A Novel Aromatisation Reaction of 11-Oxolanostanes

By **William Lawrie,* William Hamilton, John McLean,** and **James Meney,** Department of Pure and Applied Chemistry, University of Strathclyde, Cathedral Street, Glasgow G1 1XL

Oxidation of 11-oxolanostan-3β-yl acetate (1a) with selenium dioxide in acetic acid is accompanied by a C-nor-D-homo rearrangement of the steroid skeleton with aromatisation of ring D and formation of 9β-hydroxy-4,4,15-trimethyl-11-oxo-14(13→12)*abeo*-5α-cholesta-12,14,16-trien-3β-yl acetate (2a). Analogous aromatic products are obtained from 3β,7α- and 3β,7β-diacetoxy-11-oxolanostanes (1b and c), respectively. methyl 3β-acetoxy-11-oxo-25,26,27-trinorlanostan-24-oate (1e) and methyl 3β-acetoxy-24-methyl-11-oxolanostan-21-oate (1f), under the same conditions.

THE existence of the C-nor-D-homo-steroid skeleton was first shown [1] in the steroidal alkaloids jervine and veratramine. Shortly afterwards the C-nor-D-homo-steroid rearrangement was discovered.[2] The rearrangement has been achieved by solvolysis of the methanesulphonates of 12β-hydroxysapogenins [2-4] and by heating the 12-tosylhydrazone of hecogenin in the presence of alkali.[3,4] In view of the natural occurrence of the skeleton in jervine and veratramine the latter have been employed along with hecogenin in the synthesis of C-nor-D-homo analogues of testosterone,[5] epiandrosterone,[6] and pregnanolone.[7]

Oxidation of 11-oxolanostan-3β-yl acetate (1a) with selenium dioxide in a neutral solvent such as dioxan gives 9α-hydroxy-11,12-dioxolanostan-3β-yl acetate; [8] however, when the oxidation is performed in acetic acid the major product is a compound $C_{32}H_{48}O_4$ to which we ascribe the structure (2a), *viz.* 9β-hydroxy-4,4,15-trimethyl-11-oxo-14(13⟶12)*abeo*-5α-cholesta-12,14,16-trien-3β-yl acetate.

The u.v. spectrum with maxima at 218, 262, and 314 nm (ε 28 400, 13 000, and 2 500) is typical of an aromatic ketone [9] and suggested the presence of a substituted indan-1-one system; [10] the i.r. spectrum revealed the presence of hydroxy (3 580 cm^{-1}), acetate (1 731 and 1 238 cm^{-1}), and carbonyl groups (1 710 cm^{-1}). The compound is not phenolic and the hydroxy group is resistant to oxidation and to acetylation under normal conditions, indicating its tertiary nature, but it can be acetylated under forcing conditions.

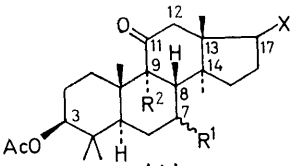
The n.m.r. spectrum shows the presence of one aromatic proton (τ 2.90), two aromatic methyl groups (τ 7.48 and 7.72), and the acetate methyl group (τ 7.99). The hydroxy proton gives a singlet at τ 7.81 (disappearing on deuteriation) and the 3α-proton a multiplet (1H) at τ 5.30, indicating that the acetate group is secondary. Hydrolysis of the acetate (2a) affords the corresponding dihydroxy-ketone (2i), which in turn is oxidised by chromium trioxide to the 9β-hydroxy-3,11-dione (2j).

The spectra of the aromatic acetate (2a) and its derivatives (see Experimental section) indicate that the aromatic ring in these compounds carries one proton and two methyl substituents and is consequently a terminal ring. Since ring A is intact, it is concluded that the formation of the aromatic acetate (2a) has involved contraction of ring C with concomitant expansion and aromatisation of ring D.

Possible locations for the tertiary hydroxy group in the aromatic compound (2a) follow from its mass spectral data and those of the derived 3,9-dihydroxy-11-ketone (2i) and the 9-hydroxy-3,11-dione (2j). The most abundant peak in each spectrum occurs at *m/e* 287 due to an ion $C_{19}H_{27}O_2^+$ (3a) which must contain the aromatic ring. The ion (3a) contains two oxygen functions, one derived from the 11-carbonyl group and the other from the tertiary hydroxy group, indicating that the latter is associated with rings C and D or the side chain X; possible sites are C-8, C-9, C-20, and C-25. The least likely of these, C-25, was excluded when it

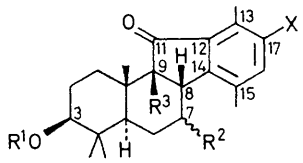
[1] J. Fried, O. Wintersteiner, M. Moore, B. M. Iselin, and A. Klingsberg, *J. Amer. Chem. Soc.*, 1951, **73**, 2970.
[2] R. F. Hirschmann, C. S. Snoddy, jun., and N. L. Wendler, *J. Amer. Chem. Soc.*, 1952, **74**, 2693.
[3] C. F. Hiskey, R. F. Hirschmann, and N. L. Wendler, *J. Amer. Chem. Soc.*, 1953, **75**, 5135.
[4] R. F. Hirschmann, C. S. Snoddy, jun., C. F. Hiskey, and N. L. Wendler, *J. Amer. Chem. Soc.*, 1954, **76**, 4013.
[5] S. M. Kupchan and S. D. Levine, *J. Amer. Chem. Soc.*, 1964, **86**, 701.
[6] H. Mitsuhashi and N. Kawahara, *Tetrahedron*, 1965, **21**, 1215.
[7] W. F. Johns and I. Laos, *J. Org. Chem.*, 1965, **30**, 4220.
[8] W. Voser, H. Günthard, H. Heusser, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 2065.
[9] A. I. Scott, 'Ultraviolet Spectra of Natural Products,' Pergamon, Oxford, 1964, p. 100.
[10] 'The Ultraviolet Atlas of Organic Compounds,' vol. IV, Butterworth, London, 1968.

was found that oxidation of methyl 3β-acetoxy-11-oxo-25,26,27-trinorlanostan-24-oate (1e) with selenium dioxide in acetic acid gave an aromatic compound (2e) containing a tertiary hydroxy group and having characteristics exactly paralleling those of the aromatic product (2a) derived from 11-oxolanostanyl acetate (1a), the difference residing in the side chain X. That the tertiary hydroxy group was not at C-20 was shown by hydrolysis of the aromatic ester (2e) to the corresponding acid, which did not form a γ-lactone.



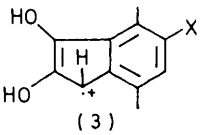
(1)

a; $R^1 = R^2 = H$, $X = C_8H_{17}$
b; $R^1 = \alpha$—OAc, $R^2 = H$, $X = C_8H_{17}$
c; $R^1 = \beta$—OAc, $R^2 = H$, $X = C_8H_{17}$
d; $R^1 = H$, $R^2 = OH$, $X = C_8H_{17}$
e; $R^1 = R^2 = H$, $X = C_6H_{11}O_2$
f; $R^1 = R^2 = H$, $X = C_{10}H_{19}O_2$



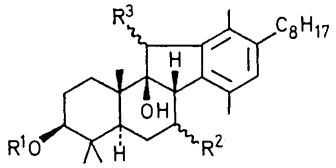
(2)

a; R^1 = Ac, $R^2 = H$, R^3 = OH, $X = C_8H_{17}$
b; R^1 = Ac, $R^2 = H$, R^3 = OAc, $X = C_8H_{17}$
c; R^1 = Ac, $R^2 = \alpha$—OAc, R^3 = OH, $X = C_8H_{17}$
d; R^1 = Ac, $R^2 = \beta$—OAc, R^3 = OH, $X = C_8H_{17}$
e; R^1 = Ac, $R^2 = H$, R^3 = OH, $X = C_6H_{11}O_2$
f; R^1 = Ac, $R^2 = H$, R^3 = OH, $X = C_{10}H_{19}O_2$
g; $R^1 = H$, $R^2 = \beta$—OH, R^3 = OH, $X = C_8H_{17}$
h; $R^1 = H$, $R^2 = \alpha$—OH, R^3 = OH, $X = C_8H_{17}$
i; $R^1 = R^2 = H$, R^3 = OH, $X = C_8H_{17}$
j; 3—ketone, $R^2 = H$, R^3 = OH, $X = C_8H_{17}$
k; R^1 = Ac, $R^2 = R^3 = H$, $X = C_8H_{17}$
l; $R^1 = R^2 = H$, R^3 = OH, $X = C_5H_9O_2$
m; R^1 = Ac, $R^2 = H$, R^3 = OH, $X = C_5H_9O_2$



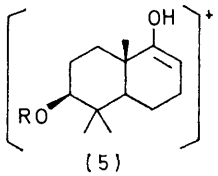
(3)

a; $X = C_8H_{17}$
b; $X = C_6H_{11}O_2$
c; $X = C_{10}H_{19}O_2$



(4)

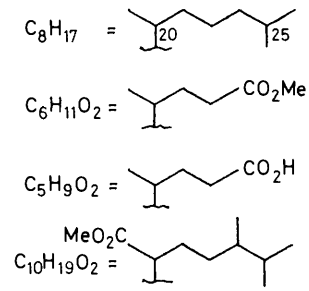
a; $R^1 = R^2 = H$, $R^3 = \alpha$—OH
b; R^1 = Ac, $R^2 = H$, $R^3 = \alpha$—OH
c; $R^1 = H$, $R^2 = \beta$—OH, $R^3 = \alpha$—OH
d; R^1 = Ac, $R^2 = \beta$—OAc, $R^3 = \alpha$—OH
e; $R^1 = R^2 = H$, $R^3 = \beta$—OH
f; R^1 = Ac, $R^2 = H$, $R^3 = \beta$—OH



(5)

a; R = H
b; R = Ac

side-chain X



That the tertiary hydroxy group is not at C-20 was confirmed by oxidising methyl 3β-acetoxy-24-methyl-11-oxolanostan-21-oate (1f) with selenium dioxide in acetic acid: an aromatic ester (2f) was formed. If this ester (2f) had contained the tertiary hydroxy group at C-20, then on reduction with lithium aluminium hydride it would have yielded a tetraol, containing an α-glycol system in the side chain. Reduction of the ester did in fact produce a tetraol, which was stable to prolonged treatment with sodium periodate. Our first reaction to this inability of periodate to cleave the side chain vicinal glycol system was to discard C-20 as the site of the tertiary hydroxy group. Moreover, if the tertiary group were at C-9, then reduction with lithium aluminium hydride should also produce an α-glycol system embracing C-9 and C-11; our evidence at this stage appeared to rule out C-9 as the location for the hydroxy group in the aromatic compound. That this tentative conclusion is not justified will become apparent in the following.

The mass spectra of the aromatic esters (2e) and (2f) showed prominent peaks at *m/e* 289 ($C_{17}H_{21}O_4^+$) and 345 ($C_{21}H_{29}O_4^+$) corresponding respectively to the fragments (3b and c). This again indicated that the tertiary hydroxy group was associated with rings C and D, and we considered C-8 and C-9 as possible locations. The mass spectrum of the triol (4a) obtained by reduction with lithium aluminium hydride of the parent indanone (2a) also supported C-8 or C-9 for the tertiary hydroxy group position in that it showed a prominent peak at *m/e* 210 ($C_{13}H_{22}O_2^+$) formulated as (5a). Acetylation of the triol (4a) at 100 °C gave the 3β-monoacetate (4b), which showed a corresponding peak at *m/e* 252 in the mass spectrum, represented as (5b). These fragments, which must contain rings A and B with an additional oxygen atom, indicate, in conjunction with earlier evidence, that the tertiary hydroxy group is at a centre common to rings B and C, *i.e.* C-8 or C-9.

Oxidation of 3β,7α-diacetoxy-11-oxolanostane (1b) with selenium dioxide in acetic acid gave the 7α-acetoxy-

analogue (2c) of the indanone (2a); the analogous 7β-acetoxyindanone (2d) was obtained by similar oxidation of the 3β,7β-diacetoxy-11-ketone (1c). Alkaline hydrolysis of the epimeric diacetates (2c) and (2d) afforded trihydroxy-ketones, each of which would contain a vicinal glycol system if the tertiary hydroxy group were at C-8. Again, however, both compounds were stable to prolonged treatment with sodium periodate, and we were hesitant to conclude, from our previous experience, that the tertiary hydroxy group was not located at C-8. The problem was solved, however, by an examination of the n.m.r. spectra of the 7α- and 7β-acetates (2c and d). The 7β-acetate (2d) shows a doublet (1 H) at τ 6.74 superimposed upon the broad multiplet observed in the τ 7 region of the spectrum of the parent indanone (2a). This doublet is attributed to a benzylic proton coupled with a neighbouring single proton, and since the spectrum of the parent aromatic acetate (2a) is simplified in this region by the introduction of the 7β-acetate group it is concluded that the 7α-proton is responsible for this splitting. The coupling constant (J 9.7 Hz) is consistent with *trans*-diaxial protons, and there is therefore a β-axial proton at C-8 and a group other than hydrogen at C-9. The spectrum of the epimeric 7α-acetate (2c) contains a similar doublet (1 H) at τ 6.72 due to the C-8 benzylic proton, and the coupling constant (J 5.2 Hz) is this time consistent with coupling between the equatorial 7β-proton and the axial β-proton at C-8.

In the spectrum of the hydroxy-trione (6) derived by Jones oxidation of the oxo-triol (2g), the signal due to the C-8 proton (now flanked by phenyl and carbonyl groups) has been shifted downfield and appears as a singlet at τ 6.03. This confirms that C-8 carries a hydrogen atom and that C-9 is fully substituted.

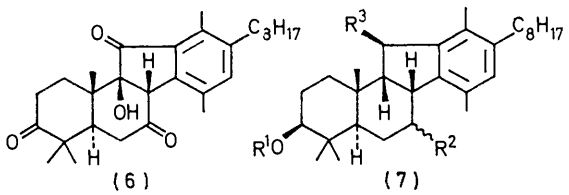
The lack of success in splitting the C-9,C-11 vicinal glycol system in the aromatic triol (4a) with sodium periodate or with lead tetra-acetate may be due to the hydroxy groups being *trans* and diaxial to one another, or it may be due to steric factors operating against the approach of these reagents. There is some evidence that this is the case in that the ketone (2a) does not form an oxime, semicarbazone, or dinitrophenylhydrazone, and the triol (4a) forms only the 3β-monoacetate (4b) on acetylation at 100 °C.

In systems which possess a five-membered ring fused to a six-membered ring the preferred stereochemistry of the ring junction is frequently *cis*; pertinent examples have been reported by House.[11] We have established above that the aromatic compounds (2) contain a β-proton at C-8, and will show later that rings B and C are indeed *cis*-β-fused. With this stereochemistry the C-11 carbonyl group is relatively hindered from attack from the α-face, and reduction of the 9β-hydroxy-ketone (2a) with lithium aluminium hydride should take place preferentially from the β-face to give the 3β,9β,11α-triol (4a) in which the vicinal hydroxy groups in ring C are *trans*. The reduction of tertiary α-ketols to *trans*-diols by lithium aluminium hydride has previously been observed in the cholestane series.[12] An attempt was therefore made to prepare the less hindered 3β,9β,11β-triol (4e) by reduction of the ketone (2a) with sodium in propanol, conditions which convert oxo-steroids into the thermodynamically more stable equatorial alcohols.[13] The main product was a 9-deoxy-compound, $C_{30}H_{48}O_2$ which proved to be the 3β,11β-diol (7a); a small amount of the desired triol (4e) was subsequently isolated and characterised as the 3β-monoacetate (4f) after cold acetylation and chromatography of the mother liquors from this reaction. Whereas in the n.m.r. spectra of the epimeric triol monoacetates (4b and f), the C-11 proton signal appears as a singlet (τ 5.06 and 4.65, respectively), confirming that in each the adjacent C-9 is fully substituted, in the spectra of the diol (7a) and its 3β-monoacetate (7b), the C-11 proton signal appears as a doublet at τ 4.68 (J 8.5 Hz), indicating that a hydrogen atom has replaced the tertiary hydroxy group during the reduction. The coupling constant is in accord with that expected between pseudodiaxial 9β- and 11α-protons and consequently the C-11 hydroxy group in the diol has the β-configuration. Mild oxidation of the monoacetate (7b) gives the corresponding 11-ketone (2k), the 9-deoxy-derivative of the parent indanone (2a). In the n.m.r. spectrum of the ketone (2k) the 9β-proton signal appears as a doublet at τ 7.71 whose coupling constant ($J_{9\beta,8\beta}$ 6 Hz) is in agreement with the *cis*-fusion of rings B and C. That this stereochemistry also prevails in the parent aromatic compounds is apparent from the n.m.r. spectra of the 7α- and 7β-acetoxy-derivatives (2c and d). The spectrum of the 3β,7β-diacetate (2d) contains a sharp 6 H singlet at τ 7.99 attributable to the methyl groups of both acetate functions. In the spectrum of the 7α-acetoxy-epimer (2c), however, whereas the signal due to the 3β-acetate appears in the normal position (τ 7.99), that of the 7α-acetate is at τ 8.77. The large upfield shift can only be explained if the methyl group of the 7α-acetate lies below the aromatic ring. With a β-proton at C-8, models show that this can occur only when the BC ring junction is *cis*-fused; the hydroxy group at C-9 therefore also has the β-configuration.

Several examples of the replacement of the hydroxy group in an α-ketol system by hydrogen during reduction with sodium in alcohol have been recorded,[12,14] and the formation of the diol (7a) by reduction of the ketone (2a) proves that the tertiary hydroxy group in the latter is correctly located at C-9. Surprisingly, the triol monoacetate (4f), isolated as a minor product from this reduction and in which the vicinal hydroxy groups are *cis* (9β,11β), was not attacked by periodic acid.

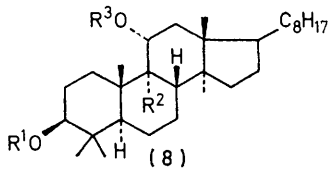
[11] H. O. House, V. Paragamian, R. S. Ro, and D. J. Wluka, *J. Amer. Chem. Soc.*, 1960, **82**, 1457.
[12] D. N. Jones, J. R. Lewis, C. W. Shoppee, and G. H. R. Summers, *J. Chem. Soc.*, 1955, 2876.
[13] D. N. Kirk and M. P. Hartshorn, 'Steroid Reaction Mechanisms,' Elsevier, Amsterdam, 1968, p. 131.
[14] D. N. Kirk and F. J. Rowell, *J. Chem. Soc.* (*C*), 1970, 1498; A. D. Boul, P. M. Fairweather, J. M. Hall, and G. D. Meakins, *ibid.*, 1971, 1199.

This led us to investigate the behaviour of the model ketol, 9α-hydroxy-11-oxolanostan-3β-yl acetate (1d) towards cleavage reagents. It was found to be stable towards prolonged treatment with sodium periodate.



(6) (7)

a; $R^1 = R^2 = H$, $R^3 = OH$
b; $R^1 = Ac$, $R^2 = H$, $R^3 = OH$
c; $R^1 = Ac$, $R^2 = \beta$-OAc, $R^3 = OH$
d; $R^1 = Ac$, $R^2 = R^3 = H$



(8)

a; $R^1 = R^3 = H$, $R^2 = OH$
b; $R^1 = Ac$, $R^2 = OH$, $R^3 = H$
c; $R^1 = R^2 = R^3 = H$
d; $R^1 = R^3 = Ac$, $R^2 = H$
e; $R^1 = R^3 = Ac$, $R^2 = OH$

Moreover, an attempt to prepare the corresponding 3β,9α,11α-trihydroxylanostane (8a) by reduction of the ketol (1d) with sodium in propanol gave the corresponding 9-deoxy-compound, 3β 11α-dihydroxylanostane (8c) which was also formed by reduction of 11-oxolanostan-3β-yl acetate under the same conditions.

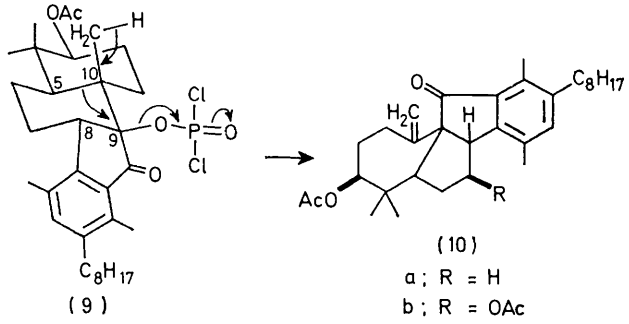
The desired model diol *viz.* 9α,11α-dihydroxylanostan-3β-yl acetate (8b), was obtained from 3β,11β-dihydroxylanostan-3β-yl acetate [15,16] by conversion into lanost-9(11)-en-3β-yl acetate followed by osmylation. The i.r. spectrum of the *cis*-diol (8b) showed peaks in the hydroxy-region at 3 605 and 3 530 cm^{-1} which are attributed [17] to the free hydroxy-absorption and the hydrogen-bonded absorption respectively of the 9α-axial, 11α-equatorial vicinal diol system. The n.m.r. spectrum showed a signal at τ 5.83 (m, 1 H) attributed to the axial 11β-proton. The axial configuration of the C-11 proton was also revealed in the n.m.r. spectrum of the 3β,11α-diacetate (8e) which shows a signal at τ 4.59 (double doublet, 1 H, *J* 12 and 6.5 Hz). The high coupling constants confirm its axial nature and hence the equatorial nature of the 11-acetate function. The model 9α,11α-*cis*-diol (8b) was again stable to prolonged treatment with sodium periodate.

[15] W. Voser, M. Montavon, H. Günthard, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1950, **33**, 1893.
[16] J. F. McGhie, M. K. Pradhan, and J. F. Cavalla, *J. Chem. Soc.*, 1952, 3176.
[17] C. W. Davey, E. L. McGinnis, J. M. McKeown, G. D. Meakins, M. W. Pemberton, and R. N. Young, *J. Chem. Soc.* (*C*), 1968, 2674.

The tertiary hydroxy group in the aromatic α-ketol (2a) is also replaced by hydrogen when the compound is reduced with zinc amalgam in ethanolic hydrochloric acid.[18] After reacetylation of the product, two isomeric acetates, $C_{32}H_{50}O_2$, were isolated by chromatography. Both had spectroscopic properties in keeping with an indane system and the major isomer *A*, m.p. 120—122°, is tentatively formulated as (7d) with the more stable *cis*-fused BC-ring junction while the less abundant isomer *B*, m.p. 166—168°, may be represented as the corresponding 9α*H*-epimer.

Dehydration of the aromatic acetate (2a) by phosphoryl chloride in pyridine afforded a non-crystalline compound (g.l.c. showed purity) which exhibited i.r. bands indicative of a vinylidene group. This was confirmed by the n.m.r. spectrum which showed characteristic sharp singlets, each equivalent to one proton, at τ 5.20 and 5.50. A model (9) (Scheme 1) of the chlorophosphate of the parent aromatic compound (2a) reveals that the 5,10-bond and the departing chlorophosphate group are *trans* and antiparallel to one another, and a plausible interpretation of the dehydration would be that shown in the Scheme. (*N.B.* The plane containing rings A and B is almost at right angles to the plane containing rings C and D.) The synchronous displacement of the leaving group by the electrons of the 5,10-bond with loss of a proton from the 10-methyl group results in the A-homo-B-nor-structure (10a).

Similar dehydration reactions, which are accompanied by ring expansion–contraction with the generation of a



(9) (10)

a; R = H
b; R = OAc

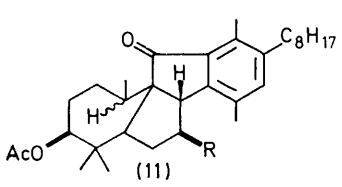
SCHEME 1

vinylidene group have been observed previously in the hopane series. Thus 7β-hydroxyhopane is converted almost exclusively into 9(8 → 7)*abeo*-hop-8(26)-ene [19] by reaction with phosphoryl chloride; similar treatment of 15α-hydroxyhopane gives 13(14 → 15)*abeo*-hop-14(27)ene.[20]

The dehydration product (10a) was hydrogenated in the presence of platinum to give the dihydro-derivative (11a). In the n.m.r. spectrum of this compound the new secondary methyl signal appeared as a doublet at τ 9.53

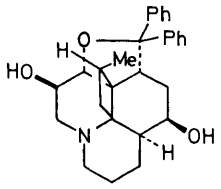
[18] L. F. Fieser and A. M. Seligman, *J. Amer. Chem. Soc.*, 1935, **57**, 942.
[19] R. E. Corbett, R. A. J. Smith, and H. Young, *J. Chem. Soc.* (*C*), 1968, 1823.
[20] R. E. Corbett and R. A. J. Smith, *J. Chem. Soc.*, (*C*), 1969, 44.

(*J* 6 Hz). This high field position is attributed to the shielding effect of either the carbonyl group at C-11 or the benzene ring. A similar effect has been reported [21] for diphenylannotinine (12) in which the secondary



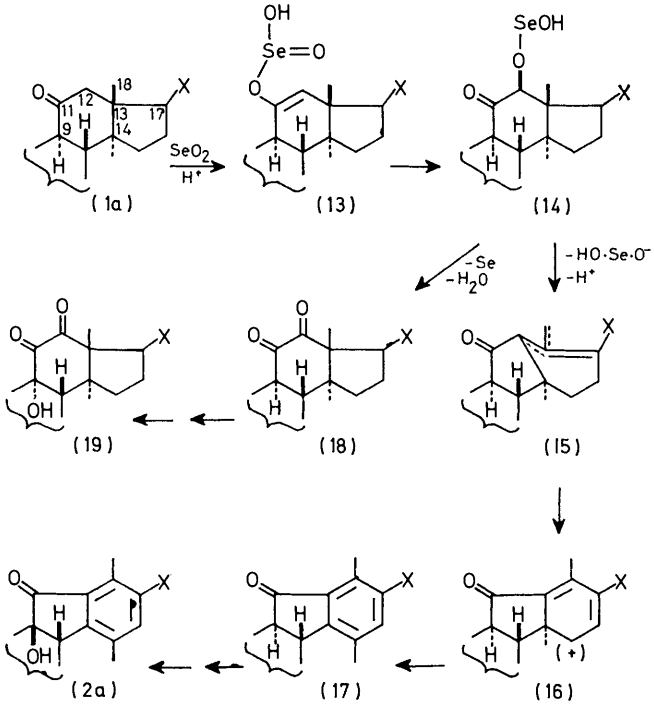
(11)

a; R = H
b; R = OAc



(12)

methyl group resonates at τ 9.8. An analogous dehydration product (10b) was obtained when the 9β-hydroxy-3β,7β-diacetate (2d) was treated with phosphoryl chloride in pyridine and this on mild catalytic



SCHEME 2

hydrogenation furnished the corresponding dihydro-derivative (11b) in which the new secondary methyl signal appears in the n.m.r. spectrum as a doublet at τ 9.54.

The mechanism proposed for the oxidation of 11-oxolanostan-3β-yl acetate (1a) to the C-nor-D-homo-steroid (2a) (Scheme 2) is in accord with that expected of a relatively hindered steroid ketone.[22] The initially formed Δ^{11}-enyl selenite ester (13) rearranges [23] to the 11-oxo-ester (14) in which the selenium(II) ester group is equatorial and antiparallel to the 13,14-bond. Displacement of the ester group by the electrons of this bond with loss of a proton from C-12, C-17, or C-18 leads to an intermediate (15) having the C-nor-D-homo skeleton. Successive allylic oxidations then lead to the cation (16) from which by methyl migration and loss of a proton, the fully aromatic ketone (17) is formed. Oxidation of the remaining α-hydrogen at C-9 *via* the $\Delta^{9(11)}$-enyl selenite ester finally produces the more stable 9β-hydroxy-11-ketone (2a) having the *cis*-BC ring junction. The 9α-hydroxy-11,12-dione [8] (19), the minor product when the reaction is carried out in acetic acid, may also arise from the intermediate (14) by collapse of the secondary selenium(II) ester group at C-12 to water, selenium, and the diketone (18), which then undergoes further oxidation at C-9. The order in which oxidation at C-9 and C-11 occurs, however, may be reversed in this case since oxidation of 9α-hydroxy-11-oxolanostan-3β-yl acetate (1d) with selenium dioxide in acetic acid gives the hydroxy-dione (19) exclusively with no trace of any aromatic products.

EXPERIMENTAL

Specific rotations were measured at room temperature (1 dm tube; chloroform as solvent). U.v. spectra were measured with absolute ethanol as solvent, using a Perkin-Elmer 137 spectrophotometer. I.r. spectra were measured with carbon disulphide as solvent, unless otherwise stated, on a Perkin-Elmer 125 spectrometer. ^{1}H N.m.r. spectra were measured with deuteriochloroform as solvent on a 60 Hz Perkin-Elmer instrument, unless otherwise stated, with tetramethylsilane as standard. Mass spectra were measured on an A.E.I. MS9 instrument; molecular formula of ions, where quoted, have been established by mass measurement. Grade II alumina and light petroleum (b.p. 40—60 °C) were used for chromatography throughout. 'In the usual way . . .' means addition of the reaction mixture to an excess of water followed by extraction with ether, washing of the extracts with water till neutral, drying (Na_2SO_4), and evaporation *in vacuo* to dryness.

11-*Oxolanostan*-3β-*yl Acetate* (1a).—The material (1a) was made in a series of reactions from 'isocholesterol' (commercially available), involving acetylation followed by hydrogenation of the acetate mixture over palladium–carbon to give a mixture whose constituents all contain the saturated lanostane side chain. Oxidation [24] then gives 7,11-dioxolanost-8-en-3β-yl acetate, which on reduction with zinc [25] affords 7,11-dioxolanostan-3β-yl acetate. The latter is converted into the 7-mono(ethylene dithioacetal),[15] which in turn is desulphurised with a ten-fold excess of Raney nickel.

4,4,15-*Trimethyl*-11-*oxo*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14-16-*triene*-3β,9β-*diol* 3-*Acetate* (2a).—11-Oxolanostan-3β-yl acetate (1a) (50 g) in acetic acid (1.5 l) was heated under reflux (24 h) with selenium dioxide (75 g). The filtered solution was evaporated to *ca.* 200 ml *in vacuo* and the crude product, isolated by addition of water (2 l) and extraction with ether, was dissolved in light petroleum–benzene (10 : 1; 200 ml) and chromatographed on neutral alumina (1 kg). Elution with petrol–benzene (3 : 1; 5.0 l)

[21] T. L. Ho, *Tetrahedron Letters*, 1969, 1307.
[22] E. N. Trachtenberg in 'Oxidation,' vol. I, ed. R. L. Augustine, Dekker, New York, 1969, p. 171.
[23] E. J. Corey and J. P. Schaefer, *J. Amer. Chem. Soc.*, 1960, **82**, 918.
[24] J. F. Cavalla and J. F. McGhie, *J. Chem. Soc.*, 1951, 834.
[25] C. Dorée, J. F. McGhie, and F. Kurzer, *J. Chem. Soc.*, 1948, 988.

and benzene (2.5 l) yielded a *fraction* (2a) (16 g) which crystallised from methylene chloride–methanol as plates (13 g), m.p. 200—202°, $[\alpha]_D$ −19° (*c* 1.92). Compound (2a) gave a yellow colour with tetranitromethane; $\lambda_{max.}$ 218 (ε 28 400), 262 (13 000), and 314 nm (2 500); $\nu_{max.}$ 3 580 (OH), 3 437 (OH, disappears on dilution), 1 731 and 1 238 (OAc), and 1 710 cm^{-1} (aromatic ketone); $\nu_{max.}$(KBr) 3 420 (OH), 1 708 (OAc and aromatic ketone), 1 603 and 1 579 (carbonyl-conj. aromatic C=C), 1 265 (OAc), and 725 cm^{-1} (aromatic); τ 2.90 (1 H, s, aromatic), 5.30 (1 H, m, 3α-H), *ca.* 7 (3 H, m, 1α-, 8β-, and 20-H), 7.48 and 7.72 (each 3 H, s, aromatic Me), 7.81 (1 H, s, tert. OH), and 7.99 (3 H, s, 3β-OAc); *m/e* 496 ($C_{32}H_{48}O_4$) (parent) and 287 ($C_{19}H_{27}O_2$) (base) (Found: C, 77.5; H, 9.7%; M^+, 496.3532. $C_{32}H_{48}O_4$ requires C, 77.4; H, 9.7%; *M*, 496.3552). Acetylation of compound (2a) with acetyl chloride and dimethylaniline in refluxing chloroform [26] afforded 4,4,15-*trimethyl*-11-*oxo*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*triene*-3β,9β-*diol diacetate* (2b), m.p. 164—165°, $[\alpha]_D$ −49°; $\lambda_{max.}$ 215 (ε 25 500), 260 (9 800), and 310 nm (2 000); τ 2.95 (1 H, s, aromatic), 5.30 (1 H, m, 3α-H), *ca.* 7 (3 H, m, 1β-, 8β-, and 20-H), 7.54 and 7.75 (each 3 H, s, aromatic CH_3), 7.99 (3 H, s, 3β-OAc), and 8.22 (3 H, s, 9β-OAc) (Found: C, 75.5; H, 9.6%; M^+, 538.3665. $C_{34}H_{50}O_5$ requires C, 75.8; H, 9.4%; *M*, 538.3658).

Further elution of the original column with benzene (2.0 l) and benzene–ether (10 : 1; 1 l) yielded a yellow gum which crystallised from methylene chloride–methanol to give 9α-hydroxy-11,12-dioxolanostan-3β-yl acetate (0.25 g), m.p. and mixed m.p. 210—212°, $[\alpha]_D$ +138° (*c* 0.58) (lit.,[8] m.p. 211—212°; $[\alpha]_D$ +140°) (Found: C, 74.4; H, 10.1%; M^+, 516.3802. Calc. for $C_{32}H_{52}O_5$: C, 74.4; H, 10.3%; *M*, 516.3814).

4,4,15-*Trimethyl*-11-*oxo*-14(13 SKS 12)abeo-5α-*cholesta*-12,14,16-*triene*-3β,7β,9β-*triol* 3,7-*Diacetate* (2d).—11-Oxolanostane-3β,7β-diol diacetate (1c) [27] (25 g) in acetic acid (750 ml) was heated under reflux (24 h) with selenium dioxide (37.5 g). The filtered solution was evaporated *in vacuo* and poured into water (2.5 l) and the crude product extracted with ether. Removal of the ether *in vacuo* left a residue which was dissolved in light petroleum (200 ml) and chromatographed on neutral alumina (750 g). Elution with light petroleum–benzene (4 : 1, 2 l; 2 : 1, 1 l) yielded a fraction (1.64 g) which crystallised from methylene chloride–methanol as needles (1.5 g), m.p. 208—210°, $[\alpha]_D$ +80° (*c* 1.58); *m/e* 468 ($C_{32}H_{52}O_2$). This compound was not investigated further. Continued elution of the column with benzene (3 l) and benzene–ether (10 : 1, 1 l) yielded the *diacetate* (2d) (6.1 g) (crystallised from ether–light petroleum as needles), m.p. 180—182°, $[\alpha]_D$ +23° (*c* 1.72); $\lambda_{max.}$ 217 (ε 24 000), 264 (11 100), and 315 nm (2 230); $\nu_{max.}$ 3 575 (OH) 1 740 and 1 230 (OAc), 1 717 (C=O), and 725 cm^{-1} (aromatic); $\nu_{max.}$(KBr) 1 579 cm^{-1} (CO-conj. aromatic C=C); τ 2.88 (1 H, s, aromatic), 5.3 (1 H, m, 3α-H), 5.66 (1 H, m, 7α-H), 6.74 (1 H, d, *J* 9.7 Hz, 8β-H), *ca.* 7.0br (2 H, m, 1α- and 20-H), 7.48 and 7.66 (each 3 H, s, aromatic Me), 7.87 (1 H, s, tertiary OH), and 7.99 (6 H, s, 3β- and 7β-OAc); *m/e* 554 ($C_{34}H_{50}O_6$) (parent) and 287 ($C_{19}H_{27}O_2$) (Found: C, 73.2; H, 8.9%; M^+, 554.3608. $C_{34}H_{50}O_6$ requires C, 73.6: H, 9.1%; *M*, 554.3607).

4,4,15-*Trimethyl*-11-*oxo*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14-16-*triene*-3β,7α,9β-*triol* 3,7-*Diacetate* (2c).——11-Oxolanostane-3β,7α-diol diacetate (1b) [27] (1.5 g) in acetic acid (45 ml) was heated under reflux (24 h) with selenium dioxide (2.25 g). The product, isolated as above, was dissolved in light petroleum (15 ml) and chromatographed on neutral alumina (50 g). Elution with petroleum–benzene (10 : 1, 200 ml; 3 : 1, 200 ml) yielded a fraction (0.569 g) which crystallised from ether–petroleum to give the *diacetate* (2c) as needles, double m.p. 122—124° and 158—160°, $[\alpha]_D$ −27° (*c* 1.32); $\lambda_{max.}$ 218 (ε 27 000), 260 (11 400), and 310 nm (2 510); $\nu_{max.}$ 3 576 (OH), 1 738 and 1 233 (OAc), 1 715 (C=O), and 730 cm^{-1} (aromatic); $\nu_{max.}$(KBr) 1 605 and 1 580 cm^{-1} (CO-conj. aromatic C=C); τ 2.91 (1 H, s, aromatic), 4.5 (1 H, m, 7β-H), 5.25 (1 H, m, 3α-H), 6.72 (1 H, d, *J* 5.2 Hz, 8β-H), 7.46 and 7.73 (each 3 H, s, aromatic Me), 7.99 (3 H, s, 3β-OAc), and 8.77 (3 H, s, 7α-OAc); *m/e* 554 ($C_{34}H_{50}O_6$) (parent) and 287 ($C_{19}H_{27}O_2$) (Found: C, 73.65; H, 8.9%; M^+, 554.3618. $C_{34}H_{50}O_6$ requires C, 73.6; H, 9.1%; *M*, 554.3607).

Further elution of the column with ether (100 ml) yielded a fraction (0.12 g) which crystallised from ether–light petroleum to give 11,12-*dioxolanostane*-3β,7α,9α-*triol* 3,7-*diacetate* as yellow needles, m.p. 235—237°, $[\alpha]_D$ +67° (*c* 1.6); $\nu_{max.}$ 3 580 (OH), 3 420 (H-bonded OH), 1 725 (CO), and 1 235 cm^{-1} (OAc); τ 4.6 (1 H, m, 7β-H), 5.40 (1 H, m, 3α-H), 6.55 (1 H, s, 9α-OH), and 7.7 and 7.95 (each 3 H, s, 3α- and 7α-OAc) (Found: C, 71.6; H, 9.2%; M^+, 574.3839. $C_{34}H_{54}O_7$ requires C, 71.0; H, 9.5%; *M*, 574.3869).

4,4,15-*Trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*triene*-3β,9β,11α-*triol* (4a).—The aromatic acetate (2a) (1 g) in dry ether (120 ml) was added to a suspension of lithium aluminium hydride (1 g) in dry ether (100 ml) and the mixture heated under reflux (3 h). After dilution with ether and addition of crushed ice, work-up in the usual manner gave an amorphous solid which crystallised in methanol to give the *triol* (4a) (0.509 g), m.p. 96—102°, $[\alpha]_D$ −38.8° (*c* 0.88); $\lambda_{max.}$ 208 (ε 28 600), 220 (10 900), 272 (570), and 282 nm (597); $\nu_{max.}$(KBr) 3 450 (OH), 1 027 (OH), and 722 cm^{-1} (aromatic); τ 3.13 (1 H, s, aromatic), 5.12 (1 H, d, *J* 4 Hz, 11β-H, becomes singlet in deuteriating medium), 6.63 (1 H, m, 3α-H), *ca.* 7.0 (2 H, m, 8- and 20-H), and 7.75br (6 H, s, aromatic Me); *m/e* 456 ($C_{30}H_{48}O_3$) (parent) and 210 ($C_{13}H_{22}O_2$) (Found: C, 79.5; H, 10.8%; M^+, 456.3605. $C_{30}H_{48}O_3$ requires C, 78.9; H, 10.6%; *M*, 456.3603). The triol (4a) (0.9 g) in dry pyridine (1 ml) and acetic anhydride (0.5 ml) was left at room temperature (18 h). Isolation of the product in the usual way afforded a gum (0.94 g) which crystallised from ether–light petroleum to give 4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*triene*-3β,9β,11α-*triol* 3-*acetate* (4b) (0.8 g), needles, double m.p. 150—152° and 173—174.5°, $[\alpha]_D$ −24° (*c* 1.21); $\nu_{max.}$ 3 579 and 3 565 (OH), 3 450 (bonded OH, disappears on dilution), 3 010 (aromatic C–H), 1 728 and 1 240 (OAc), and 722 cm^{-1} (aromatic); τ 3.12 (1 H, s, aromatic), 5.06 (1 H, d, *J* 6 Hz, 11β-H, becomes singlet in deuteriating medium), 5.34 (1 H, m, 3α-H), *ca.* 7.0 (2 H, m, 8- and 20-H), 7.75br (6 H, s, aromatic Me), and 7.98 (3 H, s, 3β-OAc); *m/e* 498 ($C_{32}H_{50}O_4$) (parent) and 252 ($C_{15}H_{24}O_3$) (Found: C, 77.1; H, 10.2%; M^+, 498.3698. $C_{32}H_{50}O_4$ requires C, 77.1; H, 10.1%; *M*, 498.3708). The 9β,11α-dihydroxy-ester (4b) was stable to prolonged treatment with sodium periodate.

[26] Pl. A. Plattner, Th. Petrzilka, and W. Lang, *Helv. Chim. Acta*, 1944, **27**, 518.

[27] C. W. Shoppee, N. W. Hughes, and R. E. Lack, *J. Chem. Soc. (C)*, 1966, 2359; D. H. R. Barton, A. Hameed, and J. F. McGhie, *Tetrahedron Letters*, 1965, 4343; C. S. Barnes and A. Palmer, *Austral. J. Chem.*, 1957, **10**, 334.

3β,7β,9β-*Trihydroxy*-4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*trien*-11-*one* (2g).—The aromatic oxo-diacetate (2d) (0.1 g) was heated under reflux (2 h) with methanolic potassium hydroxide (5%; 40 ml) and the hydrolysis product isolated in the usual manner. Crystallisation from ether–light petroleum afforded the 11-*oxo*-3β,7β,9β-*triol* (2 g) (0.08 g) as waxy prisms, m.p. 120—130°, $[\alpha]_D$ +14° (*c* 0.92); $\nu_{max.}$(KBr) 3 440 (OH), 1 705 (CO), 1 572 and 1 600 (CO-conj. aromatic C=C), and 723 cm^{-1} (aromatic); τ 2.84 (1 H, s, aromatic), *ca.* 6.9br (5 H, m, 1β-, 3α-, 7α-, 8β-, and 20-H), and 7.52 and 7.62 (aromatic Me) (Found: C, 76.5; H, 10.3%; M^+, 470.3393. $C_{30}H_{46}O_4$ requires C, 76.55; H, 9.9%; *M*, 470.3395).

Reacetylation of the aromatic oxo-triol with acetic anhydride in pyridine furnished the aromatic oxo-diacetate (2d), m.p. and mixed m.p. 180—182°.

The aromatic oxo-triol (2 g) (0.6 g) in absolute ethanol (20 ml) was treated with aqueous sodium periodate [28] (21.211 mg ml^{-1}; 3.4 ml) and volume made up to 50 ml with ethanol. Regular titration of 5 ml samples against standard sodium arsenite solution showed there had been no consumption of periodate after 100 h. Isolation of the product in the usual way yielded starting material. Repetition of the experiment using periodic acid in place of sodium periodate again furnished starting material.

3β,7α,9β-*Trihydroxy*-4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*trien*-11-*one* (2h).—Hydrolysis of the corresponding oxo-diacetate (2c) (0.1 g) with methanolic potassium hydroxide (5%; 40 ml) and isolation of the product in the usual manner gave the 11-oxo-3β,7α,9β-triol (2h) (0.06 g) as an amorphous solid, showing t.l.c. and g.l.c. homogeneity; $\nu_{max.}$ (Nujol) 3 472 (OH), 1 706 (C=O), 1 608, and 1 582 cm^{-1} (CO-conj. aromatic C=C).

9β-*Hydroxy*-4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*triene*-3,7,11-*trione* (6).—The aromatic oxo-triol (2g) (0.1 g) in acetone (10 ml) was treated with an excess of Jones reagent [29] (8N; 0.12 ml). The aromatic 9β-*hydroxy*-3,7,11-*trione* (6) was isolated in the usual manner as a pale yellow gum, shown by t.l.c. and g.l.c. to be homogeneous; $\lambda_{max.}$ 221 (ε 26 000), 266 (13 400), and 320 nm (2 900) (unchanged in the presence of alkali); $\nu_{max.}$(KBr) 3 460 (OH), 1 700 (C=O), 1 563 (CO-conj. aromatic C=C), and 720 cm^{-1} (aromatic); τ 2.67 (1 H, s, aromatic), 6.03 (1 H, s, 8β-H), and 7.40 and 7.67 (each 3 H, s, aromatic Me); *m/e* 466 ($C_{30}H_{42}O_4$) (parent) and 287 ($C_{19}H_{27}O_2$) (Found: M^+, 466.3084. $C_{30}H_{42}O_4$ requires *M*, 466.3082).

4,4,15-*Trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*triene*-3β,7β,9β,11α-*tetraol* (4c).—The aromatic oxo-triol (2g) (0.75 g) in dry ether (100 ml) was added to a stirred suspension of lithium aluminium hydride (0.75 g) in dry ether (75 ml) and the mixture heated under reflux (3 h). After dilution with ether and addition of crushed ice, the product was isolated in the usual way. Crystallisation from ether–methanol gave the *aromatic tetraol* (4c) as needles, m.p. 119—122°, $[\alpha]_D$ +24.5° (*c* 0.8); $\lambda_{max.}$ 208 (ε 27 000), 272 (550), and 282 nm (550); $\nu_{max.}$ 3 600 and 1 020 cm^{-1} (OH); τ(C_5D_5N) 2.86 (1 H, s, aromatic), 5.5br (1 H, m, 11β-H, becomes singlet in deuteriating medium), *ca.* 6.05 (m, 3α- and 7α-H), *ca.* 7.0 (2 H, m, 8β- and 20-H), and 7.29 and 7.55 (each 3 H, s, aromatic Me); *m/e* 472 ($C_{30}H_{48}O_4$) and 225 ($C_{13}H_{21}O_3$) (Found: C, 76.6; H, 10.45%; M^+, 472.3558. $C_{30}H_{48}O_4$ requires C, 76.2; H, 10.2%; *M*, 472.3553).

[28] F. E. King, T. J. King, and J. M. Ross, *J. Chem. Soc.*, 1954, 3995.

The aromatic tetraol (4c) (0.22 g) in dry pyridine (2 ml) and acetic anhydride (1 ml) was left at 16 °C (18 h). Isolation of the product furnished a gum which crystallised from methanol to give 4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*triene*-3β,7β,9β,11α-*tetraol* 3,7-*diacetate* (4d) (0.23 g) as plates, m.p. 201—203°, $[\alpha]_D$ +7° (*c* 1.32); $\nu_{max.}$ 3 590 and 3 565 (OH), 3 015 (aromatic C–H), 1 735 and 1 235 (OAc), and 724 cm^{-1} (aromatic); τ 3.1 (1 H, s, aromatic), 5.1 (1 H, d, *J* 4 Hz, 11β-H, becomes singlet in deuteriating medium), 5.2 (1 H, m, 3α-H), 5.4 (1 H, m, 7α-H), 6.83 (1 H, d, *J* 10 Hz, 8β-H), *ca.* 7.0 (1 H, m, 20-H), 7.72 (6 H, s, aromatic Me), and 7.97 (6 H, s, 3β- and 7β-OAc); *m/e* 556 ($C_{34}H_{52}O_6$) (parent) and 310 ($C_{17}H_{26}O_5$) (Found: C, 73.2; H, 9.2%; M^+, 556.3762. $C_{34}H_{52}O_6$ requires C, 73.3; H, 9.4%; *M*, 556.3763).

Lanost-9(11)-*ene*-3β,11-*diol Diacetate*.—A solution of 11-oxolanostan-3β-yl acetate (1a) (5 g) and toluene-*p*-sulphonic acid (1.9 g) in acetic anhydride (350 ml) was distilled slowly during 5 h until the volume was reduced to *ca.* 50 ml. The product was isolated in the usual way and chromatographed on a column of neutral alumina (150 g). Elution with light petroleum–benzene (4 : 1) gave a fraction (3.9 g) which crystallised from methanol to yield the *diacetate* as needles, m.p. 113—114°, $[\alpha]_D$ +83° (*c* 1.2); $\nu_{max.}$ 1 745, 1 240 (3β-acetate), 1 764, 1 220 (11-acetate), and 1 635 cm^{-1} (C=C) (Found: C, 76.1; H, 10.4. $C_{34}H_{56}O_4,\frac{1}{2}CH_3OH$ requires C, 76.05; H, 10.7%).

11-*Oxolanostane*-3β,9α-*diol* 3-*Acetate* (1d).—The foregoing diacetate (5.5 g) in glacial acetic acid (300 ml) and hydrogen peroxide (30%; 27.5 ml) were heated at 100 °C (3 h). Isolation of the product in the usual manner and chromatography on neutral alumina gave the α-*ketol* (1d) (3.1 g), crystallised from methanol as prisms, m.p. 184—186°, $[\alpha]_D$ +17° (*c* 0.87); $\nu_{max.}$ 3 585 (OH), 3 480 (H-bonded OH which disappears on dilution), 1 730 and 1 240 (OAc), and 1 710 cm^{-1} (C=O); τ 5.51 (1 H, m, 3α-H), 6.88 (1 H, d, *J* 14 Hz, 12α-H), 7.72 (1 H, s, 9α-OH, disappears in deuteriating medium), 7.75 (1 H, d, *J* 14 Hz, 12β-H), and 7.93 (3 H, s, 3β-OAc) (Found: C, 76.85; H, 10.8%; M^+, 502.4025. $C_{32}H_{54}O_4$ requires C, 76.4; H, 10.8%; *M*, 502.4022). Treatment of the α-ketol (1d) with sodium periodate as above resulted in recovery of starting material.

Reduction of 11-*Oxolanostane*-3β,9α-*diol* 3-*Acetate* (1d) *with Sodium in Propan*-1-*ol*.—The α-ketol (1d) (0.55 g) in dry propan-1-ol (25 ml) was boiled gently; sodium (0.9 g) was added in small portions and heating under reflux continued (4 h). Isolation of the product furnished lanostane-3β,11α-diol (8c) (0.32 g), m.p. 199—200° (lit.,[30] 195—196°) (Found: M^+, 446.4151. Calc. for $C_{30}H_{54}O_2$: *M*, 446.4123). Acetylation in pyridine–acetic anhydride and isolation of the product as usual yielded the diacetate (8d), m.p. 127—129°, $[\alpha]_D$ +20° (*c* 1.32) (lit.,[30] m.p. 127—128°, $[\alpha]_D$ +13°); *m/e* 470 ($C_{32}H_{54}O_2$, M^+ − HOAc) (Found: C, 76.9; H, 10.9. Calc. for $C_{34}H_{58}O_4$: C, 76.9; H, 11.0%).

Reduction of 11-*Oxolanostan*-3β-*yl Acetate* (1a) *with Sodium in Propan*-1-*ol*.—A boiling solution of the ketone (1a) (0.50 g) in propan-1-ol (20 ml) was treated with sodium (0.50 g) as above. The product was isolated in the usual way and acetylated with acetic anhydride in pyridine at room temperature to give the diacetate (8d) (0.32 g), as

[29] A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, 1953, 2548.

[30] M. V. Mijovic, W. Voser, H. Heusser, and O. Jeger, *Helv. Chim. Acta*, 1952, **35**, 964.

needles from methanol, m.p. and mixed m.p. 127—128°, $[\alpha]_D$ +24° (*c* 3.1).

Oxidation of 11-*Oxolanostane*-3β,9α-*diol* 3-*Acetate with Selenium Dioxide*.—A solution of the hydroxy-ketone (1d) (0.23 g) in acetic acid (10 ml) was heated under reflux with selenium dioxide (0.30 g) for 5 h. The product was isolated in the usual way and chromatographed on a column of neutral alumina to give 11,12-dioxolanostane-3β,9α-diol 3-acetate (19) (0.17 g) as prisms from methylene chloride–methanol, m.p. 210—212°, $[\alpha]_D$ +139° (*c* 0.75), identical with the product isolated previously.

Lanostane-3β,9α,11α-*triol* 3-*Acetate* (8b).—Lanost-9(11)-en-3β-yl acetate [15,16] (1.54 g) in dry pyridine (25 ml) and ether (25 ml) was treated with osmium tetraoxide (1 g, 1.2 mol. equiv.) in ether (25 ml) and the solution was stored in darkness at 16 °C for 3 days. The mixture was then evaporated *in vacuo* (almost to dryness); ethanol (200 ml) and sodium disulphite (7 g) in water (30 ml) were then added. The mixture was heated under reflux (6 h) and filtered, and the crude product (1.3 g) isolated the usual way. Chromatography on neutral alumina (40 g) and elution with ether–benzene (1 : 3, 500 ml) gave the *triol* (8b) (0.5 g), which crystallised from methanol as needles, m.p. 164.5—165.5°, $[\alpha]_D$ +29° (*c* 2.04); $\nu_{max.}$ 3 605 and 3 530 (OH), 1 735, and 1 240 cm^{-1} (OAc); τ 5.53 (1 H, m, 3α-H), 5.83 (1 H, m, 11β-H), 7.19 (1 H, s, OH), and 7.96 (3 H, s, 3β-OAc) (Found: C, 76.45; H, 11.2%; M^+, 504.4182. $C_{32}H_{56}O_4$ requires C, 76.1; H, 11.2%; *M*, 504.4178). Acetylation of the triol acetate (0.4 g) in dry pyridine (2 ml) and acetic anhydride (1 ml) at 90 °C (5 h) followed by isolation in the usual manner yielded the 3,11-*diacetate* (8e) as a gum, shown by t.l.c. and g.l.c. to be homogeneous; $\nu_{max.}$ 3 590 (OH), 1 735, and 1 245 cm^{-1} (OAc); τ 4.59 (1 H, dd, *J* 12 and 6.5 Hz, 11β-H), 5.60 (1 H, m, 3α-H), 7.58 (1 H, s, 9α-OH), and 7.94 and 7.97 (each 3 H, s, 3β- and 11α-OAc) (Found: M^+, 546.4282. $C_{34}H_{58}O_5$ requires *M*, 546.4284). The triol acetate (8b) when treated with sodium periodate for 72 h as above was unchanged.

Reduction of the Aromatic Hydroxy-ketone (2a) *with Sodium in Propan*-1-*ol*.—The aromatic ketone (2a) (3.0 g) in dry propan-1-ol (300 ml) was treated with sodium (5.1 g) in portions over 1 h and the mixture was refluxed (3 h). Isolation of the product in the usual way gave an amorphous solid (2.5 g), which crystallised from methanol to give 4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α,9β-*cholesta*-12,14,16-*triene*-3β,11β-*diol* (7a) as prisms (1.1 g), m.p. 103—105°, $[\alpha]_D$ −73° (*c* 1.15); $\nu_{max.}$ 3 582 cm^{-1}; τ 3.03 (1 H, s, aromatic), 4.70 (1 H, d, *J* 8 Hz, 11α-H), 6.69 (1 H, m, 3α-H), 7.61 and 7.73 (each 3 H, s, aromatic Me) (Found: C, 81.7; H, 11.5%; M^+, 440.3636. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%; *M*, 440.3654). Acetylation of the diol (7a) (0.9 g) in pyridine (2 ml) with acetic anhydride (1 ml) at 16° for 18 h afforded the 3-*acetate* (7b) (0.71 g) as prisms (from ether–light petroleum), m.p. 134—135°, $[\alpha]_D$ −63° (*c* 1.66); $\nu_{max.}$ 3 585 (OH), 1 735, and 1 243 cm^{-1} (OAc); τ 4.68 (1 H, d, *J* 8 Hz, 11α-H) (Found: C, 79.0; H, 10.5%; M^+, 482.3750. $C_{32}H_{50}O_3$ requires C, 79.6; H, 10.4%; *M*, 482.3759).

The methanolic mother liquors from the crystallisation of the diol (7a) were evaporated to dryness and the residue was acetylated with acetic anhydride in pyridine at 16 °C. Chromatography of the crude product (0.87 g) on a column of alumina (80 g) and elution with benzene and benzene–ether yielded successively the diol monoacetate (7b) (0.32 g), m.p. 133—134°, identical with that described above, and a fraction (0.22 g) which crystallised from light petroleum to give 4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*triene*-3β,9β,11β-*triol* 3-*acetate* (4f) as needles, m.p. 137—140°; $\nu_{max.}$ 3 280 (OH), 1 733, and 1 245 cm^{-1} (OAc); τ 3.18 (1 H, s, aromatic), 4.65 (1 H, s, 11α-H), 5.43 (1 H, m, 3α-H), 7.66 and 7.81 (each 3 H, s, aromatic Me), 7.97 (3 H, s, 3β-OAc); *m/e* 252 [fragment (5b)] (Found: M^+, 498.3689. $C_{32}H_{52}O_4$ requires *M*, 498.3709). The compound was inert towards sodium periodate.

4,4,15-*Trimethyl*-14(13 ⟶ 12)abeo-5α,9β-*cholesta*-12,14,16-*triene*-3β,7β,11β-*triol* 3,7-*Diacetate* (7c).—Reduction of the oxo-diacetate (2d) (0.65 g) with sodium (1.1 g) in propan-1-ol (30 ml) as above, followed by acetylation and chromatography of the crude product, gave the *triol diacetate* (7c) (0.11 g), a homogeneous gum (t.l.c. and g.l.c.); $\nu_{max.}$ 3 535 (OH), 1 740, and 1 238 cm^{-1} (OAc); τ 3.08 (1 H, s, aromatic), 4.67 (1 H, d, *J* 9.5 Hz, 11α-H), 5.32 (1 H, m, 3α-H), 5.8 (1 H, m, 7α-H), 6.6 (1 H, dd, *J* 11.4 and 7.2 Hz, 8β-H), 7.65br (6 H, s, aromatic Me), and 7.9 and 7.95 (each 3 H, s, 3β- and 7β-OAc) (Found: M^+, 540.3814. $C_{34}H_{52}O_5$ requires *M*, 540.3814).

Reduction of the Aromatic Acetate (2a) *with Zinc Amalgam and Hydrochloric Acid*.—The aromatic acetate (2a) (3 g) in ethanol (3 l) was treated with concentrated hydrochloric acid (300 ml) and water (300 ml) and the mixture heated under reflux with zinc amalgam (120 g) (8 h) (*cf.* ref. 18). The filtered solution was concentrated *in vacuo* and the product, isolated in the usual way, was dissolved in pyridine (6 ml) and acetic anhydride (3 ml). Isolation of the product in the usual way after 18 h at 16 °C gave a gum (2.8 g) which was chromatographed on alumina (90 g). Elution with light petroleum (500 ml) gave 4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α,9β-*cholesta*-12,14,16-*trien*-3β-*yl acetate* (7d) (1.39 g) (isomer *A*) as plates, m.p. 120—122° (from methanol), $[\alpha]_D$ −42° (*c* 1.04); $\lambda_{max.}$ 208 (ε 16 450), 220 (8 850), 269 (350), and 278 nm (260); $\nu_{max.}$ 1 730 and 1 235 (OAc), and 700 and 725 cm^{-1} (aromatic); τ 3.30 (1 H, s, aromatic), 4.58 (1 H, m, 3α-H), *ca.* 7 (2 H, m, 8β- and 20-H), 7.3 (2 H, d, 11-H_2), 7.77 and 7.85 (each 3 H, s, aromatic Me), and 7.95 (3 H, s, 3β-OAc) (Found: C, 82.1; H, 10.75%; M^+, 466.3818. $C_{32}H_{50}O_2$ requires C, 82.3; H, 10.8%; *M*, 466.3811). Further elution with petrol–benzene 10 : 1; 600 ml) gave a fraction (0.8 g) which crystallised from methanol to give 4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*trien*-3β-*yl acetate* (isomer *B*) (0.45 g), needles, m.p. 166—168°, $[\alpha]_D$ +8° (*c* 0.78); u.v. and i.r. spectra almost identical with those of isomer *A*; and the only relevant difference in n.m.r. is at τ *ca.* 7.2br (4 H, m, 11-H_2, 8β-H, and 20-H) (Found: C, 82.0; H, 10.7%; M^+, 466.3814. $C_{32}H_{50}O_2$ requires C, 82.3; H, 10.8%; *M*, 466.3811).

3β,9β-*Dihydroxy*-4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*trien*-11-*one* (2i).—The aromatic acetate (2a) (3 g) was heated under reflux (3 h) with methanolic potassium hydroxide (10%; 300 ml). Isolation of the product in the usual way gave the 3β,9β-*dihydroxy*-11-*oxo-aromatic compound* (2i) as prisms (from ether), m.p. 170—172°; $[\alpha]_D$ −29.8° (*c* 1.04); $\nu_{max.}$(KBr) 3 506 (OH), 1 700 (C=O), 1 584 (CO-conj. aromatic C=C), and 730 and 741 cm^{-1} (aromatic) (Found: C, 78.6; H, 10.0%; M^+, 454.3452. $C_{30}H_{46}O_3$ requires C, 79.2; H, 10.2%; *M*, 454.3486).

The 3β,9β-dihydroxy-11-oxo-compound (2i) (0.30 g) in pyridine (6 ml) was added to the complex formed by reaction of chromium trioxide (0.30 g) with pyridine (3 ml)

and left 12 h. Work-up in the usual way gave 9β-*hydroxy*-4,4,15-*trimethyl*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*triene*-3,11-*dione* (2j), needles (from methanol), m.p. 163—164°, $[\alpha]_D$ −46.2° (*c* 0.6) (Found: C, 79.6; H, 9.95. $C_{30}H_{44}O_3$ requires C, 79.6; H, 9.8%).

Dehydration of the Aromatic Acetate (2a).—The aromatic acetate (2a) (2 g) in dry pyridine (30 ml) was treated with phosphoryl chloride (3 ml) and the solution kept at 90 °C for 3 h. The *dehydration product* (10a), isolated in the usual way, was obtained as a gum (1.5 g), $\nu_{max.}$ 3 075, 1 620, and 883 (C=CH_2), 1 733 and 1 239 (OAc), and 1 699 cm^{-1} (C=O); τ 2.78 (1 H, s, aromatic), 5.10 (1 H, m, 3α-H), 5.20 and 5.50 (each 1 H, s, C=CH_2), 6.35 (1 H, pair of d, *J* 9.6 and 3.6 Hz, 8β-H), 7.44 and 7.63 (each 3 H, s, aromatic Me), and 7.93 (3 H, s, 3β-OAc) (Found: M^+, 478.3440. $C_{32}H_{46}O_3$ requires *M*, 478.3446). The dehydration product (10a) (0.5 g) in ethanol (15 ml) was hydrogenated in the presence of platinum oxide (0.05 g) until no further uptake occurred. The filtered solution was concentrated *in vacuo* to give a gum (0.49 g) which crystallised from methanol to give the *dihydro-derivative* (11a) as prisms (0.2 g), m.p. 99—101°, $[\alpha]_D$ −88.7° (*c* 1.26); $\nu_{max.}$ 1 732 and 1 249 (OAc) and 1 692 cm^{-1} (C=O); τ 2.77 (1 H, s, aromatic), 5.07 (1 H, pair of d, *J* 12 and 4 Hz, 3α-H), 6.74br (1 H, d, *J* 9 Hz, 8β-H), *ca.* 7 (1 H, m, 20-H), 7.4 and 7.68 (each 3 H, s, aromatic Me), 7.95 (3 H, s, 3β-OAc), and 9.53 (3 H, d, *J* 6 Hz, 10-Me) (Found: C, 79.4; H, 10.0%; M^+, 480.3632. $C_{32}H_{48}O_3$ requires C, 79.9; H, 10.0%; M^+, 480.3603).

Dehydration of the Aromatic 3β,7β-*Diacetate* (2d).—The 3β,7β-diacetate (2d) (1.0 g) in pyridine (30 ml) was treated with phosphoryl chloride (5 ml) at 90 °C for 4 h. Isolation of the product in the usual way followed by chromatography on a column of alumina (30 g) gave the *dehydration product* (10b) as a resin (0.8 g), $[\alpha]_D$ −40° (*c* 0.97); $\nu_{max.}$ 3 075, 1 630, and 895 (C=CH_2), 1 738 and 1 240 (OAc), and 1 707 cm^{-1} (C=O); τ 2.73 (1 H, s, aromatic), 5.1 (1 H, m, 3α-H), 5.2 (1 H, m, 7α-H), 5.16 and 5.51 (each 1 H, s, C=CH_2), 6.23 (1 H, d, *J* 5 Hz, 8β-H), 7.42 and 7.63 (each 3H, s, aromatic Me), and 7.87 and 7.90 (each 3 H, s, 3β- and 7β-OAc) (Found: M^+, 536.3486. $C_{34}H_{48}O_5$ requires *M*, 536.3501).

Hydrogenation of the dehydration product (10b) (0.50 g) in ethanol (15 ml) over platinum oxide (0.05 g) gave the *dihydro-derivative* (11b), which crystallised from methanol as needles (0.30 g), m.p. 129—130°, $[\alpha]_D$ −33° (*c* 1.44); $\nu_{max.}$ 1 738 and 1 243 (OAc), and 1 695 cm^{-1} (C=O); τ 2.72 (1 H, s, aromatic), 4.8 (1 H, m, 7α-H), 5.14 (1 H, m, 3α-H), 6.53 (1 H, d, *J* 5 Hz, 8β-H), 7.40 and 7.64 (each 3 H, s, aromatic Me), 7.85 and 7.92 (each 3 H, s, 3β- and 7β-OAc), and 9.54 (3 H, d, *J* 6 Hz, 10-Me) (Found: C, 76.1; H, 9.45%; M^+, 538.3660. $C_{34}H_{50}O_5$ requires C, 75.8; H, 9.4%; *M*, 538.3658).

Methyl 3β-*Acetoxy*-9β-*hydroxy*-4,4,15-*trimethyl*-11-*oxo*-25,26,27-*trinor*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*trien*-24-*oate* (2e).—'Isocholesterol' was converted into methyl 3β-acetoxy-11-oxo-25,26,27-trinorlanostan-24-oate[31] (1e) and the latter compound (12.9 g) in acetic acid (390 ml) was heated under reflux (6 h) with selenium dioxide (19 g). The solution was filtered and the crude product isolated in the usual way as a dark gum. Trituration of the gum with warm ether yielded the crude aromatic compound (2e), m.p. 182—195°. The ether-soluble portion was chromatographed on alumina (200 g) from benzene–light petroleum (1 : 1; 20 ml) and benzene–ether (1 : 1), which furnished an additional quantity (0.13 g) of product, m.p. 190—195°. The combined crops of crude material were chromatographed on alumina (15 g) from benzene (50 ml) and eluted with benzene then benzene–ether (1 : 1), yielding the 9β-*hydroxy*-11-*oxo*-*ester* (2e) (1.2 g), as needles, from ether, m.p. 197—199°, $[\alpha]_D$ −26°; $\lambda_{max.}$ 222, 262, and 312 nm (ε 15 300, 10 400, and 2 340); $\nu_{max.}$ 3 420 (OH), 1 736 (CO_2Me), 1 703 (CO and OAc), and 1 575 cm^{-1} (ArCO); τ 2.88 (1 H, s, aromatic), 5.28 (t, 3α-H), 6.38 (ester Me), 7.94 (3 H, s, 3β-OAc), and 7.46 and 7.69 (each 3 H, s, aromatic Me) (Found: C, 72.5; H, 8.55%; M^+, 498.2959. $C_{30}H_{42}O_6$ requires C, 72.3; H, 8.4%; *M*, 498.2981). Hydrolysis of the acetoxy-ester (0.12 g) in methanol (10 ml) with methanolic potassium hydroxide (5%; 5 ml) at room temperature (12 h) followed by acidification with hydrochloric acid (2M) and extraction with ether gave 3β,9β-*dihydroxy*-4,4,15-*trimethyl*-11-*oxo*-25,26,27-*trinor*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*trien*-24-*oic* acid (2 l) (0.10 g), m.p. 245—250°, $[\alpha]_D$ −45° (in chloroform–ethanol, 1 : 1); $\nu_{max.}$ 3 480 (OH), 3 360 and 3 300 (CO_2H), 1 695 (CO), 1 680 (CO_2H), and 1 575 cm^{-1} (benzenoid) (Found: C, 73.3; H, 8.7. $C_{27}H_{38}O_5$ requires C, 73.2; H, 8.6%). The dihydroxy-acid (2 l) (0.3 g) in pyridine (2 ml) and acetic anhydride (1 ml) was left at 18 °C (12 h). Isolation of the product gave the 3β-*acetoxy*-*acid* (2m) (0.21 g) as needles from methylene chloride–methanol, m.p. 193—195°, $[\alpha]_D$ −42° (in chloroform–ethanol, 1 : 1); $\nu_{max.}$ 3 300 (CO_2H and OH), 1 703 (CO and OAc), 1 695 (CO_2H), 1 575 (benzenoid), and 1 270 cm^{-1} (OAc) (Found: C, 70.8; H, 8.3. $C_{29}H_{40}O_6$ requires C, 71.6; H, 8.3%).

Methyl 3β-*Acetoxy*-9β-*hydroxy*-4,4,15,24-*tetramethyl*-11-*oxo*-14(13 ⟶ 12)abeo-5α-*cholesta*-12,14,16-*trien*-21-*oate* (2f).—Methyl acetyleburicoate[32] was converted in several steps[33] into methyl 3β-acetoxy-24-methyl-11-oxolanostan-21-oate (1f). The latter ester (1.0 g) in glacial acetic acid (35 ml) was heated under reflux (5 h) with selenium dioxide (1.5 g). The *product* (2f) (0.11 g) isolated in the usual way through ether, crystallised from acetone–hexane as prisms, m.p. 246—247°; $\nu_{max.}$ 3 500 (OH), 1 740 and 1 275 (ester), 1 710 (C=O), and 1 570 and 819 cm^{-1} (benzenoid); $\lambda_{max.}$ 220, 261, and 312 nm (ε 17 050, 8 500, and 1 900); τ 2.73 (1 H, s, aromatic), 5.27 (1 H, m, 3α-H), 6.36 (3 H, s, CO_2Me), 7.42 and 7.72 (each 3 H, s, aromatic Me), and 7.96 (3 H, s, OAc) (Found: C, 73.8; H, 9.0%; M^+, 554.3613. $C_{34}H_{48}O_6$ requires C, 73.9; H, 8.75%; *M*, 554.3607).

We thank the S.R.C. for a research studentship (to J. M.) and Drs. J. Blair and T. G. Watson for technical assistance. We also thank Organon Laboratories Ltd., for a generous gift of 'isocholesterol.'

[7/1183 *Received*, 5th *July*, 1977]

[31] W. Voser, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 497, 503; G. R. Pettit, P. Hofer, W. J. Bowyer, T. R. Kasturi, R. C. Bansal, R. E. Kadunce, and B. Green, *Tetrahedron*, 1963, **19**, 1143.

[32] F. N. Lahey and P. H. A. Strasser, *J. Chem. Soc.*, 1951, 873.

[33] R. M. Gascoigne, A. Robertson, and J. J. H. Simes, *J. Chem. Soc.*, 1953, 830; G. W. Krakower, J. W. Brown, and J. Fried, *J. Org. Chem.*, 1962, **27**, 4710.