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Synthesis of Lanosterol Analogs with Modified Side Chains

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Starting from lanosteryl acetate (**1b**), we synthesized twelve lanosterol analogs (cf. Chart 1—3; **9**, **11**, **14**, **16**, **18a**, **19**, **26**, **27a**, **28**, **29**, **30**, **32**) with different sizes of side chain and 20-iso-24-dihydrolanosterol (**37**), for biological studies. The analogs have shorter side chains than **1b** except for the 24-ethylidene derivative (**19**) and **37**. 20-Iso-24-dihydrolanosterol (**37**) was prepared *via* 20-iso-22-dehydro-24-dihydrolanosterol [obtained by the Wittig reaction of 20*R*,*S*-aldehyde mixture (**6**, **33**) with isoamyl triphenylphosphonium iodide, followed by column chromatographic separation].

Keywords——synthesis; lanosterol analogs; 20-iso-24-dihydrolanosterol; 20-iso-aldehyde; Wittig reaction; degradation

In the course of our investigations in the field of cholesterol biosynthesis, we became interested in preparing lanosterol analogs with modified side chains. We recently reported[2] a synthesis of the deuterated and undeuterated 21- and 22-methyl derivatives of pentanor analogs of dihydrolanosterol and chloesterol, and the relationship between their T_1 values and structures. Recently, Ikekawa and his co-workers[3] have described a novel synthesis of cholesterol analogs with a modified side chain. The degradation of the lanosterol side chain has been reported by Habermehl *et al.*,[4] Briggs *et al.*,[5] Fetizon *et al.*,[6] Ganem *et al.*[7] and Iwasaki.[8] We now wish to report a synthesis of twelve analogs of lanosterol with different sizes of side chain and 20-iso-24-dihydrolanosterol in order to investigate the effects of lanosterol analogs on cholesterol biosynthesis from lanosterol. Recent publications in this field have described potent inhibitors[9—13] of cholesterol biosynthesis.

In this investigation, we used commercial lanosteryl acetate (**1b**) as the starting material. First, treatment of **1b** with peracid afforded the 24,25-epoxide (**2**), as described by Boar *et al.*,[14] and **2** was further transformed into the 24-oxo compound (**3**)[5] together with the aldehyde (**4**)[5] by boron trifluoride-etherate treatment. Dehydrogenation of the former compound (**3**) with selenium dioxide afforded the unsaturated ketone (**5**), mp 170—171°, whose structure was determined to be 22-*trans*-3β-acetoxy-lanosta-8,22-dien-24-one on the basis of its PMR spectrum ($J_{22,23}=15$ Hz) and also its IR spectrum (α,β-unsaturated ketone band at 1690 cm^{-1}). Oxidation of **5** with potassium permanganate under neutral conditions afforded an aldehyde (**6**)[5] and a carboxylic acid (**7**)[5] in 70% and 13% yields, respectively. Subsequent reduction of **6** with sodium borohydride afforded the corresponding 22-alcohol, which was further transformed to 23,24,25,26,27-pentanorlanost-8-en-3β-ol (**9**)[15] *via* the 22-chloro compound (**8**) as described previously.[2] On treatment with lead tetraacetate[16] in the presence of Cu^{2+}-pyridine, the carboxylic acid (**7**) gave an olefin compound (**10**) in 48% yield, and this was converted to 22,23,24,25,26,27-hexanorlanost-8-en-3β-ol (**11**), mp 160—161°, by catalytic hydrogenation with 5% palladium on charcoal followed by alkaline hydrolysis. On the other hand, treatment of **10** with sodium periodate and potassium permangnate in the presence of potassium carbonate gave a carboxylic acid (**12**) which, on treatment with ethyl chloroformate and triethylamine in tetrahydrofuran and then reduction of the product with sodium borohydride, was converted to a 20-alcohol. Subsequent treatment of the alcohol, without further purification, with phosphoryl chloride in pyridine gave a chloro compound (**13**), which was converted to 21,22,23,24,25,26,27-heptanorlanost-8-en-3β-ol (**14**), mp 159—162°, by reductive dehalogenation with lithium aluminum hydride.

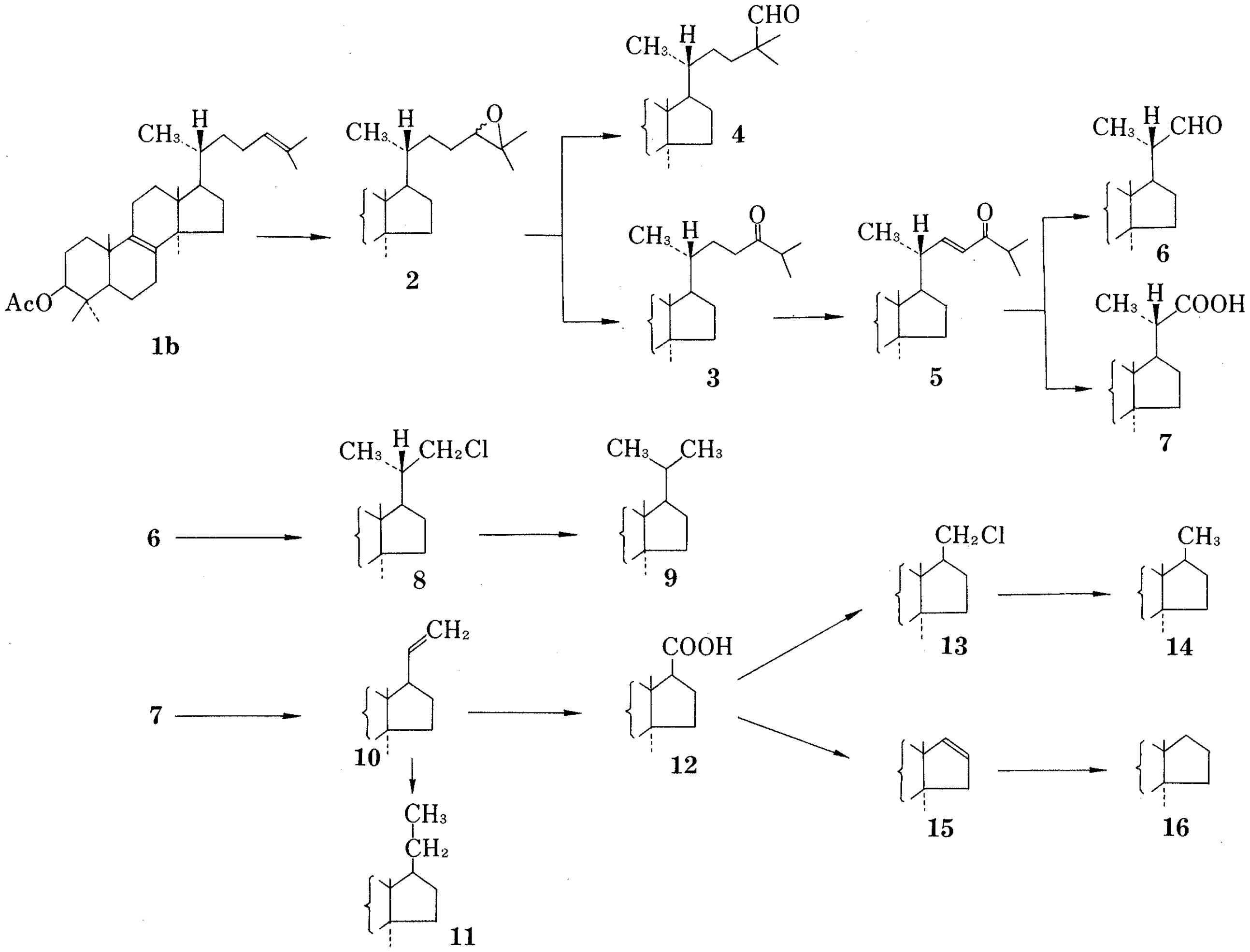


Chart 1

The compound with no alkyl side chain was prepared from the carboxylic acid (**12**). On treatment with lead tetraacetate as described above (**7**→**10**), **12** gave a decarboxylated compound (**15**), whose PMR spectrum exhibited a multiplet assigned to C-16 and C-17 olefinic protons at 5.50—5.80 ppm. Catalytic hydrogenation of **15** with 5% palladium on charcoal, followed by alkaline hydrolysis, afforded 20,21,22,23,24,25,26,27-octanorlanost-8-en-3β-ol (**16**), mp 161—162°. In order to prepare the 23-nor analog (**18b**),[4,17] the alcohol (**17**) obtained by treatment of the aldehyde (**4**) with sodium borohydride was reacted with lead tetraacetate in benzene. Alkaline hydrolysis of the product (**18b**) afforded 23-norlanost-8-en-3β-ol (**18a**), mp 136—137°. Further, the 24-ethylidene compound (**19**) was prepared by the Wittig reaction of the 24-oxo-compound (**3**) with ethyl triphenylphosphonium bromide in 82% yield. The structure of **19** was confirmed by its mass spectrum (*m/e* 454, M^+) and PMR spectrum, which showed a three-proton doublet at 1.58 ppm due to the 29-methyl group and a quartet at 5.12 ppm due to 28-H. Studies on the Z stereochemistry[19] of the ethylidene group will be reported in detail at a later date.

As a starting material for the synthesis of nor-, dinor-, and trinor-analogs of lanosterol, the 24-aldehyde (**23**)[19,20] was prepared as follows. Oxidation of lanosteryl acetate (**1b**) by the procedure of Habermehl *et al.*[4] afforded the 24-carboxylic acid (**21**) and the ketol compound (**20**). Reduction of the ketol (**20**) with sodium borohydride gave the 24ξ, 25-diol (**22**). Subsequent oxidative cleavage of the diol (**22**) with periodate in dioxane afforded 3β-acetoxy-25,-26,27-trinorlanost-8-en-24-al (**23**) in 76% yield. Reduction of **23** with sodium borohydride gave a primary alcohol (**24**), which was transformed to the chloro compound (**25**) in 60% yield by treatment with phosphoryl chloride in pyridine. Reductive dehalogenation of **25** with

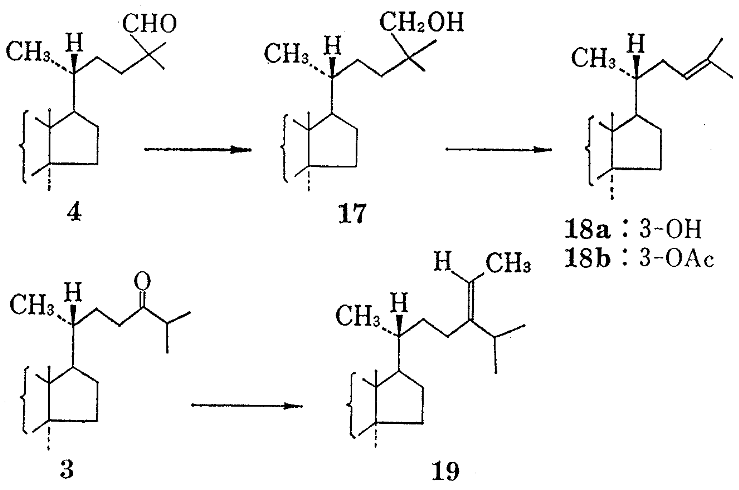


Chart 2

lithium aluminum hydride gave 25,26,27-trinorlanost-8-en-3β-ol (**26**),[18] mp 169—170°, in 90% yield. To obtain nor- and dinor-analogs, on the other hand, Wittig reactions of the aldehyde (**23**) were performed. On treatment with methyl triphenylphosphonium bromide in the presence of *n*-butyl lithium, **23** gave 26,27-dinorlanosta-8,24-dien-3β-ol (**27a**), mp 133—134°, and its acetate (**27b**), mp 143°, in 24% and 48% yields, respectively. The structure of **27a**

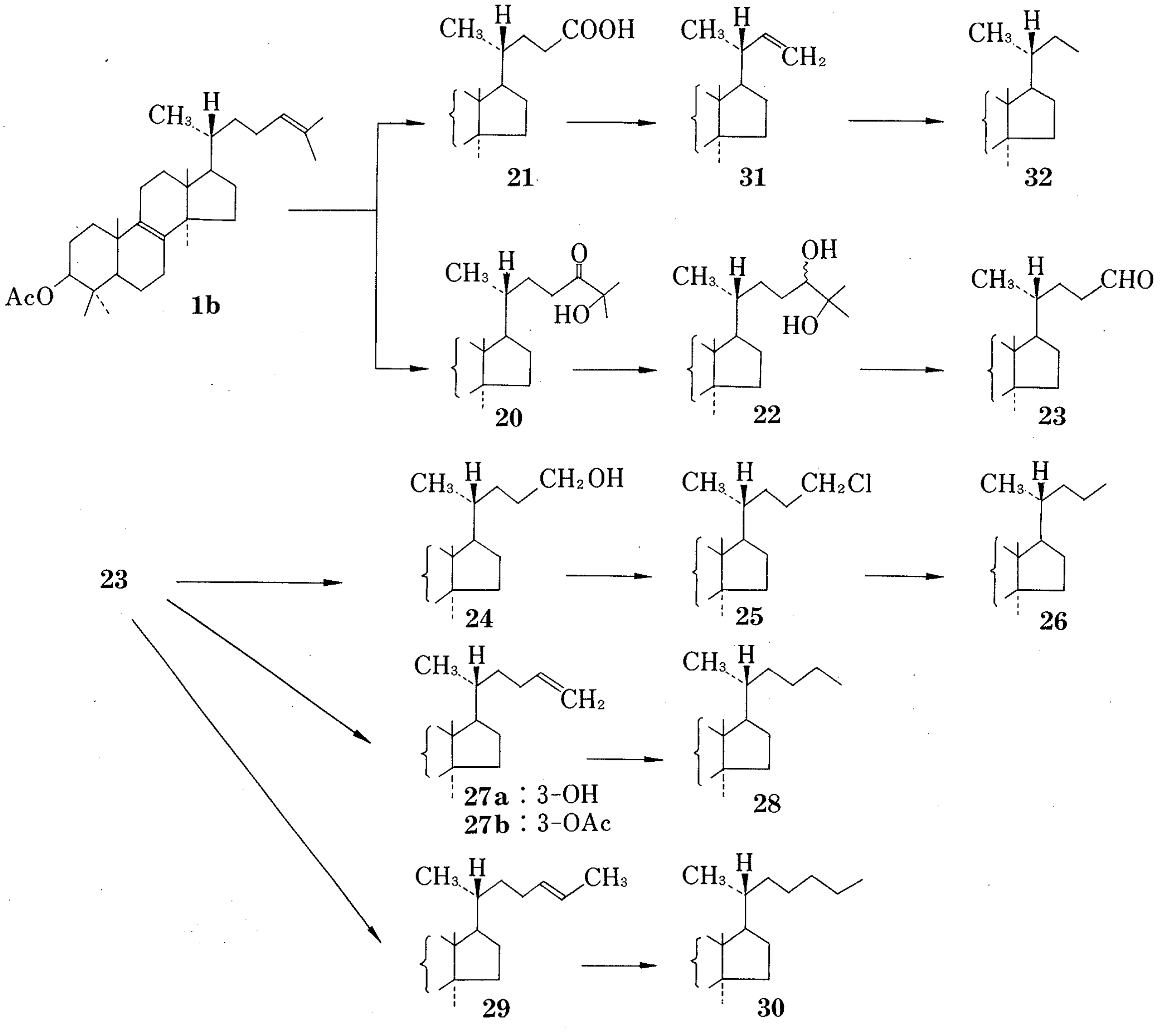
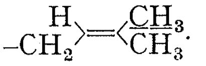


Chart 3

with its terminal vinyl group was confirmed by its PMR spectrum, which exhibited both a two-proton multiplet in the region of 4.80—5.10 ppm and a multiplet in a region of 5.60—6.00 ppm. The reaction of **23** with ethyl triphenylphosphonium bromide in a similar manner afforded 27-norlanosta-8,24-dien-3β-ol and its acetate in 21% and 39% yields, respectively. Gas liquid chromatography (GLC) and the PMR spectrum (1.58 and 1.65 ppm signals of 26-methyl) of the 3β-ol compounds showed that the 24,25-*cis* and 24,25-*trans* isomer ratio was approximately 3 : 1. Column chromatography of the mixture on 10% silver nitrate-impregnated silica gel resulted in isomerization of the *cis* isomer into the *trans* isomer, as indicated by GLC analysis of all fractions, to afford 24-*trans*-27-norlanosta-8,24-dien-3β-ol (**29**), mp 148°. Its IR spectrum was consistent with the *trans* structure[21] (965 cm^{-1}, KBr). Further, its PMR spectrum supports the *trans* structure, since the 1.65 ppm signal due to the 26-methyl group was consistent with that (1.66 ppm) of the partial structure[22]  $\overset{H}{\underset{-CH_2}{}}\!\!>\!=\!<\!\!\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}$. Catalytic hydrogenation of the 24,25-unsaturated compounds (**27a** and **29**) afforded 26,27-dinorlanost-8-en-3β-ol (**28**), mp 149—151°, and 27-norlanost-8-en-3β-ol (**30**), mp 142—143°, respectively. In order to synthesize the tetranor analog, the carboxylic acid (**21**) was treated with lead tetraacetate in the presence of Cu^{2+}-pyridine to give 3β-acetoxy-24,25,26,27-tetranorlanosta-8,22-diene (**31**).[23] Catalytic hydrogenation of **31** in the presence of 5% palladium on charcoal and subsequent alkaline hydrolysis afforded 24,25,26,27-tetranorlanost-8-en-3β-ol (**32**), mp 156°.

In addition to the synthesis of lanosterol analogs with a modified side chain, the synthesis of 20-iso-24-dihydrolanosterol was also required for biological experiments. Previous publications have described the synthesis of 20-iso-22-dehydrochloesterol,[24] 20-isocholesterol,[25—27] 20-isocholanic acid derivatives[28] and 20-iso-24,25,26,27-tetranorlanosteryl acetate.[29] Our synthetic route to 20-iso-24-dihydrolanosterol (**37**) is shown in Chart 4. As a starting material for this experiment, the 20-aldehyde (**6**) was used. Treatment of **6** with sulfuric acid in methanol[30] gave an 20-iso- and normal-aldehyde mixture, as determined by PMR spectroscopy

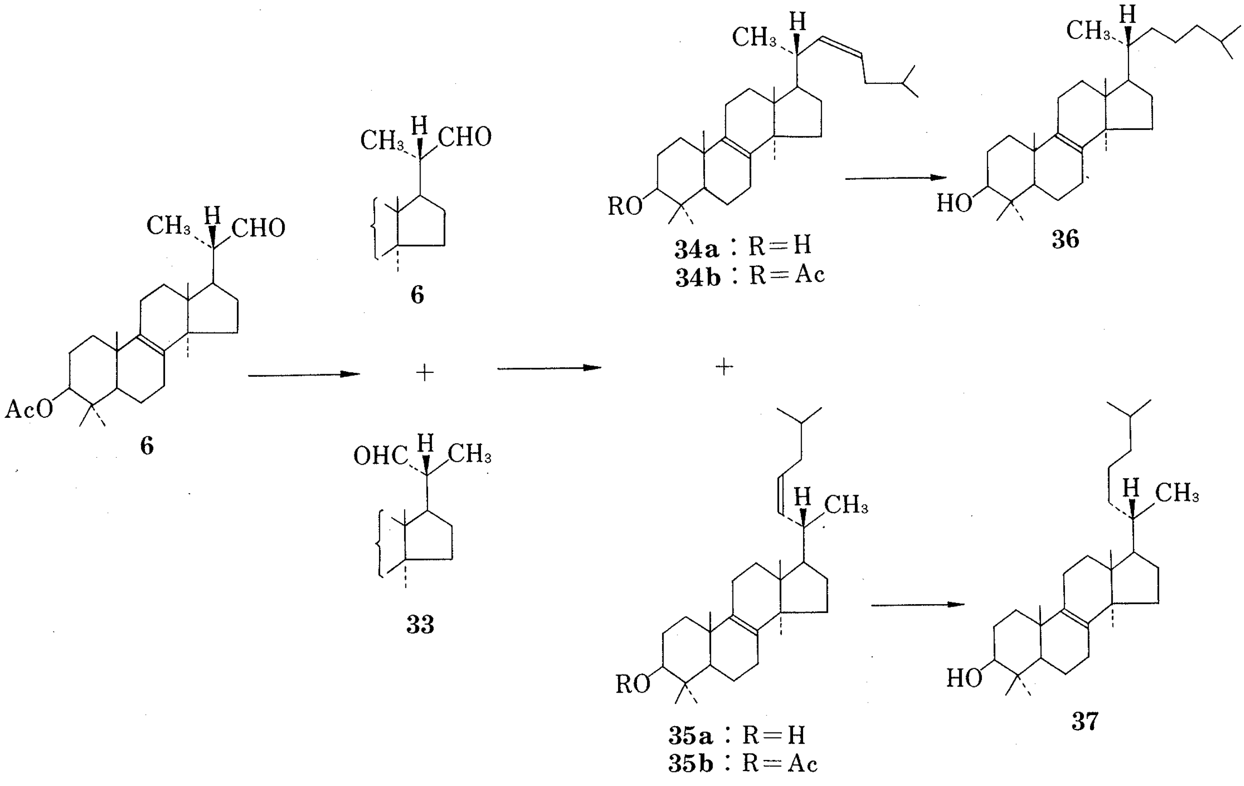


Chart 4

of the acetylation product. The PMR data indicated the formation of the 20-iso compound on the basis of the appearance of new signals at 0.72 ppm and 9.50 ppm in addition to the signals at 0.75 ppm and 9.58 ppm ascribed to the 18-methyl protons and an aldehyde proton of **6**, respectively. A comparison of ^1H signals indicated that the mixture consists of the 20-normal- (**6**) and 20-iso-aldehyde (**33**) in a 1: 1 ratio, and difficulties were encountered in the separation of the isomers on GLC and thin layer chromatography (TLC) because of the similarity in their chromatographic behavior. The Wittig reaction of an aldehyde mixture (**6** and **33**) with isoamyl triphenylphosphonium iodide afforded the 22-dehydro-24-dihydrolanosterol isomer (**34a** and **35a**) and their acetates (**34b** and **35b**), in 46% and 18% yields, respectively. The stereoisomers, **34a** and **35a**, were separated by column chromatography on silica gel, furnishing **35a** as the less polar product; the ratio of the stereoisomers was approximately 1: 1. The Δ^{22} compound (**34a**) was identical with 22-dehydro-24-dihydrolanosterol prepared by the Wittig reaction of the 20-normal aldehyde (**6**). Consequently, **35a** is the 20-iso-Δ^{22}-compound. Inspection of the PMR spectra of **34a** and **35a** revealed that the 18-methyl signals were substantially different (0.74 and 0.62 ppm, respectively). In the mass spectra of **34a** and **35a**, some appreciable differences were observed in their fragmentation patterns; they gave base peaks at *m/e* 111 and 69, respectively. The IR spectra (KBr) of **34a** and **35a** exhibited absorption bands at 735 and 730 cm^{-1}, respectively, which suggest the *cis* configuration[21] of their Δ^{22} double bonds. Catalytic reduction of the iso-compound (**35a**) afforded the corresponding dihydro compound, whose structure was elucidated as 20-iso-24-dihydrolanosterol (**37**), mp 171.5—172°, $[\alpha]_D^{19}$ +33°. Hydrogenation of **34a** in a similar manner afforded 24-dihydrolanosterol (**36**), mp 146—146.5°, $[\alpha]_D^{19}$ +63°. The PMR spectra of **36** and **37** were very similar in $CDCl_3$ but some chemical-shift differences were observed in 14- and 18-methyls in hexadeuterobenzene (1.03 and 0.84 ppm for 24-dihydrolanosterol and 1.01 and 0.82 ppm for 20-iso-24-dihydrolanosterol, respectively). The 21-methyl groups in the above compounds were not observed because of overlapping with other signals. In GLC on 1.5% OV-17, the relative retention time of the iso-compound (**37**) relative to that of the normal compound (**36**) was 0.88. Corey–Pauling–Koltun (CPK) model examination of **36** and **37** thus obtained clearly indicated that their side chains have different orientations.

Studies on the effects of these lanosterol analogs on cholesterol biosynthesis will be reported elsewhere in the near future.

Experimental

All melting points were obtained on a micro-melting point determination apparatus (type MM2, Shimadzu Seisakusho Ltd.) and are uncorrected. PMR spectra were recorded on a JEOL JNM-MH-100 spectrometer at 100 MHz, with tetramethylsilane as an internal standard in deuteriochloroform. Abbreviations used: s=singlet, d=doublet, t=triplet, q=quartet, h=heptet, m=multiplet. IR spectra were recorded on a Hitachi EPI-G3 machine as KBr pellets. The UV spectrum was determined on a Hitachi EPS-3T machine. Mass spectra (MS) were determined on a JEOL JMS D-100 spectrometer. Column chromatography was performed with Kanto Kagaku silica gel (100 mesh above) and aluminum oxide 90 (E. Merck, Darmstadt). Thin layer chromatography (TLC) was done on Merck precoated Kieselgel 60 F_{254} plates (0.25 mm thick). Gas liquid chromatography (GLC) was performed on a Shimadzu GC-6AF machine with a 1.5% OV-17 (2 m × 3 mm) column. Optical rotations were determined on a JASCO DIP-SL machine and are recorded as follows, $[\alpha]_D^{temp.}$ (% concentration, solvent). "The usual work-up" refers to dilution with water, extraction with methylene chloride, washing to neutrality, drying over anhydrous sodium sulfate, filtration, and evaporation under reduced pressure.

Epoxidation of 3β-Acetoxylanosta-8,24-diene (1b)——A solution of m-Cl-perbenzoic acid (2.1 g) in chloroform (60 ml) was added over 1 hr to a solution of **1b**[31] (7.2 g) in chloroform (300 ml) at 0°. After usual work-up of the reaction mixture, the residue was column-chromatographed on Aluminum oxide 90. Elution with benzene gave dihydrolanosteryl acetate (2.5 g) as a solid. Further elution with methylene chloride gave a solid (4.0 g) which was recrystallized from MeOH to give colorless needles of 3β-acetoxy-24ξ,25-epoxylanost-8-ene (**2**),[14] mp 195—196.5°. MS *m/e*: 484 (M^+), 469, 451, 409 (M^+-75, base peak), 391. PMR δ (ppm): 0.70 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 1.25 and 1.29 (each 3H, s, 26 and 27-CH_3), 2.03 (3H, s, 3β-$OCOCH_3$), 2.68 (1H, t, 24-H, J=6.5 Hz), 4.36—4.60 (1H, m, 3α-H).

Boron Trifluoride-Catalyzed Rearrangement of 3β-Acetoxy-24ξ,25-epoxylanost-8-ene (**2**)——Boron trifluoride–ether complex (1.2 g) was added to a solution of **2** (1.5 g) in anhydrous benzene (100 ml). The mixture was allowed to stand for 1 hr at 20°, then water was added to the reaction mixture. The usual work-up of the separated organic phase afforded a yellow oil, which was column-chromatographed on silica gel (150 g).

(i) Elution with *n*-hexane–benzene (1:1) gave a solid (0.3 g) with *Rf* 0.23 which was recrystallized from MeOH to give colorless needles, 3β-acetoxy-24,24-dimethyl-26,27-dinorlanost-8-en-25-al (**4**), mp 184° (lit.[5] mp 121—123°). MS *m/e*: 484 (M^+), 469, 409 (M^+-75, base peak). IR ν_{max}^{KBr} cm^{-1}: 2700 (aldehyde C–H), 1738 (3β-$OCOCH_3$), 1725 (aldehyde C=O). PMR δ (ppm): 0.69 (3H, s, 18-CH_3), 1.01 (3H, s, 19-CH_3), 1.06 (6H, s, 24,24-CH_3), 2.03 (3H, s, 3β-$OCOCH_3$), 4.40—4.64 (1H, m, 3α-H), 9.37 (1H, s, CHO).

(ii) Further elution with benzene gave a solid (1.0 g) with *Rf* 0.14 which was recrystallized from MeOH to give colorless needles, 3β-acetoxylanost-8-en-24-one (**3**), mp 145—147° (lit.[5] 121—123°). MS *m/e*: 484 (M^+), 469, 407 (M^+-75, base peak). IR ν_{max}^{KBr} cm^{-1}: 1710 (24 C=O), 1738 (3β-$OCOCH_3$). PMR δ (ppm): 0.68 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 1.06 (6H, d, 26 and 27-CH_3, *J*=6.5 Hz), 2.00 (3H, s, 3β-$OCOCH_3$), 2.30—2.70 (3H, m, 23-CH_2- and 25-H), 4.40—4.64 (1H, m, 3α-H).

Dehydrogenation of 3β-Acetoxylanost-8-en-24-one (**3**) **with Selenium Dioxide**——Selenium dioxide (0.5 g) was added to a solution of **3** (100 mg) in EtOH (100 ml) and the mixture was refluxed for 3 days. After cooling, the resulting black selenium was removed by filtration. After usual work-up of the filtrate, the residue was column-chromatographed on silica gel (20 g). Elution with benzene gave recovered **3** as a solid (20 mg). Further elution with benzene–methylene chloride (99:1) and recrystallization from MeOH gave 22-*trans*-3β-acetoxylanosta-8,22-dien-24-one (**5**) (55 mg) as colorless needles, mp 170—171°. *Anal.* Calcd for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.91; H, 10.21. MS *m/e*: 482 (M^+), 467, 407 (M^+-75, base peak). IR ν_{max}^{KBr} cm^{-1}: 1731 (3β-$OCOCH_3$), 1690 (24 C=O). UV λ_{max}^{MeOH} nm (ε): 235 (11470). PMR δ (ppm): 0.74 (3H, s, 18-CH_3), 1.01 (3H, s, 19-CH_3), 1.10 (6H, d, 26 and 27-CH_3, *J*=6.5 Hz), 2.03 (3H, s, 3β-$OCOCH_3$), 2.85 (1H, h, 25-H), 4.38—4.62 (1H, m, 3α-H), 6.72 (1H, q, 22-H, *J*=7.5 and 15 Hz), 6.06 (1H, d, 23-H, *J*=15 Hz).

Oxidation of 22-*trans*-3β-Acetoxylanosta-8,22-dien-24-one (**5**) **with Potassium Permanganate**——$KMnO_4$ (70 mg) was added slowly (over 50 min) to a stirred solution of **5** (100 mg) in distilled acetone (130 ml) and stirring was continued for 2 hr at room temperature. The crude yellow oil obtained from the reaction was column-chromatographed on silica gel (15 g). Elution with benzene and recrystallization from MeOH gave 3β-acetoxy-23,24,25,26,27-pentanorlanost-8-en-22-al (**6**) (60 mg) as colorless needles, mp 105—106° (lit.[5] 110—111°). MS *m/e*: 414 (M^+), 399, 339 (M^+-75, base peak), 356. PMR δ (ppm): 0.75 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 1.09 (3H, d, 21-CH_3, *J*=6.5 Hz), 2.01 (3H, s, 3β-$OCOCH_3$), 4.36—4.60 (1H, m, 3α-H), 9.58 (1H, d, 22-CHO, *J*=3 Hz). Further elution with methylene chloride–acetone (8:2) and recrystallization from acetone gave 3β-acetoxy-23,24,25,26,27-pentanorlanost-8-en-22-oic acid (**7**) (12 mg) as colorless needles, mp 245—246° (lit.[4] 247—249°). MS *m/e*: 430 (M^+), 415, 355 (M^+-75, base peak). PMR δ (ppm): 0.72 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 1.22 (3H, d, 21-CH_3, *J*=6.5 Hz), 2.01 (3H, s, 3β-$OCOCH_3$), 4.36—4.60 (1H, m, 3α-H).

3β-Acetoxy-22,23,24,25,26,27-hexanorlanosta-8,20-diene (**10**)——$Pb(OAc)_4$ (1.8 g), $Cu(OAc)_2$ (0.3 g) and pyridine (0.2 ml) were added to a solution of **7** (1.0 g) in anhydrous benzene (200 ml). The reaction mixture was refluxed for 2 hr. After cooling, an inorganic salt was filtered off, and the filtrate was extracted with benzene to give a crude product, which was column-chromatographed on silica gel (50 g). Elution with benzene gave a solid (0.42 g) which was recrystallized from MeOH to give colorless needles of **10**, mp 119—120°. *Anal.* Calcd for $C_{26}H_{40}O_2$: C, 81.20; H, 10.48. Found: C, 80.99; H, 10.18. MS *m/e*: 384 (M^+), 369, 309 (M^+-75, base peak). PMR δ (ppm): 0.63 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 4.38—4.62 (1H, m, 3α-H), 4.80—5.10 (2H, m, 21-H_2), 5.60—5.95 (1H, m, 20-H).

22,23,24,25,26,27-Hexanorlanost-8-en-3β-ol (**11**)——A solution of **10** (50 mg) in MeOH (100 ml) was hydrogenated in the presence of 5% Pd–C (150 mg) under an H_2 atmosphere at room temperature until no more hydrogen was absorbed. After removal of the catalyst by filtration, the filtrate was concentrated and the residue was hydrolyzed with 10% methanolic KOH. After usual work-up, the residue was recrystallized from MeOH to give colorless needles of **11** (35 mg), mp 160—161°. *Anal.* Calcd for $C_{24}H_{40}O$: C, 83.65; H, 11.70. Found: C, 83.23; H, 11.72. MS *m/e*: 344 (M^+), 329 (M^+-15, base peak), 311. PMR δ (ppm): 0.63 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 3.16—3.40 (1H, m, 3α-H).

3β-Acetoxy-21,22,23,24,25,26,27-heptanorlanost-8-en-20-oic Acid (**12**)——K_2CO_3 (0.48 g) was added to a solution of **10** (0.48 g) in *tert*-butanol (48 ml), then a mixture of $NaIO_4$ (1.09 g) and $KMnO_4$ (0.07 g) in water (40 ml) was added over 30 min and the whole was stirred for 20 hr at room temperature. To destroy excess oxidizing agent, 10% $NaHSO_3$ was added to the reaction mixture until decolorization occurred. After removal of *tert*-butanol from the mixture *in vacuo*, the concentrated solution was acidified with dil. HCl. The usual work-up afforded a yellow oil which was column-chromatographed on silica gel (50 g). Elution with methylene chloride gave a solid (0.26 g) which was recrystallized from MeOH to give colorless needles of **12**, mp 238—240°. *Anal.* Calcd for $C_{25}H_{38}O_4$: C, 74.59; H, 9.52. Found: C, 74.71; H, 9.64. MS *m/e*: 402 (M^+), 387, 327 (M^+-75, base peak). PMR δ (ppm): 0.71 (3H, s, 18-CH_3), 0.97 (3H, s, 19-CH_3), 2.00 (3H, s, 3β-$OCOCH_3$), 2.58—2.80 (1H, m, 17α-H), 4.36—4.60 (1H, m, 3α-H).

3β-Acetoxy-20-chloro-21,22,23,24,25,26,27-heptanorlanost-8-ene (**13**)——A solution of **12** (402 mg, 1 mmol) in tetrahydrofuran (5 ml) was stirred with ethyl chloroformate (130 mg, 1.2 mmol) and triethylamine (120 mg, 1.2 mmol) at 0° for 20 min. To this was added a solution of $NaBH_4$ (380 mg, 10 mmol) in water (2 ml) at 0°, and stirring was continued for 2 hr at 0°. The usual work-up afforded the crystalline alcohol. This crude alcohol was dissolved in pyridine (20 ml), then $POCl_3$ (6 ml) was added, and the mixture was refluxed for 12 hr. After usual work-up, the brown residue was column-chromatographed on silica gel (40 g). Elution with benzene and recrystallization from MeOH gave **13** (215 mg) as colorless needles, mp 123—124°. *Anal.* Calcd for $C_{25}H_{39}ClO_2$: C, 73.77; H, 9.66. Found: C, 73.50; H, 9.50. MS *m/e*: 406 (M^+ for ^{35}Cl-compound), 391, 331 (M^+-75, base peak). PMR δ (ppm): 0.69 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 2.01 (3H, s, 3β-$OCOCH_3$), 3.40—3.60 (2H, m, 20-CH_2-), 4.38—4.62 (1H, m, 3α-H).

21,22,23,24,25,26,27-Heptanorlanost-8-en-3β-ol (14)——$LiAlH_4$ (300 mg) was added to a solution of the 20-chloro compound (13) (150 mg) in anhydrous dioxane (20 ml) and the mixture was refluxed for 12 hr. After usual work-up, the residue was column-chromatographed on silica gel (10 g). Elution with methylene chloride and recrystallization from MeOH gave **14** (85 mg) as colorless needles, mp 159—162°. *Anal.* Calcd for $C_{23}H_{38}O$: C, 83.57; H, 11.59. Found: C, 83.61; H, 11.80. MS *m/e*: 330 (M^+), 315 (M^+-15, base peak), 297. PMR δ (ppm): 0.61 (3H, s, 18-CH_3), 0.86 (3H, d, 20-CH_3, $J=6.5$ Hz), 3.18—3.42 (1H, m, 3α-H).

3β-Acetoxy-20,21,22,23,24,25,26,27-octanorlanosta-8,16-diene (15)——$Pb(OAc)_4$ (0.45 g), $Cu(OAc)_2$ (0.07 g) and pyridine (0.05 ml) were added to a solution of **12** (0.25 g) in anhydrous benzene (25 ml), and the mixture was refluxed for 2 hr. After cooling, an inorganic salt was filtered off, and the filtrate was extracted with benzene to give a crude product, which was column-chromatographed on silica gel (15 g). Elution with benzene gave a solid (0.2 g) which was recrystallized from MeOH to give colorless needles of **15**, mp 152—154°. *Anal.* Calcd for $C_{24}H_{36}O_2$: C, 80.85; H, 10.18. Found: C, 81.15; H, 10.15. MS *m/e*: 356 (M^+), 341 (M^+-15, base peak), 281. PMR δ (ppm): 0.72 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 4.38—4.62 (1H, m, 3α-H), 5.50—5.80 (2H, m, 16,17-H_2).

20,21,22,23,24,25,26,27-Octanorlanost-8-en-3β-ol (16)——A solution of **15** (50 mg) in MeOH (30 ml) was hydrogenated in the presence of 5% Pd-C (50 mg) under an H_2 atmosphere at room temperature. After removal of the catalyst by filtration, the filtrate was concentrated and the residue was hydrolyzed with 10% methanolic KOH. After usual work-up, the residue was recrystallized from MeOH to give colorless needles of **16** (36 mg), mp 161—162°. *Anal.* Calcd for $C_{22}H_{36}O$: C, 83.48; H, 11.47. Found: C, 83.13; H, 11.28. MS *m/e*: 316 (M^+), 301, 283 (M^+-33, base peak). PMR δ (ppm): 0.75 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 3.20—3.44 (1H, m, 3α-H).

3β-Acetoxy-24,24-dimethyl-25-hydroxy-26,27-dinorlanost-8-ene (17)——$NaBH_4$ (100 mg) was added to a solution of **4** (100 mg) in MeOH (50 ml) and the mixture was stirred at room temperature for 12 hr. After usual work-up, the residue was recrystallized from MeOH to give colorless needles of **17** (76 mg), mp 208—209°. *Anal.* Calcd for $C_{32}H_{54}O_3$: C, 78.96; H, 11.18. Found: C, 79.13; H, 11.06. MS *m/e*: 486 (M^+), 471, 411 (M^+-75, base peak). PMR δ (ppm): 0.69 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 3.28 (2H, broad singlet, 25-CH_2-), 4.38—4.62 (1H, m, 3α-H).

Treatment of 3β-Acetoxy-24,24-dimethyl-25-hydroxy-26,27-dinorlanost-8-ene (17) with Lead Tetraacetate——Lead tetraacetate (300 mg) was added to a solution of **17** (100 mg) in anhydrous benzene (50 ml). The mixture was refluxed for 12 hr and extracted with benzene to give a crude product which was column-chromatographed on silica gel (20 g). Elution with benzene gave a solid (40 mg) which was recrystallized from MeOH to give colorless needles of 3β-acetoxy-23-norlanosta-8,24-diene (**18b**), mp 172—173° (lit.[4]) 164—165°). MS *m/e*: 454 (M^+), 439, 379, 69 (base peak). PMR δ (ppm): 0.70 (3H, s, 18-CH_3), 1.01 (3H, s, 19-CH_3), 1.60 (3H, s, 27-CH_3), 1.71 (3H, s, 26-CH_3), 2.03 (3H, s, 3β-$OCOCH_3$), 4.42—4.66 (1H, m, 3α-H), 5.16 (1H, t, 24-H, $J=6.5$ Hz).

18b was hydrolyzed with 10% methanolic KOH to give 23-norlanosta-8,24-dien-3β-ol (**18a**), mp 136—137°. *Anal.* Calcd for $C_{29}H_{48}O$: C, 84.40; H, 11.72. Found: C, 84.88; H, 11.67. MS *m/e*: 412 (M^+), 397 (M^+-15, base peak), 379, 69. PMR δ (ppm): 0.71 (3H, s, 18-CH_3), 1.63 (3H, s, 27-CH_3), 1.72 (3H, s, 26-CH_3), 3.15—3.39 (1H, m, 3α-H), 5.16 (1H, t, 24-H).

Wittig Reaction of 3β-Acetoxylanost-8-en-24-one (3)——NaH (50%, 0.26 g) was added to a suspension of ethyl triphenylphosphonium bromide (1.53 g) in dimethylsulfoxide (3.4 ml). To this solution was added the ketone (3) (0.34 g) in anhydrous benzene (2.4 ml) and the whole was heated with stirring at 70° for 4 hr. The reaction mixture was extracted with benzene, and the residue from the extract was column-chromatographed on silica gel (30 g). Elution with benzene gave a solid (0.26 g) which was recrystallized from MeOH to give colorless granules of 24-ethylidene-lanost-8-en-3β-ol (**19**) (0.26 g), mp 179.5—180°. *Anal.* Calcd for $C_{32}H_{54}O$: C, 84.51; H, 11.97. Found: C, 84.16; H, 11.77. MS *m/e*: 454 (M^+), 439 (M^+-15, base peak), 421. PMR δ (ppm): 0.60 (3H, s, 18-CH_3), 1.58 (3H, d, 29-CH_3, $J=6$ Hz), 2.84 (1H, h, 25-H, $J=6$ Hz), 5.12 (1H, q, 28-H, $J=6$ Hz).

Oxidation of Lanosteryl Acetate (1b)——**1b**[31]) (7.5 g) was oxidized by the procedure of Habermehl *et al.*[4]) The usual work-up of the reaction mixture afforded a yellow oil which was column-chromatographed on silica gel (200 g). Elution with benzene gave a solid (2.6 g), which was a mixture of dihydrolanosteryl acetate and **1b**.

(i) Elution with benzene gave a solid (1.6 g), which was recrystallized from MeOH to give colorless needles of 3β-acetoxy-25-hydroxylanost-8-en-24-one (**20**), mp 129—131°. *Anal.* Calcd for $C_{32}H_{52}O_4$: C, 76.75;

H, 10.47. Found: C, 76.78; H, 10.30. MS *m/e*: 500 (M^+), 485, 425 (M^+-75, base peak). PMR δ (ppm): 0.68 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 1.36 (6H, s, 26 and 27-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 4.38—4.62 (1H, m, 3α-H).

(ii) Further elution with methylene chloride gave a solid (1.0 g), which was recrystallized from MeOH to give colorless needles of 3β-acetoxy-25,26,27-trinorlanost-8-en-24-oic acid (**21**), mp 218—220° (lit.[4] 214—216°). MS *m/e*: 458 (M^+), 443, 383 (M^+-75, base peak). PMR δ (ppm): 0.68 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 4.38—4.62 (1H, m, 3α-H).

3β-Acetoxy-24ξ,25-dihydroxylanost-8-ene (**22**)——$NaBH_4$ (3.5 g) was added to a solution of **20** (3.5 g) in MeOH (500 ml) and the mixture was stirred at room temperature for 12 hr. After usual work-up, the residue was recrystallized from MeOH to give colorless needles of **22** (3.2 g), mp 183—185°. *Anal.* Calcd for $C_{32}H_{54}O_4$: C, 76.44; H, 10.83. Found: C, 76.65; H, 10.83. MS *m/e*: 502 (M^+), 487, 469, 451, 409 (M^+-93, base peak). PMR δ (ppm): 0.70 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 1.18 (6H, s and s, 26 and 27-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 3.31 (1H, t, 24-H, $J=6$ Hz), 4.40—4.64 (1H, m, 3α-H).

3β-Acetoxy-25,26,27-trinorlanost-8-en-24-al (**23**)——$HIO_4 \cdot 2H_2O$ (3.0 g) in water (5 ml) was added to a solution of **22** (3.0 g) in dioxane (100 ml) and the mixture was stirred at room temperature for 2hr. After usual work-up, the residue was column-chromatographed on silica gel (50 g). Elution with benzene gave a solid (2.0 g) which was recrystallized from MeOH to give colorless needles of **23**, mp 143—144° (lit.[20] 144—145°). MS *m/e*: 442 (M^+), 427, 367 (M^+-75, base peak). PMR δ (ppm): 0.70 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 4.38—4.62 (1H, m, 3α-H), 9.76 (1H, t, 24-CHO, $J=2$ Hz).

3β-Acetoxy-24-hydroxy-25,26,27-trinorlanost-8-ene (**24**)——$NaBH_4$ (1.0 g) was added to a solution of **23** (1.0 g) in MeOH (200 ml) and the mixture was stirred at room temperature for 12 hr. After usual work-up, the residue was recrystallized from MeOH to give colorless needles of **24**, mp 169—171°. *Anal.* Calcd for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 77.88; H, 10.84. MS *m/e*: 444 (M^+), 429, 369 (M^+-75, base peak). PMR δ (ppm): 0.68 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 3.52—3.83 (2H, m, 24-CH_2-), 4.42—4.68 (1H, m, 3α-H).

3β-Acetoxy-24-chloro-25,26,27-trinorlanost-8-ene (**25**)——Phosphoryl chloride (3 ml) was added to a solution of **24** (0.2 g) in pyridine (10 ml) and the mixture was refluxed for 12 hr. After usual work-up, the brown residue was column-chromatographed on silica gel (10 g). Elution with benzene gave a solid (0.11 g), which was recrystallized from MeOH to give colorless needles of **25**, mp 167°. *Anal.* Calcd for $C_{29}H_{47}ClO_2$: C, 75.20; H, 10.23. Found: C, 75.27; H, 10.17. MS *m/e*: 462 (M^+ for ^{35}Cl-compound), 447 (M^+-15, base peak), 387. PMR δ (ppm): 0.69 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 3.38—3.68 (2H, m, 24-CH_2-), 4.38—4.62 (1H, m, 3α-H).

25,26,27-Trinorlanost-8-en-3β-ol (**26**)——$LiAlH_4$ (0.1 g) was added to a solution of **25** (0.1 g) in anhydrous dioxane (20 ml) and the mixture was refluxed for 12 hr. After usual work-up, the residue was column-chromatographed on silica gel (10 g). Elution with methylene chloride gave a solid (85 mg), which was recrystallized from MeOH to give colorless needles of **26**, mp 169—170° (lit.[18] 170—175°). *Anal.* Calcd for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 84.36; H, 11.88. MS *m/e*: 386 (M^+), 371 (M^+-15, base peak), 353. PMR δ (ppm): 0.69 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 3.11—3.35 (1H, m, 3α-H).

Wittig Reaction of 3β-Acetoxy-25,26,27-trinorlanost-8-en-24-al (**23**)——a) A solution of *n*-butyl lithium (14%, 1.2 ml) was added to a suspension of methyl triphenylphosphonium bromide (1.2 g) in anhydrous benzene (20 ml) and the mixture was stirred at room temperature for 10 min. A solution of the aldehyde (**23**) (0.5 g) in anhydrous benzene (10 ml) was then added, and the mixture was stirred for 5 hr. After extraction with benzene, the residue was column-chromatographed on silica gel (50 g). Elution with benzene gave a solid (0.23 g), which was recrystallized from MeOH to give colorless needles of 3β-acetoxy-26,27-dinorlanosta-8,24-diene (**27b**), mp 143°. *Anal.* Calcd for $C_{30}H_{48}O_2$: C, 81.76; H, 10.98. Found: C, 82.12; H, 10.98. MS *m/e*: 440 (M^+), 425 (M^+-15, base peak), 365. PMR δ (ppm): 0.70 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 2.00 (3H, s, 3β-$OCOCH_3$), 4.38—4.62 (1H, m, 3α-H), 4.80—5.10 (2H, m, 25-H_2), 5.60—6.00 (1H, m, 24-H). Further elution with benzene gave a solid (0.10 g), which was recrystallized from MeOH to give colorless needles of 26,27-dinorlanosta-8,24-dien-3β-ol (**27a**), mp 133—134°. *Anal.* Calcd for $C_{28}H_{46}O$: C, 84.35; H, 11.63. Found: C, 84.18; H, 11.56. MS *m/e*: 398 (M^+), 383 (M^+-15, base peak), 365. PMR δ (ppm): 0.68 (3H, s, 18-CH_3), 0.98 (3H, s,19-CH_3), 3.00—3.24 (1H, m, 3α-H), 4.80—5.10 (2H, m, 25-H_2), 5.60—6.00 (1H, m, 24-H).

b) Starting from ethyl triphenylphosphonium bromide (1.2 g) and the aldehyde (**23**) (0.5 g), 27-norlanosta-8,24-dien-3β-ol and its acetate (*cis* and *trans*, 3: 1 each) were obtained in 21% and 39% yields in the manner described above (GLC analysis showed that the *cis* isomer has a slightly longer retention time than the *trans* isomer). The mixture of 3β-ol compounds (98 mg) was column-chromatographed on 10% $AgNO_3$-impregnated silica gel (15 g). Elution with benzene gave only the *trans* isomer (90 mg), which was recrystallized from MeOH to give colorless needles of 24-*trans*-27-norlanosta-8,24-dien-3β-ol (**29**), mp 148°. *Anal.* Calcd for $C_{29}H_{48}O$: C, 84.40; H, 11.72. Found: C, 84.73; H, 11.72. MS *m/e*: 412 (M^+), 397 (M^+-15, base peak), 379. PMR δ (ppm): 0.68 (3H, s, 18-CH_3), 0.98 (3H, s, 19-CH_3), 1.65 (3H, double doublet, 26-CH_3, $J=4.5$ and 1.5 Hz), 3.06—3.30 (1H, m, 3α-H), 5.20—5.60 (2H, m, 24 and 25-H). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 965.

Hydrogenation of 26,27-Dinorlanosta-8,24-dien-3β-ol (**27a**)——A solution of **27a** (80 mg) in MeOH (100 ml) was hydrogenated in the presence of 5% Pd–C (150 mg) at room temperature. Recrystallization of the product from MeOH gave colorless needles of 26,27-dinorlanost-8-en-3β-ol (**28**) (56 mg), mp 149—151°. *Anal.* Calcd for $C_{28}H_{48}O$: C, 83.93; H, 12.08. Found: C, 83.69; H, 11.87. MS *m/e*: 400 (M^+), 385 (M^+-15, base peak), 367. PMR δ (ppm): 0.69 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 3.14—3.38 (1H, m, 3α-H).

Hydrogenation of 27-Norlanosta-8,24-dien-3β-ol (29)——Starting from **29** (80 mg), 27-norlanost-8-en-3β-ol (**30**) was prepared in the manner described above. Recrystallization from MeOH gave colorless needles of **30**, mp 142—143°. *Anal.* Calcd for $C_{29}H_{50}O$: C, 83.99; H, 12.15. Found: C, 83.70; H, 11.87. MS *m/e*: 414 (M^+), 399 (M^+-15, base peak), 381. PMR δ (ppm): 0.68 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 3.00—3.24 (1H, m, 3α-H).

3β-Acetoxy-24,25,26,27-tetranorlanosta-8,22-diene (31)——**31** was prepared from **21** by the procedure of Poyser *et al.*[23] Recrystallization of the product from MeOH gave colorless needles, mp 148—149° (lit.[23] 147—148°). MS *m/e*: 412 (M^+), 397 (M^+-15, base peak), 337. PMR δ (ppm): 0.71 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 1.01 (3H, d, 21-CH_3, $J=7$ Hz), 2.03 (3H, s, 3β-$OCOCH_3$), 4.38—4.62 (1H, m, 3α-H), 4.80 (1H, q, 23-H, $J=2$ and 10 Hz), 4.90 (1H, q, 23-H, $J=2$ and 17 Hz), 5.70 (1H, octet, 22-H, $J=10$, 17 and 8 Hz).

24,25,26,27-Tetranorlanost-8-en-3β-ol (32)——A solution of **31** (80 mg) in MeOH (100 ml) was hydrogenated in the presence of 5% Pd–C (150 mg) under an H_2 atmosphere at room temperature. After removal of the catalyst by filtration, the filtrate was concentrated and the residue was hydrolyzed with 10% methanolic KOH. After usual work-up, the residue was recrystallized from MeOH to give colorless needles of **32** (52 mg), mp 156°. *Anal.* Calcd for $C_{26}H_{44}O$: C, 83.80; H, 11.90. Found: C, 84.16; H, 11.88. MS *m/e*: 372 (M^+), 358 (M^+-15, base peak), 340. PMR δ (ppm): 0.69 (3H, s, 18-CH_3), 1.00 (3H, s, 19-CH_3), 3.12—3.36 (1H, m, 3α-H).

Isomerization of (20*S*)-3β-Acetoxy-23,24,25,26,27-pentanorlanost-8-en-22-al (6)——50% H_2SO_4 (2 ml) was added to a solution of **6** (0.2 g) in MeOH (100 ml) and the mixture was refluxed for 30 min. After usual work-up, the crude product in Ac_2O (2 ml) and pyridine (4 ml) was allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water and a white solid thus obtained was column-chromatographed on silica gel (15 g). Elution with benzene gave the (20*R*)-aldehyde (**33**) and (20*S*)-aldehyde (**6**) as a 1 : 1 mixture. (20*S*)-aldehyde (**6**); PMR δ (ppm): 0.75 (18-CH_3), 9.58 (–CHO, d, $J=3$ Hz), (20*R*)-aldehyde (**33**); PMR δ (ppm): 0.72 (18-CH_3), 9.50 (–CHO, d, $J=5$ Hz).

Wittig Reaction of (20*R*,*S*)-3β-Acetoxy-23,24,25,26,27-pentanorlanost-8-en-22-al (6 and 33)——A solution of *n*-butyl lithium (14%, 0.6 ml) was added to a suspension of isoamyl triphenylphosphonium iodide (0.6 g) in anhydrous benzene (10 ml) and the mixture was stirred at room temperature for 10 min. A solution of the aldehyde mixture (**6** and **33**) (0.2 g) in anhydrous benzene (5 ml) was then added, and the mixture was stirred at room temperature for 5 hr. After extraction with benzene, the residue from the extract was column-chromatographed on silica gel (30 g). Elution with benzene (fr. 1 and 2) gave a solid (41 mg) which was recrystallized from MeOH to give colorless needles of (20*R*,*S*)-3β-acetoxylanosta-8,22-diene (**34b** and **35b**). Further elution with benzene (fr. 4 and 5) gave a solid (48 mg) which was recrystallized from MeOH to give colorless granules of (20*S*)-lanosta-8,22-dien-3β-ol (**35a**), mp 151—152°. *Anal.* Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.15; H, 12.22. MS *m/e*: 426 (M^+), 411, 393, 111 (81%), 69 (base peak). PMR δ (ppm): 0.62 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 3.13—3.37 (1H, m, 3α-H), 5.12—5.28 (2H, m, 22 and 23-H). Further elution with benzene (fr. 7 to 10) gave a solid (49 mg) which was recrystallized from MeOH to give colorless needles of (20*R*)-lanosta-8,22-dien-3β-ol (**34a**), mp 147—148°. *Anal.* Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.01; H, 11.86. MS *m/e*: 426 (M^+), 411, 393, 111 (base peak), 69 (84%). PMR δ (ppm): 0.74 (3H, s, 18-CH_3), 0.99 (3H, s, 19-CH_3), 3.13—3.37 (1H, m, 3α-H), 5.12—5.26 (2H, m, 22 and 23-H).

(20*S*)-Lanost-8-en-3β-ol (20-Iso-24-dihydrolanosterol) (37)——A solution of **35a** (25 mg) in MeOH (50 ml) was hydrogenated in the presence of 5% Pd–C (50 mg) under an H_2 atmosphere at room temperature. After removal of the catalyst by filtration, the filtrate was concentrated and the residue was recrystallized from MeOH to give colorless needles of **37** (15 mg), mp 171.5—172°. *Anal.* Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.23. Found: C, 83.65; H, 12.23. MS *m/e*: 428 (M^+), 413 (M^+-15, base peak), 395. PMR δ (ppm in $CDCl_3$): 0.68 (3H, s, 18-CH_3), 0.81 (3H, s, 4β-CH_3), 0.85 (6H, d, 26 and 27-CH_3), 0.87 (3H, s, 14-CH_3), 0.98 (3H, s, 4α-CH_3), 0.99 (3H, s, 19-CH_3), 3.13—3.37 (1H, m, 3α-H). PMR δ (ppm in C_6D_6): 0.79 (3H, s, 4β-CH_3), 0.82 (3H, s, 18-CH_3), 0.93 (6H, d, 26 and 27-CH_3), 0.95 (6H, s, 19 and 4α-CH_3), 1.01 (3H, s, 14-CH_3), 2.92—3.20 (1H, m, 3α-H). $[\alpha]_D^{19}$: +33° ($c=1.0$, $CHCl_3$).

(20*R*)-Lanost-8-en-3β-ol (20-Normal 24-Dihydrolanosterol) (36)——A solution of **34a** (25 mg) in MeOH (50 ml) was hydrogenated in the presence of 5% Pd–C (50 mg) under an H_2 atmosphere at room temperature. Recrystallization from MeOH gave colorless needles of **36** (16 mg), mp 146—146.5°; this product was identical with an authentic sample (mp 146°). PMR δ (ppm in C_6D_6): 0.79 (3H, s, 4β-CH_3), 0.84 (3H, s, 18-CH_3), 0.93 (6H, d, 26 and 27-CH_3), 0.95 (6H, s, 19 and 4α-CH_3), 1.03 (3H, s, 14-CH_3), 2.92—3.20 (1H, m, 3α-H).

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