Indian Sandalwood Oil. 1. Stereoselective Synthesis of (±)-β-Santalene and (±)-β-Santalol†,[1]

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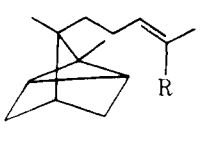
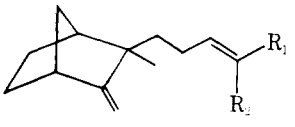
Sulfuric acid catalyzed rearrangement of γ-lactone **10** provides δ-lactone **11** as the major product. Reduction of **11** to lactols **12** with diisobutylaluminum hydride, followed by a Wittig reaction with isopropyltriphenylphosphorane, gives alcohol **13**, which is readily dehydrated to (±)-β-santalene (**5**). Acid-catalyzed alcoholysis of **11** provides ester **34**, whereas ammonolysis of **11** and dehydration of the intermediate hydroxyamide **32** with *p*-toluenesulfonyl chloride in pyridine provides nitrile **33**. Reduction of **33** or **34** with diisobutylaluminum hydride yields aldehyde **31**, which has been converted to (±)-β-santalol (**2**), (±)-*trans*-β-santalol (**7**), and dihydro-β-santalol (**3**). Compounds of the related iso series (**38**, **43**, and **46**) have been prepared from γ-lactone **10** using a similar sequence of reactions.

East Indian sandalwood oil, highly prized by perfumers for its sweet, woody fragrance, contains the sesquiterpene alcohols α-santalol (**1**) and β-santalol (**2**).[2] Other related sesquiterpenes in the oil include dihydro-β-santalol (**3**),[3] α-santalene (**4**), and β-santalene (**5**).[2] Many minor components have been identified,[4] several of which contribute to the overall odor character, but the santalols, which account for about 90% of the oil, are generally considered to be responsible for the main odor character.

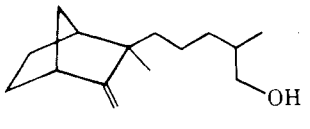
The use of large quantities of East Indian sandalwood oil by the fragrance industry, together with the relatively high price and a sometimes sporadic supply of the oil, has encouraged research chemists to search for syntheses of the odor significant components. This report describes a new stereoselective synthesis of (±)-β-santalene (**5**) and (±)-β-santalol (**2**) from racemic camphene (**6**). In addition, (±)-*trans*-β-santalol (**7**), dihydro-β-santalol (**3**), tetrahydro-β-santalol (**8**), and compounds of the related iso series have been prepared. Previous syntheses were recently reviewed.[5]



1, R = CH_2OH
4, R = CH_3



2, R_1 = CH_3; R_2 = CH_2OH
5, R_1 = R_2 = CH_3
7, R_1 = CH_2OH; R_2 = CH_3



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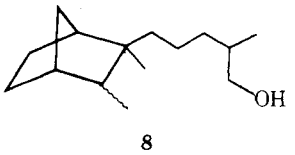

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† Dedicated to Professor Sir Derek Barton on the occasion of his 60th birthday.

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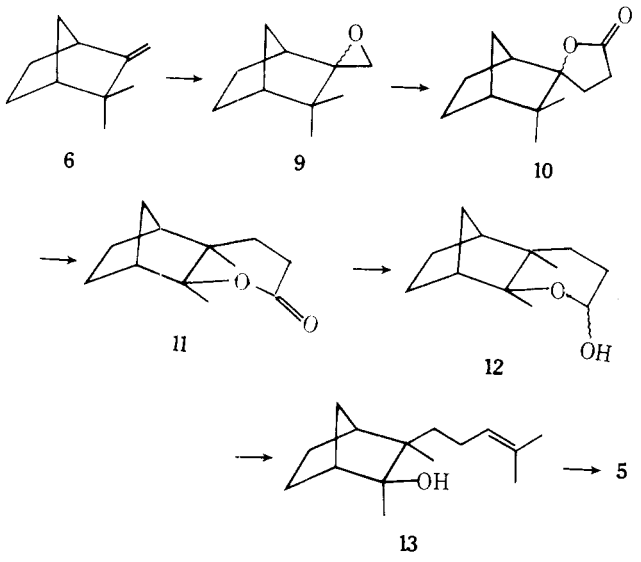
Discussion

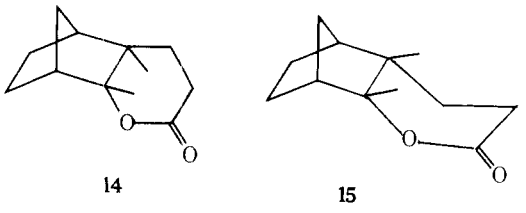
We envisaged rearranging γ-lactone **10** to the δ-lactone **11**, which should be a useful intermediate for the synthesis of β-santalene, β-santalol, and other related chemicals of potential interest to the fragrance industry. Clearly the stereoselectivity of the rearrangement **10** → **11** would effect epimer ratios in the final products.



In our hands manganic acetate oxidation of camphene[6] gave low yields of lactone **10**. We were also unable to prepare **10** from camphene and chloroacetic acid according to a recently reported procedure,[7] despite several attempts. Epoxidation of camphene with buffered peracetic acid gave **9** as a mixture of exo and endo isomers in 87% yield. Reaction of epoxide **9** with the dianion of acetic acid (lithium diisopropylamide in tetrahydrofuran), followed by lactonization, gave **10** as a mixture of exo and endo isomers in 78% yield. Although a lower yield was obtained, a more convenient method utilized lithium diethylamide, prepared from lithium shot according to the procedure of Normant.[8] Alternatively, lactone **10** was obtained in 53% yield by reacting epoxide **9** with the anion of acetonitrile (lithium diisopropylamide in tetrahydrofuran), followed by hydrolysis and lactonization.

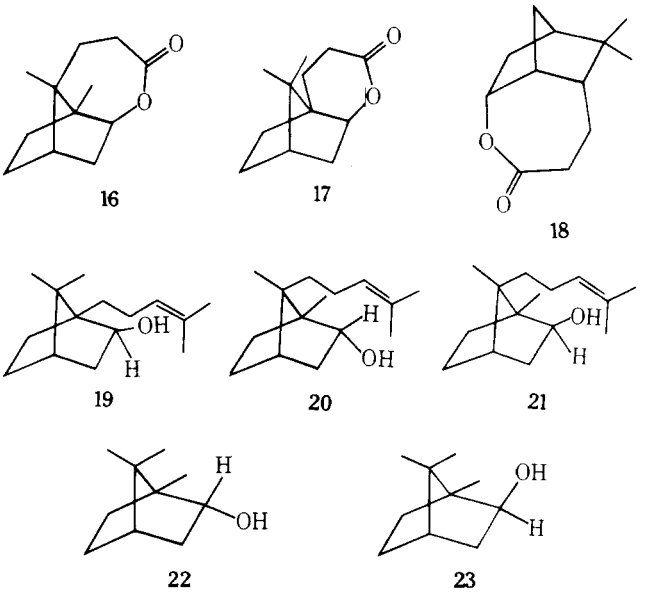
Stirring lactone **10** with concentrated sulfuric acid in the cold gave cleanly two different lactones in a 5:1 ratio.[9a] The major product was assigned the δ-lactone structure **11** based on spectral data and conversion to β-santalene (**5**) as follows. Reduction of **11** with diisobutylaluminum hydride gave the lactols **12** in quantitative yield. Reaction of **12** with isopropyltriphenylphosphorane in dimethyl sulfoxide gave the known[10] alcohol **13** in 88% yield. Dehydration of **13** with phosphorus oxychloride in pyridine gave (±)-β-santalene (**5**) in 71% yield. Comparison of spectral and GLC data for this product with data for natural β- and epi-β-santalene (isolated from East Indian sandalwood oil) showed that our synthetic material contained 93% (±)-β-santalene and 2% (±)-*epi*-β-santalene.

Although *trans*-δ-lactone **14** could also lead to β-santalene, models indicate that **14** would be much more strained than **11**. Also, spectral data for **13** are identical with those previously reported[10] for this alcohol. We thus assign the cis-exo



stereochemistry to the major rearrangement product **11**. The small amount of *epi*-β-santalene observed in the final product is probably due to the presence of a small amount of cis-endo isomer **15**.

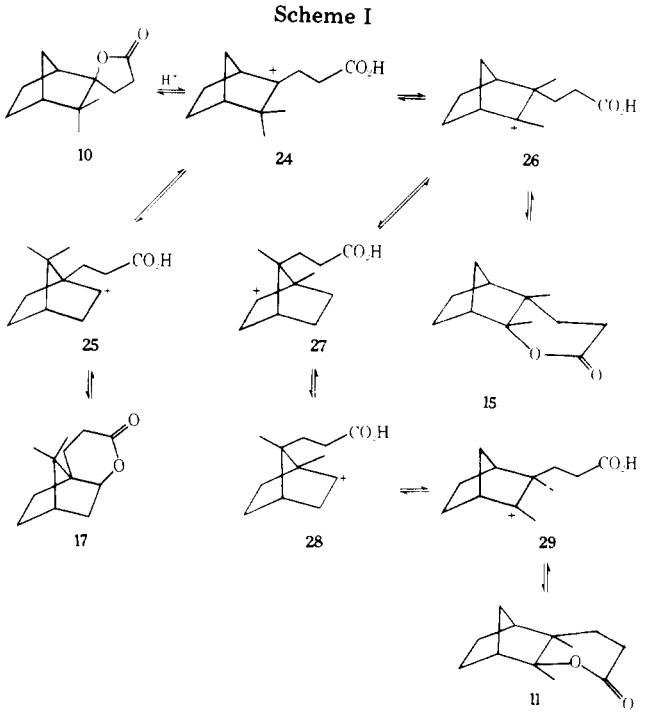
The minor product from the rearrangement of γ-lactone **10** was purified by selective hydrolysis and relactonization, followed by crystallization and preparative high pressure liquid chromatography. Spectral data suggested a six-membered (or higher) lactone of a secondary hydroxy acid. Structures **16**–**18** were considered the most likely possibilities. Reduction of the minor lactone with diisobutylaluminum hydride followed by reaction with isopropyltriphenylphosphorane gave an alcohol, to which structure **19** is assigned on



the basis of a comparison of ^{1}H NMR data with data for campherenol (**20**), isocampherenol (**21**), borneol (**22**), and isoborneol (**23**).[11] In addition, the IR spectra of **19**, the intermediate lactol, and the minor lactone all show bands characteristic of a *gem*-dimethyl group. The minor rearrangement product is thus assigned structure **17**.

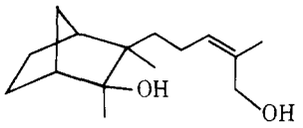
Our proposed mechanism[9b] for the acid-catalyzed rearrangement of γ-lactone **10**, outlined in Scheme I, involves

Scheme I



protonation to cation **24**, which can either undergo Wagner–Meerwein rearrangement to **25** or an *exo*-methyl shift to provide tertiary cation **26**. Since the reaction is carried out in strong acid, dications may be involved, but for simplicity only classical monocations are depicted. Dicationic species would provide additional driving force for the *exo*-methyl shift **24** → **26**, because charge separation would be greater. Successive Wagner–Meerwein/6,2-hydride/Wagner–Meerwein rearrangements via cations **27** and **28** would lead to cation **29**, and thus to the major product **11**. Cations **24** and **29** are probably not in direct equilibrium since *endo*-methyl migration would be required.[9c] Cyclization of cation **26** to *cis-endo*-δ-lactone **15** is not favored because it requires endo attack.

With a stereoselective synthesis of (±)-β-santalene in hand, we turned our attention to (±)-β-santalol (**2**). Treating lactols **12** with ethylidenetriphenylphosphorane, *n*-butyllithium, and formaldehyde[12] under a variety of conditions did not yield the desired diol **30**. Attempts to convert lactols **12** to aldehyde **31** either directly, by dehydration with methanesulfonyl chloride in pyridine (and related reagents), or indirectly, by conversion to either the ethylene glycol acetal or the dimethylhydrazone, followed by dehydration and deprotection, all proved unsuccessful. Ammonolysis of δ-lactone **11** with ammonia, or more conveniently with dimethylaluminum amide, provided hydroxy amide **32** in about 60% yield. Dehydration of **32** with *p*-toluenesulfonyl chloride in pyridine provided nitrile **33** in



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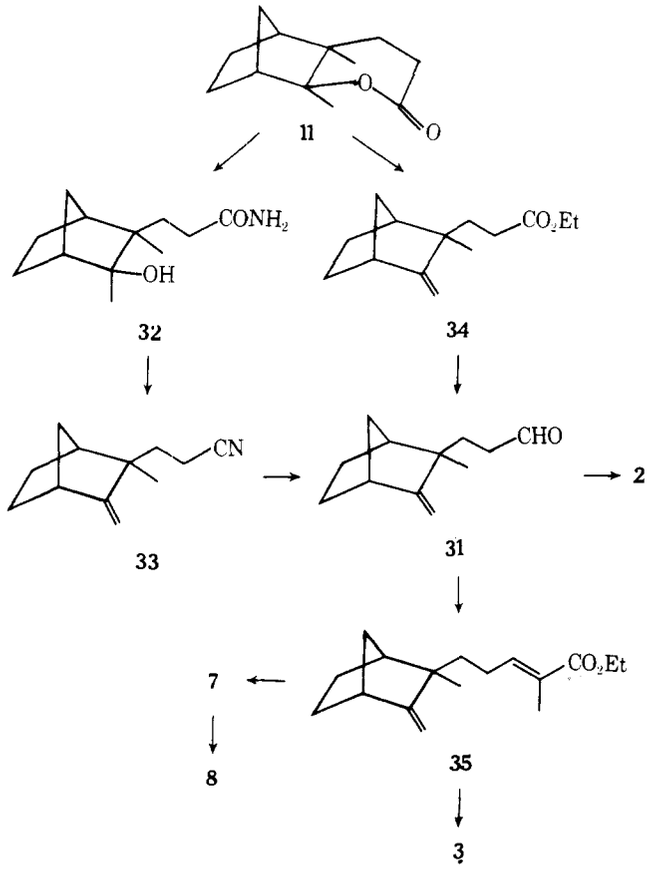
90% yield. Reduction of the nitrile with diisobutylaluminum hydride gave the acid-sensitive aldehyde **31** in 87% yield. Alternatively, lactone **11** was treated with a catalytic amount of *p*-toluenesulfonic acid in refluxing ethanol/benzene to provide ester **34** in 69% yield. Reduction of **34** with diisobutylaluminum hydride provided **31** in 90% yield. This aldehyde was treated sequentially with ethylidenetriphenylphosphorane, *n*-butyllithium, and formaldehyde[12] to give (±)-β-santalol (**2**) in 44% yield. This material was identical in all respects with material isolated from East Indian sandalwood oil by preparative GLC.



Reaction of aldehyde **31** with sodiotriphenyl phosphonopropanoate gave the known[13] ester **35** as a mixture of trans/cis (85:15) isomers in 70% yield. Aluminum hydride reduction of **35** gave (±)-*trans*-β-santalol (containing 15% of the cis isomer) in 84% yield. Lithium/ammonia reduction of **35** gave (±)-dihydro-β-santalol (**3**) in 77% yield. Hydrogenation of (±)-*trans*-β-santalol over poisoned platinum oxide catalyst gave (±)-tetrahydro-β-santalol (**8**) as a mixture of exo/endo isomers in 87% yield.

A similar sequence of reactions starting with lactone **10** provided compounds of the isosantalene series in comparable yields (Scheme II). For convenience exocyclic double bonds are drawn in the *E* configuration. Since GLC/MS analysis indicates that ester **45** is a mixture of four isomers, ester **41** and aldehyde **42** must be mixtures of *E* and *Z* isomers.[14] Attempted reduction of nitrile **40** with diisobutylaluminum hydride was unsuccessful.

Experimental Section

General. Tetrahydrofuran was distilled from lithium aluminum hydride. Dimethoxyethane, benzene, acetonitrile, toluene, and methylene chloride were dried over 4Å molecular sieves. Diethylamine, diisopropylamine, dimethyl sulfoxide, pyridine, and hexamethylphosphoramide were distilled from calcium hydride and stored over 4Å molecular sieves. Moisture- or oxygen-sensitive reactions were carried out in flame-dried glassware under a nitrogen atmosphere.

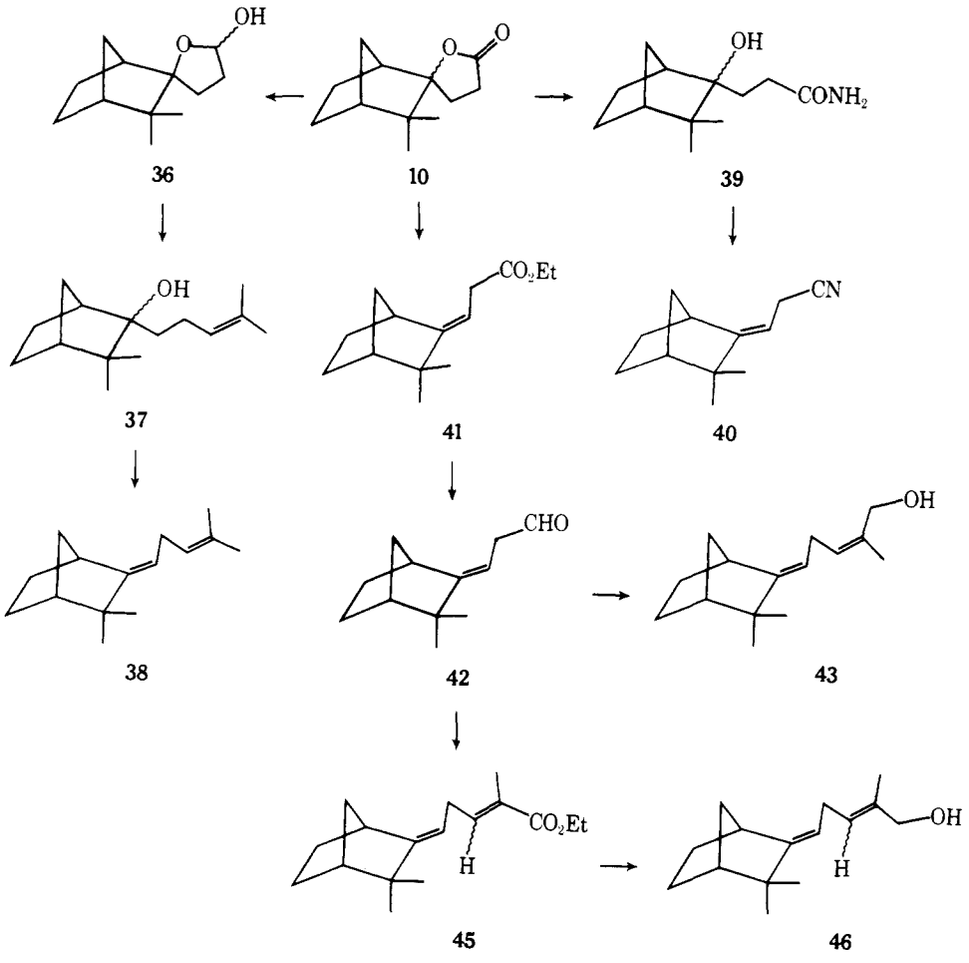
Spinning band distillations were carried out with a Perkin-Elmer NFA-200 auto-annular still. GLC analyses were obtained with a Hewlett-Packard Model 5840A or a Perkin-Elmer Model 3920 gas chromatograph using either a 10 ft, 2 mm i.d. glass column packed with 2% Carbowax 20M on Chromosorb G 100/120 or a 12 ft, 2 mm i.d. glass column packed with 3% OV-101 on Chromosorb WHP 100/120. Where indicated, percentages refer to computer calculated peak areas without correction for response. ^{1}H NMR spectra were recorded with a Varian Associates T-60A or XL 100 spectrometer, using tetramethylsilane as an internal reference. IR spectra were obtained with a Perkin-Elmer 137 Infracord. UV spectra were obtained with a Beckman Model DB-G grating spectrophotometer. Mass spectra were obtained with a Perkin-Elmer Model 270 or a Hewlett-Packard 5985 mass spectrometer. GLC, LC, and MS data were provided courtesy of the Fritzsche Dodge and Olcott Inc. Instrumental Laboratory.

Elemental microanalyses were performed by Childers Laboratories, Milford, N.J. Melting points were determined with a Thomas Model 40 micro hot stage apparatus and are uncorrected.

Spiro[3,3-dimethylbicyclo[2.2.1]heptane-2,2′-oxirane] (9). Peracetic acid (114 g of a 40% solution, 0.6 mol, saturated with anhydrous sodium acetate) was added to a stirred mixture of camphene (102.0 g, commercial grade containing 20% tricyclene, 0.6 mol) and sodium carbonate (127.2 g, 1.2 mol) in methylene chloride (900 mL) at such a rate that the reaction temperature was maintained between 15 and 25 °C (water bath cooling). After being stirred for 6 h at 25 °C, the reaction mixture was filtered and the solids were thoroughly washed with methylene chloride. The filtrate was washed successively with water (2 × 200 mL), 1 N NaOH (2 × 150 mL), and brine (150 mL) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to give 99.1 g of a white solid which ^{1}H NMR analysis indicated to be 80% camphene epoxide (**9**): NMR ($CDCl_3$) 0.87 (6 H, s, $>C(CH_3)_2$), 0.8–2.1 (8 H, m), 2.63 and 2.73 (2 H, 2s, $>C\overline{CH_2O}$); IR (CCl_4) 2940, 1545, 1460 cm^{-1} (lit.[15]).

3-(2-Hydroxy-3,3-dimethylbicyclo[2.2.1]hept-2-yl)propanoic Acid Lactone (Exo and Endo Isomers) (10). Method A. To a cold (ice/water bath) solution of diisopropylamine (5.05 g, 0.05 mol) in tetrahydrofuran (85 mL) was added *n*-butyllithium (16.7 mL of 3.02 M, 0.05 mol) at such a rate that the reaction temperature was <10 °C. Acetic acid (1.50 g, 0.025 mol) in tetrahydrofuran (10 mL) was added during 5 min, and the mixture was warmed at 30–35 °C for 30 min. A solution of camphene epoxide (2.03 g, 75% pure, 0.01 mol) in benzene (5 mL) was added, the mixture was heated at reflux for 22 h and then cooled, and water (50 mL) and ether (50 mL) were added. The

Scheme II



organic layer was washed with water (3 × 20 mL). The combined aqueous extracts were washed with ether (3 × 20 mL) and acidified with 40% sulfuric acid, and the organic product was extracted with ether (3 × 25 mL). The solvent was evaporated, and the residue was dissolved in benzene (100 mL) and heated at reflux for 1 h. The solution was cooled, washed with saturated $NaHCO_3$, and dried (Na_2SO_4). The solvent was evaporated to give 1.51 g (78%) of lactone **10**, mp 101–102 °C (lit.[9a] mp 101–103 °C). GLC analysis indicated that the material was a 65:35 mixture (exo/endo isomers): NMR ($CDCl_3$) δ 0.95 and 0.98 (6 H, 2s, $>C(CH_3)_2$); IR ($CHCl_3$) 2940, 1760 cm^{-1}.

Method B. Lithium shot (8.32 g, 1.20 mol) was added to a solution of diethylamine (88.4 g, 1.20 mol) in benzene (220 mL) and hexamethylphosphoramide (225 g, 1.25 mol), and the mixture was stirred with cooling (water bath) until all of the lithium had dissolved. Tetrahydrofuran (400 mL) was added and the solution cooled (ice/water bath). Acetic acid (36.00 g, 0.60 mol) in tetrahydrofuran (40 mL) was added dropwise to the red-colored solution. The viscous, purple-colored solution was warmed (35–40 °C) for 30 min, and a solution of camphene epoxide (**9**; 81.0 g, 75% pure, 0.40 mol) in dry benzene (30 mL) was added. The mixture was heated at gentle reflux for 22 h, cooled, and poured into ice water. The organic layer was washed with 2 N NaOH (3 × 40 mL). The combined aqueous layers were extracted with benzene (4 × 50 mL), cooled (0 °C), acidified with cold 40% sulfuric acid, and extracted with benzene (6 × 100 mL). The benzene extracts were heated at reflux for 1 h, cooled, washed successively with 2 N HCl (4 × 50 mL), water (50 mL), and saturated $NaHCO_3$ (3 × 50 mL), and dried (Na_2SO_4). Evaporation of solvent and crystallization of the residue from petroleum ether (30–60 °C) gave 39.2 g (50.5%) of colorless crystals, identical with the material obtained by method A.

Method C. To a cold (ice/water bath) solution of diisopropylamine (75.89 g, 0.75 mol) in tetrahydrofuran (1200 mL) was added *n*-butyllithium (310 mL of 2.48 M, 0.77 mol) at such a rate that the reaction temperature was <10 °C. The solution was stirred for 15 min, acetonitrile (30.78 g, 0.75 mol) in tetrahydrofuran (50 mL) was added dropwise during 10 min, and then a solution of camphene epoxide (89.4 g of 85%, 0.5 mol) in benzene (50 mL) was added. The solution was allowed to warm to room temperature and was then heated at 50–60 °C for 18 h and cooled, and water (100 mL) was added. Solvent was evaporated, and the residue was heated at reflux with potassium hydroxide (56 g) in ethanol (800 mL)/water (200 mL) for 16 h. The solution was concentrated, water (300 mL) added, and unwanted organic material extracted with ether (2 × 100 mL). The aqueous layer was cooled (ice/water bath), acidified with 40% sulfuric acid, and extracted with ether (4 × 100 mL). The solvent was evaporated, and the residue was dissolved in toluene (300 mL) and heated at reflux for 1.5 h. The solution was cooled, washed with saturated $NaHCO_3$, and dried (Na_2SO_4), and the solvent was evaporated. Crystallization from petroleum ether gave 51.4 g (53%) of lactone **10** identical with the material obtained by method A.

3-(3-Hydroxy-2,3-*endo*-dimethylbicyclo[2.2.1]hept-2-yl)-propanoic Acid Lactone (11). γ-Lactone **10** (16.16 g, 0.833 mol) was added portionwise to concentrated sulfuric acid (325 mL) at −10 °C. After being stirred for 45 min, the mixture was poured into ice water (3.0 L) and the product was extracted with chloroform (4 × 200 mL). The extracts were washed with saturated $NaHCO_3$ solution and dried (Na_2SO_4), and the solvents were evaporated to yield 15.0 g of crude product. Chromatography on silica gel (toluene/ethyl acetate, 15:1) gave 6.20 g of starting material, intermediate fractions containing mixtures of lactones **10**, **11**, and **17**, and 7.23 g (45%) of δ-lactone **11** (91% **11**, 8% **17**, and 1% **10**). Rechromatography and crystallization gave an analytical sample of **11**: mp 90–91 °C; NMR ($CDCl_3$) δ 1.02 (3 H, s, $>CCH_3$), 1.27 (3 H, s, $-OC(CH_3)<$), 0.9–2.1 (10 H, m) 2.1–2.5 (2 H, m, $-CH_2CO_2-$); IR ($CHCl_3$) 1735 cm^{-1}; MS *m/e* 194, 179, 166, 151. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.07; H, 9.28.

3-(2-*exo*-Hydroxy-7,7-dimethylbicyclo[2.2.1]hept-1-yl)propanoic Acid Lactone (17). Intermediate fractions from the chromatographic purification of lactone **11** [containing a mixture of lactones **10**, **11**, and **17** (16, 9, and 66%, respectively); 1.60 g, 0.0082 mol], 1 N KOH (5.8 mL), and ethanol (20 mL) were heated at reflux for 45 min. The solution was cooled, poured into water (100 mL), and extracted with toluene (4 × 10 mL). The aqueous layer was cooled (0 °C), acidified with 5% sulfuric acid, and extracted with ether (4 × 25 mL). The ether extracts were washed with water and the solvent evaporated. The residue was heated in refluxing toluene (50 mL) for 1.5 h,

cooled, washed with saturated $NaHCO_3$ (2 × 10 mL), and dried (Na_2SO_4), and the solvent was evaporated to yield 0.67 g of material, which was shown by GLC analysis to contain 93% of lactone **17**. Crystallization from petroleum ether (60–90 °C) gave 0.11 g of material containing none of δ-lactone **11**. Preparative LC gave 0.083 g of δ-lactone **17**: mp 79.5–81 °C (99% pure); NMR (CCl_4) δ 0.91 (3 H, s, $-CH_3$), 1.02 (3 H, s, $-CH_3$), 0.9–2.5 (11 H, m), 4.0–4.28 (1 H, dd, J = 3 and 8 Hz, >C**H**O–); IR ($CHCl_3$) 2950, 1735, 1380, 1370 cm^{-1}; MS m/e 194, 179, 166, 152. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.46; H, 9.30.

3-(3-Hydroxy-2,3-*endo*-dimethylbicyclo[2.2.1]hept-2-yl)-propanal Hemiacetal (12). Diisobutylaluminum hydride (16.3 mL of 1 M hexane solution) was added dropwise with stirring to a solution of δ-lactone **11** (2.52 g, 0.013 mol, 99% pure) in toluene (100 mL), cooled to −78 °C. After being stirred at −78 °C for 3 h, the solution was poured into 10% acetic acid (100 mL) and stirred vigorously. The aqueous layer was separated and extracted with toluene (3 × 25 mL). The combined extracts were washed with saturated $NaHCO_3$ solution (3 × 25 mL) and dried (Na_2SO_4), and the solvent was evaporated to yield 2.55 g (100%) of lactol **12**. Crystallization from petroleum ether (30–60 °C) gave colorless crystals: mp 95–98 °C; NMR ($CDCl_3$) δ 0.90 (3 H, s, $-CH_3$), 1.30 (3 H, s, $-OC(CH_3)<$), 0.9–2.5 (12 H, m), 3.95 (1 H, broad s, –OH), 5.15–5.48 (1 H, t, >C**H**OH); IR ($CHCl_3$) 3300, 2950 cm^{-1}; MS m/e 196, 178, 153. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.42; H, 10.27. Found: C, 73.82; H, 10.45.

3-(4-Methyl-3-pentenyl)-2,3-*endo*-dimethylbicyclo[2.2.1]-heptan-2-ol (13). Sodium hydride (0.106 g of 50% oil dispersion, 2.2 mmol) was washed with hexane. Dimethyl sulfoxide (5 mL) was added, and the mixture was heated to 70 °C until evolution of hydrogen ceased. The solution was cooled (20 °C), and isopropyltriphenylphosphonium iodide (0.951 g, 2.2 mmol) was added portionwise. The deep red-colored solution was stirred for 15 min, and lactol **12** (0.196 g, 1 mmol) was added in one portion. After being heated at 50–55 °C for 42 h, the solution was cooled, poured into water (20 mL), and extracted with petroleum ether (30–60 °C) (6 × 15 mL). The organic extracts were washed with water (7 × 10 mL) and dried (Na_2SO_4), and the solvent was evaporated. The residue was dissolved in petroleum ether and filtered through neutral alumina (1 g). Evaporation of the solvent and Kugelrohr distillation of the residue gave 0.195 g (88% yield) of alcohol **13**, bp 95–108 °C (0.3 mm). GLC analysis indicated one major component (94%): NMR ($CDCl_3$) δ 0.88 (3 H, s, >CCH_3), 1.18 (3 H, s, >$C(OH)CH_3$), 1.60 and 1.68 (6 H, 2s, $C{=}C(CH_3)_2$), 0.9–2.6 (13 H, m), 4.95–5.27 (1 H, m, –CH=<); IR (film) 3450, 2950, 1420 cm^{-1}; MS m/e 222, 204, 179 (lit.[10]).

2-*endo*-Methyl-2-*exo*-(4-methyl-3-pentenyl)-3-methylene-bicyclo[2.2.1]heptane (β-Santalene) (5). To a cold (ice/water bath) solution of phosphorus oxychloride (0.3 mL) in pyridine (2.2 mL) was added alcohol **13** (0.170 g, 0.77 mmol) in pyridine (1.5 mL). After being stirred for 17 h, the solution was poured into ice water and extracted with ether (5 × 10 mL). The ether extracts were washed with 5% HCl (4 × 5 mL) and saturated $NaHCO_3$ (2 × 10 mL) and dried (Na_2SO_4), and the solvent was evaporated. The residue was dissolved in petroleum ether (30–60 °C) and filtered through neutral alumina (0.5 g). Evaporation of the solvent and Kugelrohr distillation of the residue gave 0.111 g of a colorless oil, bp 105–110 °C (5 mm). GLC analysis indicated 93% β-santalene (**5**) and 2% *epi*-β-santalene: NMR (CCl_4) δ 1.04 (3 H, s, $-CH_3$), 1.59 and 1.65 (6 H, 2s, $-C{=}C(CH_3)_2$), 1.0–2.2 (11 H, m), 2.53–2.75 (1 H, m, –CH–≤), 4.43 and 4.69 (2 H, 2s, >$=CH_2$), 4.87–5.26 (1 H, m, –CH=<); IR (film) 2980, 1660, 1460 cm^{-1}; MS m/e 204, 189, 161, 122, 94. A sample of a mixture of β-santalene (**5**) and *epi*-β-santalene was isolated from East Indian sandalwood oil by preparative GLC. The 100-MHz ^1H NMR spectrum of the mixture shows the *exo*-methyl group of *epi*-β-santalene at δ 1.02 and the *endo*-methyl group of β-santalene at δ 1.04, consistent with previously reported spectral data.[11,16] Comparison of the above spectrum with the 100-MHz ^1H NMR of the synthetic material confirmed that β-santalene (**5**) had been prepared.

1-(4-Methyl-3-pentenyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-*exo*-ol (19). To a solution of lactone **17** (0.160 g, 0.82 mmol, 97% pure) in toluene (10 mL) at −78 °C was added diisobutylaluminum hydride (1 mL of 1 M hexane solution). After being stirred for 3.5 h, the solution was poured into 10% acetic acid (5 mL) and shaken vigorously and the layers were separated. The aqueous layer was extracted with toluene (3 × 10 mL). The combined organic layers were washed with saturated $NaHCO_3$ (3 × 5 mL) and dried (Na_2SO_4), and the solvent was evaporated to yield a viscous oil (0.154 g): NMR (CCl_4) δ 0.87 (3 H, s, $-CH_3$), 1.15 and 1.22 (3 H, 2s, $-CH_3$), 0.7–2.7 (11 H, m), 3.40–3.65 and 3.75–3.93 (1 H, 2 sets of dd, >CH–O–), 4.20–4.45 (1 H, broad s, –OH, exchanges with D_2O), 4.45–4.75 and 4.95–5.30 (1 H, 2 sets of m, –C**H**(OH)O); IR (CCl_4) 3400, 2750, 1480, 1420, 1380, 1370 cm^{-1}.

Sodium hydride (0.084 g of 50% mineral oil dispersion, 1.68 mmol) was washed with hexane (3 × 5 mL). Dimethyl sulfoxide (8 mL) was added, and the solution was heated at 50–60 °C until hydrogen evolution ceased. The solution was cooled to 25 °C, and isopropyltriphenylphosphonium iodide (0.728 g, 1.68 mmol) was added portionwise. The deep red-colored solution was stirred for 30 min, and the lactol (0.150 g, 0.76 mmol, crude product from above) in dimethyl sulfoxide (3 mL) was added. The solution was heated at 50–55 °C for 24 h and then was poured into water (25 mL) and extracted with petroleum ether (63–75 °C) (6 × 10 mL). The extracts were washed with water (3 × 10 mL) and dried (Na_2SO_4), and the solvent was evaporated. Most of the triphenylphosphine oxide was removed by crystallization from petroleum ether (35–60 °C). Evaporation of the filtrate and Kugelrohr distillation of the residue gave 0.115 g (68% yield) of alcohol **19**, bp 90–100 °C (0.3 mm). Preparative GLC gave an analytical sample: NMR (100 MHz) ($CDCl_3$) δ 0.80 (3 H, s, $-CH_3$), 1.02 (3 H, s, $-CH_3$), 1.64 and 1.69 (6 H, 2s, $=C(CH_3)_2$), 0.8–1.8 (8 H, m), 1.86–2.16 (2 H, m, $>CH_2CH{=}<$), 3.67–3.86 (1 H, m, >C**H**OH), 5.12–5.34 (1 H, m, –CH=<); IR (film) 3470, 2950, 1460, 1380, 1370 cm^{-1}; MS m/e 204, 189, 161. Anal. Calcd for $C_{15}H_{20}O$: 222.1983. Found: 222.1976.[17]

3-(3-Hydroxy-2,3-*endo*-dimethylbicyclo[2.2.1]hept-2-yl)propanamide (32). Method A. A mixture of lactone **11** (0.400 g, 2.06 mmol), ammonia (12 g), ammonium chloride (0.1 g), and methanol (10 mL) was heated in a sealed vessel at 100 °C for 94 h. After being cooled and partial removal of solvents, the reaction mixture was poured into water and extracted with chloroform (3 × 20 mL). Evaporation of solvent and crystallization of the residue from benzene/petroleum ether (63–73 °C) gave 0.27 g (62%) of amide **32**: mp 109–110 °C; NMR ($CDCl_3$) δ 0.83 (3 H, s, >CCH_3), 1.17 (3 H, s, >$C(OH)CH_3$), 0.90–2.55 (12 H, m), 2.25 (1 H, broad s, —OH, exchanges with D_2O), 5.6–6.4 (2 H, broad s, $-NH_2$, exchanges slowly with D_2O); IR ($CDCl_3$) 3350, shoulder at 3500, 2980, 1660, 1600 cm^{-1}; MS m/e 211, 193. Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 68.08; H, 9.91; N, 6.57.

Method B. Trimethylaluminum (6.5 mL of 25% hexane solution, 2.2 mmol) was added dropwise during 15 min to a solution of ammonia (~1 mL) in methylene chloride (25 mL). The mixture was stirred at 20 °C for 20 min, and then lactone **11** (1.94 g, 1 mmol) was added in one portion. The mixture was stirred at room temperature for 3 days, refluxed for 24 h before cooling (0 °C), and cautiously decomposed with 3 N HCl (20 mL). The aqueous layer was extracted with methylene chloride (3 × 10 mL). The combined extracts were dried (Na_2SO_4), the solvent was evaporated, and the residue was crystallized from ethanol/ether to give 1.26 g (60%) of amide **32**, identical with the material obtained by method A.

3-(2-*endo*-Methyl-3-methylenebicyclo[2.2.1]hept-2-yl)propanenitrile (33). A mixture of amide **32** (0.740 g, 3.5 mmol), *p*-toluenesulfonyl chloride (2.67 g, 14 mmol), and pyridine (40 mL) was heated at 90–100 °C for 21 h. The reactants were cooled, poured into water (200 mL), and extracted with ether (4 × 40 mL). The ether extracts were washed successively with 3 N HCl (3 × 20 mL), saturated $NaHCO_3$ (2 × 15 mL), and brine, (10 mL) and dried ($MgSO_4$), and the solvent was evaporated. Kugelrohr distillation of the residue gave 0.551 g (90%) of nitrile **33**, bp 84–88 °C (0.5 mm). GLC analysis indicated one major component (95%): NMR ($CDCl_3$) δ 1.05 (3 H, s, $-CH_3$), 1.0–2.6 (11 H, m), 2.63–2.87 (1 H, m, >CH–≤), 4.48 and 4.83 (2 H, 2s, >$=CH_2$); IR (film) 2960, 2250, 1660 cm^{-1}; MS m/e 175, 160, 146. Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78. Found: C, 82.00; H, 9.80.

Ethyl 3-(2-*endo*-Methyl-3-methylenebicyclo[2.2.1]hept-2-yl)propanoate (34). A mixture of lactone **11** (9.00 g, 4.64 mmol, 98% pure), *p*-toluenesulfonic acid hydrate (0.45 g), ethanol (200 mL), and benzene (150 mL) was heated at reflux for 75 h, using a Soxhlet extractor containing Na_2SO_4. The solution was cooled, sodium carbonate (1 g) added, and the solution concentrated. The residue was dissolved in benzene (200 mL) and water (50 mL). The organic layer was washed with saturated $NaHCO_3$ (3 × 20 mL) and dried (Na_2SO_4), and the solvent was evaporated to give 10.45 g of crude product, which was distilled through a spinning band column to provide 7.11 g (69%) of ester **34**, bp 105–107 °C (1.2 mm). GLC analysis indicated 96% **34**, 2% *epi*-**34**, and 2% **41**: NMR ($CDCl_3$) δ 1.03 (3 H, s, >CCH_3), 1.1–1.4 (3 H, t, J = 7 Hz, $-CH_2CH_3$), 1.0–2.45 (11 H, m), 2.57–2.78 (1 H, m, –CH–≤), 3.95–4.3 (2 H, q, J = 7 Hz, $-CH_2CH_3$), 4.53 and 4.80 (2 H, 2s, >$C{=}CH_2$); IR (film) 2940, 1735, 1650 cm^{-1}; MS m/e 222, 207, 194, 193, 179. Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.98. Found: C, 75.69; H, 9.98.

3-(2-*endo*-Methyl-3-methylenebicyclo[2.2.1]hept-2-yl)propanal (31). Method A. Nitrile **33** (0.123 g, 0.7 mmol) in dry hexane (12 mL) was cooled to −78 °C, and diisobutylaluminum hydride (0.84

mL of a 1 M hexane solution) was added dropwise during 5 min. The solution was stirred for 1 h at −78 °C and for 30 min at 0 °C. Ether (15 mL) and 10% acetic acid (10 mL) were added, and the mixture was stirred at 20 °C for 45 min. The aqueous layer was extracted with petroleum ether (60–90 °C) (4 × 5 mL). The combined extracts were washed with saturated $NaHCO_3$ (4 × 10 mL) and brine (10 mL) and dried (Na_2SO_4). Evaporation of solvent and Kugelrohr distillation of the residue gave 0.109 g of aldehyde **31**, bp 75–85 °C (1 mm). GLC analysis indicated one major component (87%): NMR (CCl_4) δ 1.01 (3 H, 2s, $-CH_3$), 1.0–2.6 (11 H, m), 2.6–2.8 (1 H, m, >CH–≤), 4.45 and 4.75 (2 H, 2s, >=CH_2), 9.68–9.75 (1 H, t, J = 2 Hz, –CHO); IR (film) 2940, 2700, 1725 cm^{-1}; MS *m/e* 178, 163, 160, 145 (ref 13). Semicarbazone, mp 167–168.5 °C. Anal. Calcd for $C_{13}H_{21}N_3O$: C, 66.35; H, 9.00; N, 17.87. Found: C, 66.29; H, 9.00; N, 17.96.

Method B. A solution of ester **34** (1.25 g, 5.63 mmol) in toluene (75 mL) was cooled to −78 °C, and diisobutylaluminum hydride (6.2 mL of a 1 M hexane solution) was added dropwise during 5 min. After being stirred at −78 °C for 3.5 h, the solution was poured into 5% acetic acid (30 mL) and stirred vigorously. The aqueous layer was extracted with toluene (3 × 10 mL). The organic extracts were washed with saturated $NaHCO_3$ (4 × 20 mL) and dried (Na_2SO_4), and the solvent was evaporated. Kugelrohr distillation of the residue gave 0.90 g of aldehyde **31**. GLC analysis indicated one major component (85%).

(*Z*)-2-Methyl-5-(2-*endo*-methyl-3-methylenebicyclo[2.2.1]hept-2-yl)-2-penten-1-ol (β-Santalol) (2). To a suspension of ethyltriphenylphosphonium bromide (1.436 g, 3.87 mmol) in tetrahydrofuran (10 mL) was added *n*-butyllithium (1.7 mL of a 2.3 M hexane solution, 3.87 mmol). After being stirred for 15 min, the solution was cooled to −78 °C and aldehyde **31** (0.709 g, 3.98 mmol, 81% pure) in tetrahydrofuran (3 mL) was added dropwise during 5 min. After being stirred for 5 min, *n*-butyllithium (2.3 mL of 2.3 M hexane solution, 5.3 mmol) was added dropwise and the solution was stirred at −78 °C for 20 min. The solution temperature was raised to 0 °C (ice/water bath), and gaseous formaldehyde (generated by heating paraformaldehyde to 150–160 °C in a stream of nitrogen and dried by passing over phosphorus pentoxide) was bubbled into the solution until a straw-colored solution was obtained. The solution was stirred overnight at room temperature and then poured into saturated ammonium chloride solution (40 mL) and extracted with ether (4 × 15 mL). The ether extracts were washed with water (10 mL) and brine (10 mL) and dried ($MgSO_4$). Evaporation of solvents gave 1.98 g of residue, which was chromatographed on silica gel to give, after evaporation of solvent and Kugelrohr distillation, 0.384 g (44% yield) of β-santalol (**2**), bp 110–120 °C (0.3 mm). GLC analysis indicated one major component (96%): NMR (CCl_4) δ 1.05 (3 H, s, >CCH_3), 1.73 (3 H, broad s, =$C(CH_2OH)CH_3$), 1.0–1.90 (9 H, m), 1.95–2.3 (3 H, m, $-CH_2CH$=< and bridgehead proton), 2.60–2.75 (1 H, m, >CH–≤), 4.06 (2 H, s, $-CH_2OH$), 4.43 and 4.70 (2 H, 2s, >=CH_2), 5.16–5.40 (1 H, m, –CH=<); IR (film) 3330, 2940, 1660 cm^{-1}; MS *m/e* 220, 202, 187. The 100-MHz ^1H NMR spectrum of the synthetic material was identical with that of natural β-santalol, isolated from East Indian sandalwood oil.

(*E*)-Ethyl 2-Methyl-5-(2-*endo*-methyl-3-methylenebicyclo[2.2.1]hept-2-yl)-2-pentenoate (35). Sodium hydride (0.505 g of a 50% oil dispersion, 10.5 mmol) was washed with dimethoxyethane (3 × 5 mL). To a suspension of the sodium hydride in dimethoxyethane (60 mL) was added triethyl phosphonopropanoate (2.50 g, 10.5 mmol) in dimethoxyethane (10 mL) dropwise during 5 min. When hydrogen evolution had ceased, the solution was cooled (0 °C) and aldehyde **31** (1.87 g, 10.5 mmol, 81% pure) in dimethoxyethane (10 mL) was added dropwise during 10 min. The mixture was stirred at 20 °C for 1 h and then heated at 60–70 °C for 30 min, cooled, poured into water (50 mL), and extracted with ether (3 × 40 mL). The ether extracts were washed with water (3 × 10 mL) and brine (10 mL) and dried ($MgSO_4$), and the solvents were evaporated. The residue was chromatographed on silica gel to give, after evaporation of solvent and Kugelrohr distillation, 2.41 g of esters, bp 110–113 °C (0.3 mm) [lit.[13] bp 110–120 °C (0.25 mm)]. GLC analysis indicated 76% *E* and 12% *Z* ester **35**: NMR (CCl_4) δ 1.02 (3 H, s, >CCH_3), 1.11–1.28 (3 H, t, J = 7 Hz, $-CH_2CH_3$), 1.78 (3 H, broad s, =$C(CO_2R)CH_3$), 1.0–2.4 (11 H, m), 2.55–2.80 (1 H, m, >CH–≤), 3.9–4.3 (2 H, q, J = 7 Hz, $-CH_2CH_3$), 4.43 and 4.70 (2 H, 2s, >=CH_2), 6.43–6.84 (1 H, m, –CH=$C(CO_2R)$–); IR (film) 2980, 1705, 1650, 1475 cm^{-1}.

(*E*)-2-Methyl-5-(2-*endo*-methyl-3-methylenebicyclo-[2.2.1]hept-2-yl)-2-penten-1-ol (*trans*-β-Santalol) (7). To a cold (0 °C) solution of aluminum chloride (0.346 g, 2.59 mmol) in ether (40 mL) was added portionwise lithium aluminum hydride (0.290 g, 7.63 mmol). The solution was stirred for 20 min at 0 °C, and then esters **35** (1.00 g, 3.82 mmol, 93% pure) in ether (6 mL) were added dropwise. The solution was stirred at 0 °C for 45 min and then cautiously poured into 2 N HCl (50 mL). The aqueous layer was extracted with ether (3 × 25 mL). The combined organic extracts were washed successively with water (10 mL), saturated $NaHCO_3$ (3 × 10 mL), and brine (10 mL) and dried ($MgSO_4$). Evaporation of solvent, chromatography on silica gel, and Kugelrohr distillation gave 0.708 g (84%) of a colorless oil, bp 120–130 °C (0.3 mm). GLC analysis indicated 87% *trans*-β-santalol (**7**) and 9% *cis*-β-santalol (**2**): NMR (CCl_4) δ 1.03 (3 H, s, >CCH_3), 1.62 (3 H, broad s, –CH=$C(CH_2OH)CH_3$), 1.0–2.3 (12 H, m), 2.55–2.78 (1 H, m, >CH–≤), 3.85 (2 H, s, $-CH_2OH$), 4.43 and 4.70 (2 H, 2s, >=CH_2), 5.1–5.5 (1 H, m, –CH=$C(CH_2OH)$–), and a small singlet at 4.06 for $-CH_2OH$ of *cis*-β-santalol (**2**); IR (film) 3330, 2960, 1660 cm^{-1} (lit.[13]).

2-Methyl-5-(2-*endo*,3-dimethylbicyclo[2.2.1]hept-2-yl)-2-pentan-1-ol (Tetrahydro-β-santalol) (8). A mixture of *trans*-β-santalol (0.289 g, 1.31 mmol), platinum oxide (0.050 g), sodium nitrite (0.002 g), and ethanol (10 mL) was shaken under a hydrogen atmosphere for 20 h. The mixture was then filtered through Celite, and the solids were washed with toluene (3 × 10 mL). Solvents were evaporated and the residue was chromatographed on silica gel and Kugelrohr distilled to provide 0.257 g (87%) of tetrahydro-β-santalol, bp 120–130 °C (0.3 mm). GLC analysis indicated two isomers (78 and 16%): NMR (CCl_4) δ 0.73 (3 H, s, $-CH_3$), 0.83 and 0.93 (6 H, 2d, >$CHCH_3$), 0.75–2.3 (17 H, m), 3.25–3.53 (2 H, d, $-CH_2OH$); IR (film) 3550, 2940, 1460 cm^{-1}; MS *m/e* 224, 195, 177, 123 (lit.[13]).

2-Methyl-5-(2-*endo*-methyl-3-methylenebicyclo[2.2.1]hept-2-yl)pentan-1-ol (Dihydro-β-santalol) (3). Lithium shot was added to a mixture of esters **35** (131 mg, 0.5 mmol), ethanol (2 mL), ether (2 mL), and ammonia (10 mL) until a persistent blue color was observed. The reaction was quenched with ammonium chloride (0.5 g), and ammonia was allowed to evaporate. The residue was dissolved in ether (30 mL) and water (10 mL). The aqueous layer was extracted with ether (3 × 5 mL). The ether extracts were washed with water (5 mL) and then brine (5 mL) and dried (Na_2SO_4). Evaporation of the solvent and Kugelrohr distillation gave 85 mg (77%) of dihydro-β-santalol (**3**), bp 120–130 °C (0.3 mm). GLC analysis indicated a purity of 94%: NMR (CCl_4) δ 0.90–0.92 (3 H, d, J = 7 Hz, >$CHCH_3$), 1.03 (3 H, s, $-CH_3$), 0.85–2.4 (15 H, m), 2.55–2.75 (1 H, m, >CH–≤), 3.1–3.5 (2 H, dd, J_1 = 7 Hz, J_2 = 4 Hz, $-CH_2$–OH), 4.42 and 4.70 (2 H, 2s, >=CH_2); IR (film) 3350, 2960, 1460 cm^{-1} (lit.[18]).

3-(2-Hydroxy-3,3-dimethylbicyclo[2.2.1]hept-2-yl)propanal Hemiacetal (Exo and Endo Isomers) (36). Lactone **10** (1.164 g, 6 mmol) was reduced with diisobutylaluminum hydride, according to the procedure described for the preparation of lactol **12**, to give 1.180 g (100%) of lactol **36** as a viscous oil, which solidified upon standing: mp 45–47 °C; NMR ($CDCl_3$) δ 0.90 and 0.98 (6 H, 2s, >$C(CH_3)_2$), 0.9–2.2 (10 H, m), 3.6–4.6 (1 H, broad s, exchanges with D_2O, –OH), 5.13–5.57 (1 H, m, –O–CH(OH)–); IR ($CDCl_3$) 3400, shoulder at 3600, 2940, 1460, 1380, 1370 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.42; H, 10.27. Found: C, 73.04; H, 10.21.

2-(4-Methyl-3-pentenyl)-3,3-dimethylbicyclo[2.2.1]heptan-2-ol (Exo and Endo Isomers) (37). Lactol **36** (0.455 g, 2.27 mmol) was reacted with isopropylidenetriphenylphosphorane in dimethyl sulfoxide, according to the procedure described for the preparation of alcohol **13**, to give 0.427 g (85%) of alcohol **37**, bp 85–95 °C (0.2 mm). GLC analysis indicated one major component (98%): NMR ($CDCl_3$) δ 0.90 and 0.97 (6 H, 2s, >$C(CH_3)_2$), 1.62 and 1.68 (6 H, 2s, –C=$(CH_3)_2$), 0.9–2.7 (13 H, m), 4.90–5.40 (1 H, m, –CH=<); IR (film) 3500, 2950, 1440 cm^{-1}; MS *m/e* 222, 204, 189, 179, 167. Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.68; H, 11.62.

2-(4-Methyl-3-pentenylidene)-3,3-dimethylbicyclo[2.2.1]-heptane (Isosantalene) (38). Alcohol **37** (1.95 g, 8.78 mmol) was dehydrated with phosphorus oxychloride in pyridine, according to the procedure described for the preparation of β-santalene (**5**), to give 1.28 g (72%) of isosantalene (**38**), bp 105–115 °C (3 mm). GLC analysis indicated one major component (96%): NMR (CCl_4) δ 0.98 and 1.00 (6 H, 2s, >$C(CH_3)_2$), 1.63 and 1.68 (6 H, 2s, –C=$(CH_3)_2$), 2.3–3.0 (3 H, m, >CH–≤ and $-CH_2CH$=<), 4.7–5.25 (2 H, m, olefinic H); IR (film) 2940, 1670, 1450, 1370 cm^{-1}; MS *m/e* 204, 189, 175, 161. Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.11; H, 11.70 (ref 14).

Ethyl 3-(3,3-Dimethylbicyclo[2.2.1]hept-2-ylidene)propanoate (41). Lactone **10** (25.0 g, 0.129 mol) was reacted with ethanol, as described for the preparation of ester **34**, to yield, after distillation, 20.7 g (72%) of ester **41**, bp 105–106 °C (2 mm). GLC analysis indicated one major component (97%): NMR ($CDCl_3$) δ 1.00 and 1.02 (6 H, 2s, >$C(CH_3)_2$), 1.12–1.35 (3 H, t, J = 7 Hz, $-CH_2CH_3$), 0.85–2.1 (7 H, m), 2.95–3.07 (2 H, d, J = 7 Hz, $-CH_2CO$–), 2.80–3.15 (1 H, m, >CH–≤), 3.62–3.97 (2 H, q, J = 7 Hz, $-CH_2CH_3$), 4.93–5.18 (1 H, t, J = 7 Hz, –CH=<); IR (film) 2940, 1730, 1460, 1370, 1360 cm^{-1}; MS *m/e* 222,

207, 193, 179. Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.98. Found: C, 75.39; H, 9.96.

3-(2-Hydroxy-3,3-dimethylbicyclo[2.2.1]hept-2-yl)propanamide(Exo and Endo Isomers) (39). Method A. A mixture of lactone **10** (19.4 g, 0.10 mol), ammonia (250 mL), and sodium methoxide (6.75 g, 0.125 mol) was heated in a Parr reactor at 45 °C for 6 days. After cooling and partial evaporation, the residue was poured into water (200 mL) and extracted with chloroform (3 × 50 mL). The organic extracts were washed with water (2 × 10 mL) and dried (Na_2SO_4), and the solvents were evaporated. The residue was crystallized from toluene to give 7.73 g (37%) of amide **39**, mp 126–128 °C. Lactone **10** (6.33 g) was recovered from the mother liquor.

Method B. Lactone **10** (3.88 g, 0.02 mol) was reacted with dimethylaluminum amide, as previously described for the preparation of amide **32**, to give 2.38 g (56%) of amide **39**: mp 126–128 °C; NMR ($CDCl_3$) δ 0.92 and 0.98 (3 H, 2s, $>C(CH_3)_2$), 0.9–2.70 (12 H, m), 2.4–2.75 (1 H, broad s, –OH, exchanges with D_2O), 5.7–6.4 (2 H, broad s, $-NH_2$, exchanges slowly with D_2O); IR ($CHCl_3$) 3400 with shoulder at 3300, 2960, 1670, 1590 cm^{-1}; MS *m/e* 211, 194, 178. Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 68.51; H, 9.94; N, 6.67.

3-(3,3-Dimethylbicyclo[2.2.1]hept-2-ylidene)propanenitrile (40). Amide **39** (5.10 g, 0.0242 mol) was dehydrated with *p*-toluenesulfonyl chloride in pyridine, according to the procedure described for the preparation of nitrile **33**, to give 3.69 g (87%) of nitrile **40**, bp 75–76 °C (0.5 mm). GLC analysis indicated one major component (95%): NMR (CCl_4) δ 1.02 and 1.05 (6 H, 2s, $>C(CH_3)_2$), 0.95–2.60 (7 H, m), 2.90–3.02 (2 H, d, J = 7 Hz, $-CH_2CN$), 2.80–3.15 (1 H, m, >CH–≤), 4.80–5.03 (1 H, t, J = 7 Hz, –CH=<); IR (film) 2960, 2260, 1670, 1440, 1370, 1360 cm^{-1}; MS *m/e* 175, 166, 146. Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78. Found: C, 81.91; H, 9.74.

3-(3,3-Dimethylbicyclo[2.2.1]hept-2-ylidene)propanal (42). Ester **41** (10.25 g, 0.046 mol) was reduced with diisobutylaluminum hydride, according to the procedure for the preparation of aldehyde **31**, to give 6.46 g (78%) of aldehyde **42**, bp 85–90 °C (2 mm). GLC analysis indicated a purity of 89%: NMR (CCl_4) δ 1.02 and 1.05 (6 H, 2s, $>C(CH_3)_2$), 0.9–2.2 (7 H, m), 2.92–3.07 (2 H, dd, J = 2.5 and 7 Hz, $-CH_2CHO$), 2.8–3.1 (1 H, m, >CH–≤), 4.90–5.13 (1 H, t, J = 7 Hz, –CH=<), 9.50–9.58 (1 H, t, J = 2.5 Hz, –CHO); IR (film) 2920, 2700, 1725, shoulder at 1660, 1470, 1370, 1360 cm^{-1}; MS *m/e* 178, 163, 149, 135. 2,4-DNP, mp 147–149 °C. Anal. Calcd for $C_{18}H_{22}N_4O_4$: C, 60.32; H, 6.19; N, 15.63. Found: C, 60.50; H, 6.27; N, 15.38.

(2*Z*)-2-Methyl-5-(3,3-dimethylbicyclo[2.2.1]hept-2-ylidene)-2-penten-1-ol (43). Aldehyde **42** (3.60 g, 0.0202 mol, 85% pure) was reacted sequentially with ethylidenetriphenylphosphorane, *n*-butyllithium, and formaldehyde, according to the procedure described for the preparation of *β*-santalol (**2**), to give 1.57 g (35%) of *cis*-isosantalol (**43**), bp 105–115 °C (0.3 mm). GLC analysis indicated a purity of 96%: NMR ($CDCl_3$) δ 1.00 (6 H, s, $>C(CH_3)_2$), 1.78 (3 H, broad s, $-CH_3$), 0.9–2.0 (8 H, m), 2.4–3.1 (3 H, m, >CH–≤ and $-CH_2CH$=<), 4.13 (2 H, s, $-CH_2OH$), 4.71–4.95 (1 H, t, J = 7 Hz, –CH=<), 5.1–5.5 (1 H, m, CH=C(CH_2OH)–); IR (film) 3300, 2930, 1450, 1375, 1360 cm^{-1}; MS *m/e* 220, 202, 189, 187, 173, 159. Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.89. Found: C, 81.58; H, 10.84.

Ethyl 2-Methyl-5-(3,3-dimethylbicyclo[2.2.1]hept-2-ylidene)-2-pentenoate (45). Sodium hydride (1.555 g, 0.0324 mol, 50% oil dispersion) was washed with toluene and then suspended in dimethoxyethane (150 mL). Triethyl phosphonopropanoate (7.721 g, 0.0324 mol) in dimethoxyethane (10 mL) was added rapidly. When hydrogen evolution had ceased, the mixture was cooled (0 °C) and aldehyde **42** (6.34 g, 0.0356 mol, 85% pure) in dimethoxyethane was added dropwise during 15 min. After being stirred at 0 °C for 1 h, the mixture was poured into water (150 mL) and extracted with petroleum ether (35–60 °C) (4 × 50 mL). The extracts were washed with brine (2 × 20 mL) and dried (Na_2SO_4), and the solvents were evaporated. The residue was distilled through a short-path column to give 7.77 g (83%) of esters **45**, bp 108–120 °C (0.3 mm), as a mixture of isomers. Redistillation gave analytically pure material, bp 108–112 °C (0.3 mm). GLC analysis indicated four isomers: NMR (CCl_4) δ 1.02 (6 H, s, $>C(CH_3)_2$), 1.18–1.42 (3 H, t, J = 7 Hz, $-CH_2CH_3$), 1.82 (3 H, s, =C(CH_3)–), 0.95–2.2 (7 H, m), 2.55–3.2 (3 H, m, >CH–≤ and $-CH_2CH$=<), 3.99–4.32 (2 H, q, J = 7 Hz, $-CH_2CH_3$), 4.76–5.00 (1 H, t, J = 7 Hz, –CH=<), 5.6–5.8 and 6.49–6.74 (1:4 ratio, 1 H, t, J = 8 Hz, –CH=C(CO_2Et)–); IR (film) 2980, 1715, 1650 cm^{-1}; MS *m/e* 262, 246, 189, 173; UV (95% EtOH) 217 nm (calcd 217) (ϵ 13 400). Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.81; H, 9.98. Found: C, 78.08; H, 10.15.

(2*E*)-2-Methyl-5-(3,3-dimethylbicyclo[2.2.1]hept-2-ylidene)-2-penten-1-ol (46). Esters **45** (0.917 g, 3.5 mmol, mixture of isomers) were reduced with aluminum hydride, according to the procedure described for the preparation of *trans*-*β*-santalol (**7**), to yield 0.711 g (92%) of alcohols **46**, bp 115–125 °C (0.3 mm). GLC analysis indicated a mixture of allylic alcohols totalling 100%: NMR ($CDCl_3$) δ 1.00 (6 H, s, $>C(CH_3)_2$), 1.70 (3 H, s, –CH=C(CH_3)—), 0.9–2.0 (7 H, m), 2.60–3.10 (3 H, m, >CH–≤ and $-CH_2CH$=<), 4.00 and 4.15 (2 H, 2s, $-CH_2OH$, 4:1 ratio), 4.75–5.07 (1 H, m, –CH=<), 5.25–5.65 (1 H, m, CH=C(CH_2OH)–); IR (film) 3400, 2960, 1670, 1430, 1385, 1370 cm^{-1} (ref 14).

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