Studies on a Steroidal Plant-growth Regulator. Part 26.† Stereoselective Construction of the Brassinolide Side-chain: New Practical Syntheses of Brassinolide Analogues from Hyodeoxycholic Acid‡

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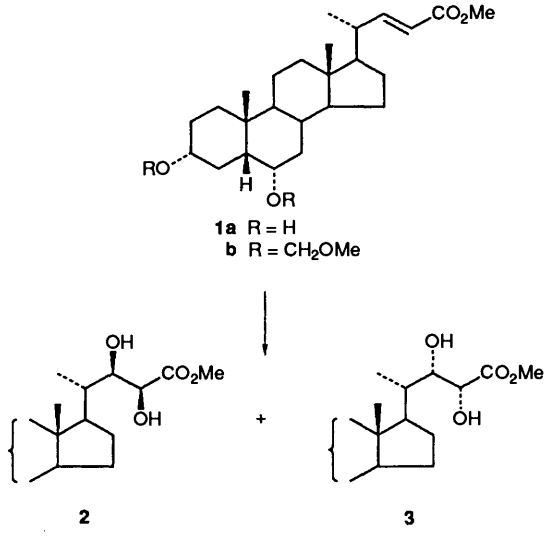
High stereoselectivity in an osmium tetroxide-catalysed asymmetric dihydroxylation of the 5β-cholan-22-en-24-oate **1b** has been achieved and the (22*R*,23*S*)-22,23-dihydroxycholanoate **2b** has been used as the key intermediate for syntheses of brassinolide analogues.

A number of useful methods for construction of the side-chain of brassinolide, a plant growth regulator, have been described.[1] Unfortunately, the osmium tetroxide catalysed dihydroxylation of the (22*E*)-alkenic compound produces the unnatural (22*S*,23*S*)-isomer as the major product,[2] particularly when a 24-alkyl substituent is present [(24*S*) natural configuration]. However, very recently, we have found that dihydroxylation of the (22*E*,24*R*)- and (22*E*,24*S*)-methyl steroid unsaturated side-chain by the osmium tetroxide-catalysed asymmetric method[3] affords the natural isomer as the major product.[4] As an extension of the work on the dihydroxylation of (22*E*)-alkenic compounds, we applied this new methodology to the hyodeoxycholate **1**, producing the (22*R*,23*S*)-22,23-diol **2** with high diastereoselectivity (at least 4:1).[5] It is particularly noteworthy that when osmium tetroxide catalysed dihydroxylation of **1b** was carried out without the cinchona alkaloid, a 1:8 mixture of the (22*R*,23*S*)-diol **2b** and (22*S*,23*R*)-diol **3b** was obtained (Scheme 1).[6]



Scheme 1 *Reagents:* Dihydroquinidine *p*-chlorobenzoate, $K_3Fe(CN)_6$, K_2CO_3, Bu^{t}OH–H_2O (1:1, v/v), OsO_4 (cat.)

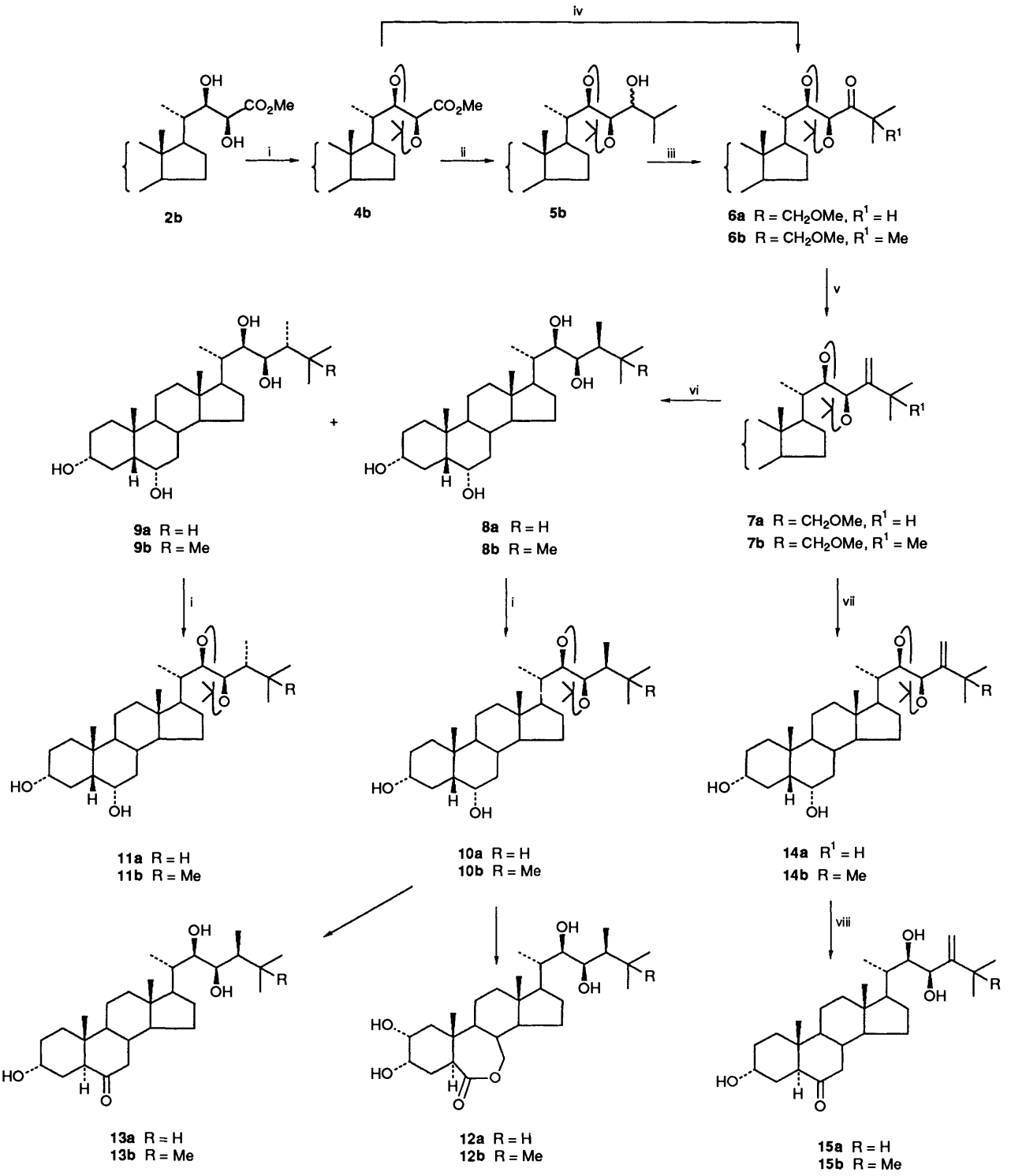
† Part 25. W. S. Zhou and L. F. Huang, *Tetrahedron*, 1992, **48**, 1837.
‡ Hyodeoxycholic acid = 3α,6α-dihydroxycholan-24-oic acid.
Acronymns: DMAP, 4-(dimethylamino)pyridine; PCC, pyridinium chlorochromate; PDC, pyridinium dichromate; PPTS, pyridinium toluene-*p*-sulfonate; THF, tetrahydrofuran.

In order to construct the brassinolide side-chain, the (22*R*,23*S*)-diol **2b** was first protected with 2,2-dimethoxypropane as an acetonide **4b**, which could be used as starting material for the side-chain elaboration.

Diastereoselective Construction of the Brassinolide and 25-Methylbrassinolide Side-chains (Scheme 2).—The acetonide **4b** was treated with $LiBH_4$–Pr^{i}MgCl[7] to give the alcohol **5b** in 86% yield, oxidation of which with PCC gave the ketone **6a** in 91.5% yield. The Wittig reaction of compound **6a** with $Ph_3(Me)PI$ provided compound **7a** in 89% yield, which was hydrogenated in the presence of palladium on charcoal in ethyl acetate followed by treatment with HCl–MeOH (2.5%) to give a 4:1 mixture of the products (22*R*,23*R*,24*S*)-**8a** and (22*R*,23*R*,24*R*)-**9a** which were easily separated by column chromatography on silica gel. The overall yield of these two steps was 82%. Treatment of compounds **8a** and **9a** with 2,2-dimethoxypropane gave the acetonides **10a**[8] and **11a** in almost quantitative yield. The five-step overall yield from compound **4b** to **10a** and **11a** was *ca.* 46% and *ca.* 11% respectively. Selective deprotection of the 3α,6α-bis(methoxymethyl) groups[9] of compound **7a** gave the 3α,6α-diol **14a** in 80% yield. Treatment of compound **14a** with PDC in CH_2Cl_2 followed by acid treatment afforded the new brassinolide **15a** (41% yield). The conversion of compound **10a** into brassinolide **12a** and typhasterol **13a** is known.[1g]

Treatment of compound **4b** with Bu^{t}Li in THF gave the ketone **6b** in 84% yield. The required 25-methylacetonide **10b** used as the key intermediate for a synthesis of 25-methylbrassinolide and compound **11b** were obtained from ketone **6b** in a ratio of 3:2 through intermediates **7b**, **8b** and **9b**, with the same conditions employed for **6a**–**10a**. The overall yield from **4b** to products **10b** and **11b** was *ca.* 34 and *ca.* 23% in five steps, respectively. Selective removal of the 3α,6α-bis(methoxymethyl) groups[9] of compound **7b** provided the 3α,6α-diol **14b** (82.3% yield). In the same way as described for the preparation of compound **15a**, compound **15b**, which was isolated from the kidney bean (*Phaseolus vulgaris*),[11] was obtained from compound **14b** in 38% yield. The conversion of compound **10b** into the 25-methylbrassinolide **12b**,[12] which is a more potent plant growth regulator than brassinolide, and 25-methyltyphasterol **13b** is known.[10]

Diastereoselective Construction of the Demethylated Brassinolide Side-chain (Scheme 3).—Reaction of compound **4b** with MeLi followed by dehydration of the resulting tertiary alcohol **16** with $MeSO_2Cl$–Et_3N in the presence of a catalytic amount of DMAP[13] produced compound **17** in 87% yield. Finally, selective deprotection of the 3α,6α-bis(methoxymethyl) groups[9]

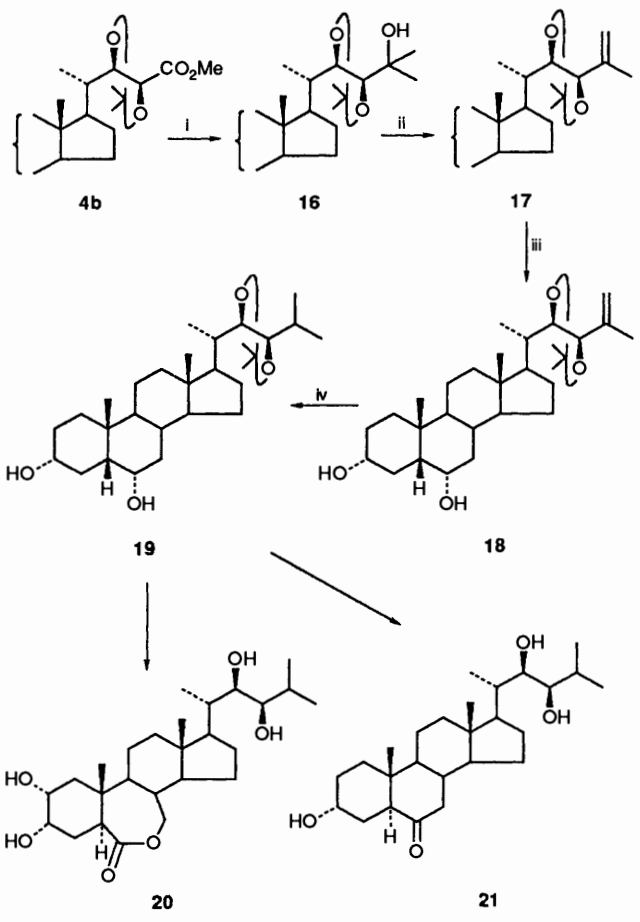


Scheme 2 *Reagents:* i, $Me_2C(OMe)_2$, *p*-TsOH, CH_2Cl_2; ii, $LiBH_4$–Pr^iMgCl, THF; iii, PCC–NaOAc, CH_2Cl_2; iv, Bu^tLi, THF; v, $Ph_3(Me)I$, Bu^tOK, PhH; vi, Pd–C (10%), H_2, EtOAc, then HCl–MeOH (2.5%); vii, PPTS, Bu^tOH; viii, PDC, CH_2Cl_2 then HCl–MeOH (2.5%)

followed by catalytic hydrogenation of the resulting compound **18** yielded the known compound **19**, m.p. 199–200 °C (lit.,[10] 202–203 °C) in *ca.* 80% yield in two steps. The overall yield of the four-step synthesis of **19** is *ca.* 69%. Compound **19** could be converted into the demethylated brassinolide **20**,[14] which has almost the same activity as brassinolide, and the demethylated typhasterol **21** by a known procedure.[10]

Experimental

M.p.s were determined on a Büchi 535 instrument and are uncorrected. IR spectra were recorded on Shimadzu 440 spectrometer. ^1H NMR spectra were obtained on a Varian XL-200 (200 MHz) spectrometer, using $CDCl_3$ as solvent and TMS as an internal standard (*J* values in Hz). Mass spectra were run on a JMS-01U spectrometer. High-resolution mass spectra were recorded with a Finnigan MAT 8430 spectrometer. The optical rotation was measured on Autpol III polarimeter. Elemental analyses were performed by the Analytical Department of the Shanghai Institute. The usual work-up means that the extract was washed with HCl (5%) (or saturated $NaHCO_3$) and brine, and dried ($MgSO_4$), and then concentrated under reduced



Scheme 3 *Reagents:* i, MeLi; ii, $MeSO_2Cl$–Et_3N, DMAP (cat.), CH_2Cl_2; iii, PPTS, Bu^{t}OH; iv, Pd–C (10%), H_2, EtOAc

pressure. Flash column chromatography was performed on silica gel H (10–40 μ). Light petroleum refers to the fraction boiling in the range 60–90 °C.

Methyl (22R,23S)- *and* (22S,23R)-22,23-*Dihydroxy*-3α,6α-*bis*-(*methyoxymethyl*)-5β-*cholan*-24-*oate* **2b** *and* **3b**.—To a well-stirred mixture of dihydroquinidine *para*-chlorobenzoate (46.5 mg, 0.1 mmol), potassium ferricyanide (198 mg, 0.6 mmol), potassium carbonate (83 mg, 0.6 mmol) and osmium tetroxide (0.05 mol dm^{-3} in Bu^{t}OH; 0.05 cm^3, 2.5 × 10^{-3} mmol) in Bu^{t}OH–H_2O [1:1 (v/v), 4 cm^3] at room temp., was added compound **1b** (98 mg, 0.2 mmol) in one portion.[10] The reaction mixture was stirred at room temp. for 24 h, after which it was concentrated to dryness under reduced pressure and the residue was extracted with ethyl acetate (20 cm^3) and worked-up in the usual way. The mixture was separated by column chromatography (light petroleum–acetone, 10:1) to afford compound **3b** (18 mg, 17%) and **2b** (73 mg, 70%).

Compound **2b**, amorphous solid, $[\alpha]_D^{26}$ +14.44 (*c* 0.72, $CHCl_3$) (Found: C, 65.9; H, 9.7. $C_{29}H_{50}O_8$ requires C, 66.13; H, 9.57%); *m/z* 527 (M^+ + 1), 509 (M^+ − OH) and 494 (M^+ − MeOH); ν_{max}(film)/cm^{-1} 3400 (OH) and 1740 (C=O); δ_H(200 MHz, $CDCl_3$) 0.65 (3 H, s, 18-H), 0.91 (3 H, s, 19-H), 1.00 (3 H, d, *J* 6.2, 21-H), 3.36 (3 H, s, OMe), 3.37 (3 H, s, OMe), 3.52 (1 H, m, 3β-H), 3.82 (3 H, s, CO_2Me), 3.89 (1 H, d, *J* 4.3, 22-H), 3.92 (1 H, m, 6β-H), 4.11 (1 H, d, *J* 4.3, 23-H), 4.65 (2 H, s, OCH_2O), 4.70 and 4.72 (each 1 H, each d, *J* 6.8, OCH_2O).

Compound **3b**, amorphous solid; $[\alpha]_D^{26}$ −5.94 (*c* 1.985, $CHCl_3$) (Found: C, 65.8; H, 9.6. $C_{29}H_{50}O_8$ requires C, 66.13; H, 9.57%); *m/z* 527 (M^+ + 1), 494 (M^+ − MeOH), 445 (M^+ − 2MeOH); ν_{max}(film)/cm^{-1} 3400 (OH) and 1740 (C=O); δ_H(200 MHz, $CDCl_3$) 0.68 (3 H, s, 18-H), 0.91 (3 H, s, 19-H), 1.01 (3 H, d, *J* 6.8, 21-H), 3.39 (3 H, s, OMe), 3.40 (3 H, s, OMe), 3.52 (1 H, m, 3β-H), 3.84 (3 H, s, O_2Me), 3.92 (1 H, m, 6β-H), 3.94 (1 H, d, *J* 4.0, 22-H), 4.27 (1 H, s, 23-H), 4.61 (2 H, s, OCH_2O), 4.70 and 4.73 (each 1 H, each d, *J* 6.8, OCH_2O).

Methyl (22R,23S)-22,23-*Isopropylidenedioxy*-3α,6α-*bis*(*methoxymethyl*)-5β-*cholan*-24-*oate* **4b**.—To a solution of compound **2b** (1.578 g, 3 mmol) in CH_2Cl_2 (20 cm^3) was added 2,2-dimethoxypropane (8 cm^3) and *p*-TsOH (50 mg) and the mixture was stirred for 2 h at room temp. Work-up followed by chromatography (light petroleum–EtOAc 15:1) afforded the acetonide **4b** (1.610 g, 95%) as an amorphous solid; ν_{max}(film)/cm^{-1} 1760 (C=O) (Found: C, 67.7, H, 9.2. $C_{32}H_{54}O_8$ requires C, 67.84; H, 9.61%); *m/z* 566 (M^+), 551 (M^+ − Me) and 534 (M^+ − MeOH); δ_H(200 MHz, $CDCl_3$) 0.68 (3 H, s, 18-H), 0.95 (3 H, s, 19-H), 1.00 (3 H, d, *J* 6.5, 21-H), 1.40 and 1.46 (2 × 3 H, 2 s, acetonide), 3.39 (3 H, s, OMe), 3.40 (3 H, s, OMe), 3.50 (1 H, m, 3β-H), 3.81 (3 H, s, CO_2Me), 3.94 (1 H, m, 6β-H), 4.25 (2 H, s, 22,23-H), 4.66 (2 H, s, OCH_2O), 4.71 and 4,73 (each 1 H, each d, *J* 6.8, OCH_2O).

(22R,23R)-22,23-*Isopropylidenedioxy*-3α,6α-*bis*(*methoxymethyl*)-5β-*cholestan*-24-*ol* **5b**.—To a stirred solution of $LiBH_4$ (21 mg, 1.0 mmol) in THF (10 cm^3) was added a solution of Pr^{i}MgCl (2.0 mol dm^{-3} in THF; 3.0 cm^3) under argon at 0 °C. This mixture was cooled to −25 °C and compound **4b** (450 mg, 0.8 mmol) in THF (5 cm^3) added dropwise *via* a syringe. After being stirred for a further 1 h at −25 °C, the reaction mixture was quenched by careful addition of HCl (5%). Work-up, followed by purification on a silica gel column (light petroleum–EtOAc 10:1) gave compound **5b** (397 mg, 86%) as an amorphous solid; ν_{max}(film)/cm^{-1} 3450 (OH), 1140, 1100 and 1050 (Found: C, 70.7, H, 10.5. $C_{34}H_{60}O_7$ requires C, 70.31; H, 10.41%); *m/z* 566 (M^+ + 1 − Me), 565 (M^+ − Me), 549 (M^+ − OMe), 507 (M^+ − C_4H_9O); δ_H(200 MHz, $CDCl_3$) 0.64 (3 H, s, 18-H), 0.91 (3 H, s, 19-H), 0.97 (6 H, d, *J* 6.5, 26-H, 27-H), 1.39 and 1.40 (2 × 3 H, 2 s, acetonide), 3.12 (1 H, m, 24-H), 3.36 (3 H, s, OMe), 3.37 (3 H, s, OMe), 3.50 (1 H, m, 3β-H), 3.77 and 3.78 (1 H, each d, each *J* 8.5, 22-H), 4.03 and 4.14 (1 H, each d, each *J* 8.5, 23-H), 4.63 (2 H, s, OCH_2O), 4.67 and 4.72 (2 H, each 1 H, each d, *J* 6.8, OCH_2O).

(22R,23S)-22,23-*Isopropylidenedioxy*-3α,6α-*bis*(*methoxymethyl*)-5β-*cholestan*-24-*one* **6a**.—To a stirred suspension of PCC (310 mg) and NaOAc (100 mg) in dry CH_2Cl_2 (10 cm^3) was added compound **5** (260 mg, 0.45 mmol) in CH_2Cl_2 (5 cm^3) and the mixture was stirred for 24 h at room temp. Work-up followed by column chromatography (light petroleum–EtOAc, 15:1) provided the ketone **6a** (237 mg, 91.5%) as an amorphous solid; $[\alpha]_D^{25}$ −25.05 (*c* 0.455, $CHCl_3$); ν_{max}(film)/cm^{-1} 1710 (C=O), 1140, 1100 and 1040 (C=O) (Found: C, 69.4; H, 10.0. $C_{34}H_{58}O_7 \cdot \frac{1}{2}H_2O$ requires C, 69.47; H, 10.12%); *m/z* 517 (M^+ − OCH_2OMe), 507 (M^+ − C_3H_7O); δ_H(200 MHz, $CDCl_3$) 0.65 (3 H, s, 18-H), 0.91 (3 H, s, 19-H), 0.98 (3 H, d, *J* 6.5, 21-H), 1.07 (3 H, d, *J* 6.8, 26-H), 1.14 (3 H, d, *J* 7.0, 27-H), 3.15 (1 H, m, 25-H), 3.36 (3 H, s, OMe), 3.37 (3 H, s, OMe), 3.52 (1 H, m, 3β-H), 3.90 (1 H, m, 6β-H), 4.13 (2 H, s, 22,23-H), 4.63 (2 H, s, OCH_2O), 4.67 and 4.72 (each 1 H, each d, *J* 6.8, OCH_2O).

(22R,23S)-22,23-*Isopropylidenedioxy*-3α,6α-*bis*(*methoxymethyl*)-25-*methyl*-5β-*cholestan*-24-*one* **6b**.—To a stirred solution of compound **4b** (1.3 g, 2.5 mmol) in dry THF (100 cm^3) was added slowly *via* a syringe a solution of Bu^{t}Li (1.7 mol dm^{-3} in heptane; 1.6 cm^3) at −78 °C under argon and the mixture was kept at −78 °C for 5 min. A further portion of Bu^{t}Li (0.8 cm^3) was added to the reaction mixture, which was stirred for 10 min, and then quenched with aq. NH_4Cl. Work-up followed

by chromatography (light petroleum–EtOAc, 30:1) gave the ketone **6b** (1.14 g, 84%) as an amorphous solid; $[\alpha]_D^{25}$ +11.93 (*c* 1.02, $CHCl_3$) (Found: C, 71.2; H, 10.25. $C_{35}H_{60}O_7$ requires C, 70.9; H, 10.2%); ν_{max}(film)/cm^{-1} 1700, 1140, 1100 and 1040 (C–O); *m/z* 593 (M^+ + 1), 531 (M^+ − OCH_2OMe) and 507 (M^+ + C_5H_9O); δ_H(200 MHz, $CDCl_3$) 0.63 (3 H, s, 18-H), 0.91 (3 H, s, 19-H), 0.97 (3 H, d, *J* 5.9, 21-H), 1.22 (9 H, s, 25-Me, 26-H, 27-H), 1.37 and 1.43 (2 × 3 H, 2 s, acetonide), 3.36 (3 H, s, OMe), 3.37 (3 H, s, OMe), 3.52 (1 H, m, 3β-H), 3.92 (1 H, m, 6β-H), 4.33 (2 H, s, 22,23-H), 4.63 (2 H, s, OCH_2O), 4.67 and 4.72 (each 1 H, each d, *J* 6.8, OCH_2O).

(22R,23R)-22,23-*Isopropylidenedioxy*-3α,6α-*bis*(*methoxymethyl*)-24-*methylene*-5β-*cholestane* **7a**.—A mixture of Ph_3PCH_3I (1.2 g, 3 mmol) and Bu^{t}OK (330 mg, 3 mmol) in dry benzene (10 cm^3) was stirred under argon for 1 h at room temp. and then ketone **6a** (270 mg, 0.47 mmol) in benzene (5 cm^3) was added and the mixture stirred for 1.5 h. The resulting solid was filtered off and the solvent removed to give the crude product, which was purified by chromatography (light petroleum–EtOAc, 20:1) to afford compound **7a** (239 mg, 89%) as an amorphous solid; $[\alpha]_D^{25}$ +10.09 (*c* 0.515, $CHCl_3$) (Found: C, 73.0; H, 10.7. $C_{35}H_{60}O_6$ requires C, 72.88; H, 10.48%); ν_{max}(film)/cm^{-1} 1640 (C=C); *m/z* 577 (M^+ + 1), 575 (M^+ − 1), 561 (M^+ − Me) and 515 (M^+ − OCH_2OMe); δ_H(200 MHz, $CDCl_3$) 0.62 (3 H, s, 18-H), 0.91 (3 H, s, 19-H), 1.00 (3 H, d, *J* 6.0, 21-H), 1.07 (3 H, d, J 6.7, 26-H), 1.10 (3 H, d, *J* 5.7, 27-H), 2.31 (1 H, m, 25-H), 3.36 (3 H, s, OMe), 3.37 (3 H, s, OMe), 3.50 (1 H, m, 3β-H), 3.80 (1 H, d, *J* 8.5, 22-H), 3.90 (1 H, m, 6β-H), 4.20 (1 H, d, *J* 8.5, 23-H), 4.63 (2 H, s, OCH_2O), 4.67 and 4.72 (each 1 H, each d, *J* 6.8, OCH_2O), 5.01 (1 H, s, 28-H) and 5.08 (1 H, s, 28-H).

(22R,23R)-22,23-*Isopropylidenedioxy*-3α,6α-*bis*(*methoxymethyl*)-25-*methyl*-5β-*cholestane* **7b**.—The Wittig reaction was carried out as for compound **6a** using the ketone **6b** (510 mg, 0.86 mmol), $Ph_3(Me)PI$ (2.02 g, 5 mmol), Bu^{t}OK (560 mg, 5 mmol) and dry benzene (20 cm^3). Work-up gave the title compound **7b** (441 mg, 87%) as an amorphous solid; $[\alpha]_D^{25}$ +28.56 (*c* 1.96, $CHCl_3$) (Found C, 73.1; H, 10.6. $C_{36}H_{62}O_6$ requires C, 73.18; H, 10.58%); ν_{max}(film)/cm^{-1} 1640 (C=C); *m/z* 576 (M^+ + 1-Me), 529 (M^+ − OCH_2OMe), 183, 153 and 139; δ_H(200 MHz, $CDCl_3$) 0.59 (3 H, s, 18-H), 0.91 (3 H, s, 19-H), 1.01 (3 H, d, *J* 5.8, 21-H), 1.10 (9 H, s, 25-CH, 26-H, 27-H), 1.38 and 1.45 (2 × 3 H, 2 s, acetonide), 3.36 (3 H, s, OMe), 3.37 (3 H, s, OMe), 3.50 (1 H, m, 3β-H), 3.88 (1 H, d, *J* 9.1, 22-H), 3.90 (1 H, m, 6β-H), 4.28 (1 H, d, *J* 9.1, 23-H), 4.63 (2 H, s, OCH_2O), 4.67 and 4.72 (each 1 H, each d, *J* 6.8, OCH_2O), 5.20 (1 H, s, 28-H) and 5.24 (1 H, s, 28-H).

(22R,23R)-22,23-*Isopropylidenedioxy*-5β-*ergostane*-3α,6α-*diol* **10a** *and* (22R,23R)-22,23-*Isopropylidenedioxy*-5β-*campestane*-3α,6α-*diol* **11a**.—To a solution of compound **7a** (100 mg, 0.17 mmol) in EtOAc (5 cm^3) was added Pd–C (10%; 20 mg) and the mixture was hydrogenated for 3 h at room temp., after which the catalyst was filtered off, the solvent removed and the residue dissolved in HCl–MeOH (2.5%; 5 cm^3) and left for 24 h at room temp. Work-up followed by separation on a silica gel column afforded compounds **9a** (13 mg, $CHCl_3$–MeOH, 30:1) and **8a** (51 mg, $CHCl_3$–MeOH, 20:1).

Compound **8a** (51 mg) in CH_2Cl_2 (1.5 cm^3) was treated with $Me_2C(OMe)_2$ (0.2 cm^3) and *p*-TsOH (2 mg) at room temp. for 20 min after which work-up followed by chromatography (light petroleum–EtOAc, 1:1) furnished the title compound **10a** in almost quantitative yield.

In the same manner, the acetonide **11a** was obtained from compound **9a**.

Compound **10a**, m.p. 189–190 °C (lit.,[8] 190–190.9 °C); $[\alpha]_D^{26}$ +23.41 (*c* 0.82, $CHCl_3$) (Found: C, 74.6; H, 11.2. $C_{31}H_{54}O_4 \cdot \frac{1}{2}H_2O$ requires C, 74.50; H, 11.09%); ν_{max}(KBr)/cm^{-1} 3350 (OH), 1230 (OH) and 1030 (C–O); *m/z* 490 (M^+), 475 (M^+ − Me), 419 (M^+ − C_5H_{11}), 171, 142 and 99; δ_H(200 MHz, $CDCl_3$) 0.64 (3 H, s, 18-H), 0.84 (3 H, s, 19-H), 0.89 (6 H, d, *J* 8.2, 26-H, 27-H), 0.94 (3 H, d, *J* 7.0, 24-Me), 0.97 (3 H, d, *J* 5.2, 21-H), 1.34 and 1.37 (2 × 3 H, 2 s, acetonide), 3.62 (1 H, m, 3β-H), 3.72 (1 H, dd, *J* 8.6, 4.2, 23-H), 3.83 (1 H, d, *J* 8.6, 22-H) and 4.06 (1 H, m, 6β-H).

Compound **11a**, amorphous solid; $[\alpha]_D^{26}$ +11.95 (*c* 0.435, $CHCl_3$) (M^+ + 1 − Me, 476.3868. *M*, 476.3865); ν_{max}(KBr)/cm^{-1} 3350 (OH), 1230 and 1030; *m/z* 489 (M^+ − 1), 475 (M^+ − Me), 419 (M^+ − C_5H_{11}), 171, 142 and 99; δ_H(200 MHz, $CDCl_3$) 0.64 (3 H, s, 18-H), 0.70 (3 H, d, *J* 7, 24-Me), 0.81 (3 H, d, *J* 6.6, 26-H), 0.90 (3 H, d, *J* 6.6, 27-H), 0.9 (3 H, s, 19-H), 0.96 (3 H, d, *J* 5.9, 21-H), 1.34 and 1.38 (2 × 3 H, 2 s, acetonide), 3.55 (1 H, dd, *J* 6.9, 9.3, 23-H), 3.62 (1 H, m, 3β-H), 3.94 (1 H, d, *J* 6.9, 22-H) and 4.06 (1 H, m, 6β-H).

(22R, 23R)-22,23-*Isopropylidenedioxy*-25-*methyl*-5β-*ergostane*-3α,6α-*diol* **10b** *and* (22R,23R)-22,23-*Isopropylidenedioxy*-25-*methyl*-5β-*campestane*-3α,6α-*diol* **11b**.—In the same manner as described for the preparation of compounds **10a** and **11a**, compound **7b** (100 mg, 0.17 mmol) in EtOAc (4 cm^3) was hydrogenated over Pd-C (10%; 25 mg) and the resulting mixture was treated with HCl–MeOH (2.5%; 4 cm^3) to give compounds **9b** (26 mg) and **8b** (39 mg), treatment of which with 2,2-dimethoxypropane afforded (almost quantitatively) the acetonides **10b** and **11b**, respectively.

Compound **10b**, m.p. 267–269 °C, $[\alpha]_D^{27}$ +30.24 (*c* 0.615, $CHCl_3$) (lit.,[10] m.p. 268–270 °C, $[\alpha]_D^{27}$ +31.2 (*c* 0.52, $CHCl_3$) (Found: C, 74.8; H, 11.2. $C_{32}H_{56}O_4 \cdot \frac{1}{2}H_2O$ requires C, 74.81; H, 11.18%); ν_{max}(KBr)/cm^{-1} 3350 (OH), 1230 (OH), 1050 and 1020; *m/z* 489 (M^+ − Me), 419 (M^+ − C_6H_{13}), 185, 156 and 99; δ_H(200 MHz, $CDCl_3$) 0.65 (3 H, s, 18-H), 0.87 (3 H, d, *J* 7.0, 24-Me), 0.89 (3 H, s, 19-H), 0.91 (9 H, s, 25-Me, 26-H, 27-H), 0.97 (3 H, d, *J* 6.5, 21-H), 1.34 (6 H, s, acetonide), 3.62 (1 H, m, 3β-H), 3.66 (1 H, d, *J* 9.3; 23-H), 3.93 (1 H, d, *J* 9.3, 22-H) and 4.08 (1 H, m, 6β-H).

Compound **11b**, m.p. 211.5–213 °C; $[\alpha]_D^{27}$ +6.00 (*c* 0.55, $CHCl_3$) (Found: C, 75.9; H, 11.3. $C_{32}H_{56}O_4$ requires C, 76.14; H, 11.18%); ν_{max}(KBr)/cm^{-1} 3350 (OH) and 1040 (C–O); *m/z* 503 (M^+ − 1), 489 (M^+ − Me), 471 (M^+ − Me − H_2O), 419 (M^+ − C_6H_{13}), 185, 156 and 99; δ_H(200 MHz, $CDCl_3$) 0.64 (3 H, s, 18-H), 0.75 (3 H, d, *J* 7.0, 24-Me), 0.91 (3 H, d, 19-H), 0.95 (9 H, s, 25-Me, 26-H, 27-H), 1.34 and 1.36 (2 × 3 H, 2 s, acetonide), 3.62 (1 H, m, 3β-H), 3.63 (1 H, dd, *J* 7.0, 8.9, 23-H), 3.97 (1 H, d, *J* 7.0, 22-H) and 4.06 (1 H, m, 6β-H).

(22R,23R)-22,23-*Isopropylidenedioxy*-24-*methylene*-5β-*cholestane*-3α,6α-*diol* **14a**.—A stirred mixture of compound **7a** (60 mg, 0.1 mmol), PPTS (45 mg) and Bu^{t}OH (5 cm^3) was heated under reflux for 2.5 h. After work-up the residue was chromatographed (light petroleum–EtOAc 1.5:1) to afford the title compound **14a** (42 mg, 80%), colourless needles, m.p. 189–190 °C; $[\alpha]_D^{25}$ +3.78 (*c* 0.318, $CHCl_3$) (Found: C, 75.4; H, 10.8. $C_{31}H_{52}O_4 \cdot \frac{1}{2}H_2O$ requires C, 75.49; H, 10.73%); ν_{max}(KBr)/cm^{-1} 3350 (OH), 1640 (C=C) and 1050 (C–O); *m/z* 473 (M^+ − Me), 419 (M^+ − C_5H_9), 169, 140 and 125; δ_H(200 MHz, $CDCl_3$) 0.63 (3 H, s, 18-H), 0.92 (3 H, s, 19-H), 1.00 (3 H, d, *J* 5.8, 21-H), 1.07 (3 H, d, *J* 6.7, 26-H), 1.10 (3 H, d, *J* 6.7, 27-H), 1.41 (6 H, s, acetonide), 3.67 (1 H, m, 3β-H), 3.80 (1 H, d, *J* 8.9, 22-H), 4.10 (1 H, m, 6β-H), 4.20 (1 H, d, *J* 8.9, 23-H), 5.01 (1 H, s, 28-H) and 5.08 (1 H, s, 28-H).

(22R,23R)-22,23-*Isopropylidenedioxy*-25-*methyl*-24-*methylene*-5β-*cholestane*-3α,6α-*diol* **14b**.—In the same manner as described for the preparation of compound **14a**, compound **7b** (50 mg, 0.08 mmol), PPTS (70 mg) and Bu^{t}OH (3 cm^3) were

used. Work-up afforded compound **14b** (35 mg, 82.3%), as colourless needles, m.p. 192–193.5 °C, $[\alpha]_D^{28}$ +10.71 (*c* 1.68, $CHCl_3$) (Found: C, 73.8; H, 10.9. $C_{32}H_{54}O_4 \cdot H_2O$ requires C, 73.80; H, 10.84%); ν_{max}(KBr)/cm^{-1} 3350 (OH), 1640 (C=C) and 1030 (C–O); *m/z* 503 (M^+ + 1), 487 (M^+ − Me), 419 (M^+ − C_6H_{11}), 183, 154 and 139; δ_H(200 MHz, $CDCl_3$) 0.60 (3 H, s, 18-H), 0.92 (3 H, s, 19-H), 1.01 (3 H, d, *J* 5.6, 21-H), 1.10 (9 H, s, 25-Me, 26-H, 27-H), 1.38 and 1.45 (2 × 3 H, 2 s, acetonide), 3.68 (1 H, m, 3β-H), 3.88 (1 H, d, *J* 9.0, 22-H), 4.11 (1 H, m, 6β-H), 4.28 (1 H, d, *J* 9.0, 23-H), 5.20 (1 H, s, 28-H) and 5.24 (1 H, s, 28-H).

(22R,23R)-3α,22,23-*Trihydroxy*-24-*methylene*-5α-*cholestan*-6-*one* **15a**.—A solution of compound **14a** (80 mg, 0.16 mmol) in CH_2Cl_2 (10 cm^3) was treated with PDC (100 mg) at room temp. for 2.5 h, after which the mixture was diluted with dry diethyl ether (10 cm^3) and the mixture filtered. After removal of solvent, the residue was dissolved in HCl–MeOH (2.5%; 10 cm^3) and the solution set aside for 48 h and then worked up. On chromatography (light petroleum–EtOAc 1:1.5) compound **15a** was obtained (30 mg, 41%), colourless needles, m.p. 186–187 °C; $[\alpha]_D^{28}$ − 7.18 (*c* 0.39, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3400 (OH) and 1650 (C=C) (Found: C, 74.5; H, 10.6. $C_{28}H_{46}O_4 \cdot \frac{1}{4}H_2O$ requires C, 74.54; H, 10.39%); *m/z* 447 (M^+ + 1), 446 (M^+), 429 (M^+ − OH); δ_H(200 MHz, $CDCl_3$) 0.62 (3 H, s, 18-H), 0.73 (3 H, s, 19-H), 0.95 (3 H, d, *J* 6.2, 21-H), 1.08 (3 H, d, *J* 6.7, 26-H), 1.10 (3 H, d, *J* 6.7, 27-H), 2.30 (1 H, dd, *J* 4.3 and 12.7, 7β-H), 2.72 (1 H, t, *J* 7.7, 5α-H), 3.63 (1 H, d, *J* 8.0, 22-H), 4.03 (1 H, d, *J* 8.0, 23-H), 4.17 (1 H, $W_{\frac{1}{2}}$ 8 Hz, 3β-H), 5.03 (1 H, s, 28-H) and 5.06 (1 H, s, 28-H).

(22R,23R)-3α,22,23-*Trihydroxy*-24-*methylene*-25-*methyl*-5α-*cholestan*-6-*one* **15b**.—In the same manner as described for the preparation of compound **15a**, **14b** (80 mg, 0.16 mmol), was treated with PDC (100 mg) followed by acid treatment to give compound **15b** (28 mg, 38%), colourless needles (EtOAc), m.p. 171–172 °C; ν_{max}(KBr)/cm^{-1} 3400 (OH) and 1650 (C=C); *m/z* 461 (M^+ + 1), 460 (M^+) and 443 (M^+ − OH); δ_H(200 MHz, $CDCl_3$) 0.61 (3 H, s, 18-H), 0.73 (3 H, s, 19-H), 0.96 (3 H, d, *J* 6.4, 21-H), 1.11 (9 H, s, 25-Me, 26-H, 27-H), 2.30 (1 H, dd, *J* 4.4, 12.8, 7β-H), 2.73 (1 H, t, *J* 7.9, 5α-H), 3.76 (1 H, d, *J* 8.0, 22-H), 4.06 (1 H, d, *J* 8.0, 23-H), 4.15 (1 H, $W_{\frac{1}{2}}$ 8 Hz, 3β-H), 5.08 (1 H, s, 28-H) and 5.15 (1 H, s, 28-H).

(22R,23R)-22,23-*Isopropylidenedioxy*-3α,6α-*bismethoxy*-*methyl*-24-*methyl*-24-*methylene*-5β-*cholane* **17**.—To a solution of the acetonide **4b** (566 mg, 1 mmol) in THF (50 cm^3) under argon at −78 °C was added methyllithium (1.6 mol dm^{-3} in EtOEt; 2 cm^3). The mixture was stirred for 1 h, and then warmed to room temp. and quenched with aq. NH_4Cl solution. Work-up afforded the crude product **16** which was dissolved in CH_2Cl_2 (10 cm^3) and Et_3N (0.43 cm^3, 3 mmol), and DMAP (5 mg) were added. The stirred mixture was cooled to 0 °C, and CH_3SO_2Cl (0.12 cm^3, 1.5 mmol) added dropwise. The mixture was stirred at room temp. for 4 h after which it was worked up and the residue chromatographed (light petroleum–EtOAc 10:1) to furnish compound **17** (482 mg, 87%) as an amorphous solid; ν_{max}(film)/cm^{-1} 1650 (C=C) (Found: C, 72.3; H, 10.1. $C_{33}H_{56}O_6$ requires C, 72.22; H, 10.28%); *m/z* 548 (M^+), 533 (M^+ − Me), 507 (M^+ − C_3H_5), 487 (M^+ − $MeOCH_2OH$); δ_H(200 MHz, $CDCl_3$) 0.64 (3 H, s, 18-H), 0.92 (3 H, s, 19-H), 1.00 (3 H, d, *J* 5.6, 21-H), 1.41 (6 H, s, acetonide), 1.86 (3 H, s, 25-H), 3.38 (3 H, s, OMe), 3.39 (3 H, s, OMe), 3.52 (1 H, m, 3β-H), 3.85 (1 H, d, *J* 9.0, 22-H), 3.94 (1 H, m, 6β-H), 4.16 (1 H, d, *J* 9.0, 23-H), 4.65 (2 H, s, OCH_2O), 4.70 and 4.72 (each 1 H, each d, *J* 6.8, OCH_2O) and 4.94 (2 H, s, 28-H).

(22R,23R)-22,23-*Isopropylidenedioxy*-24,24-*dimethyl*-5β-*cholane*-3α,6α-*diol* **19**.—A stirred mixture of compound **17** (110 mg, 0.2 mmol), PPTS (100 mg) and Bu^tOH (5 cm^3) was heated under reflux for 2 h. After work-up the resulting compound **18** dissolved in EtOAc (10 cm^3) was hydrogenated over Pd-C (10%; 10 mg) for 2 h at room temp. The catalyst was filtered off and the solvent removed. Chromatography on silica gel (light petroleum–EtOAc, 1:2) afforded compound **19** (74 mg, 80%), m.p. 199–200 °C (needles, EtOAc–hexane) (lit.,[10] m.p. 202–203 °C). The ^{1}H NMR, MS and IR data were identical with those reported.[10]

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