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SYNTHESIS OF NATURALLY OCCURRING BRASSINOSTEROIDS EMPLOYING CLEAVAGE OF 23,34-EPOXIDES AS KEY REACTIONS. SYNTHESIS OF BRASSINOLIDE, CASTASTERONE, DOLICHOLIDE, DOLICHOSTERONE, HOMODOLICHOLIDE, HOMODOLICHOSTERONE, 6-DEOXOCASTASTERONE AND 6-DEOXODOLICHOSTERONE†

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Abstract—Eight new plant growth-promoting steroids (brassinolide, castasterone, dolicholide, dolichosterone, homodolicholide, homodolichosterone, 6-deoxocastasterone and 6-deoxodolichosterone) were synthesized by the regio- and stereoselective ring-opening reactions of 23,24-epoxides prepared from stigmasterol.

The discovery of brassinolide **1** in 1979 by Grove *et al.* was a breakthrough in recent phytochemistry, because it was shown to be a potent plant growth-promotor like the gibberellins.[1,2] Since then several related steroids with plant growth-promoting activity have been isolated from plants by Takahashi *et al.* They are castasterone **2** from the insect galls of *Castanea* spp.,[3] four unsaturated steroids from immature seeds of *Dolichos lablab* (Fujimame in Japanese): dolicholide **3**,[4] dolichosterone **4**,[5] homodolicholide **5**,[6] and homodolichosterone **6**,[5] and two deoxo compounds from *Phaseolus vulgaris* (var. Kentucky wonder): 6-deoxocastasterone **7**[7] and 6-deoxodolichosterone **8**[7] (Fig. 1). The structures of these brassinosteroids were proposed on the basis of their physical data obtained with very small amounts of the isolated materials: 4 mg of **1**, 12 ~ 160 μg of **2** ~ **6** and several μg of **7** and **8**. In order to confirm the proposed structures and also to secure sufficient materials for biological evaluation, we undertook synthetic studies on brassinosteroids.

All eight naturally occurring brassinosteroids **1** ~ **8** were synthesized as detailed in this paper. The three types of the steroidal sidechain of brassinosteroids as seen in brassinolide **1**, dolicholide **3** and homodolicholide **5** were all constructed by the regio- and stereoselective cleavage of an appropriate epoxide as shown in Fig. 2.

Synthesis of brassinolide, castasterone and 6-deoxocastasterone

Our earlier synthesis of brassinolide **1**, like those by others, suffered from low overall yield (1.3% in 19 steps) and not so efficient as to yield multi-gram quantities of brassinolide.[8] We therefore became interested in developing a more efficient synthesis of **1**.[9] Among the existing synthesis of brassinolide by others,[10-13] one achieved by Ikekawa *et al.* involves an epoxide similar to **12** (Fig. 3).[11] However, they reported that their attempts to introduce a Me group at C-24 of their epoxide using various organocopper reagents were unsuccessful.[11] We envisaged that some other organometallic reagent might work. Then a Me group can directly be attached to C-24 with the correct (*S*)-configuration. This was indeed realized as shown in Fig. 3. The starting aldehyde **9** was prepared from stigmasterol as reported previously.[8] Addition of $LiC \equiv CPr^i$ to **9** yielded a diastereomeric mixture of two alkynyl alcohols **10** and **10′** in 68% yield. These two isomers **10** and **10′** were separable by HPLC. The unwanted alcohol **10′** could be converted into **10** by treating the corresponding mesylate with KO_2 followed by a reductive work-up.[14] Alternatively, **10′** yielded a mixture of **10** and **10′** by its successive oxidation (MnO_2) and reduction ($NaBH_4$). Catalytic hydrogenation of the mixture of **10** and **10′** over P-2 Ni[15] in the presence of ethylenediamine gave a diastereomeric mixture of an allylic alcohol **11** and its (22*S*)-isomer **11′** in 84% yield. The mixture was epoxidized with MCPBA to give a mixture of two epoxides **12** and its (22*S*)-isomer. These were separated by SiO_2 chromatography to give 49.1% yield of the desired **12** and 43.5% of the undesired isomer. The structure **12** was assigned to an isomer whose acetate showed $J_{H(20)-H(22)} = 0$ Hz in its ^{1}H-NMR spectrum, because it later yielded brassinolide. The crucial ring-cleavage of the epoxide **12** was effected with 10 eq of Me_3Al in the presence of *n*-BuLi (*n*-BuLi:Me_3Al = 1:2.3 in dry n-hexane).[16] Castasterone **2** was obtained in 55.3% yield from **12**. Its physical properties were identical to those of the natural product. Castasterone tetraacetate **13** was subsequently converted to brassinolide **1** by the existing method.[8] The overall yield of brassinolide **1** from

†Brassinolide and its analogs, Part V. This work was presented by K. M. at the *Xth International Symposium on Natural Products Chemistry*, Monterrey, Mexico, on 28 April 1983. Part IV, M. Kondo and K. Mori, *Agric. Biol. Chem.* **47**, 97 (1983).

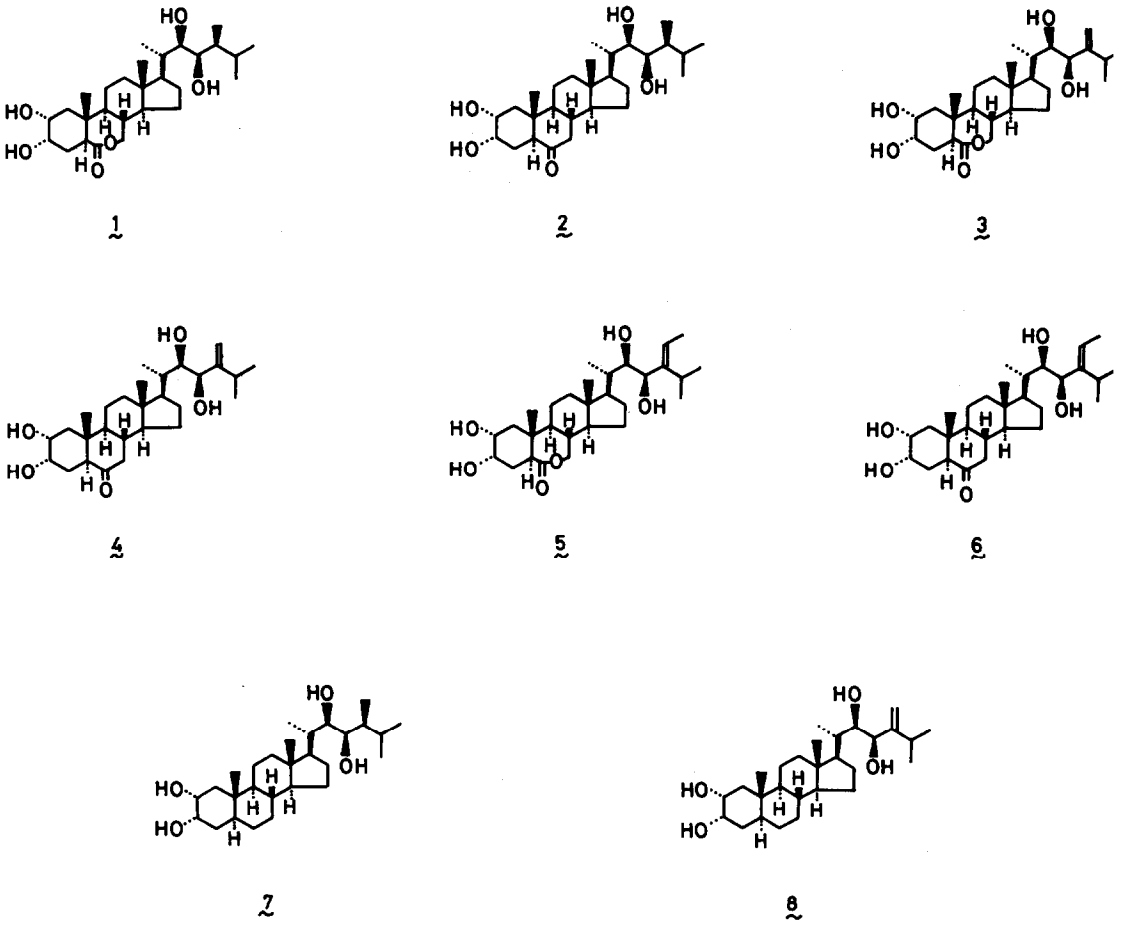

Fig. 1. Structures of brassinolide and related steroids.

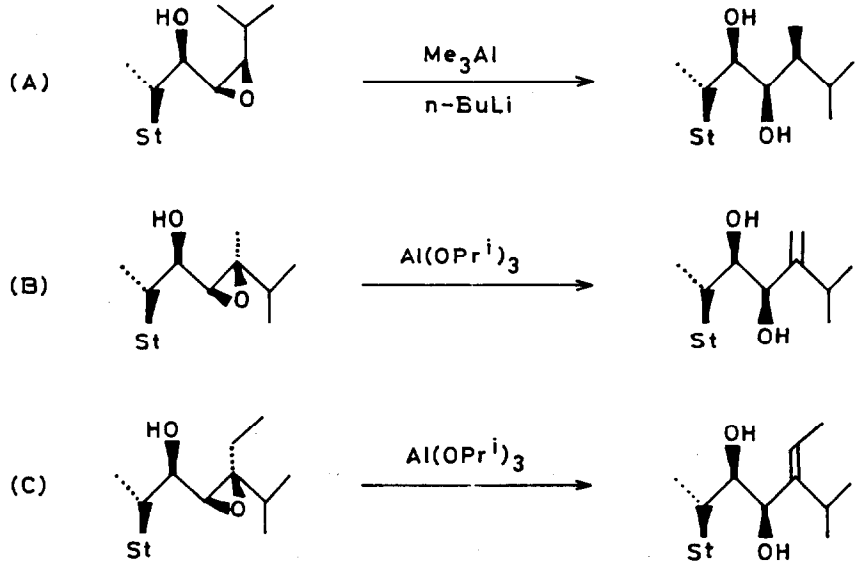

Fig. 2. Epoxide cleavage reactions employed for the construction of the steroidal side-chains.

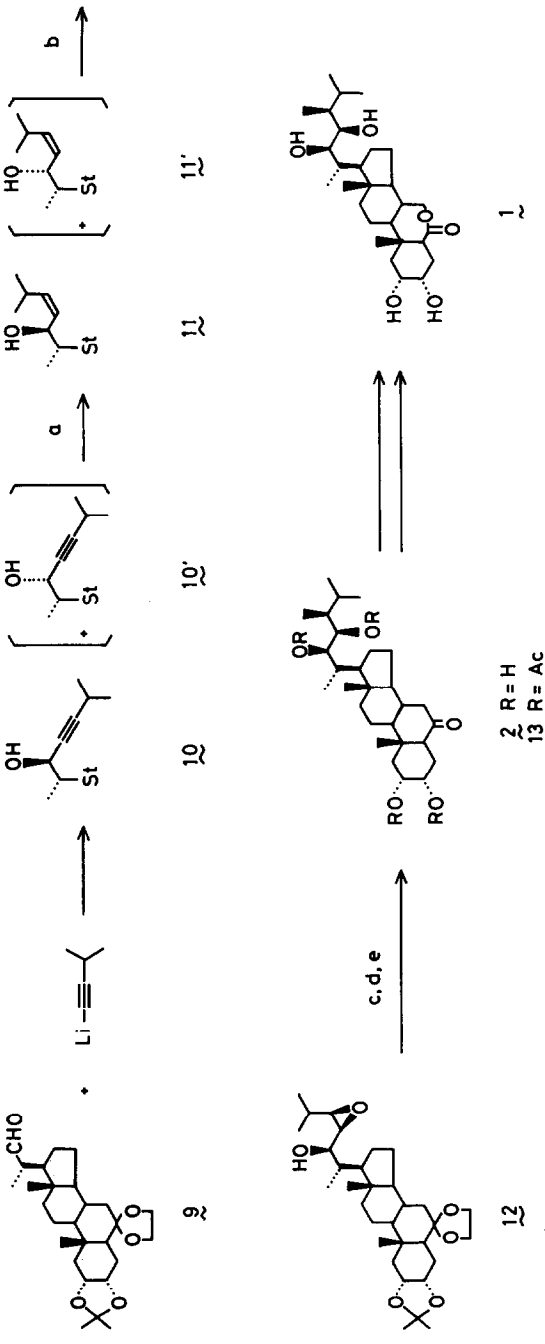

Fig. 3. An improved synthesis of brassinolide.

(a) H_2/P2-Ni, $H_2N(CH_2)_2NH_2$, (b) MCPBA, (c) Me_2Al, n-BuLi/C_6H_{14}, (d) AcOH-H_2O (4:1), (e) Ac_2O, DMAP/C_5H_5N

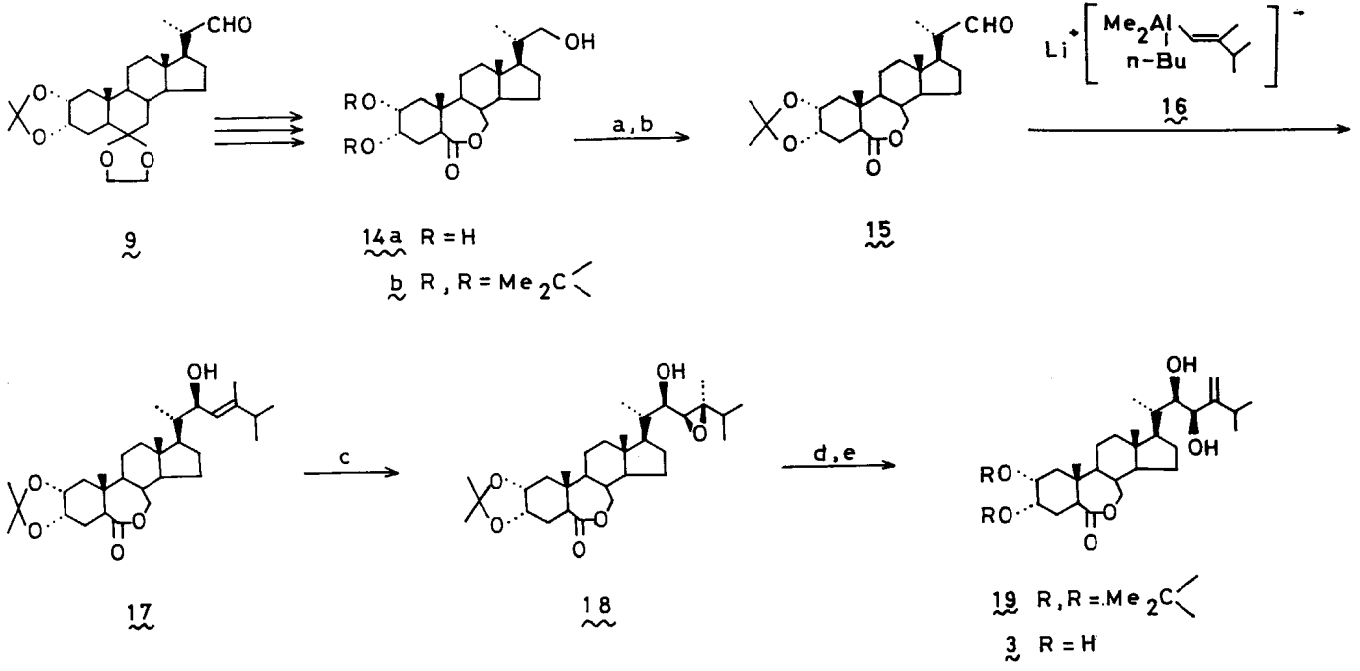

Fig. 4. Synthesis of dolicholide.

(a) $Me_2C(OMe)_2$, p-TsOH, (b) PCC, (c) MCPBA, (d) $Al(OPr^i)_3$/toluene, (e) AcOH–H_2O (4:1)

stigmasterol by this improved route was 3.0% in 16 steps. The Huang Minlon reduction of castasterone **2** yielded 6-deoxocastasterone **7**, identified with the natural product by GC-MS.

Synthesis of dolicholide, dolichosterone and 6-deoxodolichosterone

The synthesis of dolicholide **3** was achieved as shown in Fig. 4.[17] Stigmasterol was converted to a trihydroxy lactone **14a**[18] via our common intermediate **9**.[8] The glycol system of the triol **14a** was protected as an acetonide **14b**, which was oxidized to a lactonic aldehyde **15**. Extension of the side-chain was achieved in the manner similar to that employed by Fung and Siddall in their synthesis of brassinolide **1**.[10] Treatment of **15** with a lithium alanate **16** stereoselectively yielded an allylic alcohol **17** with (*E*)-geometry. The alanate **16** was prepared by the method of Negishi *et al.* as shown in Fig. 5.[19,20] Epoxidation of the olefin **17** with MCPBA proceeded stereoselectively to give an epoxide **18**. Finally treatment of **18** with $Al(OPr^i)_3$ in toluene[21] smoothly effected the cleavage of the epoxy ring.

An alternative route to **15** as shown in Fig. 6 was also explored. A known unsaturated ketone **i**[8] was converted to a silyl enol ether **ii**. Oxidation of **ii** with MCPBA yielded **iii** (16.7%) and **iv** (52.8%) after separation by SiO_2 chromatography. Oxidative cleavage of **iv** with HIO_4 was followed by reduction ($NaBH_4$) to give a lactone **v** after acidification and relactonization. Finally the steroidal side-chain of **v** was cleaved by ozonolysis to give **15** in 9.3% overall yield. This process, however, was no more satisfactory than the procedure shown in Fig. 4 with regard to the overall yield (9.8% from **i** by the route shown in Fig. 4), and the purity of **15** obtained by this

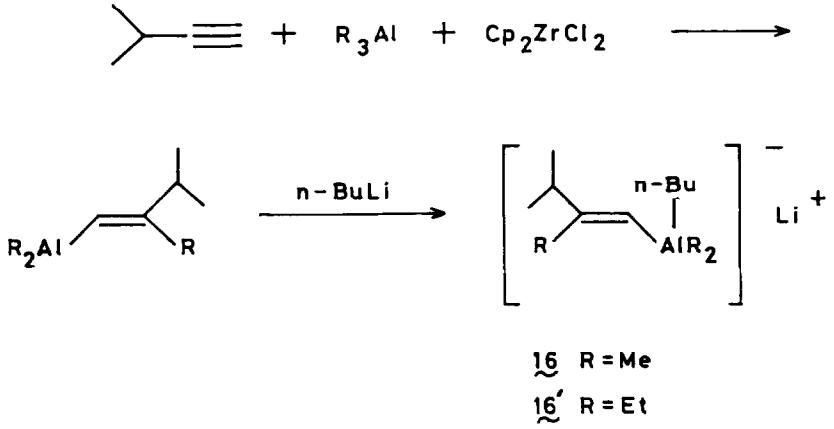

Fig. 5. Preparation of the organoaluminum reagents.

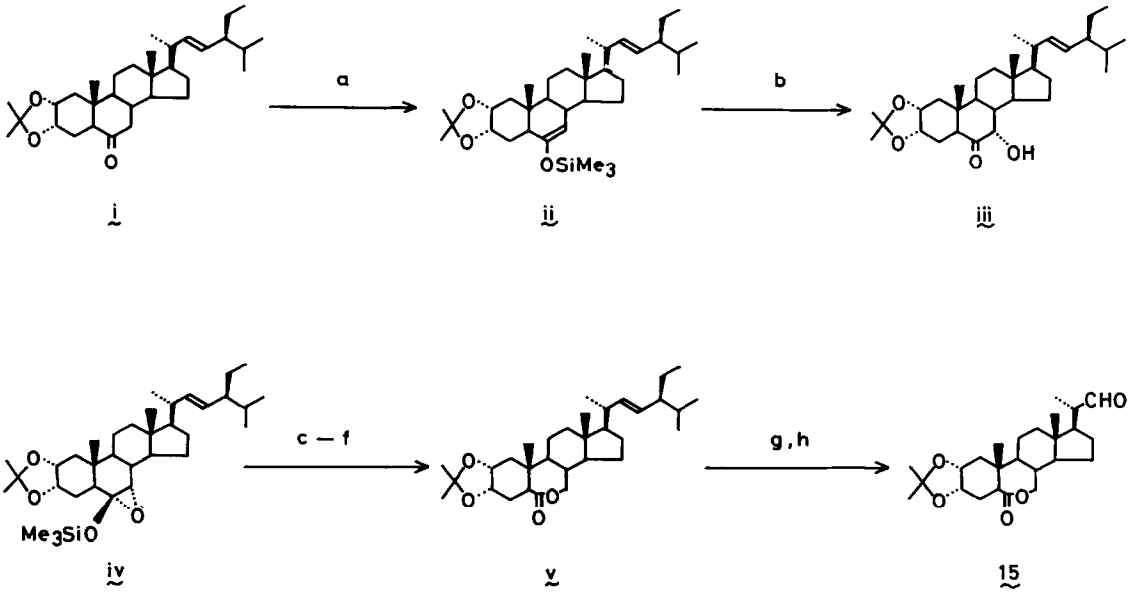

Fig. 6. An alternative route to the lactonic aldehyde **15**.

(a) LDA, Me_3SiCl, (b) MCPBA, (c) HIO_4, (d) $NaBH_4$, (e) dil HCl, (f) $Me_2C(OMe)_2$, p-TsOH, (g) O_3, (h) Me_2S

route was somewhat lower than that shown in Fig. 4. The resultant allylic alcohol **19** was treated with AcOH–H_2O to remove the protective group yielding dolicholide **3**, m.p. 235–237°, $[\alpha]_D^{22}$ +26.5° ($CHCl_3$). Its 400 MHz ^{1}H-NMR spectrum was completely identical to that of the natural product. Very recently, another synthesis of dolicholide **3** was reported by Takatsuto and Ikekawa.[22]

Dolichosterone **4** was synthesized in a similar fashion starting from the common intermediate **9** (Fig. 7). Addition of **9** to **16** smoothly yielded an allylic alcohol **20**. Its epoxidation with MCPBA gave **21**, which was treated with $Al(OPr^i)_3$ to afford an allylic alcohol **22**. Removal of both the acetal and acetonide protective groups of **22** yielded dolichosterone **4**, m.p. 230–232.5°, $[\alpha]_D^{21.5}$ +4.0° (MeOH), identical with the natural product.

Our synthesis of 6-deoxocastasterone **8** is shown in Fig. 8. The known triacetoxy ketone **23**[18] was converted to a thioacetal **24**, whose desulfurization with Raney Ni yielded **25**. This was hydrolyzed to a triol **26**. The glycol system of **26** was protected as an acetonide **27**. Oxidation of **27** with PCC (pyridinium chlorochromate) yielded an aldehyde **28**. The remaining steps to the target **8** were same as those employed in the synthesis of dolicholide **3**. Reaction of the alanate **16** with **28** gave an allylic alcohol **29**. This was epoxidized to give **30**. Treatment of **30** with $Al(OPr^i)_3$ yielded **31**. Finally removal of the acetonide group gave 6-deoxodolichosterone **8**, m.p. 219–220.5°, $[\alpha]_D^{23.5}$ +33.2° (MeOH), identified with the natural product by GC–MS.

Synthesis of homodolicholide and homodolichosterone

The same strategy as employed in the synthesis of dolicholide was also successful in the synthesis of brassinosteroids with an ethylidene group at C-24. As shown in Fig. 9, the crucial step was the addition of a lithium alanate **16′** to the appropriate aldehydes **15** and **9**. The new organoaluminum reagent **16′** was prepared according to the general procedure of Negishi as shown in Fig. 6.[19,20] The formation of the alkenylalane proceeded rather sluggishly in this case due to the diminished reactivity of Et_3Al compared with that of Me_3Al. The resultant alkenylalane was mixed with *n*-BuLi to yield **16′**. Addition of **15** to the soln of **16′** yielded an allylic alcohol **32**. This was epoxidized to **33**. Cleavage of the epoxy ring of **33** with $Al(OPr^i)_3$ proceeded selectively to give only the desired (*E*)-isomer **34**. Finally removal of the acetonide protective group of **34** gave homodolicholide **5**, m.p. 214–216°, $[\alpha]_D^{21}$ +35.4° ($CHCl_3$-MeOH = 9:1). This was identified with the natural product by 400 MHz ^{1}H-NMR and GC-MS comparisons. For the synthesis of homodolichosterone **6**, the aldehyde **9** was reacted with the alanate **16′** and the resulting allylic alcohol **35** was epoxidized to **36**. Treatment of the epoxide **36** with $Al(OPr^i)_3$ gave a mixture of an (*E*)-olefin **37** and its (*Z*)-isomer in a ratio of 4:1. Finally removal of the acetonide group of **37** yielded homodolichosterone **6**, m.p. 225–226° $[\alpha]_D^{22}$ −9.8° ($CHCl_3$MeOH = 9:1), which was identical with the natural product on the basis of its 400 MHz ^{1}H-NMR and GC-MS comparisons. Similarly **37′** gave the (Z)-isomer **6′** of homodolichosterone.

The present synthesis of homodolicholide **5** and homodolichosterone **6** was unique and conceptually simple, employing the regio- and stereo-selective ring-opening of 23, 24-epoxides **33** and **36**. However, the

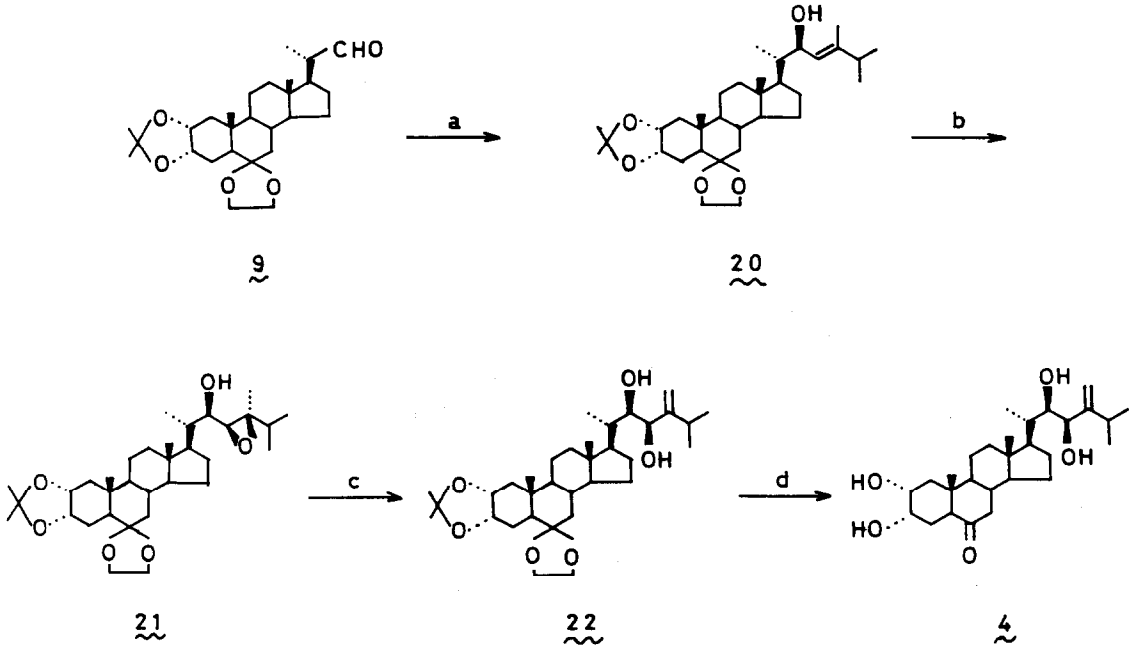

Fig. 7. Synthesis of dolichosterone.

(a) **16**, (b) MCPBA, (c) $Al(OPr^i)_3$/toluene, (d) AcOH–H_2O (4:1)

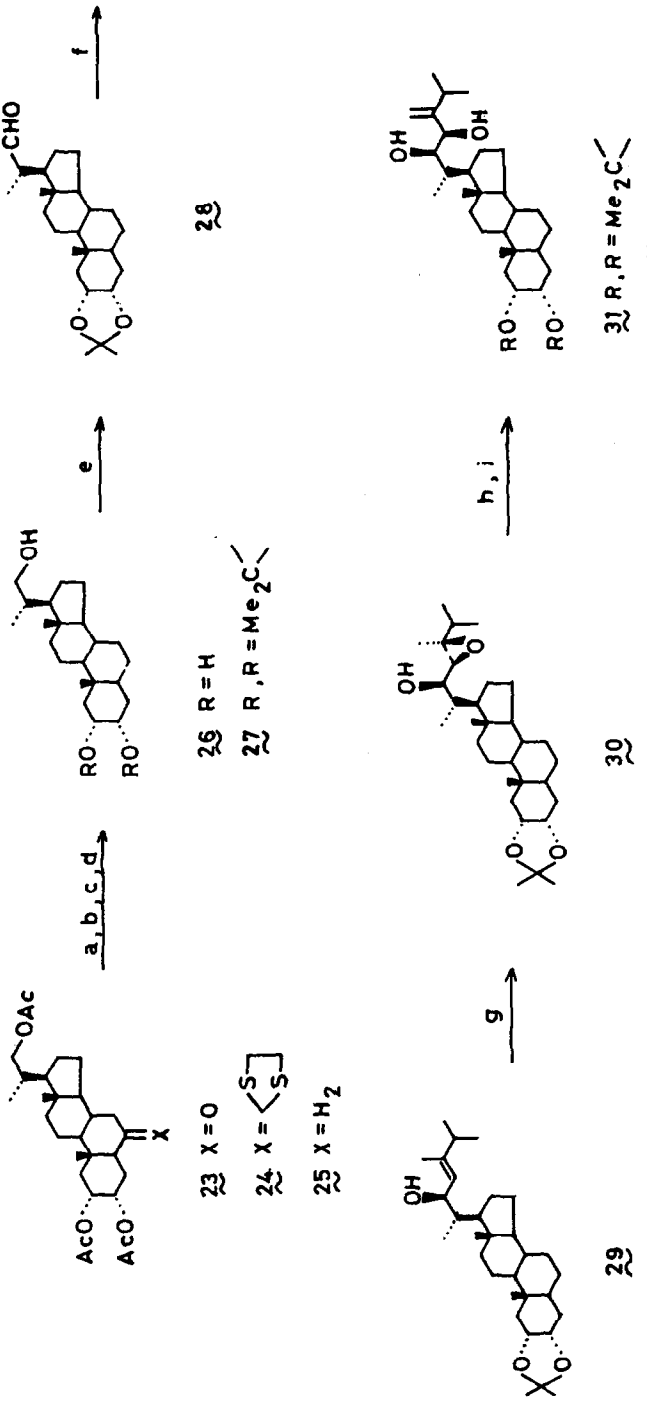

Fig. 8. Synthesis of 6-deoxodolichosterone.

(a) $(CH_2SH)_2$, BF_3, (v) Raney Ni, (c) NaOH, (d) $Me_2C(OMe)_2$, p-TsOH, (e) PCC, (f) **16**, (g) MCPBA, (h) $Al(OPr^i)_3$/toluene, (i) AcOH–H_2O (4:1)

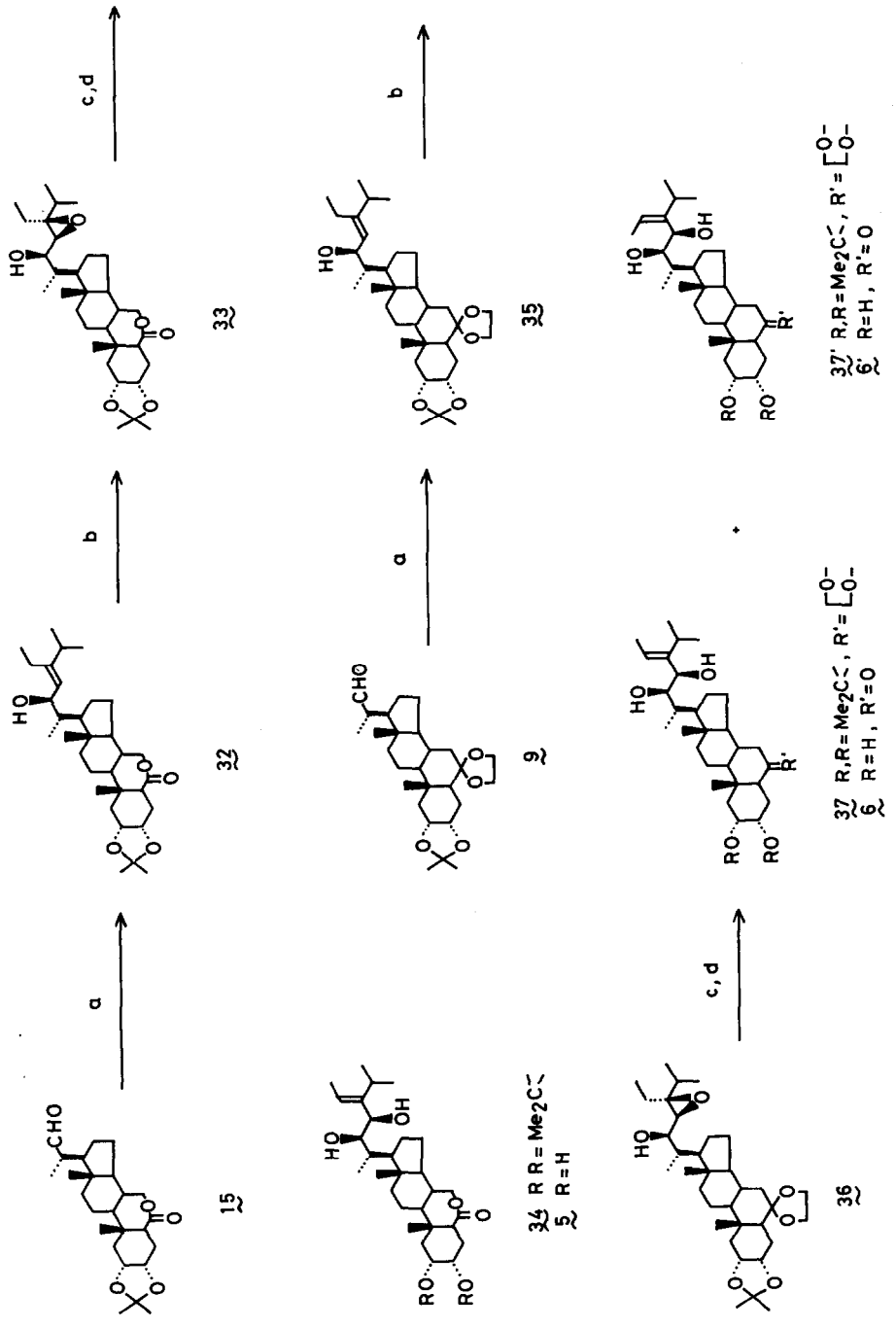

Fig. 9. Synthesis of homodolicholide and homodolichosterone.
(a) **16**, (b) MCPBA, (c) $Al(OPr^i)_3$/toluene, (d) AcOH–H_2O (4:1)

synthetic route was rather lengthy, involving the cleavage and reconstruction of the steroidal side-chain, and resulted in low overall yields. Another strategy was to utilize the whole carbon skeleton of stigmasterol without cleaving the side-chain. Preliminary accounts of our alternative synthesis of **5** and **6** along this line have already been published.[23,24] The details will be reported later.

In conclusion the present synthetic work firmly establishes the structures proposed for the new brassinosteroids and provides sufficient amounts of samples for further biological studies. The usefulness of 23,24-epoxides in the synthesis of brassinosteroids was demonstrated definitively.

EXPERIMENTAL

All m.ps were uncorrected. IR spectra were measured as films for oils or as Nujol mulls for solids on a Jasco A-102 spectrometer. NMR spectra were recorded at 60 MHz with TMS as an internal standard on a Hitachi-R24A spectrometer unless otherwise stated. Optical rotations were measured on a Jasco DIP-140 polarimeter. HPLC analyses were performed on a Shimadzu LC-2 chromatograph.

A mixture of (2R, 3S, 22R)- *and* (2R, 3S, 22S)-6,6-*ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-5α-*cholest*-23-*yne* **10** + **10′**

A soln of n-BuLi in n-hexane (1.32M, 13.6 ml) was added dropwise to a stirred and cooled soln of 1,1-dibromo-3-methyl-1-butene (2.1 g) in dry THF (40 ml) at −70 ~ −60° under Ar. The stirring was continued for 2 h at −60 ~ −50°. Then a soln of **9** (2.04 g) in dry THF (25 ml) was added dropwise during 15 min to the stirred and cooled mixture at −68 ~ −66°. The stirring was continued for 30 min at −69°. The cooling bath was then removed and the reaction temp was raised to room temp during 25 ~ 30 min. The reaction was quenched by the addition of sat NH_4Cl soln (3 ml) and water (5 ml). The mixture was extracted with ether. The ether soln was washed with water, dried (Na_2SO_4) and concentrated *in vacuo* to give a syrup (3 g). This was chromatographed over SiO_2 (Mallinckrodt CC-7, 120 g). Elution with EtOAc–n–hexane (15:85) gave 1.59 g (67.8%) of a mixture of **10** and **10′**, $[\alpha]_D^{23}$ +47.5° (c = 1.103, $CHCl_3$); ν_{max} 3460 (s), 1060 (s), 1040 (s) cm^{-1}; δ (CCl_4) 0.67 (3H, s), 0.77 (3H, s), 1.13 (6H, d, J = 7 Hz), 1.15 (3H, s), 1.29 (3H, s), 1.94 (1H, s), 0.8–2,8 (m), 3.3–4.4 (7H, m); MS: *m/z* 514 (M^+), 513 ($M^+ - 1$), 499 ($M^+ - Me$), 445, 431, 303, 235. This mixture was used in the next step without further purification.

A mixture of (2R, 3S, 22R, 23Z)- *and* (2R, 3S, 22S, 23Z)-6,6-*ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-5α-*cholest*-23-*ene* **11** + **11′**

P2-Ni catalyst was prepared from 1M $NaBH_4$ in EtOH and $Ni(OAc)_2 \cdot 4H_2O$ (498 mg) in 95% EtOH (4.0 ml).[15] To this were added under H_2 ethylenediamine (260 μl, 4.0 mmol) and a soln of **10** and **10′** (3.08 g) in 95% EtOH (15 ml). The mixture was stirred for 24 h under H_2 at room temp. It was then diluted with ether (50 ml) and filtered. The filtrate was concentrated *in vacuo*. The residue was dissolved in ether. The ether soln was washed with water, dried (K_2CO_3) and concentated *in vacuo*. The residue (3.1 g) was chromatographed over SiO_2 (Mallinckrodt CC-7, 186 g) to give pure **11** + **11′**. Impure **11** + **11′** was rechromatographed over SiO_2 (CC-7, 18 g). The total amount of pure **11** + **11′** was 2.61 g (83.9%), $[\alpha]_D^{23}$ +31.1° (c = 1.433, $CHCl_3$); ν_{max} 3480 (s), 1060 (s) cm^{-1}; δ (CCl_4) 5.0 ~ 5.4 (2H, m); MS: *m/z* 516 (M^+), 515 ($M^+ - 1$), 512, 501 ($M^+ - Me$), 483, 401, 359, 329, 305.

(2R, 3S, 22R, 23S, 24R)-23,24-*Epoxy*-6,6-*ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-5α-*cholestane* **12** *and its* (2R, 3S, 22S, 23R, 24S)-*isomer*

MCPBA (80%, 2.4 g) was added to a stirred and ice-cooled soln of **11** + **11′** (2.4 g) in dry CH_2Cl_2 (180 ml). The stirring was continued for 7 h at room temp. The mixture was washed with 1N-NaOH soln (235 ml) and water (235 ml). The CH_2Cl_2 soln was dried (Na_2SO_4) and concentrated *in vacuo*. The residue (2.6 g) was chromatographed over SiO_2 (Mallinckrodt CC-η, 208 g). Elution with EtOAc–n–hexane (10:90 ~ 15:85) gave the undesired (22*S*)-isomer in earlier fractions and the desired **12** in later fractions. The total yield of **12** was 1.15 g (49.1% on the basis of the consumed **11** + **11′**; 125 mg of **11** + **11′** was recovered), $[\alpha]_D^{22.5}$ +28.7° (c = 1.237, $CHCl_3$); ν_{max} 3460 (s), 1058 (s) cm^{-1}; δ ($CDCl_3$) 0.68 (3H, s), 0.83 (3H, s), 1.24 (3H, s), 1.39 (3H, s), 2.00 (1H, s), 0.8 ~ 2.3 (m), 2.61 (1H, dd, J = 4 and 9 Hz), 3.00 (1H, dd, J = 4 and 6 Hz), 3.5 ~ 4.3 (7H, m); MS: *m/z* 532 (M^+), 531 ($M^+ - 1$), 518, 517 ($M^+ - Me$), 499 ($M^+ - Me - H_2O$), 445, 431, 359, 321, 249, 235. The total yield of the undesired isomer was 1.02 g (43.5%), $[\alpha]_D^{22.5}$ +34.9° (c = 1.407, $CHCl_3$); ν_{max} 3460 (s), 1058 (s), 910 (s); δ ($CDCl_3$) 0.71 (3H, s), 0.83 (3H, s), 1.24 (3H, s), 1.38 (3H, s), 1.99 (1H, s), 0.8–2.3 (m), 2.63 (1H, dd, J = 4 and 9 Hz), 2.99 (1H, t, J = 4 Hz), 3.5 ~ 4.4 (7H, m). Its MS was identical to that of **12**.

(2R, 3S, 22R, 23R, 24R,)-2,3,22,23-*Tetrahydroxy*-24-*methyl*-5α-*cholestan*-6-*one* (*castasterone*) **2**

A soln of Me_3Al in n-hexane (15%, 1.8M, 7.8 ml, 14.0 mmol) and a soln of n-BuLi (1.2M, 0.5 ml, 0.6 mmol) were added to a stirred and cooled soln of **12** (750 mg, 1.4 mmol) in dry n-hexane (100 ml) at −70° under Ar. The cooling bath was removed after 30 min and the mixture was stirred for 69 h at room temp. The mixture was then cooled to −70° and the reaction was quenched by the addition of 1N-HCl (75 ml). The mixture was extracted with EtOAc. The EtOAc soln was dried (Na_2SO_4) and concentrated *in vacuo*. The residual semi-crystalline solid (0.9 g) was dissolved in 80% AcOH (20 ml) and the soln was stirred at 50° for 30 min. It was then neutralized with Na_2CO_3 and extracted with EtOAc. The EtOAc soln was dried (Na_2SO_4) and concentrated *in vacuo* to give crystals. The crystalline mass was washed with redistilled n-hexane to give 0.53 g of colorless crystals. This was further purified by HPLC [Partisil 5, 25 cm × 4.6 mm, $CHCl_3$–MeOH (9:1)] to give 294 mg (45.2%) of pure **2**, m.p. 258 ~ 260°[from $CHCl_3$–MeOH (9:1)], (lit[3] m.p. 259 ~ 261°). Slightly impure **2** (66 mg, 10.1%) was also obtained from the later eluted fractions. The pure **2** showed the following properties: $[\alpha]_D^{24.5}$ +0.03° [c = 1.170, $CHCl_3$–MeOH (9:1)], ν_{max} 3370 (s), 1710 (s), 1042 (s), 980 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.69 (3H, s), 0.76 (3H, s), 0.85 (3H, d, J = 6.8 Hz), 0.91 (3H, d, J = 6.6 Hz), 0.95 (3H, d, J = 6.8 Hz), 0.97 (3H, d, J = 6.8 Hz), 1.05 ~ 2.10 (m), 2.30 (1H, dd, J = 4.5 and 13.0 Hz), 2.69 (1H, dd, J = 2.8 and 12.6 Hz), 3.56 (1H, ddd, J = 1.5, 4.4 and 8.3 Hz), 3.72 (1H, ddd, J = 2.0, 4.6 and 8.5 Hz), 3.77 (1H, ddd, J = 3.2, 6.1 and 11.2 Hz), 4.05 (1H, dt, J = 2.5 and 4.2 Hz). (Found: C, 72.12; H, 10.29, Calc for $C_{28}H_{48}O_5$: C, 72.37; H, 10.41%). The spectral data were identical with those of the natural **2**. The corresponding tetraacetate **13**, m.p. 215 ~ 218° (lit[8] 221 ~ 222°), was obtained in the usual manner by the acetylation of **2** with Ac_2O, C_5H_5N and DMAP (N, N-4-dimethylaminopyridine). This could be converted into brassinolide **1**.[8]

Conversion of (2*R*, 3*S*, 22*S*)-6,6-*ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-5α-*cholest*-23-*yne* **10′** *into its* (2*R*, 3*S*, 22*R*)-*isomer* **10**

MsCl (50 μl) and DMAP (1 mg) were added to a stirred and ice-cooled soln of **10′** (23 mg) in dry C_5H_5N (1 ml). The stirring was continued for 1.5 h at room temp. The mixture was poured into iced-water and extracted with ether. The ether soln was washed with aq $CuSO_4$, water, aq $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give 20 mg of the mesylate as a gum: ν_{max} 1360 (s), 1173 (s), 1060 (s), 912 (s), 890 (s) cm^{-1}; δ (CCl_4) 0.73 (3H, s), 0.77 (3H, s), 1.19 (6H, d, J = 7 Hz), 1.30 (3H, s), 0.9 ~ 2.2 (m), 2.90 (3H, s), 3.6 ~ 4.2 (6H, m), 5.00 (1H, m). KO_2 (10 mg) and dicyclohexyl-18-crown ether-6 (50 mg) were added to a

stirred and ice-cooled soln of the mesylate (20 mg) in dry DMSO (1 ml) and dry DMF (1 ml). The mixture was stirred for 1 h at 0° and for 18.5 h at room temp, poured into brine and extracted with EtOAc. The EtOAc soln was washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in 99% EtOH (2 ml). $NaBH_4$ (3 mg) was added to the soln and the mixture was stirred for 3 h at room temp. Excess $NaBH_4$ was destroyed by the addition of NH_4Cl. The soln was concentrated *in vacuo* and the residue was partitioned between ether and water. The ether soln was washed with water, dried (Na_2SO_4) and concentrated *in vacuo* to give 41 mg of a gum. Purification of this by prep TLC gave 1.0 mg of **10**.

Conversion of (2R, 3S, 22S)-6,6-*ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-5α-*cholest*-23-*yne* **10′** *into a mixture of* **10′** *and its* (2R, 3S, 22R)-*isomer* **10** *by oxidation-reduction*

MnO_2 (590 mg) and $NaHCO_3$ (5 mg) were added to a soln of **10′** (59 mg) in ether (5 ml). The mixture was stirred for 4 h at room temp, filtered, and the filtrate was concentrated *in vacuo*. The residual gum (58 mg) was homogeneous when checked by TLC, ν_{max} 2200 (s), 1665 (s); MS:*m/z* 512 (M^+), 511 (M^+–1), 497 (M^+–Me), 455, 437, 417, 301. $NaBH_4$ (2 mg) was added to a soln of the gummy ketone (58 mg) in MeOH (5 ml). After stirring for 1 h at room temp, the mixture was concentrated *in vacuo* at 30°. The residue was diluted with water and extracted with ether. The ether soln was dried (K_2CO_3) and concentrated *in vacuo* to give a gum (63 mg). This was purified by prep TLC to give 4.8 mg of a mixture of **10** and **10′** (3:2 as determined by its 400 MHz ^{1}H-NMR spectrum in which 22-H of **10** appeared at δ 4.44, while that of **10′** appeared at δ 4.40).

(2R, 3S, 22R, 24S)-2,3,22,23-*Tetrahydroxy*-24-*methyl*-5α-*cholestane* (6-*deoxocastasterone*) **7**

A mixture of **2** (5 mg), 80% $N_2H_4 \cdot H_2O$ (140 μl), KOH (140 mg) and diethylene glycol (1 ml) was stirred and heated under reflux for 2 h. Subsequently the excess $N_2H_4 \cdot H_2O$ and water were removed by concentrating *in vacuo*. The residue was stirred and heated at ~200° for 30 min. After cooling, the mixture was diluted with water and dil HCl and extracted with $CHCl_3$. The $CHCl_3$ soln was washed with water and $NaHCO_3$aq, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by prep TLC (Merck Kieselgel 60 F_{254}, Art 5714; Solvent, $CHCl_3$–EtOH = 7:1) to give 1.7 mg of **7**, m.p. 225 ~ 226° (sinter at 218°), ν_{max} 3400 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.68 (3H, s), 0.81 (3H, s), 0.85 (3H, d, J = 7 Hz), 0.90 (3H, d, J = 7 Hz), 0.95 (3H, d, J = 7 Hz), 0.97 (3H, d, J = 7 Hz), 1.02 ~ 2.00 (m), 3.56 (1H, d, J = 8 Hz), 3.72 (1H, dd, J = 2 and 8 Hz), 3.76 (1H, ddd, J = 3, 4 and 9 Hz), 3.96 (1H, br. s); MS of the corresponding bismethaneboronate: *m/z* 498.4053 (M^+, Calc for $C_{30}H_{52}O_4B_2$: 498.4052). This MS was identical to that of the bismethaneboronate of the natural **7**.

(2R, 3S, 20S)-20-*Hydroxymethyl*-2,3-*isopropylidenedioxy*-*B*-*homo*-7-*oxa*-5α-*pregnan*-6-*one* **14b**

p-TsOH (100 mg) was added to a stirred soln of **14a** (1.1 g) and $Me_2C(OMe)_2$ (10 ml) in CH_2Cl_2 (10 ml). The stirring was continued for 3 h at room temp. The mixture was poured into $NaHCO_3$ aq and extracted with CH_2Cl_2. The extract was washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Merck Kieselgel 60, Art 7734, 20 g). Elution with n-hexane–EtOAc (3:2) gave 0.85 g (82%) of **14b**, m.p. 192 ~ 198° (from ether) (lit.[22] m.p. 193–195°), $[\alpha]_D^{20}$ +27.5° (c = 1.03, $CHCl_3$); ν_{max} 3450 (m), 1060 (s) cm^{-1}; δ (400 HMz, $CDCl_3$) 0.73 (3H, s), 0.88 (3H, s), 1.05 (3H, d, J = 7 Hz), 1.32 (3H, s), 1.52 (3H, s), 1.56 (1H, m), 3.29 (1H, dd, J = 6 and 10 Hz), 3.37 (1H, dd, J = 7 and 10 Hz), 3.63 (1H, dd, J = 4 and 10 Hz), 4.08 (1H, dd, J = 1.8 and 13.2 Hz), 4.12 (1H, dd, J = 11.2 and 13.2 Hz), 4.35 ~ 4.40 (2H, m); MS:*m/z* 405 (M^+–Me).

(2R, 3S, 20S)-20-*Formyl*-2,3-*isopropylidenedioxy*-*B*-*homo*-7-*oxa*-5α-*pregnan*-6-*one* **15**

A soln of **14b** (800 mg) in CH_2Cl_2 (5 ml) was added to a stirred suspension of PCC (620 mg) and NaOAc (50 mg) in CH_2Cl_2 (5 ml). The mixture was stirred for 2 h at room temp and left aside for a few min. The supernatant was removed and the residue was washed with CH_2Cl_2 (X2) and ether (X2). The combined (supernatant and washings) soln was filtered through florisil (30 g) and concentrated *in vacuo* to give 680 mg (85%) of **15**, ν_{max} 2720 (w), 1730 (s), 1180 (s), 1060 (s) cm^{-1}; δ ($CDCl_3$) 0.75 (3H, s), 0.90 (3H, s), 1.15 (3H, d, J = 7 Hz), 1.35 (3H, s), 1.55 (3H, s, 3.35 (1H, m), 4.05 ~ 4.30 (2H, br.), 4.30 ~ 4.60 (2H, br. s), 9.75 (1H, d, J = 3 Hz). Since **15** was quite unstable, it was employed in the next step without further purification.

(2R, 3S, 22R, 23E)-22-*Hydroxy*-2,3-*isopropylidenedioxy*-24-*methy*.-*B*-*homo*-7-*oxa*-5α-*cholest*-23-*en*-6-*one* **17**

(a) *Preparation of the organoaluminum reagent* **16**: A soln of Me_3Al in n-hexane (15%, 4 ml) was added to a stirred suspension of Cp_2ZrCl_2 (1.0 g) in CH_2Cl_2 (10 ml) under Ar. The mixture was stirred for 30 min at room temp to give a homogeneous yellow soln. i-PrC ≡ CH (560 mg) was added to the mixture and the stirring was continued for 2 h. The stirring was continued for 1 h at 30° under a reduced press of 30 mmHg to remove excess Me_3Al and the solvents. Dry n-hexane (5 ml) was added to the residue to precipitate Cp_2ZrCl_2. The supernatant was transferred to another flask under Ar. This hexane-extraction of the organoalane was repeated two more times. A soln of n-BuLi in n-hexane (1.50M, 2.6 ml) was added to the stirred and cooled hexane soln of the organoalane at −10°. After 30 min, the bath temp was raised to 2 ~ 5° and the mixture was stirred for 1 hr at that temp. The soln contained **16**.

(b) *Preparation of* **17**: A soln of **15** (680 mg) in ether (5 ml) was added to the stirred and cooled soln of **16** prepared as described above at −10°. After 5 min the bath temp was raised to 2 ~ 5°. The mixture was stirred overnight at room temp, then diluted with THF (7 ml) and quenched with NH_4Cl aq with ice-cooling. It was extracted with ether and EtOAc. The extract was washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Merck Kieselgel 60, Art 7734, 16 g). Elution with CH_2Cl_2–ether (3:1) gave 290 mg (36%) of **17**, m.p. 225–226° (needles from EtOAc–CH_2Cl_2), $[\alpha]_D^{20.5}$ +35.9° (c = 0.518, $CHCl_3$); ν_{max} 3470 (s), 1745 (s), 1660 (w) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.72 (3H, s), 0.88 (3H, s), 0.96 (3H, d, J = 6 Hz), 1.06 (6H, d, J = 7 Hz), 1.31 (3H, s), 1.52 (3H, s), 1.62 (3H, d, J = 1 Hz), 2.23 (1H, sept, J = 7 Hz), 3.30 (1H, dd, J = 5 and 10 Hz), 4.05 ~ 4.16 (2H, m), 4.34 ~ 4.41 (2H, m), 4.45 (1H, d, J = 7.8 Hz); 5.42 (1H, d, J = 7.8 Hz), ^{13}C-NMR (25 HMz, $CDCl_3$) 70.3, 71.2, 72.5, 73.1, 107.6, 124.7, 143.0, 176.6; MS:*m/z* 484 (M^+–18). (Found: C, 73.83; H, 9.84. Calc for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03%).

(2R, 3S, 22R, 23S, 24R)-23,24-*Epoxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-24-*methyl*-*B*-*homo*-7-*oxa*-5α-*cholestan*-6-*one* **18**

MCPBA (80%, 214 mg) was added to a stirred and ice-cooled soln of **17** (200 mg) in dry CH_2Cl_2 (2 ml). The stirring was continued for 4 h at 0 ~ 5° and overnight at room temp. The soln was washed with aq $NaHCO_3$, dried (Na_2SO_4) and concentrated *in vacuo* to give 200 mg (97%) of **18**, $[\alpha]_D^{22}$ +24.7° (c = 1.78, $CHCl_3$), ν_{max} 3470 (m), 1740 (s), 1260 (s), 1180 (s), 1060 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.73 (3H, s), 0.89 (3H, s), 0.93 (3H, d, J = 7 Hz), 1.00 (3H, d, J = 8 Hz), 1.05 (3H, d, J = 8 Hz), 1.21 (3H, s), 1.31 (3H, s), 1.52 (3H, s), 1.6 ~ 2.4 (m), 2.82 (1H, d, J = 7.8 Hz), 3.30 (1H, dd, J = 5 and 10 Hz), 3.58 (1H, d, J = 7.8 Hz), 4.05 ~ 4.14 (2H, m), 4.34 ~ 4.41 (2H, m); MS:*m/z* 518 (M^+).

(2R, 3S, 22R, 23R) - 22,23 - *Dihydroxy* - 2,3 - *isopropylidenedioxy* - *B* - *homo* - 7 - *oxa* - 5α - *ergost* - 24(28) - *en* - 6 - *one* **19**

$Al(OPr^i)_3$ (70 mg) was added to a soln of **18** (178 mg) in toluene (2 ml). The mixture was stirred and heated under reflux for 30 min under Ar. Then the mixture was acidified with 1N-HCl with ice-cooling and extracted with CH_2Cl_2. The CH_2Cl_2 soln was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by prep TLC(SiO_2) to give 167 mg (94%) of **19**, $[\alpha]_D^{22}$ +26.5° (c = 1.27, $CHCl_3$); ν_{max} ($CHCl_3$) 3450 (s), 1730 (s) cm^{-1}; δ ($CDCl_3$) 0.67 (3H, s), 0.89 (3H, s), 0.95 ~ 1.20 (9H, m), 1.31 (3H, s), 1.52 (3H, s), 3.30 (1H, m), 3.65 (1H, d, J = 8 Hz), 3.90 ~ 4.25 (3H, m), 4.30 ~ 4.50 (2H, br. s), 5.00 ~ 5.15 (2H, br. s); MS:*m/z* 518 (M^+).

(2*R*, 3*S*, 22*R*, 23*R*) - 2,3,22,23 - *Tetrahydroxy* - **B** - *homo* - 7 - *oxa* - 5α - *ergost* - 24(28) - *en* - 6 - *one* (*dolicholide*) **3**

A soln of **19** (126 mg) in AcOH-H_2O (4:1, 1.5 ml) was stirred and heated at 50° for 40 min. It was then poured into aq $NaHCO_3$ and extracted with $CHCl_3$. The $CHCl_3$ soln was washed with water, dried (Na_2SO_4) and concentrated *in vacuo* to give 55 mg (47%) of **3**. Recrystallization from MeOH gave needles, m.p. 235–237° (lit.[4] m.p. 234 ~ 238°), $[\alpha]_D^{22}$ +56.3° (c = 0.405, MeOH); ν_{max} 3420 (s), 1730 ~ 1695 (s, br.), 1640 (w), 1180 (m), 1060 (s), 1025 (m) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.66 (3H, s), 0.92 (3H, s), 0.96 (3H, d, J = 7 Hz), 1.08 (3H, d, J = 8 Hz), 1.11 (3H, d, J = 8 Hz), 1.2 ~ 2.2 (m), 2.26 (1H, m), 3.11 (1H, dd, J = 4 and 12 Hz), 3.62 (1H, d, J = 8 Hz). 3.72 (1H, m), 4.02 (1H, br. s), 4.03 (1H, d, J = 8 Hz), 4.09 (2H, m), 5.04 (1H, s), 5.07 (1H, s); MS:*m/z* 397, 100. (Found: C, 68.10; H, 9.65. Calc for $C_{28}H_{46}O_2 \cdot H_2O$: C, 67.71; H, 9.74%). The spectral data was identical to those of the natural 3.

(2R, 3S, 24S, 22E) - 24 - *Ethyl* - 2,3 - *isopropylidenedioxy* - 6 - *trimethylsilyloxy* - 5α - *cholesta* - 6,22 - *diene* **ii**

A soln of LDA was prepared by the addition of a soln of n-BuLi in n-hexane (1.75M, 4.3 ml) to a stirred and cooled soln of i-Pr_2NH (1.1 ml) in dry DME (20 ml) at −78° under Ar. After stirring for 30 min, a soln of **i** (2.07 g) in dry DME (20 ml) was slowly added to the stirred soln at −78°. After 15 min, Me_3SiCl (1.0 ml) and Et_3N (0.2 ml) were added rapidly at −78°. The cooling bath was removed and the stirring was continued for 1 h. The mixture was poured into aq $NaHCO_3$ and extracted with n-pentane. The extract was dried (K_2CO_3) and concentrated *in vacuo* to give 2.85 g (quantitative) of amorphous **ii**, ν_{max} 1658 (s), 1250 (s), 1220 (s), 1170 (s), 1060 (s), 865 (s), 842 (s) cm^{-1}; δ ($CDCl_3$) 0.16 (9H, s), 0.70 (6H, s), 0.7 ~ 2.6 (m), 1.32 (3H, s), 1.46 (3H, s), 4.20 (2H, m), 4.62 (1H, br. s), 5.15 (2H, m). This was employed directly in the next step.

(2R, 3S, 7S, 24S, 22E) - 24 - *Ethyl* - 7 - *hydroxy* - 2,3 - *isopropylidenedioxy* - 5α - *cholest* - 22 - *en* - 6 - *one* **iii** *and* (2R, 3S, 6S, 7S, 24S, 22E) - 6,7 - *epoxy* - 24 - *ethyl* - 7 - *hydroxy* - 2,3 - *isopropylidenedioxy* - 6 - *trimethylsilyloxy* - 5α - *cholest* - 22 - *ene* **iv**

MCPBA (80% purity, 883 mg) was added to a stirred soln of **ii** (2.07 g) in dry CH_2Cl_2 (100 ml). After stirring for 1 h the mixture was washed with aq Na_2SO_3 and aq $NaHCO_3$ dried (K_2CO_3) and concentrated *in vacuo* to give 2.34 g of an amorphous solid. This was chromatographed over SiO_2 (Merck Kieselgel G, Art 7734, 140 g). Elution with EtOAc–n-hexane first gave **iv** (1.12 g, 52.8%), $[\alpha]_D^{23}$ +28.2° (c = 0.834. $CHCl_3$). ν_{max} 1372 (s), 1365 (s), 1241 (s), 1210 (s), 1050 (s), 835 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.19 (9H, s), 0.69 (3H, s), 0.77 (3H, s), 0.79 (3H, d, J = 6.4 Hz), 0.80 (3H, t, J = 7.0 Hz), 0.84 (3H, d, J = 6.4 Hz), 1.02 (3H, d, J = 6.8 Hz), 1.33 (3H, s), 1.47 (3H, s), 1.0 ~ 2.1 (m), 2.27 (1H, ddd, J = 1.8, 3.0 and 15.0 Hz), 3.55 (1H, br. s, W 1/2 = 5.0 Hz, β-H at C-7), 4.06 (1H, ddd, J = 5.0, 6.5 and 10.5 Hz), 4.30 (1H, m), 5.02 (1H, dd, J = 8.5 and 15.0 Hz), 5.16 (1H, dd, J = 8.5 and 15.0 Hz); MS:*m/z* 572 (M^+), 557 (M^+–Me), 499, 485, 469. Then 310 mg (16.7%) of **iii** was eluted, m.p. 153–154° (from EtOAc–n-hexane), $[\alpha]_D^{23}$ +20.6° (c = 0.804, $CHCl_3$); ν_{max} 3410 (s), 1698 (s), 1660 (w), 1375 (s), 1365 (s), 1235 (s), 1210 (s), 1050 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.64 (3H, s), 0.66 (3H, s), 0.79 (3H, d, J = 6.8 Hz), 0.80 (3H, t, J = 7.0 Hz), 0.85 (3H, d, J = 6.8 Hz), 1.02 (3H, d, J = 6.8 Hz), 1.34 (3H, s), 1.50 (3H, s), 1.0 ~ 2.1 (m), 2.70 (1H, br. d, J = 3.2 Hz), 3.28 (1H, dd, J = 4.5 and 12.5 Hz), 3.80 (1H, br. s, W 1/2 = 6.0 Hz, β-H at C-7), 4.08 (1H, ddd, J = 5.0, 6.5 and 10.5 Hz), 4.29 (1H, ddd, J = 1.8, 4.0 and 4.0 Hz), 5.03 (1H, dd, J = 8.8 and 15.0 Hz), 5.15 (1H, dd, J = 8.8 and 15.0 Hz); MS:*m/z* 500 (M^+), 485 (M^+–Me). (Found: C, 76.68; H, 10.13. Calc for $C_{32}H_{52}O_4$: C, 76.75; H, 10.47%.)

(2R, 3S, 24S, 22E) - 24 - *Ethyl* - 2,3 - *isopropylidenedioxy* - 7 - *oxa* - *B* - *homo* - 5α - *cholest* - 22 - *en* - 6 - *one* **v**

$HIO_4 \cdot 2H_2O$ (180 mg) was added to a stirred and ice-cooled soln of **iv** (439 mg) in dry ether (50 ml). After 30 min, the ice-bath was removed and the stirring was continued for 2 h at room temp. The mixture was filtered and the solid was washed with dry ether. The combined filtrate and washings were concentrated *in vacuo* to give 378 mg of a crude gum. This was dissolved in EtOH (50 ml) and treated with $NaBH_4$ (22 mg) with stirring and ice-cooling. The ice-bath was removed after 1 h and the stirring was continued for 16 h at room temperature. The mixture was concentrated *in vacuo*. The residue was dissolved in THF (20 ml) and 6N-HCl (20 ml), and the resultant soln was stirred at room temp for 4.5 h. It was then concentrated *in vacuo*. The residue was neutralized with $NaHCO_3$ and extracted with $CHCl_3$. The extract was dried ($NaSO_4$) and concentrated *in vacuo* to give 391 mg of a gummy material. This was dissolved in CH_2Cl_2 (40 ml). *p*-TsOH (5 mg) and $Me_2C(OMe)_2$ (2 ml) were added to the soln and the mixture was stirred for 17 h at room temp. It was then neutralized with K_2CO_3. The mixture was washed with $NaHCO_3$ aq, dried ($MgSO_4$) and concentrated *in vacuo* to give 400 mg of crude **v**. This was chromatographed over SiO_2 (Merck Kieselgel, Art 7734, 24 g) to give 162 mg (41.0%) of **v**, $[\alpha]_D^{21}$ +19.3° (c = 0.365, $CHCl_3$); ν_{max} 1738 (s), 1255 (s), 1203 (s), 1175 (s), 1070 (s), 1058 (s), 1040 (s), 963 (s)cm^{-1}; δ (400 MHz, $CDCl_3$) 0.72 (3H, s), 0.79 (6H, d, J = 7.0 Hz), 0.80 (3H, t, J = 7.0 Hz), 0.88 (3H, s), 1.02 (3H, d, J = 6.8 Hz), 1.1 ~ 2.1 (m), 1.32 (3H, s), 1.52 (3H, s), 2.32 (1H, dd, J = 3.5 and 10.5 Hz), 3.29 (1H, dd, J = 5.0 and 9.5 Hz), 4.07 (1H, dd, J = 9.5 and 12.5 Hz), 4.11 (1H, dd, J = 3.0 and 12.5 Hz), 4.37 (2H, m), 5.03 (1H, dd, J = 8.8 and 15.0 Hz), 5.14 (1H, dd, J = 8.5 and 15.0 Hz); MS:*m/z* 500 (M^+), 485 (M^+–Me), 471, 399.

(2R, 3S, 20S)-20-*Formyl*-2,3-*isopropylidenedioxy*-7-*oxa*-B-*homo*-5α-*pregnan*-6-*one* **15**

O_3 was bubbled into a stirred and cooled soln of **v** (61 mg in MeOH (10 ml)–CH_2Cl_2 (10 ml) in the presence of $NaHCO_3$ (61 mg) at −70°. After 8 h, N_2 was bubbled through the soln to remove excess O_3. Me_2S (5 ml) was added at −70°. The mixture was stirred overnight. N_2 was bubbled through the soln to remove Me_2S. The mixture was then diluted with ether (100 ml). The ether soln was washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The residue (44 mg) was purified by prep TLC to give 19 mg (37.3%) of **15**. The IR and NMR spectra were identical to those of an authentic sample. MS:*m/z* 418 (M^+), 403 (M^+–Me).

(3R, 3S, 22R, 23E)-6-*Ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-24-*methyl*-5α-*cholest*-23-*ene* **20**

In the same manner as described for the synthesis of **17**, **9** (1.40 g) and the lithium alanate prepared from i-PrC ≡ CH (1.00 g), Cp_2ZrCl_2 (2.16 g), Me_3Al (15% hexane soln, 8.5 ml) and n-BuLi (1.31M-hexane soln, 5.6 ml) gave 700 mg (42%) of **20**, $[\alpha]_D^{22}$ +35.6° (c = 3.28, $CHCl_3$); ν_{max} 3470 (s), 1060 (s)

cm^{-1}; δ (400 MHz, $CDCl_3$) 0.68 (3H, s), 0.84 (3H, s), 0.95 (3H, d, J = 6 Hz), 1.10 (6H, d, J = 7 Hz), 1.27 (3H, s), 1.41 (3H, s), 1.61 (3H, s), 2.23 (1H, m), 3.76 (1H, m), 3.92 (3H, m), 4.10 (1H, m), 4.27 (1H, m), 4.45 (1H, d, J = 7 Hz), 5.33 (1H, d, J = 7 Hz); MS:*m/z* 512 (M^+-H_2O).

(2R, 3S, 22R, 23S, 24R)-23,24-*Epoxy*-6-*ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-24-*methyl*-5α-*cholestane* **21**

In the same manner as described for the preparation of **18**, **20** (200 mg) was epoxidized with MCPBA (80% purity, 163 mg) to give 198 mg (96%) of **21**. Recrystallization of **21** from EtOAc–n–hexane gave pure **21**, m.p. 223–224.5°. $[\alpha]_D^{21}$ +31.6° (c = 0.414, $CHCl_3$); ν_{max} 3530 (s), 1060 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.69 (3H, s), 0.84 (3H, s), 0.92 (3H, d, J = 7 Hz), 0.99 (3H, d, J = 7 Hz), 1.04 (3H, d, J = 7 Hz), 1.21 (3H, s), 1.27 (3H, s), 1.42 (3H, s), 2.81 (1H, d, J = 6 Hz), 3.59 (1H, d, J = 6 Hz), 3.76 (1H, m), 3.92 (3H, m), 4.10 (1H, m), 4.27 (1H, m); MS:*m/z* 546 (M^+). (Found: C, 72.23; H, 9.87. Calc for $C_{33}H_{54}O_6$: C, 72.49; H, 9.96%.)

(2R, 3S, 22R, 23R)-6-*Ethylenedioxy*-22,23-*dihydroxy*-2,3-*isopropylidenedioxy*-5α-*ergost*-24(28)-*ene* **22**

In the same manner as described for the preparation of **19**, **21** (180 mg) was treated with $Al(OPr^i)_3$ (70 mg) to give 150 mg (83%) of **22**, $[\alpha]_D^{22}$ +35.2°(c = 1.66, $CHCl_3$); ν_{max} 3450 (s), 1080 (s), 1060 (s), 1040 (s) cm^{-1}; δ ($CDCl_3$) 0.64 (3H, s), 0.85 (3H, s), 0.55 (3H, d, J = 6 Hz), 1.10 (6H, d, J = 7 Hz), 1.30 (3H, s), 1.43 (3H, s), 3.7 ~ 4.4 (8H, m), 5.10 (2H, br. s); MS:*m/z* 546 (M^+). This was employed in the next step without further purification.

(2R, 3S, 22R, 23R)-2,3,22,23-*Tetrahydroxy*-5α-*ergost*-24(28)-*en*-6-*one* (*dolichosterone*) **4**

In the same manner as described for the synthesis of **3**, **22** (145 mg) was treated with AcOH aq to give 95 mg (77%) of **4**, m.p. 230–232.5° (from MeOH) (lit[5] m.p. 233–237°), $[\alpha]_D^{21.5}$ +4.0° (c = 0.2, MeOH); ν_{max} 3350 (s), 1710 (s), 1640 (w), 1080 (m), 1040 (m), 1010 (m), 985 (m) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.62 (3H, s), 0.75 (3H, s), 0.96 (3H, d, J = 6 Hz), 1.08 (3H, d, J = 7 Hz), 1.11 (3H, d, J = 7 Hz), 1.2 ~ 2.3 (m), 2.69 (1H, dd, J = 4 and 12 Hz), 3.63 (1H, d, J = 8 Hz), 3.77 (1H, m), 4.03 (1H, dd, J = 3 and 8 Hz), 4.05 (1H, br. s), 5.04 (1H, s), 5.06 (1H, s); MS:*m/z* 363, 100. (Found: C, 69.86; H, 9.76. Calc for $C_{28}H_{46}O_5 \cdot H_2O$: C, 69.96; H, 10.07%.) The spectral data was identical to those of the natural **4**.

(2R, 3S, 20S)-2,3-*Diacetoxy*-20-*acetoxymethyl*-6-*ethylenedithio*-5α-*pregnane* **24**

$(CH_2SH)_2$ (1 g) and $BF_3 \cdot Et_2O$ (0.5 ml) were added to a soln of **23** (1.9 g) in CH_2Cl_2 (30 ml) and the soln was left to stand overnight at room temp. It was then poured into 5% aq Na_2CO_3 and extracted with CH_2Cl_2. The extract was washed with water, dried ($MgSO_4$) and concentrated *in vacuo* to give 1.95 g (89%) of **24**, m.p. 196–197° (form 99% EtOH), $[\alpha]_D^{21.5}$ +26.6° (c = 1.13, $CHCl_3$), ν_{max} 1745 (s) 1250 (s), 1240 (s), 1220 (s) cm^{-1}; δ ($CDCl_3$) 0.72 (3H, s), 1.00 (3H, d, J = 6 Hz), 1.05 (3H, s), 2.00 (3H, s), 2.07 (3H, s), 2.12 (3H, s), 3.10 ~ 3.30 (4H, m), 3.7 ~ 4.1 (2H, m), 4.8 ~ 5.2 (1H, m), 5.3 ~ 5.5 (1H, br. s); MS:*m/z* 566 (M^+), 506 (M^+-60). (Found: C, 63.29; H, 8.02. Calc for $C_{30}H_{46}O_2S_2$: C, 63.58; H, 8.18%).

(2R, 3S, 20S)-2,3-*Diacetoxy*-20-*acetoxymethyl*-5α-*pregnane* **25**

Raney-Ni (prepd from 10 g of Raney Ni–Al alloy) was added to a soln of **24** (600 mg) in EtOH (20 ml). The mixture was stirred and heated under reflux for 30 min at 70 ~ 80°. It was then filtered and the filtrate was concentrated *in vacuo* to give 450 mg (89%) of **25**, m.p. 191.5–192.5° (from EtOH–$CHCl_3$), $[\alpha]_D^{21.5}$ +21.5° (c = 1.15, $CHCl_3$); ν_{max} 1740 (s), 1250 (s), 1230 (s), 1035 (s) cm^{-1}; δ ($CDCl_3$) 0.68 (3H, s), 0.88 (3H, s), 1.00 (3H, d, J = 6 Hz), 2.00 (3H, s), 2.07 (3H, s), 2.11 (3H, s), 3.75 ~ 4.20 (2H, m), 4.80 ~ 5.20 (1H, m), 5.20 ~ 5.40 (1H, br. s); MS:*m/z* 476 (M^+), 416 (M^+–AcOH). (Found: C, 70.34; H, 9.24. Calc for $C_{28}H_{44}O_6$: C, 70.55; H, 9.31%).

(2R, 3S, 20S)-2,3-*Dihydroxy*-20-*hydroxymethyl*-5α-*pregnane* **26**

50% NaOH aq (7 ml) was added to a soln of **25** (1.5 g) in MeOH (30 ml) and the mixture was stirred and heated under reflux for 1 h. Crude **26** was collected on a filter as a solid, ν_{max} 3600 ~ 3200 (s), 1040 (s) cm^{-1}. The yield was almost quantitative (1.10 g). This was employed directly in the next step.

(2R, 3S, 20S)-20-*Hydroxy*-2,3-*isopropylidenedioxy*-5α-*pregnane* **27**

p-TsOH (50 mg) was added to a soln of **26** (1.3 g) in $Me_2C(OMe)_2$ (10 ml) and CH_2Cl_2 (10 ml). After stirring for 4 h at room temp, the mixture was poured into $NaHCO_3$ aq and extracted with CH_2Cl_2. The CH_2Cl_2 soln was washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (15 g). Elution with n-hexane–EtOAc (95:5 ~ 90:10) gave 1.10 g (76%) of **27**, $[\alpha]_D^{22.5}$ +52.3° (c = 1.59, $CHCl_3$); ν_{max} 3450 (s), 1240 (s), 1230 (s), 1210 (s), 1050 (s), 1035 (s), 910 (s) cm^{-1}; δ ($CDCl_3$) 0.68 (3H, s), 0.75 (3H, s), 1.05 (3H, d, J = 6 Hz), 1.35 (3H, s), 1.51 (3H, s), 3.15 ~ 3.80 (2H, m), 4.05 ~ 4.40 (2H, m); MS:*m/z* 375 (M^+–Me)

(2R, 3S, 20S)-20-*Formyl*-2,3-*isopropylidenedioxy*-5α-*pregnane* **28**

In the same manner as described for the preparation of **15**, **27** (1.10 g) was oxidized with PCC (920 mg) in the presence of NaOAc (70 mg) to give 735 mg (67%) of **28**, m.p. 99 ~ 100.5°, ν_{max} 2720 (w), 1720 (s), 1365 (s), 1240 (s), 1230 (s), 1210 (s), 1050 (s) cm^{-1}; δ ($CDCl_3$) 0.70 (3H, s), 0.75 (3H, s), 1.11 (3H, d, J = 7 Hz), 1.35 (3H, s), 1.50 (3H, s), 4.10 ~ 4.30 (2H, m), 9.68 (1H, d, J = 4 Hz); MS:*m/z* 388 (M^+), 373 (M^+-15).

(2R, 3S, 22R, 23E)-22-*Hydroxy*-2,3-*isopropylidenedioxy*-24-*methyl*-5α-*cholest*-23-*ene* **29**

In the same manner as described for the synthesis of **17**, **28** (735 mg) was treated with the lithium alanate prepared from Cp_2ZrCl_2 (1.20 g), Me_3Al (15% hexane soln, 4 ml) and i-PrC ≡ CH (0.60 g) to give 713 mg (80%) of **29**, m.p. 168–169° (from EtOAc-n-hexane), $[\alpha]_D^{23}$ +53.6° (c = 0.83, $CHCl_3$); ν_{max} 3530 (s), 1660 (w), 1050 (s) cm^{-1}; δ ($CDCl_3$) 0.65 (3H, s), 0.70 (3H, s), 0.98 (9H, seemingly d, J = 7 Hz), 1.30 (3H, s), 1.48 (3H, s), 1.60 (3H, d, J = 2 Hz), 3.95 ~ 4.25 (2H, m), 4.42 (1H, d, J = 8 Hz), 5.30 (1H, d, J = 8 Hz); MS:*m/z* 454 (M^+-H_2O). (Found: C, 78.76; H, 10.94. Calc for $C_{31}H_{52}O_3$: C, 78.76; H, 11.09%).

(2R, 3S, 22R, 23S, 24R)-23,24-*Epoxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-24-*methyl*-5α-*cholestane* **30**

In the same manner as described for the preparation of **18**, **29** (390 mg) was epoxidized with MCPBA (80%, 445 mg) to give 380 mg (95%) of **30**, m.p. 193 ~ 194° (from EtOAc-CH_2Cl_2–n-hexane), $[\alpha]_D^{23}$ +43.0° (*c* = 0.8, $CHCl_3$); ν_{max} 3470 (s), 1245 (s), 1210 (s), 1055 (s) cm^{-1}; δ ($CDCl_3 + D_2O$) 0.68 (3H, s), 0.72 (3H, s), 0.85 ~ 1.10 (9H, m), 1.20 (3H, s), 1.32 (3H, s), 1.50 (3H, s), 2.80 (1H, d, J = 7 Hz), 3.58 (1H, d, J = 7 Hz), 4.00 ~ 4.30 (2H, m); MS:*m/z* 488 (M^+), 473 (M^+-15). (Found: C, 76.16; H, 10.61. Calc for $C_{31}H_{52}O_4$: C, 76.18; H, 10.72%).

(2R, 3S, 22R, 23R)-22,23-*Dihydroxy*-2,3-*isopropylidenedioxy*-5α-*ergost*-24(28)-*ene* **31**

In the same manner as described for the synthesis of **19**, **30** (424 mg) was treated with $Al(OPr^i)_3$ (180 mg) to give 403 mg (95%) of **31**, m.p. 163–164° (from ether–n-hexane), $[\alpha]_D^{23.5}$ +52.3° (c = 0.78, $CHCl_3$); ν_{max} 3550 (s), 3090 (w), 1645 (w), 1250 (s), 1210 (s), 1050 (s) cm^{-1}; δ ($CDCl_3 + D_2O$) 0.60 (3H, s), 0.70 (3H, s), 0.85 ~ 1.20 (9H, m), 1.31 (3H, s), 1.48

(3H, s), 3.58 (1H, d, J = 9 Hz), 3.85 ~ 4.25 (3H, m), 5.01 (2H, br. s); MS:*m/z* 488 (M^+), 473 (M^+–Me). (Found: C, 76.12; H, 10.68. Calc for $C_{31}H_{52}O_4$: C, 76.18; H, 10.72%.)

(2R, 3S, 22R, 23R)-2,3,22,23-*Tetrahydroxy-5α-ergost*-24(28)-*ene* (*6-deoxodolichosterone*) **8**

A soln of **31** (235 mg) in AcOH–H_2O (4:1, 5 ml) was stirred and heated at 55 ~ 60° for 30 min. Subsequent workup gave 211 mg (quantitative) of **8**, m.p. 219–220.5° (from EtOAc–MeOH), $[\alpha]_D^{23.5}$ +33.2° (c = 0.51, MeOH); ν_{max} 3600 ~ 3100 (s), 1670 (w), 1065 (m), 1040 (m), 1020 (m), 990 (m), 910 (m) cm^{-1}; δ (400 MHz, $CDCl_3$ + D_2O) O.63 (3H, s), 0.80 (3H, s), 0.94 (3H, d, J = 6.7 Hz), 1.08 (3H, d, J = 8 Hz), 1.11 (3H, d, J = 8 Hz), 1.2 ~ 2.2 (m), 2.27 (1H, m), 3.63 (1H, m), 3.75 (1H, m), 3.95 (1H, br. s), 4.03 (1H, dd, J = 2 and 8 Hz), 5.03 (1H, s), 5.06 (1H, s); MS of the corresponding bismethaneboronate: *m/z* 498 ($M^+ = C_{30}H_{50}O_4B_2$), 481 (M^+–Me), 453 (M^+–C_3H_7), 342, 313, 288, 273, 205, 153, 124. This was identical to the MS of the bismethaneboronate of the natural **8**. (Found: C, 72.11; H, 10.57. Calc for $C_{28}H_{48}O_4 \cdot H_2O$: C, 72.06; H, 10.80%.)

(2R, 3S, 22R, 23E)-22-*Hydroxy*-2,3-*isopropylidenedioxy*-24-*ethyl*-B-*homo*-7-*oxa*-5α-*cholest*-23-*en*-6-*one* **32**

A soln of Et_3Al in toluene (15%, 7.1 ml) was added to a stirred suspension of Cp_2ZrCl_2 (1.15 g) in dry CH_2Cl_2 (10 ml) under Ar at room temp to yield a light orange-colored soln. After 30 min i-PrC ≡ CH (272 mg) was added at room temp. The stirring was continued for 14 h to give a deep orange-colored soln. This was concentrated *in vacuo* (20 mm Hg). Dry n-hexane (10 ml) was added to the residue and the supernatant soln was transferred to another flask under Ar. This was repeated for three times. To the stirred and ice-cooled n-hexane soln was added a soln of n-BuLi in n-hexane (1.4M, 2.86 ml) to give the lithium alanate soln. After stirring for 30 min, a soln of **15** (819 mg) in dry THF (10 ml) was added. The cooling bath was removed and the stirring was continued for 17 h at room temp. The reaction was quenched by the addition of NH_4Cl aq (5 ml) to the stirred and ice-cooled soln. The mixture was extracted with EtOAc. The extract was washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The residual amorphous solid (0.89 g) was chromatographed over SiO_2 (Merck Kieselgel Art 7734, 54 g). Elution with n-hexane–EtOAc (4:1 ~ 3:1) gave 361 mg (35.9%) of **32** as colorless needles from MeOH, m.p. 219–222° (sinter at 217°), $[\alpha]_D^{22}$ +27.7° (c = 0.475, $CHCl_3$); ν_{max} 3500 (s), 1748 (s), 1655 (w), 1210 (s), 1165 (s), 1050 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.72 (3H, s), 0.88 (3H, s), 0.97 (3H, d, J = 6.8 Hz), 1.01 (3H, t, J = 7.4 Hz), 1.02 (6H, d, J = 7.0 Hz), 1.05 ~ 2.13 (m), 1.32 (3H, s), 1.52 (3H, s), 2.06 (2H, q, J = 7.5 Hz), 2.26 (1H, sept, J = 7.0 Hz), 2.32 (1H, dd, J = 3.5 and 16.0 Hz), 3.30 (1H, dd, J = 4.8 and 10.0 Hz), 4.08 (1H, dd, J = 9.5 and 13.0 Hz), 4.13 (1H, dd, J = 3.0 and 13.0 Hz), 4.37 (2H, m), 4.47 (1H, br. d., J = 8.3 Hz), 5.30 (1H, d, J = 8.3 Hz); MS:*m/z* 499 (M^+–OH), 498 (M^+–H_2O), 484 (M^+–OH–Me), 483 (M^+–H_2O–Me), 440, 390, 389, 331, 323, 301. (Found: C, 74.17; H, 10.23. Calc for $C_{32}H_{52}O_5$: C, 74.37; H, 10.14%).

(2R, 3S, 22R, 23S, 24R)-23,24-*Epoxy*-24-*ethyl*-22-*hydroxy*-2, 3-*isopropylidendioxy*-B-*homo*-7-*oxa*-5α-*cholestan*-6-*one* **33**

MCPBA (80%, 72 mg) was added to a stirred soln of **32** (72 mg) in dry CH_2Cl_2 (20 ml). The stirring was continued for 1 h at room temp. The mixture was then washed with N-NaOH (10 ml) and water (10 ml), dried (Na_2SO_4) and concentrated *in vacuo* to give 67 mg (90.5%) of **33** as a gum. A portion of it was further purified by SiO_2 chromatography to give pure **33**, $[\alpha]_D^{22.5}$ +21° (c = 0.55, $CHCl_3$); ν_{max} 3475 (s), 1725 (s), 1250 (s), 1202 (s), 1173 (s), 1150 (s), 1055 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.73 (3H, s), 0.87 (3H, d, J = 7.0 Hz), 0.89 (3H, s), 0.97 (3H, d, J = 7.0 Hz), 1.01 (3H, t, J = 7.4 Hz), 1.05 (3H, d, J = 6.8 Hz), 1.1 ~ 2.1 (m), 1.32 (3H, s), 1.52 (3H, s), 2.32 (1H, dd, J = 3.5 and 15.5 Hz), 2.88 (1H, d, J = 6.0 Hz), 3.29 (1H, dd, J = 4.8 and 10.0 Hz), 3.60 (1H, d, J = 6.0 Hz), 4.10 (2H, m), 4.37 (2H, m); MS:*m/z* 517 (M^+–Me), 417, 403, 343.

(2R, 3S, 22R, 23R, 24(28)E)-24(28)-*Ethylidene*-22,23-*dihydroxy*-2,3-*isopropylidenedioxy*-B-*homo*-7-*oxa*-5α-*cholestan*-6-*one* **34**

$Al(OPr^i)_3$ (30 mg) was added to a soln of **33** (67 mg) in dry toluene (10 ml) and the mixture was stirred and heated under reflux for 1 h. After cooling, the mixture was acidified with 2N-HCl and extracted with $CHCl_3$. The $CHCl_3$ soln was washed with water, dried (Na_2SO_4 + K_2CO_3) and concentrated *in vacuo*. The residue (86 mg) was chromatographed over SiO_2 (Merck Kieselgel Art 7734, 5.2 g). Elution with n-hexane–EtOAc (3:2) yielded **34** (55 mg) in later fractions, $[\alpha]_D^{22}$ +18° (c = 0.55, $CHCl_3$); ν_{max} 3450 (s), 1730 (s), 1660 (sh), 1255 (s), 1202 (s), 1177 (s), 1058 (s), 1040 (s) cm^{-1}; δ ($CDCl_3$) 0.65 (3H, s), 0.86 (3H, s), 1.30 (3H, s), 1.50 (3H, s), 1.68 (3H, d, J = 7 Hz), 0.9 ~ 4.5 (m), 5.44 (1H, q, J = 7 Hz); MS:*m/z* 517 (M^+–Me), 514 (M^+–H_2O), 496 (M^+–$2H_2O$), 419, 405, 403, 361, 343, 331.

(2R, 3S, 22R, 23R, 24(28)E)-24(28)-*Ethylidene*-2,3,22,23-*tetrahydroxy*-B-*homo*-7-*oxa*-5α-*cholestan*-6-*one* (*homodolicholide*) **5**

A soln of **34** (44 mg) in AcOH (2 ml)–H_2O (0.5 ml) was stirred and heated at 50° for 1 h. After cooling, the mixture was neutralized with solid $NaHCO_3$ and extracted with $CHCl_3$ (× 13). The extract was dried (Na_2SO_4) and concentrated *in vacuo* to give 39 mg (96%) of **5**. This was recrystallized from MeCN–H_2O to give needles, m.p. 214–216° (dec) (sinter at 200°) (lit[6] m.p. 227–228°), $[\alpha]_D^{21}$ +35.4° [c = 0.480, $CHCl_3$–MeOH (4:1)] ν_{max} (KBr) 3500 (s), 3425 (s), 1740 (s), 1705 (s), 1650 (w), 1335 (s), 1182 (s) cm^{-1}; δ (400 MHz, $CDCl_3$, measured at 50°) 0.66 (3H, s), 0.91 (3H, s), 0.93 (3H, d, J = 6.4 Hz), 1.07 (3H, d, J = 7.1 Hz), 1.14 (3H, d, J = 7.1 Hz), 1.71 (3H, d, J = 7.1 Hz), 1.16 ~ 2.00 (m), 2.11 (1H, br. s), 2.14 (1H, br. s), 2.18 (1H, br. s), 2.27 (1H, d, J = 4.3 Hz), 2.76 (1H, sept, J = 7.1 Hz), 3.10 (1H, dd, J = 4.5 and 12.0 Hz), 3.67 (1H, ddd, J = 1.0, 3.5 and 8.3 Hz), 3.71 (1H, m), 3.95 (1H, dd, J = 4.3 and 8.3 Hz), 4.01 (1H, br. s), 4.07 (2H, m), 5.51 (1H, q, J = 7.1 Hz); MS (as bismethaneboronate): *m/z* 540.3836 (M^+, Calc for $C_{31}H_{50}O_6B_2$: 540.3793). This was identical to the MS of the bismethaneboronate of the natural **5**. (Found: C, 67.76; H, 9.64. Calc for $C_{29}H_{48}O_6 \cdot H_2O$: C, 68.20; H, 9.87%.)

(2R, 3S, 22R, 23E)-24-*Ethyl*-6,6-*ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-5α-*cholest*-23-*ene* **35**

In the same manner as described for the preparation of **32**, Et_3Al (15% toluene soln, 8 ml) was added to a suspension of Cp_2ZrCl_2 (2 g) in dry CH_2Cl_2 (20 ml) with stirring under Ar at room temp. After 30 min i-PrC ≡ CH (500 mg) was added to this mixture. The stirring was continued for 3 h at room temp to give a deep orange soln. This was concentrated *in vacuo* and the residue was mixed with n-hexane (10 ml). The supernatant soln was transferred to another flask under Ar. This operation was repeated for 3 times. n-BuLi (1.3 M in n-hexane, 6.15 ml) was added to the stirred and ice-cooled soln of the organoalane. The stirring was continued for 30 min. Subsequently a soln of **9** (3.12 g) in dry THF (10 ml) was added dropwise to the soln. The ice-bath was removed and the stirring was continued for 40 h at room temp. The reaction was quenched by the addition of aq NH_4Cl (30 ml), and the mixture was extracted with ether. The ether soln was washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The residue (3.3 g) was chromatographed over SiO_2 (Mallinckrodt CC-7, 200 g). Elution with n-hexane–EtOAc (9:1) gave 1.06 g (27.7%) of **35** as a gum, $[\alpha]_D^{21.5}$ +32.6° (c = 0.685, $CHCl_3$); ν_{max} 3500 (s), 1650 (w), 1190 (s), 1165 (s), 1120 (s), 1080 (s), 1075 (s), 1060 (s), 1045 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.67 (3H, s), 0.83 (3H, s), 0.96 (3H, d, J = 6.4 Hz), 1.00 (3H, t,

J = 7.8 Hz), 1.02 (6H, d, J = 6.8 Hz), 1.27 (3H, s), 1.42 (3H, s), 1.05 ~ 2.19 (m), 2.25 (1H, sept, J = 6.8 Hz), 3.76 (1H, m), 3.93 (3H, m), 4.10 (1H, m), 4.27 (1H, m), 4.48 (1H, dd, J = 1.0 and 7.8 Hz), 5.30 (1H, d, J = 7.8 Hz); MS:*m/z* 529 (M^+–Me), 526 (M^+–H_2O), 511 (M^+–Me–H_2O), 468 (M^+–Me–H_2O–Ac), 401, 359, 329.

(2R, 3S, 22R, 23S, 24S)-23,24-*Epoxy*-24-*ethyl*-6,6-*ethylenedioxy*-22-*hydroxy*-2,3-*isopropylidenedioxy*-5α-*cholestane* **36**

In the same manner as described for the preparation of **33**, **35** (580 mg) and MCPBA (80%, 580 mg) in dry CH_2Cl_2 (70 ml) yielded 502 mg (95.8% based on the consumed **35**; 12.2% of **35** was recovered.) of **36** as a gum, $[\alpha]_D^{21.5}$ +33.1° (c = 0.740, $CHCl_3$); ν_{max} 3490 (s), 1192 (s), 1167 (s), 1080 (s), 1060 (s), 1045 (s), 980 (s), 955 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.68 (3H, s), 0.83 (3H, s), 0.87 (3H, d J = 7.3 Hz), 0.96 (3H, d, J = 6.8 Hz), 1.01 (3H, t, J = 7.5 Hz), 1.04 (3H, d, J = 6.8 Hz), 1.27 (3H, s), 1.42 (3H, s), 1.05 ~ 2.19 (m), 2.88 (1H, d, J = 6.3 Hz), 3.61 (1H, ddd, J = 1.0, 4.0 and 6.3 Hz), 3.76 (1H, m), 3.92 (3H, m), 4.10 (1H, m), 4.27 (1H, m); MS:*m/z* 560 (M^+), 559 (M^+–H), 545 (M^+–Me), 527 (M^+–Me–H_2O), 511, 445, 431, 235.

(2R, 3S, 22R, 23R, 24(28)E) - 6,6 - *Ethylenedioxy* - 24(28) - *ethylidene* - 22,23 - *dihydroxy* - 2,3 - *isopropylidenedioxy*-5α - *cholestane* **37** *and its* (*Z*)- *isomer* **37′**

$Al(OPr^i)_3$ (140 mg) was added to a soln of **36** (300 mg) in dry toluene (30 ml) and the soln was stirred and heated under reflux for 1.5 h. After cooling, the mixture was acidified with 2N-HCl and extracted with $CHCl_3$. The extract was washed with water, dried (Na_2SO_4 and K_2CO_3) and concentrated *in vacuo*. The residual gum was chromatographed over SiO_2 (Mallinckrodt CC-7, 33 g). The order of elution was: (i) pure (*Z*)-isomer (5.3%); (ii) an (*E*, *Z*)-mixture enriched in the (*Z*)-isomer (5.3%); (iii) an (*E*, *Z*)-mixture (14.7%); (iv) an (*E*, *Z*)-mixture enriched in the (*E*)-isomer (14.3%); and (v) the pure (*E*)-isomer (55.0%). The desired (*E*)-isomer **37** showed the following properties: $[\alpha]_D^{21.5}$ +28.9° (c = 0.784, $CHCl_3$); ν_{max} 3400 (s), 1650 (w), 1080 (s), 1060 (s), 1040 (s) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.62 (3H, s), 0.83 (3H, s), 0.92 (3H, d, J = 7.3 Hz), 1.06 (3H, d, J = 6.8 Hz), 1.14 (3H, d, J = 7.3 Hz), 1.27 (3H, s), 1.42 (3H, s), 1.71 (3H, d, J = 6.8 Hz), 1.45 ~ 2.27 (m), 2.76 (1H, sept, J = 7.3 Hz), 3.69 (1H, dd, J = 3.5 and 8.3 Hz), 3.76 (1H, m), 3.92 (3H, m), 3.95 (1H, dd, J = 3.9 and 8.3 Hz), 4.10 (1H, m), 4.27 (1H, m), 5.51 (1H, q, J = 6.8 Hz); MS:*m/z* 560 (M^+), 546 (M^+–CH_2), 542 (M^+–H_2O), 539, 527 (M^+–Me–H_2O), 511, 509, 431, 401, 389, 359, 331, 329. The physical properties of the (*Z*)-isomer **37′** was: δ (400 MHz, $CDCl_3$) 0.69 (3H, s), 0.83 (3H, s), 1.03 (3H, d, J = 6.8 Hz), 1.04 (3H, d, J = 6.8 Hz), 1.07 (3H, d, J = 6.8 Hz), 1.27 (3H, s), 1.41 (3H, s), 1.70 (3H, d, J = 7.3 Hz), 1.1 ~ 2.27 (m), 2.33 (1H, sept, J = 6.8 Hz), 3.73 (1H, dd, J = 1.0 and 9.3 Hz), 3.75 (1H, m), 3.92 (3H, m), 4.10 (1H, br. s), 4.27 (1H, m), 4.49 (1H, d, J = 9.3 Hz), 5.54 (1H, q, J = 7.3 Hz).

(2R, 3S, 22R, 23R, 24(28)E-24(28)-*Ethylidene*-2,3,22,23-*tetrahydroxy*-5α-*cholestan*-6-*one* (*homodolichosterone*) **6**

A soln of **37** (158 mg) in AcOH (4 ml)-H_2O (1 ml) was stirred and heated at 50° for 1 h. After cooling, the mixture was neutralized with Na_2CO_3 and extracted with $CHCl_3$ (× 13). The extract was dried (Na_2SO_4)and concentrated *in vacuo* to give 128 mg (95.6%) of **6**, m.p. 225–226° (sinter at 222°; from $CHCl_3$–MeOH = 9:1) (lit[5] m.p. 204–208°), $[\alpha]_D^{22}$ −9.8° (c = 0.598, $CHCl_3$–MeOH = 9:1); ν_{max} (KBr)3525 (s), 1710 (s), 1650 (w), 1090 (m), 1050 (m), 1045 (m), 1015 (m), 990 (m) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.62 (3H, s), 0.75 (3H, s), 0.93 (3H, d, J = 6.6 Hz), 1.06 (3H, d, J = 7.1 Hz), 1.14 (3H, d, J = 7.1 Hz), 1.71 (3H, d, J = 7.1 Hz), 1.05 ~ 2.33 (m), 2.69 (1H, dd, J = 3.1 and 12.5 Hz), 2.77 (1H, sept, J = 7.1 Hz), 3.69 (1H, ddd, J = 0.5, 3.0 and 8.5 Hz), 3.76 (1H, br. m), 3.96 (1H, dd, J = 4.4 and 8.5 Hz), 4.05 (1H, br. s), 5.51 (1H, q, J = 7.1 Hz); MS of the corresponding bismethaneboronate: *m/z* 524.3824 (M^+, Calc for $C_{31}H_{50}O_5B_2$: 524.3844), 523.3735 (M^+–H). The MS was identical to that of the bismethaneboronate of the natural **6**.

(2R, 3S, 22R, 23R, 24(28)Z)-24(28)-*Ethylidene*-2,3,22,23-*tetrahydroxy*-5α-*cholestan*-6-*one* **6′**.

A soln of **37′** (16 mg) in AcOH (2 ml) and water (0.5 ml) was stirred and heated at 50° for 1 h. Subsequent work-up gave 13 mg of **6′**. This was recrystallized from MeOH to give crystals, m.p. 216–218°. Further recrystallization of this from MeCN–H_2O gave needles, m.p. 233–244° (dec, sinter at 225°), ν_{max} (KBr) 3400 (s), 1705 (s), 1650 (w), 1043 (s)cm^{-1}; δ (400 MHz, $CDCl_3$) 0.61 (3H, s), 0.75 (3H, s), 0.94 (3H, d, J = 6.6 Hz), 1.04 (3H, d, J = 7.0 Hz), 1.07 (3H, d, J = 7.0 Hz), 1.2 ~ 2.05 (m), 1.70 (3H, d, J = 7.0 Hz), 2.00 (1H, br. s), 2.05 (1H, d, J = 2.8 Hz), 2.11 (1H, br. s), 2.25 (1H, d, J = 3.8 Hz), 2.29 (1H, dd, J = 4.5 and 13.0 Hz), 2.33 (1H, sept, J = 7.0 Hz), 2.68 (1H, dd, J = 3.0 and 12.8 Hz), 3.72 ~ 3.80 (2H, m), 4.05 (1H, br. s), 4.49 (1H, dd, J = 2.8 and 9.3 Hz), 5.54 (1H, q, J = 7.0 Hz); MS of the corresponding bismethaneboronate: *m/z* 524.3747 (M^+, Calc for $C_{31}H_{50}O_5B_2$: 524.3844).

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