564 *Steroids of Unnatural Configuration. Part IV.* Oxidation of Lumisterol and Lumisteryl Acetate with Perbenzoic Acid.*

By P. A. Mayor and G. D. Meakins.

Lumisterol and its acetate are converted by perbenzoic acid into 5β,6β-epoxides, ring opening of which leads ultimately to two known triols. These compounds are now shown to be lumista-7,22-diene-3β,5β,6β-triol (IIIa) and -3β,5β,6α-triol (IVa). The stereochemical aspects of the sequences leading to these triols have been examined, and the structures of intermediates and related compounds determined.

Previous work on triols derived from lumisterol may be summarised as follows. Oxidation of lumisterol (Ia) by perbenzoic acid yielded a triol monobenzoate from which triol-I was obtained by boiling methanolic potassium hydroxide.[1] When lumisteryl acetate (Ib) was similarly oxidised an acetate oxide was obtained. With boiling water the acetate oxide produced a triol monoacetate which was converted into triol-II by saponification.[2] Oxidation of the triols to the same hydroxy-diketone,[3] coupled with indirect evidence that the 5,6-double bond of lumisteryl acetate is attacked by the peracid treatment,[4] led to representation of the triols as 3,5,6-trihydroxy-compounds differing only in their configurations at position 6.

The main object of the present work was to elucidate the structures and stereochemistry of these triols. To simplify discussion the structures finally established for the triols are used from the outset, and it is assumed that they arise by oxidation of the 5,6-double bond in lumisterol and its acetate. This assumption is verified below.

The original oxidation of lumisterol (Ia) to triol-I monobenzoate (IIId) with perbenzoic acid in chloroform solution [1] was complete in 18 hours at 0°. Attempts were first made to isolate intermediates by stopping the reaction at various stages, but the mixtures so obtained were difficult to separate. However, with benzene as solvent the oxidation

* Part III, preceding paper.

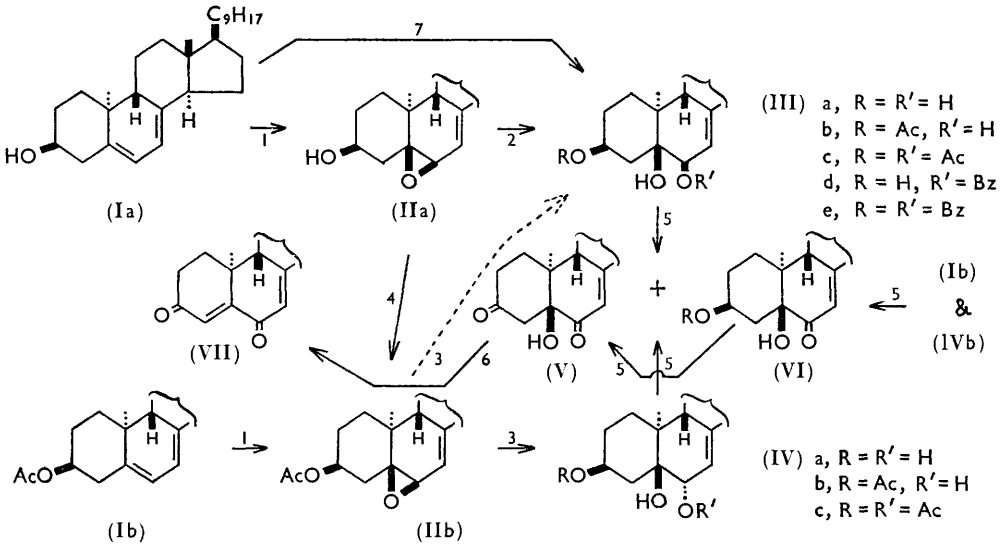
[1] Heilbron, Spring, and Stewart, *J.*, 1935, 1221.
[2] Dimroth, *Ber.*, 1936, **69**, 1123.
[3] Heilbron, Moffet, and Spring, *J.*, 1937, 411.
[4] Burawoy, *J.*, 1937, 409.

was much slower, formation of triol-I monobenzoate requiring 5 days at 5°, and by interrupting the reaction after 22 hr. a hydroxy-oxide (IIa) was isolated in good yield. Treatment of this hydroxy-oxide with benzoic acid in benzene (containing a trace of perbenzoic acid) caused smooth opening of the epoxide ring and afforded triol-I monobenzoate (IIId). Triol-I (IIIa) was obtained from the benzoate (IIId) by alkaline hydrolysis at 20°.

Perbenzoic acid converted lumisteryl acetate (Ib) into an acetate oxide [2] (IIb) which was unchanged by contact with benzoic acid. This acetate oxide was also obtained by acetylating the hydroxy-oxide (IIa): the reverse process (IIb ⟶ IIa) was already known.[2] Attempts to open the epoxide ring of the acetate oxide (IIb) with dilute mineral acid gave intractable oils. Controlled ring-fission could be achieved only by boiling the oxide with water [2] which yielded mainly triol-II monoacetate (IVb) accompanied by a little triol-I monoacetate (IIIb). Saponification of acetate (IVb) at 20° afforded triol-II.

Oxidation of triols-I and -II by chromic acid in acetone under mild conditions led in both cases to two products, the hydroxy-diketone [3] (V) and the dihydroxy-ketone (VI; R = H). These oxidations, together with the assumption that epoxidation of lumisterol and its acetate occurs at the 5,6-double bond, confirm the view that the triols differ only in their configurations at position 6.

At this stage experiments were carried out to confirm the relations (apart from stereochemical details) between the compounds already described. Acetylation of triol-I (IIIa) and its monoacetate (IIIb) afforded the diacetate (IIIc): triol-II (IVa) and its monoacetate (IVb) gave an isomeric diacetate (IVc). The ease of these reactions showed the acetoxyl groups in the diacetates to be at positions 3 and 6. The light absorption of the dihydroxy-ketone (VI; R = H) proved it to be an αβ-unsaturated ketone: its hydroxyl groups are therefore at positions 3 and 5, and on oxidation the expected hydroxy-diketone



Reagents: 1, BzO_2H–C_6H_6. 2, BzOH–C_6H_6. 3, H_2O at 100°. 4, Ac_2O–C_5H_5N. 5, CrO_3–$COMe_2$ at 20° (various times). 6, AcOH at 100°. 7, OsO_4.

(V) was formed. The derived acetate (VI; R = Ac) must contain a 3-acetoxyl group since it was obtained by mild acetylation of the diol (VI; R = H) and by direct chromic oxidation of lumisteryl acetate (Ib).[4] Formation of acetate (VI; R = Ac) from triol-II monoacetate (IVb), the major product in the ring opening of the acetate oxide (IIb), confirms the 3-acetoxy-structure of these compounds. [The minor product of ring opening,

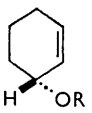
triol-I monoacetate (IIIb) is thus almost certainly a 3-acetate although this is not rigorously proved.] Chromic oxidation of triol-I monobenzoate (IIId) gave a monoketone (X) containing a non-conjugated (*i.e.*, 3-) carbonyl group, indicating that the benzoyloxy-group is at position 6 rather than 5. Proof of this point is given below.

Triols-I (IIIa) and -II (IVa) are formed by opening of the epoxide rings in the oxides (IIa) and (IIb). Although the configurations of the epoxide rings are uncertain at this stage it is established that the orientations are the same (both α or both β) in the two cases. The production of different triols must then be a consequence of different modes of ring opening, or of stereochemical inversion at $C_{(6)}$ during the conversion of the products of ring opening into the triols. Triol-II is formed by mild hydrolysis of a 3-acetoxy-5,6-diol (IVb), which is unlikely to cause inversion at $C_{(6)}$. A similar conclusion for the formation of triol-I followed from its formation by reduction of triol-I monobenzoate (Id) with lithium aluminium hydride, as well as by saponification of this ester. Benzoylation at 20° of triol-I and its monobenzoate to the same dibenzoate (IIIe) confirmed this and also the 6-benzoyloxy-structure of the monobenzoate (Id). The stereochemical difference between the two series arises, then, during the hydrolysis of the 5,6-epoxides (IIa) and (IIb).

The formation of triol-I in high yield from lumisterol (Ia) and osmium tetroxide indicated a 5,6-*cis*-structure for this triol, and a 5,6-*trans*-orientation for triol-II. In accordance with this only triol-I formed an isopropylidene derivative (VIII) when solutions of the triols in acetone were refluxed with anhydrous copper sulphate. The possibility that this derivative possessed a 3,5- or 3,6-bridge was excluded by its oxidation to an isopropylidenedioxy-ketone (IX) with a non-conjugated carbonyl group.

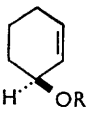
The molecular rotations of the triols and their acetates provided evidence about the configurations at position 6 in these compounds. On Mills's generalisation [5] that allylic alcohols and derivatives of type (A) have more positive rotations than their enantiomers (B), the figures in the following Table suggest that triol-I has the 6β- and triol-II the 6α-configuration, though application of the rule is rendered somewhat uncertain [5] by the presence of vicinal hydroxyl groups.

Type (A)



	$[M]_D$
Triol II (IVa)	+198°
Triol II 3-monoacetate (IVb)	+264°
Triol II 3,6-diacetate (IVc)	+792°

Type (B)



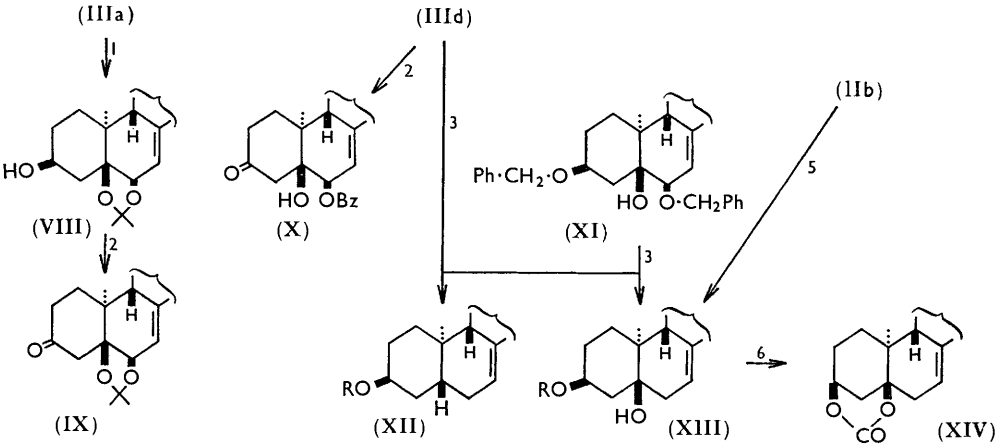
	$[M]_D$
Triol I (IIIa)	−21°
Triol I 3-monoacetate (IIIb)	+28°
Triol I 3,6-diacetate (IIIc)	−211°

Unambiguous proof of the orientations of the 5-hydroxy-groups was obtained by the following sequences. Lithium aluminium hydride reduced the acetate oxide (IIb) to a diol (XIII; R = H) which formed only a monoacetate (XIII; R = Ac), and therefore has hydroxyl groups at positions 3 and 5. With carbonyl chloride the diol gave a cyclic carbonate (XIV). (The possibility that carbonyl chloride had coupled two molecules of triol to a " dimeric " carbonate was excluded by a molecular-weight determination.) It follows that the 5-hydroxyl group in the diol (XIII; R = H) must have the same (β) configuration as the 3-hydroxyl group.

The diol monoacetate (XIII; R = Ac) was next prepared from triol-I monobenzoate (IIId). Benzylation [to the dibenzyl ether (XI)] followed by reduction with lithium in ethylamine and acetylation of the product gave the diol monoacetate (XIII; R = Ac) and dihydrolumisteryl acetate [6] (XII; R = Ac), the latter predominating. [It was found later that direct reduction of triol-I monobenzoate with lithium in ethylamine

[5] Mills, *J.*, 1952, 4976.
[6] Part III, preceding paper.

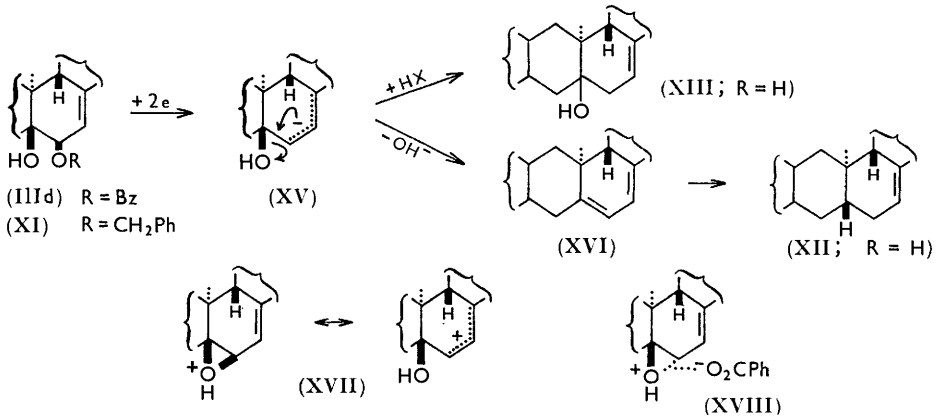
led to the same products. These reductions probably proceed by reductive fission of the allylic C–O bond in the ester or ether to give the mesomeric anion (XV). Addition of a proton affords the diol (XIII; R = H), but prior loss of hydroxide ion gives lumisterol



Reagents: 1, $COMe_2$–$CuSO_4$. 2, CrO_3–$COMe_2$ at 20°. 3, Li–Et·NH_2. 4, C_6H_5·CH_2Cl–KOH. 5, $LiAlH_4$. 6, $COCl_2$–C_5H_5N–C_6H_5·Me.

(XVI) which is known to form dihydrolumisterol (XII; R = H) under the reaction conditions.]

Triol-I monobenzoate (IIId) and, in turn, triols-I and -II [and their oxidation products (V) and (VI)] are thus shown to possess 5β-hydroxyl groups. This feature, together with the relative orientations of the 5- and the 6-hydroxyl group already established, leads to formulation of triol-I as the 3β,5β,6β-triol (IIIa) and triol-II as the 3β,5β,6α-isomer (IVa). These structures agree with the configurations at position 6 deduced from the molecular-rotation data.



The intermediate oxides (IIa) and (IIb) contain 5β,6β-epoxide rings. Formation of triol-II monoacetate (IVb) from the acetate oxide (IIb) under neutral conditions (boiling water) is an S_N2-type reaction with concomitant inversion at $C_{(6)}$. On the other hand, opening of the epoxide ring in the hydroxy-oxide (IIa) under acidic conditions proceeds with retention of configuration at positions 5 and 6. Analogous cases of acid-catalysed ring opening with retention are known;[7] Brewster's explanation[7b] is applicable to the

[7] (*a*) Wasserman and Aubrey, *J. Amer. Chem. Soc.*, 1956, **78**, 1726; (*b*) Brewster, *ibid.*, p. 4061; (*c*) Curtin, Bradley, and Hendrickson, *ibid.*, p. 4064.

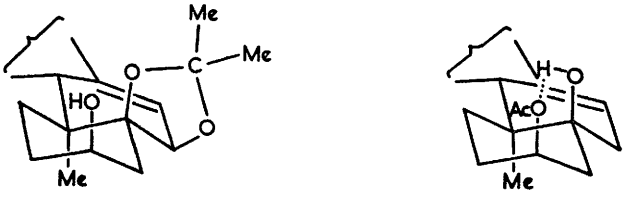
present example as follows. In the protonated epoxide (XVII) the presence of the 7,8-double bond leads to a considerable contribution of the 6-carbonium ion form. Ring opening by a reaction of S_N1 character is thus facilitated and, since completion of the reaction does not require an appreciable " push " from the entering nucleophilic reagent, rear approach to the epoxide ring is not necessarily favoured. The observed fact that the benzoyloxy-anion attacks on the β-face may be a consequence of hindrance by the 10-methyl group to approach at the α-face. Alternatively some form of bonding between the two ions (cf. XVIII) may be involved [the dotted line from $C_{(6)}$ in formula (XVIII) represents a partial bond of β-configuration, not a normal α-bond].

Two pieces of evidence confirm the assumption that the 5,6- rather than the 7,8-double bond in lumisterol and its acetate are oxidised by perbenzoic acid. Attack at the 7,8-bond would have led to a Δ^5-3,8-diol structure for diol (XIII; R = H), and models show that such hydroxyl groups are too far apart to be bridged by carbonyl chloride in the formation of carbonate (XIV). Dehydration of the hydroxy-diketone (V) with acetic acid at 100° afforded a diketone with $\lambda_{max.}$ 2910 Å, $\nu_{max.}$ 1684 and 1656 cm.$^{-1}$. These values are in consonance with structure (VII) for the diketone rather than with any of the possibilities (*e.g.*, a $\Delta^{5,8}$-3,7-dioxo-structure) that would have resulted from a sequence based on attack at the 7,8-double bond.[8]

Oxidation at the 5,6-double bond of lumisterol to products of β-configuration differs from the behaviour of " normal " steroids which are attacked at the α-face. The stereochemistry of the products is clearly determined by the configuration of the 10-methyl group, the reagent approaching from the side opposite to this group. Titrations with perbenzoic acid (see following Table) indicate that β-face attack also occurs in the oxidation of the 7,8-double bond in lumisterol derivatives. The results with 3β,6β-diacetoxy-5β-lumist-22-ene show that the side-chain double bond was oxidised under these conditions (large excess of perbenzoic acid in benzene) in about 2 hours. In the triol diacetates (IIIc) and (IVc) the additional 7,8-double bonds were also completely oxidised under these conditions, but with the 5β,6β-isopropylidene derivative (VIII) the 7,8-double bond was not appreciably affected during 6 hours. Since the isopropylidene group in compound (VIII) reduces

Compound	Equivalents of perbenzoic acid consumed at 20°					
Time (hr.):	0·5	1	2	6	48	100
3β,6β-Diacetoxy-5β-lumist-22-ene [9]	0·48	0·75	0·97	0·97	—	—
3β,6β-Diacetoxylumista-7,22-dien-5β-ol (IIIc)	1·22	1·61	1·97	1·97	—	—
3β,6α-Diacetoxylumista-7,22-dien-5β-ol (IVc)	1·25	1·62	1·96	1·97	—	—
5β,6β-Isopropylenedioxylumista-7,22-dien-3β-ol (VIII)	0·51	0·78	1·01	1·10	1·78	2·10

access to the 7,8-double bond only from the β-face (see Figure), attack of peracid presumably occurs from this side on the triol diacetates although not necessarily with the isopropylidene derivative (IX) itself. (From the results of Henbest and Nicholls [10] it appears unlikely that the masking of the 5β-hydroxyl group in the isopropylidene derivative plays a major rôle in determining the rate of oxidation.) Hindrance at both faces of the



compound (VIII) is shown by the failure of its 3β-hydroxyl group to react with acetic anhydride–pyridine at 20°.

[8] Ruzicka and Jeger, *Helv. Chim. Acta*, 1942, **25**, 775.
[9] Mayor and Meakins, unpublished work.
[10] Henbest and Nicholls, *J.*, 1957, 4608.

In the infrared spectra of all the compounds containing the 3β-acetoxy-5β-hydroxy-system, for example, compound (XIII; R = Ac), the acetate C=O stretching frequency was unusually high (*ca.* 1750 cm.$^{-1}$). Similar results have been observed [11] with 3α-acetoxy-5α-hydroxy-derivatives of cholesterol and attributed to intramolecular hydrogen bonding of type $-O-H\cdots O-CO-$. Clearly such bonding between β-substituents can occur in 10α-methyl steroids (see Figure).

Experimental

For general directions see *J.*, 1958, 2156.

5β,6β-*Epoxylumista*-7,22-*dien*-3β-*ol* (IIa).—A solution of perbenzoic acid in dry benzene (6·3 c.c. of an 0·438M-solution diluted to 25 c.c. with benzene) was added to lumisterol (1 g.) in benzene (25 c.c.) at 5°. After 22 hr. at 5° the mixture was poured on a column of deactivated alumina (100 g.). Elution with benzene afforded successive fractions consisting of 6β-benzoyloxylumista-7,22-diene-3β,5β-diol (100 mg.) (see below) and the epoxy-alcohol (450 mg.), m. p. 129—132° (from acetone), $[\alpha]_D$ +180° (*c* 0·9) (Dimroth [2] gives m. p. 132°, $[\alpha]_D$ +173°).

6β-*Benzoyloxylumista*-7,22-*diene*-3β,5β-*diol* (IIId).—(a) *From lumisterol* (Ia). Lumisterol (1 g.) was treated with perbenzoic acid as in the preceding experiment and the solution kept at 5° for 5 days. Adsorption on alumina followed by elution with benzene as above gave the triol monobenzoate (700 mg.), m. p. 189—191° (after two crystallisations from benzene), $[\alpha]_D$ −66° (*c* 1·0) (Heilbron *et al.*[1] record m. p. 185—186°, $[\alpha]_D$ −68°).

(b) *From* 5β,6β-*epoxylumista*-7,22-*dien*-3β-*ol* (IIa). A solution of the epoxy-alcohol (250 mg.), benzoic acid (85 mg.), and perbenzoic acid (0·1 c.c. of an 0·395M-solution in benzene) in dry benzene (12 c.c.) was kept at 5° for 3 days, and then washed with aqueous sodium hydrogen carbonate. Removal of solvent and crystallisation of the residue from acetone gave the triol monobenzoate as needles (70 mg.), m. p. and mixed m. p. 184—186°, $[\alpha]_D$ −63°.

6β-*Benzoyloxy*-5β-*hydroxylumista*-7,22-*dien*-3-*one* (X).—The preceding triol monobenzoate (500 mg.) in acetone (50 c.c.) was oxidised with 8N-chromic acid (1·3 c.c.) for 30 sec. The product obtained on dilution with water and extraction with ether was chromatographed on neutral alumina (40 g., prepared from Grade H material with ethyl acetate [12]). Elution with light petroleum–benzene (1 : 1) gave 6β-*benzoyloxy*-5β-*hydroxylumista*-7,22-*dien*-3-*one* (300 mg.), m. p. 209—211° (needles from methanol), $[\alpha]_D$ −63° (*c* 0·7) (Found: C, 78·9; H, 9·6. $C_{35}H_{48}O_4$ requires C, 78·9; H, 9·1%), $\nu_{max.}$ (in Nujol) 3575, 1705 (broad, 3-oxo- and 6-oxo-groups), 1283, and 711 cm.$^{-1}$.

5β,6β-*Epoxylumista*-7,22-*dien*-3β-*yl Acetate* (IIb).—Lumisteryl acetate (1 g.) in benzene (35 c.c.) was oxidised with perbenzoic acid (5·7 c.c. of an 0·458M-solution) at 5° for 18 hr. Passage of the solution through alumina, removal of solvent, and crystallisation of the residue from acetone afforded the epoxy-acetate (700 mg.), m. p. 132·5—134·5°, $[\alpha]_D$ +124° (*c* 0·5) (lit.,[2] m. p. 133°, $[\alpha]_D$ +119°) (Found: C, 79·45; H, 10·25. Calc. for $C_{30}H_{46}O_3$: C, 79·2; H, 10·2%).

This epoxy-acetate was also obtained (identification by mixed m. p. and comparison of infrared spectra with the above material) from the epoxy-alcohol (IIa) with acetic anhydride–pyridine at 20°.

Lumista-7,22-*diene*-3β,5β,6β-*triol* (*Triol-I*) (IIIa).—(a) *By hydrolysis of* 6β-*benzoyloxylumista*-7,22-*diene*-3β,5β-*diol* (IIId). A solution of the triol monobenzoate (350 mg.) in 5% methanolic potassium hydroxide (20 c.c.) was refluxed for 3 hr. A similar solution was kept at 20° for 24 hr. The solutions were separately poured into water and extracted with ether. Both experiments gave the triol (200 mg.), m. p. 180—182° (from light petroleum), $[\alpha]_D$ −5° (*c* 0·5) (cf. lit.,[1] m. p. 180—181°, $[\alpha]_D$ −9°) (Found: C, 78·1; H, 10·9. Calc. for $C_{28}H_{46}O_3$: C, 78·1; H, 10·8%).

(b) *By reduction of* 6β-*benzoxylumista*-7,22-*diene*-3β,5β-*diol*. Lithium aluminium hydride (1 g.) was added to the triol monobenzoate (0·5 g.) in ether (100 c.c.), and the mixture refluxed for 2 hr. The triol (0·3 g.) isolated in the usual way crystallised from aqueous methanol as needles, m. p. and mixed m. p. 179—181°, $[\alpha]_D$ −4°.

(c) *By oxidation of lumisterol* (Ia). Osmium tetroxide (1 g.) in ether (50 c.c.) was added to lumisterol (1·4 g.) in ether–pyridine (50 : 3; 53 c.c.), and the mixture kept at 20° for 3 days. Lithium aluminium hydride (1 g.) was added and the mixture was refluxed for 2 hr. After

[11] Henbest and Lovell, *J.*, 1957, 1965.
[12] Douglas, Ellington, Meakins, and Swindells, *J.*, 1959, 1720.

addition of ethyl acetate followed by 3N-sulphuric acid the product was isolated with ether and crystallised from aqueous methanol. The triol (0·7 g.) so obtained had m. p. and mixed m. p. 179—181°, $[\alpha]_D$ −5°.

With acetic anhydride–pyridine at 20° the triol gave 3β,6β-diacetoxylumista-7,22-dien-5β-ol (IIIc), m. p. 129—131°, $[\alpha]_D$ −41° (*c* 0·6) (lit.,[1] m. p. 128—130°, $[\alpha]_D$ −48° in acetone) (Found: C, 75·0; H, 10·0. Calc. for $C_{32}H_{50}O_5$: C, 74·7; H, 9·8%).

Treatment of either the triol (IIIa) or the triol monobenzoate (IIId) with benzoyl chloride–pyridine at 20° gave 3β,6β-*dibenzoyloxylumista*-7,22-*dien*-5β-*ol* (IIIe) which crystallised from methanol as needles, m. p. 146—148°, $[\alpha]_D$ +7° (*c* 0·9) (Found: C, 78·8; H, 9·0. $C_{46}H_{54}O_5$ requires C, 79·0; H, 8·5%).

Ring Opening of 5β,6β-*Epoxylumista*-7,22-*dien*-3β-*yl Acetate* (IIb).—A Soxhlet thimble containing the epoxy-acetate (3·5 g.) was submerged in boiling water for 1 hr. The thimble was extracted with ether and the material so obtained chromatographed on neutral alumina (300 g.). Elution with benzene–ether (9 : 1) and evaporation of solvent gave two fractions, A and B. Fraction A consisted of 3β-*acetoxylumista*-7,22-*diene*-5β,6β-*diol* (IIIb) (150 mg.), needles (from methanol), m. p. 168—170°, $[\alpha]_D$ +6° (*c* 0·5) (Found: C, 76·1; H, 10·6. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·2%), $\nu_{max.}$ 3605, 1755, and 1219 cm.$^{-1}$. Treatment of this material with acetic anhydride–pyridine at 20° gave 3β,6β-diacetoxylumista-7,22-dien-5β-ol (IIIc), m. p. and mixed m. p. 129—131°.

Crystallisation of fraction B from aqueous methanol afforded 3β-acetoxylumista-7,22-diene-5β,6α-diol (IVb) (850 mg.), m. p. 181—188°, $[\alpha]_D$ +56° (*c* 0·7), which was acetylated at 20° to 3β,6α-diacetoxylumista-7,22-dien-5β-ol (IVc), m. p. 142—145°, $[\alpha]_D$ +154° (*c* 0·6) (Found: C, 74·5; H, 9·7. Calc. for $C_{32}H_{50}O_5$: C, 74·7; H, 9·8%). Dimroth [2] records m. p. 178—179°, $[\alpha]_D$ +28°, and m. p. 143°, $[\alpha]_D$ +114° (in acetone) for the mono- and the di-acetate respectively.

Lumista-7,22-*diene*-3β,5β,6α-*triol* (*Triol-II*) (IVa).—A solution of 3β-acetoxylumista-7,22-diene-5β,6α-diol (IVb) (2 g.) in 5% methanolic potassium hydroxide (300 c.c.) was kept at 20° for 24 hr. The material obtained by dilution with water and extraction with ether crystallised from aqueous methanol to give the triol (1·6 g.), m. p. 176—183° (decomp.), $[\alpha]_D$ +46° (*c* 0·6) (lit.,[2] m. p. 180—183°, $[\alpha]_D$ +38°).

Oxidation of Lumista-7,22-*diene*-3β,5β,6β-*triol* (IIIa) *and Lumista*-7,22-*diene*-3β,5β,6α-*triol* (IVa).—A solution of the 3β,5β,6β-triol (1·5 g.) in acetone (150 c.c.) was treated with 8N-chromic acid (2·1 c.c.). After 10 sec. water was added and the mixture extracted with ether. The oil so obtained was chromatographed on neutral alumina (150 g.). Elution with benzene–ether (9 : 1) gave 5β-hydroxylumista-7,22-diene-3,6-dione (V) (200 mg.) which crystallised from methanol as needles, double m. p. 180—184° and 187—189° (Heilbron *et al.*[3] record m. p. 182—183°), $[\alpha]_D$ −17° (*c* 0·6) (Found: C, 78·8; H, 10·1. Calc. for $C_{28}H_{42}O_3$: C, 78·8; H, 9·9%), $\lambda_{max.}$ 250 mμ (ε 16,500), $\nu_{max.}$ (in Nujol) 3365, 1715, and 1678 cm.$^{-1}$.

Further elution with benzene–ether (9 : 1) afforded 3β,5β-*dihydroxylumista*-7,22-*dien*-6-*one* (VI; R = H) (150 mg.), m. p. 189—192° (from methanol), $[\alpha]_D$ +6° (*c* 0·5) (Found: C, 78·2; H, 10·2. $C_{28}H_{44}O_3$ requires C, 78·45; H, 10·35%), $\lambda_{max.}$ 250 mμ (ε 12,900), $\nu_{max.}$ (in Nujol) 3350 and 1662 cm.$^{-1}$. Treatment of this compound in acetone with 8N-chromic acid yielded the hydroxy-diketone (IV), identified by its double m. p. 180—184° and 187—189°, and comparison of infrared spectra with authentic material.

Similar oxidation of the 3β,5β,6α-triol (1·5 g.) gave 5β-hydroxylumista-7,22-diene-3,6-dione (500 mg.) and 3β,5β-dihydroxylumista-7,22-dien-6-one (300 mg.).

3β-*Acetoxy*-5β-*hydroxylumista*-7,22-*dien*-6-*one* (VI; R = H).—(a) *From lumisteryl acetate* (Ib). 8N-Chromic acid (35 c.c.) was added to lumisteryl acetate (10 g.) in acetone (1 l.). After 30 sec. the mixture was diluted with water and extracted with ether. The material so obtained was chromatographed on deactivated alumina (500 g.). Elution with benzene gave an oil (1·4 g.) which was discarded and then 3β-acetoxy-5β-hydroxylumista-7,22-dien-6-one (2·2 g.), m. p. 180—182° (needles from propan-2-ol), $[\alpha]_D$ +16° (*c* 0·6) (Found: C, 76·8; H, 10·2. Calc. for $C_{30}H_{46}O_4$: C, 76·55; H, 9·85%), $\lambda_{max.}$ 2490 Å (ε 14,100) and 3240 Å (ε 116), $\nu_{max.}$ 3585, 1755, 1678, 1250, 1210, and 1026 cm.$^{-1}$. (Burawoy [4] used chromic oxide in acetic acid for this oxidation and obtained a comparable yield of product m. p. 177—178°, $[\alpha]_D$ +11·7°.)

(b) *From* 3β-*acetoxylumista*-7,22-*diene*-5β,6α-*diol* (IVb). The triol monoacetate (400 mg.) in acetone (50 c.c.) was oxidised with 8N-chromic acid (0·5 c.c.) for 30 sec. 3β-Acetoxy-5β-hydroxylumista-7,22-dien-6-one (225 mg.) was isolated in the usual way and had m. p. 182—184° undepressed on admixture with an authentic specimen.

(c) *From* 3β,5β-*dihydroxylumista*-7,22-*dien*-6-*one* (VI; R = H). Acetylation of the dihydroxy-ketone was carried out with acetic anhydride–pyridine at 20°. The product, m. p. 181·5—183°, was identified by mixed m. p. and comparison of infrared spectra with material obtained as in (a) above.

5β,6β-*Isopropylenedioxylumista*-7,22-*dien*-3β-*ol* (VIII).—A solution of lumista-7,22-diene-3β,5β,6β-triol (250 mg.) in dry acetone (100 c.c.) was refluxed with anhydrous copper sulphate (2·5 g.) for 28 hr. Filtration and evaporation of the solvent gave the *derivative* which crystallised from methanol as needles, m. p. 154—156°, $[\alpha]_D$ +43° (*c* 0·8) (Found: C, 79·4; H, 10·7. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%), $\nu_{max.}$ 3555 and 1030 cm.$^{-1}$.

The isopropylidene derivative was recovered unchanged after treatment with acetic anhydride–pyridine at 20° for 24 hr.

The derivative (80 mg.) in acetone (10 c.c.) was oxidised with 8N-chromic acid (0·2 c.c.) for 30 sec. Standard manipulation gave 5β,6β-*isopropylidenedioxylumista*-7,22-*dien*-3-*one* (IX), m. p. 204—207° (from methanol), $[\alpha]_D$ +20° (*c* 0·4) (Found: C, 79·5; H, 10·1. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%), $\nu_{max.}$ 1725 and 1020 cm.$^{-1}$.

Lumista-7,22-*diene*-3β,5β-*diol* (XIII; R = H).—Lithium aluminium hydride (2 g.) was added in portions to a solution of 5β,6β-epoxylumista-7,22-dien-3β-yl acetate (IIb) (1 g.) in ether (200 c.c.), and the mixture was refluxed for 2 hr. The product obtained by the usual treatment was chromatographed on deactivated alumina (100 g.). Elution with benzene gave the *diol* (77 mg.), needles (from methanol), m. p. 191—193°, $[\alpha]_D$ +8° (*c* 0·5) (Found: C, 80·3; H, 11·2%). After sublimation *in vacuo* the material had m. p. 192—194° (Found: C, 80·4; H, 11·05. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%), $\nu_{max.}$ 3620, 3530, and 3350 cm.$^{-1}$.

Treatment with acetic anhydride–pyridine at 20° afforded 3β-*acetoxylumista*-7,22-*dien*-5β-*ol* (XIII; R = Ac), m. p. 145—147° (from methanol), $[\alpha]_D$ +29° (*c* 0·6) (Found: C, 79·2; H, 11·05. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%), $\nu_{max.}$ 3590, 1749, 1230, and 1207 cm.$^{-1}$.

Lumista-7,22-*dien*-3β,5β-*ylene Carbonate* (XIV).—Toluene (150 c.c.) saturated with carbonyl chloride at 5° was added to a solution of the above diol (480 mg.) in a mixture of pyridine (10 c.c.) and chloroform (50 c.c.). After being kept at 20° for 2 days the mixture was washed successively with aqueous potassium hydrogen carbonate (to remove excess of reagent), 3N-hydrochloric acid, and aqueous potassium hydrogen carbonate. After removal of solvent from the dried solution the residue was chromatographed on deactivated alumina (50 g.). Light petroleum–benzene (1 : 1) eluted the *carbonate* (160 mg.) which crystallised from methanol as needles, m. p. 230—233°, $[\alpha]_D$ +19° (*c* 0·6) (Found: C, 79·0; H, 10·2%; *M*, 420. $C_{29}H_{44}O_3$ requires C, 79·0; H, 10·1%; *M*, 441), $\nu_{max.}$ 1760, 1229, 1187, 1107, and 1068 cm.$^{-1}$.

3β,6β-*Dibenzyloxylumista*-7,22-*dien*-5β-*ol* (XI).—A solution of 6β-benzoyloxylumista-7,22-diene-3β,5β-diol (IIId) (500 mg.) and benzyl chloride (2 c.c.) in dioxan (50 c.c.) was heated with powdered potassium hydroxide (4 g.) at 100° for 15 min. After filtration the solution was evaporated at 100°, first at 20 mm., then at 0·01 mm. The residue was extracted with light petroleum, and the material so obtained was chromatographed on deactivated alumina (50 g.). Elution with light petroleum–benzene (4 : 1) gave the *dibenzyl ether*, needles (from methanol), m. p. 105—107°, $[\alpha]_D$ −31° (*c* 0·6) (Found: C, 82·75; H, 9·7. $C_{42}H_{58}O_3$ requires C, 82·6; H, 9·6%), $\nu_{max.}$ 3495, 1088, and 1070 cm.$^{-1}$.

Reductions by Lithium in Ethylamine.—(*a*) A mixture of the dibenzyl ether (XI) (200 mg.), finely cut lithium (100 mg.), and ethylamine (25 c.c.) was shaken in a stoppered flask until a blue colour persisted and then for a further 15 min. Water was added cautiously and the mixture was extracted with ether. The material so obtained was dissolved in pyridine (2 c.c.), acetic anhydride (2 c.c.) was added, and the mixture kept at 20° for 24 hr. The acetylated product was chromatographed on deactivated alumina (20 g.). Light petroleum–benzene (9 : 1) eluted 5β-lumista-7,22-dien-3β-yl acetate [6] (XII; R = Ac) (70 mg.), m. p. and mixed m. p. 141—143°. Elution with light petroleum–benzene (1 : 1) gave 3β-acetoxylumista-7,22-dien-5β-ol (XIII; R = Ac) (33 mg.), m. p. 144—147°, identified by mixed m. p. and comparison of infrared spectra with the product obtained from the epoxy-acetate (IIb) (see above).

(*b*) 6β-Benzoyloxylumista-7,22-diene-3β,5β-diol (IIId) (1 g.) was reduced with lithium (700 mg.) in ethylamine (50 c.c.), and the product acetylated and chromatographed as in the preceding experiment. This reduction yielded the acetoxy-diene (XII; R = Ac) (300 mg.) and the hydroxy-acetoxy-diene (XIII; R = Ac) (90 mg.).

Lumista-4,7,22-*triene*-3,6-*dione* (VII).—A solution of 5β-hydroxylumista-7,22-diene-3,6-dione (V) (500 mg.) in acetic acid (100 c.c.) was kept at 100° for 1 hr. The material obtained

by dilution with water and extraction with ether was chromatographed on neutral alumina (40 g.). Benzene eluted the *triene-dione* (135 mg.) which crystallised from methanol as pale yellow plates, m. p. 157—159°, $[\alpha]_D$ +154° (*c* 0·5) (Found: C, 82·7; H, 10·0. $C_{28}H_{40}O_2$ requires C, 82·3; H, 9·9%), $\lambda_{max.}$ 291 mμ (ε 12,500), $\nu_{max.}$ 1684, 1656, and 1250 cm.$^{-1}$. Elution with benzene–ether (9 : 1) gave starting material (95 mg.).

The authors are indebted to Professor E. R. H. Jones, F.R.S., for his interest and advice, to the Ministry of Education for a grant (to P. A. M.), to Miss W. Peadon for recording the spectroscopic data, and to Mr. E. S. Morton for performing the microanalyses.

THE UNIVERSITY, MANCHESTER, 13.
THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, January 8th*, 1960.]