Regio- and Stereoselective Ruthenium Catalyzed Hydrovinylation of 1,3-Dienes: Application to the Generation of a 20S-Steroidal Sidechain

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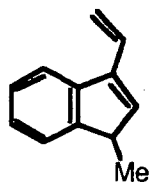
Supporting Information

Experimental Section

General Data: All ^1H NMR and ^{13}C NMR spectra were recorded at 300 and 75 MHz respectively. For those products that are mixtures of stereoisomers, diastereomeric ^{13}C NMR resonances are noted in square brackets. Melting points were obtained on a Mel-Temp melting point apparatus and are uncorrected. Elemental analyses were obtained from Midwest Microlabs, Ltd., Indianapolis, IN and high resolution mass spectra were obtained from the Washington University Resource for Mass Spectroscopy.

Solvents were distilled from Na, Na-benzophenone, or CaH_2, and degassed prior to use. All reactions were carried out in a nitrogen-filled glove-box or using standard Schlenk techniques unless otherwise noted. Catalysts **1** and **2** were prepared according to the literature procedures.[1] The conjugated 1,3-diene substrates were prepared by Wittig olefination of the corresponding enal (**3b-d**), or prepared by palladium catalyzed Stille coupling of the enoltriflate with tributylvinyltin[2] (**3e-h**). Dienes **3b**,[3] **3c**,[4] **3d**,[5] **3e**,[6] **3f**,[7] and **3h**[8] were identified by comparison of their spectral data with the literature values.



1-Methyl-3-vinyl-1H-indene (3g): ^1H NMR ($CDCl_3$) δ 7.59 (d, J = 7.8 Hz, 1H), 7.43 (d, J = 6.9 Hz, 1H), 7.34-7.22 (m, 2H), 6.77 (ddd, J = 0.9, 10.5, 18.0 Hz, 1H), 6.49 (t, J = 2.4 Hz, 1H), 5.85 (d, J = 18.0 Hz, 1H), 5.36 (d, J = 10.5 Hz, 1H), 3.53 (q, J = 7.5 Hz, 1H), 1.36 (d, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 149.4, 141.9, 139.3, 137.9, 130.1, 125.8, 124.6, 122.4, 119.7, 115.5, 43.9, 16.7.

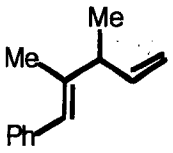
General Procedure for Ru-catalyzed hydrovinylation with Catalyst 1.

A 25 mL medium walled vacuum Schlenk tube (Kontes catalog # 218710-0025) equipped with stirring bar and Teflon stopcock was charged with degassed diene (1.0-2.0 mmol), catalyst **1** (1.0-2.0 mol%), and methylene chloride (3.0 mL) in a nitrogen-filled glove box. The tube was removed from the glove box, cooled in a liquid N_2 bath, and excess ethylene (ca. 6.4 mmol) was condensed into the tube. The tube was stoppered, removed from the liquid N_2 bath, warmed to rt, and immersed in a 75 °C oil bath for a specified period of time (Table 1). (CAUTION: These conditions result in an increase in pressure in the medium wall reaction vessel. Heating of the

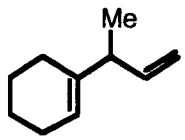
reaction flask should be conducted in a fume hood behind a closed safety sash). After this time, the reaction mixture was cooled to rt, and the tube opened to the air. The reaction mixture was concentrated and the residue was dissolved in hexanes/methylene chloride (5 mL) and passed through a short column of silica gel in a disposable pipet (ca. 5 cm). Evaporation of the solvent gave the crude product. The crude product was dissolved in methylene chloride (10 mL) and to the stirred solution was added small amounts of N-phenyltriazodione (PTAD), until the red color of PTAD persisted. The mixture was concentrated and the residue purified by column chromatography (hexanes).

General Procedure for Ru-catalyzed hydrovinylation with Catalyst 2.

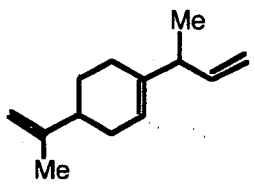
In a 25 mL medium walled vacuum Schlenk tube (Kontes catalog # 218710-0025) equipped with magnetic stirring bar and Teflon stopcock, the diene (1.0-2.0 mmol) was added and the tube was degassed. The tube was placed into a glovebox, where catalyst **2** (8.0 mg., 0.01 mmol) was added, followed by the addition of benzene (3.0 mL). The sealed tube was removed from the glove box and under a stream of dry N_2, HBF_4:OEt_2 in ether (4.0 μl., ca. 2.0 μmol) was injected by the means of a syringe. The mixture was stirred at rt for 15 min. The reaction tube was cooled in a liquid N_2 bath, and excess ethylene (ca. 6.4 mmol) was condensed into the tube. The tube was stoppered, removed from the liquid N_2bath, warmed to rt, and immersed in a 75 °C oil bath for a specified period of time (Table 1). (CAUTION: These conditions result in an increase in pressure in the medium wall reaction vessel. Heating of the reaction flask should be conducted in a fume hood behind a closed safety sash). After this time, the reaction mixture was cooled to rt, and the tube opened to the air. The reaction mixture was concentrated and the residue was dissolved in hexanes/methylene chloride (5 mL) and passed through a short column of silica gel in a disposable pipet (ca. 5 cm). In all cases, *except for* ***4h***, the crude product was dissolved in methylene chloride (10 mL) and to the stirred solution was added small amounts of N-phenyltriazodione (PTAD), until the red color of PTAD persisted. The mixture was concentrated and the residue purified by column chromatography (hexanes).



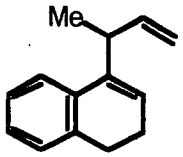
2,3-Dimethyl-1-phenyl-1,4-pentadiene (4b): ^{1}H NMR ($CDCl_3$) δ 7.37-7.21 (m, 5H), 6.36 (s, 1H), 5.89 (ddd, J = 17.1, 10.2, 6.9 Hz, 1H), 5.15-5.05 (m, 2H), 3.03-2.90 (m, 1H), 1.84 (d, J = 1.2 Hz, 3H), 1.28 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 142.2, 142.0, 138.4, 128.9, 128.0, 125.9, 124.5, 113.6, 46.8, 18.1, 15.7. Anal. calcd. for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.41; H, 9.47.



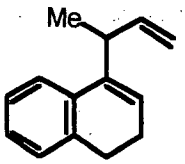
1-(1-Methyl-2-propenyl)-cyclohexene (4c): ^{1}H NMR ($CDCl_3$) δ 5.79 (ddd, J = 17.1, 10.2, 7.2 Hz, 1H), 5.47 (br s, 1H), 5.01 (d, J = 17.1 Hz, 1H), 4.96 (d, J = 10.2 Hz, 1H), 2.78-2.65 (m, 1H), 2.10-1.88 (m, 4H), 1.65-1.50 (m, 4H), 1.11 (d, J = 7.2 Hz, 3H). This compound was identified by comparison of its spectral data with the literature values.[9]



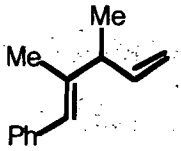
1-(1-Methyl-2-propenyl)-4-(1-methylethylene)cyclohexene (4d): ^{1}H NMR ($CDCl_3$) δ 5.77 (ddd, J = 17.4, 10.2, 7.2 Hz, 1H), 5.48 (br s, 1H), 5.03-4.94 (m, 2H), 4.71 (br s, 2H), 2.80-2.70 (m, 1H), 2.20-1.78 (m, 6H), 1.75 (s, 3H), 1.54-1.40 (m, 1H), 1.13 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 149.58 [149.55], 142.3 [142.2], 139.9 [139.7], 119.6 [119.4], 112.6 [112.5], 108.1, 44.8 [44.7], 41.7 [41.6], 31.26 [31.23], 28.4, 27.3 [27.2], 21.3, 18.9 [18.4]; Anal. calcd. for $C_{13}H_{20}$: C, 88.57; H, 11.43. Found: C, 88.37; H, 11.38.



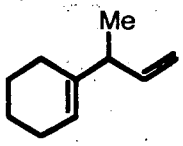
1,2-Dihydro-4-(1-methyl-2-propenyl)naphthalene (4e): ^{1}H NMR ($CDCl_3$) δ 7.34 (d, J = 7.8 Hz, 1H), 7.26-7.10 (m, 3H), 5.99 (ddd, J = 16.8, 9.9, 6.0 Hz, 1H), 5.93 (t, J = 4.8 Hz, 1H), 5.15-5.05 (m, 2H), 3.53 (dq, J = 6.9, 6.9 Hz, 1H), 2.76 (t, J = 7.8 Hz, 1H), 2.35-2.26 (m, 2H), 1.32 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 142.3, 139.2, 136.4, 134.2, 127.1, 126.0, 125.7, 123.6, 122.4, 113.1, 38.3, 28.9, 23.6, 19.8. This compound was identified by comparison of its spectral data with the literature values.[10]



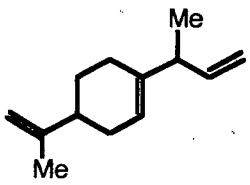
1,2-Dihydro-1-methyl-4-(1-methyl-2-propenyl)naphthalene (4f): ^{1}H NMR ($CDCl_3$) δ 7.40-7.34 (m, 1H), 7.26-7.18 (m, 3H), 6.07-5.93 (m, 1H), 5.85 and 5.84 (2 x t, J = 4.0 Hz, 1H total), 5.18-5.03 (m, 2H), 3.55 (dq, J =



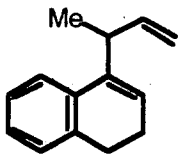
2,3-Dimethyl-1-phenyl-1,4-pentadiene (4b): ^{1}H NMR ($CDCl_3$) δ 7.37-7.21 (m, 5H), 6.36 (s, 1H), 5.89 (ddd, J = 17.1, 10.2, 6.9 Hz, 1H), 5.15-5.05 (m, 2H), 3.03-2.90 (m, 1H), 1.84 (d, J = 1.2 Hz, 3H), 1.28 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 142.2, 142.0, 138.4, 128.9, 128.0, 125.9, 124.5, 113.6, 46.8, 18.1, 15.7. Anal. calcd. for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.41; H, 9.47.



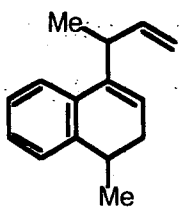
1-(1-Methyl-2-propenyl)-cyclohexene (4c): ^{1}H NMR ($CDCl_3$) δ 5.79 (ddd, J = 17.1, 10.2, 7.2 Hz, 1H), 5.47 (br s, 1H), 5.01 (d, J = 17.1 Hz, 1H), 4.96 (d, J = 10.2 Hz, 1H), 2.78-2.65 (m, 1H), 2.10-1.88 (m, 4H), 1.65-1.50 (m, 4H), 1.11 (d, J = 7.2 Hz, 3H). This compound was identified by comparison of its spectral data with the literature values.[9]



1-(1-Methyl-2-propenyl)-4-(1-methylethylene)cyclohexene (4d): ^{1}H NMR ($CDCl_3$) δ 5.77 (ddd, J = 17.4, 10.2, 7.2 Hz, 1H), 5.48 (br s, 1H), 5.03-4.94 (m, 2H), 4.71 (br s, 2H), 2.80-2.70 (m, 1H), 2.20-1.78 (m, 6H), 1.75 (s, 3H), 1.54-1.40 (m, 1H), 1.13 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 149.58 [149.55], 142.3 [142.2], 139.9 [139.7], 119.6 [119.4], 112.6 [112.5], 108.1, 44.8 [44.7], 41.7 [41.6], 31.26 [31.23], 28.4, 27.3 [27.2], 21.3, 18.9 [18.4]; Anal. calcd. for $C_{13}H_{20}$: C, 88.57; H, 11.43. Found: C, 88.37; H, 11.38.



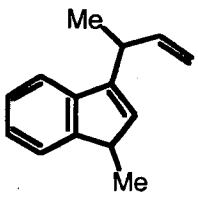
1,2-Dihydro-4-(1-methyl-2-propenyl)naphthalene (4e): ^{1}H NMR ($CDCl_3$) δ 7.34 (d, J = 7.8 Hz, 1H), 7.26-7.10 (m, 3H), 5.99 (ddd, J = 16.8, 9.9, 6.0 Hz, 1H), 5.93 (t, J = 4.8 Hz, 1H), 5.15-5.05 (m, 2H), 3.53 (dq, J = 6.9, 6.9 Hz, 1H), 2.76 (t, J = 7.8 Hz, 1H), 2.35-2.26 (m, 2H), 1.32 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 142.3, 139.2, 136.4, 134.2, 127.1, 126.0, 125.7, 123.6, 122.4, 113.1, 38.3, 28.9, 23.6, 19.8. This compound was identified by comparison of its spectral data with the literature values.[10]



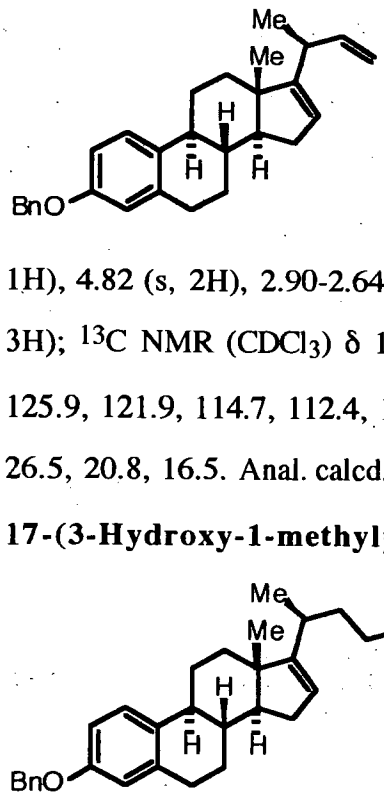
1,2-Dihydro-1-methyl-4-(1-methyl-2-propenyl)naphthalene (4f): ^{1}H NMR ($CDCl_3$) δ 7.40-7.34 (m, 1H), 7.26-7.18 (m, 3H), 6.07-5.93 (m, 1H), 5.85 and 5.84 (2 x t, J = 4.0 Hz, 1H total), 5.18-5.03 (m, 2H), 3.55 (dq, J =

6.6, 6.6 Hz, 1H), 2.89 (ddq, J = 7.2, 7.2, 7.2 Hz, 1H), 2.53-2.42 (br d, J = 16.8 Hz, 1H), 2.19-2.07 (m, 1H), 1.33 and 1.32 (2 x d, J = 6.9 Hz, 3H total), 1.28 and 1.25 (2 x d, J = 6.9 Hz, 3H total); ^{13}C NMR ($CDCl_3$) δ 142.3, 141.23 [141.16], 138.6 [138.4], 133.3, 126.3, 125.73 [125.71], 125.56 [125.52], 122.6 [122.5], 122.04 [121.97], 113.1; 38.25 [38.20], 32.61 [32.58], 31.42 [31.36], 20.3, 19.7. Anal. calcd. for $C_{15}H_{18}$:1/4H_2O: C, 88.83; H, 9.62. Found: C, 88.87; H, 9.65.

1-Methyl-3-(1-methyl-2-propenyl)-1H-indene (4g): ^{1}H NMR ($CDCl_3$) δ 7.42-7.16 (m, 4H), 6.18 (s, 1H), 6.01 (ddt, J = 17.1, 10.5, 7.2 Hz, 1H), 5.12 (br d, J = 17.1 Hz, 1H), 5.06 (br d, J = 10.5 Hz, 1H), 3.55-3.40 (m, 2H), 1.41 and 1.40 (2 x d, J = 6.9 Hz, 3H total), 1.32 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 149.4, 145.1, 143.2, 141.3, 134.0, 125.5, 124.2, 122.2, 119.4, 113.3, 43.8, 36.7 [36.6], 19.6, 16.94 [16.86]. EI-HRMS m/z 184.1249 (calcd for $C_{14}H_{16}$ (M^+) m/z 184.1252).



17-(1-Methyl-2-propenyl)-3-(phenylmethoxy)-estra-1,3,5(10),16-tetraene (4h): $[\alpha]_D$ +80.6 (c 1.6, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.33 (d, J = 7.5 Hz, 1H), 7.24-7.08 (m, 5H), 6.87 (dd, J = 7.5, 2.0 Hz, 1H), 6.79 (d, J = 2.0 Hz, 1H), 5.86 (ddd, J = 17.1, 9.9, 7.2 Hz, 1H), 5.41 (br s, 1H), 5.06 (d, J = 17.1 Hz, 1H), 4.98 (d, J = 9.9 Hz, 1H), 4.82 (s, 2H), 2.90-2.64 (m, 3H), 2.28-1.40 (m, 11H), 1.21 (d, J = 7.2Hz, 3H), 0.78 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 158.4, 156.5, 143.6, 137.9, 137.2, 133.2, 128.4, 127.7, 127.3, 125.9, 121.9, 114.7, 112.4, 112.0, 69.9, 56.4, 47.6, 44.4, 37.4, 36.7, 35.2, 30.9, 29.8, 27.8, 26.5, 20.8, 16.5. Anal. calcd. for $C_{29}H_{34}O$: C, 87.39; H 8.60. Found: C, 87.22; H, 8.60.

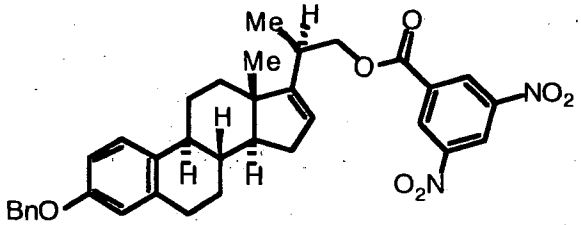


17-(3-Hydroxy-1-methylpropyl)-3-(phenylmethoxy)-estra-1,3,5(10),16-tetraene (5): To a solution of **4h** (0.33 g, 0.83 mmol) in THF (10 mL), under N_2 at 0 °C, was added dropwise a solution of 9-BBN (2.0 mL, 0.5 M in THF, 1.0 mmol). After 1 h, the reaction mixture was warmed to rt, stirred overnight, and

treated with a mixture of 30% H_2O_2 (1 mL) and 1.0 M aqueous KOH (2 mL). The reaction mixture was stirred for 30 min and poured into a separatory funnel containing brine (20 mL) and ether (70 mL). The layers were separated and the ether layer was washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-EtOAc = 5:1) to afford **5** as a white solid (0.30 g, 87%).

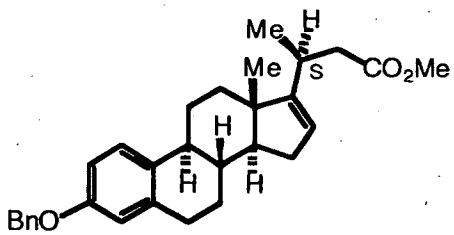
5: mp 90-92 °C; $[\alpha]_D$ +61.8 (c 3.7, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 7.46-7.30 (m, 5H), 7.20 (d, *J* = 8.4 Hz, 1H), 6.79 (dd, *J* = 8.4, 2.7 Hz, 1H), 6.74 (d, *J* = 2.9 Hz, 1H), 5.45 (br s, 1H), 5.05 (s, 2H), 3.77-3.63 (m, 2H), 2.95-2.87 (m, 2H), 2.42-1.40 (m, 15H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 160.2, 155.9, 137.5, 136.7, 132.8, 128.0, 127.3, 127.0, 125.5, 121.3, 114.4, 111.8, 70.0, 61.6, 56.4, 47.9, 44.6, 40.2, 37.7, 35.4, 31.3, 30.2, 29.0, 28.2, 26.9, 21.1, 17.1. Anal. calcd. for $C_{29}H_{36}O_2$: C, 83.61; H, 8.71. Found: C, 83.47; H, 8.65.

3,5-Dinitrobenzoate ester of 5. A sample of **4h** (0.18 g, 0.45 mmol) was treated with 9-BBN as above, followed by oxidation with alkaline H_2O_2. The crude alcohol was dissolved in THF (10 mL) and 3,5-dinitrobenzoyl chloride (0.11 g, 0.48 mmol), NEt_3 (0.07 g, 0.72 mmol) and DMAP (one crystal) were added. The reaction mixture was stirred overnight, and then diluted with ether (50 mL) and washed with saturated aqueous $NaHCO_3$ (2 x 15 mL), followed by water. The ethereal layer was dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes- CH_2Cl_2 = 2:1) to give a pale yellow solid (0.090 g, 33%). ^1H NMR ($CDCl_3$) δ 9.24-9.15 (m, 3H), 7.46-7.28 (m, 5H), 7.19 (d, *J* = 8.4 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.73 (br s, 1H), 5.50 (br s, 1H), 5.04 (s, 2H), 4.55-4.40 (m, 2H), 2.95-2.82 (m, 2H), 2.50-1.30 (m, 15H), 1.22 (d, *J* = 6.6 Hz, 3H), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 162.3, 159.3, 156.5, 148.5, 137.9, 137.2, 134.0, 133.0, 129.3, 128.4, 127.7, 127.3, 125.9, 122.4, 122.2, 114.8, 112.1, 69.9, 65.7, 56.3, 47.7, 44.3, 37.4, 35.7, 35.2, 31.0, 29.8, 28.6, 27.8,

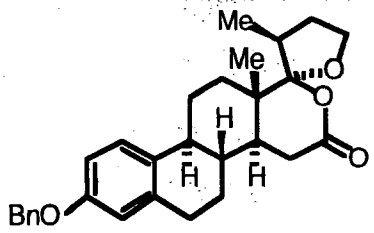


26.5, 21.8, 16.8. Anal. calcd. for $C_{36}H_{38}N_2O_7$: C, 70.81; H, 6.27; N, 4.59. Found: C, 71.05; H, 6.35; N, 4.52.

Preparation of 6 and 7. A sample of **4h** (0.389 g, 0.98 mmol) was treated with 9-BBN as above, followed by oxidation with alkaline H_2O_2. The crude alcohol was dissolved in acetone (10 mL) and Jones reagent (0.30 g CrO_3/mL concentrated H_2SO_4) was added portionwise until the orange color persisted. The reaction mixture was stirred for 50 min. The mixture was concentrated on a rotary evaporator, and then 2N HCl (10 mL) was added and the mixture was extracted with ether (70 mL). The ethereal extracts were dried (Na_2SO_4) and concentrated. The residue (0.310 g) was dissolved in ether (10 mL) in a plastic beaker and the mixture was cooled in a ice-water bath. To the mixture was cautiously added an ethereal solution of diazomethane (prepared from MNNG and KOH) until the yellow color persisted. The reaction mixture was flushed with N_2 until colorless, and then dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (hexanes-EtOAc -CH_2Cl_2 = 5:1:1) to give **6** as a colorless oil (0.156 g, 36% based on **4h**) followed by **7** as a white solid (0.059 g, 14%). Slow recrystallization of **7** from methanol-CH_2Cl_2 gave colorless flakes which were suitable for X-ray diffraction analysis.

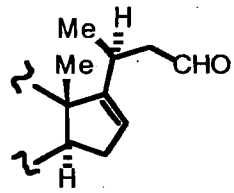


(20*S*)-3-Benzyloxy-19,24-dinorchola-1,3,5(10),16-tetraen-23-oic acid, methyl ester (6): ^1H NMR ($CDCl_3$) δ 7.50-7.30 (m, 5H), 7.20 (d, J = 8.7 Hz, 1H), 6.78 (dd, J = 8.7, 2.4 Hz, 1H), 6.73 (d, J = 2.4 Hz, 1H), 5.43 (br s, 1H), 5.04 (s, 2H), 3.68 (s, 3H), 3.00-2.64 (m, 3H), 2.56 (dd, J = 14.7, 5.1 Hz, 1H), 2.40-1.30 (m, 12H), 1.14 (d, J = 6.6 Hz, 3H), 0.84 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.0, 159.2, 156.5, 137.9, 137.2, 133.1, 128.4, 127.7, 127.3, 125.9, 122.0, 114.7, 112.0, 69.9, 56.4, 51.4, 47.4, 44.3, 41.8, 37.4, 34.9, 30.9, 29.8, 27.8, 26.5, 21.1, 16.7. Anal. calcd. for $C_{30}H_{36}O_3$: C, 81.04; H, 8.16. Found: C, 80.83; H, 8.29.

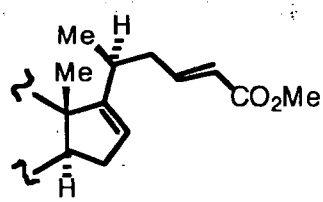


7: mp 221-223 °C, ^{1}H NMR ($CDCl_3$) δ 7.45-7.30 (m, 5H), 7.19 (d, J = 8.7 Hz, 1H), 6.80 (dd, J = 8.7, 2.4 Hz, 1H), 6.72 (d, J = 2.4 Hz, 1H), 5.03 (s, 2H), 4.08 (dt, J = 8.7, 3.9 Hz, 1H), 3.79 (q, J = 8.1 Hz, 1H), 2.90-2.78 (m, 3H), 2.50-1.26 (m, 13H), 1.21 (d, J = 6.6 Hz, 3H), 1.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.3, 156.7, 137.5, 137.0, 132.0, 128.4, 127.8, 127.3, 126.1, 115.5, 114.4, 112.5, 69.9, 67.0, 42.3, 39.0, 38.6, 37.2, 33.5, 32.6, 32.0, 29.9, 25.8, 25.7, 15.4, 14.8. Anal. calcd. for $C_{29}H_{34}O_4$: C, 78.00; H, 7.67. Found: C, 77.21; H, 7.63.

(20*S*)-3-Benzyloxy-19,24-dinorchola-1,3,5(10),16-tetraen-23-al (8a). To a



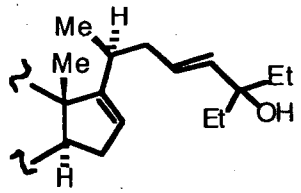
solution of alcohol **5** (0.15 g, 0.36 mmol) in THF was added a solution of allyl magnesium bromide (0.4 mL, 1.0M in ether, 0.4 mmol). The solution was stirred at room temperature for 15 min, at which time solid (azodicarbonyl)dipiperidine (0.10 g, 0.40 mmol) was added in one portion. The reaction mixture was stirred for 1 h, and then brine was added. The reaction mixture was extracted with ether, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes-EtOAc = 10:1) to give **8a** as a colorless solid (0.10 g, 70% based on consumed **5**) followed by recovered **5** (0.03 g, 20%). **8a:** mp 100-102 °C, $[\alpha]_D$ +56.7 (c 0.36, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 9.71 (t, *J* = 2.1 Hz, 1H), 7.45-7.25 (m, 5H), 7.19 (d, *J* = 8.4 Hz, 1H), 6.78 (dd, *J* = 8.4, 2.7 Hz, 1H), 6.73 (d, *J* = 2.1 Hz, 1H), 5.45 (br s, 1H), 5.04 (s, 2H), 2.95-2.78 (m, 3H), 2.62 (ddd, *J* = 16.5, 6.3, 2.1 Hz, 1H), 2.41 (ddd, *J* = 16.5, 7.6, 2.1 Hz, 1H), 2.36-1.30 (m, 11H), 1.20 (d, *J* = 6.9 Hz, 3H), 0.87 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 201.7, 158.2, 155.9, 137.5, 136.7, 132.6, 128.0, 127.4, 127.0, 125.5, 122.7, 114.5, 111.8, 70.0, 56.6, 50.8, 47.7, 44.6, 37.7, 35.3, 31.3, 30.1, 28.1, 27.5, 26.9, 21.9, 17.2. Anal. calcd. for $C_{29}H_{34}O_2$: C, 84.02; H, 8.27. Found: C, 83.73; H, 8.18.



(20*S*)-3-Benzyloxy-19,26(27)-dinorchola-1,3,5(10),16,23*E*-pentaen-25-oic acid, methyl ester (i). To a solution of aldehyde **8a** (0.20 g, 0.48 mmol) in CH_2Cl_2 (15 mL),

cooled to 0 °C, was added solid (carbomethoxymethylene)triphenylphosphorane (0.187 g, 0.53 mmol). The reaction mixture was stirred at 0 °C for 4 h, and then at rt for 20 h. The reaction mixture was concentrated, and the residue was taken up in ether (20 mL). The by-product insoluable Ph_3PO was removed by filtration and the solid washed with ether. The combined ethereal extracts were washed with water, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes-EtOAc = 10:1) to give **i** as a colorless oil (0.19 g, 84%). **i:** $[\alpha]_D$ +30.6 (c 2.30, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 7.46-7.30 (m, 5H), 7.20 (d, J = 8.4 Hz, 1H), 6.94 (dt, J = 15.0, 7.2 Hz, 1H), 6.78 (dd, J = 8.4, 2.7 Hz, 1H), 6.73 (d, J = 2.7 Hz, 1H), 5.83 (d, J = 15.9 Hz, 1H), 5.42 (br s, 1H), 5.05 (s, 2H), 3.75 (s, 3H), 2.94-2.86 (m, 2H), 2.50-2.15 (m, 6H), 2.00-1.88 (m, 3H), 1.64-1.40 (m, 5H), 1.12 (d, J = 6.9 Hz, 3H), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.2, 158.5, 155.9, 147.7, 137.5, 136.7, 132.7, 128.0, 127.3, 127.0, 125.5, 121.9, 121.6, 114.4, 111.8, 70.0, 56.4, 51.7, 47.8, 44.6, 40.0, 37.7, 35.3, 31.6, 31.3, 30.2, 28.2, 26.9, 21.3, 17.1. Anal. calcd. for $C_{32}H_{38}O_3$: C, 81.66; H, 8.14. Found: C, 81.26; H, 8.05.

19-Nor-26,27-homo-cholesta-1,3,5(10),16,23E-pentaene-3,25-diol (9a). To a solution of the enoate **i** (0.275 g, 0.585 mmol) in ether (10 mL), under N_2, cooled to –78 °C, as added dropwise a solution of ethyl lithium (4.68 mL, 0.5 M in benzene/hexane, 2.34 mmol). The reaction mixture was stirred at –78 °C for 1 h, and then warmed to 0 °C and stirred for 2 h. At this time, water (5 mL) was cautiously added. The ethereal layer was separated and the aqueous layer was extracted with ether (20 mL). The combined ethereal extracts were washed with water (2 x 10 mL), dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexanes-EtOAc = 10:1) to give **9a** as a colorless viscous oil (0.168 g, 58%). **9a:** $[\alpha]_D$ +26.6 (c 0.44, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 7.46-7.30 (m, 5H), 7.20 (d, J = 8.4 Hz, 1H), 6.78 (br d, J = 8.4 Hz, 1H), 6.73 (br s, 1H), 5.57 (dt, J = 15.6, 6.6 Hz, 1H), 5.39 (d, J = 15.6 Hz, 1H), 5.36 (br s, 1H), 5.04 (s, 2H), 2.95-2.84 (m, 2H), 2.40-1.86 (m, 8H), 1.66-1.26 (m, 11H), 1.09 (d, J = 6.3 Hz, 3H), 0.89 (t, J = 7.4 Hz, 6H), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 159.5, 155.9,



137.5, 136.8, 136.1, 132.8, 128.0, 127.3, 127.0, 126.8, 125.5, 121.0, 114.5, 111.8, 75.4, 70.0, 56.4, 47.8, 44.7, 40.3, 37.8, 35.4, 33.6, 32.4, 31.3, 30.2, 28.2, 27.0, 21.0, 17.1, 8.5. Anal. calcd. for $C_{35}H_{46}O_2$:1/3H_2O: C, 83.28; H, 9.32. Found: C, 83.30; H, 9.21.

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