Epoxides of Lanosterol and Some Related Compounds

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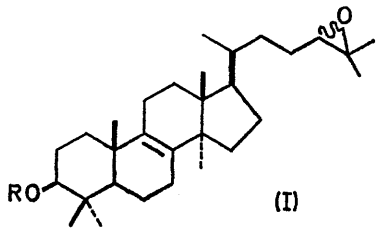
A convenient method for the separation of the two isomers of 24ξ,25-epoxy-5α-lanost-8-en-3β-yl acetate is described. The absolute configuration of these compounds is established by their conversion into the corresponding 5α-lanost-8-ene-3β,24ξ-diol 3-acetates, and thence by Horeau's method (treatment with α-phenylbutyric anhydride), and by the method of molecular rotation differences. A number of related compounds have also been prepared and their absolute configurations determined by correlation with the above compounds.

A RECENT publication [1] described the separation of the C-24 stereoisomers of 24,25-epoxy-5α-lanost-8-en-3β-yl acetate (I; R = Ac). Previous workers [2] had always dealt with a mixture of the two diastereoisomers. We devised a convenient method for the separation of the acetates (I; R = Ac), based upon the considerably different solubilities of the two isomers in methanol, the details of which and the determination of the absolute configuration of each isomer we now report.

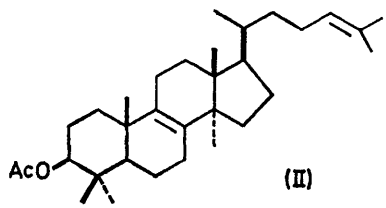
Pure 5α-lanosta-8,24-dien-3β-yl acetate (II) [3] was treated at 0° with 1·1 equiv. of perbenzoic acid in chloroform with efficient external cooling. The n.m.r. spectrum of the product indicated that attack of the peroxy-acid had occurred exclusively at the trisubstituted, and *a priori* less reactive, 24,25-double bond. This reflects the considerable steric hindrance of the tetrasubstituted 8,9-double bond, although other more subtle factors may be involved. Ourisson and his co-workers have previously discussed some analogous observations.[4] The product was treated with boiling methanol. After recrystallisation, the insoluble material gave 24ξ,25-epoxy-5α-lanost-8-en-3β-yl acetate

[1] D. H. R. Barton, D. M. Harrison, G. P. Moss, and D. A. Widdowson, *J. Chem. Soc.* (*C*), 1970, 775.
[2] C. Doree and V. Petrow, *J. Chem. Soc.*, 1936, 1562; G. Ponsinet and G. Ourisson, *Phytochemistry*, 1965, **4**, 799.
[3] D. A. Lewis and J. F. McGhie, *Chem. and Ind.*, 1956, 550.
[4] G. Charles, G. Ponsinet, and G. Ourisson, *Bull. Soc. chim. France*, 1967, 4453.

isomer A (IA; R = Ac). The methanol-soluble material yielded the acetate isomer B (IB; R = Ac). T.l.c. of the separated isomers (IA; R = Ac) and (IB; R = Ac) involving repeated elution with a relatively non-polar solvent showed them as two distinct spots (R_F 0·19 and 0·25, respectively). These separated cleanly when run together, thus demonstrating the rat-liver enzymes gave 24,25-epoxy-5α-lanost-8-en-3β-ol (I; R = H),[6] and with microsomes of *Rubus fruticosa* gave 24,25-epoxycycloartanol.[7] In both these cases the 24,25-epoxide was a 1 : 1 mixture of the C-24 epimers. There are, however, a number of naturally occurring 24,25-epoxytriterpenes,[8] and it is likely that these compounds are sterically homogeneous. As a



(I)



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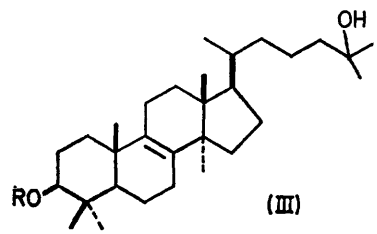

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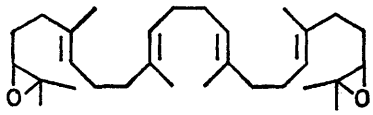

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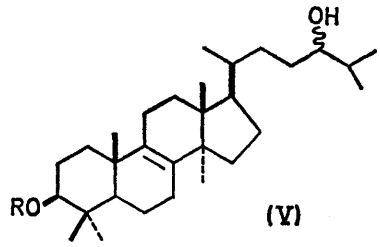

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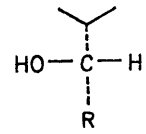

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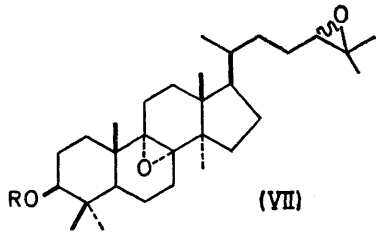

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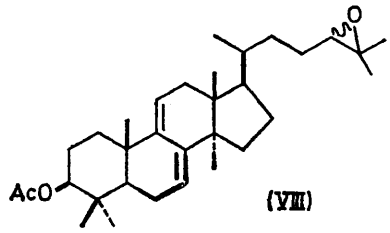

(VIII)

A = (24*R*)-
B = (24*S*)-

stereochemical purity of each. Examination of the total product in this way showed the two isomers to be present in approximately equal amounts (*cf.* the reaction of cycloartenol acetate with *p*-nitroperbenzoic acid, which also gives a 1 : 1 mixture of the diastereoisomeric 24,25-epoxides [4]). Compounds (IA; R = Ac) and (IB; R = Ac) had essentially identical i.r. and n.m.r. spectra. Their relation was further confirmed by reduction with lithium aluminium hydride in tetrahydrofuran, when each isomer gave the same product, 5α-lanost-8-ene-3β,25-diol (III; R = H).

In order to elucidate the mechanism of the enzyme-controlled cyclisation of 2,3-epoxysqualene, modified substrates [5-7] such as 2,3;22,23-diepoxysqualene (IV) [6,7] have been utilised. Thus, incubation of (IV) with preliminary to the investigation of such compounds, we sought a method for the determination of the absolute configuration of the isomers of 24ξ,25-epoxy-5α-lanost-8-en-3β-yl acetate (I; R = Ac).

We determined the configuration of the 24,25-epoxide by converting it into the corresponding 24-alcohol and then investigating this compound by the method of Horeau [9] and by the method of molecular rotation differences.[10] For the conversion of 24ξ,25-epoxy-5α-lanost-8-en-3β-yl acetate (I; R = Ac) into 24-hydroxy-5α-lanost-8-en-3β-yl acetate (V; R = Ac) we used diborane–sodium borohydride,[11] a system that reacts with neither the 3β-acetate nor Δ^8-function of (I;

[5] E. E. van Tamelen, R. P. Hanzlik, R. B. Clayton, and A. L. Burlingame, *J. Amer. Chem. Soc.*, 1970, **92**, 2137, and references cited therein.

[6] E. J. Corey and S. K. Gross, *J. Amer. Chem. Soc.*, 1967, **89**, 4561.

[7] R. Heintz, P. C. Schaefer, and P. Benveniste, *Chem. Comm.*, 1970, 946.

[8] See, for example, D. Shiengthong, A. Verasarn, P. Na-Nonggai-Suwanrath, and E. W. Warnhoff, *Tetrahedron*, 1965, **21**, 917; C. W. L. Bevan, D. E. U. Ekong, T. G. Halsall, and P. Toft, *J. Chem. Soc.* (*C*), 1967, 820.

[9] A. Horeau, *Tetrahedron Letters*, 1961, 506; 1962, 965; A. Horeau and H. B. Kagan, *Tetrahedron*, 1964, **20**, 2431.

[10] W. Klyne and W. M. Stokes, *J. Chem. Soc.*, 1954, 1979.

[11] H. C. Brown and Nung-Min Yoon, *J. Amer. Chem. Soc.*, 1968, **90**, 2686.

R = Ac) but which reduces the 24,25-epoxide predominantly in the required anti-Markownikov sense.

Treatment of the epoxy-acetate (IA or IB; R = Ac) with diborane–sodium borohydride in tetrahydrofuran–diglyme gave a readily separable mixture of 24-hydroxy- (VA or VB respectively; R = Ac) and 25-hydroxy-5α-lanost-8-en-3β-yl acetate (III; R = Ac) in a ratio of *ca.* 5 : 3. The tendency for hydrolysis to occur during work-up with formation of the corresponding 3β-hydroxy-compounds was suppressed by the use of an appropriate buffer. The alcohols (VA and VB; R = Ac) were both crystallised from light petroleum and, as for the corresponding epoxides, the stereochemical homogeneity of each isomer was established by t.l.c. After repeated elution in a relatively non-polar solvent the R_F values for compounds (VA and VB; R = Ac) were 0·08 and 0·30, respectively; the M_D values were +293 and +223°. 5α-Lanost-8-en-3β-yl acetate, prepared by hydrogenation of pure 5α-lanosta-8,24-dien-3β-yl acetate,[3] had M_D +270°. It is well established that the alcohols (VI; R = Et, Pr^n, Bu^n, or n-pentyl) of *S*-configuration all have negative rotations.[10] It follows that compounds (IA; R = Ac) and (VA; R = Ac) are (24*R*)-24,25-epoxy-5α-lanost-8-en-3β-yl acetate and (24*R*)-24-hydroxy-5α-lanost-8-en-3β-yl acetate, respectively, and that compounds (IB; R = Ac) and (VB; R = Ac) are the corresponding (24*S*)-isomers.

To confirm these findings both compounds (VA and VB; R = Ac) were treated with racemic α-phenylbutyric anhydride[12] in application of the Horeau method according to Herz and Kagan.[13] The alcohol (VA; R = Ac) gave a residue of (+)-α-phenylbutyric acid, indicative of a 24*R*-configuration, whilst the alcohol (VB; R = Ac) afforded (−)-α-phenylbutyric acid indicating a 24*S*-configuration.

Recently Brieskorn and Dertinger[14] have described (24*R*)-5α-lanost-8-ene-3β,24-diol (V; R = H), m.p. 167° (from aqueous ethanol), the product of hydrogenation of a novel natural product to which they assign the structure (24*R*)-5α-lanosta-8,25-diene-3β,24-diol. The configuration at C-24 of both compounds was based upon the high positive rotation of the former ($[\alpha]_D$ +91·5°), a value that we considered to be abnormal. Consequently, we prepared a sample of the diol (V; R = H) by mild base hydrolysis of stereochemically pure (24*R*)-24-hydroxy-5α-lanost-8-en-3β-yl acetate (VA; R = Ac). The product crystallised from acetone–ethanol as an ethanol solvate (n.m.r.), m.p. 179—181°, $[\alpha]_D$ +57·7°. We feel therefore that the result of Brieskorn and Dertinger should be regarded with some reservation.

We have also prepared some other epoxides in the lanosterol series, and by correlations we have established the absolute configuration of these. Thus, treatment of 5α-lanosta-8,24-dien-3β-yl acetate (II) with an excess of perbenzoic acid in chloroform gives (24*R*)-8α,9;24,25-diepoxy-5α-lanostan-3β-yl acetate (VIIA; R = Ac) and the corresponding (24*S*)-isomer (VIIB; R = Ac). The configuration of these compounds followed from their alternative preparation from the (24*R*)- and (24*S*)-monoexpoides (I; R = Ac), respectively. The ease with which 8α,9-epoxides are converted into 7,9(11)-dienes is well-known,[15] and forms the basis for a convenient synthetic route to the latter system. By the action of hydrobromic acid, the (24*R*)- and (24*S*)-diepoxides (VII; R = Ac) afforded the corresponding 7,9(11)-diene-24,25-bromohydrins (as a mixture of 24-bromo-25-hydroxy- and 25-bromo-24-hydroxy-compounds), which on treatment with base followed by reacetylation gave (24*R*)- and (24*S*)-24,25-epoxy-5α-lanosta-7,9(11)-dien-3β-yl acetate (VIII) respectively. The dienes (VIII) are also the products of the mono-epoxidation of 5α-lanosta-7,9(11),24-trien-3β-yl acetate.

The presence on the lanosterol skeleton of an 8α,9- or a 24,25-epoxide gives rise to a diagnostic set of peaks in the n.m.r. spectrum. In the latter case the two 25-methyl groups appear as singlets at τ 8·69 and 8·73, and the 24-proton as an apparent triplet (*J* 5 Hz) at τ *ca.* 7·32. As already noted compounds differing only in the stereochemistry at C-24 show essentially identical n.m.r. spectra. The positions of the signals for the nuclear methyl groups in some compounds of the former type are summarised in the Table. The singlets at τ 8·86, 9·04, 9·09, 9·19, and 9·20 in the 3β-hydroxy-series are replaced by ones at τ 8·87, 9·11, 9·16, 9·19, and 9·22 in the corresponding 3β-acetates (average values ±0·02). The assignments in the Table are

Methyl resonances (τ values) in the n.m.r. spectra of some 8α,9-epoxides

Compound	Methyl resonance (τ) 4α-	4β-	10β-	13β-	14α-
8α,9-Epoxy-5-lanostan-3β-yl acetate	9·19	9·16	9·11	9·24	8·88
8α-9-Epoxy-5α-lanostan-3β-ol	9·04	9·18	9·09	9·20	8·86
8α,9;24,25-Diepoxy-5α-lanostan-3β-yl acetate	9·20	9·16	9·12	9·23	8·87
8α,9;24 25-Diepoxy-5α-lanostan-3β-ol	9·04	9·20	9·09	9·20	8·86
8α,9-Epoxy-5α-lanost-24-en-3β-yl acetate [3]	9·18	9·15	9·12	9·22	8·85
8α,9-Epoxy-5α-lanost-24-en-3β-ol	9·04	9·20	9·10	9·20	8·86
24ξ,25-Dibromo-8α,9-epoxy-5α-lanostan-3β-yl acetate [3]	9·18	9·16	9·10	9·21	8·88

based on the following considerations. The singlet at lowest field is ascribed to the 14α-methyl group which from models can be seen to be positioned within the deshielding zone of an 8α,9-epoxide group. The signals at τ 9·09 and 9·20 (3β-hydroxy) and τ 9·11 and 9·22 (3β-acetate) are assigned to the 10β- and 13β-methyl groups, respectively, from a consideration of their chemical shifts[16] and from the fact that they are

[12] H. Falk and K. Schlogl, *Monatsh.*, 1965, **96**, 283.
[13] W. Herz and H. B. Kagan, *J. Org. Chem.*, 1967, **32**, 216.
[14] C. H. Brieskorn and G. Dertinger, *Arch. Pharm.*, 1970, **303**, 960.
[15] M. J. Birchenough and J. F. McGhie, *J. Chem. Soc.*, 1949, 2038; J. Fried, J. W. Brown, and M. A. Applebaum, *Tetrahedron Letters*, 1965, 849.
[16] F. Hemmert, B. Lacoume, J. Levisalles, and G. R. Pettit, *Bull. Soc. chim. France*, 1966, 976.

relatively unaffected by the change at C-3. It is well established that the conversion of lanost-8-en-3β-ols into lanost-8-en-3β-yl acetates causes a shift in the position of the signals for the 4α- and 4β-methyl groups of 6·5 Hz upfield and 5·0 Hz downfield, respectively.[16] On this basis we attribute the peaks at τ 9·04 and 9·19 (3β-hydroxy) and τ 9·19 and 9·16 (3β-acetate) to the 4α- and 4β-methyl groups, respectively, with the corollary that the presence of an 8α,9-epoxide group changes the conformation of the molecule such that the shifts occurring on acetylation are 9·0 Hz upfield (4α-methyl) and 2·0 Hz downfield (4β-methyl).

EXPERIMENTAL

N.m.r. data refer to deuteriochloroform solutions with tetramethylsilane as internal standard, and were recorded on a Perkin-Elmer R10 instrument. Unless otherwise stated rotations refer to chloroform solutions and u.v. spectra to solutions in absolute ethanol. Column chromatography was on Laporte type O alumina, and t.l.c. on plates prepared using Merck Silica Gel GF_{254}. Light petroleum refers to the fraction b.p. 60—80°. Isomers A and B are the compounds of absolute stereochemistry (24*R*)- and (24*S*)-, respectively.

Monoepoxidation of 5α-Lanosta-8,24-dien-3β-yl Acetate.—A solution of pure 5α-lanosta-8,24-dien-3β-yl acetate [3] (10 g) in chloroform (20 ml) was cooled to −10° and so treated with a solution of perbenzoic acid in chloroform (34 ml, 1·1 mol) that the temperature did not rise above 0°. The solution was left overnight at 0° and then washed thoroughly with 2N-sodium hydroxide followed by water (failure at this stage to remove all traces of acid leads to the formation of 24-hydroxy-25-methoxy-derivatives during the subsequent treatment with methanol). The solvent was evaporated, and the residue was treated with boiling methanol (120 ml) and filtered whilst hot. The insoluble material was recrystallised twice from acetone to give lustrous plates of 24ξ,25-*epoxy-5α-lanost-8-en-3β-yl acetate* (IA; R = Ac) (3·3 g), m.p. 194—197°, $[\alpha]_D$ +58·6° (*c* 2·79), $\nu_{max.}$ (CCl_4) 1735 and 1245 cm^{-1}, τ 5·50 (1H, q, 3α-H), 7·32 (1H, t, 24-H), 7·96 (3H, s, AcO), 8·70 and 8·74 (each 3H, s, 26-, 27-H_3), 9·00 (3H, s), 9·12 (9H, s), and 9·30 (3H, s), M^+ (mass spectrum), 484, *m/e* 469 (M^+ − Me) and 409 (base peak, M^+ − Me − HOAc) (Found: C, 79·3; H, 10·85. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

The filtrate was evaporated to small volume and left to crystallise. Recrystallisation from acetone gave needles of *isomer B* (IB; R = Ac) (3·5 g), m.p. 137—139°, resolidifying and remelting 143·5—144·5°, $[\alpha]_D$ +49·2° (*c* 2·23), $\nu_{max.}$ (CCl_4) 1735 and 1245 cm^{-1}, τ 5·47 (1H, q, 3α-H), 7·27 (1H, t, 24-H), 7·91 (3H, s, AcO), 8·66 and 8·70 (each 3H, s, 26- and 27-H_3), 9·00 (3H, s), 9·12 (9H, s) and 9·30 (3H, s) (Found: C, 79·2; H, 10·7. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Comparison (t.l.c.) of the 24,25-epoxy-isomers A and B [eluting 17 times with benzene–light petroleum (1 : 1, v/v)] showed that each was stereochemically pure.

24,25-Epoxy-5α-lanost-8-en-3β-ol (*Isomer A*) (I; R = H). The foregoing 24,25-epoxyacetate isomer A was treated with 10% potassium hydroxide in ethanol to give the corresponding alcohol, m.p. (from acetone) 131—134°, $[\alpha]_D$ +63·1° (*c* 0·65), $\nu_{max.}$ (Nujol) 3500—3200br cm^{-1}.

Reduction of 24,25-Epoxy-5α-lanost-8-en-3β-yl Acetate (Isomers A and B) with Lithium Aluminium Hydride.—A solution of 24,25-epoxy-5α-lanost-8-en-3β-yl acetate isomer A (1 g) in dry tetrahydrofuran (100 ml) was treated with lithium aluminium hydride (1 g). The mixture was heated under reflux for 12 h and then the excess of lithium aluminium hydride was destroyed by the careful addition of water. The organic layer was separated and the aqueous layer was extracted twice with ether. The combined organic extracts were washed with water, dried, and evaporated to leave 5α-lanost-8-ene-3β,25-diol (III; R = H) (820 mg), m.p. 184—186° (from ethyl acetate), $[\alpha]_D$ +59° (*c* 1·20), $\nu_{max.}$ (Nujol) 3350br and 1040 cm^{-1}, τ 6·78 (1H, complex, 3α-H), 8·62 (2H, s imposed on methyl envelope, exchangeable with D_2O, 2 × OH), 8·80 [6H, s, $Me_2C(OH)$], 9·00 (6H, s), 9·12 (3H, s), 9·19 (3H, s), and 9·31 (3H, s). Similar reduction of the 24,25-epoxide isomer B gave an identical product (t.l.c., i.r., and mixed m.p.).

Reduction of 24,25-Epoxy-5α-lanost-8-en-3β-yl Acetate (Isomers A and B) with Diborane–Sodium Borohydride.—An approximately 1M-solution of diborane in tetrahydrofuran (25 ml) was cooled on an ice-bath and a solution of sodium borohydride (1 g) in diglyme (10 ml) was added. The mixture was stirred under nitrogen for 15 min and then a solution of 24,25-epoxy-5α-lanost-8-en-3β-yl acetate (isomer A) (2·0 g) in dry tetrahydrofuran (25 ml) was added. After 4 h (t.l.c. control), the mixture was poured into a sodium hydroxide–potassium dihydrogen phosphate buffer. The organic layer was rapidly separated and the aqueous layer was extracted twice with chloroform. The combined extracts were processed in the usual way and the product thus obtained was chromatographed [alumina (80 g); benzene–chloroform (1 : 1 v/v)] to give *24-hydroxy-5α-lanost-8-en-3β-yl acetate* (*isomer A*) (VA; R = Ac) (950 mg), plates, m.p. 152—154° (from light petroleum), $[\alpha]_D$ +60·1° (*c* 2·09), M_D +293°, $\nu_{max.}$ (CCl_4) 3630, 1735, and 1240 cm^{-1}, τ 5·55 (1H, complex, 3α-H), 6·65 (1H, complex, 24-H), 7·98 (3H, s, AcO), and 8·5 (1H, imposed on methylene envelope, exchangeable with D_2O, OH) (Found: C, 78·8; H, 11·0. $C_{32}H_{54}O_3$ requires C, 79·0; H, 11·2%).

Similarly, 24,25-epoxy-5α-lanost-8-en-3β-yl acetate (isomer B) afforded the *24-hydroxy-acetate* (*isomer B*) (VB; R = Ac), needles, m.p. 144—145° (from light petroleum), partly resolidifying and then remelting 154—155°, $[\alpha]_D$ +47° (*c* 2·00), M_D +229° (Found: C, 79·1; H, 11·2. $C_{32}H_{54}O_3$ requires C, 79·0; H, 11·2%). Comparison (t.l.c.) of the above 24-hydroxy-isomers A and B [eluting 8 times with light petroleum–benzene (1 : 3 v/v)] showed that each was stereochemically pure.

Determination of the Absolute Configuration of 24-Hydroxy-5α-lanost-8-en-3β-yl Acetate (*Isomers A and B*).—A solution of the 24-alcohol (isomer A) (51 mg) and α-phenylbutyric anhydride (120 mg) in dry pyridine (1 ml) was left at room temperature for 2 days. Water (0·5 ml) was added, and the solution was left for a further 4 h. More water (10 ml) was added, and the solution was extracted with ether (4 × 10 ml). The combined extracts were washed with water, 5% sodium hydrogen carbonate (3 × 10 ml), and again twice with water. The combined aqueous extracts were washed with chloroform, and then acidified with an excess of 2N-sulphuric acid. The acidified solution was extracted with chloroform (4 × 10 ml), and the combined extracts were dried and evaporated. This yielded α-phenylbutyric acid (82 mg, constant weight after drying *in vacuo*) which was pure (t.l.c.) and which had a rotation of +0·093° (2 ml solution in dry benzene, 1 dm

tube). This is equivalent to $[\alpha]_D$ +2·27°, and an optical yield, calculated according to Herz and Kagan,[13] of 15%. The original ether layer was washed thoroughly with water, 2N-sulphuric acid, and again with water, and evaporated. The residual ester contained none of the starting alcohol (t.l.c.). In an identical fashion the isomer B (72 mg) and α-phenylbutyric anhydride (253 mg) afforded α-phenylbutyric acid (215 mg), $[\alpha]_D$ −1·27° (*c* 10·7), equivalent to an optical yield of 13%. It follows that the absolute configurations of isomers A and B are (24*R*)- and (24*S*)- respectively.

(24R)-5α-*Lanost*-8-*ene*-3β,24-*diol* (V; R = H).—A solution of (24*R*)-24-hydroxy-5α-lanost-8-en-3β-yl-acetate (40 mg) in ethanol (25 ml) containing 5% potassium hydroxide was left at room temperature for 4 h. During this time the product began to crystallise out. The solution was diluted with water and extracted with ether. Work-up in the usual manner afforded needles of the diol (V; R = H) (34 mg), m.p. 179—181° [from acetone–ethanol (4 : 1 v/v)], $[\alpha]_D$ +57·7° (*c* 1·26), τ 6·28 (2H, q, $CH_3 \cdot CH_2 \cdot OH$), 6·70 (2H, complex, 3-H and 24-H), 8·60 (2H, s, exchangeable with D_2O, 2 × OH), 8·79 (3H, t, $CH_3 \cdot CH_2 \cdot OH$), 8·99 (6H, s), 9·10 (3H, s), 9·17 (3H, s), and 9·30 (3H, s).

Diepoxidation of 5α-*Lanosta*-8,24-*dien*-3β-*yl Acetate*.—Pure 5α-lanosta-8,24-dien-3β-yl acetate [3] (10 g) in chloroform (100 ml) was treated as in the monoepoxidation (see before) but with 100 ml (2·5 mol) of perbenzoic acid in chloroform. After the washing, pyridine (1 ml) was added to the solution and the solvent was evaporated. The residue was treated with boiling methanol (200 ml) and filtered whilst hot. The insoluble material was recrystallised from acetone to give plates of (24R)-8α,9;24,25-*diepoxy*-5α-*lanostan*-3β-*yl acetate* (VII; R = Ac) (2·6 g), m.p. 203—204°, $[\alpha]_D$ +15·3° (*c* 1·02), $\nu_{max.}$ (Nujol) 1735 and 1255 cm^{-1}, τ 5·55 (1H, q, 3α-H), 7·32 (1H, t, 24-H), 7·97 (3H, s, AcO), 8·70 and 8·74 (each 3H, s, 26- and 27-H_3), 8·87 (3H, s), 9·12 (3H, s), 9·16 (3H, s), 9·20 (3H, s), and 9·23 (3H, s), M^+ (mass spectrum), 500, *m/e* 482, 467, 425, 407, 353, 305, 136 (base peak), and 121 (Found: C, 76·5; H, 10·2. $C_{32}H_{52}O_4$ requires C, 76·8; H, 10·5%).

The filtrate quickly deposited crystals, m.p. 183—186°, a mixture of (24*R*)- and (24*S*)-isomers. On cooling the filtrate further material was obtained which was recrystallised three times from acetone to give needles of the (24*S*)-*isomer* (VII; R = Ac) (3·1 g), m.p. 160—161°, $[\alpha]_D$ +6·7° (*c* 1·01), $\nu_{max.}$ (Nujol) 1735 and 1260 cm^{-1}, τ 5·57 (1H, q, 3α-H), 7·31 (1H, t, 24-H), 7·96 (3H, s, AcO), 8·69 and 8·72 (each 3H, s, 26- and 27-H_3), 8·87 (3H, s), 9·12 (3H, s), 9·16 (3H, s), 9·19 (3H, s), and 9·23 (3H, s) (Found: C, 76·9; H, 10·5. $C_{32}H_{52}O_4$ requires C, 76·8; H, 10·5%).

Conversion of (24R)- *and* (24S)-24,25-*Epoxy*-5α-*lanost*-8-*en*-3β-*yl Acetate into* (24R)- *and* (24S)-8α,9;24,25-*Diepoxy*-5α-*lanostan*-3β-*yl Acetate, Respectively*.—(24*R*)-24,25-Epoxy-5α-lanost-8-en-3β-yl acetate (1·5 g) in chloroform (20 ml) was treated with a solution of perbenzoic acid in chloroform (10 ml, 2 mol) at 0°. After 3 days the solution was washed thoroughly with 2N-sodium hydroxide, then with water. Pyridine (0·5 ml) was added and the solvent was evaporated off. The residue crystallised from acetone–methanol as plates of (24*R*)-8α,9;24,25-diepoxy-5α-lanostan-3β-yl acetate (1·3 g), m.p. 200—201°, $[\alpha]_D$ +15·4° (*c* 1·00). Similarly the (24*S*)-24,25-monoepoxide gave the (24*S*)-8α,9;24,25-diepoxide, m.p. 158—160°, $[\alpha]_D$ +5·5° (*c* 1·02).

In an analogous experiment, 5α-lanost-8-en-3β-yl acetate was converted into 8α,9-epoxy-5α-lanostan-3β-yl acetate, needles, m.p. 139—140° (from acetone–methanol), $[\alpha]_D$ +13·4° (*c* 1·06) (lit.,[15] m.p. 140—141°, $[\alpha]_D$ +15°), M^+ (mass spectrum), 486, *m/e* 468, 453, 411, 393, 339, 291, 136 (base peak), and 121.

Conversion of (24R)- *and* (24S)-8α,9;24,25-*Diepoxy*-5α-*lanostan*-3β-*yl Acetate* (VII; R = Ac) *into* (24R)- *and* (24S)-24,25-*Epoxy*-5α-*lanosta*-7,9(11)-*dien*-3β-*yl Acetate* (VIII), *Respectively*.—A solution of (24*R*)-8α,9;24,25-diepoxy-5α-lanostan-3β-yl acetate (1·0 g) in ether (100 ml) was shaken with 48% constant-boiling hydrobromic acid (3 ml) for 30 min. Water (10 ml) was added and the aqueous layer separated. The organic layer was washed with 2N-sodium carbonate and then water, dried, and evaporated. The residue was dissolved in benzene and heated under reflux with 5% potassium hydroxide in ethanol for 3 h. Usual work-up afforded material, m.p. 155—156° (from acetone–methanol), $[\alpha]_D$ +67·4° (*c* 1·02). This was acetylated (acetic anhydride–pyridine, room temperature, overnight) to yield (24R)-24,25-*epoxy*-5α-*lanosta*-7,9(11)-*dien*-3β-*yl acetate*, m.p. 226—227°, $[\alpha]_D$ +94° (*c* 1·00), $\nu_{max.}$ (Nujol) 1730 and 1255 cm^{-1}, $\lambda_{max.}$ 235, 243, and 253 nm (log ε 4·21, 4·26, and 4·10), τ 4·58 (2H, complex, 7- and 11-H), 5·47 (1H, t, 3α-H), 7·30 (1H, t, 24-H), 7·93 (3H, s, AcO), 8·68 and 8·72 (each 3H, s, 26- and 27-H_3), 9·00 (3H, s), 9·05 (3H, s), 9·12 (6H, s), and 9·42 (3H, s) (Found: C, 79·5; H, 10·5. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%).

Similarly, the (24*S*)-diepoxide (VII; R = Ac) afforded (24S)-24,25-*epoxy*-5α-*lanosta*-7,9(11)-*dien*-3β-*yl acetate*, m.p. 206—207°, $[\alpha]_D$ +89·4° (*c* 0·87) (Found: C, 79·5; H, 10·5. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%).

Monoepoxidation of 5α-*Lanosta*-7,9(11),24-*trien*-3β-*yl Acetate*.—A solution of 5α-lanosta-7,9(11),24-trien-3β-yl acetate [3] (2·0 g) in chloroform (20 ml) was treated at −10° with a solution of perbenzoic acid in chloroform (7 ml, 1·05 mol). After 3 days at 0° the solution was worked-up in the usual manner. The product (910 mg) was crystallised from benzene–methanol, m.p. 215—216°, and was recrystallised from acetone to afford (24*R*)-24,25-epoxy-5α-lanosta-7,9(11)-dien-3β-yl acetate, fine plates, m.p. 223—224°, $[\alpha]_D$ +91·5 (*c* 1·03), identical with a sample prepared from the (24*R*)-diepoxide (VII; R = Ac). The mother liquors from the above crystallisations were combined and evaporated to dryness. The residue was treated with boiling acetone (25 ml) and filtered whilst hot. On addition of methanol the filtrate gave (24*S*)-24,25-epoxy-5α-lanosta-7,9(11)-dien-3β-yl acetate (320 mg), fine needles, m.p. 205—207°, $[\alpha]_D$ +90·8° (*c* 0·99), $\lambda_{max.}$ 235, 243, and 252 nm (log ε 4·25, 4·29, and 4·12), identical with a sample prepared from the (24*S*)-diepoxide (VII; R = Ac).

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