cm^{-1} (OH); NMR ($CDCl_3$, $CHCl_3$ reference) δ 0.03–0.75 (m, 3 H, cyclopropyl hydrogens), 0.96 (s, 3 H, angular CH_3), 1.11 and 1.13 (2 s, 6 H, $C(CH_3)_2OH$); mass spectrum, *m/e* (rel intensity) 222 (5) (M^+), 204 (18, $(M - H_2O)^+$), 189 (12), 149 (29), 105 (33), 59 (100), 41 (27).

The IR and NMR spectra of **1** were identical with those obtained by Moss and co-workers[2,13] and were in close agreement with those reported by Ando, Sayama, and Takase.[3]

Registry No. (+)-**1**, 71962-31-7; (−)-**4**, 18541-52-1; *cis*-**5a**, 71962-32-8; (+)-**5b**, 57605-76-2; (+)-**6**, 71911-57-4; (−)-**7a**, 71911-58-5; (+)-**7b**, 71911-59-6.

Synthesis of 14β,17β(H)-Cholest-5-en-3β-ol

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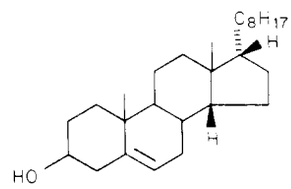
Sterols with a modified stereochemistry with respect to that of natural compounds appear to exhibit different noticeable activities on the enzyme systems which catalyze both the biosynthesis and catabolism of cholesterol. The first example is represented by the inhibitory effect on the cholesterol biosynthesis of the triterpenoid euphol, which differs from lanosterol only in the stereochemistry.[1] These observations prompted us to synthesize 5α,14β-cholest-7-en-3β-ol[2] and 14β-cholest-5-en-3β-ol,[3] both containing a cis C/D ring junction due to the β configuration of the hydrogen at C-14. Studies on in vitro catabolism of these compounds showed that rat liver enzymes are able to transform the former[4] into 5α-cholest-7-en-3β-ol, a cholesterol precursor, but leave unaffected the latter which, however, significantly modifies the lecithin cholesterol acyl transferase activity in plasma.[5] In addition Schroepfer et al.[6] were able to demonstrate that two 14β steroids (i.e., 5α,14β-cholest-7-en-3β,15β-diol and 5α,14β-cholest-7-en-3β,15α-diol) are inhibitors of sterol biosynthesis in L cells and in primary cultures of liver cells. More recently Koreeda and Koizumi[7] reported that (20*S*)-cholesterol exhibits a significant in vitro inhibitory activity in the conversion of cholesterol to pregnenolone and that side chain cleaving enzymes appear to be fastidious in their steric requirement with respect to side chain stereochemistry.

In continuation of our work we now report a stereochemically controlled synthesis of 14β,17β(H)-cholest-5-en-3β-ol (**1**), which differs from cholesterol in side chain configuration and in C/D ring junction, in order to check its influence on cholesterol biosynthesis and/or catabolism. A simple method to obtain 17β(H) steroids from 17α(H) steroids was proposed recently by us[8,9] and Caspi et al.[10,11] simultaneously. The side chain inversion is effected on a 7-, 8(14)- and 14-ene steroid by hydrogen chloride at controlled temperature to yield a 14β-chloro,17β(H) steroid which is transformed by either triethylamine treatment or chromatography on silica into the 14-ene,17β(H) compound. Catalytic hydrogenation of the Δ^{14} double bond of a 17β(H) steroid gives a 14β,17β(H) compound. The cis geometry of C/D rings was established by Caspi et al.[10] on the basis of ^{13}C NMR evidence and by Brunke et al.[12] by X-ray diffraction analysis. With this in mind, the key compound chosen for the synthesis of **1** was 5α-cholest-



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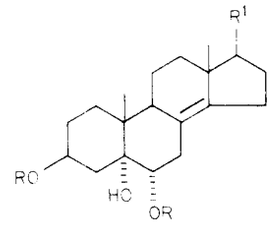
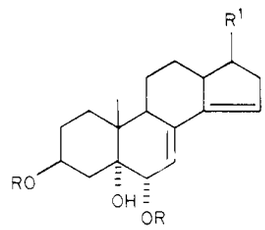
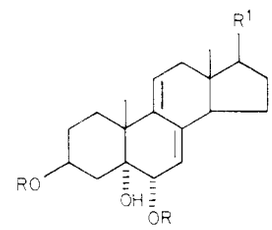


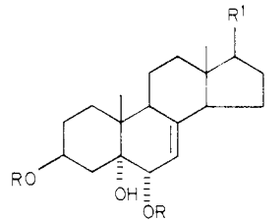
2a, R = H; R^1 = C_8H_{17}
b, R = H; R^1 = C_9H_{19}
c, R = Ac, R^1 = C_8H_{17}



3a, R = H; R^1 = C_8H_{17}
b, R = H; R^1 = C_9H_{17}
c, R = Ac; R^1 = C_8H_{17}



4a, R = H; R^1 = C_8H_{17}
b, R = H; R^1 = C_9H_{17}
c, R = Ac; R^1 = C_8H_{17}



5a, R = H; R^1 = C_8H_{17}
b, R = H; R^1 = C_9H_{17}
c, R = Ac; R^1 = C_8H_{17}

8(14)-ene-3β,5,6α-triol 3,6-diacetate (**2c**) containing a $\Delta^{8(14)}$ double bond suitable for the side chain inversion and a masked 5α,6α-diol system useful for the introduction of a Δ^5 double bond. The diacetate (**2c**) and the parent triol (**2a**) are unknown. However, their homologues with a C_9H_{19} side chain were obtained by M. Fieser et al.[13] by hydrogenation of a material considered to be 5α-ergosta-7,14,22-triene-3β,5,6α-triol (**3b**) derived from permanganate oxidation of ergosterol. Actually the supposed **3b** was shown[14] to be a mixture of three different compounds: 5α-ergosta-7,9(11),22-triene-3β,5,6α-triol (**4b**), 5α-ergost-

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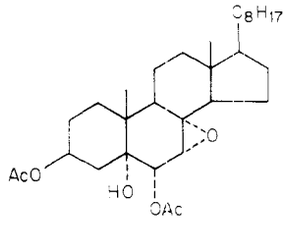
7,22-diene-3β,5,6α-triol (**5b**), and 5α-ergosta-7,14,22-triene-3β,5,6α-triol (**3b**). The diene **5b** and the trienic compounds **3b** and **4b** (these latter being formed during the oxidation workup) are transformed by hydrogenation into the monoene **2b**.[14] We obtained the same set of compounds (i.e., **3a**, **4a**, and **5a**) in the permanganate oxidation of cholesta-5,7-dien-3β-ol which the workup of the oxidation products was performed according to Fieser et al.[13] By consequence **2c** was obtained by direct catalytic hydrogenation of **3c**, **4c**, and **5c** and of their mixture. We also obtained **2c** by hydrogenation in acetic acid of the acetylated primary oxidation products of cholesta-5,7-dien-3β-ol[15] (i.e., **5c**, **6**, **7**, and **8**) and of their mixture. This



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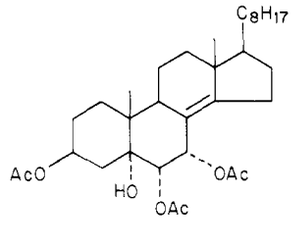

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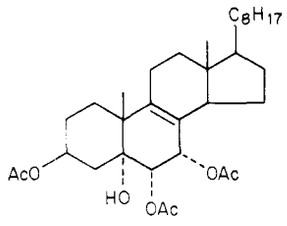

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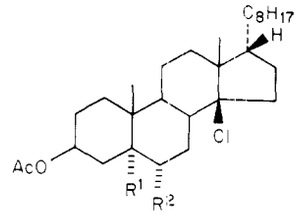
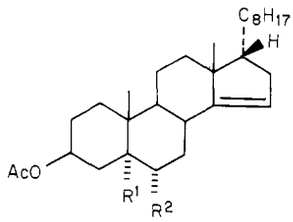
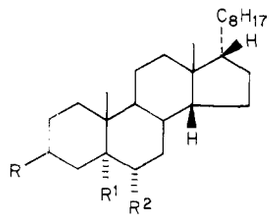
result is in accordance with the reported reactivity of analogous compounds of the ergosterol series.[14] When a 20 mM solution of **2c** in diethyl ether was treated with hydrogen chloride at −60 °C for 8 h, 14-chloro-5α,14β,17β(H)-cholestane-3β,5,6α-triol 3,6-diacetate (**9a**)



9a, R^1 = OH; R^2 = OAc
b, R^1 = R^2 = H



10a, R^1 = OH; R^2 = OAc
b, R^1 = R^2 = H



11a, R^1 = OH; R = R^2 = OAc
b, R = R^1 = R^2 = OH
c, R = OH; R^1 = R^2 = H

was obtained. The elemental analysis was in accord with the molecular formula $C_{31}H_{51}O_5Cl$. The ^1H NMR spectrum exhibits two signals for acetate methyl groups, and the positions of the C-18 and C-19 methyl signals are in accordance with the values calculated by Zurcher's rules.[16] These values were computed from the additive chemical shift of the appropriate 5α-OH and 6α-$OCOCH_3$ entities to the values observed for the known[8,9] **9b**. As observed for **9b**, **9a** was dehydrohalogenated either on silica or by treatment with triethylamine in methanol at 50 °C to give 5α,17β(H)-cholest-14-ene-3β,5,6α-triol 3,6-diacetate (**10a**) which shows ^1H NMR signals at δ 5.18 for the vinylic proton at C-15 and at δ 1.08 ppm for the C-18 and C-19 methyl groups in accordance with calculated values.[8,16] Catalytic hydrogenation of **10a** afforded as the only product 5α,14β,17β(H)-cholestane-3β,5,6α-triol 3,6-diacetate (**11a**). This means that hydrogen was entered from the front side of the molecule in accord with the results of Caspi et al.[10] and Brunke et al.[12] for the hydrogenation of 17β(H)-Δ^{14}-ene steroids. The 14β configuration for **11a** was established on the basis of its ^1H NMR spectrum and chemical transformations which will be described later. The positions of the C-18 and C-19 methyl signals in the ^1H NMR spectrum of **11a** are in accord with the calculated values.[16,17] The next step in the synthesis of **1** is concerned with formation of the Δ^5 double bond from the 5α,6α-diol system present in **11b** obtained by saponification of **11a**. Following the procedure of Eastwood and Grank[18] the triol **11b** was reacted with triethyl orthoformate and pyrolyzed at reduced pressure under acidic conditions to give **1** after saponification of the crude reaction material. It is noteworthy that this procedure does not require selective protection of the 3β-OH group. The spectral properties of 14β,17β(H)-cholest-5-en-3β-ol are very similar to those of cholesterol. Both the mass and IR spectra of **1** are almost identical with those of the natural compound. However, the ^1H NMR spectrum of **1** shows the signal for the C-18 methyl group at δ 0.97 ppm which is 0.30 ppm further downfield than the C-18 methyl resonance of cholesterol at δ 0.67 ppm.[19] This large downfield shift is expected for the change from a trans to a cis C/D ring junction.[16] The chemical shift of the C-18 methyl of **1** is comparable to the 0.98-ppm resonance of the C-18 methyl of 14β-cholest-5-en-3β-ol,[3] thus confirming that the epimerization of the side chain has a small effect on the chemical shift of the C-18 methyl group.[9] The other ^1H NMR signals for the protons at C-3 and C-6 have similar chemical shifts to the corresponding protons in both cholesterol and 14β-cholest-5-en-3β-ol. The structure of **1** was confirmed by hydrogenation and transformation to crystalline **11c** which was also obtained by hydrogenation of **10b** and saponification. The availability of **1** opens the way to various biological investigations. The inhibition of cholesterol biosynthesis is a first possibility. The transformation of **1** in tissues should also be examined with special regard to the possible role of the compound in modulating the synthesis of steroid hormones.

Experimental Section

All melting points are uncorrected. Infrared spectra were obtained for solutions in chloroform, UV spectra were recorded for solutions in absolute ethanol, NMR spectra were taken on a Varian HA-100 spectrometer as chloroform-*d* solutions and are reported as δ units relative to Me_4Si, and optical rotations were taken as chloroform solutions when not otherwise indicated. The mass spectra were determined on a MAT Varian 112 S spectrometer by direct inlet. The progress of all reactions and column

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chromatographs (silica gel G–C elite, 1:1 (v/v)) was monitored by TLC on silica gel (HF_{254}) microplates. Benzene–ethyl acetate (80:20) and dichloromethane–acetone (100:6) were used as developing solvents, and spots were detected by spraying with 70% sulfuric acid, followed by heating.

Permanganate Oxidation of Cholesta-5,7-dien-3β-ol. Cholesta-5,7-dien-3β-ol (4 g) was dissolved in methylcyclohexane (100 mL) at 100 °C, and aqueous potassium permanganate (3.2 g/80 mL), preheated to 100 °C, was added at once to the hot solution of the sterol. The flask was stoppered and shaken vigorously. The permanganate was all consumed in 10 min, the thin suspension of brown manganese dioxide was destroyed with sulfur dioxide (2.9 g) after cooling of the mixture at room temperature, and the resulting suspension of white solid was transferred to a separatory funnel and shaken gently with three successive portions of water to extract inorganic salts. The milky organic layer consisting of a suspension of the sparingly soluble oxidation products was then steam-distilled for separation of the solvent. The distillation was stopped after 1 h when the foaming became excessive. The mixture was then transferred to a large porcelain dish and evaporated on a steam bath (3 h, internal temperature 90 °C) to a thick gelatinous curd. After drying under high vacuum the crude product was acetylated at room temperature with acetic anhydride and pyridine to yield, after the usual workup, a crystalline material (2.5 g). TLC analysis of this material on silica gel G–$AgNO_3$ revealed the presence of three different components. Chromatography on silica gel G-Celite-$AgNO_3$ (1:1:0.3) (150 g), eluting with 20% benzene–hexane, afforded 5α-cholest-7-ene-3β,5,6α-triol 3,6-diacetate (**5c**) (370 mg): mp 188–189 °C (from methanol); $[\alpha]^{23}_D$ +58°; IR 3560, 3420, 1730 cm^{-1}; ^1H NMR δ 0.57 (s, 3 H, 18-CH_3; calcd[16,17] 0.54), 1.04 (s, 3 H, 19-CH_3; calcd[16,17] 1.01), 2.00, 2.10 (2 s, 6 H, OAc), 4.94 (m, 1 H, 6β-H, $w_{1/2} \simeq 6$ Hz), 5.0–5.3 (overlapping, 3α-H, 7-H); mass spectrum m/e 442 (14%, M − AcOH).

Anal. Calcd for $C_{31}H_{50}O_5 \cdot 0.5H_2O$: C, 72.8; H, 10.0. Found: C, 73.1; H, 9.8.

Saponification of **5c** with 0.2 N methanolic potassium hydroxide gave the triol **5a**: mp 231–232 °C (from methanol); $[\alpha]^{23}_D$ +26.4°. The compound regenerated **5c** when acetylated.

30% Benzene–hexane eluted 5α-cholesta-7,9(11)-diene-3β,5,6α-triol 3,6-diacetate (**4c**) (1.5 g): mp 191–192 °C (from methanol); $[\alpha]^{23}_D$ +103°; IR 3560, 3420, 1720 cm^{-1}; UV λ_{max} 236, 242, 250 nm (log ε 4.20, 4.23, 4.05); ^1H NMR δ 0.52 (s, 3 H, 18-CH_3; calcd[17] 0.52), 1.14 (s, 3 H, 19-CH_3; calcd[17] 1.12), 2.00, 2.13 (2 s, 6 H, OAc), 5.02 (m, 1 H, 6β-H, $w_{1/2} \simeq 7$ Hz), 5.1 (m, 1 H, 3α-H, $w_{1/2} \simeq 14$ Hz), 5.43 (m, 1 H, 7-H, $w_{1/2} \simeq 7$ Hz), 5.7 (m, 1 H, 11-H, $w_{1/2} \simeq 10$ Hz); mass spectrum m/e 500 (8%, M^+), 362 (100, M − 2AcOH + H_2O).

Anal. Calcd for $C_{31}H_{48}O_5 \cdot 0.5H_2O$: C, 73.1; H, 9.6. Found: C, 73.1; H, 9.5.

Saponification of **4c** with methanolic potassium hydroxide gave the triol **4a**: mp 201–202 °C; $[\alpha]^{23}_D$ +100°; IR 3450, 3330 cm^{-1}; UV λ_{max} 236, 242, 250 nm (log ε 4.20, 4.23, 4.05); ^1H NMR δ 0.53 (s, 3 H, 18-CH_3; calcd[16] 0.51), 1.05 (s, 3 H, 19-CH_3; calcd[16] 1.03), 4.00 (m, 1 H, 3α-H, $w_{1/2} \simeq 14$ Hz), 5.14 (m, 1 H, 7-H, $w_{1/2} \simeq 6$ Hz), 5.65 (m, 1 H, 11-H). Acetylation of **4a** regenerated **4c**.

40% Benzene–hexane eluted last 5α-cholesta-7,14-diene-3β,5,6α-triol 3,6-diacetate (**3c**) (600 mg): mp 179–180 °C (from methanol); $[\alpha]^{23}_D$ −80°; IR 3450, 1725, 1635 cm^{-1}; UV λ_{max} 242 nm (log ε 3.99); ^1H NMR δ 0.82 (s, 3 H, 18-CH_3; calcd[16,17] 0.78), 1.02 (s, 3 H, 19-CH_3; calcd[16,17] 1.01), 2.01, 2.12 (2 s, 6 H, OAc), 5.21, (overlapping, 2 H, 3α-H, 6β-H), 5.41 (m, 1 H, 7-H, $w_{1/2} \simeq 7$ Hz), 5.60 (m, 1 H, 15-H, $w_{1/2} \simeq 7$ Hz); mass spectrum m/e 500 (2%, M^+), 380 (100%, M − 2 AcOH).

Anal. Calcd for $C_{31}H_{48}O_5$: C, 73.9; H, 9.6. Found: C, 73.8; H, 9.8.

Saponification of **3c** with methanolic potassium hydroxide gave the triol **3a**: mp 182–184 °C (from methanol); $[\alpha]^{23}_D$ −137° (dioxane); IR 3450, 3330 cm^{-1}; UV λ_{max} 242 (log ε 3.99); ^1H NMR δ 0.79 (s, 3 H, 18-CH_3; calcd[16,17] 0.75), 0.96 (s, 3 H, 19-CH_3; calcd[16,19] 0.93). Acetylation of **3a** regenerated **3c**.

Synthesis of 5α-Cholest-8(14)-ene-3β,5,6α-triol 3,6-Diacetate (2c). Compound **2c** was obtained by action of hydrogen on **3c**, **4c**, **5c** (and their mixture), **6**, **7**, and **8** (and their mixture containing also **5c**) in acetic acid in the presence of PtO_2 by the following general procedure. The steroid (250 mg), PtO_2 (100 mg), and acetic acid (20 mL) were stirred for 1–4 h at room temperature under a slight positive pressure of hydrogen. After the usual workup **2c** was recovered (200 mg) by crystallization from methanol: mp 159–160 °C; $[\alpha]^{23}_D$ −5°; IR 3410, 1730 cm^{-1}; ^1H NMR δ 0.83 (s, 3 H, 18-CH_3; calcd[17] 0.83), 0.90 (s, 3 H, 19-CH_3; calcd[17] 0.89), 2.00; 2.07 (2 s, 6 H, OAc), 4.7–5.4 (br m, 2 H, 3α-H and 6β-H); mass spectrum m/e 502 (12%, M − AcOH).

Anal. Calcd for $C_{31}H_{50}O_5$: C, 74.0; H, 10.0. Found: C, 74.1; H, 9.8.

When the reaction was performed on alcohols **3a**, **4a**, and **5a**, the product obtained was **2a**: mp 218–219 °C; $[\alpha]^{23}_D$ −4° (dioxane).

Anal. Calcd for $C_{27}H_{46}O_3$: C, 77.4; H, 11.1. Found: C, 77.4; H, 11.4.

Synthesis of 14-Chloro-5α,14β,17β(H)-cholestane-3β,5,6α-triol 3,6-Diacetate (9a). Diacetate **2c** (500 mg) in diethyl ether (100 mL) was treated with HCl at −60 °C for 8 h. The pressure in the reaction vessel was then lowered to about 20 mm without interruption of the cooling. The residue was poured into ice–water and extracted with diethyl ether. The organic layer was dried (Na_2SO_4) and evaporated in vacuo to give solid 14-chloro-5α,14β,17β(H)-cholestane-3β,5,6α-triol 3,6-diacetate (**9a**) (510 mg): mp 148–149 °C (from hexane); ^1H NMR δ 1.18 (s, 3 H, 18-CH_3; calcd[8,16] 1.18), 1.0 (s, 3 H, 19-CH_3; calcd[8,16] 0.99); mass spectrum m/e 500 (M^+ − HCl).

Anal. Calcd for $C_{31}H_{51}O_5Cl$: C, 69.1; H, 9.5; Cl, 6.5. Found: C, 69.2; H, 9.6; Cl, 6.4.

5α,17β(H)-Cholest-14-ene-3β,5,6α-triol 3,6-Diacetate (10a). 14-Chloro-5α,14β,17β(H)-cholestane-3β,5,6α-triol 3,6-diacetate (**9a**) (500 mg) in methanol (50 mL) and triethylamine (5 mL) were refluxed for 30 min. After the usual workup **10a** (460 mg) was obtained as an oil. Crystallization from methanol gave pure **10a**: mp 68–71 °C; $[\alpha]^{23}_D$ +79°; ^1H NMR δ 1.08 (2 s, 6 H, overlapping, 18- and 19-CH_3; calcd[8,16,17] 1.09 and 1.06), 5.18 (s, 1 H, 15-H); mass spectrum m/e 500 (M^+).

Anal. Calcd for $C_{31}H_{50}O_5$: C, 72.8; H, 10.0. Found: C, 73.1; H, 10.2.

5α,14β,17β(H)-Cholestane-3β,5,6α-triol 3,6-Diacetate (11a). 5α,17β(H)-cholest-14-ene-3β,5,6α-triol 3,6-diacetate (**10a**) (500 mL) in ethyl acetate (25 mL) was hydrogenated in the presence of 10% Pd-on-C at room temperature and atmospheric pressure. One equivalent of hydrogen was absorbed in 10 h. The catalyst was removed by filtration and the solution was concentrated to give 5α,14β,17β(H)-cholestane-3β,5,6α-triol 3,6-diacetate (**11a**): mp 136–137 °C (from methanol); $[\alpha]^{23}_D$ +22°; IR 3480, 1730 cm^{-1}; ^1H NMR δ 1.02 (overlapping, 6 H, 18-CH_3 and 19-CH_3; calcd[16,17] 1.01 and 1.03, respectively).

Anal. Calcd for $C_{31}H_{52}O_5$: C, 73.8; H, 10.4. Found: C, 73.6; H, 10.6.

Saponification of **11a** with methanolic potassium hydroxide gave the triol **11b**: mp 204–205 °C (from methanol); $[\alpha]^{23}_D$ +21°; IR 3450, 3330 cm^{-1}; ^1H NMR δ 1.00 (2 s, 6 H, overlapping, C-18 and C-19 CH_3; calcd[16,17] 1.00 and 0.986).

Anal. Calcd for $C_{27}H_{48}O_3$: C, 77.1; H, 11.5. Found: C, 77.3; H, 11.4.

14β,17β(H)-Cholest-5-en-3β-ol (1). A solution of triol **11b** (300 mg), ethyl orthoformate (4 mL), and benzoic acid (10 mg) was stirred at 110 °C for 1 h. To the crude 1,3-dioxolane, after evaporation of the solvent in vacuo, 100 mg of benzoic acid was added. The mixture was heated at 180 °C for 15 min at 5 torr. During the reaction the 3β-OH group was partially formylated. In fact, the reaction mixture showed a band at 1730 cm^{-1} in the IR spectrum. The oil product was refluxed with methanolic KOH, extracted with diethyl ether, dried, and evaporated. The crude product was chromatographed to yield **1** (180 mg). An analytical sample was preparated by recrystallization from hexane: mp 127–128 °C; $[\alpha]^{23}_D$ +11°; IR 3420 cm^{-1}; ^1H NMR δ 0.97 (s, 3 H, 18-CH_3; calcd[8,16] 0.984), 1.04 (s, 3 H, 19-CH_3; calcd[8,16] 0.991), 3.50 (m, 1 H, 3α-H), 5.36 (m, 1 H, 6 H); mass spectrum m/e 386 (M^+), 371, 368, 301, 273, 255.

Anal. Calcd for $C_{27}H_{46}O$: C, 83.9; H, 12.0. Found: C, 84.1, H, 12.2.

5α,14β,17β(H)-Cholestan-3β-ol (11c). **14β,17β(H)-Cholest-5-en-3β-ol (1)** (170 mg) was dissolved in ethyl acetate and hydrogenated over PtO_2 (20 mg) at room temperature and atmospheric pressure. After the stoichiometric amount of hydrogen was taken up the catalyst was removed and the solvent

eliminated. The residue was crystallized from methanol to give 5α,14β,17β(H)-cholestan-3β-ol (**11c**) (140 mg): mp 103–104 °C; $[\alpha]^{23}_D$ +24°; ^{1}H NMR δ 0.84 (s, 3 H, 18-CH_3), 1.01 (s, 3 H, 19-CH_3), 3.6 (m, 1 H, 3α-H); mass spectrum *m/e* 388 (M^+), 373, 355, 257, 234, 217.

Anal. Calcd for $C_{27}H_{48}O$: C, 83.4; H, 12.4. Found: C, 83.4; H, 12.6.

The product was identical (melting point and NMR and mass spectra) with that obtained[10] by hydrogenation of 5α,17β(H)-cholest-14-en-3β-ol (**10b**).

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Registry No. **1**, 71869-93-7; **2a**, 71831-80-6; **2c**, 71831-81-7; **3a**, 71831-82-8; **3c**, 71831-83-9; **4a**, 71831-84-0; **4c**, 71831-85-1; **5a**, 71831-86-2; **5c**, 71831-87-3; **6**, 71831-88-4; **7**, 71831-89-5; **8**, 71831-90-8; **9a**, 71831-91-9; **10a**, 71831-92-0; **10b**, 56193-33-0; **11a**, 71869-94-8; **11b**, 71869-95-9; **11c**, 56193-35-2; cholesta-5,7-dien-3β-ol, 434-16-2.

Synthesis of a Protected Glycoside of α-D-Purpurosamine C by Cycloaddition

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The pseudotrisaccharide mixture Gentamicin[1,2] is a broad-spectrum aminoglycoside antibiotic complex, designated as gentamicins C_1, C_2, and C_{1a}, produced by *Micromonospora purpurea*. Each pseudotrisaccharide contains the branched-chain amino sugar garosamine, the aglycon 2-deoxystreptamine, and one of three different 2,6-diamino-2,3,4,6-tetradeoxyaldoses, which have been named purpurosamine A, B, and C from gentamicins C_1, C_2, and C_{1a}, respectively. The *meso*-2-deoxystreptamine is asymmetrically α-glycosylated in the gentamicins at C-4 with the purpurosamine subunits. The pseudodisaccharide gentamines,[3] which are deprived of the garosamine subunit, exhibit interesting antibacterial activity. Recently, a new type of aminoglycoside antibiotic pseudodisaccharide, the *Fortimicins*,[4] was isolated, containing only one sugar unit, *epi*-purpurosamine *B*. The position and nature of all linkages to the novel aminocyclitol fortamine have been firmly established. Several syntheses of purpurosamine C derivatives have been already reported.[5-11]

No synthetic method can compete with fermentation in the production of natural antibiotics of even moderate complexity. Efforts in this field seem mainly interesting as a test of new methods or as a route to modified derivatives for biological evaluation. Simple sugars generally are not endowed with antibiotic activity, so that some kind of coupling reaction should be considered as one of the last steps of the syntheses. In the gentamicins, purpurosamines are linked to 2-deoxystreptamine by α-glycosidic bonds cis to a 2-amino group. Such a configuration can generally be built only in low overall yield when calculated from the starting 2-amino(acetamido)-2-deoxyhexopyranosyl component sugar. To avoid long synthetic sequences terminating with the most hazardous steps, we have adapted in recent years the cycloaddition experiments of Zamojski et al.[12] to the synthesis of oligo- and pseudodisaccharides. This new method consists of the cycloaddition between the dienyl ether of a protected sugar and a glyoxylic ester, the sugar moiety acting as an inducer of chirality in the product. In this way the anomeric configuration is determined at the very beginning of the sequence. We have previously reported the synthesis by this method of the blood group A trisaccharide antigenic determinant[13] and the enantiomer of kasuganobiosamine.[14] We shall now describe the first synthesis of a protected derivative of a disaccharide with α-D-*N*,*N*′-diacetylpurpurosamine C as the nonreducing unit and compare our method with more classical approaches.

The starting material was the lyxo epoxide **1**. The first preparation[15] has been substantially improved to 23% overall yield from "diacetone-glucose" by using diethyl 2-oxomalonate as the dienophile.[16] The method has been scaled up to 50-g quantities as the five-step sequence involves only two chromatographic separations at the end. Lithium aluminum hydride reduction of **1**, followed by *p*-toluenesulfonylation of the crude reduction product, gave in 84% overall yield a ditosylate **5** which could also be prepared from the known,[15] allylic alcohol **2** by catalytic hydrogenation followed by esterification. Thus, $LiAlH_4$ reduction of epoxide **1** had given mainly the diol **4**, a product of diaxial opening.

So far, very few instances have been reported of S_N2 displacements by external nucleophiles at the 2-position of pyranosides with axial anomeric substituents. We wondered whether the lack of 3- and 4-substituents on the ring in diester **5** would increase the reactivity at C-2 in this case. Treatment with sodium azide of diester **5** in dimethylformamide solution for 16 h at 110 °C gave in quantitative yield the unsaturated derivative **6**, having the correct ^{1}H NMR and analytical parameters. Thus elimination had proceeded more quickly than substitution. Under milder conditions, at 60 °C, only one product was formed. Its ^{1}H NMR spectrum was compatible with a saturated primary azide structure. Reaction at 100 °C gave a mixture of the same monoazide and the unsaturated compound **6**. TLC examination showed no other product. A similar observation has been recorded, in the course of a total synthesis of DL-purpurosamine B.[17]

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