The Synthesis and Configuration of Some 32-Norlanosterol Derivatives

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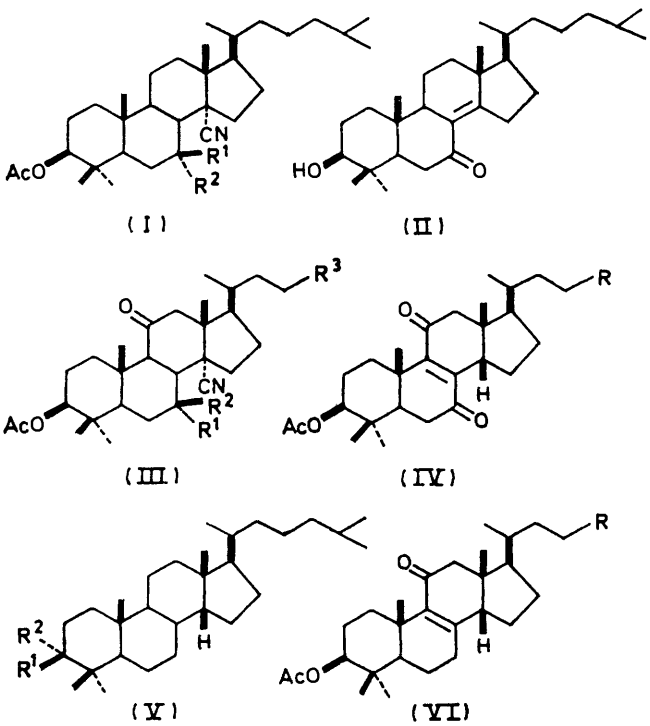
Methods are described for the removal of carbon atom 32 from certain 32-functionalised lanosterol derivatives. It is shown unequivocally that the compounds thus obtained have the unnatural 14β-configuration.

In the preceding paper the synthesis of various 32-functionalised lanostane derivatives was described.[1] Those compounds possessing a nitrile function at C-32 appeared well suited for the synthesis of 32-norlanostenes (4,4-dimethylcholestenes). This work parallels that of Fried and his co-workers, who have described a variety of methods for the conversion of lanost-7-ene-3β,32-diol and 3β-hydroxylanost-7-en-32-al into 32-norlanostenes.[2]

Oxidation of 3β-acetoxy-7α-hydroxylanostan-32-onitrile [1] (I; R^1 = H, R^2 = OH) with Kiliani's chromic acid gave 3β-acetoxy-7-oxolanostan-32-onitrile (I;



R^1R^2 = O). The nitrile function was smoothly eliminated by treatment with potassium t-butoxide in t-butyl alcohol to give 3β-hydroxy-4,4-dimethylcholest-8(14)-en-7-one (II). Wolff–Kishner reduction of the ketone (II), even under strictly anhydrous conditions,[3] gave, after reacetylation, a mixture of isomeric 3β-acetoxy-4,4-dimethylcholestenes, the expected 3β-acetoxy-4,4-dimethylcholest-7-ene being present to the extent of *ca.* 40% (n.m.r. spectroscopy). Isomerisation of this mixture over platinum allowed the isolation of pure 3β-acetoxy-4,4-dimethylcholest-8(14)-ene, but the overall yield was low.

To avoid this difficulty, the starting material for the foregoing synthesis was modified by the introduction of an 11-ketone function. However, the 4,4-dimethylcholestenes thus obtained were shown to possess the unnatural 14β-configuration. It is well established, that, in general *cis*-8-methylhydrindanes are more stable than their *trans*-isomers.[4] In particular, there are a number of examples of the isomerisation of Δ^8-11-oxo-14α-steroids (*trans*-CD-ring junction) to the corresponding 14β-isomers (*cis*-CD-ring junction).[5]

Oxidation of 3β-acetoxy-7α-hydroxy-11-oxolanostan-32-onitrile [1] (III; R^1 = OH, R^2 = H, R^3 = Bu^i) gave the 7,11-dione (III; R^1R^2 = O, R^3 = Bu^i), which when treated with potassium t-butoxide in t-butyl alcohol afforded, after reacetylation, 3β-acetoxy-4,4-dimethyl-14β-cholest-8-ene-7,11-dione (IV; R = Bu^i). The assignment of the 14β-configuration to the latter followed from its conversion into 4,4-dimethyl-14β-cholestan-3β-ol (V; R^1 = OH, R^2 = H) by treatment with zinc in glacial acetic acid and Wolff–Kishner reduction of the resulting 3β-acetoxy-4,4-dimethyl-14β-cholestane-7,11-dione. The physical constants of compound (V; R^1 = OH, R^2 = H) and the derived 3β-acetate (V; R^1 = OAc, R^2 = H) and 3-ketone (V; R^1R^2 = O) differed from those for the corresponding known 14α-compounds (see Table).[6-8]

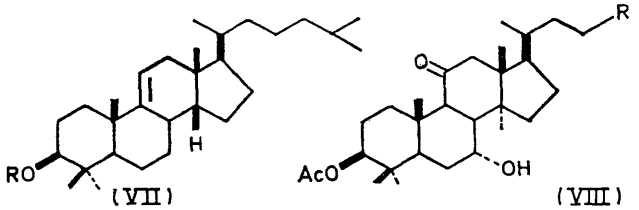
Physical constants of some 4,4-dimethyl-14α- and 14β-cholestanes

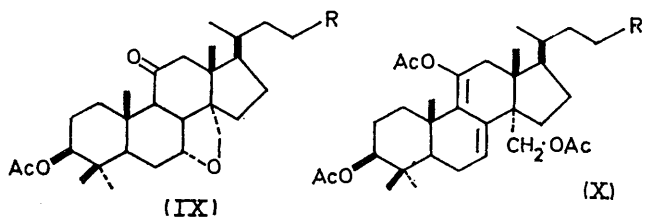
	14β-Isomer		14α-Isomer		
	M.p. (°C)	$[\alpha]_D$	M.p. (°C)	$[\alpha]_D$	Ref.
3β-Hydroxy-4,4-dimethylcholestane	173—174	+43·0°	157—158	+14°	6, 7
3β-Acetoxy-4,4-dimethylcholestane	87—88	+51·8	138—139	+19	7
4,4-Dimethylcholestan-3-one	78—79	+32·9	100—101	+8	8

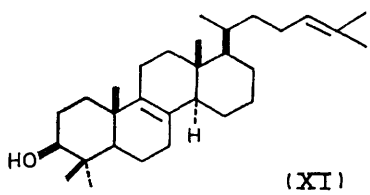
[1] D. H. R. Barton, P. L. Batten, T. J. Bentley, R. B. Boar, R. W. Draper, D. F. McGhie, preceding paper.
[2] J. Fried and N. W. Brown, *Tetrahedron Letters*, 1967, 925.
[3] J. F. Cavalla, J. F. McGhie, and M. K. Pradhan, *J. Chem. Soc.*, 1951, 3142; D. H. R. Barton, J. S. Fawcett, and B. R. Thomas, *J. Chem. Soc.*, 1951, 3147; D. H. R. Barton, D. A. J. Ives, and B. R. Thomas, *J. Chem. Soc.*, 1955, 2056.
[4] M. Hanack, 'Conformation Theory,' Academic Press, New York, 1965, p. 176 *et seq.*
[5] C. Djerassi, W. Frick, G. Rosenkranz, and F. Sondheimer, *J. Amer. Chem. Soc.*, 1953, **75**, 3496; ref. 4, pp. 223—225; A. S. Dreiding, *Chem. and Ind.*, 1954, 992.
[6] N. W. Attwater, *J. Amer. Chem. Soc.*, 1960, **82**, 2847.
[7] Y. Mazur and F. Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.
[8] J. L. Beton, T. G. Halsall, E. R. H. Jones, and P. C. Phillips, *J. Chem. Soc.*, 1957, 753.

The n.m.r. spectra of compounds (V; R^1 = OAc, R^2 = H) and (V; R^1R^2 = O) provided additional evidence for their 14β-configuration. In both of these compounds the signal for the 13-methyl group appeared at τ 9·02, whereas calculations [9] suggest that in the corresponding 14α-compounds the signals would be at τ 9·36 and 9·33, respectively.

Reduction of the diketone (IV; R = Bu^i) with sodium borohydride gave 3β-acetoxy-7β-hydroxy-4,4-dimethyl-14β-cholest-8-en-11-one, which was further reduced with zinc in glacial acetic acid to give 3β-acetoxy-4,4-dimethyl-14β-cholest-8-en-11-one (VI; R = Bu^i). Wolff–Kishner reduction of (VI; R = Bu^i), in contrast to that of compound (II), above, proceeded cleanly and gave 4,4-dimethyl-14β-cholest-9(11)-en-3β-ol (VII; R = H) in high yield. The n.m.r. spectrum of the acetate (VII; R = Ac) showed a signal at τ 4·85 attributable to the vinylic proton at C-11. Further proof of the structure (VII; R = Ac) followed from catalytic hydrogenation to 3β-acetoxy-4,4-dimethyl-14β-cholestane, identical with authentic material prepared by Wolff–Kishner reduction of 3β-acetoxy-4,4-dimethyl-14β-cholestane-7,11-dione and reacetylation.







Next, we established the identity of our 3β-acetoxy-4,4-dimethyl-14β-cholest-8-en-11-one (VI; R = Bu^i) with the acetate of the 3β-hydroxy-4,4-dimethyl-14α-cholest-8-en-11-one described by Shoppee and his co-workers.[10] The assignment of the 14-configuration by the latter authors was, in fact, not proven. In our hands treatment of 3β-acetoxy-7α-hydroxylanostan-11-one [1] (VIII; R = Bu^i) with lead tetra-acetate in dry benzene for 42 h under reflux gave the 7α,32-ether (IX; R = Bu^i) consistently in yields of *ca.* 70%. Treatment of this ether with boron trifluoride–ether in acetic anhydride and alkaline hydrolysis of the resulting 3β,11,32-triacetoxylanosta-7,9(11)-diene (X; R = Bu^i), as described by Shoppee,[10] afforded 3β-hydroxy-4,4-dimethyl-14β-cholest-8-en-11-one, the acetate of which was identical (i.r., mixed m.p., and t.l.c.) with compound (VI; R = Bu^i) prepared as already described.

In a similar series of reactions, methyl 3β-acetoxy-7α-hydroxy-32-nitrilo-11-oxo-25,26,27-trinorlanostan-24-oate [1] (III; R^1 = OH, R^2 = H, R^3 = CO_2Me) was converted into methyl 3β-acetoxy-4,4-dimethyl-7,11-dioxo-25,26,27-trinor-14β-cholest-8-en-24-oate (IV; R = CO_2Me) and methyl 3β-acetoxy-4,4-dimethyl-11-oxo-25,26,27-trinor-14β-cholest-8-ene-24-oate (VI; R = CO_2Me). The latter compound was also prepared from methyl 3β-acetoxy-7α-hydroxy-11-oxo-25,26,27-trinorlanostan-24-oate [1] (VIII; R = CO_2Me) *via* the 7α,32-ether (IX; R = CO_2Me). In view of the unnatural 14β-configuration of these compounds our original intention of further converting (VI; R = CO_2Me) into the biosynthetically interesting compound 3β-hydroxy-4,4-dimethylcholesta-8,24-diene (XI) *via* Wolff–Kishner reduction and rebuilding of the side chain (Wittig reaction) was not pursued.

As a final confirmation of the foregoing configurational assignments we carried out unambiguous syntheses of 3β-acetoxy-4,4-dimethyl-14α-cholest-8-ene-7,11-dione (XVII) and 3β-acetoxy-4,4-dimethyl-14α-cholest-8-en-11-one (XV), and demonstrated the tendency of these compounds to epimerise to the corresponding 14β-compounds. Cholesterol was converted into 3β-acetoxy-4,4-dimethyl-14α-cholest-7-ene (XII) by known methods.[11] Oxidation of compound (XII) with mercury(II) acetate in acetic acid–chloroform gave 3β-acetoxy-4,4-dimethyl-14α-cholesta-7,9(11)-diene (XIII) in 70% yield. The physical constants of this compound differed somewhat from those previously reported,[12] but the spectroscopic data fully supported the assigned structure. Treatment of the diene (XIII) with 1·1 mol. equiv. of perbenzoic acid in chloroform at 0° gave 3β-acetoxy-9α,11α-epoxy-4,4-dimethyl-14α-cholest-7-ene (XIV), identified from spectroscopic data, from further reactions, and by analogy with the behaviour on epoxidation of similar 7,9(11)-dienes.[13] Rearrangement of the unsaturated epoxide (XIV) by boron trifluoride–ether in refluxing benzene [13a] gave 3β-acetoxy-4,4-dimethyl-14α-cholest-8-en-11-one (XV). This differed from the 14β-isomer (VI; R = Bu^i) prepared by

[9] J. N. Shoolery and M. T. Rogers, *J. Amer. Chem. Soc.*, 1958, **80**, 5121; R. F. Zurcher, *Helv. Chim. Acta*, 1961, **44**, 1380; 1963, **46**, 2054; M. Fetizon, M. Golfier, and P. Laszlo, *Bull. Soc. chim. France*, 1965, 3205.

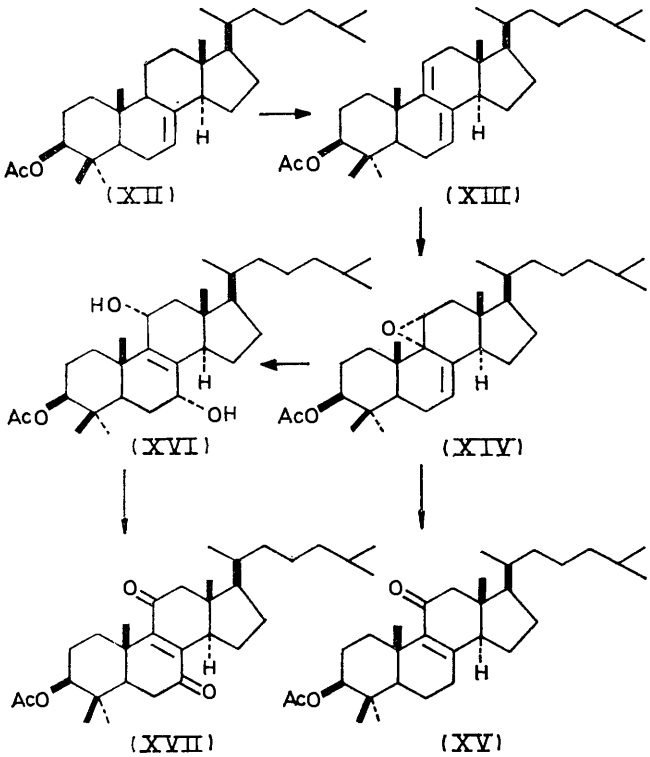
[10] C. W. Shoppee, N. W. Hughes, and R. E. Lack, *J. Chem. Soc.* (*C*), 1966, 2359; *Tetrahedron Letters*, 1966, 5235.

[11] (*a*) R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1957, 1131; (*b*) F. Gautschi and K. Bloch, *J. Biol. Chem.*, 1958, **233**, 1343.

[12] E. Ohki, *Chem. and Pharm. Bull.* (*Japan*), 1960, **8**, 229.

[13] (*a*) H. Heusser, K. Eichenberger, P. Kurath, H. R. Dallenbach, and O. Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106; (*b*) C. Djerassi, W. Frick, G. Rosenkranz, and F. Sondheimer, *J. Amer. Chem. Soc.*, 1953, **75**, 3496 and references cited therein.

elimination of the 32-carbon atom from the lanosterol derivatives (III; $R^1R^2 = O$, $R^3 = Bu^i$) and (X; R = Bu^i). Hydrolysis of the acetate function of (XV) with 5% sodium hydroxide in ethanol was accompanied by



epimerisation at C-14, as evidenced by the fact that re-acetylation of the product with pyridine–acetic anhydride gave material identical with the 14β-isomer (VI; R = Bu^i). The greater stability of the *cis*-CD-ring junction in this type of compound was thus confirmed. Full support for the foregoing changes in configuration was forthcoming from the n.m.r. spectra of the products (see Experimental section).

In keeping with the analogous findings of other workers,[14] attempts to oxidise the 7,9(11)-diene (XIII) directly to the 8-ene-7,11-dione (XVII) did not proceed satisfactorily. In consequence, the unsaturated epoxide (XIV) was converted by treatment with 2N-sulphuric acid in dioxan[13a] into 3β-acetoxy-4,4-dimethyl-14α-cholest-8-ene-7α,11α-diol (XVI), which was readily oxidised to the required 3β-acetoxy-4,4-dimethyl-14α-cholest-8-ene-7,11-dione (XVII). There was no evidence for the formation of 3β-acetoxy-8α,9α-epoxy-4,4-dimethyl-14α-cholest-8-ene-7,11-dione in the latter reaction.[13a] The authentic 14β-isomer (XVII) thus obtained differed from compound (IV; R = Bu^i) prepared by elimination of the nitrile function from (III; $R^1R^2 = O$, $R^3 = Bu^i$). As with 3β-acetoxy-4,4-dimethyl-14α-cholest-8-en-11-one (XV), mild alkaline hydrolysis of (XVII) proceeded with epimerisation at C-14 to give 3β-hydroxy-4,4-dimethyl-14β-cholest-8-ene-7,11-dione, identical with authentic material prepared from compound (III; $R^1R^2 = O$, $R^3 = Bu^i$).

[14] L. F. Fieser, Wei-Yuan Huang, and J. C. Babcock, *J. Amer. Chem. Soc.*, 1953, **75**, 116; L. F. Fieser and J. E. Herz, *ibid.*, p. 121; J. Elks, R. M. Evans, A. G. Long, and G. H. Thomas, *J. Chem. Soc.*, 1954, 451.

EXPERIMENTAL

General directions are as described in the preceding paper.[1]

3β-*Acetoxy*-7,11-*dioxolanostan*-32-*onitrile* (III; $R^1R^2 = O$, $R^3 = Bu^i$).—Kiliani's chromic acid (22·5 ml) was added to a solution of 3β-acetoxy-7α-hydroxy-11-oxolanostan-32-onitrile[1] (5 g) in acetone (225 ml). The mixture was shaken at room temperature for 10 min. The excess of oxidant was destroyed by addition of aqueous sodium hydrogen sulphite, and the mixture was poured into water. Extraction with ether gave the *dione* (4·5 g, 90%), m.p. (from chloroform–methanol) 243—244°, $[\alpha]_D$ +51·2° (*c* 0·49), $\nu_{max.}$ 2230, 1735, 1710, and 1250 cm^{-1} (Found: C, 75·1; H, 9·6; N, 2·5. $C_{32}H_{49}NO_4$ requires C, 75·1; H, 9·65; N, 2·7%).

Similarly, methyl 3β-acetoxy-7α-hydroxy-32-nitrilo-11-oxo-25,26,27-trinorlanostan-24-oate[1] (6 g) was converted into *methyl* 3β-*acetoxy*-32-*nitrilo*-7,11-*dioxo*-25,26,27-*trinorlanostan*-24-*oate* (III; $R^1R^2 = O$, $R^3 = CO_2Me$) (5·1 g, 85%), m.p. (from methanol) 245—246°, $[\alpha]_D$ +39·7° (*c* 0·50), $\nu_{max.}$ 2230, 1735, 1725, 1710, and 1250 cm^{-1} (Found: C, 70·2; H, 8·3; N, 2·55. $C_{30}H_{43}NO_6$ requires C, 70·15; H, 8·4; N, 2·7%); and 3β-acetoxy-7α-hydroxylanostan-32-onitrile[1] (84 mg) was converted into 3β-*acetoxy*-7-*oxolanostan*-32-*onitrile* (I; $R^1R^2 = O$) (73 mg, 87%), m.p. (from chloroform–methanol) 282—285°, $[\alpha]_D$ +18° (*c* 1·00), $\nu_{max.}$ 2230, 1735, 1710, and 1240 cm^{-1} (Found: C, 77·1; H, 10·5; N, 2·65. $C_{32}H_{51}NO_3$ requires C, 77·2; H, 10·35; N, 2·8%).

3β-*Hydroxy*-4,4-*dimethylcholest*-8(14)-*en*-7-*one* (II).—3β-Acetoxy-7-oxolanostan-32-onitrile (305 mg) dissolved in dry, refluxing t-butyl alcohol (25 ml) was treated with a solution of potassium t-butoxide (240 mg) in t-butyl alcohol (5 ml). The mixture was refluxed in an atmosphere of nitrogen for 1 h, acidified with 2N-hydrochloric acid, and poured into water. Extraction with ether gave a pale yellow solid (252 mg). This crystallised from methanol to give needles of 3β-*hydroxy*-4,4-*dimethylcholest*-8(14)-*en*-7-*one* (212 mg, 81%), m.p. 163—166°, $[\alpha]_D$ −34° (*c* 1·01), $\nu_{max.}$ 3250, 1680, and 1620 cm^{-1}, $\lambda_{max.}$ 263 nm (log ε 3·97) (Found: C, 81·3; H, 11·35. $C_{29}H_{48}O_2$ requires C, 81·25; H, 11·3%).

Wolff–Kishner Reduction of 3β-*Hydroxy*-4,4-*dimethylcholest*-8(14)-*en*-7-*one*.—Sodium (540 mg) was dissolved in redistilled digol (27 ml) and anhydrous hydrazine was distilled into the heated solution until it refluxed freely at 180°. 3β-Hydroxy-4,4-dimethylcholest-8(14)-en-7-one (150 mg) was added and the mixture was refluxed overnight. Hydrazine was distilled out until the temperature of the mixture rose to 210° before refluxing ensued. Refluxing was continued at this temperature for 16 h. The mixture was cooled and poured on ice to give a solid (142 mg), $\nu_{max.}$ 3400 cm^{-1}. Acetylation (pyridine–acetic anhydride at room temperature overnight) gave an oil (134 mg) which crystallised from ethyl acetate–methanol as needles and was a mixture of isomeric 3β-acetoxy-4,4-dimethylcholestenes, m.p. 100—110°, $[\alpha]_D$ +23° (*c* 0·46), $\nu_{max.}$ 1730 and 1245 cm^{-1}, τ 4·8 (*ca.* 0·4H, C-7 vinylic H), 5·6 (1H, 3α-H), and 8·01 (3H, OAc). This mixture (45 mg) in ethyl acetate (5 ml)

and acetic acid (5 ml) was shaken with Adams platinum oxide (100 mg) in an atmosphere of hydrogen for 3 days. The catalyst was filtered off and the solvent evaporated to give an oil, which was chromatographed on type H alumina (5 g). Elution with light petroleum gave a solid (31 mg) which crystallised from ethyl acetate–methanol as needles of 3β-acetoxy-4,4-dimethylcholest-8(14)-ene (12 mg), m.p. 107—111°, $[\alpha]_D$ +29° (*c* 1·53) (lit.,[11b] m.p. 115—117°, $[\alpha]_D$ +30°).

3β-*Acetoxy*-4,4-*dimethyl*-14β-*cholest*-8-*ene*-7,11-*dione* (IV; R = Bu^i).—3β-Acetoxy-7,11-dioxolanostan-32-onitrile (7 g) dissolved in dry, refluxing t-butyl alcohol (500 ml) in an atmosphere of nitrogen was treated with a solution of potassium (1·7 g) in dry t-butyl alcohol (125 ml). The mixture was refluxed for 3 h, poured into water, and extracted with ether to give a yellow oil. Acetylation (pyridine–acetic anhydride, room temperature overnight) gave an oil which crystallised from acetone–methanol to yield yellow needles of 3β-*acetoxy*-4,4-*dimethyl*-14β-*cholest*-8-*ene*-7,11-*dione* (5·8 g, 88%), m.p. 119—120°, $[\alpha]_D$ +96° (*c* 0·37), $\nu_{max.}$ 1730, 1695, 1680, and 1250 cm^{-1}, $\lambda_{max.}$ 266 nm (log ε 3·78) (Found: C, 76·7; H, 9·80. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0%).

3β-*Hydroxy*-4,4-*dimethyl*-14β-*cholest*-8-*ene*-7,11-*dione*.— A solution of 3β-acetoxy-4,4-dimethyl-14β-cholest-8-ene-7,11-dione (400 mg) in ethanol (50 ml) containing sodium hydroxide (2·5 g) was refluxed for 2 h. Work-up in the usual way gave the 3β-*hydroxy-compound* (243 mg), m.p. (from ethanol) 88—89°, $[\alpha]_D$ +98·5° (*c* 0·41), $\nu_{max.}$ 3520, 3360, 3240, 1680, 1670, and 1610 cm^{-1}, $\lambda_{max.}$ 267 nm (log ε 3·94) (Found: C, 76·5; H, 10·5. $C_{29}H_{46}O_3$,EtOH requires C, 76·2; H, 10·7%); *benzoate*, m.p. (from methanol) 135—136°, $[\alpha]_D$ +120·7° (*c* 0·42), $\nu_{max.}$ 1725, 1690, 1680, and 1270 cm^{-1}, $\lambda_{max.}$ 230 and 267 nm (log ε 4·22 and 3·93) (Found: C, 79·1; H, 9·1. $C_{36}H_{50}O_4$ requires C, 79·1; H, 9·2%).

Methyl 3β-*Acetoxy*-4,4-*dimethyl*-7,11-*dioxo*-25,26,27-*trinor*-14β-*cholest*-8-*en*-24-*oate* (IV; R = CO_2Me).—Methyl 3β-acetoxy-32-nitrilo-7,11-dioxo-25,26,27-trinorlanostan-24-oate (2 g) dissolved in dry, refluxing t-butyl alcohol (300 ml) in an atmosphere of nitrogen was treated with a solution of potassium (500 mg) in dry t-butyl alcohol (50 ml). The mixture was refluxed for 3 h, then acidified with 2N-hydrochloric acid, diluted with water, and extracted with ether. The resulting oil (1·85 g) in absolute methanol (50 ml) containing boron trifluoride–ether complex (0·5 ml) was refluxed for 20 min. Acetylation of the product (pyridine–acetic anhydride at room temperature overnight) gave a yellow oil. This was chromatographed on type H alumina (40 g). Elution with light petroleum afforded yellow plates of *methyl* 3β-*acetoxy*-4,4-*dimethyl*-7,11-*dioxo*-25,26,27-*trinor*-14β-*cholest*-8-*en*-24-*oate* (1·3 g, 68%), m.p. (from acetone–methanol) 84—85°, $[\alpha]_D$ +77·2° (*c* 0·50), $\nu_{max.}$ 1735, 1725, 1695, 1680, and 1250 cm^{-1}, $\lambda_{max.}$ 267 nm (log ε 3·88) (Found: C, 71·5; H, 8·8. $C_{29}H_{42}O_6$ requires C, 71·6; H, 8·7%); the *benzoate* crystallised from methanol; m.p. 135—136°, $[\alpha]_D$ +110° (*c* 0·51), $\nu_{max.}$ 1740, 1720, 1685, 1670, and 1270 cm^{-1}, $\lambda_{max.}$ 229 and 266 nm (log ε 4·2 and 3·8) (Found: C, 74·2; H, 7·9. $C_{34}H_{44}O_6$ requires C, 74·2; H, 8·1%).

3β-*Acetoxy*-7β-*hydroxy*-4,4-*dimethyl*-14β-*cholest*-8-*en*-11-*one*.—A suspension of sodium borohydride (500 mg) in absolute ethanol (15 ml) was added during 30 min to a solution of 3β-acetoxy-4,4-dimethyl-14β-cholest-8-ene-7,11-dione (2·4 g) in absolute ethanol (50 ml) and benzene (30 ml). The mixture was stirred at room temperature for 2 h, evaporated to small bulk, diluted with water, and extracted with ether to yield 7β-*hydroxy*-11-*one* (1·62 g, 67%), m.p. (from methanol) 203—204°, $[\alpha]_D$ +83·6° (*c* 0·47), $\nu_{max.}$ 3400, 1735, 1660, 1605, and 1240 cm^{-1}, $\lambda_{max.}$ 248 nm (log ε 3·92) (Found: C, 76·35; H, 10·35. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4%).

Similarly, methyl 3β-acetoxy-4,4-dimethyl-7,11-dioxo-25,26,27-trinor-14β-cholest-8-en-24-oate (230 mg) was converted into *methyl* 3β-*acetoxy*-7β-*hydroxy*-4,4-*dimethyl*-11-*oxo*-25,26,27-*trinor*-14β-*cholest*-8-*en*-24-*oate* (151 mg, 66%), m.p. (from methanol) 196—197°, $[\alpha]_D$ +79·9 (*c* 0·15), $\nu_{max.}$ 3400, 1740, 1730, 1660, 1600, and 1240 cm^{-1}, $\lambda_{max.}$ 248 nm (log ε 3·87) (Found: C, 71·3; H, 9·0. $C_{29}H_{44}O_6$ requires C, 71·3; H, 9·1%).

3β-*Acetoxy*-4,4-*dimethyl*-14β-*cholest*-8-*en*-11-*one* (VI; R = Bu^i).—Zinc dust (6 g) was added during 30 min to a refluxing solution of 3β-acetoxy-7β-hydroxy-4,4-dimethyl-14β-cholest-8-en-11-one (1·6 g) in glacial acetic acid (70 ml). The solution was refluxed for a further 2 h, and then decanted on to ice. The residual zinc was extracted with boiling glacial acetic acid (2 × 15 ml) and these extracts were added to the ice. The total precipitate so obtained was filtered off, washed with water, and dried, and on crystallisation from methanol yielded needles of 3β-*acetoxy*-4,4-*dimethyl*-14β-*cholest*-8-*en*-11-*one* (1·2 g, 78%), m.p. 107—108°, $[\alpha]_D$ +124·7° (*c* 0·54), $\nu_{max.}$ 1735, 1660, 1605, and 1245 cm^{-1}, $\lambda_{max.}$ 248 nm (log ε 3·9) (Found: C, 79·2; H, 10·9. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%).

Similarly, methyl 3β-acetoxy-7β-hydroxy-4,4-dimethyl-11-oxo-25,26,27-trinor-14β-cholest-8-en-24-oate (125 mg) afforded *methyl* 3β-*acetoxy*-4,4-*dimethyl*-11-*oxo*-25,26,27-*trinor*-14β-*cholest*-8-*en*-24-*oate* (VI; R = CO_2Me) (79 mg, 65%), m.p. (from methanol) 122—123°, $[\alpha]_D$ +122·2 (*c* 0·50), $\nu_{max.}$ 1740, 1730, 1660, 1610, and 1250 cm^{-1}, $\lambda_{max.}$ 249 nm (log ε 3·9) (Found: C, 73·9; H, 9·6. $C_{29}H_{44}O_5$ requires C, 73·7; H, 9·4%).

3β-*Acetoxy*-4,4-*dimethyl*-14β-*cholestane*-7,11-*dione*.— 3β-Acetoxy-4,4-dimethyl-14β-cholest-8-ene-7,11-dione (4 g) was reduced with zinc dust (5 g) in glacial acetic acid (100 ml) as described for 3β-acetoxy-7β-hydroxy-4,4-dimethyl-14β-cholest-8-en-11-one. The 3β-*acetoxy*-4,4-*dimethyl*-14β-*cholestane*-7,11-*dione* thus obtained (2·4 g, 60%) crystallised from methanol, m.p. 160—161°, $[\alpha]_D$ +9·1° (*c* 0·61), $\nu_{max.}$ 1735, 1710, 1700 and 1250 cm^{-1} (Found: C, 76·3; H, 10·5. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4%).

Similarly, 3β-benzoyloxy-4,4-dimethyl-14β-cholest-8-ene-7,11-dione (300 mg) gave 3β-*benzoyloxy*-4,4-*dimethyl*-14β-*cholestane*-7,11-*dione* (220 mg, 73%), m.p. (from methanol) 158—159°, $[\alpha]_D$ +34·8° (*c* 0·31), $\nu_{max.}$ 1725, 1715, 1705, 1270, and 710 cm^{-1} (Found: C, 78·6; H, 9·6. $C_{36}H_{52}O_4$ requires C, 78·8; H, 9·55%).

Wolff–Kishner Reduction of 3β-*Acetoxy*-4,4-*dimethyl*-14β-*cholestane*-7,11-*dione*.—This was carried out as described for 3β-hydroxy-4,4-dimethylcholest-8(14)-en-7-one. The 4,4-*dimethyl*-14β-*cholestan*-3β-*ol* (V; R^1 = OH, R^2 = H) so obtained (66%) crystallised (from ethyl acetate), m.p. 173—174°, $[\alpha]_D$ +43·0° (*c* 0·27), $\nu_{max.}$ 3260 cm^{-1} (Found: C, 83·4; H, 12·55. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%). Acetylation in the usual manner afforded 3β-*acetoxy*-4,4-*dimethyl*-14β-*cholestane* (V; R^1 = OAc, R^2 = H), m.p. 87—88°, $[\alpha]_D$ +51·8° (*c* 0·54), $\nu_{max.}$ 1730 and 1245 cm^{-1} (Found: C, 81·0; H, 11·8. $C_{31}H_{54}O_2$ requires C, 81·2; H, 11·9%).

4,4-*Dimethyl*-14β-*cholestan*-3-*one* (V; R^1R^2 = O).—4,4-Dimethyl-14β-cholestan-3β-ol (200 mg) in acetone (30 ml) was oxidised with Kiliani's chromic acid (2 ml) as described for 3β-acetoxy-7,11-dioxolanostan-32-onitrile. The 4,4-*di*-

methyl-14β-*cholestan*-3-*one* thus obtained (150 mg, 75%) crystallised from methanol; m.p. 78—79°, $[\alpha]_D$ +32·9° (*c* 0·61), $\nu_{max.}$ 1710 cm^{-1} (Found: C, 83·8; H, 12·3. $C_{29}H_{50}O$ requires C, 84·0; H, 12·15%).

Wolff–Kishner Reduction of 3β-*Acetoxy*-4,4-*dimethyl*-14β-*cholest*-8-*en*-11-*one*.—This was carried out as described for 3β-hydroxy-4,4-dimethylcholest-8(14)-en-7-one. The 4,4-*dimethyl*-14β-*cholest*-9(11)-*en*-3β-*ol*, after crystallisation from methanol, was isolated in 67% yield, m.p. 132—133°, $[\alpha]_D$ +41·6° (*c* 0·32), $\nu_{max.}$ 3300 cm^{-1} (Found: C, 84·0; H, 12·4. $C_{29}H_{50}O$ requires C, 84·0; H, 12·15%).

The acetate, 3β-*acetoxy*-4,4-*dimethyl*-14β-*cholest*-9(11)-*ene*, had m.p. 99—100° (from methanol), $[\alpha]_D$ +51·7° (*c* 0·29), $\nu_{max.}$ 1730 and 1245 cm^{-1} (Found: C, 81·4; H, 11·5. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·5%).

3β-*Acetoxy*-4,4-*dimethyl*-14β-*cholestane*.—A solution of 3β-acetoxy-4,4-dimethyl-14β-cholest-9(11)-ene (250 mg) in ethyl acetate (15 ml) and glacial acetic acid (15 ml) containing Adams platinum oxide (50 mg) and perchloric acid (70%; 4 drops) was shaken in an atmosphere of hydrogen until the uptake of gas was complete. The solution was filtered. The filtrate was diluted with ether (20 ml), and washed thoroughly with 2N-sodium carbonate and finally with water. The organic layer was dried and on evaporation yielded 3β-acetoxy-4,4-dimethyl-14β-cholestane, m.p. and mixed m.p. 87—88°.

3β-*Acetoxy*-7α,32-*epoxylanostan*-11-*one* (IX; R = Bu^i).—A solution of 3β-acetoxy-7α-hydroxylanostan-11-one [1] (6 g) and lead tetra-acetate (24 g) in dry benzene (500 ml) was refluxed with stirring for 42 h. The mixture was diluted with water (300 ml) and filtered through Celite. The Celite was washed thoroughly with ether and the combined filtrates were processed to give 3β-acetoxy-7α,32-epoxylanostan-11-one (4·2 g, 70%), m.p. (from methanol) 176—178°, $[\alpha]_D$ +48° (*c* 0·51), $\nu_{max.}$ 1730, 1710, and 1255 cm^{-1} (lit.,[10] m.p. 173—174°, $[\alpha]_D$ +46°). Similarly, methyl 3β-acetoxy-7α-hydroxy-11-oxo-25,26,27-trinorlanostan-24-oate [1] (570 mg) when treated with lead tetra-acetate (2·2 g) in benzene (150 ml) afforded *methyl* 3β-*acetoxy*-7α,32-*epoxy*-11-*oxo*-25,26,27-*trinorlanostan*-24-*oate* (IX; R = CO_2Me) (365 mg, 64%), m.p. (from methanol) 195—197°, $[\alpha]_D$ +44·3° (*c* 0·61), $\nu_{max.}$ 1735, 1725, 1705, and 1245 cm^{-1} (Found: C, 71·5; H, 9·2. $C_{30}H_{46}O_6$ requires C, 71·7; H, 9·2%).

3β-*Acetoxy*-4,4-*dimethyl*-14β-*cholest*-8-*en*-11-*one*.—A solution of 3β-acetoxy-7α,32-epoxylanostan-11-one (800 mg) in acetic anhydride (60 ml) containing boron trifluoride–ether (2 ml) was stirred at room temperature for 10 min, poured into water, and extracted with ether. The resulting oil was chromatographed on type H alumina (40 g). Initially elution with light petroleum gave starting material (IX; R = Bu^i) followed by an oil (625 mg). This oil, dissolved in ethanol (50 ml) containing potassium hydroxide (5 g), was refluxed for 90 min. Isolation in the normal way afforded an oil which was chromatographed on type H alumina (20 g). Elution with light petroleum gave a solid (423 g) which was crystallised from methanol to give 3β-hydroxy-4,4-dimethyl-14β-cholest-8-en-11-one, m.p. 127—128°, $[\alpha]_D$ +133° (*c* 0·45), $\nu_{max.}$ 3300, 1665, and 1610 cm^{-1}, $\lambda_{max.}$ 249 nm (log ε 3·9) (lit.,[10] m.p. 119—122°). On acetylation 3β-acetoxy-4,4-dimethyl-14β-cholest-8-en-11-one, m.p. 107—108°, $[\alpha]_D$ +125° (*c* 0·48), was obtained, identical with the material prepared by zinc dust reduction of 3β-acetoxy-7β-hydroxy-4,4-dimethyl-14β-cholest-8-en-11-one.

Similarly, methyl 3β-acetoxy-7α,32-epoxy-11-oxo-25,26,27-trinorlanostan-24-oate (300 mg) gave 3β-hydroxy-4,4-dimethyl-11-oxo-25,26,27-trinor-14β-cholest-8-en-24-oic acid which when re-esterified [boron trifluoride–ether (4 drops) in refluxing methanol (30 ml) for 30 min] and re-acetylated (pyridine–acetic anhydride, room temperature overnight) yielded methyl 3β-acetoxy-4,4-dimethyl-11-oxo-25,26,27-trinor-14β-cholest-8-en-24-oate (155 mg), m.p. 122—123°, $[\alpha]_D$ +121° (*c* 0·50), identical with authentic material prepared by the zinc dust reduction of methyl 3β-acetoxy-7β-hydroxy-4,4-dimethyl-11-oxo-25,26,27-trinor-14β-cholest-8-en-24-oate.

3β-*Acetoxy*-4,4-*dimethyl*-14α-*cholesta*-7,9(11)-*diene* (XIII).—3β-Acetoxy-4,4-dimethyl-14α-cholest-7-ene [11] (7·8 g) in chloroform (360 ml) was added to a solution of mercury(II) acetate (20 g) in glacial acetic acid (320 ml). The reaction vessel was flushed with nitrogen, sealed, and left at 25° for 24 h. The precipitated mercury(I) acetate was filtered off. The filtrate was diluted with water and extracted with ether, and the resulting yellow oil was chromatographed on type H alumina (150 g). Elution with light petroleum–benzene (9 : 1 v/v) gave 3β-*acetoxy*-4,4-*dimethyl*-14α-*cholesta*-7,9(11)-*diene* (5·6 g, 72%), m.p. (from acetone–methanol) 142—143°, $[\alpha]_D$ +77·9° (*c* 0·5), $\nu_{max.}$ 1740 and 1240 cm^{-1}, $\lambda_{max.}$ 235, 242, and 251 nm (log ε 4·12, 4·17, and 3·9) (Found: C, 81·2; H, 11·1. $C_{31}H_{50}O_2$ requires C, 81·9; H, 11·1%) (lit.,[12] m.p. 126—128°, $[\alpha]_D$ +49·3°).

3β-*Acetoxy*-9α,11α-*epoxy*-4,4-*dimethyl*-14α-*cholest*-7-*ene* (XIV).—A solution of 3β-acetoxy-4,4-dimethyl-14α-cholesta-7,9(11)-diene (3·8 g) in chloroform (100 ml) was cooled to −5° and a solution of perbenzoic acid in chloroform (1·1 mol. equiv.) was slowly added. After 12 h at 0° the solution was washed with 2N-sodium hydroxide (2 × 50 ml), followed by hot water until the washings were neutral to litmus. Evaporation of the chloroform and chromatography of the residue on type H alumina (50 g), followed by elution with light petroleum afforded starting material (330 mg), m.p. 142—143°. Continued elution with light petroleum benzene (6 : 1 v/v) gave 3β-*acetoxy*-9α,11α-*epoxy*-4,4-*dimethyl*-14α-*cholest*-7-*ene* (2·1 g), m.p. (from methanol) 189—190°, $[\alpha]_D$ +2·3° (*c* 0·5), $\nu_{max.}$ 1735 and 1255 cm^{-1} (Found: C, 79·3; H, 10·5. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%).

3β-*Acetoxy*-4,4-*dimethyl*-14α-*cholest*-8-*en*-11-*one* (XV).—A solution of 3β-acetoxy-9α,11α-epoxy-4,4-dimethyl-14α-cholest-7-ene (1·9 g) in dry benzene (45 ml) containing redistilled boron trifluoride–ether complex (560 mg) was refluxed for 48 h. The solution was diluted with water and extracted with ether to yield a solid (1·26 g), which crystallised from methanol as needles. This was 3β-*acetoxy*-4,4-*dimethyl*-14α-*cholest*-8-*en*-11-*one*, m.p. 175—176°, $[\alpha]_D$ +122·9° (*c* 0·54), $\nu_{max.}$ 1740, 1645, 1585, and 1240 cm^{-1}, $\lambda_{max.}$ 252 nm (log ε 3·97); o.r.d. (*c* 0·1 in MeOH; 20°) $[\phi]_{589}$ +637°, $[\phi]_{438}$ +982°, $[\phi]_{366}$ −769°, $[\phi]_{285}$ 20,030°, τ 9·31 and 8·82 (18- and 19-H_3) (Calc.[9] 9·28 and 8·80, respectively) (Found: C, 79·3; H, 10·7. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). A solution of the foregoing material (933 mg) in ethanol (50 ml) containing sodium hydroxide (2·5 g) was refluxed in an atmosphere of nitrogen for 2 h. Isolation in the normal manner afforded 3β-hydroxy-4,4-dimethyl-14β-cholest-8-en-11-one (753 mg), m.p. (from methanol) 127—128°, $[\alpha]_D$ +134·8° (*c* 0·36), $\nu_{max.}$ 3300, 1665, and 1610 cm^{-1}, $\lambda_{max.}$ 249 nm (log ε 3·9), identical with authentic material prepared from 3β-acetoxy-7α,32-epoxylanostane-11-one. Acetylation gave 3β-acetoxy-4,4-dimethyl-14β-cholest-8-en-11-one, m.p. 107—108°, $[\alpha]_D$ +125° (*c* 0·51), $\nu_{max.}$ 1735, 1660, 1605, and 1245 cm^{-1}, $\lambda_{max.}$ 248 nm

(log ε 3·9), o.r.d. (*c* 0·1 in MeOH; 20°) $[\phi]_{589}$ +604°, $[\phi]_{394}$ +1290°, $[\phi]_{372}$ +1097°, $[\phi]_{285}$ +9057°, τ 8·99 and 8·77 (18- and 19-H_3), identical with material prepared by the action of zinc dust in acetic acid on 3β-acetoxy-7β-hydroxy-4,4-dimethyl-14β-cholest-8-en-11-one.

3β-*Acetoxy*-4,4-*dimethyl*-14α-*cholest*-8-*ene*-7α,11α-*diol* (XVI).—2N-Sulphuric acid (27 ml) was added to a solution of 3β-acetoxy-9α,11α-epoxy-4,4-dimethyl-14α-cholest-7-ene (200 mg) in dioxan (150 ml). After 3 min the reaction was terminated by addition of N-sodium hydrogen carbonate (56 ml). The solution was extracted with ether to give the *diol* (110 mg, 52%), m.p. (from acetone–methanol) 234—236°, $[\alpha]_D$ +106·9° (*c* 0·12), $\nu_{max.}$ 3200, 1740, and 1245 cm^{-1}, (Found: C, 76·35; H, 10·7. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%).

3β-*Acetoxy*-4,4-*dimethyl*-14α-*cholest*-8-*ene*-7,11-*dione* (XVII).— 3β-Acetoxy-4,4-dimethyl-14α-cholest-8-ene-7α,11α-diol (130 mg) in acetone (20 ml) was oxidised with Kiliani's chromic acid (3 ml) as described for 3β-acetoxy-7,11-dioxolanostan-32-onitrile. The product was chromatographed on silica gel (4 g). Elution with benzene–light petroleum (4 : 1 v/v) yielded the *dione* (73 mg) as yellow needles (from methanol), m.p. 178—179°, $[\alpha]_D$ +35·5° (*c* 0·3), $\nu_{max.}$ 1730, 1690, 1680, and 1245 cm^{-1}, $\lambda_{max.}$ 267 nm (log ε 3·90) (Found: C, 76·7; H, 9·9. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0%). This material (60 mg) in ethanol (20 ml) containing sodium hydroxide (1 g) was refluxed in an atmosphere of nitrogen for 1·5 h. Isolation in the normal manner gave 3β-hydroxy-4,4-dimethyl-14β-cholest-8-ene-7,11-dione, m.p. 88—89°, $[\alpha]_D$ +98·5° (*c* 0·41), $\lambda_{max.}$ 267 nm (log ε 3·94), identical with material prepared from (III; R^1R^2 = O, R^3 = Bu^i).

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