

## Photo-oxygenation of Lanosteryl Acetate

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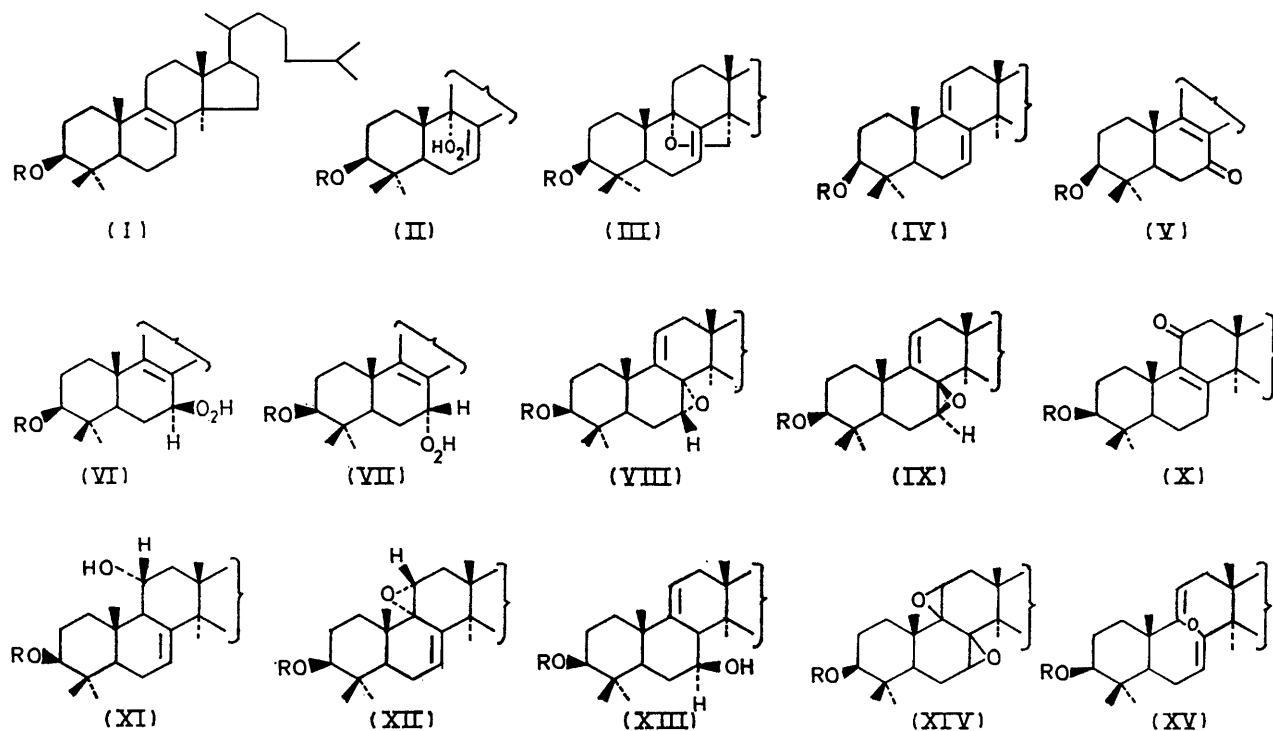
3 $\beta$ -Acetoxylanost-8-ene has been photo-oxygenated in the presence of a dye and *p*-nitrobenzenesulphonyl chloride to yield, among other products, the Criegee rearrangement product 3 $\beta$ -acetoxy-8,9-epoxy-8,9-secolanosta-7,9(11)-diene (XV; R = Ac) and 3 $\beta$ -acetoxy-7 $\alpha$ -hydroperoxylanost-8-ene (VII; R = Ac). These are thought to arise from 3 $\beta$ -acetoxy-9 $\alpha$ -hydroperoxylanost-7-ene (II; R = Ac); their transformations are reported. The bridged cyclodeca-1,6-diene system in (XV) takes part in transannular reactions.

It is generally accepted that in the conversion of lanosterol into cholesterol in mammalian systems, the 14-methyl group is the first to be metabolised.<sup>1</sup> Several groups of workers have introduced functional groups at this position (C-32).<sup>2-7</sup>

We considered that the lability of the 14-methyl group *in vivo* might in some way be due to the proximity of the 8,9-double bond. If dihydrolanosterol (I; R = H) were to be treated with oxygen in the presence of light

this latter process in the work of Corey and White<sup>9</sup> on 1,5,5-trimethylcyclohexane hydroperoxide.

Preliminary experiments in which the photo-oxidation of 3 $\beta$ -acetoxylanost-8-ene (I; R = Ac) in the presence of the dye haematoporphyrin was attempted yielded intractable mixtures rather than the expected 9 $\alpha$ -hydroperoxide (II; R = Ac) and it was concluded that the failure to isolate this might be due to its extreme instability. It was decided, therefore, to conduct the



and a photosensitiser, then the 9 $\alpha$ -hydroperoxy-7-ene (II; R = H) might be expected.<sup>8</sup> Esterification of this compound would be expected to give a peroxyester (a good leaving group), which on solvolysis would yield the 9,14-epoxide (III; R = H). There is an analogy for

photo-oxygenation in the presence of *p*-nitrobenzenesulphonyl chloride so that if any 9 $\alpha$ -hydroperoxide were formed it might be esterified and the resultant peroxyester solvolysed *in situ* to yield the 9,14-epoxide (III; R = Ac).

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<sup>1</sup> For leading references see R. B. Clayton, *Quart. Rev.*, 1965, 19, 168, 201.

<sup>2</sup> D. H. R. Barton, J. S. Bentley, and J. F. McGhie, *Tetrahedron Letters*, 1965, 2497.

<sup>3</sup> J. Fried, J. W. Brown, and L. Borckenhagen, *Tetrahedron Letters*, 1965, 2499.

<sup>4</sup> C. W. Shoppee, J. C. Coll, N. W. Hughes, and R. E. Lack, *Tetrahedron Letters*, 1965, 3249.

<sup>5</sup> D. H. R. Barton, A. Hameed, and J. F. McGhie, *Tetrahedron Letters*, 1965, 4343.

<sup>6</sup> C. W. Shoppee, N. W. Hughes, and R. E. Lack, *Tetrahedron Letters*, 1966, 5235; *J. Chem. Soc. (C)*, 1966, 2359.

<sup>7</sup> J. Fried, J. W. Brown, and M. Applebaum, *Tetrahedron Letters*, 1965, 849.

<sup>8</sup> G. O. Schenck, *Angew. Chem.*, 1957, 69, 579.

<sup>9</sup> E. J. Corey and R. W. White, *J. Amer. Chem. Soc.*, 1958, 80, 6686.

3 $\beta$ -Acetoxy lanost-8-ene<sup>10</sup> (I; R = Ac) was dissolved in pyridine with *p*-nitrobenzenesulphonyl chloride and haematoporphyrin, and oxygen was passed through the solution with irradiation from two 20 W fluorescent tubes. The mixture yielded 3 $\beta$ -acetoxy lanosta-7,9(11)-diene<sup>11</sup> (IV; R = Ac) and 3 $\beta$ -acetoxy lanost-8-en-7-one<sup>12</sup> (V; R = Ac), together with four compounds of unknown structure.

The first of these, m.p. 175–176°, had a band at 3500 cm<sup>-1</sup> in its i.r. spectrum and so was at first considered to be an alcohol. The n.m.r. spectrum had signals at  $\tau$  1.49 (1H, s, OH) and *ca.* 5.5 (2H, m, CH·OAc and allylic CH·OH?) but showed no olefinic protons. In an attempt to verify the allylic nature of the 'alcohol', we treated the compound with manganese dioxide in chloroform and obtained 3 $\beta$ -acetoxy lanosta-7,9(11)-diene<sup>11</sup> (IV; R = Ac). Attempted acetylation yielded the ketone<sup>12</sup> (V; R = Ac). These results could be explained if the compound were a 3 $\beta$ -acetoxy-7-hydroperoxy lanost-8-ene, and since Horn and Ilse<sup>13</sup> had prepared the 7 $\beta$ -hydroperoxide (VI; R = Ac), the product of this photosensitised oxidation must be 3 $\beta$ -acetoxy-7 $\alpha$ -hydroperoxy lanost-8-ene (VII; R = Ac). The presence of the hydroperoxide group was verified by a positive iron(II) thiocyanate test,<sup>14</sup> and molecular rotation differences supported the stereochemical assignment since the  $\Delta M_D$  values of the new compound (–95°), the 7 $\beta$ -hydroperoxide<sup>13</sup> (+64°), and 3 $\beta$ -acetoxy lanost-8-ene were of similar magnitude to the values quoted<sup>15</sup> for steroidal alcohols (–59° for 7 $\alpha$ -ols and +110° for 7 $\beta$ -ols). Significantly the differences between the two isomeric hydroperoxides (–159°) and the two isomeric alcohols (–169°) were very similar. The 7 $\alpha$ -hydroperoxy-8-ene (VII; R = Ac) might possibly arise from the expected 9 $\alpha$ -hydroperoxy-7-ene (III; R = Ac) by an allylic rearrangement of the type observed by Schenck *et al.*<sup>16</sup> in analogous systems.

A further two products of the photosensitised reaction appeared to be 1,2-epoxides. The first of these, m.p. 182–183°,  $[\alpha]_D$  –4.5°, at first appeared to us to be the compound which had been obtained by treatment with monoperoxyphthalic acid of the diene (IV; R = Ac) and designated as 3 $\beta$ -acetoxy-7,8-epoxy lanost-9(11)-ene (VIII or IX; R = Ac) by Jeger *et al.*,<sup>17</sup> (m.p. 185–186°,  $[\alpha]_D$  –8°). The n.m.r. spectrum of this compound showed the signal for the epoxide proton as a doublet at  $\tau$  6.84 (*J* 5 Hz) and the olefinic proton at 4.28 as part of an ABX system with  $J_{AX} = J_{BX} = 4$  Hz and  $J_{AB}$  8 Hz,  $\tau_A = 7.85$ ,  $\tau_B = 7.93$ . That no further coupling was

present in this system was verified by decoupling experiments. Treatment with boron trifluoride of the epoxide yielded the enone<sup>17</sup> (X; R = Ac), m.p. and mixed m.p. 133–135°. Reduction of the epoxide with lithium and ethylamine yielded 3 $\beta$ -hydroxy lanost-8-ene (I; R = H) and a diol, which was most probably lanost-7-ene-3 $\beta$ ,11 $\alpha$ -diol<sup>18</sup> (XI; R = H). The epoxide photoproduct was therefore 3 $\beta$ -acetoxy-9 $\alpha$ ,11 $\alpha$ -epoxy lanost-7-ene (XII; R = Ac).

The second of the epoxides showed an n.m.r. spectrum, which was similar to that of the above epoxide (see Experimental section); the olefinic proton signal at  $\tau$  4.36 was part of an A<sub>2</sub>X system as proven by decoupling. No further coupling was present in this system. Treatment of this second epoxide with chromatographic silica gel yielded 3 $\beta$ -acetoxy lanost-9(11)-en-7-one,<sup>17</sup> while thermal treatment or boron trifluoride treatment yielded 3 $\beta$ -acetoxy lanost-8-en-7-one<sup>12</sup> (V; R = Ac). Reduction of the epoxide with lithium and ethylamine gave lanost-8-en-3 $\beta$ -ol (I; R = H) and lanost-9(11)-ene-3 $\beta$ ,7 $\beta$ -diol<sup>19</sup> (XIII; R = H), indicating that this epoxide must be 3 $\beta$ -acetoxy-7 $\beta$ ,8 $\beta$ -epoxy lanost-9(11)-ene (IX; R = Ac). Treatment of 3 $\beta$ -acetoxy lanosta-7,9(11)-diene (IV; R = Ac) with *m*-chloroperbenzoic acid yielded not only epoxides (IX; R = Ac) and (XII; R = Ac), but a third epoxide, which was concluded (see Experimental section) to be 3 $\beta$ -acetoxy-7,8:9,11-diepoxylanostane (XIV; R = Ac).

The final product of the photosensitised reaction was an ether, C<sub>32</sub>H<sub>52</sub>O<sub>3</sub>, m.p. 142–144°,  $[\alpha]_D$  +164°. This had a three-proton multiplet at  $\tau$  5.4 in the n.m.r. spectrum, one of these protons being the 3 $\alpha$ -proton. To simplify the  $\tau$  5.4 region, the ether was converted into an alcohol, C<sub>30</sub>H<sub>50</sub>O<sub>2</sub>, m.p. 129–131°,  $[\alpha]_D$  +177.6°, from which the original ether could be regenerated on acetylation. The 3 $\alpha$ -proton signal now appeared at  $\tau$  6.7 and the remaining two protons gave rise to a quartet at 5.22. One proton was part of an ABX system ( $\tau_A$  8.04,  $\tau_B$  7.64, and  $\tau_X$  5.22,  $J_{AX}$  5,  $J_{BX}$  8,  $J_{AB}$  14 Hz), and the other appeared as a triplet at 5.47 (1H, *J* 3.5 Hz). The chemical shifts of these protons compare well with that of the  $\beta$ -olefinic proton of dihydropyranyl ether at 5.46<sup>20</sup> and the structure (XV; R = Ac) is in accord with the above data. This compound could arise by Criegee rearrangement<sup>21</sup> of the hypothetical 9 $\alpha$ -hydroperoxide (II; R = Ac) in an analogous manner to the rearrangement of 10-hydroperoxy- $\Delta^{8,9}$ -octalin,<sup>22</sup> which gives rise to bridged cyclodecane systems.

Treatment of this seco-ether (XV; R = Ac) with

<sup>10</sup> R. E. Marker, E. L. Wittle, and L. A. Mixon, *J. Amer. Chem. Soc.*, 1937, **59**, 1368.

<sup>11</sup> L. Ruzicka, R. Denss, and O. Jeger, *Helv. Chim. Acta*, 1946, **29**, 204.

<sup>12</sup> D. H. R. Barton, J. S. Fawcett, and B. R. Thomas, *J. Chem. Soc.*, 1951, 3147.

<sup>13</sup> D. H. S. Horn and D. Ilse, *J. Chem. Soc.*, 1957, 2280.

<sup>14</sup> F. Feigl, 'Spot Tests in Organic Analysis,' Elsevier, Amsterdam 1960, p. 534.

<sup>15</sup> W. Klyne, 'The Chemistry of the Steroids,' Methuen, London 1965, p. 55.

<sup>16</sup> G. O. Schenck, O.-A. Neumuller, and W. Eisfeld, *Annalen*, 1958, **618**, 202.

<sup>17</sup> M. V. Mijovic, W. Voser, H. Heusser, and O. Jeger, *Helv. Chim. Acta*, 1952, **35**, 964.

<sup>18</sup> C. W. Shoppee, J. C. Coll, and R. E. Lack, *J. Chem. Soc. (C)*, 1968, 1581.

<sup>19</sup> J. F. Cavalla, J. F. McGhie, and M. K. Pradhan, *J. Chem. Soc.*, 1951, 3142.

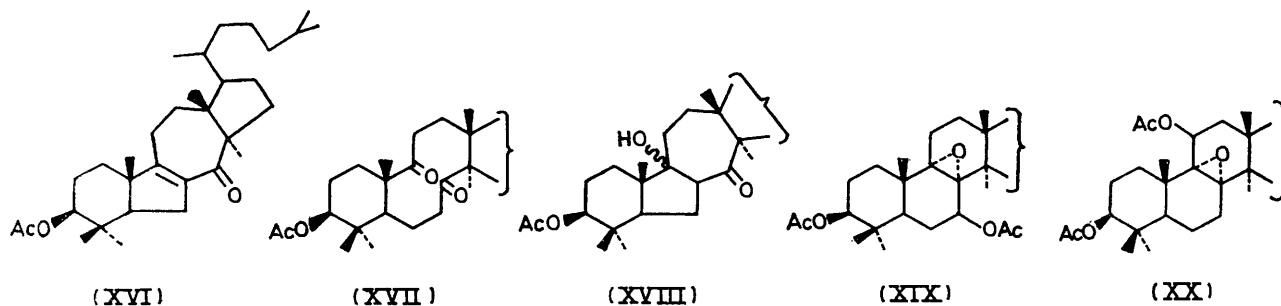
<sup>20</sup> L. M. Jackman, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, London 1959, p. 62.

<sup>21</sup> R. Criegee, *Ber.*, 1944, **77**, 722.

<sup>22</sup> G. O. Schenck and K. H. Schulte-Elte, *Annalen*, 1958, **618**, 185.

potassium iodide in acetic acid gave the diene (IV; R = Ac), a product of transannular reaction. Treatment with boron trifluoride-ether in glacial acetic acid, however, gave a mixture of three products, the first of which, an enone, was identical to the compound assigned structure (XVI) by Snatzke *et al.*<sup>23,24</sup> A second product was a ketol, m.p. 176–177°,  $[\alpha]_D -61.7^\circ$ , with carbonyl and hydroxy-absorptions in the i.r. spectrum. Snatzke<sup>23</sup> had reported a gummy mixture containing the enone (XVI) and material with  $\nu_{\max}$  3595 and 3510 (OH) and

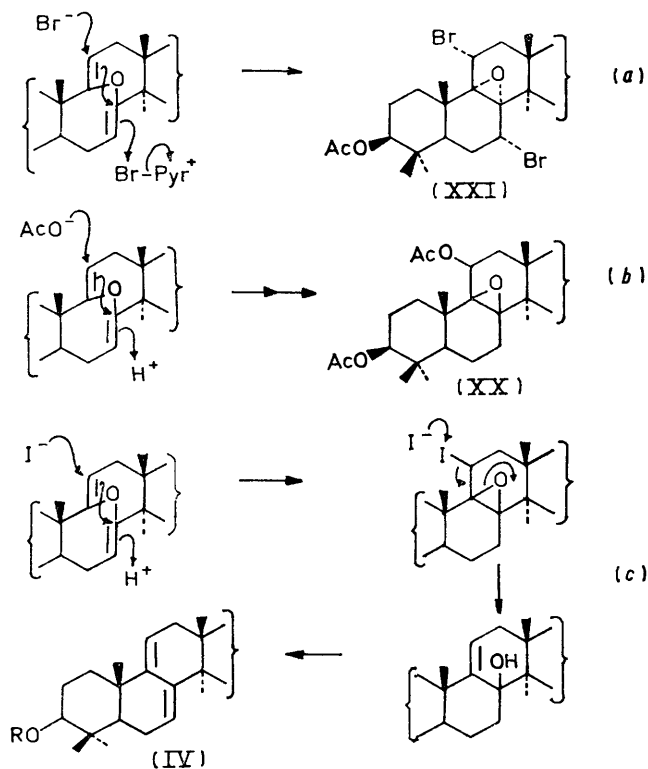
which both multiplets were absent. It was concluded that the diacetate was the product of transannular reaction, either 3 $\beta$ ,7-diacetoxy-8 $\alpha$ ,9 $\alpha$ -epoxy lanostane (XIX) or 3 $\beta$ ,11-diacetoxy-8 $\alpha$ ,9 $\alpha$ -epoxy lanostane (XX). The latter assignment was concluded to be the correct one, as the 4-72 multiplet was part of an ABX system with  $\tau_A$  8.22,  $\tau_B$  8.22,  $\tau_X$  4.72,  $J_{AX}$  2 Hz,  $J_{BX}$  6 Hz,\* and no further coupling with any other protons. It would be expected that in the 3,7-isomer (XIX), further coupling of the AB protons at C(6) with 5-H would be observed.



1691 (C=O)  $\text{cm}^{-1}$  from treatment with acetic acid of the seco-dione (XVII). We have self-condensed the latter compound (XVII) on grade III neutral alumina to obtain a mixture containing the enone (XVI) (21%), the ketol (29%), and a second ketol (67%), m.p. 220–222°,  $[\alpha]_D +29^\circ$ . On treating the seco-dione (XVII) with acetic acid, we obtained the second ketol as the sole product. This showed absorptions due to bands at hydroxy- and carbonyl groups in the i.r. Both ketols could be dehydrated to the enone (XVI) and were assumed to be the epimeric  $\beta$ -hydroxy-ketones (XVIII). The carbonyl absorption in the i.r. spectra of the two ketols showed no change in position on dilution, indicating intramolecular hydrogen bonding, the ketol with lower m.p. being obviously the more hydrogen-bonded of the two. Rates of dehydration of the two ketols were similar, and the proton  $\alpha$  to the carbonyl group and to the carbon atom bearing the alcoholic function gave rise to a quartet at  $\tau$  6.84 in the n.m.r. spectrum of the first ketol and to a triplet at  $\tau$  6.69 in the spectrum of the second. No stereochemical inferences have been drawn from these data.

The third product from the boron trifluoride-ether treatment of the seco-ether (XV; R = Ac) was a diacetate, m.p. 190–193°,  $[\alpha]_D -16.8^\circ$ . The n.m.r. spectrum (see Experimental section) contained two distinct acetate methyl singlets and signals for two secondary CH-OAc protons as multiplets at  $\tau$  4.72 and 5.6. Saponification of the diacetate yielded a diol, in which the two multiplets at  $\tau$  4.72 and 5.6 had been shifted to  $\tau$  5.92 and 6.84, respectively. Oxidation of the diol with ruthenium tetroxide yielded a diketone, in the n.m.r. spectrum of

Further verification of the seco-ether structure (XV; R = Ac) for the photo-oxygenation product was that



SCHEME

on bromination, a dibromide was obtained. This has been analysed by X-ray crystallography<sup>25</sup> and shown to be 3 $\beta$ -acetoxy-7 $\alpha$ ,11 $\alpha$ -dibromo-8 $\alpha$ ,9 $\alpha$ -epoxy lanostane (XXI), which could arise by a concerted transannular

<sup>23</sup> G. Snatzke and H. W. Fehlhaber, *Annalen*, 1963, **663**, 123.

<sup>24</sup> G. Snatzke and A. Nisar, *Annalen*, 1965, **683**, 159.

<sup>25</sup> J. K. Fawcett and J. Trotter, *J. Chem. Soc. (B)*, 1966, 174.

\* It is considered that, since the chemical shifts of protons A and B are so similar, the outer bands are small and hidden under the other absorption present. The values shown refer only to the central parts of the AB spectrum and  $J_{AB}$  is not obtainable. The assignments, are however, in agreement with results of decoupling experiments.

reaction (see Scheme). Such transannular reactions have been observed recently<sup>26</sup> in the case of a cyclodeca-1,6-diene without the epoxide bridge; the bromination, the conversion of the seco-ether (XV; R = Ac) into the diene (IV; R = Ac), and the boron trifluoride-ether treatment to yield the diacetate (XX) are all examples of this transformation. Mechanisms for these three reactions are suggested in the Scheme.

Attempts to functionalise the 14-methyl group *via* the 7 $\alpha$ -hydroperoxide (VI; R = Ac) were not successful.

#### EXPERIMENTAL

I.r. spectra were determined for solutions in carbon tetrachloride (unless otherwise stated) on Perkin-Elmer 237 and Infracord instruments. U.v. spectra were recorded for solutions in methanol with a Unicam SP 800 spectrophotometer. N.m.r. spectra for deuteriochloroform solutions with tetramethylsilane as internal standard were recorded with Varian A 60 and HA 100 instruments, and mass spectra on an A.E.I. MS 9 instrument. We thank R. J. Suffolk and F. G. Bloss respectively, for n.m.r. and mass spectra. Microanalyses were determined by J. M. R. Cameron, The University of Glasgow, and B. J. Sanderson, The University of Sussex, and their respective staffs. M.p.s were recorded on a Kofler hot-stage apparatus and rotations were measured for solutions in chloroform on a Perkin-Elmer 141 polarimeter.

*Photosensitised Oxygenation of 3 $\beta$ -Acetoxy lanost-8-ene (I; R = Ac) in the Presence of *p*-Nitrobenzenesulphonyl Chloride.*—3 $\beta$ -Acetoxy lanost-8-ene (10 g), *p*-nitrobenzenesulphonyl chloride (4.66 g), and haematoporphyrin (130 mg) were dissolved in AnalaR pyridine (200 ml). Oxygen was passed through the solution for 6 days with irradiation from two 20 W, 250 V fluorescent tubes. The solvent was removed under reduced pressure and the residual gum was dissolved in ether, washed with water, and dried (MgSO<sub>4</sub>). Removal of the solvent *in vacuo* yielded a semi-solid which was chromatographed on grade III alumina.

Elution with light petroleum ether (b.p. 60–80°) yielded first aromatic material derived from *p*-nitrobenzenesulphonyl chloride, and then 3 $\beta$ -acetoxy lanosta-7,9(11)-diene (IV; R = Ac) as needles, m.p. 160–165° [from light petroleum (b.p. 60–80°)],  $\lambda_{\max}$  236, 245, and 254 nm (lit.,<sup>11</sup> 160–161°).

Elution with light petroleum (b.p. 60–80°)-benzene (9:1) gave 3 $\beta$ -acetoxy-8,9-epoxy-8,9-secolanosta-7,9(11)-diene (XV; R = Ac) as needles (153 mg), m.p. 142–144° [from light petroleum (b.p. 60–80°)],  $[\alpha]_D +164^\circ$  (*c* 1.57) (Found: C, 79.0; H, 10.5. C<sub>32</sub>H<sub>52</sub>O<sub>3</sub> requires C, 79.3; H, 10.8%), *M* (mass spectroscopy), 484,  $\nu_{\max}$  1730 and 1240 (both OAc) cm<sup>-1</sup>,  $\tau$  5.4 (3H, m, 3 $\alpha$ -H and 2 other protons).

Elution with light petroleum (b.p. 60–80°)-benzene (4:1) gave 3 $\beta$ -acetoxy lanost-8-en-7-one (V; R = Ac) as needles (1.6 g), m.p. 146–151° [from light petroleum (b.p. 60–80°)],  $[\alpha]_D +19^\circ$  (*c* 1.02),  $\lambda_{\max}$  255 nm ( $\epsilon$  13,050) (lit.,<sup>12</sup> 149–155°,  $[\alpha]_D +22^\circ$ ).

Elution with benzene-ether (19:1) yielded 3 $\beta$ -acetoxy-7 $\alpha$ -hydroperoxy lanost-8-ene (VII; R = Ac) as needles (640 mg), m.p. 175–176° (from ethyl acetate),  $[\alpha]_D +35.2^\circ$  (*c* 0.83) (Found: C, 76.95; H, 10.4. C<sub>32</sub>H<sub>54</sub>O<sub>4</sub> requires C, 76.75; H, 10.85%),  $\nu_{\max}$  3500 (O·OH), 1737, and 1270 (OAc) cm<sup>-1</sup>, *M*<sup>+</sup> (mass spectroscopy), 484; the compound gave a red colouration with iron(II) thiocyanate.<sup>14</sup>

Rechromatography of fractions eluted immediately after the seco-ether (XV; R = Ac) yielded 3 $\beta$ -acetoxy-9 $\alpha$ ,11 $\alpha$ -epoxy lanost-7-ene (XII; R = Ac) (200 mg), m.p. 182–183° [from light petroleum (b.p. 60–80°)],  $[\alpha]_D -4.5^\circ$  (*c* 0.431) (Found: C, 79.7; H, 10.75. C<sub>32</sub>H<sub>52</sub>O<sub>3</sub> requires C, 79.3; H, 10.8%).

Rechromatography of fractions eluted immediately before the seco-ether (XV; R = Ac) yielded 3 $\beta$ -acetoxy-7 $\beta$ ,8 $\beta$ -epoxy lanost-9(11)-ene (IX; R = Ac) as prisms [101 mg from 3 $\beta$ -acetoxy lanost-8-ene (40 g)], m.p. 171.5–174°,  $[\alpha]_D +94.3^\circ$  (*c* 1.24) (Found: C, 79.35; H, 10.2. C<sub>32</sub>H<sub>52</sub>O<sub>3</sub> requires C, 79.3; H, 10.8%),  $\nu_{\max}$  1730 and 1240 (OAc) cm<sup>-1</sup>, *M*<sup>+</sup> (mass spectroscopy), 484,  $\tau$  4.36 (1H, A<sub>2</sub>X,  $\tau_{AX}$  7.84,  $J_{AX}$  4 Hz, 11-H) and 7.0 (1H, m, 7-H).

*Treatment of 3 $\beta$ -Acetoxy-7 $\alpha$ -hydroperoxy lanost-8-ene (VII; R = Ac) with Manganese Dioxide.*—The hydroperoxide (VII; R = Ac) (37 mg) was dissolved in chloroform (4 ml) and shaken with manganese dioxide (350 mg) for 3 days at room temperature. The solution was filtered through Celite and the residue was washed well with an excess of chloroform. The solvent was removed from the combined filtrate and washings *in vacuo* to yield a gum which was chromatographed on grade III alumina. Elution with light petroleum (b.p. 60–80°) gave 3 $\beta$ -acetoxy lanosta-7,9(11)-diene (IV; R = Ac) (3 mg), m.p. and mixed m.p. 160–163°,  $\lambda_{\max}$  236, 244 ( $\epsilon$  19,400), and 252 nm. The infrared spectrum was identical with that of an authentic sample.

*Treatment of 3 $\beta$ -Acetoxy-7 $\alpha$ -hydroperoxy lanost-8-ene (VII; R = Ac) with Acetic Anhydride.*—The hydroperoxide (VII; R = Ac) (20 mg) was dissolved in acetic anhydride (1 ml) and pyridine (1 ml) and left overnight at room temperature. Water was added to the solution, which was extracted with ether. The extracts were washed with water and dried (MgSO<sub>4</sub>). The solvent was removed *in vacuo* to yield the enone (V; R = Ac) as needles, m.p. and mixed m.p. 145–149° [from light petroleum (b.p. 60–80°)] (Found: C, 79.2; H, 10.1. Calc. for C<sub>32</sub>H<sub>52</sub>O<sub>3</sub>: C, 79.6; H, 10.4%),  $\lambda_{\max}$  257 nm ( $\epsilon$  13,750).

*3 $\beta$ -Acetoxy lanost-8-en-11-one (X; R = Ac).*—3 $\beta$ -Acetoxy-9 $\alpha$ ,11 $\alpha$ -epoxy lanost-9(11)-ene (XII; R = Ac) (70 mg) was dissolved in 45% boron trifluoride-ether (4 ml) and left for 12 h at room temperature. Water was added and the solution was extracted with ether. The extracts were washed well with water and dried (MgSO<sub>4</sub>). The solvent was removed *in vacuo* to yield a gum which was chromatographed on 1-mm thick plates of silica gel. Elution with benzene-chloroform (1:1) gave the ketone (X; R = Ac)<sup>17</sup> (38 mg) as needles, m.p. and mixed m.p. 133–135° (from methanol),  $[\alpha]_D +140^\circ$  (*c* 0.252),  $\lambda_{\max}$  257 nm.

*Reduction of 3 $\beta$ -Acetoxy-9 $\alpha$ ,11 $\alpha$ -epoxy lanost-7-ene (XII; R = Ac).*—The epoxide (XII; R = Ac) (73 mg) was dissolved in ethylamine (30 ml) with metallic lithium (100 mg) and stirred at room temperature overnight. Excess of methanol was added with caution, followed by excess of 2*N*-sulphuric acid, and the solution was extracted with ether. The extracts were washed with water and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed *in vacuo* to yield a solid (118 mg), which was chromatographed on grade II alumina. Elution with benzene gave needles of lanost-8-en-3 $\beta$ -ol<sup>27</sup> (I; R = H) (14 mg), m.p. 140–143° [from light petroleum (b.p. 60–80°)],  $[\alpha]_D +49^\circ$  (*c* 0.018),

<sup>26</sup> R. M. Gipson, H. W. Guin, S. H. Simonsen, C. G. Skinner, and W. Shive, *J. Amer. Chem. Soc.*, 1966, **88**, 5366.

<sup>27</sup> R. G. Curtis and H. Silberman, *J. Chem. Soc.*, 1952, 1187.

$M^+$ , 428, identical with an authentic specimen (i.r. and n.m.r.). Elution with light petroleum (b.p. 60–80°)–ethyl acetate (1 : 1) yielded a solid,  $C_{30}H_{52}O_2$ , m.p. 204–207°,  $[\alpha]_D - 4^\circ$  ( $c$  0.216),  $M^+$  (mass spectroscopy), 444,  $\nu_{\max}$  3620 (OH)  $cm^{-1}$ ; this was most likely lanost-7-ene-3 $\beta$ ,11 $\alpha$ -diol (XI; R = H) (lit.,<sup>18</sup> m.p. 197–198°).

*Treatment with Silica Gel of 3 $\beta$ -Acetoxy-7 $\beta$ ,8 $\beta$ -epoxylanost-9(11)-ene* (IX; R = Ac).—The epoxide (IX; R = Ac) (65 mg) was applied to a column of chromatographic silica gel (B.D.H.; 10 g) in light petroleum (b.p. 60–80°) in the usual way and left for 3 h before commencing elution. Elution with benzene yielded 3 $\beta$ -acetoxylanost-9(11)-en-7-one, m.p. 158–163° (from methanol-ether),  $[\alpha]_D + 117.6^\circ$  ( $c$  1.03) (lit.,<sup>17</sup> m.p. 153–154°,  $[\alpha]_D + 119^\circ$ ). The i.r., n.m.r., and u.v. spectra were in accord with this structure.

*Thermal Treatment of 3 $\beta$ -Acetoxy-7 $\beta$ ,8 $\beta$ -epoxylanost-9(11)-ene* (IX; R = Ac).—A sample of the epoxide (IX; R = Ac) was left in a vacuum-drying pistol at 100° overnight and the resultant 3 $\beta$ -acetoxylanost-8-en-7-one (V; R = Ac) was crystallised from light petroleum (b.p. 60–80°), m.p. and mixed m.p. 144–152°,  $[\alpha]_D + 18.2^\circ$  ( $c$  0.77) {lit.,<sup>12</sup> m.p. 155°,  $[\alpha]_D + 24^\circ$  ( $c$  0.23)}.

*Treatment with Boron Trifluoride of 3 $\beta$ -Acetoxy-7 $\beta$ ,8 $\beta$ -epoxylanost-9(11)-ene* (IX; R = Ac).—The epoxide (50 mg) was dissolved in glacial acetic acid (2.5 ml) with 45% boron trifluoride-ether (10 drops) and left at room temperature for 3 h. Water was added and the solution was extracted with ether. The extracts were washed with water and dried (MgSO<sub>4</sub>). The solvent was removed *in vacuo* to yield 3 $\beta$ -acetoxylanost-8-en-7-one (V; R = Ac) as needles, m.p. 152–154° [from light petroleum (b.p. 60–80°)],  $[\alpha]_D + 18.6^\circ$  ( $c$  1.72),  $\lambda_{\max}$  257 nm ( $\epsilon$  9250).

*Reduction of 3 $\beta$ -Acetoxy-7 $\beta$ ,8 $\beta$ -epoxylanost-9(11)-ene* (IX; R = Ac).—The epoxide (48 mg) was dissolved in ethylamine (20 ml) with lithium (200 mg) and stirred at 4° for 9 h. Excess of methanol was added and the solution was acidified and extracted with ether. The extracts were washed with water and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed *in vacuo* to yield a solid (47 mg) which was chromatographed on grade II alumina. Elution with light petroleum (b.p. 60–80°)–benzene (1 : 1) yielded lanost-8-en-3 $\beta$ -ol<sup>27</sup> (I; R = H) (29 mg) which was crystallised from light petroleum (b.p. 60–80°) containing one drop of methanol, m.p. 141–143°,  $[\alpha]_D^{25} + 52^\circ$  ( $c$  0.68), identical with an authentic specimen. Elution with benzene afforded prisms of lanost-9(11)-ene-3 $\beta$ ,7 $\beta$ -diol<sup>19</sup> (XIII; R = H) (13 mg), m.p. 206–209° [from light petroleum (b.p. 60–80°)],  $[\alpha]_D + 91.5^\circ$  ( $c$  0.236) (lit.,<sup>19</sup> m.p. 213–214°,  $[\alpha]_D + 94^\circ$ ); the spectra are in accord with this structure.

*Treatment of 3 $\beta$ -Acetoxy-7,9(11)-diene* (IV; R = Ac) with *m*-Chloroperbenzoic Acid.—The diene (IV; R = Ac) (25.2 g) was dissolved in AnalaR chloroform (100 ml) with 85% *m*-chloroperbenzoic acid (18 g; Aldrich) and stirred for 2 days at 4°. Excess of aqueous potassium iodide solution was added, and the iodine formed was destroyed with 0.05N-sodium thiosulphate solution. The solution was extracted with ether and the extracts were washed with aqueous sodium hydrogen carbonate solution and water, and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed *in vacuo* to yield an oil (33 g), 15 g of which was chromatographed on grade II alumina. Elution with light petroleum (b.p. 60–80°)–benzene (9 : 1 and 4 : 1) yielded 3 $\beta$ -acetoxy-7 $\beta$ ,8 $\beta$ -epoxylanost-9(11)-ene (IX; R = Ac) (1.5 g), needles, m.p. 174–175° [from light petroleum (b.p. 60–80°)],  $[\alpha]_D + 94.4^\circ$  ( $c$  0.72) (Found: C, 79.2; H, 10.7. Calc. for

$C_{32}H_{52}O_3$ : C, 79.3; H, 10.8%), identical with an authentic specimen. Elution with light petroleum (b.p. 60–80°)–benzene (1 : 1) yielded 3 $\beta$ -acetoxy-9 $\alpha$ ,11 $\alpha$ -epoxylanost-7-ene (XII; R = Ac) (150 mg), m.p. 180–182°,  $[\alpha]_D - 9.1^\circ$  ( $c$  2.12), identical with an authentic sample. Elution with light petroleum (b.p. 60–80°)–benzene (1 : 3 and 1 : 9) yielded 3 $\beta$ -acetoxy-7,8 : 9,11-diepoxylanostane (XIV; R = Ac) (900 mg) as needles, m.p. 204–205° (from light petroleum),  $[\alpha]_D + 46.3^\circ$  ( $c$  0.19) (Found: C, 76.7; H, 10.6.  $C_{32}H_{52}O_4$  requires C, 76.75; H, 10.5%),  $M$  (mass spectroscopy), 500,  $\nu_{\max}$  1736 (OAc)  $cm^{-1}$ ,  $\tau$  5.5 (1H, m, 3 $\alpha$ -H), 6.4 (1H, d,  $J$  3.5 Hz), and 6.99 (1H, d,  $J$  5 Hz).

*8,9-Epoxy-8,9-secolanosta-7,9(11)-dien-3 $\beta$ -ol* (XV; R = H).—3 $\beta$ -Acetoxy-8,9-epoxy-8,9-secolanosta-7,9(11)-diene (121 mg) was suspended in aqueous methanolic potassium hydroxide solution (10 ml) [from potassium hydroxide (4.0 g), water (10 ml), and methanol (40 ml)] and stirred at room temperature for 6 h. The mixture was extracted with ether and the extracts were washed with water and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed *in vacuo* to yield the alcohol as needles, m.p. 129–131° (from aqueous methanol),  $[\alpha]_D + 177.6^\circ$  ( $c$  0.31) (Found: C, 81.2; H, 11.6.  $C_{30}H_{50}O_2$  requires C, 81.4; H, 11.4%),  $\nu_{\max}$  3620  $cm^{-1}$ ,  $M$  (mass spectroscopy), 442.

*3 $\beta$ -Acetoxy-8,9-epoxy-8,9-secolanosta-7,9(11)-diene* (XV; R = Ac).—The foregoing alcohol (38 mg) was dissolved in AnalaR pyridine (2 ml) with AnalaR acetic anhydride (2 ml) and left at room temperature overnight. Water was added, and the solution was extracted with ether. The extracts were washed with water and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed *in vacuo* to yield 3 $\beta$ -acetoxy-8,9-epoxy-8,9-secolanosta-7,9(11)-diene (XV; R = Ac) as needles, m.p. and mixed m.p. 145–147° [from light petroleum (b.p. 60–80°)],  $[\alpha]_D + 175^\circ$  ( $c$  0.25); for n.m.r. data, see text.

*Treatment with Potassium Iodide of 3 $\beta$ -Acetoxy-8,9-epoxy-8,9-secolanosta-7,9(11)-diene* (XV; R = Ac).—The epoxide (XV; R = Ac) (21 mg) was heated with a saturated solution of potassium iodide in glacial acetic acid (5 mg) on the steam-bath for 30 min. The red solution was treated with an excess of aqueous sodium thiosulphate solution and extracted with ether. The extracts were washed with aqueous sodium hydrogen carbonate solution and water and dried (MgSO<sub>4</sub>). The solvent was removed *in vacuo* to yield a semi-solid which contained a considerable amount of starting material (t.l.c.). The treatment with a saturated solution of potassium iodide in glacial acetic acid (10 ml) was therefore continued for a further 4 h and the reaction was worked-up as before. The resultant gum (12 mg) was chromatographed on grade III alumina; elution with light petroleum (b.p. 60–80°) gave 3 $\beta$ -acetoxy-7,9(11)-diene (IV; R = Ac) (6 mg) as needles, m.p. and mixed m.p. 166–169° [from light petroleum (b.p. 60–80°)],  $\lambda_{\max}$  236, 244 ( $\epsilon$  13,500), and 253 nm, identical in all respects with an authentic sample.

*Treatment of 3 $\beta$ -Acetoxy-8,9-epoxy-8,9-secolanosta-7,9(11)-diene* (XV; R = Ac) with Acid.—The seco-epoxide (XV; R = Ac) (150 mg) was dissolved in glacial acetic acid (7 ml) with 45% boron trifluoride-ether (17 drops) and left at room temperature for 4 h. Water was added and the solution was extracted with ether. The extracts were washed with water and dried (MgSO<sub>4</sub>). The solvent was removed *in vacuo* to yield a gum which was chromatographed on grade III alumina. Elution with light petroleum (b.p. 60–80°) gave the homo-nor-ketone (XVI)<sup>23,24</sup> (36 mg) as needles, m.p. and mixed m.p. 162–163°

[from light petroleum (b.p. 60—80°)],  $[\alpha]_D - 8.5^\circ$  (*c* 1.02) (Found: C, 79.35; H, 10.5. Calc. for  $C_{32}H_{52}O_3$ : C, 79.3; H, 10.8%),  $\lambda_{\max}$  251 nm ( $\epsilon$  11,200).

Elution with light petroleum (b.p. 60—80°)—benzene (19 : 1 to 1 : 1) gave 3 $\beta$ ,11-diacetoxy-8 $\alpha$ ,9 $\alpha$ -epoxyxylanostane (XX), which crystallised from acetone and sublimed at 170° and 10<sup>-7</sup> mmHg, m.p. 190—193°,  $[\alpha]_D - 16.8$  (*c* 0.62) (Found: C, 74.8; H, 10.2.  $C_{34}H_{56}O_5$  requires C, 74.95; H, 10.35%),  $\nu_{\max}$  1740 (OAc)  $cm^{-1}$ ,  $\tau$  4.72 (m, CH·OAc), 5.6 (m, CH·OAc), 7.96 (s, OAc), and 8.03 (s, OAc).

Elution with benzene gave 3 $\beta$ -acetoxy-3 $\xi$ -hydroxy-*c*(14a)-homo-*B*-norlanostan-14a-one (XVIII) as plates (32 mg), m.p. 176—177° [from light petroleum (b.p. 60—80°)],  $[\alpha]_D - 61.7^\circ$  (*c* 0.34) (Found: C, 76.15; H, 10.7.  $C_{32}H_{54}O_4$  requires C, 76.45; H, 10.8%),  $\nu_{\max}$  3615, 3520 (OH), 1735 (OAc), 1710, and 1680  $cm^{-1}$ ,  $\tau$  5.51 (1H, m, 3 $\alpha$ -H) and 6.84 (1H, q, J, 6, J<sub>2</sub> 10 Hz, CO·CH·C·OH).

*Condensation of 3 $\beta$ -Acetoxy-8,9-secolanostane-8,9-dione* (XVII).—The seco-dione (XVII) (23 mg) was dissolved in an excess of light petroleum (b.p. 60—80°) and left in the presence of grade III alumina (10 g) overnight. The alumina was extracted well with ether and the extracts were chromatographed in the usual way on grade III alumina. Elution with light petroleum (b.p. 60—80°)—benzene (4 : 1) gave the homo-nor-enone (XVI) (4.9 mg) as needles, m.p. and mixed m.p. 160—162° (from light petroleum).

Elution with light petroleum (b.p. 60—80°)—benzene (1 : 1) gave the other epimer of the ketol (XVIII) (16 mg) as needles, m.p. 220—222° (from light petroleum),  $[\alpha]_D + 29^\circ$  (*c* 0.206) (Found: C, 76.4; H, 10.8.  $C_{32}H_{54}O_4$  requires C, 76.45; H, 10.8%),  $\nu_{\max}$  3600 (OH), 1736 (OAc), and 1695 (C=O)  $cm^{-1}$ ,  $\tau$  6.69 (1H, t, J 8 Hz, CO·CH·C·OH).

Elution with benzene gave needles of the ketol (XVIII) (68 mg), m.p. and mixed m.p. 172—176° [from light petroleum (b.p. 60—80°)], identical with the ketol obtained in the previous experiment,  $[\alpha]_D - 61.8^\circ$  (*c* 0.168).

*Treatment of 3 $\beta$ -Acetoxy-8,9-secolanostane-8,9-dione* (XVII) with Acetic Acid.—The dione (XVII) (181 mg) was heated under reflux with glacial acetic acid (20 ml) for 1 h and added to excess of saturated aqueous sodium hydrogen carbonate solution. The solution was extracted with ether and the extracts were washed with water and dried ( $Na_2SO_4$ ). The solvent was removed *in vacuo* to give a solid (154 mg) which was chromatographed on grade II alumina. Elution with benzene yielded the epimer of the 3 $\xi$ -hydroxy-homo-nor-lanostane (XVIII), which had m.p. 220—222° [from light petroleum (b.p. 60—80°)],  $[\alpha]_D + 28.2^\circ$  (*c* 0.23), identical with the ketol, m.p. 220—222°, from the previous reaction.

*Dehydration of the Ketol* (XVIII) of *M.p.* 176—177°.—The ketol (19 mg) was dissolved in AnalaR benzene (30 ml) with toluene-*p*-sulphonic acid monohydrate (one crystal) and heated under reflux overnight under a Soxhlet containing calcium hydride. The benzene solution was washed with water and dried ( $Na_2SO_4$ ). The solvent was removed *in vacuo* to yield the enone (XVI) as plates (18 mg), m.p. and mixed m.p. 163—164° [from light petroleum (b.p. 60—80°)],  $[\alpha]_D - 8.5^\circ$  (*c* 0.387), identical spectrally with an authentic sample.

*Dehydration of the Ketol* (XVIII) of *M.p.* 220—222°.—The ketol (7 mg) was dissolved in AnalaR benzene (10 ml)

with toluene-*p*-sulphonic acid monohydrate (one crystal) and treated as before. The benzene solution was washed with water and dried ( $Na_2SO_4$ ). The solvent was removed *in vacuo* to yield the enone (XVI), which was purified by p.l.c. on 0.5-mm thick silica gel using chloroform—benzene (1 : 1) as eluant; m.p. and mixed m.p. 163—165° [from light petroleum (b.p. 60—80°)], identical spectrally with an authentic sample.

*Rate Studies on the Dehydration of the Foregoing Ketols* (XVIII).—The ketol (1.1 mg) was dissolved in ether (10 ml) and a portion (3 ml) of this solution was placed in a u.v. cell with concentrated sulphuric acid (0.1 ml). The absorbance at 247.5 nm was plotted with time and the rates of dehydration of the ketols were obtained from this plot. Both ketols were dehydrated with first-order kinetics, the rate constant for the ketol, m.p. 176—177°, being 0.1 h<sup>-1</sup> and that for the ketol, m.p. 220—222°, being 0.25 h<sup>-1</sup>.

*Hydrolysis of 3 $\beta$ ,11-Diacetoxy-8,9-epoxyxylanostane* (XX).—The diacetate (XX) (70 mg) was dissolved in aqueous methanolic potassium hydroxide solution (30 ml) [from potassium hydroxide (4 g), water (10 ml), and methanol (40 ml)] and ethanol (30 ml) and left for 9 h at room temperature. The solution was acidified and extracted with ether. The extracts were washed with water and dried ( $Na_2SO_4$ ). The solvent was removed *in vacuo* to give 8 $\alpha$ ,9 $\alpha$ -epoxyxylanostane-3,11-diol (58 mg) as needles, m.p. 191—196° (from methanol),  $[\alpha]_D + 5.5^\circ$  (*c* 0.217) (Found: C, 77.5; H, 11.5.  $C_{30}H_{52}O_3$  requires C, 78.2; H, 11.4%),  $\tau$  5.94 (m, CH·OAc) and 6.84 (m, CH·OAc).

*Oxidation of 8,9-Epoxyxylanostane-3 $\beta$ ,11-diol*.—The diol (18 mg) was dissolved in carbon tetrachloride (10 ml) with ruthenium tetroxide (46.2 mg) and stirred for 30 min at room temperature. Methanol was added cautiously to destroy the excess of ruthenium tetroxide and the mixture was filtered through Celite. The residue was washed thoroughly with carbon tetrachloride and the filtrate and washings were washed well with water and dried ( $Na_2SO_4$ ). The solvent was removed *in vacuo* to yield a gum which was purified by p.l.c. on 0.5-mm thick silica gel plates with chloroform—benzene (1 : 1) as eluant. The major product was 8,9-epoxyxylanostane-3,11-dione, m.p. 131—133° [from light petroleum (b.p. 60—80°)],  $[\alpha]_D - 28^\circ$  (*c* 0.312) [*M* (mass spectroscopy), 456.36590.  $C_{30}H_{48}O_3$  requires 456.36035].

*Bromination of 3 $\beta$ -Acetoxy-8,9-epoxy-8,9-secolanostane-7,9(11)-diene* (XV; R = Ac).—The epoxide (29 mg) was dissolved in dioxan (5 ml) with pyridine perbromide (29 mg) and the solution was stirred for 3 h at room temperature. Excess of sodium thiosulphate solution was added and the solution was extracted with ether. The extracts were washed with water and dried ( $Na_2SO_4$ ). The solvent was removed *in vacuo* to yield 3 $\beta$ -acetoxy-7 $\alpha$ ,11 $\alpha$ -dibromo-8 $\alpha$ ,9 $\alpha$ -epoxyxylanostane (XXI) as laths (27 mg), m.p. 198—199° [from light petroleum (b.p. 60—80°)],  $[\alpha]_D + 79.6^\circ$  (*c* 0.79) (Found: C, 59.95; H, 7.9.  $C_{32}H_{52}Br_2O_3$  requires C, 59.7; H, 8.0%).

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