Unsaturated Steroids. Part 4.[1] Some Steroidal Hydroxy-4,4-dimethyl-5,7-dienes and 4,4-Dimethyl-5,7,14(15)-trienes

By **Jitka Brynjolffssen, John M. Midgley,** and **W. Basil Whalley,*** The School of Pharmacy, The University, London WC1N 1AX

Prepared from 4,4-dimethylcholesta-1,5-dien-3-one (1), the corresponding 1α,2α-epoxide was brominated at C-7, and the product dehydrobrominated to yield 1α,2α-epoxy-4,4-dimethylcholesta-5,7-dien-3-one (4). This ketone was reduced by various methods to the diastereoisomeric 1α,3α- and 1α,3β-diols.

Bromination of 4,4-dimethylergosta-5,7,22-triene-3-one (14; R = H) furnished the 2α-bromo-derivative (14; R = Br) from which was obtained the corresponding 4,4-dimethylergosta-1,5,7,22-tetraen-3-one (15). This ketone gave the corresponding 1α,3α- and 1α,3β-diols by way of the 1α,2α-epoxide (5).

4,4-Dimethylcholesta-5,7-dien-3-one and 4-phenyl-1,2,4-triazoline-3,5-dione formed a 1 :1 adduct which was converted by acids into 4,4-dimethylcholesta-5,7,14(15)-trien-3-one (17). Analogous compounds were prepared similarly.

Irradiation (u.v.) of 17β-acetoxy-4,4-dimethylandrosta-5,7-dien-3β-ol gave two major products, one of which is formulated as the corresponding vitamin D analogue (19).

THE elaboration [2] by certain transplantable tumours of an intensely hypercalcaemic factor, which may be steroidal [3] but which is apparently not identical with any of a wide variety of steroids,[2,3] together with present interest in the biologically similar 1α-hydroxycholecalciferol, prompted us to synthesise some 4,4-dimethyl analogues of 1α-hydroxycholecalciferol for biological investigation.

Although epoxidation of 4,4-dimethylcholesta-1,5-dien-3-one [4] (1) with *m*-perchlorobenzoic acid gave the 5α,6α-epoxide (2), the use of a nucleophilic epoxidising agent, namely hydrogen peroxide in sodium hydroxide solution, formed the 1α,2α-epoxide (3; R = H). The

[1] Part 3, A. B. Garry, J. M. Midgley, W. B. Whalley, and B. J. Wilkins, preceding paper.

[2] B. F. Rice, L. M. Roth, F. E. Cole, A. A. MacPhee, K. Davis, R. L. Ponthier, and W. H. Sternberg, *Internat. Academy of Pathology*, 1975, **33**, 428.

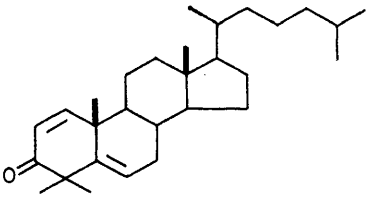
[3] B. F. Rice, personal communication.

[4] W. J. Adams, D. K. Patel, V. Petrow, I. A. Stuart-Webb, and B. Sturgon, *J. Chem. Soc.*, 1956, 4490.

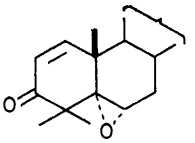
configuration of the oxiran is in accord with general mechanistic principles and with the ultimate conversion of this epoxide into 4,4-dimethylcholesta-5,7-diene-1α,3α-diol (10) (see later). The n.m.r. spectrum of (3; R = H) has signals at τ 6.45 (2 H, q, *J* 5.3 Hz), which replace signals at τ 4.13 and 3.10 (2 H, q, *J* 10 Hz) for H-1 and -2 in structure (1). This epoxide was brominated with 1,3-dibromo-5,5-dimethylhydantoin to give the 7-bromo-derivative (3; R = Br), which with triethyl phosphite gave 1α,2α-epoxy-4,4-dimethylcholesta-5,7-dien-3-one (4). In accord with precedent,[5] reduction of (4) with sodium borohydride afforded a mixture of the corresponding 3α- and 3β-ols, (6) and (8), respectively, with (6) predominating. The 3α-configuration of (6) was assigned by analogy [5,6] and confirmed by the formation of 4,4-dimethylcholesta-5,7-diene-1α,3α-diol (10) on reduction of (6) with lithium aluminium hydride. In agreement with its *cis*-diol structure, compound (10) showed $\nu_{max.}$ 3 620 (m, free OH stretch) and 3 470 cm^{-1} (s, hydrogen-bonded OH); the relative intensities were unchanged on dilution, thus confirming the presence of strong intramolecular hydrogen bonding. In contrast to (10), and as required by its formulation as a 1α,3β-diol, (12) showed $\nu_{max.}$ 3 610 cm^{-1} (single intense band, free OH stretch). The diol (10) was the major product from reduction of (4) with lithium aluminium hydride.

Reduction of (4) with aluminium amalgam [7] gave 1α-hydroxy-4,4-dimethylcholesta-5,7-dien-3-one, the n.m.r. spectrum of which had signals at τ 7.38 (2 H, q, H_2-2), 6.16br (1 H, t, H-1), and 4.50 and 4.14 (2 H, distorted ABq characteristic of H-6 and -7 in this series of 5,7-dienes). Reduction of 1α-hydroxy-4,4-dimethylcholesta-5,7-dien-3-one with lithium aluminium hydride gave a 1 : 1 mixture of the 1α,3α- (10) and 1α,3β- (12) diols; the greater proportion of 1α,3β-diol (12) was in accord with precedent.

By a similar sequence of reactions the ergostatriene-1α,3α- (11) and -1α,3β- (13) diols were prepared. Bromination of 4,4-dimethylergosterone (14; R = H) with either bromine–acetic acid or tri-*N*-methylanilinium tribromide gave the 2α-bromo-derivative (14; R = Br). The location of the bromine is in agreement with the n.m.r. spectrum (Experimental) and the formation of 4,4-dimethylergosta-1,5,7,22-tetraen-3-one (15) by the action of lithium chloride–dimethylformamide. The orientation of the halogen in (14; R = Br) is presumed to be axial on the basis of the i.r. spectrum in which the ring A ketone group exhibits absorption at 1 713 cm^{-1}, *i.e.* at the same position as in (14; R = H). The u.v. spectrum of (14; R = Br) is uninformative on this point because of the intense absorption of the 5,7-diene system. Since ring A in (14; R = Br) probably exists in a boat or quasi-boat conformation, the halogen will be in the α-orientation. Reduction of (15) with sodium borohydride furnished the corresponding 3β-alcohol, the orientation of which is assigned on the basis of, *inter alia*, (*a*) the n.m.r. spectrum, which exhibits a signal at τ 6.00 (1 H, d, *J* 2 Hz), implying [8] that the C-3 proton is axial,



(1)



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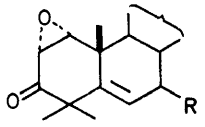
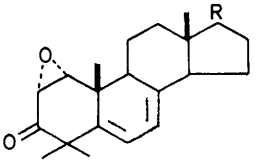
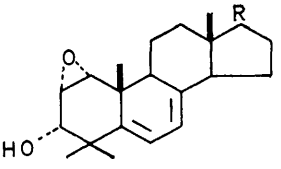


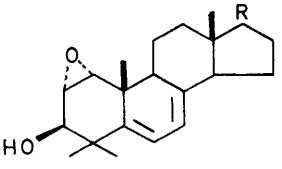
(3)



(4) R = C_8H_{17}
(5) R = $C_9H_{17}(\Delta^{22})$

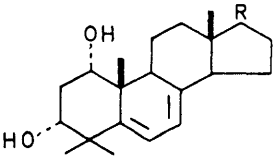


(6) R = C_8H_{17}
(7) R =

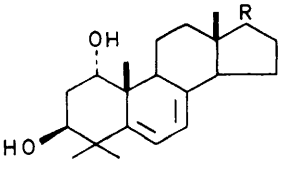


(8) R = C_8H_{17}
(9) R = $C_9H_{17}(\Delta^{22})$

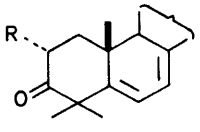
(*b*) analogy [9] with the reduction of 4,4-dimethyl ketones in general to 3β-ols, and (*c*) the positive molecular rotation difference [10] (+481°) between the alcohol (−752°) and the acetate (−271°).



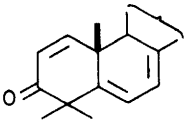
(10) R = C_8H_{17}
(11) R = $C_9H_{17}(\Delta^{22})$



(12) R = C_8H_{17}
(13) R = $C_9H_{17}(\Delta^{22})$



(14)



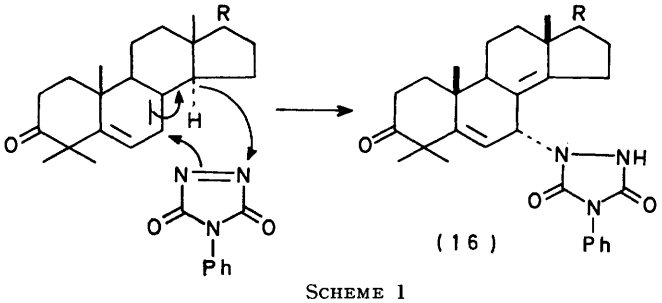
(15)

Treatment of (15) with alkaline hydrogen peroxide gave 1α,2α-epoxy-4,4-dimethylergosta-5,7,22-trien-3-one

[5] T. Okuno and T. Matsumoto, *Tetrahedron Letters*, 1969, 4077.
[6] H. Mühle and Ch. Tamm, *Helv. Chim. Acta*, 1963, **46**, 268.
[7] T. A. Narwid, J. F. Blount, J. A. Iacobelli, and M. R. Uskokovic, *Helv. Chim. Acta*, 1974, **57**, 781.
[8] D. H. Williams and I. Fleming, 'Spectroscopic Methods in Organic Chemistry,' McGraw-Hill, 1966, p. 105.
[9] R. Albrecht and Ch. Tamm, *Helv. Chim. Acta*, 1957, **40**, 2216.
[10] W. Klyne and M. W. Stokes, *J. Chem. Soc.*, 1954, 1979.

(5), τ 4.29 (2 H, q, H-6 and -7), 4.76 (2 H, m, H-22 and -23), and 6.47 (2 H, H-1 and -2). The u.v. absorption was compatible with retention of the 5,7-diene system. Reduction of the carbonyl group in (5) with sodium borohydride gave (as for the cholestane series) the 3α- and 3β-alcohols, (7) and (9), respectively. Reduction of (7) and (9) with lithium aluminium hydride afforded the 1α,3α- (11) and the 1α,3β-diol (13), respectively, as in the cholestane series.

The reaction [11] of steroidal 5,7-dienes with 4-phenyl-1,2,4-triazoline-3,5-dione to form adducts prompted us to investigate the behaviour of 4,4-dimethyl-5,7-dienes with this dienophile. With 4,4-dimethylcholesta-5,7-dien-3-one, a 1,4-cycloadduct was not formed, but a slow reaction occurred to yield the 1 : 1 adduct of type (16). The n.m.r. spectrum of (16) had signals at τ 4.60 (2 H, ABq, J 8.5 Hz) [contrast the corresponding signals [12] at τ 3.6 (2 H, ABq, J 9 Hz) for 1,4-cycloadducts] and 0.95—0.90 (1 H, s, replaceable with D_2O). That this singlet may be ascribed to NH absorption is confirmed by the i.r. spectrum [$\nu_{max.}$ 3 450 and 3 160 cm^{-1}]. The 7α-orientation of the triazolidinedione residue is consistent with the genesis of (16) by an α-face approach of the reagent which results in an 8(14)-, as opposed to an 8(9)-double bond (Scheme 1). The

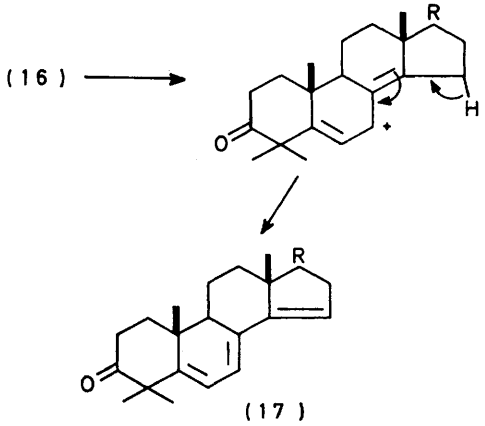


SCHEME 1

presence of an 8(14)-double bond is consistent with the downfield shift [13] of the C-13 methyl signal from τ *ca.* 9.36 in the parent steroid to τ *ca.* 9.10 in (16), and with the n.m.r. spectra [14] of cognate 7α-8(14)-ene adducts.

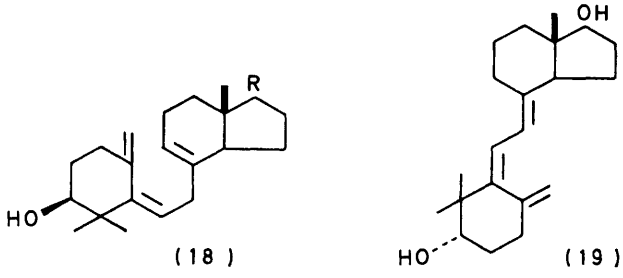
The formation of a derivative of type (16) is undoubtedly due to the inaccessibility of C-5, occasioned by either (*a*) flattening of ring A, by the 1,3-diaxial interactions between the C-10 and C-4β methyl groups or (*b*) the likelihood that ring A in a 4,4-dimethyl-5,7-diene adopts a boat-like conformation in which the C-4α methyl group becomes axial.

When a solution of (16) in 'aged' chloroform (or in ethanolic 0.001M-hydrochloric acid) was refluxed for 10 min, 4-phenyltriazolidine-3,5-dione and 4,4-dimethylcholesta-5,7,14(15)-trien-3-one (17) were produced.[15] The same products were formed almost immediately when a solution of (16) in benzene was treated with boron trifluoride–ether. The n.m.r. spectrum of (17) showed signals at τ 4.10 and 3.72 (3 H, m, H-6, -7, and -15), and the signal of the C-13 methyl group had shifted downfield to τ 8.63, relative to the parent 5,7-diene (τ 9.00), thus indicating that the third double bond was at position 14(15). The position of the u.v. maximum 325 nm (ε 12 054) was consistent with the calculated value of 323 nm. The structure (17) is in accord with its genesis as in Scheme 2.



SCHEME 2

In a model experiment for the conversion of 4,4-dimethyl-5,7-dien-3β-ols into vitamin D analogues of type (19), u.v. irradiation of 17-acetoxy-4,4-dimethylandrosta-5,7-dien-3β-ol [16] was investigated. The reaction seems to proceed less readily than with simple 5,7-dienes. The major product is formulated as (18) on the basis of spectral evidence; the minor product had all the



characteristics of the desired vitamin D analogue (19), including the characteristic u.v. absorption [$\lambda_{max.}$ 258 nm (ε 16 317)], n.m.r. signals at τ 5.09 (2 H, ABq, J 2.7 Hz, H_2-19) and 3.74 (2 H, ABq, J 10.6 Hz, H-6 and -7), and $\nu_{max.}$ 893 cm^{-1} (=CH_2).

EXPERIMENTAL

Unless otherwise stated optical rotations were determined for solutions in chloroform. Light petroleum refers

[11] D. H. R. Barton, T. Shioiri, and D. A. Widdowson, *J. Chem. Soc.* (*C*), 1971, 1968.

[12] N. Bosworth, A. Emke, J. M. Midgley, C. J. Moore, W. B. Whalley, G. Ferguson, and W. C. Marsh, *J.C.S. Perkin I*, 1977, 805.

[13] N. S. Bhacca and D. H. Williams, 'Applications of NMR Spectroscopy in Organic Chemistry,' Holden–Day, San Francisco, 1964, p.22.

[14] A. van der Gen, J. Lakeman, M. A. M. P. Gras, and H. O. Huisman, *Tetrahedron*, 1964, **20**, 2521; A. van der Gen, J. Lakeman, U. K. Pandit, and H. O. Huisman, *ibid.*, 1965, **21**, 3641; J. Lakeman, W. N. Speckamp, and H. O. Huisman, *ibid.*, 1968, **24**, 5151; A. Abramovitch and P. W. Le Quesne, *J. Org. Chem.*, 1974, **39**, 2197.

[15] J. Brynjolffssen, A. Emke, D. Hands, J. M. Midgley, and W. B. Whalley, *J.C.S. Chem. Comm.*, 1975, 633.

[16] G. A. Lane and W. B. Whalley, unpublished results.

to the fraction of b.p. 60—80 °C. Silica gel used for chromatography was Kieselgel G254.

1α,2α-*Epoxy*-4,4-*dimethylcholesta*-5,7-*dien*-3-*one* (4).—Treatment of a solution of 4,4-dimethylcholesta-1,5-dien-3-one (0.05 g) in boiling dichloromethane (20 ml) with *m*-chloroperbenzoic acid (0.2 g) during 12 h gave 5α,6α-*epoxy*-4,4-*dimethylcholest*-1-*en*-3-*one*, which formed needles (0.03 g), m.p. 99—101° (from ethanol) (Found: C, 82.0; H, 10.8. $C_{29}H_{46}O_2$ requires C, 81.6; H, 10.9%), $\lambda_{max.}$ 228 nm (ε 7 940), τ 6.68 (1 H, t, H-6), and 4.16 and 3.18 (2 H, ABq, *J* 10.6 Hz, H-1 and -2), $\nu_{max.}$ 1 685 cm^{-1} (C=C–C=O).

1,3-Dibromo-5,5-dimethylhydantoin (1.25 g) was added to a refluxing solution of 1α,2α-epoxy-4,4-dimethylcholest-5-en-3-one [5] (2 g) in benzene (25 ml) and light petroleum (15 ml). After 0.5 h at the b.p. the reaction mixture was cooled and filtered; xylene (10 ml) was added to the filtrate, which was reduced in volume to 10 ml and added to boiling xylene (20 ml) containing an excess of triethyl phosphite (2 ml). The mixture was refluxed for 1 h, the solvent removed *in vacuo*, and the product purified from ethanol to yield 1α,2α-*epoxy*-4,4-*dimethylcholesta*-5,7-*dien*-3-*one* (1.8 g) in glittering plates, m.p. 157—159°, $[\alpha]_D^{20}$ +41° (*c* 2.1) (Found: C, 82.0; H, 10.3%; M^+, 424. $C_{29}H_{44}O_2$ requires C, 82.0; H, 10.4%; *M*, 424), $\lambda_{max.}$ 282 (ε 10 627) and 274 nm (10 536), $\nu_{max.}$ 1 710 cm^{-1} (C=O), τ 6.49 (2 H, s, H-1 and -2), and 4.56 and 3.98 (2 H, ABq, *J* 10 Hz, H-6 and -7).

4,4-*Dimethylcholesta*-5,7-*diene*-1α,3α-*diol* (10) *and* -1α,3β-*diol* (12).—(*a*) Reduction of the preceding ketone (0.5 g) with sodium borohydride (0.65 g) gave a mixture of the 3α- and 3β-alcohols, which was purified from acetone to yield 1α,2α-*epoxy*-4,4-*dimethylcholesta*-5,7-*dien*-3α-*ol* (0.3 g) in plates, m.p. 173—175°, $[\alpha]_D^{20}$ −111° (*c* 2.12), $\lambda_{max.}$ 282 (ε 11 465) and 272 nm (11 998), τ 6.34—6.59 (3 H, m, H-1, -2, and -3), and 4.36 (2 H, dd, *J* 5.3 Hz, H-6 and -7) (Found: C, 81.6; H, 11.0. $C_{29}H_{46}O_2$ requires C, 81.6; H, 10.9%).

A solution of 1α,2α-epoxy-4,4-dimethylcholesta-5,7-dien-3α-ol (50 mg) in boiling ether (30 ml) was reduced during 4 h with an excess of lithium aluminium hydride to yield 4,4-*dimethylcholesta*-5,7-*diene*-1α,3α-*diol* [R_F 0.51 on silica; ethyl acetate–benzene (1 : 1)] as flat needles (40 mg), m.p. 193—196° (from ethanol), $[\alpha]_D^{20}$ −127° (*c* 1.28), $\lambda_{max.}$ 284 (ε 10 161) and 275 nm (11 391), τ 4.02 and 4.50 (2 H, dd, *J* 6 Hz, H-6 and -7) (Found: C, 81.4; H, 11.0%; M^+, 428. $C_{29}H_{48}O_2$ requires C, 81.3; H, 11.3%; *M*, 428).

(*b*) Reduction of a solution of 1α,2α-epoxy-4,4-dimethylcholesta-5,7-dien-3-one (0.9 g) in boiling ether (70 ml) with lithium aluminium hydride (0.2 g) during 4 h gave a mixture of 1α,3α- and 1α,3β-diols which was purified from ethanol to yield 4,4-dimethylcholesta-5,7-diene-1α,3α-diol (0.5 g), identical (i.r., u.v., t.l.c., and n.m.r.) with the product from route (*a*). Purification of the residue remaining after isolation of the 1α,3α-diol by t.l.c. [benzene–ethyl acetate (4 : 1)] gave 4,4-*dimethylcholesta*-5,7-*diene*-1α,3β-*diol* (0.05 g) in micro-needles, m.p. 150—153° (from aqueous ethanol), $[\alpha]_D^{22}$ −123° (*c* 1.0), M^+ 428, $\lambda_{max.}$ 273 (ε 10 700) and 284 nm (10 700).

(*c*) An excess of freshly prepared aluminium amalgam (2 g) was added to a stirred suspension of 1α,2α-epoxy-4,4-dimethylcholesta-5,7-dien-3-one (0.3 g) in ether (30 ml) and ethanol (96%) (10 ml). After 24 h the mixture was diluted with chloroform (20 ml) and clarified by filtration. Purification of the residue obtained by removal of solvent *in vacuo* gave 1α-*hydroxy*-4,4-*dimethylcholesta*-5,7-*dien*-3-*one* (0.2 g) in needles, m.p. 194—196° (from acetone), $[\alpha]_D^{20}$ −61° (*c* 2.02), $\nu_{max.}$ 1 695 cm^{-1}, $\lambda_{max.}$ 283 (ε 9 966) and 274 nm (10 165) (Found: C, 81.3; H, 10.9. $C_{29}H_{46}O_2$ requires C, 81.6; H, 10.9%).

Reduction of this 1α-hydroxy-ketone (50 mg) with lithium aluminium hydride at room temperature during 0.5 h, in ether (50 ml), gave a mixture of 4,4-dimethylcholesta-5,7-diene-1α,3β-diol and -1α,3α-diol [*cf.* method (*b*)].

1α,2α-*Epoxy*-4,4-*dimethylergosta*-5,7,22-*trien*-3-*one* (5).—Tri-*N*-methylanilinium tribromide (4.5 g) was added to a stirred solution of 4,4-dimethylergosta-5,7,22-trien-3-one (5 g) in tetrahydrofuran (300 ml). A precipitate of trimethylanilinium bromide formed rapidly, and after 0.5 h an excess of aqueous sodium hydrogen sulphite was added to the mixture. Extraction with ether gave 2α-*bromo*-4,4-*dimethylergosta*-5,7,22-*trien*-3-*one* (4.3 g), which separated in plates, m.p. 128—131° (from acetone–ethanol), $\lambda_{max.}$ 273 nm (ε 9 789), $\nu_{max.}$ 1 713 cm^{-1} (C=O), τ 9.37, 9.20, 9.11, 9.00, 8.90, 8.63, and 8.53 (7 × 3 H, Me), 5.31 (1 H, q, *J* 8 Hz, H-2), 4.78 (2 H, m, H-22 and -23), and 4.46 and 4.14 (2 H, q, *J* 6 Hz, H-6 and -7) (Found: C, 71.8; H, 9.1; Br, 15.8%; M^+, 501. $C_{30}H_{45}BrO$ requires C, 71.8; H, 9.0; Br, 15.9%; *M*, 501). The same product (i.r., n.m.r., and u.v.) (1.8 g) was obtained when a solution of bromine (1.6 g) in acetic acid (12 ml) was added dropwise to a stirred solution of 4,4-dimethylergosta-5,7,22-trien-3-one (2 g) in ether (200 ml) and the reaction quenched 10 min later with aqueous sodium hydrogen sulphite.

A solution of this bromo-derivative (3.5 g) in dimethylformamide (55 ml) containing an excess of lithium carbonate was refluxed during 3 h. After isolation with ether 4,4-*dimethylergosta*-1,5,7,22-*tetraen*-3-*one* (2.5 g) formed tiny plates, m.p. 105—107° (from acetone–ethanol), $[\alpha]_D^{20}$ +39° (*c* 0.54), $\lambda_{max.}$ 275 (ε 7 446) and 280 nm (7 436), $\nu_{max.}$ 1 690 cm^{-1} (C=O), τ 9.35, 9.21, 9.02, 8.90, 8.78, and 8.69 (8 × 3 H, Me), 4.69 (2 H, m, 22- and 23-H), and 3.08—4.59 (4 H, m, H-1, -2, -6, and -7) (Found: C, 85.9; H, 10.7%; M^+, 420. $C_{30}H_{44}O$ requires C, 85.7; H, 10.5%; *M*, 420).

Reduction of this ketone (0.3 g) dissolved in benzene (20 ml) and ethanol (20 ml) with sodium borohydride (0.4 g) gave 4,4-*dimethylergosta*-1,5,7,22-*tetraen*-3β-*ol* (0.27 g) in needles, m.p. 175—177° (from acetone–ether), $[\alpha]_D^{20}$ −180° (*c* 0.6), $\lambda_{max.}$ 272 nm (ε 10 103), τ 9.37, 9.20, 9.11, 9.01, 8.98, 8.94, and 8.79 (8 × 3 H, Me), 6.00 (1 H, d, *J* 2 Hz, H-3α), 4.76 (2 H, m, H-22 and -23), and 4.32 (4 H, m, H-1, -2, -6, and -7) (Found: C, 83.6; H, 10.8%; M^+, 422. $C_{30}H_{46}O$ requires C, 85.2; H, 11.0%; *M*, 422. $C_{30}H_{46}O,-0.5H_2O$ requires C, 83.1; H, 10.9%). The *acetate* formed plates, m.p. 185° (from chloroform–methanol), $[\alpha]_D^{20}$ −58.3° (*c* 1.2), $\lambda_{max.}$ 281 (ε 9 250) and 272 nm (9 800), $\nu_{max.}$ 1 730 cm^{-1} (ester C=O), τ 7.89 (3 H, s, OAc) (Found: C, 82.4; H, 10.2. $C_{32}H_{48}O_2$ requires C, 82.7; H, 10.4%).

A solution of 4,4-dimethylergosta-1,5,7,22-tetraen-3-one (2 g) in ether (100 ml) and methanol (200 ml) was cooled to 10 °C. Aqueous 4N-sodium hydroxide (1 ml) was added, followed immediately by hydrogen peroxide (100 vol.; 2 ml). After 2 h, the product was isolated and purified from acetone–methanol to yield 1α,2α-*epoxy*-4,4-*dimethylergosta*-5,7,22-*trien*-3-*one* (1.6 g) in plates, m.p. 129—131°, $[\alpha]_D^{20}$ +24° (*c* 2.64), $\lambda_{max.}$ 293 (ε 6 163), 282 (10 090), and 271 nm (9 931), $\nu_{max.}$ 1 715 cm^{-1} (Found: C, 82.6; H, 10.2%; M^+, 436. $C_{30}H_{44}O_2$ requires C, 82.5; H, 10.2%; *M*, 436).

4,4-*Dimethylergosta*-5,7,22-*triene*-1α,3α-*diol* (11) *and* -1α,3β-*diol* (13).—(*a*) Reduction of 1α,2α-epoxy-4,4-dimethylergosta-5,7,22-trien-3-one (0.3 g) with aluminium amalgam (3 g) as for the cholestane analogue gave 1α-*hydroxy*-4,4-*dimethylergosta*-5,7,22-*trien*-3-*one* (0.2 g) in plates, m.p. 195—197° (from acetone–methanol), $[\alpha]_D^{20}$ −86° (*c* 1.88), $\lambda_{max.}$ 283 (ε 9 537) and 274 nm (9 577), $\nu_{max.}$ 1 702 cm^{-1} (C=O), τ 7.23 (2 H, q, *J* 2.6 Hz, H_2-2), 5.90 (1 H, t, H-1β), 4.74 (2 H, m, H-22 and -23), and 4.43 and 4.04 (2 H, q, *J* 6 Hz, H-6 and -7) (Found: C, 82.1; H, 10.6. $C_{30}H_{46}O_2$ requires C, 82.1; H, 10.6%). Reduction of this ketone (0.5 g) with lithium aluminium hydride (0.2 g) in boiling ether (50 ml) during 5 h gave a mixture of epimeric 3-ols, which was purified by chromatography on silica [ether–light petroleum (4 : 1)] to yield (a) 4,4-*dimethylergosta*-5,7,22-*triene*-1α,3α-*diol* in needles (0.32 g), m.p. 190—192° (from methanol), $[\alpha]_D^{22}$ −123° (*c* 0.83), $\lambda_{max.}$ 283 (ε 10 833) and 272 nm (10 971), $\nu_{max.}$ 3 610 and 3 465 cm^{-1} (free OH and hydrogen bonded OH-unchanged on dilution), τ 9.38, 9.19, 9.10, 9.00, 8.89, 8.78, and 8.68 (8 × 3 H, Me), 6.30br (2 H, t, H-1 and -3), 4.75 (2 H, m, H-22 and -23), and 4.50—3.98 (2 H, q, *J* 6 Hz, H-6 and -7) (Found: C, 82.0; H, 11.1%; M^+, 440. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%; *M*, 440); and (b) 4,4-*dimethylergosta*-5,7,22-*triene*-1α,3β-*diol* (0.1 g), which formed prisms, m.p. 192—195° (from aqueous ethanol), $[\alpha]_D$ −139° (*c* 0.7), $\nu_{max.}$ 3 610 cm^{-1} (free OH stretch), M^+ 440.

(*b*) Reduction of 1α,2α-epoxy-4,4-dimethylergosta-5,7,22-trien-3-one (0.2 g) with sodium borohydride (0.25 g) gave a mixture of epimeric 3-ols which was purified by t.l.c. on silica to yield 1α,2α-*epoxy*-4,4-*dimethylergosta*-5,7,22-*trien*-3α-*ol* (0.13 g) in needles, m.p. 185° (from methanol–ether), $[\alpha]_D^{22}$ −97° (*c* 1.62), $\lambda_{max.}$ 273 nm (ε 11 468), τ 6.99—6.53 (3 H, m, H-1, -2, and -3), 4.78 (2 H, m, H-22 and -23), and 4.36—4.00 (2 H, q, *J* 6 Hz, H-6 and -7) (Found: C, 82.4; H, 10.8. $C_{30}H_{46}O_2$ requires C, 82.1; H, 10.6%).

Reduction of this epoxide (50 mg) with lithium aluminium hydride gave 4,4-dimethylergosta-5,7,22-triene-1α,3α-diol (35 mg), identical (t.l.c., i.r., u.v., and n.m.r.) with the product from method (*a*).

Reaction of 4,4-*Dimethyl*-5,7-*dien*-3-*ones with* 4-*Phenyl*-1,2,4-*triazoline*-3,5-*dione*.—(*a*) A solution of 4-phenyl-1,2,4-triazoline-3,5-dione in acetone was added dropwise to a stirred solution of 4,4-dimethylcholesta-5,7-dien-3-one (0.5 g) in dichloromethane (100 ml) until a pink colouration persisted. Purified from ether, the *adduct* (16) (0.3 g) formed plates, m.p. 160° (decomp.), $[\alpha]_D^{22}$ −185° (*c* 2.32 in Me_2CO) (Found: C, 75.7; H, 8.6; N, 7.2. $C_{37}H_{51}N_3O_3$ requires C, 75.9; H, 8.8; N, 7.2%). A solution of this adduct (0.25 g) in reagent grade chloroform (10 ml) was refluxed for 10 min. The cooled mixture was filtered (to remove phenyltriazolidinedione), and the filtrate evaporated to yield 4,4-*dimethylcholesta*-5,7,14(15)-*trien*-3-*one* in needles (0.16 g), m.p. 157°, $[\alpha]_D^{22}$ −303° (*c* 0.7) (Found: C, 84.8; H, 10.6%; M^+, 408. $C_{29}H_{44}O$ requires C, 85.2; H, 10.9%; *M*, 408), $\lambda_{max.}$ 325 nm (ε 12 054), τ 4.10—3.72 (3 H, H-6, -7, and -15).

Reduction of this ketone (0.1 g) with lithium aluminium hydride in ether gave 4,4-*dimethylcholesta*-5,7,14(15)-*trien*-3β-*ol* (0.1 g) in flat needles, m.p. 137—139° (from ethanol), $[\alpha]_D^{22}$ −296° (*c* 0.4) (Found: C, 84.4; H, 11.2%; M^+, 410. $C_{29}H_{46}O$ requires C, 84.8; H, 11.3%; *M*, 410), $\lambda_{max.}$ 321 nm (ε 12 700), τ 6.59 (1 H, t, H-3α) and 4.29—3.57 (3 H, m, H-6, -7, and -15).

(*b*) Prepared (in 75% yield) as in (*a*) from 4-phenyl-1,2,4-triazoline-3,5-dione and 1α,2α-epoxy-4,4-dimethylcholesta-5,7-dien-3-one, the *adduct* separated from methanol (containing 0.01% pyridine) in plates, m.p. 201—203° (decomp.), $[\alpha]_D^{23}$ −176° (*c* 0.78 in Me_2CO) (Found: C, 73.8; H, 8.4; N, 7.0. $C_{37}H_{49}N_3O_4$ requires C, 74.1; H, 8.2; N, 7.0%). Boron trifluoride–ether (1 drop) was added to a stirred solution of this adduct (0.15 g) in benzene (10 ml). After 5 min the product was isolated and purified from ethanol to yield 1α,2α-*epoxy*-4,4-*dimethylcholesta*-5,7,14(15)-*trien*-3-*one* (0.06 g) in plates, m.p. 126—128°, $[\alpha]_D^{19}$ −244° (*c* 0.54), τ 6.42 (2 H, s, H-1 and -2) and 3.93 (3 H, m, H-6, -7, and -15) (Found: C, 81.9; H, 10.1. $C_{29}H_{42}O_2$ requires C, 82.4; H, 10.0%).

(*c*) Similarly the *adduct* from 4-phenyl-1,2,4-triazoline-3,5-dione and 1α,2α-epoxy-4,4-dimethylergosta-5,7,22-trien-3-one formed needles, m.p. 202—205° (decomp.) [from methanol containing pyridine (0.01%)], $[\alpha]_D^{19}$ −195° (*c* 0.44 in Me_2CO) (Found: C, 74.4; H, 8.2; N, 6.8. $C_{38}H_{49}N_3O_4$ requires C, 74.6; H, 8.1; N, 6.9%). Treatment of this adduct with boron trifluoride–ether gave (in 50% yield) 1α,2α-*epoxy*-4,4-*dimethylergosta*-5,7,14(15),22-*tetraen*-3-*one* in needles, m.p. 101—103° (from ethanol), $[\alpha]_D^{19}$ −268° (*c* 0.51), τ 6.43 (2 H, s, H-1 and -2), 4.73 (2 H, m, H-22 and -23), and 3.94 (3 H, m, H-6, -7, and -15) (Found: C, 82.5; H, 9.5. $C_{30}H_{42}O_2$ requires C, 82.9; H, 9.7%).

4,4-*Dimethyl*-9,10-*secoandrosta*-5,7,10(19)-*triene*-3β,17β-*diol* (19).—Prepared from 17β-acetoxy-4,4-dimethylandrosta-5,7-dien-3-one [16] (1 g) by reduction with sodium borohydride, the 3β-*ol* formed plates (0.72 g), m.p. 175—176° (from methanol), $[\alpha]_D^{22}$ −269° (*c* 2.0), $\nu_{max.}$ 1 730 cm^{-1} (ester C=O) (Found: C, 76.9; H, 9.3. $C_{23}H_{34}O_3$ requires C, 77.1; H, 9.6%). A solution of the 3β-ol (0.3 g) in ether (800 ml) was irradiated with a low pressure mercury vapour lamp in a Hanovia 1 l reactor for 4 h, in a stream of nitrogen. Solvent was removed under reduced pressure, and the residue was treated with maleic anhydride (0.3 g) in benzene (50 ml) at 75 °C for 0.5 h. The solvent was removed *in vacuo* and the residue was dissolved in methanolic 2N-potassium hydroxide (50 ml). After 30 min the mixture was diluted with water and extracted with ether to furnish a product which was purified by t.l.c. on silica [ethyl acetate–chloroform (1 : 9)] to yield (a) 4,4-*dimethyl*-9,10-*secoandrosta*-5,7,10(19)-*triene*-3β,17β-*diol* in needles (60 mg), m.p. 77—80° (from cyclohexane), $\lambda_{max.}$ 258 nm (ε 16 317) (Found: C, 79.7; H, 10.2%; M^+, 316. $C_{21}H_{32}O_2$ requires C, 79.7; H, 10.2%; *M*, 316); and (b) 4,4-*dimethyl*-9,10-*secoandrosta*-5,8(9),10(19)-*triene*-3β,17β-*diol* (0.1 g), R_F 0.34 on silica in ethyl acetate–chloroform (3 : 7). This triene failed to crystallise and had increasing u.v. absorption from 300 nm with a shoulder at 260 nm (ε 2 000); $\nu_{max.}$ 3 420, 3 080, 1 710, 1 638, 1 593, 1 055, and 900 cm^{-1}, τ 9.13 (3 H, s, H_3-18), 8.87 (6 H, s, 4-Me_2), 7.18 (2 H, d, *J* 7 Hz, H_2-7), 6.51 (2 H, m, H-3 and -17), 5.20 and 4.99 (2 H, ABq, *J* 2.7 Hz, H_2-19), and 4.67 and 4.44 (2 H, m, H-9 and -6), M^+ 316.

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