SYNTHESIS AND BIOLOGICAL ACTIVITY OF 7a-HOMO- AND 7a,7b-DIHOMO-5α-CHOLESTANE ANALOGUES OF BRASSINOLIDE+

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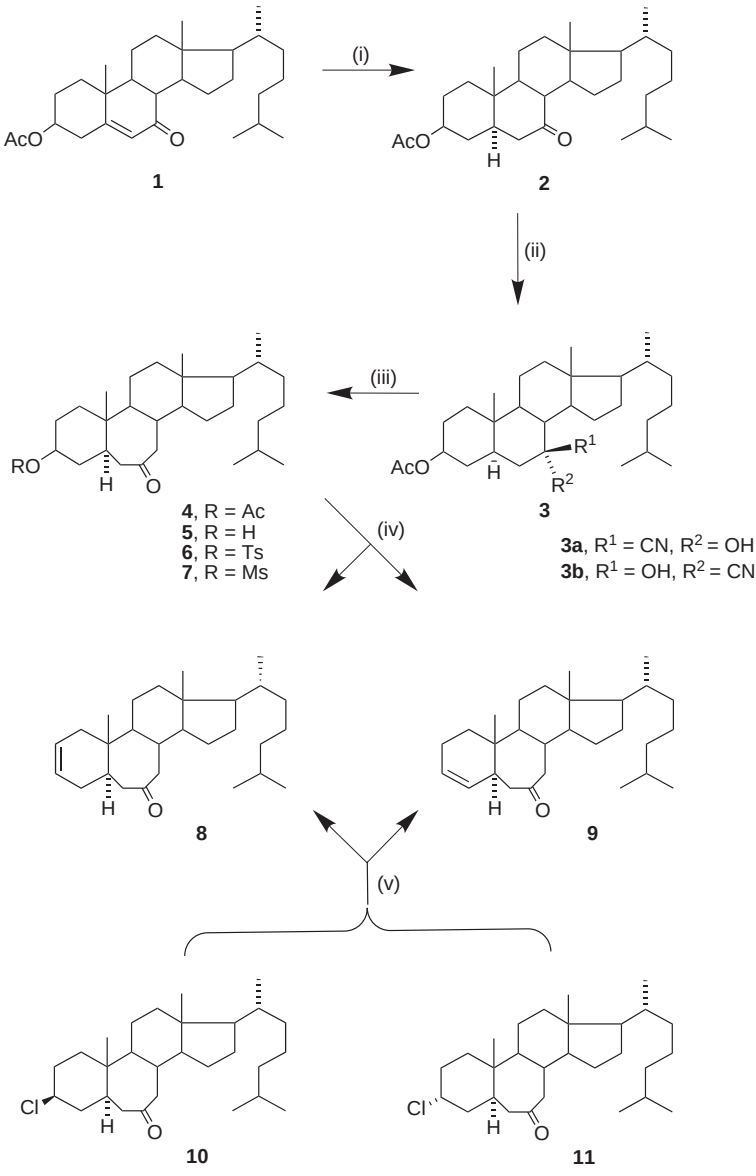
New analogues of castasterone, (20*R*)-2α,3α-dihydroxy-7a-homo-5α-cholestan-7-one (**12**) and (20*R*)-3α,4α-dihydroxy-7a-homo-5α-cholestan-7-one (**14**), and brassinolide, (20*R*)-2α,3α-dihydroxy-7a,7b-dihomo-7a-oxa-5α-cholestan-7-one (**15**), (20*R*)-3α,4α-dihydroxy-7a,7b-dihomo-7a-oxa-5α-cholestan-7-one (**16**) and (20*R*)-7-oxa-7a-homo-5α-cholestan-2α,3α-diol (**24**), were synthesized and their biological and spectral properties studied.

Keywords: Steroids; Brassinosteroids; NMR spectroscopy; Homocholestanes; Dihomocholestanes; Plant growth regulators; Bayer–Villiger oxidation.

Brassinosteroids, a class of potent plant growth regulators, have a promise of potential use in agriculture due to their ability to improve crop yields, overcome environmental stress[2] and being environmentally friendly. Since the chemical structure of brassinolide[3] was established, structurally related compounds have been synthesized and their biological activities evaluated. In this connection, two problems should be addressed. The first is the structure–activity relationships of brassinosteroids, the second is their activity in different bioassays. Having studied[4–8] the structure–activity relationships of brassinosteroids, we now turn our attention to brassinolide analogues of 7a-homo- and 7a,7b-dihomo-5α-cholestanes[9].

To elaborate the synthesis, (20*R*)-7-oxo-cholest-5-en-3β-yl acetate (**1**) was used as a starting material (Scheme 1). This compound was hydrogenated over the Adams catalyst to afford (20*R*)-7-oxo-5α-cholestan-3β-yl acetate (**2**). The reaction of ketone **2** with powdered potassium cyanide and acetic acid provided a mixture of epimeric cyanohydrins **3a** and **3b**; pure isomer

+ Part CDXV in the Series On Steroids; Part CDXIV see ref.[1]



(i) H_2/PtO_2; (ii) KCN; (iii) $NaNO_2$; (iv) collidine, Δ; (v) LiBr

SCHEME 1

3a was obtained on crystallization. The second epimer **3b** was isolated from the mother liquor using preparative thin layer chromatography (TLC). The determination of configuration at C(7) in both epimers was not straightforward due to the absence of a hydrogen atom at C(7). All alternative attempts – (i) *in situ* TAI-acylation method[10], (ii) NOE measurements, and/or (iii) coupling constants *J*(C,H) – required a complete structural assignment of proton and carbon signals. This was achieved for both epimers **3a** and **3b** by the combination of 2D homo- and heteronuclear correlation NMR techniques; the results are given in Table I. The observed induced TAI-acylation shifts (Δδ) of the protons in the vicinity of the acylated OH group supported the configuration assignment shown in Fig. 1a, with some negative Δδ values for the protons in 1,3-diaxial orientation to the OTAC group: this effect can be explained by the reduction of van der Waals effect of the acylated OH group. Further arguments could be obtained from interproton NOEs, where different NOE contacts (characteristic for each epimer) were expected, as shown in Fig. 1b. Unfortunately, the signal of the OH proton was clearly visible only for **3b**. In the ROESY spectrum of **3b**, the characteristic NOE contacts of OH to H-6α, H-6β, H-8, H-15α and H-15β were observed, indicating the structure **3b** (in agreement with the TAI-acylation results). Final evidence of the configuration at C(7) was derived from the observed *J*(C,H) couplings of the C≡N carbon. In accordance with the situation illustrated in Fig. 1c, the C≡N carbon signal appears as a quartet with three small *J*(C,H) ≈ 2 Hz in epimer **3a** (C≡N carbon in *gauche*-orientation to H-6α, H-6β and H-8), while in the second epimer **3b**, this signal shows as a doublet of triplets with two large *J*(C,H) ≈ 9 Hz and one smaller *J*(C,H) ≈ 5 Hz coupling (C≡N carbon in *trans*-orientation to H-6β, H-8 and *gauche*-orientation to H-6α).

Cyanohydrins **3a** and **3b** were converted to (20*R*)-7-oxo-7a-homo-5α-cholestan-3β-yl acetate (**4**), as described in the literature[11]. Hydrolysis of acetate **4** with potassium carbonate in methanol afforded (20*R*)-3β-hydroxy-7a-homo-5α-cholestan-7-one (**5**), which furnished the corresponding sulfonates **6** and **7** on treatment with 4-toluenesulfonyl chloride or methanesulfonyl chloride, respectively. Chlorides **10** and **11** were also obtained from this reaction as side products. On reaction[12] with sym-collidine, both sulfonates **6** and **7** gave a mixture of two isomeric olefins (2,3- and 3,4-olefins) **8** and **9**. The same mixture was also obtained on treatment of chlorides **10** and **11** with lithium bromide. The position of the double bond was evident from the analysis of their ^{1}H NMR spectra as well as from subsequent reactions. These olefins were hydroxylated with osmium tetroxide[5] in the presence of *N*-methylmorpholine *N*-oxide. The

TABLE I
^{1}H and ^{13}C NMR chemical shifts of cyanohydrins **3a** and **3b** in $CDCl_3$

Proton	**3a**	**3b**	Carbon	**3a**	**3b**
1α	1.04	1.08	1	36.30	36.18
1β	1.76	1.77	2	27.21	27.17
2α	1.83	1.87	3	72.94	72.71
2β	1.48	1.47	4	32.70	32.82
3	4.68	4.72	5	36.85	40.39
4α	1.58	1.68	6	41.93	40.77
4β	1.35	1.40	7	69.03	74.39
5	1.67	1.54	8	42.32	44.60
6α	1.80	1.83	9	47.54	50.33
6β	1.90	1.64	10	34.96	36.08
8	1.79	1.64	11	21.16	21.16
9	1.11	0.98	12	39.36	39.10
11α	1.58	1.60	13	43.70	43.78
11β	1.31	1.35	14	50.32	52.42
12α	1.12	1.19	15	24.88	26.07
12β	1.98	2.00	16	28.32	28.58
14	1.40	1.48	17	55.51	54.78
15α	1.92	1.87	18	12.05	12.07
15β	1.62	1.44	19	11.35	12.26
16α	1.33	1.33	20	35.68	35.56
16β	1.91	1.96	21	18.70	18.73
17	1.12	1.15	22	36.05	35.06
18	0.714	0.688	23	23.75	23.72
19	0.856	0.860	24	39.45	39.47
20	1.36	1.37	25	28.00	28.01
21	0.910	0.920	26	22.78	22.79
22	1.33; 1.02	1.35; 1.05	27	22.54	22.55
23	1.33; 1.13	1.34; 1.13	CN	123.42	120.51
24	≈1.13 (2 H)	≈1.12 (2 H)	C=O (Ac)	170.72	170.48
25	1.52	1.53	CH_3	21.37	21.34
26	0.867	0.872			
27	0.863	0.865			
OH	[a]	2.57			
OAc	2.03	2.03			

[a] The position of the OH signal was not determined.

2,3-olefin **8** gave (20*R*)-2α,3α-dihydroxy-7a-homo-5α-cholestan-7-one (**12**), accompanied with a small amount of (20*R*)-2β,3β-dihydroxy-7a-homo-5α-cholestan-7-one (**13**). The 3,4-olefin **9** yielded a single diol, (20*R*)-3α,4α-dihydroxy-7a-homo-5α-cholestan-7-one (**14**) (Scheme 2). Diols **12** and **14** can be considered as cholestane homo-analogues of castasterone.

Baeyer–Villiger oxidation of castasterone analogues **12** and **14** produced cholestane homo-analogues of brassinolide. Ketone **12** was oxidized to yield one product, (20*R*)-2α,3α-dihydroxy-7a-oxa-7a,7b-dihomo-5α-cholestan-7-one (**15**) and, similarly, ketone **14** gave a single product, (20*R*)-3α,4α-dihydroxy-7a-oxa-7a,7b-dihomo-5α-cholestan-7-one (**16**). The structures of dihydroxylactones **15** and **16** were confirmed by ^{1}H and ^{13}C NMR spectros-

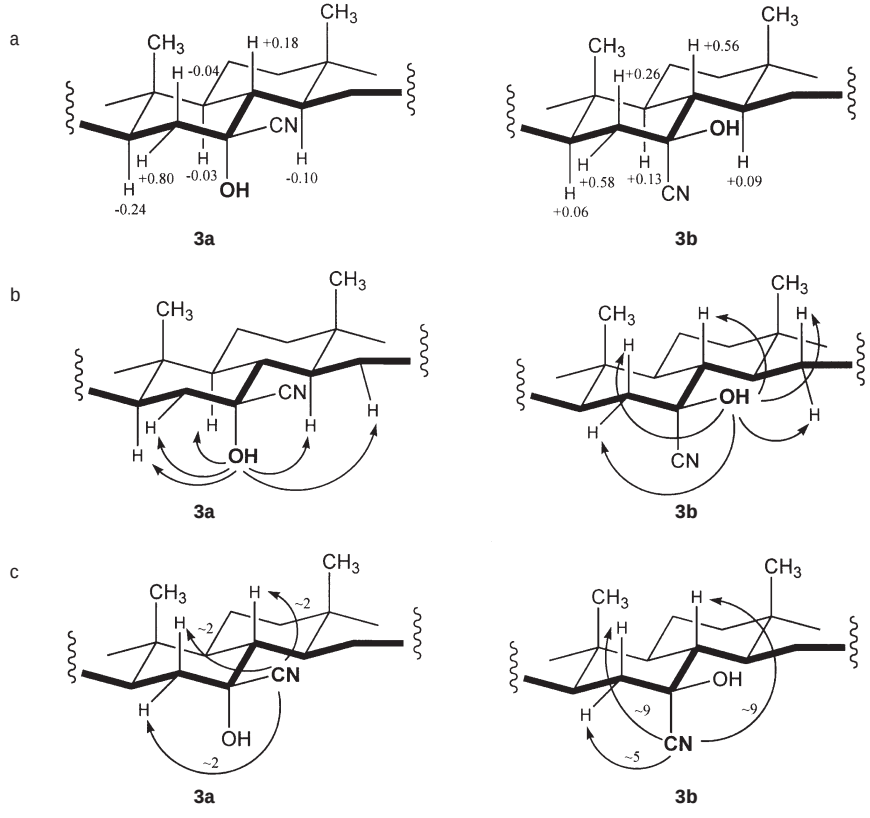
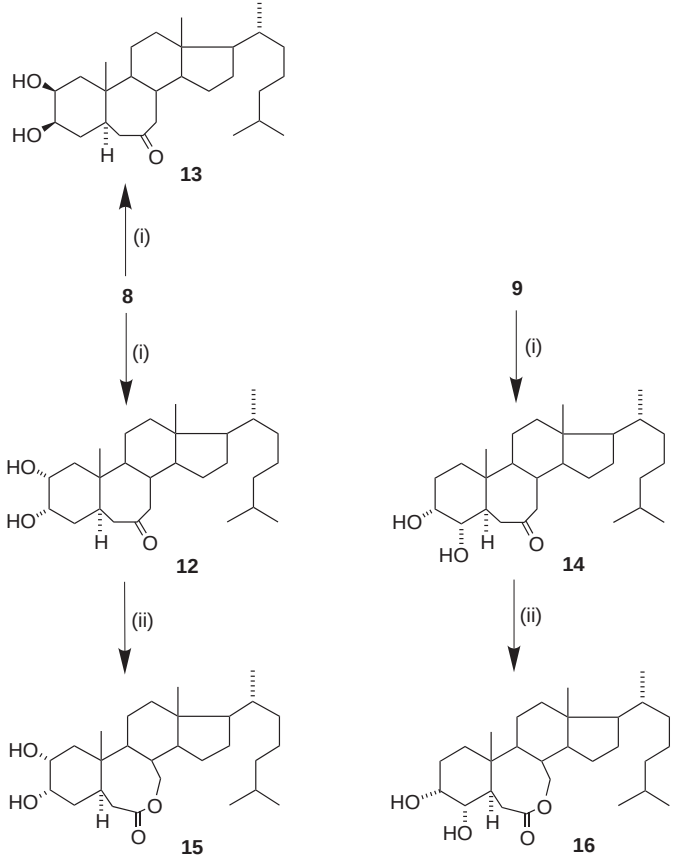


FIG. 1

The induced TAI-acylation shifts of protons (a) in epimers **3a** and **3b**; characteristic NOE contacts (b), expected for compounds **3a** and **3b**; the vicinal *J*(C,H) couplings (c), observable in epimers **3a** and **3b**

copy. A complete structural assignment of proton and carbon signals was again done by the combination of 2D homo- and heteronuclear correlation NMR techniques; the results are given in Table II. The proton coupling constants $J(7a\alpha,8) < 1$, $J(7a\beta,8) \approx 1.5$, $J(5,6\alpha) \approx 2.2$ and $J(5,6\beta) \approx 12.2$ Hz indicate that the eight-membered ring adopts a "chair-boat" form in both compounds (Fig. 2) in accordance with the lowest energy conformation, calculated using molecular dynamics and energy minimization (molecular mechanics MM+ method with HyperChem version 6.01 from Hypercube Inc.). The six-membered ring A assumes the chair form with 2-OH(eq), 3-OH(ax) in compound **15** and 3-OH(ax), 4-OH(eq) in compound **16**.



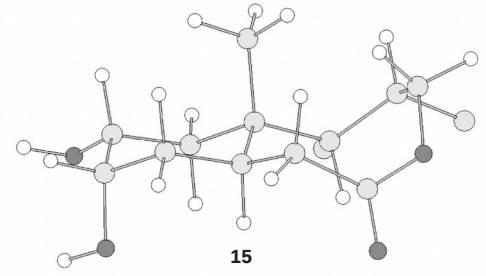
SCHEME 2

TABLE II
^{1}H and ^{13}C NMR chemical shifts of dihydroxylactones **15** and **16** in $CDCl_3$

Proton	**15**	**16**	Carbon	**15**	**16**
1α	≈1.58	1.33	1	41.39	32.00
1β	≈1.58	1.59	2	68.27	27.79
2α	–	1.80	3	68.66	68.79
2β	3.78	1.77	4	38.00	70.97
3	3.96	4.03	5	41.27	49.66
4α	≈1.73	–	6	35.61	28.24
4β	≈1.73	3.34	7	176.19	178.40
5	2.24	2.04	7a	69.56	69.87
6α	2.17	3.21	8	41.30	41.74
6β	2.69	2.50	9	46.64	47.14
7aα	4.53	4.67	10	40.22	40.69
7aβ	4.15	4.19	11	24.92	25.12
8	1.56	1.60	12	40.17	40.34
9	1.15	1.12	13	41.90	41.84
11α	1.81	1.83	14	51.54	51.70
11β	1.35	1.34	15	24.96	24.98
12α	1.13	1.12	16	27.81	27.57
12β	1.94	1.93	17	56.15	56.18
14	1.58	1.58	18	11.72	11.70
15α	≈1.55	≈1.55	19	13.08	13.04
15β	≈1.55	≈1.55	20	35.84	35.85
16α	1.27	1.25	21	18.44	18.44
16β	1.81	1.75	22	35.89	35.89
17	1.12	1.14	23	23.70	23.70
18	0.673	0.716	24	39.47	39.46
19	1.008	0.999	25	27.98	27.98
20	1.35	1.35	26	22.79	22.78
21	0.885	0.874	27	22.55	22.55
22	1.33; 1.00	1.33; 1.00			
23	1.33; 1.13	1.33; 1.13			
24	≈1.14 (2 H)	≈1.13 (2 H)			
25	1.52	1.52			
26	0.866	0.866			
27	0.860	0.860			

The synthesis of analogues without any oxygen function in ring B was carried out from acetate **4**, which was transformed into (20*R*)-7a-homo-5α-cholestan-3β-ol (**17**) by the Kishner–Wolff reduction[11]. We attempted to obtain two diols, (20*R*)-7a-homo-5α-cholestan-2α,3α-diol (**21**) and (20*R*)-7a-homo-5α-cholestan-3α,4α-diol (**22**), in a similar way, as described above for the synthesis of diols **12** and **14**. However, we encountered a problem with the separation of olefins **19** and **20**, as their polarities were practically identical. Therefore, we hydroxylated the mixture, and obtained a mixture of two diols, **21** and **22** (Scheme 3). Their structures were confirmed by independent synthesis from ketones **12** and **14**. The Kishner–Wolff reduction converted ketone **12** to diol **21** and ketone **14** to diol **22**. The last compound of this series, (20*R*)-7a-homo-7-oxa-5α-cholestan-2α,3α-diol (**24**) was obtained on reduction[13] of the previously synthesized[14] lactone **23** with sodium borohydride in the presence of boron trifluoride etherate in a good yield (Scheme 4). This method seems to be useful for the preparation of oxa-steroids.

The above synthesis yielded products, which were employed in our screening project. Their brassinosteroid activities were determined by the modified bean second internode bioassay[15]. Among all the substances



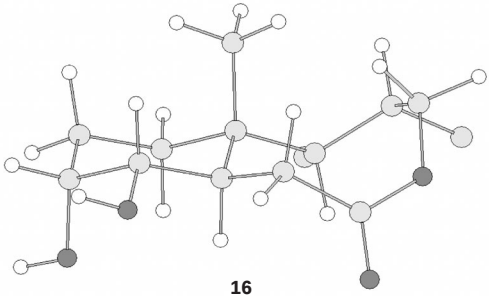
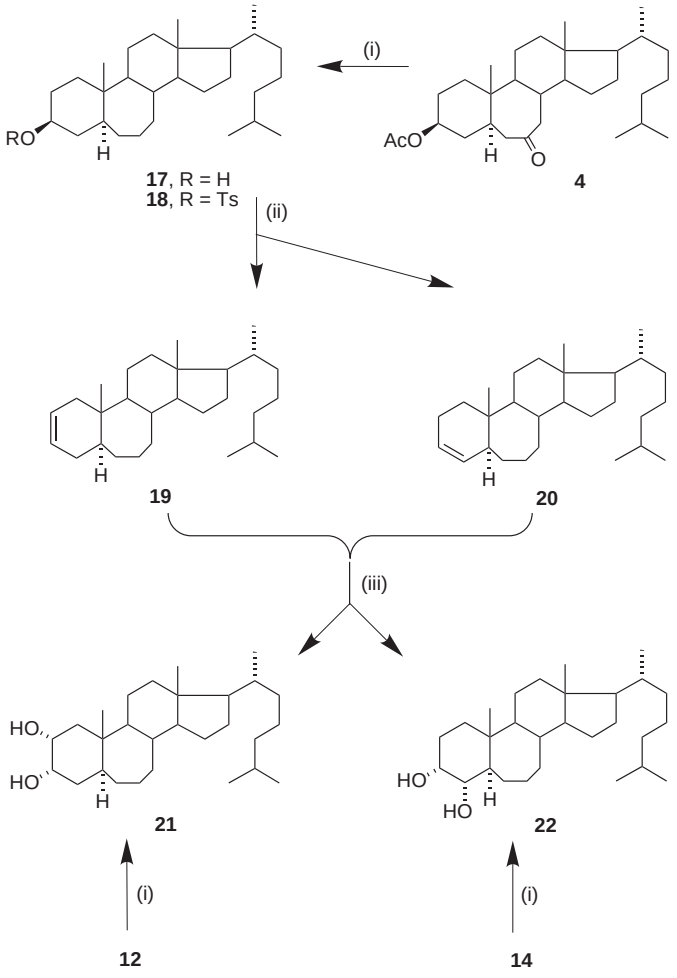
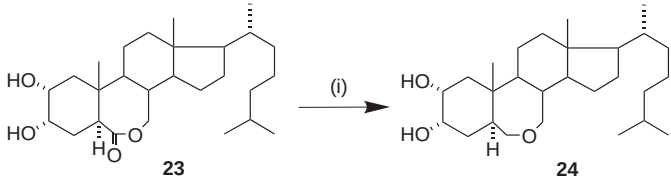


FIG. 2
The conformations of rings A and B in compounds **15** and **16**



(i) $N_2H_2 \cdot H_2O$, KOH; (ii) collidine, Δ; (iii) OsO_4

SCHEME 3



(i) $BF_3 \cdot Et_2O$

SCHEME 4

tested, the highest biological activity was displayed by compounds **14**, **16** and **22**, *i.e.* by compounds, which have a 3α,4α diol moiety and a carbonyl in position 7a. However, their activities were lower in comparison with that of 24-epibrassinolide [(22*R*,23*R*,24*R*)-2α,3α,22,23-tetrahydroxy-24-methyl-7-oxa-7a-homo-5α-cholestan-6-one] (Table III).

EXPERIMENTAL

The melting points were determined on a Kofler block. Optical rotations were measured at 25 °C in chloroform (unless otherwise stated) and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded on a Bruker IFS 88 spectrometer in tetrachloromethane (unless otherwise stated), the wavenumbers are given in cm^{-1}. ^{1}H NMR spectra were taken in deuteriochloroform on a Varian UNITY-200 (at 200 MHz) instrument in deuteriochloroform solutions with tetramethylsilane as an internal reference unless otherwise stated. Detailed NMR structure analyses of cyanohydrins **3a**, **3b** and dihydroxylactones **15**, **16** were done on a Varian UNITY-500 (^{1}H at 500 MHz; ^{13}C at 125.7 MHz). Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) and multiplet half-widths ($W_{1/2}$) in Hz. All values were obtained by first-order analysis. Mass spectra were obtained with a ZAB-EG spectrometer at 70 eV. The identity of prepared samples was checked by melting points, thin-layer chromatography (TLC) on silica gel G (ICN Biochemicals, detection by spraying with sulfuric acid and heating), IR and ^{1}H NMR spectra. Preparative TLC was carried out on 200 × 200 mm

TABLE III
Bean second internode bioassay

Compound	Lengthening of the second internode, mm[a]	The amount applied, mol[b]
24-epiBR[c]	32.3	10^{-10}
12	5.6	10^{-9}
14	21.8	10^{-9}
14	19.4	10^{-10}
15	–5.4	10^{-10}
16	17.2	10^{-10}
21	8.3	10^{-11}
22	18.0	10^{-10}
24	8.8	10^{-9}

[a] The lengthening of the second internode means its lengthening as compared to that of the reference plant for the applied amount given. [b] The applied amount means the amount causing the maximum lengthening of the second internode (all compounds were applied in the amounts from 1×10^{-12} to 1×10^{-7} mol per one plant). [c] 24-epiBR means 24-epibrassinolide [(22*R*,23*R*,24*R*)-2α,3α,22,23-tetrahydroxy-24-methyl-7-oxa-7a-homo-5α-cholestan-6-one].

plates coated with 0.7 mm layer of silica gel Woelm DC, detection by spraying the plates with 0.2% methanolic morine solution, by UV detection or by spraying with sulfuric acid and heating the side strips of the plates. For column chromatography, neutral silica gel 60–120 μm was used (Service Laboratories of the Institute).

"Worked up as usual" means extraction with a given organic solvent, washing the organic phase with 5% hydrochloric acid, water, saturated aqueous potassium hydrogen carbonate, water, drying over anhydrous sodium sulfate, filtering and evaporating the solvent to dryness under reduced pressure.

Light petroleum refers to a fraction boiling at 40–65 °C.

Bean Second Internode Bioassay

Bean seeds (*Phaseolus vulgaris* L., cv. Pinto) were germinated for two days. Selected germinated seeds were planted into pots containing perlite and modified Hoagland's solution (half concentration, pH 5.7). The pots were placed in light-controlled cultivation room (25 to 27 °C, light: 48 W/m^2, light/dark period: 16 h/8 h). Groups of eight 7-day-old seedlings with 1–2 mm long second internodes were treated with different amounts of the tested compounds in lanoline (2 ml). The control plants were treated with lanoline. The measurements were taken after 5 days. The difference in the length of the second internodes of the treated and control plants was used as a measure of the activity.

(20*R*)-7-Oxo-5α-cholestan-3β-yl Acetate (**2**)

(20*R*)-7-Oxo-cholest-5-en-3β-yl acetate (**1**; 1 g, 2.26 mmol) was dissolved in acetic acid (30 ml). The Adams catalyst (50 mg, 0.22 mmol) was added and the mixture was hydrogenated. The reaction mixture was poured into water and worked up as usual. The consumed amount of hydrogen (*ca* 110 ml, theoretical amount about 60 ml) and TLC indicated that the 7-one group was also hydrogenated. The evaporated residue was therefore dissolved in acetone (20 ml) and treated with the Jones reagent until a permanent orange colour persisted. After 10 min, the excess reagent was destroyed by the addition of methanol. After 5 min and filtration, the solution was diluted with ether and worked up as usual. Evaporation of the solvent *in vacuo* afforded 1 g of a solid residue, which was chromatographed on silica gel (100 g); elution with light petroleum–ether (7:3) gave 900 mg (2.02 mmol; 89%) of pure ketone **2**. Analytical sample was crystallized from methanol to afford: m.p. 146–149 °C, $[\alpha]_D$ –46 (*c* 1.040), giving identical physical constants, as described in the literature[11]. IR: 1737, 1027 (OAc); 1712 (C^7=O); 1380 (Me, i-Pr); 1367 (i-Pr). ^{1}H NMR: 0.658 s, 3 H (3 × H-18); 0.858 d, 3 H, *J* = 6.5 and 0.862 d, 3 H, *J* = 6.5 (3 × H-26 and 3 × H-27); 0.905 d, 3 H, *J* = 6.7 (3 × H-21); 1.097 s, 3 H (3 × H-19); 2.025 s, 3 H (3α-OAc); 4.66 m, 1 H, $W_{1/2}$ = 19.0 (H-3α). EI MS, *m/z*: 444 (M^+), 429 ($M^+ - CH_3$), 384 (M^+ – AcOH). For $C_{29}H_{48}O_3$ (444.7) calculated: 78.33% C, 10.88% H; found: 78.30% C, 10.79% H.

(20*R*)-7β-Cyano-7α-hydroxy-5α-cholestan-3β-yl Acetate (**3a**)

Ketone **2** (550 mg, 1.24 mmol) was dissolved in dioxane (5 ml) and ethanol (5 ml) and the solution was cooled to 0 °C. The stirred solution was treated with powdered potassium cyanide (730 mg, 11.21 mmol), and acetic acid was then added dropwise over 30 min under constant stirring at the same temperature. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for another 2 h. It was then poured into ice–water mixture and,

after standing for 1 h, the precipitate was separated by suction. The product was dissolved in ether, the ethereal solution washed with a sodium hydrogen carbonate solution, water, dried, and evaporated. The solid residue (510 mg) was chromatographed on silica gel (50 g); elution with light petroleum–ether (8:2) gave 290 mg (0.62 mmol; 50%) of a product, which contained two isomers. This mixture was crystallized from ethyl acetate to afford practically one product, the more polar one of the two isomers. Another crystallization of his material from ethyl acetate afforded an analytical sample of cyanohydrin **3a**: m.p. 164–167 °C, in accordance with the literature[11]. IR: 3602, 3447, 1052 (OH); 2231 (C≡N); 1723 (C=O); 1254 (C–O); 1027 (OAc); 1382 (Me, i-Pr); 1366 (i-Pr). ^{1}H and ^{13}C NMR data, see Table I. EI MS, *m/z*: 471 (M^+), 444 (M^+ – HCN), 426 (444 – H_2O), 384 (444 – AcOH). For $C_{30}H_{49}NO_3$ (471.7) calculated: 76.39% C, 10.71% H, 2.97% N; found: 75.95% C, 10.71% H, 2.71% N.

(20*R*)-7α-Cyano-7β-hydroxy-5α-cholestan-3β-yl Acetate (**3b**)

The mixture of the two isomers (50 mg), obtained in the previous experiment, was separated by preparative TLC on 4 plates in light petroleum–ether (8:2) to afford isomer **3a** (40 mg) and isomer **3b** (10 mg), which was more lipophilic then the former and much more unstable (disappearance on TLC in several hours). ^{1}H and ^{13}C NMR data, see Table I.

(20*R*)-7-Oxo-7a-homo-5α-cholestan-3β-yl Acetate (**4**)

A mixture of cyanohydrins **3a** and **3b** from the above experiments (5 g, 10.60 mmol) was dissolved in acetic acid (200 ml), the Adams catalyst was added (750 mg) and the resultant mixture was hydrogenated until the theoretical amount of hydrogen had been taken up (477 ml). The catalyst was filtered off and the filtrate was treated with water (20 ml). A solution of sodium nitrite (10 g) in water (30 ml) was then added dropwise with stirring at 0 °C. The reaction mixture was then stirred at room temperature for additional 2 h, treated with water (100 ml) and, after standing overnight, the precipitate was isolated by suction. The product was dissolved in ether, the ethereal solution washed with a sodium hydrogen carbonate solution, water, dried, and evaporated. The semicrystalline residue (3.4 g) was chromatographed on silica gel (250 g); elution with toluene and toluene–ether (99:1) gave 1.1 g (2.40 mmol; 23%) of the 7a-homoketone **4**. Analytical sample was crystallized from methanol: m.p. 119–120 °C, $[\alpha]_D$ –34 (*c* 0.684), giving identical physical constants, as described in the literature[11]. IR: 1735, 1243, 1025 (OAc); 1705 (cycloheptanone); 1383, 1365 (i-Pr); 1373 (Me). ^{1}H NMR: 0.662 s, 3 H (3 × H-18); 0.847 2d, 6 H, *J* = 8.2 (3 × H-26 and 3 × H-27); 0.879 s, 3 H (3 × H-19); 0.908 d, 3 H, *J* = 5.8 (3 × H-21); 2.030 s, 3 H (3α-OAc); 4.63 m, 1 H, $W_{1/2}$ = 23.1 (H-3α). EI MS, *m/z*: 458 (M^+), 440 (M^+ – H_2O), 398 (M^+ – AcOH), 380 (440 – AcOH and 398 – H_2O). For $C_{30}H_{50}O_3$ (458.7) calculated: 78.55% C, 10.99% H; found: 76.78% C, 10.89% H.

(20*R*)-3β-Hydroxy-7a-homo-5α-cholestan-7-one (**5**)

A solution of acetate **4** (1 g, 2.18 mmol) in methanol (100 ml) was treated with a solution of potassium carbonate (1 g) in water (10 ml). After standing overnight at room temperature, methanol was removed under reduced pressure, the residue was dissolved in ether and the ethereal solution worked up as usual. The crude product (90 mg, 2.16 mmol; 99%) was crystallized from acetone–water (10:1): m.p. 116–118 °C, $[\alpha]_D$ –31 (*c* 0.518), giving identical physical constants, as described in the literature[11]. IR: 3622, 3448, 1038 (OH); 1704 (C=O);

1384, 1366 (i-Pr); 1378 (Me). ^{1}H NMR: 0.661 s, 3 H (3 × H-18); 0.801 s, 3 H (3 × H-19); 0.858 d, 3H, *J* = 6.7 and 0.861 d, 3 H, *J* = 6.7 (3 × H-26 and 3 × H-27); 0.891 d, 3 H, *J* = 6.2 (3 × H-21); 3.56 m, 1 H, $W_{1/2}$ = 29.4 (H-3α). FAB MS, *m/z*: 417 (M^+ + H), 399 (417 – H_2O). For $C_{27}H_{48}O_2$ (416.7) calculated: 80.71% C, 11.62% H; found: 80.18% C, 11.14% H.

(20*R*)-7-Oxo-7a-homo-5α-cholestan-3β-yl Toluenesulfonate (**6**)

A solution of alcohol **5** (800 mg, 2.16 mmol) in pyridine (10 ml) was treated with 4-toluenesulfonyl chloride (800 mg) and the mixture was allowed to stand at room temperature overnight. The reaction mixture was decomposed with ice and water, the product taken up into ether and the solution worked up as usual. The evaporated residue was dissolved in a very small amount of chloroform and ether was added to precipitate product **6** (600 mg, 1.05 mmol; 49%). Analytical sample was crystallized from acetone: m.p. 124–126 °C, $[\alpha]_D$ –32 (*c* 1.140). IR: 1705 (C=O); 1371, 1178, 557, 575 (SO_2); 1600, 1496 (aromatic). ^{1}H NMR: 0.641 s, 3 H (3 × H-18); 0.769 s, 3 H (3 × H-19); 0.858 d, 6 H, *J* = 6.4 (3 × H-26 and 3 × H-27); 0.885 d, 3 H, *J* = 4.2 (3 × H-21); 2.452 s, 3 H (CH_3 (Tos)); 4.38 m, 1 H, $W_{1/2}$ = 24.1 (H-3α); 7.33 m, 2 H and 7.79 m, 2 H (C_6H_4 (Tos)). EI MS, *m/z*: 398 (M^+ – tosylate). For $C_{35}H_{54}O_4S$ (570.9) calculated: 73.64% C, 9.33% H, 5.62% S; found: 73.84% C, 9.77% H, 5.31% S.

(20*R*)-7-Oxo-7a-homo-5α-cholestan-3β-yl Methanesulfonate (**7**)

A solution of alcohol **5** (1 g, 2.40 mmol) in pyridine (15 ml) was treated with methanesulfonyl chloride (1.5 ml) and the solution was allowed to stand for 2 h. The reaction mixture was decomposed with ice and water, the product taken up into ether and the ethereal solution worked up as usual. The evaporated residue was dissolved in 2 ml of chloroform and ether was added to precipitate crystalline product **7** (1.1 g, 2.22 mmol; 93%). Analytical sample was crystallized from methanol: m.p. 143–144 °C, $[\alpha]_D$ –30 (*c* 0.900), giving identical physical constants, as described in the literature[12]. IR: 1705 (C=O); 1367, 1344, 1176, 938, 598, 528 (SO_2). ^{1}H NMR: 0.661 s, 3 H (3 × H-18); 0.816 s, 3 H (3 × H-19); 0.861 d, 6 H, *J* = 6.1 (3 × H-26 and 3 × H-27); 0.908 d, 3 H, *J* = 6.5 (3 × H-21); 3.010 s, 3 H (CH_3 (Mes)); 4.68 m, 1 H, $W_{1/2}$ = 24.5 (H-3α). EI MS, *m/z*: 494 (M^+), 398 (M^+ – mesylate), 383 (398 – CH_3). For $C_{29}H_{50}O_4S$ (494.8) calculated: 70.40% C, 10.19% H, 6.48% S; found: 69.20% C, 10.13% H, 6.70% S.

(20*R*)-7a-Homo-5α-cholest-2-en-7-one (**8**)

a) From (20R)-7-oxo-7a-homo-5α-cholestan-3β-yl methanesulfonate (**7**): Mesylate **7** was heated to reflux (700 mg, 1.41 mmol) in sym-collidine (15 ml) under nitrogen atmosphere for 2 h. Sym-collidine was then distilled off under reduced pressure, the residue treated with water, and the product taken up into ether. Usual work-up and evaporation left 650 mg of a product, which was chromatographed on silica gel (100 g) in heptane–ether (19:1). The fractions with a more polar compound were collected, and the solvent evaporated to afford 142 mg (0.36 mmol; 25%) of compound **8**, which was crystallized from methanol: m.p. 108–109 °C, $[\alpha]_D$ –40 (*c* 0.920), giving identical physical constants, as described in the literature[12]. IR: 3023 (=CH); 1704 (C=O); 1666 (C=C); 1384 (i-Pr, Me); 1367 (i-Pr). ^{1}H NMR: 0.683 s, 3 H (3 × H-18); 0.861 d, 3 H and 0.865 d, 3 H, *J* = 6.1 (3 × H-26 and 3 × H-27); 0.907 s, 3 H (3 ×

H-19); 0.910 d, 3 H, *J* = 6.4 (3 × H-21); 5.58 m, 2 H (H-2 and H-3). EI MS, *m/z*: 398 (M^+), 383 ($M^+ - CH_3$). For $C_{28}H_{46}O$ (398.7) calculated: 84.36% C, 11.63% H; found: 83.34% C, 11.64% H.

b) From (20R)-7-oxo-7a-homo-5α-cholestan-3β-yl toluenesulfonate (**6**): Tosylate **6** (800 mg, 1.40 mmol) in sym-collidine (15 ml) was treated in the same way, as given above under *a*). Usual work-up and evaporation left 640 mg of a product, which was chromatographed on a silica gel (100 g) in heptane–ether (19:1). The fractions with a more polar component afforded 140 mg (0.35 mmol; 25%) of olefin **8**, identical in all respects with the compound obtained above under *a*).

c) From (20R)-3β-chloro-7a-homo-5α-cholestan-7-one (**10**) *and (20R)-3α-chloro-7a-homo-5α-cholestan-7-one* (**11**): Lithium bromide (65 mg, 0.75 mmol) and pyridinium 4-toluenesulfonate (5.5 mg, 0.028 mmol) were added to a mixture of chlorides **10** and **11** (60 mg, 0.14 mmol) in *N*,*N*-dimethylacetamide (2 ml) and the mixture was heated at 160 °C for 2.5 h. After cooling, the reaction mixture was poured into water and extracted with ether. The ethereal extract was worked up in the usual manner to give 52 mg (0.13 mmol; 92%) of a mixture of olefins **8** and **9**. Preparative TLC on 4 plates in light petroleum–ether (7:3) afforded 15 mg (0.04 mmol; 29%) of isomer **8**, identical in all respects with the compound obtained above under *a*).

(20*R*)-7a-Homo-5α-cholest-3-en-7-one (**9**)

a) From (20R)-7-oxo-7a-homo-5α-cholestan-3β-yl methanesulfonate (**7**): The layers with a more lipophilic compound from the preparation of **8** under *a*) afforded 380 mg (0.80 mmol; 57%) of olefin **9**, which was crystallized from methanol: m.p. 70–72 °C, $[\alpha]_D$ +27 (*c* 0.810), giving identical physical constants, as described in the literature[12]. IR: 3028 (=CH); 1704 (C=O); 1384 (i-Pr, Me); 1367 (i-Pr). ^{1}H NMR: 0.665 s, 3 H and 0.676 s, 3 H (3 × H-18 and 3 × H-19); 0.861 d, 3 H and 0.865 d, 3 H, *J* = 6.4 (3 × H-26 and 3 × H-27); 0.896 d, 3 H, *J* = 6.4 (3 × H-21); 5.20 dd, 1 H, *J*(4,3) = 8.7, *J*(4,5α) = 1.2 (H-4); 5.73 m, 1 H, $W_{1/2}$ = 16.2 (H-3). EI MS, *m/z*: 398 (M^+), 383 ($M - CH_3$). For $C_{28}H_{46}O$ (398.7) calculated: 84.36% C, 11.63% H; found: 83.99% C, 11.71% H.

b) From (20R)-7-oxo-7a-homo-5α-cholestan-3β-yl toluenesulfonate (**6**): Work-up of the fractions with a more lipophilic component from the preparation of **8** under *b*) afforded 355 mg (0.89 mmol; 64%) of olefin **9**, identical in all respects with the compound obtained above under *a*).

c) From (20R)-3β-chloro-7a-homo-5α-cholestan-7-one (**10**) *and (20R)-3α-chloro-7a-homo-5α-cholestan-7-one* (**11**): Work-up of the preparative TLC zones with a more lipophilic compound from the synthesis of **8** under *c*) afforded 34 mg (0.08 mmol; 57%) of isomer **9**, identical in all respects with the compound obtained above under *a*).

(20*R*)-3β-Chloro-7a-homo-5α-cholestan-7-one (**10**)

Work-up of the mother liquor (100 mg) from the crystallization of the crude residue from the synthesis of tosylate **6** afforded, in addition to a further amount of tosylate **6**, a mixture of two chloro compounds **10** and **11**, which were separated by preparative TLC on 4 plates in light petroleum–ether (7:3). Work-up of the layers with a more lipophilic compound afforded 39 mg (0.09 mmol; 6%) of chloride **10**. ^{1}H NMR: 0.656 s, 3 H (3 × H-18); 0.823 s, 3 H (3 × H-19); 0.857 d, 6 H, *J* = 6.4 (3 × H-26 and 3 × H-27); 0.877 d, 3 H, *J* = 6.4 (3 × H-21); 3.79 m, 1 H, $W_{1/2}$ = 24.4 (H-3α). EI MS, *m/z*: 434 and 436 (M^+), 398 ($M^+ - HCl$). For

$C_{28}H_{47}ClO$ (435.1) calculated: 77.29% C, 10.89% H, 8.15% Cl; found: 77.01% C, 10.71% H, 7.73% Cl.

(20*R*)-3α-Chloro-7a-homo-5α-cholestan-7-one (**11**)

Work-up of the TLC plates from the above experiment with a more polar compound afforded 27 mg (0.06 mmol; 4%) of chloride **11**. ^{1}H NMR: 0.665 s, 3 H (3 × H-18); 0.778 s, 3 H (3 × H-19); 0.863 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.896 d, 3 H, J = 6.7 (3 × H-21); 4.46 m, 1 H, $W_{1/2}$ = 7.3 (H-3β). EI MS, *m/z*: 434 and 436 (M^+), 398 (M^+ – HCl). For $C_{28}H_{47}ClO$ (435.1) calculated: 77.29% C, 10.89% H, 8.15% Cl; found: 77.12% C, 10.76% H, 7.74% Cl.

(20*R*)-2α,3α-Dihydroxy-7a-homo-5α-cholestan-7-one (**12**)

A solution of osmium tetroxide (12 mg, 0.05 mmol) in 2-methylpropan-2-ol (0.12 ml) was added to a solution of alkene **8** (234 mg, 0.59 mmol) in acetone (12 ml). *N*-Methylmorpholine *N*-oxide (234 mg, 2.00 mmol) was added and the mixture was stirred under nitrogen for 5 h. A solution of sodium sulfite (5 ml; 10%) was then added and the mixture was stirred for 30 min, poured into water, extracted with chloroform and the extract worked up as usual. The residue (212 mg) was purified by preparative TLC on 12 plates in $CHCl_3$–propan-2-ol–diethyl ether (14:1:5). Work-up of the zones with a more polar compound afforded 106 mg (0.25 mmol; 42%) of (20*R*)-2α,3α-dihydroxy-7a-homo-5α-cholestan-7-one (**12**): m.p. 142–144 °C, $[\alpha]_D$ –27 (*c* 0.300). IR: 3387, 1079, 1047, 1021 (OH); 1702 (C=O); 1383, 1367 (i-Pr); 1378 (Me). ^{1}H NMR: 0.662 s, 3 H (3 × H-18); 0.806 s, 3 H (3 × H-19); 0.865 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.894 d, 3 H, J = 6.4 (3 × H-21); 3.66 m, 1 H, $W_{1/2}$ = 21.5 (H-2β); 3.93 m, 1 H, $W_{1/2}$ = 7.4 (H-3β). FAB MS, *m/z*: 433 (M^+ + H), 415 (433 – H_2O). For $C_{28}H_{48}O_3$ (432.7) calculated: 77.33% C, 11.18% H; found: 76.99% C, 10.81% H.

(20*R*)-2β,3β-Dihydroxy-7a-homo-5α-cholestan-7-one (**13**)

Work-up of the zones of the preparative TLC plates from the above experiment with a more lipophilic compound afforded 22 mg (0.05 mmol; 9%) of 2β,3β-diol **13**: m.p. 154–155 °C, $[\alpha]_D$ –19 (*c* 0.057). IR: 3617, 3573, 3457, 1038, 1053 (OH); 1694 (C=O); 1384, 1367 (Me, i-Pr). ^{1}H NMR: 0.663 s, 3 H (3 × H-18); 0.859 d, 3 H and 0.863 d, 3 H, J = 6.6 (3 × H-26 and 3 × H-27); 0.893 d, 3 H, J = 6.2 (3 × H-21); 0.907 s, 3 H (3 × H-19); 3.64 m, 1 H, $W_{1/2}$ = 19.6 (H-2β); 4.00 m, 1 H, $W_{1/2}$ = 8.5 (H-3β). EI MS, *m/z*: 432 (M^+), 414 (433 – H_2O). For $C_{28}H_{48}O_3$ (432.7) calculated: 77.33% C, 11.18% H; found: 76.96% C, 11.25% H.

(20*R*)-3α,4α-Dihydroxy-7a-homo-5α-cholestan-7-one (**14**)

A solution of osmium tetroxide (15 mg, 0.06 mmol) in 2-methylpropan-2-ol (0.15 ml) was added to a solution of alkene **9** (305 mg, 0.71 mmol) in acetone (15 ml). *N*-Methylmorpholine *N*-oxide (305 mg, 2.60 mmol) was then added and the mixture was stirred under nitrogen for 5 h. A solution of sodium sulfite (5 ml; 10%) was added and the mixture was stirred for 30 min, poured into water, extracted with chloroform and the extract worked up as usual. The crystalline residue (290 mg, 0.67 mmol; 94%) contained only 3α,4α-isomer **14** (TLC). Analytical sample was crystallized from methanol: m.p. 146–148 °C, $[\alpha]_D$ –52 (*c* 0.283). IR: 3399, 1027, 1017 (OH); 1700 (C=O); 1383, 1367 (i-Pr); 1377 (Me). ^{1}H NMR:

0.659 s, 3 H (3 × H-18); 0.799 s, 3 H (3 × H-19); 0.860 d, 6 H, *J* = 6.5 (3 × H-26 and 3 × H-27); 0.888 d, 3 H, *J* = 6.1 (3 × H-21); 3.00 dd, 1 H, *J*(5α,4β) = 3.0, *J*(5α,6α) = 17.9 (H-5α); 3.29 dd, 1 H, *J*(5α,4β) = 3.0, *J*(5α,6α) = 10.1 (H-4β); 3.95 m, 1 H, $W_{1/2}$ = 8.0 (H-3β). EI MS, *m/z*: 432 (M^+), 414 (432 – H_2O). For $C_{28}H_{48}O_3$ (432.7) calculated: 77.33% C, 11.18% H; found: 77.01% C, 10.96% H.

(20*R*)-2α,3α-Dihydroxy-7a-oxa-7a,7b-dihomo-5α-cholestan-7-one (**15**)

A solution of trifluoroperoxyacetic acid, freshly prepared from trifluoroacetic anhydride (650 mg, 3.10 mmol) and hydrogen peroxide (30%; 110 mg) in dichloromethane (4 ml), was added to a solution of diol **12** (200 mg, 0.46 mmol) in dichloromethane (10 ml). After standing at room temperature for 2 h, the reaction mixture was poured into water and taken up in chloroform. The chloroform extract was washed with water, saturated solution of potassium hydrogen carbonate, water, and dried over anhydrous sodium sulfate. Removal of the solvent gave 180 mg of a residue. Purification by preparative TLC on 12 plates in $CHCl_3$–propan-2-ol–diethyl ether (14:1:5) afforded 87 mg (0.19 mmol; 42%) of product **15**: m.p. 230–203 °C, $[\alpha]_D$ –11 (*c* 0.700). IR: 3556, 3515, 3462, 3438, 1042 (OH); 1740, 1711 (C=O); 1385, 1366 (i-Pr, Me). ^1H and ^{13}C NMR data, see Table II. FAB MS, *m/z*: 471 (M^+ + Na), 449 (M^+ + H), 431 (449 – H_2O), 413 (431 – CO). For $C_{28}H_{48}O_4$ (448.7) calculated: 74.95% C, 10.78% H; found: 73.75% C, 10.66% H.

(20*R*)-3α,4α-Dihydroxy-7a-oxa-7a,7b-dihomo-5α-cholestan-7-one (**16**)

A solution of trifluoroperoxyacetic acid, freshly prepared from trifluoroacetic anhydride (650 mg, 3.10 mmol) and hydrogen peroxide (30%; 110 mg) in dichloromethane (4 ml), was added to a solution of diol **14** (200 mg, 0.46 mmol) in dichloromethane (10 ml). After standing at room temperature for 2 h, the reaction mixture was poured into water and taken up in chloroform. The chloroform extract was washed with water, saturated solution of potassium hydrogen carbonate, water, and dried over sodium sulfate. Removal of the solvent gave 185 mg of a residue. Preparative TLC on 12 plates in $CHCl_3$–propan-2-ol–diethyl ether (14:1:5) afforded 90 mg (0.19 mmol; 44%) of product **16**: m.p. 224–227 °C, $[\alpha]_D$ –8 (*c* 1.120). IR: 3461, 3354, 1054, 1036, 1011 (OH); 1719 (C=O); 1383, 1371, 1367 (i-Pr, Me). ^1H and ^{13}C NMR data, see Table II. FAB MS, *m/z*: 471 (M^+ + Na), 413 ((M^+ + H) – H_2O – CO). For $C_{28}H_{48}O_4$ (448.7) calculated: 74.95% C, 10.78% H; found: 74.15% C, 10.84% H.

(20*R*)-7a-Homo-5α-cholestan-3β-ol (**17**)

Ketone **4** (100 mg, 0.22 mmol) was treated with hydrazine hydrate (5 ml; 90%) and the mixture heated under reflux for 2 h (until the disappearance of the starting material on TLC). The mixture was then cooled to room temperature, and ethylene glycol (5 ml) and potassium hydroxide (250 mg) were added. The reaction mixture was heated carefully to 195 °C (without reflux in order to remove hydrazine hydrate) and then at reflux for 2 h (until the decomposition of the hydrazone was apparent on TLC). The reaction mixture was poured into a saturated sodium chloride solution (40 ml) and the product was extracted with diethyl ether. Usual work-up gave a residue (88 mg), which was purified by preparative TLC on 4 plates in light petroleum–ether (1:1) to afford 75 mg (19 mmol; 85%) of compound **17**. Analytical sample was crystallized from acetone: m.p. 89–91 °C, $[\alpha]_D$ +25 (*c* 0.200), giving identical physical constants, as described in the literature[11]. IR: 3620, 3350, 1043 (OH);

1383, 1367 (i-Pr, Me). ^{1}H NMR: 0.658 s, 3 H (3 × H-18); 0.826 s, 3 H (3 × H-19); 0.861 d, 3 H and 0.864 d, 3 H, J = 6.7 (3 × H-26 and 3 × H-27); 0.894 d, 3 H, J = 6.7 (3 × H-21); 3.52 m, 1 H, $W_{1/2}$ = 24.3 (H-3α). EI MS, *m/z*: 402 (M^+), 384 (402 – H_2O), 369 (384 – Me). For $C_{28}H_{50}O$ (402.7) calculated: 83.51% C, 12.51% H; found: 82.34% C, 12.68% H.

(20*R*)-7a-Homo-5α-cholestan-3β-yl Toluenesulfonate (**18**)

A solution of alcohol **17** (90 mg, 0.22 mmol) in pyridine (1 ml) was treated with 4-toluenesulfonyl chloride (90 mg, 0.52 mmol) and then allowed to stand at room temperature overnight. The reaction mixture was decomposed with ice and water, the product was taken up into ether and the ethereal solution was worked up as usual to afford 118 mg (0.21 mmol; 96%) of tosylate **18**: m.p. 88–90 °C, $[\alpha]_D$ +22 (*c* 0.318). IR: 3068, 3032 (=CH); 1370, 1179, 558, 557 (SO_2); 1600, 1496, 1306, 1290, 2111, 1189, 1119, 1100, 1021, 832, 815, 706, 669, 458 (aromatic); 1039 (Me). ^{1}H NMR: 0.633 s, 3 H (3 × H-18); 0.790 s, 3 H (3 × H-19); 0.855 d, 3 H and 0.859 d, 3 H, J = 6.6 (3 × H-26 and 3 × H-27); 0.880 d, 3 H, J = 6.4 (3 × H-21); 2.44 s, 3 H (CH_3 (Tos)); 4.35 m, 1 H, $W_{1/2}$ = 25.1 (H-3α); 7.32 m, 2 H and 7.79 m, 2 H (C_6H_4 (Tos)). EI MS, *m/z*: 556 (M^+), 384 (M^+ – TosOH), 369 (384 – Me). For $C_{35}H_{54}O_4S$ (556.9) calculated: 75.49% C, 10.14% H, 5.76% S; found: 75.60% C, 9.94% H, 5.14% S.

(20*R*)-7a-Homo-5α-cholest-2-ene (**19**) and (20*R*)-7a-Homo-5α-cholest-3-ene (**20**)

Tosylate **18** (110 mg, 0.20 mmol) was heated in sym-collidine (5 ml) under nitrogen atmosphere for 2 h. Sym-collidine was then distilled off under reduced pressure, the residue treated with water, and the product was taken up into ether. Usual work-up and evaporation left 85 mg of a product, containing a mixture of two isomeric olefins **19** and **20**, which were inseparable due to their practically identical polarity.

(20*R*)-7a-Homo-5α-cholestan-2α,3α-diol (**21**)

a) From (20R)-2α,3α-dihydroxy-7a-homo-5α-cholestan-7-one (**12**): A solution of ketone **12** (40 mg, 0.09 mmol) was treated with hydrazine hydrate (5 ml; 90%) and then heated under reflux for 2 h (until the disappearance of the starting material on TLC). The mixture was then cooled to room temperature, and ethylene glycol (5 ml) and potassium hydroxide (150 mg) were added. The reaction mixture was heated carefully to 195 °C (without reflux in order to remove hydrazine hydrate) and then at reflux for 2 h (until TLC monitoring showed a complete decomposition of the hydrazone). The reaction mixture was poured into a saturated sodium chloride solution (20 ml) and the product was isolated with diethyl ether. Usual work-up and evaporation gave a residue (37 mg), which was purified by preparative TLC on 4 plates in light petroleum–ether (1:1) to afford 30 mg (0.07 mmol; 78%) of diol **21**. Analytical sample was crystallized from acetone: m.p. 135–137 °C, $[\alpha]_D$ +50.2 (*c* 0.215). IR: 3625, 3585, 3391, 1052, 1020 (OH); 1384, 1367 (i-Pr, Me). ^{1}H NMR: 0.657 s, 3 H (3 × H-18); 0.844 s, 3 H (3 × H-19); 0.862 d, 6 H, J = 6.5 (3 × H-26 and 3 × H-27); 0.898 d, 3 H, J = 6.6 (3 × H-21); 3.65 m, 1 H, $W_{1/2}$ = 21.8 (H-2β); 3.89 m, 1 H, $W_{1/2}$ = 7.3 (H-3β). FAB MS, *m/z*: 401 $[\alpha]_D$ (M^+ + H) – H_2O], 383 (401 – H_2O). For $C_{28}H_{50}O_2$ (418.7) calculated: 80.32% C, 12.04% H; found: 80.02% C, 12.06% H.

b) From a mixture of (20R)-7a-homo-5α-cholest-2-ene (**19**) *and (20R)-7a-homo-5α-cholest-3-ene* (**20**): A solution of osmium tetroxide (4 mg, 0.02 mmol) in 2-methylpropan-2-ol (0.04 ml) was added to a solution of alkenes **19** and **20** (85 mg, 0.20 mmol) in acetone (4 ml).

N-Methylmorpholine *N*-oxide (85 mg, 0.73 mmol) was added and the mixture was stirred under nitrogen for 5 h. A solution of sodium sulfite (2 ml; 10%) was then added and the mixture stirred for 30 min, poured into water, extracted with chloroform and the extract was worked up as usual. The semicrystalline residue (76 mg, 0.18 mmol; 91%) contained mainly two diols, **21** and **22**. This residue was purified by preparative TLC on 4 plates in $CHCl_3$–propan-2-ol–diethyl ether (14:1:5). Work-up of the zones with a more polar compound afforded 27 mg (0.07 mmol; 32%) of (20*R*)-7a-homo-5α-cholestan-2α,3α-diol (**21**).

(20*R*)-7a-Homo-5α-cholestan-3α,4α-diol (**22**)

a) From (20R)-3α,4α-dihydroxy-7a-homo-5α-cholestan-7-one (**14**): The solution of dihydroxy ketone **14** (40 mg, 0.09 mmol) was treated with hydrazine hydrate (5 ml; 90%) and then heated at reflux for 2 h (until the disappearance of the starting material on TLC). The mixture was then cooled to room temperature and ethylene glycol (5 ml) and potassium hydroxide (150 mg) were added. The reaction mixture was heated carefully to 195 °C (without reflux in order to remove hydrazine hydrate) and then at reflux for 2 h (until the decomposition of the hydrazone was indicated by TLC). The reaction mixture was poured into a saturated sodium chloride solution (20 ml) and the product was extracted with diethyl ether. Usual work-up and evaporation gave a residue (38 mg), which was purified by preparative TLC on 2 plates in light petroleum–ether (1:1) to afford 30 mg (0.07 mmol; 78%) of diol **22**. Analytical sample was crystallized from acetone: m.p. 86–90 °C, $[\alpha]_D$ +6 (*c* 1.001). IR (KBr): 3619, 3567 (OH). ^{1}H NMR: 0.655 s, 3 H (3 × H-18); 0.835 s, 3 H (3 × H-19); 0.861 d, 6 H, *J* = 7.0 (3 × H-26 and 3 × H-27); 0.895 d, 3 H, *J* = 6.4 (3 × H-21); 3.34 dd, 1 H, *J*(4β,5α) = 10.2, *J*(4β,3β) = 3.5 (H-4β); 3.93 m, 1 H, $W_{1/2}$ = 12.6 (H-3β). EI MS, *m/z*: 418 (M^+), 400 (418 – H_2O). For $C_{28}H_{50}O_2$ (418.7) calculated: 80.32% C, 12.04% H; found: 80.18% C, 12.35% H.

b) From a mixture of (20R)-7a-homo-5α-cholest-2-ene (**19**) *and (20R)-7a-homo-5α-cholest-3-ene* (**20**): Work-up of the corresponding zones with a more lipophilic compound from the purification of compound **21** under *b*) afforded 40 mg (0.10 mmol; 48%) of 3α,4α-diol **22**, identical in all respects with compound **22** obtained under *a*).

(20*R*)-7-Oxa-7a-homo-5α-cholestan-2α,3α-diol (**24**)

A solution of (20*R*)-2α,3α-dihydroxy-7-oxa-7a-homo-5α-cholestan-6-one[14] (**23**) (100 mg, 0.23 mmol) in boron trifluoride etherate (2.5 ml) was dropped at 0 °C over 10 min to a solution of sodium borohydride (150 mg) in diglyme (2.5 ml)[13]. The reaction mixture was allowed to stand at 0 °C for 2 h, and then decomposed with potassium carbonate. The reaction mixture was poured into water, the product extracted with ether and the ethereal solution was worked up as usual. Evaporation afforded 80 mg of a residue, which was purified by preparative TLC on 8 plates in toluene–ether (1:1) to afford 45 mg (0.11 mmol; 48%) of product **24** (more lipophilic) and 20 mg (0.05 mmol; 20%) of the starting compound **23**: m.p. 145–147 °C, $[\alpha]_D$ +45 (*c* 0.259). IR: 3379, 1056, 1047, 1032, 1022 (OH); 1142, 1130 (COC); 1383, 1377, 1367 (i-Pr, Me). ^{1}H NMR: 0.693 s, 3 H (3 × H-18); 0.862 d, 6 H, *J* = 6.7 (3 × H-26 and 3 × H-27); 0.897 d, 3 H, *J* = 7.0 (3 × H-21); 0.976 s, 3 H (3 × H-19); 3.17–3.35 m, 2 H (H-7aα and H-7aβ); 3.62–3.75 m, 3 H (H-6α, H-6β and H-2β); 3.94 m, 1 H, $W_{1/2}$ = 8.8 (H-3β). EI MS, *m/z*: 420 (M^+), 405 (420 – Me), 402 (420 – H_2O). For $C_{28}H_{48}O_3$ (420.7) calculated: 77.09% C, 11.50% H; found: 75.54% C, 11.62% H.

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