(R = p-$CH_3OC_6H_4$), 100-07-2; RCOCl (R = o-ClC_6H_4), 609-65-4; RCOCl (R = m-$NO_2C_6H_4$), 121-90-4; RCOCl (R = o-$NO_2C_6H_4$), 122-04-3; RCOCl (R = 2-furyl), 527-69-5; RCOCl (R = 2-thienyl), 5271-67-0; RCOCl (R = cyclopropyl), 4023-34-1; RCOCl (R = $(CH_3)_3C$), 3282-30-2; RCOCl (R = CH_3), 75-36-5; RCOCl (R = C_2H_5), 79-03-8; ClCOOR (R = CH_3), 79-22-1; ClCOOR (R = C_2H_5), 541-41-3; ClCOOR (R = $(CH_3)_2CHCH_2$), 543-27-1; hydrogen cyanide, 74-90-8; thallium, 7440-28-0; thallium(I) cyanide, 13453-34-4; trimethylcyanosilane, 7677-24-9; trimethylchlorosilane, 75-77-4.

References and Notes

(1) For the previous paper in this series, see E. C. Taylor, R. A. Conley, D. K. Johnson, and A. McKillop, *J. Org. Chem.*, **42**, 4167 (1977).
(2) We are indebted to the National Science Foundation (Grant No. CHE7616506) and to Eli Lilly & Co., Indianapolis, Ind., for support of this work.
(3) On leave from Cuttington University College, Suacoco, Liberia, as Postdoctoral Scholar of the Episcopal Church.
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(10) (a) From silver cyanide and trimethylchlorosilane (12 h under pressure; 38% yield): T. A. Bither, W. H. Knoth, R. V. Lindsey, Jr., and W. H. Sharkey, *J. Am. Chem. Soc.*, **80**, 4151 (1958); (b) from potassium cyanide, trimethylchlorosilane and 18-crown-6 (24 h; 45% yield): J. W. Zubrick, B. I. Dunbar, and H. D. Durst, *Tetrahedron Lett.*, 71 (1975).

Total Synthesis of *Racemic* α-Santalene and of *Racemic* Teresantalic Acid[1a]

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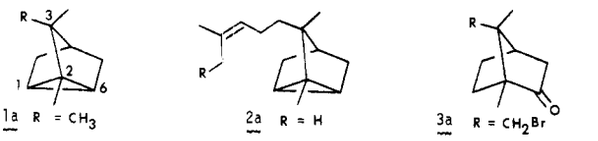
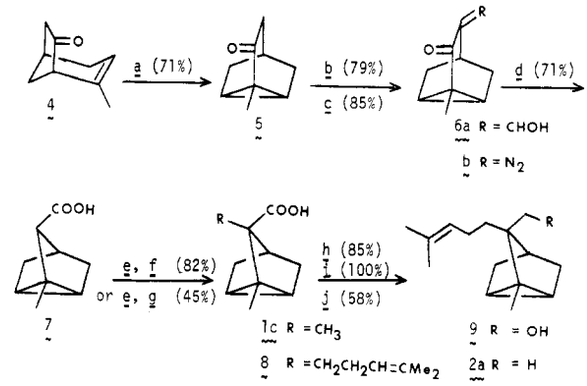
Representative examples of the tricyclene family of terpenes, characterized structurally by the presence of a 3,3-disubstituted 2-methylbicyclo[2.2.1.$0^{2,6}$]heptane skeleton, include the parent monoterpene tricyclene (**1a**) and its C-3 derivatives teresantalol (**1b**) and teresantalic acid (**1c**), as well as the sesquiterpenes α-santalene (**2a**) and α-santalol (**2b**).[2,3]



Although devoid of relative stereochemical relationships due to symmetry, these tricyclic carbon skeletons have attracted considerable synthetic interest. These efforts[4] have involved initial preparation of 7,7-disubstituted bicyclo[2.2.1]heptanones such as π-bromocamphor (**3a**)[4a] or chloro ketone **3b**[4b], cyclopropane ring closure via a carbene or carbenoid intermediate to generate the tricyclic skeleton, and subsequent functional group modification to yield the desired mono- and sesquiterpenes. We wish to report an alternative route to this general class of natural products which, via the intermediacy of tricyclic acid **7**, allows selective synthetic manipulation of *both* C-3 substituents of the tricyclene nucleus. This approach is illustrated by the total synthesis of *racemic* α-santalene (**2a**) and of *racemic* teresantalic acid (**1c**).

As shown in Scheme I, irradiation of the β,γ-unsaturated ketone **4**[5] in acetone resulted in a smooth rearrangement[6] to give the tricyclic α-methyl cyclopropyl ketone **5**. Conversion of **5** into the α′-formyl derivative **6a**, followed by treatment with tosyl azide yielded the diazo ketone **6b**,[7] which upon photolysis underwent ring contraction[8] to furnish the key intermediate, tricyclic acid **7**. Satisfactory generation of the dianion of acid **7** was achieved by exposure of **7** to lithium diisopropylamide (2.5 equiv, 50 °C)[9] *followed by* addition of n-butyllithium (1 equiv, 50 °C).[10,11] Alkylation of this dianion with methyl iodide yielded racemic teresantalic acid (**1c**). Alternatively treatment of the dianion with 5-iodo-2-methyl-2-pentene gave the 3,3-disubstituted acid **8**, which upon lithium aluminum hydride reduction yielded alcohol **9**, a structural isomer of the important natural product α-santalol (**2b**). Tosylation of alcohol **9** and reduction with lithium triethylborohydride furnished *racemic* α-santalene (**2a**).

Scheme I



[a] $h\nu$, acetone, 25 °C, 10 h. [b] NaH, ethyl formate, Et_2O/EtOH, 25 °C, 42 h. [c] Tosyl azide, Et_3N, CH_2Cl_2, 25 °C, 78 h. [d] $h\nu$, $NaHCO_3$, THF/H_2O, 25 °C, 45 min. [e] Lithium diisopropylamide (2.5 equiv), THF, 50 °C, 1 h; then n-BuLi (1 equiv) 50 °C, 1 h. [f] CH_3I, 25 °C, 16 h. [g] $Me_2C{=}CHCH_2CH_2I$, 25 °C, 20 h. [h] Lithium aluminum hydride, THF, reflux, 22 h. [i] Tosyl chloride, pyridine, 5 °C, 32 h. [j] Lithium triethylborohydride, THF, 25 °C, 72 h.

Experimental Section

General. All reactions were carried out in an inert nitrogen atmosphere and were routinely monitored by TLC or VPC using a Varian Aerograph 1200 instrument equipped with 5% SE-30 on Gas Chromosorb Q (100/120 mesh) ⅛ in. × 10 ft or 15% FFAP on Gas Chromosorb Q (100/120 mesh) ⅛ in. × 7 ft columns. Photochemical reactions were performed using a Hanovia 450 W, 3.7 A quartz high pressure mercury vapor lamp in a circulating ice-water cooled double-walled quartz immersion well. Photochemical solutions were deoxygenated by purging with dry nitrogen for 30 min and maintained at ca. 10 °C during irradiation. Melting points were determined on a Mel-temp apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer Model 237B grading infrared spectrometer; ^{1}H-NMR spectra were measured on a Perkin-Elmer R-12 spectrometer, a Varian A-60 instrument equipped with cross correlation, or a Varian HA-100 instrument and chemical shifts are reported in ppm downfield (δ) from internal Me_4Si. ^{13}C-NMR spectra were obtained on a Bruker WH90 instrument and chemical shifts are reported in ppm downfield (δ) from internal Me_4Si. High-resolution mass spectra were obtained using a CEC Model 21-100 mass spectrometer. The microanalytical determination was done by Chemalytics, Inc., Tempe, Ariz.

2-Methyltricyclo[3.2.1.$0^{2,7}$]octan-3-one (5). Irradiation of 4-methylbicyclo[3.2.1]oct-3-en-6-one (3.91 g, 28.7 mmol) in acetone (300 mL) for 10 h resulted in complete disappearance of starting material. After evaporation of the acetone at reduced pressure, the dark residue was dissolved in Et_2O and filtered through aluminum oxide (30 g, activity III) and after evaporation of the solvent distilled to give 2.80 g (71%) of tricyclic ketone **5**: bp 45–47 °C (0.1 mm); IR (CCl_4) 3025 and 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 3), 1.1–1.5 (m, 1), 1.5–2.0 (m, 4), 1.94–2.08 (br d, 2, J = 4 Hz), 2.0–2.6 (m, 2); ^{13}C NMR ($CDCl_3$) 209.8 (s), 44.2 (t), 35.6 (s), 31.9 (t), 30.6 (d), 28.8 (d), and 16.8 (q); mass spectrum, m/e (rel intensity) 136 (molecular ion, 24), 93 (32), 92 (100), and 79 (36). Anal. Calcd for $C_9H_{12}O$: m/e 136.0888. Found: m/e 136.0890.

4-Formyl-2-methyltricyclo[3.2.1.$0^{2,7}$]octan-3-one (6a). Sodium hydride (0.60 g, 25 mmol), ethyl formate (9.50 g, 12.8 mmol), ethanol (0.50 g, 10 mmol), and tricyclic ketone **5** (1.72 g, 12.6 mmol) were stirred at 25 °C for 42 h in diethyl ether (100 mL). The reaction mixture was extracted with 10% KOH (2 × 50 mL) and the organic

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phase was washed with brine and dried ($MgSO_4$) and the excess solvent was evaporated under reduced pressure to give 0.31 g of recovered tricyclic ketone **5**. The basic aqueous phase was chilled in an ice bath, acidified by addition of 10% HCl, and extracted with ether. The aqueous phase was saturated by addition of sodium chloride and re-extracted with ether. The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated at reduced pressure to give a residue which was distilled to yield 1.34 g (79%) of formyl ketone **6a**; bp 55–58 °C (0.1 mm); IR (CCl_4) 3040, 1655, 1585, and 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (s, 3), 1.1–1.7 (m, 3), 1.7–2.7 (m, 4), 2.4–2.7 (m, 1), and 7.08 (s, 1).

4-Diazo-2-methyltricyclo[3.2.1.0^{2,7}]octan-3-one (6b). *p*-Toluenesulfonyl azide (3.00 g, 15 mmol), triethylamine (3.90 g, 38 mmol), and formyl ketone **6a** (1.40 g, 8.6 mmol) were stirred at 25 °C in methylene chloride (30 mL) in a light-protected flask for 3 days. The mixture was diluted with ether (100 mL), washed with 10% KOH (2 × 25 mL) and brine, dried ($MgSO_4$), and then evaporated at reduced pressure to give a residue which was purified by chromatography on silica gel (35 g) using pentane–ether mixtures (7:3 to 5:5, v/v) to yield 1.17 g (85%) of diazo ketone **6b**, a bright yellow oily residue which solidified upon standing: mp 50–52 °C; IR (CCl_4) 3035, 2075, 1645, 1635, 1375, 1250, 1150, 1025, 950, and 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (s, 3), 1.5–2.3 (m, 6), and 2.95–3.20 (m, 1).

2-Methyltricyclo[2.2.1.0^{2,6}]heptane-3-carboxylic Acid (7). The crude diazo ketone **6b** (0.280 g, 1.73 mmol) was irradiated in water (250 mL) containing tetrahydrofuran (50 mL) and sodium bicarbonate (2.0 g) for 45 min. The reaction was monitored by observing the disappearance of the characteristic diazo absorption (2075 cm^{-1}) in the infrared spectrum. Sodium hydroxide (5 g) was dissolved in the reaction mixture, and then this mixture was extracted with diethyl ether (discarded), acidified by addition of 10% HCl, saturated with sodium chloride, and finally extracted several times with ether. The ether extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure to give a residue that was purified by chromatography on silica gel (10 g) with ether to give 0.187 g (71%) of tricyclic acid **7** as a waxy solid, which was further purified by sublimation (60 °C, 0.3 mm): mp 71–72 °C; IR (CCl_4) 1700, 1425, 1420, 1300, 1295, 1240, 1230, 1220, and 855 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (d of d, 1, J = 1 5, 5 Hz). 1.08 (d of d, 1, J = 1.5, 5 Hz), 1.15–1.6 (m, 3) 1.29 (s, 3), 1.83 (d, 1, J = 11 Hz), 2.15–2.35 (m, 1), and 2.29 (d, 1, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 180.9 (s), 53.1 (d), 36.4 (d), 34.6 (t), 31.9 (t), 20.8 (s), 18.9 (d), 17.7 (d), and 13.7 (q); mass spectrum, *m/e* (rel intensity) 152 (molecular ion, 100), 111 (28), 107 (96), 93 (50), 92 (28), 91 (90), 81 (44), 79 (78), 77 (36), and 66 (36). Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95; *m/e*, 152.0837. Found: C, 71.03; H, 7.80; *m/e*, 152.0835.

Teresantalic Acid (1c). To a stirred solution of diisopropylamine (0.40 g, 3.9 mmol) in THF (10 mL), a solution of *n*-butyllithium in hexane (1.5 M, 2.3 mL, 3.4 mmol) was added at −5 °C. This mixture was stirred for 15 min and then tricyclic acid **7** (0.210 g, 1.38 mmol) in THF (3 mL) was added. The resulting mixture was heated at ~50 °C for 1 h and then cooled to ca. −30 °C and *n*-butyllithium in hexane (1.0 mL, 1.5 mmol) was added. After warming to 10 °C for ca. 15 min, the mixture was heated at 50 °C for 1 h. A small aliquot of this mixture was quenched in D_2O, acidified with 10% HCl, and extracted with ether to give recovered acid **7**, which, when analyzed by GC/MS (3% OV-101), revealed a ratio of d_0/d_1 (*m/e* 152/153) of ca. 2.9, respectively.[10] The original dianion solution above was chilled to −5 °C, methyl iodide (1.0 g, 7 mmol) in THF (2 mL) was added, and the resulting mixture was stirred for 18 h at room temperature. The contents were poured into water (100 mL), acidified with 10% HCl, and extracted with ether. The aqueous phase was saturated with sodium chloride and extracted with additional ether. The combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated at reduced pressure to give a residue, which after filtration through silica gel (5 g) with ether and sublimation (80 °C, 0.3 mm) yielded 190 mg of material which on the basis of VPC analysis was composed of 91% teresantalic acid (**1c**) and 9% recovered starting acid **7**. This corresponds to a yield of 82% of teresantalic acid (**1c**). Pure **1c** was obtained by recrystallization (EtOH): mp 160–162 °C (lit. mp [chiral material][12] 158 °C); IR (CCl_4) 1700, 1445, 1405, 1290, 1200, 1155, 1140, 1080, 1040, 975, 940, and 855 cm^{-1}; ^1H NMR δ 0.86 (br d, 1, J = 6 Hz), 1.0–1.9 (m, 3), 1.15 (s, 3), 1.23 (s, 3), 1.58, 1.77 (br d, 2, J = 5 Hz), and 1.9–2.1 (m, 1); mass spectrum, *m/e* (rel intensity) 166 (molecular ion, 54), 121 (100), 93 (80), and 74 (64). Anal. Calcd for $C_{10}H_{12}O_2$: *m/e* 166.0994. Found: *m/e* 166.0988.

2-Methyl-3-(4-methylpent-3-en-1-yl)tricyclo[2.2.1.0^{2,6}]heptane-3-carboxylic Acid (8). As described above for teresantalic acid (**1c**), tricyclic acid **7** (0.230 g, 1.5 mmol) was treated with lithium diisopropylamide (2.6 equiv) in THF for 1 h at ~50 °C, followed by addition of *n*-butyllithium (1 equiv), first at −30 °C and then at 50 °C for 1 h. The reaction mixture was cooled to −78 °C and 5-iodo-2-methyl-2-pentene[13] (1.3 g, 6.2 mmol) was added. The mixture was allowed to warm to room temperature and was stirred for 20 h. The mixture was poured into cold 10% KOH (50 mL) and extracted with pentane (3 × 50 mL). The aqueous phase was cooled in an ice bath, acidified with 10% HCl, saturated with sodium chloride, and then extracted with ether. The combined organic extracts were washed with brine and evaporated at reduced pressure to give a residue that was partitioned between pentane (150 mL) and saturated sodium bicarbonate (50 mL). After extraction of the aqueous phase with additional pentane (3 × 50 mL), the combined organic phases were dried ($MgSO_4$) and evaporated under reduced pressure to give crude alkylated acid **8**. Acidification of the bicarbonate phase (10% HCl), followed by normal workup, yielded 0.140 g of recovered starting acid **7**. Product **8** was purified by crystallization (CH_3CN) to give 62 mg (45%) of **8**: mp 97–98 °C; IR (CCl_4) 1695, 1450, 1410, 1375, 1290, 1260, 1230, 1200, 1175, and 860 cm^{-1}, ^1H NMR δ 0.86 (br d, 1, J = 6 Hz), 1.08 (br, 1, J = 6 Hz), 1.0–1.4 (m, 4), 1.26 (5.3), 1.4–1.8 (m, 2), 1.64 (d, 6, J = 8 Hz), 1.8–2.4 (m, 3), and 4.98–5.24 (br t, 1); ^{13}C NMR ($CDCl_3$) δ 12.6, 17.6, 19.7, 20.5, 23.9, 25.0, 25.7, 30.2, 31.4, 33.0, 37.5, 58.6, 124.3, 131.8, 183.5; mass spectrum, *m/e* (rel intensity) 254 (molecular ion, 10), 164 (14), 150 (22), 107 (24), 82 (100), and 69 (20). Anal. Calcd for $C_{15}H_{22}O_2$: *m/e*, 234.1620. Found: *m/e*, 234.1624.

3-Hydroxymethyl-2-methyl-3-(4-methylpent-3-en-1-yl)tricyclo[2.2.1.0^{2,6}]heptane (9). A mixture of tricyclic acid **8** (0.10 g, 0.43 mmol) and lithium aluminum hydride (0.03 g, 0.88 mmol) in THF (15 mL) was heated at reflux for 22 h. To the cooled solution ethyl acetate (0.1 g) was added, the volume was reduced by evaporation at reduced pressure, and the residue was treated with 10% KOH (5 mL), saturated sodium potassium tartrate (5 mL), and water. This mixture was extracted several times with pentane and the combined organic extracts were dried (Na_2SO_4) and then evaporated under reduced pressure to give 0.080 g (85%) of crude alcohol **9**. A sample of pure **9** (preparative VPC, 5% SE-30) showed: IR (CCl_4) 3620, 2450, 3040, 1450, 1370, 1285, 1080, 1030, 1005, 850, and 835 cm^{-1}; ^1H NMR δ 0.90 (AB d of d, 2, J = 6, 4 Hz), 1.0–1.6 (m, 5), 1.06 (s, 3), 1.66 (d, 6, J = 8 Hz), 1.6–1.9 (m, 3), 1.9–2.3 (m, 2), 3.64 (s, 2), and 5.06–5.30 (br t, 1); mass spectrum *m/e* (rel intensity) 220 (molecular ion, 14), 184 (44), 138 (18), 120 (26), 110 (36), 105 (34), 93 (32), and 69 (100). Anal. Calcd for $C_{15}H_{24}O$: *m/e*, 220.1827. Found: *m/e*, 220.1831.

α-Santalene (2a). Tricyclic alcohol **9** (0.040 g, 0.18 mmol) was treated with *p*-toluenesulfonyl chloride (0.06 g, 0.31 mmol) in pyridine (1 mL) at 5 °C for 32 h. Evaporation at reduced pressure and extraction with CCl_4 furnished, after evaporation, 0.07 g (102%) of crude tosylate **9** (R = OTs): ^1H NMR δ 1.00 (s, 3), 0.7–2.1 (m, 12), 1.63 (d, 6, J = 7 Hz), 2.47 (s, 3), 3.97 (s, 2), 4.88–5.25 (br, t, 1), 7.35 (d, 2, J = 8 Hz), and 7.85 (d, 2, J = 8 Hz). The crude tosylate (0.045 g, 0.12 mmol) was dissolved in THF (5 mL) and a THF solution of lithium triethyl borohydride (1 M, 2.0 mL, 2 mmol) was added. After this mixture was allowed to stand at room temperature for 3 days, it was cooled in an ice–water bath, and cold 10% KOH (5 mL) and 30% hydrogen peroxide (0.3 g) were cautiously added. After stirring for 1 h, the mixture was diluted with water (50 mL) and extracted with pentane. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure to give 0.017 g of a residue which by VPC analysis contained α-santalene (**2a**) and the starting alcohol **9** in the ratio of 2.3:1. This corresponds to a 58% yield of **2a**. Pure **2a** was obtained by preparative VPC on 5% SE-30 and it was identical to natural α-santalene as judged by IR,[14] NMR,[15] and mass spectral data.[15] Synthetic racemic **2a** showed: IR (CCl_4) 3040, 1455, 1370, 1340, 1315, 1285, 1270, 1260, 1230, 1195, 1165, 1155, 1120, 1095, 1055, 1040, 970, 935, 905, 875, 850, 835, and 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80 (s, 3), 0.98 (s, 3), 0.7–1.4 (m, 6), 1.64 (d, 6, J = 7 Hz), 1.4–2.2 (m, 5), and 4.96–5.74 (br t, 1); mass spectrum, *m/e* (intensity) 204 (molecular ion, 20), 189 (24), 161 (18), 122 (28), 121 (46), 107 (40), 95 (54), 94 (100), 93 (96), 91 (28), 89 (26), and 69 (36).

Registry No.—**1c**, 562-66-3; **2a**, 512-61-8; **5**, 65878-89-9; **6a**, 65878-90-2; **6b**, 65878-91-3; **7**, 65878-92-4; **8**, 65878-93-5; **9** tosylate, 65899-41-4; **9**, 65878-94-6; 4-methylbicyclo[3.2.1]oct-3-en-6-one, 53216-75-4; 5-iodo-2-methyl-2-pentene, 43161-11-1.

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(10) Quenching of the dianion with D_2O resulted in ca. 85% incorporation of deuterium at C-3; when the *n*-BuLi treatment was omitted, ca. 20–30% deuterium incorporation was observed.
(11) Preliminary attempts to generate the enolate of the methyl ester of **7** using lithium diisopropylamide were unsuccessful as judged by deuterium incorporation; however, see P. A. Grieco and Y. Masaki, *J. Org. Chem.*, **40**, 150 (1975).
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(15) We are indebted to Dr. Bruno Willhalm, Fermenish SA, Geneva for spectral data of natural α-santalene.

A New Synthesis for Δ^{24}-Sterols: Preparation of Cholesta-5,24-dien-3β-ol (Desmosterol)[1a,2]

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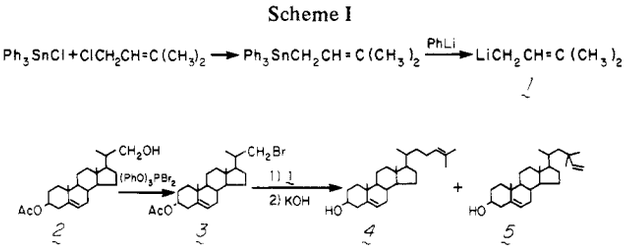
The new synthesis of Δ^{24} unsaturated sterols which involves the coupling reaction between dimethylallyllithium and a bromide is exemplified by the production of cholesta-5,24-dien-3β-ol (desmosterol; **4**) in Scheme I. The anticipated value of the new synthesis is in the preparation of other Δ^{24}- sterols. Reactions such as reductions of double bonds may be performed on the nuclear part of the sterol before the side chain with the labile Δ^{24} bond is added.

In this synthesis of desmosterol, 3β-acetoxy-23,24-dinorchol-5-en-22-ol (**2**), a known compound,[3,4] is converted into 3β-acetoxy-22-bromo-23,24-dinorchol-5-ene (**3**) with $(PhO)_3PBr_2$ in the presence of 1 mol of pyridine. This combination of reagents has been used[5] for the conversion of alkene or alkyne alcohols into bromides.

Preparation of compounds **4** was based on the analogous coupling reaction of allyllithium with 1-iodopentane to give 1-octene.[6] The required dimethylallyllithium reagent (**1**) was prepared by the transmetallation procedure of Seyferth and Weiner[7] involving a triphenyltin intermediate.

Scheme I



The coupling reaction produces the desired product and a minor by-product (**5**, ca. 3:1). The by-product has the same mol wt (as determined by MS) as the main product. The spectral data from **5** which include ^{13}C-NMR, ^{1}H-NMR, and IR determinations support structure **5**. The ^{13}C-NMR peaks at 109.7 and 149.8 ppm downfield from Me_4Si are comparable to the 108.1- and 148.1-ppm values for the vinyl protons of 3,3-dimethyl-1-butene.[8,9] The ^{1}H-NMR spectrum includes vinyl protons with chemical shifts and coupling constants similar to those of model compounds 3,3-dimethyl-1-butene[10] and 17 α-vinylestradiol.[11] The compound absorbs strongly at 907 cm^{-1} which is consistent with the IR absorption of a terminal methylene group. Previous studies[12,13] with allylic Grignard reagents indicate that the products formed are derived from the starting halide and/or the corresponding allylic isomer. This phenomenon appears to be occurring with the dimethylallyllithium in the coupling reaction causing the formation of 23,23-dimethyl-26,27-dinorcholesta-5,24-dien-3β-ol (**5**).

The new synthesis of desmosterol (**4**) is more practical than previously published preparations of this compound. The overall yield of desmosterol from the new synthesis is 14% when the 3β-acetoxy-23,24-dinorchol-5-en-22-ol starting material is prepared from commercially available 3β-acetoxy-23,24-dinorchol-5-en-22-oic acid by the Hayatsu method.[4] Compound **4** is produced from 3β-acetoxychol-5-en-24-oic acid in 9% yield,[14] and from 3β-acetoxy-26-norcholest-5-en-25-one in 36% yield,[15] but 3β-acetoxy-23,24-dinorchol-5-en-22-oic acid is a much more economical starting material. The nickel tetracarbonyl used to prepare π-(dimethylallyl)-nickel bromide in one synthesis[16] is highly toxic, and no yield is reported for the first step (Arndt–Eistert homologation) in another preparation.[16] The latter synthesis also uses 3β-acetoxy-23,24-dinorchol-5-en-22-oic acid as the starting material, and the yield of desmosterol from the homologue is 21%.

The new coupling reaction can be used for preparing Δ^{24} sterols with modified nuclear systems. Reactions such as hydrogenation which the Δ^{24} bond would not survive are performed before the addition of the Δ^{24} bond. The Fagerlund and Idler synthesis of desmosterol[14] can also be adapted for the preparation of other Δ^{24}-sterols. However, the limitations of yield and cost discussed in the synthesis of desmosterol would obtain.

Experimental Section

Melting points were determined on a Hoover Uni-Melt apparatus, under vacuum, and are uncorrected. IR spectra were taken on a Perkin-Elmer Model 521 spectrophotometer equipped with a KBr micropellet attachment. High-resolution MS spectra were determined on an A.E.I.M.S. 30. The ^{1}H-NMR spectrum was determined on a Bruker 270 MHz instrument, and the natural abundance, ^{1}H-decoupled, ^{13}C-NMR spectrum was obtained with an XL-100-15/VFT-100 instrument. The spectra were determined in $CDCl_3$, and chemical shifts are reported downfield from the Me_4Si internal standard. Microanalyses were carried out by M-H-W Laboratories, Garden City, Mich.

Dimethylallyltriphenyltin. This compound was produced from triphenyltin chloride (ICN Pharmaceuticals, Inc., Plainview, N.Y.; 10.9 g, 28.3 mmol) and 1-chloro-3-methyl-2-butene (Eastman, 4.6 g, 44 mmol).[7] The white solid was recrystallized from hexanes (50 mL), and the product (7.2 g, 17.19 mmol, 60.7%) which melted over several degrees was recrystallized from hexanes by removing the solvent at room temperature with nitrogen until crystals began to form. The many-sided irregular crystals melt at 71–72.5 °C and decompose in boiling hexanes: IR (KBr) 3060, 3050, 2964, 2910, 1694, 1657, 1651, 1426, 848, 807, 724, 710, 448 cm^{-1}. Anal Calcd for $C_{23}H_{25}Sn$ (420.147): C, 65.74; H, 5.99. Found: C, 65.82; H, 5.99.

3β-Acetoxy-22-bromo-23,24-dinorchol-5-ene (3). A 250-mL three-neck distilling flask equipped with a dropping funnel, drying tube, nitrogen inlet, and magnetic stirring bar was flame dried under a nitrogen atmosphere. Triphenyl phosphite (Aldrich, 5.4 g, 17.4 mmol) and ether (18 mL, freshly distilled from lithium aluminum

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