AcC-3), 2.17 (s, 3, AcC-19), 4.90 (heptet, 1 H, J = 3.8 Hz, HC-3), 5.99 and 6.30 (AB q, 2 H, J = 11 Hz, HC-6, HC-7), 7.04 (s, 1 H, HC-19); mass spectrum, m/e (relative intensity) 484 (M^+, 5), 364 (100), 351 (17), 349 (12), 259 (251), 251 (42), 197 (25), 157 (26), 156 (23), 147 (22), 145 (17), 143 (24). Anal. ($C_{31}H_{48}O_4$) C, H. A third fraction consisted of a material for which we assigned the structure 11 on the basis of its UV (λ_{max} 260 nm) which shifted to λ_{max} 278 nm on addition of traces of I_2 and exposure to sunlight, forming the tachysterol derivative 13. When purification of 11 was attempted on a TLC plate, it isomerized to 12, as was evident from its it UV (λ_{max} 219, 267 nm) and NMR spectra.

An isooctane solution of 11 (5 mg, 5 mL) was heated for 2 h at 50 °C, whereupon the UV changed (λ_{max} 219, 267 nm). The isolated material was identical (NMR) with 12.

Hydrolysis of 19-Acetoxyvitamin D_3 Acetate (12) and of 19-Acetoxyprevitamin D_3 Acetate (11). A solution of 12 (10 mg) in methanolic KOH (5 mL, 0.05%) was left at room temperature, its UV being monitored. A change in the UV was observed after only 5 min, the bands at 267 and 219 decreasing in intensity while new ones with λ_{max} between 240 and 260 appeared. After 2 h these (λ_{max} 242, 252, and 257 nm) reached their maximum value, indicating the formation of 14. The solution was then brought to neutral pH, and the solvent was evaporated to dryness at room temperature. The residue showed in the NMR signals at δ 9.50 and 9.55 due to the aldehydic protons.

On being left for a longer time, the UV maximum of 14 decreased, and a new band appeared at 298 nm. The same λ_{max} value was obtained when a solution of 12 in methanolic KOH (5 mL, 0.5%) was left for 5 min. This UV band was assigned to the structure 15.

Similar hydrolysis (0.5% KOH in MeOH) of 11 also resulted in 15 (UV λ_{max} 298 nm).

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Registry No. 5, 1107-90-0; 6, 73197-94-1; 7, 73197-95-2; 8, 73197-96-3; 9, 73197-97-4; 10, 13640-06-7; 11, 55105-86-7; 12, 73245-72-4; 13, 73210-06-7; 14, 73197-98-5; 15, 73197-99-6; 3β,19-diacetoxycholesta-4,6-diene, 73198-00-2.

Asymmetric Synthesis of (-)-3β-Hydroxy-17-methoxy-*D*-homo-18-nor-5α-androsta-13,15,17-triene

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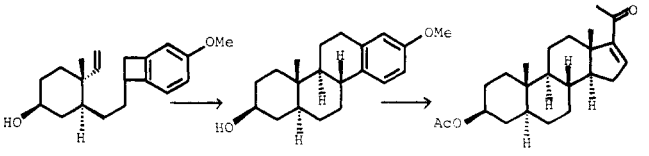
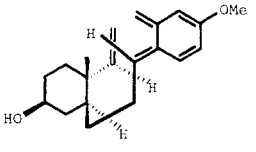
A stereoselective synthesis of (-)-3β-hydroxy-17-methoxy-*D*-homo-18-nor-5α-androsta-13,15,17-triene (2), an important intermediate in the synthesis of 20-oxo-5α-Δ^{16}-pregnen-3β-ol acetate (3), has been achieved by thermolysis of optically active 1-ethenyl-4-hydroxy-2-[2-(4-methoxybenzocyclobutenyl)ethyl]-1-methylcyclohexane (1).

There have appeared many reports[1-3] on the stereocontrolled synthesis of steroid hormones, a class of compounds which show pharmaceutically interesting activities as sex hormones, and recently attention has been focussed on the development of asymmetric syntheses[4-9] of this type of compound. Although synthetic approaches to the A-ring aromatic and 19-nor steroid nuclei, based on novel BC ring construction via intramolecular cycloaddition to *o*-quinodimethanes derived from benzocyclobutenes or other precursors, have proved to be effective methods,[10-16] none of these provides a synthetic route to the pregnane-type steroids in either racemic or optically active form. Pregnane-type steroids constitute an important class of steroid hormones and could also be key intermediates in the synthesis of other classes of steroid hormones.[1] In this paper we wish to report an efficient synthesis of optically active 3β-hydroxy-17-methoxy-*D*-homo-18-nor-5α-androsta-13,15,17-triene (2) [which has already been transformed into 20-oxo-5α-Δ^{16}-pregnen-3β-ol acetate (3) in its *dl* form[17]] by a stereoselective reaction. The synthesis is based on the chiral cyclohexane derivative 1 which un-

Scheme I





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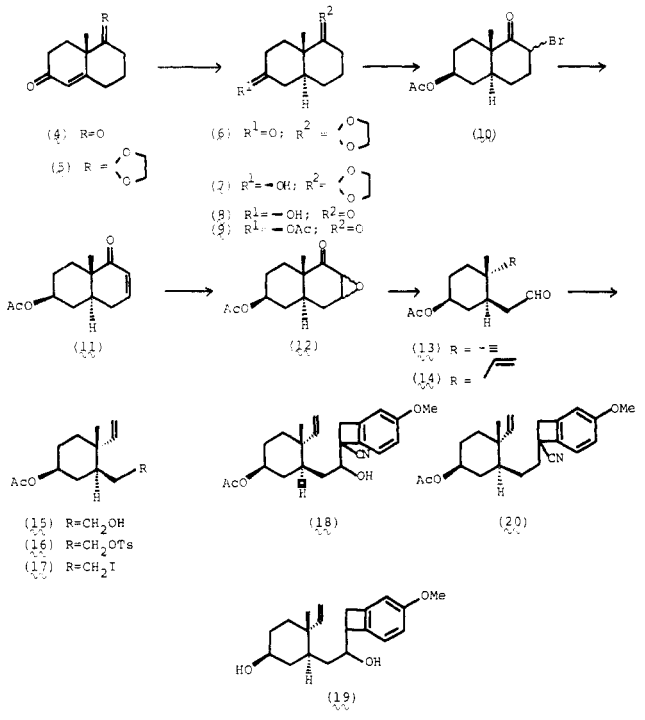
0022-3263/80/1945-2204$01.00/0

Scheme II



dergoes an intramolecular cycloaddition reaction to produce the B and C rings of the steroid system in one step (Scheme I).

The key intermediate, optically active [2-(benzocyclobutenyl)ethyl]cyclohexane **1**, was prepared from (*S*)-3,4,8,8a-tetrahydro-8a-methyl-(2*H*,7*H*)-naphthalene-1,6-dione [**4**; $[\alpha]^{25}_D$ +113° ($CHCl_3$)][18] as follows. The ketal **5** ($[\alpha]_D$ + 124.2°),[19] derived from **4** by a standard procedure, was reduced with sodium in liquid ammonia in the presence of ethanol to give the compound **6** ($[\alpha]_D$ +20.7°),[19] which was converted, on treatment with sodium borohydride in methanol, to the ketal alcohol **7** ($[\alpha]_D$ −38.5°)[19] (Scheme II). The keto acetate **9** ($[\alpha]_D$ −61°)[19] was prepared from the keto alcohol **8** ($[\alpha]_D$ −52.3°),[19] which was in turn obtained from treatment of **7** with 5% hydrochloric acid in acetone. The enone **11** ($[\alpha]_D$ −38.9°)[19] was obtained as the result of treatment of **9** with bromine in chloroform in the presence of sodium acetate and elimination of the resulting bromide **10** with lithium bromide and lithium carbonate in dimethylformamide. Oxidation of enone **11** with 30% hydrogen peroxide in 10% aqueous sodium hydroxide and methanol afforded the epoxide **12**, Eschenmoser ring opening of which was found to proceed well on using the Corey modification.[20] Thus, epoxide **12** was treated with [(2,4-dinitrophenyl)sulfonyl]hydrazine in dichloromethane–acetic acid (1:1) to give the acetylenic aldehyde **13** ($[\alpha]_D$ −7.72°),[19] which on hydrogenation on palladium on calcium carbonate in acetone under an atmosphere of hydrogen yielded the olefinic aldehyde **14** ($[\alpha]_D$ −14.0°).[19]

Condensation of this olefinic aldehyde **14** with 1-cyano-4-methoxybenzocyclobutene[21] in liquid ammonia in the presence of sodium amide, followed by reductive removal (sodium in liquid ammonia) of the cyano and hydroxyl groups of the resulting compound **18** [*m/e* 383 (M^+)], was achieved by our method[13,14] to furnish the key intermediate **1** [*m/e* 300 (M^+)]. Typical vinylic proton resonances at δ 4.80–6.05 appeared in the NMR spectrum of this derivative. As the key intermediate **1** was only a minor component of the product in the last step of the reaction sequence described above, dihydroxy derivative **19** being the major product, an alternative synthesis was carried out as follows. The olefinic alcohol **15** ($[\alpha]_D$ +0.72°),[19] which was obtained by reduction of **14** with sodium borohydride in methanol, was treated with *p*-toluenesulfonyl chloride in pyridine to give the tosylate **16** ($[\alpha]_D$ −6.20°)[19] which was then converted to the iodide **17** ($[\alpha]_D$ +13.2°).[19] Condensation of 1-cyano-4-methoxybenzocyclobutene[21] with iodide **17**, in the presence of sodium amide in liquid ammonia, furnished the compound **20** [*m/e* 367 (M^+)] which on treatment with sodium in liquid ammonia in the presence of ethanol[10] afforded the key intermediate **1**, identical with the compound obtained above with respect to the spectral data. The key step in our synthesis was carried out as follows. Heating the benzocyclobutene **1** in *o*-dichlorobenzene at 195 °C for 4.5 h in a current of nitrogen gave 3β-hydroxy-17-methoxy-*D*-homo-18-nor-5α-androsta-13,15,17-triene [**2**; $[\alpha]_D$ −43.64°,[19] *m/e* 300 (M^+)] which showed methyl group resonances at δ 0.85 (C_{10} Me) and 3.83 (OMe) in its NMR spectrum. The structure, including stereochemistry, of this compound was established by a direct comparison of its IR ($CHCl_3$) and NMR ($CDCl_3$) spectra with those of an authentic racemic sample.[17] The stereoselective outcome of this intramolecular cyclization can be explained by intervention of the intermediate A, and, indeed, this is the one expected to be most stable in light of the preceding papers.[10-16]

Thus an efficient asymmetric synthesis of 3β-hydroxy-17-methoxy-*D*-homo-18-nor-5α-androsta-13,15,17-triene (**2**) has been developed, and the method, in connection with the established methods,[17] should provide a general route for the asymmetric synthesis of a wide range of pregnane-type steroids.

Experimental Section

General Methods. All melting points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi EPI-3 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were measured on a JEOL JNM-PMX-60 spectrometer. Chemical shifts are reported as δ values relative to internal tetramethylsilane (Me_4Si). Mass spectra were taken on a Hitachi RMU-7 spectrometer. All optical rotations were measured in chloroform solution on a JASCO PIP-SL polarimeter using a 1-dm cell.

(+)-(8a*S*)-1,1-(1,2-Ethylenedioxy)-1,2,3,4,6,7,8,8a-octahydro-8a-methyl-6-oxonaphthalene (5). To a solution of 32 g (0.179 mol) of diketone **4** in 250 mL of benzene were added a catalytic amount of *p*-toluenesulfonic acid and 80 g (1.20 mol) of ethylene glycol. The reaction mixture was refluxed in a flask fitted with a Dean–Stark trap. After 55 min, 0.9 equiv of water had collected, and the reaction mixture was cooled. The benzene layer was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 250 g of silica gel by using benzene–ethyl acetate (5:1) as eluent to give 38.6 g (96.7%) of **5** as a colorless oil: IR ($CHCl_3$) 1660 cm^{-1}; NMR ($CDCl_3$) δ 1.31 (3 H, s, CH_3), 3.93 (4 H, s, OCH_2CH_2O], 5.68 (1 H, s, olefinic H); mass spectrum, *m/e* 222 (M^+); $[\alpha]^{20}_D$ +124.2° (*c* 0.153). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.09; H, 8.43.

(+)-(4a*S*,8a*S*)-1,1-(1,2-Ethylenedioxy)-1,2,3,4,4aα,5,6,7,8,8a-decahydro-8aβ-methyl-6-oxonaphthalene (6). To a solution of 8 g (0.348 mol) of sodium in 1500 mL of liquid ammonia at −78 °C were added a solution of 28.6 g (0.129 mol) of ketal **5** in 1000 mL of anhydrous tetrahydrofuran and 1 mL of absolute ethanol, and the reaction mixture was stirred for 2 h at the same temperature. After addition of solid ammonium

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chloride followed by evaporation of the solvent, 300 mL of water was added, and the resulting mixture was extracted three times with 500-mL portions of benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 300 g of silica gel with dichloromethane as eluent to give 23.2 g (80.4%) of **6** as a colorless oil: IR ($CHCl_3$) 1705 cm^{-1}; NMR ($CDCl_3$) δ 1.16 (3 H, s, CH_3), 3.90 (4 H, s, OCH_2CH_2O); mass spectrum, m/e 224 (M^+); $[\alpha]^{20}_D$ +20.7° (*c* 0.107). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.51; H, 8.53.

(−)-(4a*S*,6*S*,8a*S*)-1,1-(1,2-Ethylenedioxy)-1,2,3,4,4aα,5,6,7,8,8a-decahydro-6β-hydroxy-8aβ-methylnaphthalene (7). To a stirred solution of 116 g (0.518 mol) of ketal **6** in 1000 mL of methanol at 0 °C was added 10 g (0.264 mol) of sodium borohydride. After stirring had been continued for 1 h at 0 °C, methanol was removed by evaporation, 500 mL of water was added, and the mixture was extracted three times with 500-mL portions of benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude porduct which was chromatographed on 1 kg of silica gel with dichloromethane–ethyl acetate (5:1) as eluent to give 110 g (99.2%) of **7** as a colorless oil: IR ($CHCl_3$) 3600 cm^{-1}; NMR ($CDCl_3$) δ 0.98 (3 H, s, CH_3), 3.30–3.90 (1 H, m, CHOH), 3.95 (4 H, s, OCH_2CH_2O); mass spectrum, m/e 226 (M^+); $[\alpha]^{20}_D$ −38.5° (*c* 0.223). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.40; H, 9.91.

(−)-(4a*S*,6*S*,8a*S*)-1,2,3,4,4aα,5,6,7,8,8a-Decahydro-6β-hydroxy-8aβ-methyl-1-oxonaphthalene (8). To a solution of 110 g (0.487 mol) of ketal **7** in 800 mL of acetone was added 2 mL of 5% aqueous hydrochloric acid solution, and the reaction mixture was stirred for 16 h at room temperature. The solvent was removed by evaporation, and the residue was diluted with 300 mL of water and extracted three times with 500-mL portions of benzene. The combined benzene extract was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 800 g of silica gel with dichloromethane–ethyl acetate (5:1) as eluent to give 81.5 g (92.0%) of **8** as a colorless oil: IR ($CHCl_3$) 3600, 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (3 H, s, CH_3), 3.43–3.98 (1 H, m, CHOH); mass spectrum, m/e 182 (M^+); $[\alpha]^{20}_D$ −52.3° (*c* 0.192). Anal. Calcd for $C_{11}H_{18}O_2 \cdot {}^1/_{10}H_2O$: C, 71.78; 9.97. Found: C, 71.80; H, 9.94.

(−)-(4a*S*,6*S*,8a*S*)-6β-Acetoxy-1,2,3,4,4aα,5,6,7,8,8a-decahydro-8aβ-methyl-1-oxonaphthalene (9). To a solution of 14.5 g (79.7 mmol) of ketone **8** in 200 mL of pyridine at room temperature under nitrogen was added 10.0 g (98 mmol) of acetic anhydride, and the mixture was stirred for 14 h. The reaction mixture was added to 500 mL of water and extracted three times with 300-mL portions of benzene. This benzene extract was washed with saturated potassium hydrogen sulfate solution, saturated sodium bicarbonate solution, and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 200 g of silica gel with benzene as eluent to give 13.1 g (73.4%) of **9** as a colorless oil: IR ($CHCl_3$) 1720, and 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.08 (3 H, s, CH_3), 1.96 (3 H, s, CH_3), 4.36–5.13 (1 H, m, CHOAc); mass spectrum, m/e 224 (M^+); $[\alpha]^{20}_D$ −61.0° (*c* 0.4). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.23; H, 8.98.

(−)-(4a*S*,6*S*,8a*S*)-6β-Acetoxy-2-bromo-1,2,3,4,4aα,5,6,7,8,8a-decahydro-8aβ-methyl-1-oxonaphthalene (10). To a stirred mixture of 13.1 g (58.5 mmol) of acetate **9** and 4.1 g (62.2 mmol) of sodium acetate in 200 mL of chloroform at 0 °C under nitrogen was added dropwise a solution of 9.6 g (60 mmol) of bromine in 50 mL of chloroform. When stirring had been continued for 12 h at 0 °C, the reaction mixture was poured into 500 mL of water. The organic layer was separated, washed with saturated sodium bicarbonate solution and saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was chromatographed on 200 g of silica gel with benzene as eluent to give 17 g (96.6%) of **10** as a colorless oil: IR ($CHCl_3$) 1720 cm^{-1}; NMR ($CDCl_3$) δ 1.13 (3 H, s, CH_3), 1.99 (3 H, s, CH_3), 4.34–5.28 (2 H, m, CHOAc and CHBr); mass spectrum, m/e 302 (M^+), 304 (M^+ + 2); $[\alpha]^{20}_D$ −17.2° (*c* 0.32). Anal. Calcd for $C_{13}H_{19}O_3Br$: C, 51.49; H, 6.32. Found: C, 51.63; H, 6.54.

(−)-(4a*S*,6*S*,8a*S*)-6β-Acetoxy-1,4,4aα,5,6,7,8,8a-octahydro-8aβ-methyl-1-oxonaphthalene (11). A mixture of 28 g (92.7 mmol) of the bromide **10**, 15 g (142.8 mmol) of lithium bromide, and 12 g (162.2 mmol) of lithium carbonate in 100 mL of anhydrous dimethylformamide was stirred for 2 h at 125–130 °C under an atmosphere of nitrogen. After cooling, the reaction mixture was diluted with 500 mL of water and extracted three times with 300-mL portions of benzene. The combined organic extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 300 g of silica gel with benzene as eluent to give 6.9 g (78.2%) of **11** as a colorless oil: IR ($CHCl_3$) 1725, 1675 cm^{-1}; NMR ($CDCl_3$) δ 1.07 (3 H, s, CH_3), 2.02 (3 H, s, CH_3), 4.30–5.20 (1 H, m, CHOAc), 5.93 (1 H, d, J = 5 Hz, olefinic H), 6.68–7.03 (1 H, m, olefinic H); mass spectrum, m/e 222 (M^+); $[\alpha]^{20}_D$ −38.9° (*c* 0.46). Anal. Calcd for $C_{13}H_{18}O_3 \cdot {}^1/_5H_2O$: C, 69.12; H, 8.21. Found: C, 68.88; H, 8.23.

(−)-(4a*R*,6*S*,8a*S*)-6β-Acetoxy-2,3-epoxy-1,2,3,4,4aα,5,6,7,8,8a-decahydro-8aβ-methyl-1-oxonaphthalene (12). To a solution of 16.1 g (72.5 mmol) of the enone **11** in 20 mL of methanol at 0 °C were added 9.2 mL of 30% hydrogen peroxide and 5.3 mL of 10% aqueous sodium hydroxide solution. The reaction mixture was stirred for 10 min at 0 °C and was diluted with 200 mL of water. After extraction three times with 300-mL portions of chloroform, the combined organic extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent gave a crude product which was chromatographed on 200 g of silica gel with benzene as eluent to give 13.1 g (75.9%) of **12** as a colorless oil: IR ($CHCl_3$) 1720, 1705 cm^{-1}; NMR ($CDCl_3$) δ 0.94 (3 H, s, CH_3), 1.91 (3 H, s, CH_3), 3.03 (1 H, d, J = 1.5 Hz, C(O)–CH–C–O, 3.40 (1 H, br s, C(O)C(O)CH), 4.27–5.00 (1 H, m, CH); mass spectrum, m/e 238 (M^+); $[\alpha]^{20}_D$ −38.9° (*c* 0.46). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.70; H, 7.90.

[(−)-(1*S*,2*R*,4*S*)-4β-Acetoxy-1α-ethynyl-1β-methylcyclohex-2-yl]acetaldehyde (13). A solution of 1 g (4.2 mmol) of epoxide **12** and 1.18 g (4.5 mmol) of 2,4-dinitrophenylsulfonylhydrazine in 20 mL of acetic acid and 20 mL of dichloromethane was stirred for 72 h at 0 °C. Water (200 mL) was then added to the reaction mixture, and the organic layer was separated and washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a gum which was dissolved in a mixture of 20 mL of dichloromethane and 20 mL of acetic acid. This mixture was refluxed for 18 h, diluted with 200 mL of water, and extracted three times with 100-mL portions of dichloromethane. This organic extract was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent left a crude product which was chromatographed on 20 g of silica gel with benzene as eluent to give 220 mg (23.6%) of **13** as a colorless oil: IR ($CHCl_3$) 3310, 1720 cm^{-1}; NMR ($CDCl_3$) δ 1.12 (3 H, s, CH_3), 1.99 (3 H, s, CH_3), 4.38–5.16 (1 H, m, CHOAc), 9.78 (1 H, br s, CHO); mass spectrum, m/e 222 (M^+); $[\alpha]^{20}_D$ −7.72° (*c* 0.114). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.69; H, 8.33.

[(−)-(1*R*,2*R*,4*S*)-4-Acetoxy-1α-ethenyl-1-methylcyclohex-2-yl]acetaldehyde (14). To a solution of 1.4 g (6.3 mmol) of acetylene **13** in 120 mL of acetone was added 0.7 g of palladium on calcium carbonate. Hydrogenation occurred smoothly at 3 atm of H_2 and was complete in 2 h. The solution was filtered and the catalyst washed with acetone. The combined filtrates were evaporated to yield a crude product which was chromatographed on 30 g of silica gel with benzene as eluent to give 1.25 g (88.7%) of **14** as a colorless oil: IR ($CHCl_3$) 1720^{-1}; NMR ($CDCl_3$) δ 0.96 (3 H, s, CH_3), 1.99 (3 H, s, CH_3), 4.5–5.95 (4 H, m, olefinic H and CHOAc), 9.70 (1 H, br s, CHO); mass spectrum, m/e 224 (M^+). $[\alpha]^{20}_D$ −14.0° (*c* 0.285). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.29; H, 8.92.

4-Acetoxy-1-ethenyl-2-[2-(1-cyano-4-methoxybenzocyclobutenyl)-2-hydroxyethyl]-1-methylcyclohexane (18). To a stirred solution of sodium amide (from 32 mg of sodium) and 85.2

mg (0.536 mmol) of 1-cyano-4-methoxybenzocyclobutene in 50 mL of liquid ammonia and 10 mL of anhydrous tetrahydrofuran at −78 °C was added 120 mg (0.536 mmol) of aldehyde **14** in 10 mL of anhydrous tetrahydrofuran. After being stirred for 2 h at −78 °C, the reaction mixture was treated with excess solid ammonium chloride, and the solvent was evaporated. The reddish residue was diluted with 100 mL of saturated aqueous ammonium chloride solution, and the resulting mixture was extracted three times with 100-mL portions of benzene. This benzene extract was washed with sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a reddish gum which was chromatographed on 5 g of silica gel with dichloromethane as eluent to give 126 mg (61.4%) of **18** as a colorless oil: IR ($CHCl_3$) 3600, 2250, 1720, 1605 cm^{-1}; NMR ($CDCl_3$) δ 0.97 (3 H, s, CH_3), 1.97 (3 H, s, CH_3), 3.75 (3 H, s, CH_3), 4.50–6.00 (4 H, m, olefinic H and CHOAc), 6.7–7.4 (3 H, m, ArH); mass spectrum, m/e 383 (M^+).

Reduction of (18). To a solution of 24 mg (1.04 mmol) of sodium in 50 mL of liquid ammonia at −78 °C was added a solution of 80 mg (0.209 mmol) of cyclohexane **18** in 30 mL of anhydrous tetrahydrofuran. Three drops of absolute ethanol were added, and the reaction mixture was stirred for 2 h at −78 °C. After addition of ethanol followed by evaporation of the solvent, 100 mL of water was added, and the resulting mixture was extracted three times with 100-mL portions of benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 2 g of silica gel with benzene as eluent to give 9 mg (14.4%) of 1-ethenyl-4-hydroxy-2-[2-(4-methoxybenzocyclobutenyl)ethyl]-1-methylcyclohexane (**1**) as a colorless oil: IR ($CHCl_3$) 3600, 1600 cm^{-1}; NMR ($CDCl_3$) δ 0.94 (3 H, s, CH_3), 3.76 (3 H, s, CH_3), 4.83–6.05 (3 H, m, olefinic H), 6.66–7.20 (3 H, m, ArH); mass spectrum, m/e 300 (M^+). Anal. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 79.55; H, 9.40. Further elution with chloroform gave 52 mg (78.8%) of 1-ethenyl-4-hydroxy-2-[2-(4-methoxybenzocyclobutenyl)-2-hydroxyethyl]-1-methylcyclohexane (**19**) as a colorless oil: IR ($CHCl_3$) 3600, 1600 cm^{-1}; NMR ($CDCl_3$) δ 0.96 (3 H, s, CH_3), 3.77 (3 H, s, CH_3), 4.83–6.03 (3 H, m, olefinic H), 6.65–7.20 (3 H, m, ArH); mass spectrum, m/e 316 (M^+).

2-[(+)-(1*R*,2*S*,4*S*)-4β-Acetoxy-1α-ethenyl-1β-methylcyclohex-2-yl]ethanol (15). To a stirred solution of 4.65 g (20.8 mmol) of aldehyde **14** in 200 mL of methanol at 0 °C was added 400 mg (10.5 mmol) of sodium borohydride, and the reaction mixture was stirred for 30 min at 0 °C. After removal of the solvent, 200 mL of water was added and the mixture extracted with benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude gum which was chromatographed on 20 g of silica gel with chloroform as eluent to give 4.64 g (99.1%) of **15** as a colorless oil: IR ($CHCl_3$) 3620, 1720 cm^{-1}; NMR ($CDCl_3$) δ 0.96 (3 H, s, CH_3), 2.05 (3 H, s, CH_3), 3.43–3.91 (2 H, m, CH_2OH), 4.50–6.10 (4H, m, olefinic H and CHOAc); mass spectrum, m/e 226 (M^+); $[\alpha]^{20}_D$ +0.72° (c 0.835). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.99; H, 9.95.

2-[(−)-(1*R*,2*S*,4*S*)-4β-Acetoxy-1α-ethenyl-1β-methylcyclohex-2-yl]ethyl Tosylate (16). To a solution of 4.56 g (20.18 mmol) of alcohol **15** in 40 mL of pyridine was added 4.61 g (24.3 mmol) of *p*-toluenesulfonyl chloride, and stirring was continued for 2 h at room temperature. After water (100 mL) was added, the mixture was extracted with benzene. This benzene extract was washed with saturated potassium hydrogen sulfate solution, saturated sodium bicarbonate solution, and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude gum which was chromatographed on 20 g of silica gel with benzene as eluent to give 5.12 g (66.8%) of **16** as a colorless oil: IR ($CHCl_3$) 1720 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (3 H, s, CH_3), 2.03 (3 H, s, CH_3), 2.47 (3 H, s, CH_3), 3.90–4.28 (2 H, m, CH_2OTs), 4.40–5.95 (4 H, m, olefinic H and CHOAc), 7.35–8.05 (4 H, m, ArH); mass spectrum, m/e 380 (M^+); $[\alpha]^{20}_D$ −6.20° (c 0.65). Anal. Calcd for $C_{20}H_{28}O_5S$: C, 63.14; H, 7.42. Found: C, 63.20; H, 7.53.

2-[(+)-(1*R*,2*R*,4*S*)-4β-Acetoxy-1α-ethenyl-1β-methylcyclohex-2-yl]ethyl Iodide (17). To a solution of 5.02 g (13.2 mmol) of tosylate **16** in 150 mL of acetone was added 2.37 g (15.8 mmol) of sodium iodide, and the mixture was heated at reflux for 4 h. Removal of the solvent afforded a crude product to which was added 100 mL of water, and the mixture was extracted with benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude gum which was chromatographed on 40 g of silica gel with benzene as eluent to give 3.41 g (76.8%) of **17** as a colorless liquid: IR ($CHCl_3$) 1720 cm^{-1}; NMR ($CDCl_3$) δ 0.96 (3 H, s, CH_3), 2.04 (3 H, s, CH_3), 2.81–3.60 (2 H, m, CH_2I), 4.5–6.06 (4 H, m, olefinic H and CHOAc); mass spectrum, m/e 336 (M^+); $[\alpha]^{20}_D$ +13.2° (c 0.5). Anal. Calcd for $C_{13}H_{21}O_2I$: C, 46.44; H, 6.30. Found: C, 46.57; H, 6.53.

4-Acetoxy-1-ethenyl-2-[2-(1-cyano-4-methoxybenzocyclobutenyl)ethyl]-1-methylcyclohexane (20). To a stirred suspension of sodium amide [prepared from 238 mg (10.3 mmol) of sodium] in 50 mL of liquid ammonia at −78 °C under nitrogen was added 1.37 g (8.6 mmol) of 1-cyano-4-methoxybenzocyclobutene in 25 mL of anhydrous tetrahydrofuran. After 30 min at −78 °C, 2 g (5.95 mmol) of iodide **17** in 10 mL of anhydrous tetrahydrofuran was added to the reaction mixture. After being stirred for 1 h at −78 °C, the reaction mixture was treated with excess solid ammonium chloride, and the solvent was evaporated. The residual reddish gum was diluted with 100 mL of saturated sodium chloride solution and extracted with benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on silica gel with benzene as eluent to give 2.08 g (95.4%) of **20** as a colorless oil: IR ($CHCl_3$) 2230, 1720 cm^{-1}; NMR ($CDCl_3$) δ 1.00 (3 H, s, CH_3), 2.04 (3 H, s, CH_3), 3.46 (2 H, q, J = 7.5 Hz, CH_2Ar), 3.80 (3 H, s, CH_3), 4.30–6.05 (4 H, m, olefinic H and CHOAc), 6.72–7.93 (3 H, m, ArH); mass spectrum, m/e 367 (M^+). Anal. Calcd for $C_{23}H_{29}O_3 \cdot H_2O$: C, 71.66; H, 8.11; N, 3.63. Found: C, 71.67; H, 7.75; N, 3.63.

1-Ethyl-4-hydroxy-2-[2-(4-methoxybenzocyclobutenyl)-ethyl]-1-methylcyclohexane (1). To a solution of 780 mg (33.9 mmol) of sodium in 300 mL of liquid ammonia at −78 °C were added a solution of 2.38 g (6.49 mmol) of cyclohexane **20** in 30 mL of anhydrous tetrahydrofuran and three drops of absolute ethanol. The reaction mixture was stirred for 2 h at −78 °C. After addition of ethanol followed by evaporation of the solvent, 100 mL of water was added, and the resulting mixture was extracted three times with 100-mL portions of benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 30 g of silica gel with benzene as eluent to give 1.67 g (85.6%) of **1** as a colorless oil, identical (IR and NMR spectra) with the sample prepared above.

3β-Hydroxy-17-methoxy-*D*-homo-18-nor-5α-androsta-13,15,17-triene (2). A solution of 102 mg (0.34 mmol) of **1** in 20 mL of *o*-dichlorobenzene was stirred under an atmosphere of nitrogen at 195 °C for 4.5 h. After evaporation of the solvent, the residue was chromatographed on 3 g of silica gel with benzene as eluent to give 95 mg (93.1%) of **2** as colorless needles (acetone): mp 187–189 °C; IR ($CHCl_3$) 3600, 1600 cm^{-1}; NMR ($CDCl_3$) δ 0.85 (3 H, s, CH_3), 3.38–4.00 (1 H, m, CHOH), 3.80 (3 H, s, CH_3), 6.60–7.30 (3 H, m, ArH); mass spectrum, m/e 300 (M^+); $[\alpha]^{20}_D$ −43.64° (c 0.22). Anal. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 79.96; H, 9.40.

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