565. *Steroids of Unnatural Configuration. Part VII.* Reduction Products of 9α-Lumisterol (Pyrocalciferol).*

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A systematic study of the reduction of 9α-lumisterol (pyrocalciferol) has been made and the results compared with those obtained in a corresponding examination of lumisterol.

In catalytic reduction the 5,6-double bond of 9α-lumisterol is attacked first to give *cis*-A/B-compounds formed by rear-wise (α-face) addition of hydrogen. The three products [(II), (V), and (VI)] obtained under various conditions all possess the 5α-configuration. However, reduction of 9α-lumisterol with dissolving metals leads to products of different types: three isomeric dihydro-compounds [the 5α-$\Delta^{7,22}$-compound (II), the 5β-$\Delta^{7,22}$-compound (III), and the 8β-$\Delta^{5,22}$-compound (IV)] were formed, depending on the nature of the metal and the reducing medium.

These results are the converse of those found with lumisterol where catalytic reduction gave a mixture of *cis*- and *trans*-A/B-products, and a variety of reductions with dissolving metals led to a single dihydro-compound, the 5β-$\Delta^{7,22}$-product.

In continuing the investigation of steroids of unnatural configuration we have studied the reduction products of 9α-lumisterol (pyrocalciferol), one of the two isomeric alcohols obtained by thermal cyclisation of vitamin D_2 (calciferol). Since the methods used in determining the structures and stereochemistry of the products are similar to those described in previous work with lumisterol [1,2] they are not presented here in detail. The main outcome of the work is the observation of marked differences between the behaviour on reduction of lumisterol and its 9α-epimer. These differences illustrate further the general thesis that behaviour regarded as characteristic of the natural steroids may be profoundly modified by stereochemical changes.

Reduction of 9α-lumisterol (I; R = H) with sodium in ethanol to a dihydro-derivative of undetermined structure was described by Busse.[3] This reduction, which proceeds much more easily than that of lumisterol,[2] gave the dihydro-compound [shown below to

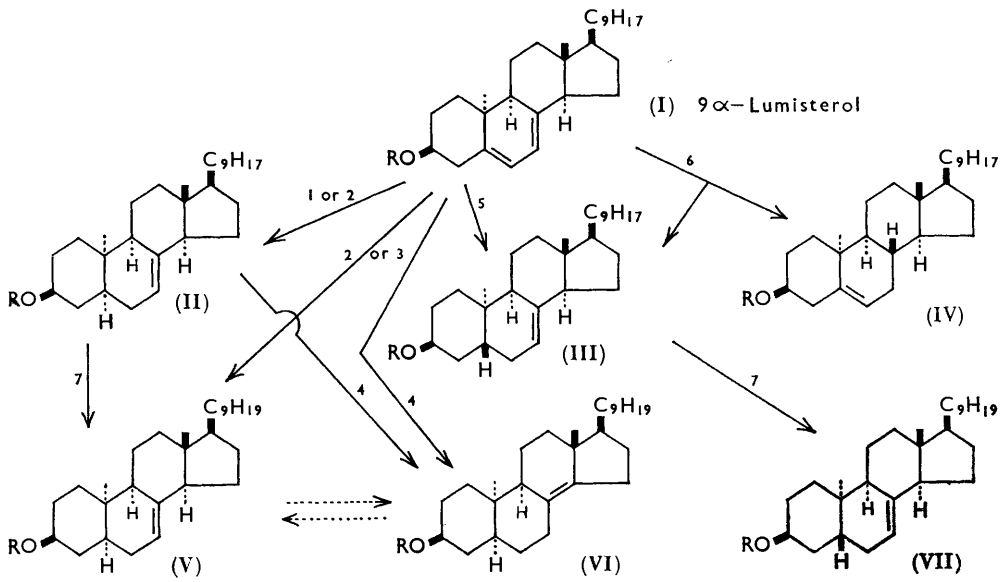
* Part VI, *J.*, 1961, 4676.

[1] Part II, *J.*, 1960, 2627.
[2] Part III, *J.*, 1960, 2785.
[3] Busse, *Z. physiol. Chem.*, 1933, **214**, 211.

be (II; R = H)] in 74% yield; the same product was more conveniently prepared (87% yield) by partial hydrogenation of 9α-lumisterol with Raney nickel. Reduction of 9α-lumisterol with sodium and ethanol in liquid ammonia afforded a second dihydro-derivative (III; R = H) (83% yield); this was the major product (46%) when lithium instead of sodium was used in the liquid-ammonia reduction, but a third dihydro-compound (IV; R = H) (15%) with a high negative rotation was then also formed. When the lithium reduction was carried out with carefully dried materials the second and the third compound (III and IV; R = H) were each obtained in 35% yield.

Hydrogenation of the first and the second dihydro-compound (II and III; R = H) in ethyl acetate with platinum afforded, respectively, the tetrahydro-derivatives (V and VII; R = H); the former of these (V; R = H) was obtained directly by hydrogenating 9α-lumisterol in ethyl acetate over Raney nickel, the reduction being greatly accelerated by the addition of a little Adams catalyst. Hydrogenation over platinum of both 9α-lumisterol and the first dihydro-compound (II; R = H) in acetic acid, or of the dihydro-compound (II; R = H) in ethyl acetate at elevated temperature and pressure, gave an isomeric tetrahydro-compound (VI; R = H). None of these tetrahydro-compounds could be further reduced under the conditions used in their preparations, a significant result in connection with the structure of hexahydro-9α-lumisterol (see below).

Structures for products (II)—(VII) and their derivatives were readily established. Side-chain double bonds were detected by infrared examination, and nuclear double bonds were shown to be either tri- or tetra-substituted by their ultraviolet and infrared absorption. The results were confirmed by applying the osmium tetroxide–lead tetra-acetate sequence [4]



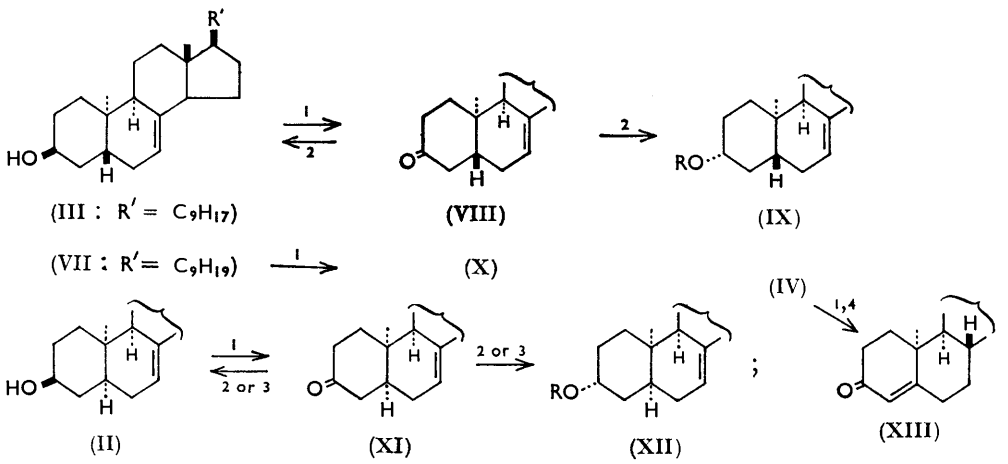
Reagents: 1, Na–EtOH. 2, H_2–Ni–EtOAc. 3, H_2–Ni–Pt–EtOAc. 4, H_2–Pt–AcOH. 5 Na–NH_3–EtOH. 6, Li–NH_3–EtOH. 7, H_2–Pt–EtOAc.

to the tetrahydro-compounds (V, VI, and VII; R = H), the spectrum of the ketonic product [ν(CO) 1738 and 1705 cm.$^{-1}$, but no aldehyde band at 2700 cm.$^{-1}$] from the last compound denoting the presence of a tetrasubstituted double bond at the 8,14-position. Trisubstituted nuclear double bonds were located either at 7,8 (II, III, and VII) or at 5,6 (IV) by spectrographic examination of the 3-oxo-derivatives (VIII, X, XI, and XIII), the αβ-unsaturated ketone (XIII) being produced from the 5,6-ethylenic compound (IV).

[4] Castells and Meakins, *Chem. and Ind.*, 1956, 248.

Allocation of the Δ^7-compounds into the *cis*- and *trans*-A/B-series was based in the first place on the molecular rotation data for pairs of 5-epimers shown in the Table, the comparison being facilitated by the compounds' high molecular rotations. In each pair the compound with the more positive rotation has the 5β-configuration, *i.e.*, the *trans*-A/B-fusion, and the ΔM_D (5β — 5α) values are in agreement with the corresponding figures for lumisterol derivatives.[2] [Conversion of both 5α,9α-lumist-8(14)-en-3β-yl acetate (VI; R = Ac) and the 9β-epimer, obtained from lumisterol,[2] into the same compound (5α,14β-lumist-8-en-3β-yl acetate) by treatment with hydrobromic acid [5] provided a gratifying confirmation of deductions about the $C_{(5)}$-orientations in products derived from lumisterol and 9α-lumisterol.]

Recent work [6,7] has shown that the course of carbanion reductions may be controlled



Reagents: 1, CrO_3–Me_2CO. 2, Na–Pr^{i}OH. 3, $LiAlH_4$. 4, KOH–EtOH.

Molecular rotations and infrared absorption bands of 5β- and 5α-$\Delta^{7,22}$-compounds, and conformations of their $C_{(3)}$-groups.

5β-Compound	$[M]_D$	C–O stretching of alcohol (cm.$^{-1}$)	1240 cm.$^{-1}$ Acetate band	Conformation of $C_{(3)}$-group
(III; R = H)	+605°	1007		Axial
(III; R = Ac)	+594		Complex	Axial
(III; R = DNB)	+426			
(IX; R = H)	+645	1046		Equat.
(IX; R = Ac)	+625		Simple	Equat.

5α-Compound	$[M]_D$	C–O stretching of alcohol (cm.$^{-1}$)	1240 cm.$^{-1}$ Acetate band	Conformation of $C_{(3)}$-group	ΔM_D (5β — 5α)
(II; R = H)	+279°	1043		Equat.	+326°
(II; R = Ac)	+185		Simple	Equat.	+409
(II; R = DNB)	+130				+296
(XII; R = H)	+199	1050		Equat.	+446
(XII; R = Ac)	+154		Simple	Equat.	+471

DNB = 3,5-$(NO_2)_2C_6H_3$·CO·O.

by factors other than the relative thermodynamic stabilities of the possible products, and that [7-9] the use of lithium rather than sodium or potassium can lead to small variations

[5] Castells, Ph.D. thesis, Manchester, 1955.
[6] Johnson, Ackerman, Eastham, and DeWalt, *J. Amer. Chem. Soc.*, 1956, **78**, 6302.
[7] Birch, Smith, and Thornton, *J.*, 1957, 1339.
[8] Arth, Poos, Lukes, Robinson, Johns, Feurer, and Sarett, *J. Amer. Chem. Soc.*, 1954, **76**, 1715.
[9] Johnson, Rogier, Szmuszkovicz, Hadler, Ackerman, Bhattacharyya, Bloom, Stalmann, Clement, Bannister, and Wynberg, *J. Amer. Chem. Soc.*, 1956, **78**, 6289.

in the proportions of different products. However, so far as we are aware, there is no comparable case in which various carbanion reductions (sodium–ethanol, sodium–ethanol–ammonia, and lithium–ethanol–ammonia) have produced such widely divergent results. With lumisterol all three methods gave 5β-lumista-7,22-dien-3β-ol as the sole product.[2]

Catalytic hydrogenation of the Δ^5-bond in lumisterol and 9α-lumisterol provides an interesting contrast to the carbanion reductions. From lumisterol, mixtures of *cis*- and *trans*-A/B-products are obtained, whereas 9α-lumisterol gives only *cis*-A/B derivatives. Models show that the most important changes caused by inversion from the 9β- to the 9α-configuration are (i) displacement of the 19-methyl group away from the Δ^5-bond on the α-face of the molecule, and (ii) a corresponding movement of the 3β-hydroxyl and 18-methyl groups towards the Δ^5-bond on the β-face. The consequential increase of hindrance at the β-face is thus responsible for the observed preference for α-attack (*i.e.*, formation of *cis*-A/B-products) with 9α-lumisterol.

Conformational analysis reveals that in the rigid all-chair *trans*-A/B-Δ^7-compounds (III and VII) the 3β- and 3α-substituents should be, respectively, axial and equatorial. The predominance (74% yield) of the 3α-alcohol (IX; R = H) in the sodium–propan-2-ol reduction of the 3-oxo-compound (VIII), and the spectrographic properties of the 3-epimeric alcohols and acetates (III, IX, and VII; R = H and Ac) are in consonance with these requirements. With the *cis*-A/B-Δ^7-compounds (II and V) the position is not so straightforward. While reduction of the 3-ketone (XI) with lithium aluminium hydride gave the 3-epimeric alcohols (II and XII; R = H) in a 3β : 3α ratio of 3 : 2, the use of sodium in propan-2-ol reversed the relative amounts of products (3β : 3α ~ 1 : 2). Further, the 3β-alcohol (II; R = H) was eluted from alumina more easily than the 3α-compound (XII; R = H). These results cannot be accommodated by assuming that the conformations of the 3-substituents are the reverse of those established in the *trans*-A/B-Δ^7-series. The infrared data (see Table) for the *cis*-A/B-Δ^7-compounds indicate that both 3α- and 3β-substituents are equatorial: such a situation is made possible by the flexibility of the ring system,[2] and equatorial conformations for both epimers would fit the chemical results. (Comparison with previous work [2] shows that *cis*-A/B-Δ^7-derivatives of lumisterol and of 9α-lumisterol differ in their conformational preferences. The 3α- and 3β-*cis*-A/B-Δ^7-derivatives of lumisterol adopt a common skeletal conformation such that the 3α- and 3β-substituents are equatorial and axial respectively.)

A hexahydro-9α-lumisterol was obtained (as acetate) by Busse[3] (from 9α-lumisterol), and later by Dimroth[10] (from dehydrolumisterol) (see Chart). We were not able to repeat Busse's catalytic reduction of his dihydro-9α-lumisteryl acetate [5α,9α-lumista-7,22-dien-3β-yl acetate (II; R = Ac)] to a hexahydro-compound. Under a variety of conditions the product isolated was the $\Delta^{8(14)}$-tetrahydro-compound (VI; R = Ac) provided no mineral acid was present during the reduction. This compound was also obtained in repetition of Dimroth's reduction of dehydrolumisteryl acetate (XIV),* and clearly corresponds to his " unsaturated acetate."

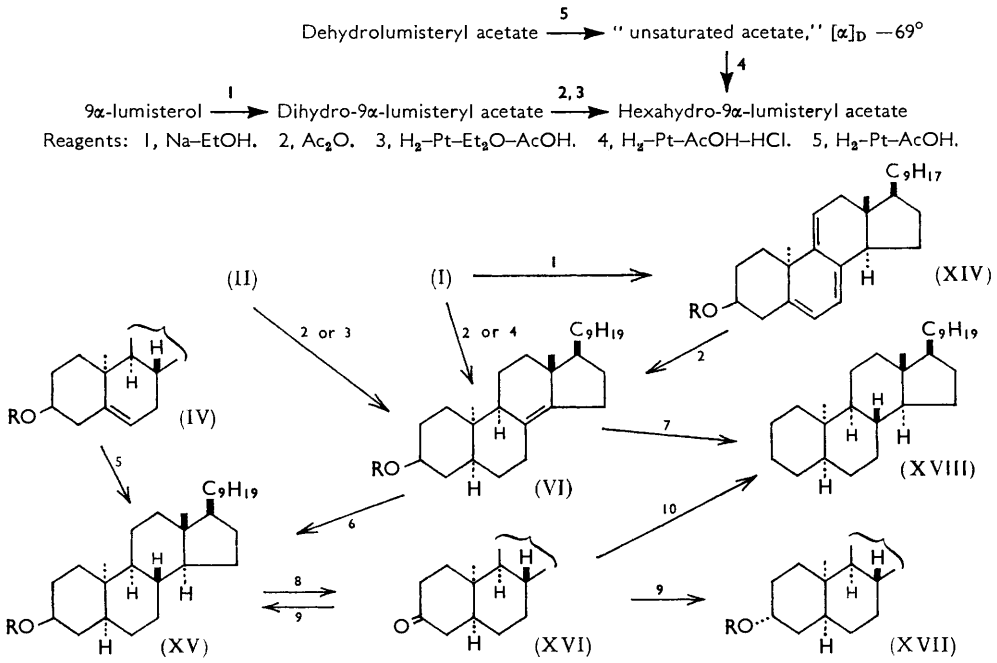
The $\Delta^{8(14)}$-tetrahydro-acetate (VI; R = Ac), $[\alpha]_D$ −70°, was not reduced by attempted hydrogenation with platinum and acetic acid. However, the product had $[\alpha]_D$ −40°, and this was separated into the $\Delta^{8(14)}$-acetate (VI; R = Ac, 50%) and material with $[\alpha]_D$ −12°, which could not be purified. Attempted hydrogenation of this material

* The preparation of dehydrolumisteryl acetate from lumisteryl acetate with mercuric acetate in chloroform–acetic acid at room temperature [11] was extremely unsatisfactory. However, when the filtrate from the mixture obtained in this way was evaporated slowly at normal pressure dehydrolumisteryl acetate was formed in 40% yield. The initial product is a mercurated intermediate which is thermally decomposed to the products, the sequence being analogous to that established by Tishler and his co-workers in similar cases.[12]

[10] Dimroth, *Ber.*, 1936, **69**, 1123.
[11] Heilbron, Spring, and Stewart, *J.*, 1935, 1221.
[12] Ruyle, Jacob, Chemerda, Chamberlin, Rosenbury, Sita, Erikson, Aliminosa, and Tishler, *J. Amer. Chem. Soc.*, 1953, **75**, 2604.

regenerated the mixture with $[\alpha]_D$ −40°, which was again separated. By continuing this process the $\Delta^{8(14)}$-tetrahydro-acetate was recovered in 92% yield.

These results show that under hydrogenation conditions the $\Delta^{8(14)}$-tetrahydro-acetate becomes equilibrated with an isomeric compound: when some of the $\Delta^{8(14)}$-tetrahydro-acetate is removed from the mixture (by crystallisation) and the remaining material



re-treated, part of the isomeric compound is converted back into the $\Delta^{8(14)}$-tetrahydro-acetate in order to maintain the equilibrium proportions. A Δ^{14}-structure for the isomer is unlikely since the material with $[\alpha]_D$ −12° did not show the characteristic olefinic CH stretching band associated with Δ^{14}-compounds.[13] It is also unlikely that the isomer contains an 8,9-double bond (with hydrobromic acid the $\Delta^{8(14)}$-tetrahydro-acetate gave a Δ^{8}-isomer,[5] which was recovered quantitatively after attempted hydrogenation with platinum in acetic acid, both in the presence and absence of hydrochloric acid). The most plausible explanation is that the isomeric compound is the Δ^{7}-tetrahydro-acetate (V; R = Ac, $[\alpha]_D$ +46°) and the material with $[\alpha]_D$ −12° a mixture of this acetate and the $\Delta^{8(14)}$-tetrahydro-acetate (VI; R = Ac, $[\alpha]_D$ −70°). The conversion of the Δ^{7}- and $\Delta^{8(14)}$-tetrahydro-acetates into an equilibrium mixture under hydrogenation conditions would also account for the low yields (~50%) obtained in preparing the $\Delta^{8(14)}$-compound, since the three routes shown probably proceed through the Δ^{7}-compound.

The above results show that neither the $\Delta^{8(14)}$-tetrahydro-acetate nor the Δ^{7}-isomer is reduced by attempted hydrogenation over platinum with acetic acid. However, hydrogenation of the $\Delta^{8(14)}$-compound in acetic acid containing hydrochloric acid afforded a hexahydro-acetate in 85% yield. The properties of this acetate [shown below to be (XV; R = Ac)] agree with those of the hexahydro-compound reported by Busse [3] and Dimroth.[10]

[13] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.

[It is probable that Busse's success in preparing the hexahydro-acetate was due to the presence of some mineral acid in the solvents used for hydrogenating the *cis*-A/B-dihydro-compound (II; R = Ac): this would agree with Dimroth's observation that his "unsaturated acetate" could be further reduced only after the addition of hydrochloric acid.] When perchloric acid was used instead of hydrochloric acid, reduction of the $\Delta^{8(14)}$-tetrahydro-acetate was accompanied by hydrogenolysis of the 3β-acetoxyl group.[14] The product, a hydrocarbon (XVIII), was later obtained by Wolff–Kishner reduction of the 3-oxo-compound (XVI).

It is extremely probable that hexahydro-9α-lumisterol (XV) retains the 5α-orientation established for its progenitor (VI; R = Ac). The same hexahydro-compound was obtained by hydrogenating the $\Delta^{5,22}$-dihydro-compound (IV; R = H) *under neutral conditions*. This preparation shows that the hexahydro-compound is not formed by skeletal rearrangement and that it possesses the α-configuration at positions 5, 9, and 14. The remaining uncertainty, orientation at position 8, was resolved by establishing that the 3β- and 3α-substituents in derivatives of hexahydro-9α-lumisterol are, respectively, axial and equatorial. [This follows from the infrared data (see Experimental) for the 3-alcohols and acetates, and from the formation of the 3α-alcohol (XVII; R = H) as the major product in the sodium–propan-2-ol reduction of the 3-ketone (XVI).] In an all-chair 5α,8α,9α-structure the 3β-hydroxyl group is equatorial, and only by forcing ring C into a boat form could the established conformational requirements be satisfied. The all-chair 5α,8β,9α-structure (XV; R = H), which leads to a 3β-axial conformation, is therefore preferred, and the 8β-configuration will also apply to the $\Delta^{5,22}$-dihydro-compound (IV). The *anti*-relationship of the hydrogen atoms at positions 8 and 14 in the hexahydro-compound provides confirmatory evidence that reduction of the $\Delta^{8(14)}$-tetrahydro-compound (VI; R = Ac) does not proceed by straightforward hydrogenation of the 8,14-double bond, but is preceded by protonation.

During this work it was found that the convenient hydrolysis of 3,5-dinitrobenzoates by passing their solutions in benzene through a column of alumina impregnated with potassium hydroxide [15] can also be used with benzoates and acetates. With these esters a longer time (3—4 hr.) is required: a typical case is described in the Experimental section under the hexahydro-acetate (XV; R = Ac).

The optical rotatory dispersion characteristics of the ketones described here and those derived from lumisterol [1,2] are in consonance with the structures proposed, and will be discussed in a forthcoming paper by Professors C. Djerassi and W. Klyne.

Experimental

For general directions see *J.*, 1958, 2156. Acetates and 3,5-dinitrobenzoates are described in the sections dealing with the parent alcohols. Assignments of infrared bands are not quoted here, but may be found by reference to those of similar lumisterol derivatives.[1,2]

5α,9α-*Lumista*-7,22-*dien*-3β-*ol* (II; R = H).—Sodium (10 g.) was added during 3 hr. to a refluxing solution of 9α-lumista-5,7,22-trien-3β-ol (9α-lumisterol)[16] (I; R = H) (990 mg.) in dry ethanol (150 c.c.). Dilution with water and extraction with ether gave a product whose ultraviolet spectrum showed it to contain 7% of starting material. After a further reduction with sodium in ethanol the product (950 mg.) was adsorbed from light petroleum on deactivated alumina (120 g.). Elution with benzene gave the following fractions: 1, 78 mg., $[\alpha]_D$ +21°; 2, 187, +73°; 3, 218, +70°; 4, 306, +69°; 5, 133, +60°; 6, 35, +26°. Fractions 2—5 were combined and crystallised from ethanol to give 5α,9α-lumista-7,22-dien-3β-ol (730 mg.), m. p. 122—125°, $[\alpha]_D$ +70° (*c* 1·2), $\nu_{max.}$ 3625, 1043, 972, and 800 cm.$^{-1}$. The acetate (II; R = Ac), prepared with acetic anhydride–pyridine at 20° and crystallised from ethanol, had m. p. 130—

[14] Barton, Campos-Neves, and Scott, *J.*, 1957, 2698.
[15] Castells and Fletcher, *J.*, 1956, 3245.
[16] Following paper.

133°, $[\alpha]_D$ +42° (*c* 0·9), $\nu_{max.}$ 1735, 1243, 971, and 800 cm.$^{-1}$. {Busse [3] records m. p. 121—122°, $[\alpha]_D$ +70° for the dihydro-alcohol (II; R = H), and m. p. 131—133°, $[\alpha]_D$ +45° for the acetate (II; R = Ac).} The 3,5-*dinitrobenzoate* (II; R = DNB) crystallised from ethyl acetate–ethanol as plates, m. p. 174—175°, $[\alpha]_D$ +22° (*c* 0·7) (Found: C, 70·6; H, 7·8; N, 4·85. $C_{35}H_{48}N_2O_6$ requires C, 70·9; H, 8·2; N, 4·7%).

The dihydro-compound (II; R = H) was also prepared by shaking a solution of 9α-lumisterol (4 g.) in ethyl acetate (100 c.c.) in hydrogen with Raney nickel (*ca.* 4 c.c. of sludge, prepared by the method of Pavlic and Adkins [17]). When 1 mol. of hydrogen had been absorbed (*ca.* 20 min.) the solution was filtered and evaporated, to give dihydro-alcohol (3·5 g.), m. p. 121—125° (from methanol).

5β,9α-*Lumista*-7,22-*dien*-3β-*ol* (III; R = H).—Sodium (1 g.) was added to a stirred solution of 9α-lumisterol (1·3 g.) in ether (50 c.c.) and liquid ammonia (50 c.c.). Ethanol was added slowly until the blue colour disappeared. More sodium (1 g.) was added, and the ethanol treatment was then repeated. Chromatography of the product (1·3 g.; $[\alpha]_D$ +147°) obtained by the usual working up gave fractions with very similar rotations. These were combined, dissolved in pyridine, and treated with 3,5-dinitrobenzoyl chloride to give 5β,9α-*lumista*-7,22-*dien*-3β-*yl* 3,5-*dinitrobenzoate* (1·6 g.), m. p. 152—155° (needles from ethyl acetate–ethanol), $[\alpha]_D$ +72° (*c* 0·8) (Found: C, 71·2; H, 8·2; N, 4·7. $C_{35}H_{48}N_2O_6$ requires C, 70·9; H, 8·2; N, 4·7%). Saponification of this ester on alkaline alumina [15] afforded the *dihydro-alcohol* (III; R = H), double m. p. 77—80° and 116—118°, $[\alpha]_D$ +152° (*c* 1·0) (Found: C, 84·1; H, 11·8. $C_{28}H_{46}O$ requires C, 84·35; H, 11·6%), $\nu_{max.}$ 3632, 1007, 971, and 809 cm.$^{-1}$. The *acetate* (III; R = Ac) had m. p. 96—97° (needles from methanol), $[\alpha]_D$ +135° (*c* 1·6) (Found: C, 81·6; H, 11·0. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%), $\nu_{max.}$ 1737, 1251, 1234, 970, and 807 cm.$^{-1}$.

Reduction of 9α-*Lumisterol with Lithium and Ethanol in Liquid Ammonia.*—Lithium (500 mg.) was added to a stirred solution of 9α-lumisterol (760 mg.) in ether (30 c.c.) and liquid ammonia (30 c.c.). After the addition of ethanol the mixture was worked up in the usual way and the product (730 mg.; $[\alpha]_D$ +87°) treated with 3,5-dinitrobenzoyl chloride–pyridine. A solution of the ester mixture in benzene was filtered through deactivated alumina and evaporated. The residue crystallised from ethyl acetate–ethanol, to give 5β,9α-lumista-7,22-dien-3β-yl 3,5-dinitrobenzoate (III; R = DNB) (520 mg.), m. p. and mixed m. p. 150—154°, $[\alpha]_D$ +71°, further identified by conversion into the related alcohol (III; R = H).

Concentration of the ethyl acetate–ethanol mother-liquor gave material (330 mg.), m. p. 114—130°, $[\alpha]_D$ +8°, which was saponified.[15] The product, $[\alpha]_D$ +22°, was treated with acetic anhydride–pyridine, and the material so obtained crystallised from ethyl acetate–ethanol to give 9α-*lumista*-5,22-*dien*-3β-*yl acetate* (IV; R = Ac) (126 mg.) as plates, m. p. 162—164°, $[\alpha]_D$ −84°) (*c* 0·8) (Found: C, 81·5; H, 10·95. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%), $\nu_{max.}$ 1736, 1246, 1225, 970, 829, and 799 cm.$^{-1}$. The *dihydro-alcohol* (IV; R = H) had m. p. 137—139°, $[\alpha]_D$ −46° (*c* 0·8) (Found: C, 84·05; H, 11·8. $C_{28}H_{46}O$ requires C, 84·35; H, 11·6%), $\nu_{max.}$ 3620, 1010, 830, and 801 cm.$^{-1}$.

The above experiment was repeated with carefully dried materials, atmospheric moisture being excluded. By addition of ethanol to lithium (1 g.) and 9α-lumisterol (1·5 g.) in ether (100 c.c.) and liquid ammonia (100 c.c.; distilled from sodium) material with $[\alpha]_D$ +60° was obtained. This was adsorbed on deactivated alumina (100 g.) and eluted with light petroleum–benzene (4 : 1; 15 × 100 c.c.). The earlier fractions, with negative rotations, were combined (0·71 g.) and acetylated, to give the $\Delta^{5,22}$-dihydro-acetate (IV; R = Ac) (0·58 g.), m. p. 163—164° (from ethanol), $[\alpha]_D$ −84° (*c* 0·7). The later fractions, with positive rotations, were combined (0·76 g.) and treated with 3,5-dinitrobenzoyl chloride–pyridine to give the $\Delta^{7,22}$-dihydro-ester (III; R = DNB) (0·8 g.), m. p. 150—154° after crystallisation from ethyl acetate–ethanol, $[\alpha]_D$ +72° (*c* 0·5).

5α,9α-*Lumist*-7-*en*-3β-*ol* (V; R = H).—5α,9α-Lumista-7,22-dien-3β-yl acetate (400 mg.), in ethyl acetate (55 c.c.) was hydrogenated over Adams catalyst (200 mg.) until no more hydrogen was absorbed. Hydrolysis of the product followed by treatment with 3,5-dinitrobenzoyl chloride–pyridine gave the *tetrahydro-ester* (V; R = DNB) (520 mg.), m. p. 198—201° after crystallisation from ethyl acetate–ethanol, $[\alpha]_D$ +21° (*c* 1·4) (Found: C, 70·45; H, 8·6; N, 4·6. $C_{35}H_{50}N_2O_6$ requires C, 70·7; H, 8·5; N, 4·7%). Saponification gave the *tetrahydro-alcohol* (V; R = H), m. p. 129—131°, $[\alpha]_D$ +75° (*c* 0·7) (Found: C, 83·85; H, 12·3. $C_{28}H_{48}O$

[17] Pavlic and Adkins, *J. Amer. Chem. Soc.*, 1946, **68**, 1471.

requires C, 83·9; H, 12·1%), $\nu_{max.}$ 3625, 1043, and 804 cm.$^{-1}$, ε_{2100} 4400. The *tetrahydro-acetate* (V; R = Ac) had double m. p. 102—104° and 116—117°, $[\alpha]_D$ +46° (*c* 1·3) (Found: C, 81·5; H, 11·7. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%), $\nu_{max.}$ 1736, 1244, 813, and 800 cm.$^{-1}$, ε_{2100} 4300.

Hydrogenation of 5α,9α-lumista-7,22-dien-3β-yl acetate (1 g.) in ethyl acetate (50 c.c.) over Adams catalyst (0·5 g.) for 7 days at 70°/100 atm. gave the tetrahydro-acetate (V; R = Ac) (0·85 g.), m. p. 114—117° (from methanol), $[\alpha]_D$ +45°.

The tetrahydro-alcohol (V; R = H) was also prepared by hydrogenating 9α-lumisterol (2 g.) in ethyl acetate (50 c.c.) with Raney nickel (2 c.c. of sludge) and Adams catalyst (50 mg.). Absorption of hydrogen (2 mol.) was complete in 15 min., and standard manipulation gave the tetrahydro-alcohol (1·9 g.), m. p. 128—130°, $[\alpha]_D$ +74° (*c* 1·1).

Hydrogenation of 9α-lumisterol in ethyl acetate with Raney nickel alone gave the same tetrahydro-alcohol (85% yield) but reduction was slow (24 hr. for uptake of 2 mol. of hydrogen).

5β,9α-*Lumist-7-en-3β-ol* (VII; R = H).—5β,9α-Lumista-7,22-dien-3β-ol (III; R = H) (1 g.) in ethyl acetate (30 c.c.) was hydrogenated over Adams catalyst (200 mg.) until no more hydrogen was absorbed. Treatment of the product with 3,5-dinitrobenzoyl chloride–pyridine gave the *tetrahydro-ester* (VII; R = DNB) (1·3 g.), m. p. 132—133° (needles from ethyl acetate–ethanol), $[\alpha]_D$ +64° (*c* 0·6) (Found: C, 70·55; H, 8·2; N, 4·65. $C_{35}H_{50}N_2O_6$ requires C, 70·7; H, 8·5; N, 4·7%). Saponification gave the *tetrahydro-alcohol* (VII; R = H), m. p. 96—99° (from 90% ethanol), $[\alpha]_D$ +154° (*c* 1·5) (Found: C, 84·2; H, 12·2. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%), $\nu_{max.}$ 3640, 1007, and 809 cm.$^{-1}$, ε_{2100} 4300. The *tetrahydro-acetate* (VII; R = Ac) had m. p. 115—116° (from ethanol), $[\alpha]_D$ +131° (*c* 1·3) (Found: C, 81·3; H, 11·5. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%), $\nu_{max.}$ 1737, 1251, 1234, and 805 cm.$^{-1}$, ε_{2100} 4500.

5α,9α-*Lumist*-8(14)-*en*-3β-*ol* (VI; R = H).—(*a*) *From* 5α,9α-*lumista*-7,22-*dien*-3β-*ol* (II; R = H). A solution of the dienol (200 mg.) in acetic acid (20 c.c.) was shaken in hydrogen with Adams catalyst (100 mg.) until no more hydrogen was absorbed. Acetylation of the material so obtained and crystallisation of the product from methanol gave 5α,9α-lumist-8(14)-en-3β-yl acetate (80 mg.) as plates, m. p. 145—147°, $[\alpha]_D$ −68° (*c* 0·8), ε_{2100} 10,000. Dimroth [10] gives m. p. 142—143°, $[\alpha]_D$ −69°.

In an attempt to repeat Busse's work [3] the diene-acetate (II; R = Ac) (1 g.) in ether (50 c.c.) and acetic acid (50 c.c.) was shaken in hydrogen with Adams catalyst (0·5 g.) at 20° for 3 days, and then at 60° for 24 hr. The product, $[\alpha]_D$ −39°, crystallised from methanol to give the $\Delta^{8(14)}$-tetrahydro-acetate (VI; R = Ac) (0·51 g.), m. p. 147—150°, $[\alpha]_D$ −70° (*c* 1·0), $\nu_{max.}$ 1732 and 1248 cm.$^{-1}$.

The 3,5-*dinitrobenzoate* (VI; R = DNB) had m. p. 143—145° (plates from ethyl acetate–ethanol), $[\alpha]_D$ −40° (*c* 1·4) (Found: C, 70·7; H, 8·4; N, 5·05. $C_{35}H_{50}N_2O_6$ requires C, 70·7; H, 8·5; N, 4·7%). The *tetrahydro-alcohol* (VI; R = H) had m. p. 140—143°, $[\alpha]_D$ −63° (*c* 0·8) (Found: C, 84·05; H, 11·95. $C_{28}H_{48}O$ requires C, 83·95; H, 12·1%), ε_{2100} 10,200.

(*b*) *From* 9α-*lumisterol* (I; R = H). A solution of 9α-lumisterol (200 mg.) in ethyl acetate (10 c.c.) and acetic acid (10 c.c.) was shaken in hydrogen with Adams catalyst (100 mg.) until hydrogen absorption ceased. Crystallisation of the product from methanol gave the $\Delta^{8(14)}$-tetrahydro-alcohol (90 mg.), m. p. 139—143°, $[\alpha]_D$ −60° (*c* 0·8).

In another experiment 9α-lumisterol (1 g.) in acetic acid (60 c.c.) was hydrogenated over Adams catalyst (0·2 g.) at 60°. After acetylation of the product and crystallisation from methanol the $\Delta^{8(14)}$-tetrahydro-acetate (0·49 g.), m. p. 146—149°, $[\alpha]_D$ −69°, was obtained.

(*c*) *From lumista*-5,7,9(11),22-*tetraen*-3β-*yl acetate* (*dehydrolumisteryl acetate*) (XIV; R = Ac). The acetate (200 mg.) in acetic acid (30 c.c.) was hydrogenated over Adams catalyst (200 mg.). After 30 min. the uptake of hydrogen stopped (absorption of 3 mol.). The product crystallised from ethanol to give the $\Delta^{8(14)}$-tetrahydro-acetate (105 mg.), m. p. 145—149°, $[\alpha]_D$ −70° (*c* 1·0).

Isomerisation Experiments with 5α,9α-*Lumist*-8(14)-*en*-3β-*yl Acetate* (VI; R = Ac) *in Acetic Acid.*—(*a*) *Treatment with platinum and hydrogen.* The $\Delta^{8(14)}$-tetrahydro-acetate (2 g.) in acetic acid (120 c.c.) was shaken in hydrogen with Adams catalyst (0·5 g.) for 30 min. The product (2 g.; $[\alpha]_D$ −40°) crystallised from methanol to give the $\Delta^{8(14)}$-tetrahydro-acetate (VI; R = Ac) (0·99 g.; m. p. 146—149°, $[\alpha]_D$ −70°) and a mother-liquor which yielded material (1·0 g.; $[\alpha]_D$ −12°) shown by titration with perbenzoic acid to contain one C=C bond. This material was dissolved in acetic acid (100 c.c.) and shaken in hydrogen with Adams catalyst (0·3 g.) for 30 min. The product was separated into the $\Delta^{8(14)}$-tetrahydro-acetate (0·45 g.) and material

(0·5 g.), $[\alpha]_D$ −14°. After three more such treatments the total recovery of the $\Delta^{8(14)}$-tetrahydro-acetate was 92% (1·83 g.).

(*b*) *Treatment with hydrochloric acid.* 10N-Hydrochloric acid (1 c.c.) was added to a solution of the $\Delta^{8(14)}$-tetrahydro-acetate (0·5 g.) in acetic acid (75 c.c.) at 20°. The optical rotation of the solution remained constant ($[\alpha]_D$ −72° ± 3°) during 4 days. Evaporation at 20°/15 mm. gave starting material (0·47 g.), m. p. and mixed m. p. 146—148°.

5α,9α-*Lumistan*-3β-*ol* (XV; R = H).—(*a*) *From* 5α,9α-*lumist*-8(14)-*en*-3β-*yl acetate* (VI; R = Ac). A solution of the $\Delta^{8(14)}$-tetrahydro-acetate (0·5 g.) in acetic acid (60 c.c.) and 10N-hydrochloric acid was hydrogenated over Adams catalyst (0·5 g.) at 20° for 24 hr. The product crystallised from methanol to give 5α,9α-lumistan-3β-yl acetate (XV; R = Ac) (0·43 g.), m. p. 140—141°, $[\alpha]_D$ +26° (*c* 0·9) (lit.,[3] m. p. 139—140°, $[\alpha]_D$ +26·1°), no colour with tetranitromethane, $\nu_{max.}$ 1736, 1250, and 1240 (complete acetax band) cm.$^{-1}$.

This acetate (0·5 g.) was adsorbed on a column of alumina (40 g.) impregnated with potassium hydroxide.[15] After 4 hr. the column was eluted with benzene–ether (1·1; 200 c.c.), giving 5α,9α-lumistan-3β-ol (0·41 g.), m. p. 130—132° after crystallisation from methanol, $[\alpha]_D$ +26° (*c* 1·1) (lit.,[3] m. p. 130—131°, $[\alpha]_D$ +34°), $\nu_{max.}$ 3630 and 990 (OH) cm.$^{-1}$.

(*b*) *From* 9α-*lumista*-5,22-*dien*-3β-*yl acetate* (IV; R = Ac). The diene-acetate (0·6 g.) in ethyl acetate (50 c.c.) was hydrogenated over Adams catalyst (0·3 g.). After 25 min. (hydrogen uptake 2 mol.) the solution was filtered and evaporated to give 5α,9α-lumistan-3β-yl acetate (0·49 g.), m. p. 139—140°, $[\alpha]_D$ +26°, which was hydrolysed as above to the alcohol (XV; R = H), m. p. and mixed m. p. 130—132°, $[\alpha]_D$ +25°, no colour with tetranitromethane.

Lumista-5,7,9(11),22-*tetraen*-3β-*yl Acetate* (*Dehydrolumisteryl Acetate*) (XIV; R = Ac).—Solutions of lumisteryl acetate (2 g.) in chloroform (24 c.c.) and mercuric acetate (5 g.) in acetic acid (50 c.c.) were mixed and shaken for 48 hr. at 20°. The solution obtained after filtration was divided into two equal parts. The first part was evaporated rapidly at 60°/14 mm. and gave a product, $\lambda_{max.}$ 2870 Å (ε 10,000), from which only a small amount of dehydrolumisteryl acetate was obtained. The second part was distilled slowly at atmospheric pressure under a short air condenser, the boiling solution being between 70° and 120° for 3 hr. The residue, $\lambda_{max.}$ 3210 Å (ε 6700), crystallised from methanol to give dehydrolumisteryl acetate (0·4 g.), m. p. 142—142·5°, $[\alpha]_D$ +227° (*c* 1·0) (lit.,[11] m. p. 142—143°, $[\alpha]_D$ +226·4°), $\lambda_{max.}$ 3200 Å (ε 10,550).

Preparation and Reduction of 3-*Oxo-compounds*.—Oxidations of the 3β-alcohols to the corresponding 3-ketones specified below were carried out by adding 8N-chromic acid to solutions of the 3β-alcohols in acetone at 20°: reductions of the 3-ketones to mixtures of 3α- and 3β-alcohols were carried out by adding sodium to refluxing solutions of the 3-ketones in propan-2-ol. Details of similar experiments are given in previous Parts.[1,2]

5β,9α-Lumista-7,22-dien-3β-ol (III; R = H) (1·8 g.) gave 5β,9α-*lumista*-7,22-*dien*-3-*one* (VIII) (1·3 g.), m. p. 169—170°, $[\alpha]_D$ +174° (*c* 0·5) (Found: C, 84·9; H, 11·35. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%), $\nu_{max.}$ 1718, 974, and 800 cm.$^{-1}$, no selective ultraviolet absorption between 2100 and 2600 Å before or after treatment with alkali. The mixture formed by reducing the 3-ketone (VIII) (0·5 g.) was chromatographed on deactivated alumina (40 g.). Light petroleum–benzene (3 : 1; 250 c.c.) eluted 5β,9α-lumista-7,22-dien-3β-ol (0·11 g.), m. p. 115—118°, $[\alpha]_D$ +152° (*c* 0·9), identified by its infrared spectrum. Benzene (250 c.c.) eluted 5β,9α-*lumista*-7,22-*dien*-3α-*ol* (IX; R = H) (0·37 g.), m. p. 139—140° (from ethanol), $[\alpha]_D$ +162° (*c* 0·7) (Found: C, 84·7; H, 11·8. $C_{28}H_{46}O$ requires C, 84·45; H, 11·55%), $\nu_{max.}$ 3610, 1046, 980, and 800 cm.$^{-1}$. Treatment with acetic anhydride–pyridine at 20° gave the *acetate* (IX; R = Ac), m. p. 103—107°, $[\alpha]_D$ +142° (*c* 0·8) (Found: C, 81·6; H, 11·1. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%), $\nu_{max.}$ 1732 and 1245 cm.$^{-1}$.

5β,9α-Lumist-7-en-3β-ol (VII; R = H) (0·5 g.) gave 5β,9α-*lumist*-7-*en*-3-*one* (X) (0·38 g.), m. p. 153—155°, $[\alpha]_D$ +155° (*c* 0·9) (Found: C, 84·6; H, 11·8. $C_{28}H_{46}O$ requires C, 84·4; H, 11·55%), $\nu_{max.}$ 1715 and 810 cm.$^{-1}$, no selective absorption between 2100 and 2600 Å before or after treatment with alkali.

5α,9α-Lumista-7,22-dien-3β-ol (II; R = H) (0·2 g.) gave 5α,9α-*lumista*-7,22-*dien*-3-*one* (XI) (0·145 g.), m. p. 154—159° (plates from acetone–methanol), $[\alpha]_D$ −17° (*c* 0·9) (Found: C, 83·35; H, 11·1. $C_{28}H_{44}O$,0·5MeOH requires C, 83·05; H, 11·25%), $\nu_{max.}$ 1708, 974, and 804 cm.$^{-1}$, no selective ultraviolet absorption between 2100 and 2600 Å before or after treatment with alkali. The mixture formed by reducing the 3-ketone (XI) (200 mg.) was chromatographed on deactivated alumina (25 g.). Light petroleum–benzene (1 : 1) eluted 5α,9α-lumista-7,22-dien-3β-ol (70 mg.), m. p. and mixed m. p. 124—125°, $[\alpha]_D$ +67° (*c* 1·1). Light petroleum–benzene (1 : 4)

eluted 5α,9α-lumista-7,22-dien-3α-ol (XII; R = H) (120 mg.), m. p. 139—142° (from acetone–methanol), $[\alpha]_D$ +50° (*c* 0·9) (lit.,[3] m. p. 138—139°, $[\alpha]_D$ +54°), $\nu_{max.}$ 3620, 1050, 971, and 803 cm.$^{-1}$. Treatment with acetic anhydride–pyridine at 20° gave the acetate (XII; R = Ac), m. p. 98—100°, $[\alpha]_D$ +35° (*c* 0·8) (lit.,[3] m. p. 98—99°, $[\alpha]_D$ +36°), $\nu_{max.}$ 1731 and 1249 cm.$^{-1}$. [Reduction of the 3-ketone (XI) (200 mg.) with lithium aluminium hydride gave the 3β- and 3α-alcohols (II and XII; R = H) in a ratio of ~3 : 2.]

9α-Lumista-5,22-dien-3β-ol (IV; R = H) (0·2 g.) was oxidised with 8N-chromic acid and the product, isolated in the usual way, was dissolved in 2% ethanolic potassium hydroxide (10 c.c.). After 1 hr. at 20° the mixture was diluted with water and extracted with ether to give 9α-*lumista*-4,22-*dien*-3-*one* (XIII) (0·16 g.), m. p. 132—135° (from methanol), $[\alpha]_D$ −137° (*c* 0·3) (Found: C, 84·7; H, 11·3. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%), $\lambda_{max.}$ 2440 Å (ε 13,200), $\nu_{max.}$ 1674, 972, and 866 cm.$^{-1}$.

5α,9α-Lumistan-3β-ol (XV; R = H) (0·9 g.) gave 5α,9α-*lumistan*-3-*one* (XVI) (0·65 g.), m. p. 142—145° (from methanol), $[\alpha]_D$ +10° (*c* 0·6) (Found: C, 84·1; H, 11·95. $C_{28}H_{48}O$ requires C, 84·0; H, 12·0%), $\nu_{max.}$ 1719 cm.$^{-1}$. The mixture formed by reducing the 3-ketone (XVI) (0·5 g.) was chromatographed on deactivated alumina (40 g.). Light petroleum–benzene (3 : 2; 125 c.c.) eluted 5α,9α-lumistan-3β-ol (80 mg.), m. p. and mixed m. p. 129—132°, $[\alpha]_D$ +25° (*c* 1·0), further identified by its infrared spectrum. Benzene (250 c.c.) eluted 5α,9α-lumistan-3α-ol (XVII; R = H) (380 mg.), m. p. 140—141° (needles from methanol), $[\alpha]_D$ +28° (*c* 0·8) (lit.,[3] m. p. 137—138°, $[\alpha]_D$ +31°), $\nu_{max.}$ 3614 and 1051 cm.$^{-1}$. Treatment with acetic anhydride–pyridine at 20° gave the *acetate* (XVII; R = Ac), m. p. 80—83°, $[\alpha]_D$ +21° (*c* 0·4) (Found: C, 81·3; H, 11·8. $C_{30}H_{52}O_2$ requires C, 81·1; H, 11·7%), $\nu_{max.}$ 1732 and 1244 (simple acetate band) cm.$^{-1}$.

5α,9α-*Lumistane* (XVIII).—(*a*) *From* 5α,9α-*lumist*-8(14)-*en*-3β-*yl acetate* (VI; R = Ac). A solution of the $\Delta^{8(14)}$-tetrahydro-acetate (0·5 g.) in acetic acid (60 c.c.) and 60% perchloric acid (1 c.c.) was hydrogenated over Adams catalyst (0·5 g.) at 20° for 48 hr. The product crystallised from methanol to give 5α,9α-*lumistane* (0·24 g.), m. p. 85—87°, $[\alpha]_D$ +32° (*c* 0·8) (Found: C, 86·85; H, 12·9. $C_{28}H_{50}$ requires C, 87·05; H, 12·95%).

(*b*) *From* 5α,9α-*lumistan*-3-*one* (XVI). The ketone (0·2 g.) was reduced by the standard Huang-Minlon procedure, and the product chromatographed on alumina (20 g.; Grade 0). Elution with light petroleum gave the hydrocarbon (0·13 g.), m. p. 84—87°, $[\alpha]_D$ +33° (*c* 0·9).

Attempted Hydrogenation of 5α,14β-*Lumist*-8-*en*-3β-*yl Acetate*.[5]—The acetate (0·5 g.; m. p. 100—102°, $[\alpha]_D$ −28°) in acetic acid (75 c.c.) was shaken in hydrogen with Adams catalyst (0·5 g.) at 20° for 24 hr. Standard manipulation gave starting material (0·41 g.; m. p. and mixed m. p. 99—102°, $[\alpha]_D$ −29°). In a second experiment 10N-hydrochloric acid (1 c.c.) was added to the mixture before hydrogenation was attempted. Starting material (0·39 g.) was again recovered.

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