566. *Steroids of Unnatural Configuration. Part VIII.* Isomerisation of Lumisterol and its Derivatives with Acids. A New Method for Locating Double Bonds in Steroids.*

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Isolumisterol,[1] the compound obtained in high yield by treating lumisterol (I; R = H) with hydrogen chloride in chloroform, is shown to be 5β-lumista-8,14,22-trien-3β-ol (II; R = H).

During this work a new method for locating double bonds in steroids was developed,[2] and the isomerisation of 10α-methyl Δ^7-steroids with hydrobromic acid was studied. In these unnatural compounds the 7,8-double bond migrates to the 8,14- and 8,9-positions, rather than to the 8,14- and 14,15-positions as in normal steroids.

The work described here started with an investigation into the structure of isolumisterol, the product obtained when the ring B diene system of lumisterol isomerises under the influence of hydrogen chloride.[1] As the study progressed it became necessary to examine the behaviour of various Δ^7-lumisterol derivatives towards acids. Interpretation of the results was hindered by uncertainty about the positions of unsaturation in certain isomerisation products, and a new method for locating double bonds in steroids was therefore developed. To simplify presentation this method is described first, and in the isomerisation work the structures established are shown at the outset.

Many of the standard methods for determining the position of an isolated nuclear double bond in a steroid (*e.g.*, the use of molecular rotation data) are based on the common stereochemical pattern of these compounds, and therefore cannot be applied directly to steroids of unnatural configuration. Spectrographic methods are probably the least affected by alterations in stereochemistry, and from them it is usually possible to establish the degree of substitution, although not necessarily the position, of a double bond. However, there are cases, particularly in distinguishing between tri- and tetra-substituted double bonds, in which the result is uncertain.

The new method [2] involves oxidation of an ethylenic bond to a dicarbonyl system by successive reactions with osmium tetroxide (formation of an osmate ester), lithium aluminium hydride (reduction of the ester to a diol),[3] and lead tetra-acetate (fission of the diol). In this way a double bond generates two groups (aldehyde or ketone) with easily recognised and reliable infrared bands. The degree of readiness of the three stages varies considerably according to the position of the original double bond: the following general procedure was devised after trial experiments with known steroids, the sequence being followed by examining the spectrum of the total product after each operation.

The 3β-hydroxyl group was protected by benzylation, and the product refluxed for one hour with osmium tetroxide in ether containing a little pyridine. [With the very unreactive ergost-8(14)-en-3β-ol only a small amount of osmate ester was formed under these conditions, but this was sufficient for continuation with the subsequent stages. A more complete osmylation was achieved by a slow reaction at 20°.] The resulting osmate ester was reduced to the diol by lithium aluminium hydride in boiling tetrahydrofuran. (At the lower temperature of boiling ether several of the esters were unexpectedly stable to lithium aluminium hydride.) Oxidation of the diol was carried out with lead tetra-acetate in acetic acid containing a little t-butyl alcohol. In the absence of t-butyl alcohol the last stage frequently resulted in the appearance of small bands due to acetoxyl groups in the spectrum of the product, these groups presumably arising from free radical

* Part VII, preceding paper.

[1] Windaus, Dithmar, and Fernholts, *Annalen*, 1932, **493**, 259.
[2] A preliminary account was given by Castells and Meakins, *Chem. and Ind.*, 1956, 248.
[3] Barton, Ives, and Thomas, *J.*, 1954, 903.

α-acetolysis of the aldehydes or ketones formed in the oxidation.[4] With t-butyl alcohol present the acetoxyl band near 1240 cm.$^{-1}$, which is known to be more intense than the 1735 cm.$^{-1}$ band, was so weak that interference in the carbonyl region by acetoxyl groups could be neglected.

The osmium tetroxide–lead tetra-acetate sequence for locating double bonds. Infrared frequencies (cm.$^{-1}$) refer to CS_2 solutions: the bands near 2700 cm.$^{-1}$ were weak, and those in the 1750—1690 cm.$^{-1}$ range were strong.

Reference compounds	Infrared bands of product		
Cholest-1-ene	2704	1729	
Cholest-5-en-3β-ol	2704	1725	1705
Ergost-7-en-3β-ol	2700	1725	1710
Ergost-14-en-3β-ol	2704	1728	1705
Cholest-8-en-3β-ol			1705
Ergost-8(14)-en-3β-ol		1735	1712
Derivatives of lumisterol			
5β-Lumist-7-en-3β-ol (XVII; R = H)	2702	1728	1705
5β,9α-Lumist-7-en-3β-ol	2699	1727	1713
5α-Lumist-7-en-3β-ol (IX; R = H)	2704	1725	1705
5α,9α-Lumist-7-en-3β-ol (XII; R = H)	2699	1729	1714
5β-Lumist-8-en-3β-ol (VII; R = H)			1705
5β,14β-Lumist-8-en-3β-ol (VIII; R = H)			1696
5α,14β-Lumist-8-en-3β-ol (XI; R = H)			1695
5α-Lumist-8(14)-en-3β-ol (X; R = H)		1737	1713
5α,9α-Lumist-8(14)-en-3β-ol (XIII; R = H)		1737	1707

In applications of the method about 15 mg. of the compound under investigation were taken through the sequence without purification at any stage, and the spectrum of the total product recorded. (Later work showed that the results were not significantly changed when the first stage, benzylation, was omitted.) The results with the reference compound (see Table) show that a disubstituted double bond generates two aldehyde groups (expected absorption near 2700 and 1730 cm.$^{-1}$), while a trisubstituted double bond produces an aldehyde group and a ketone group in a six-membered ring (expected to absorb near 1710 cm.$^{-1}$). The Δ^8-tetrasubstituted double bond leads to two keto-groups in a ten-membered ring (expected absorption near 1700 cm.$^{-1}$), but the product from the 8,14-double bond has one of its carbonyl groups in a five-membered ring (expected absorption near 1740 cm.$^{-1}$). This distinction between the two tetrasubstituted ethylenic bonds is a useful supplement to the direct ultraviolet method.[5,6]

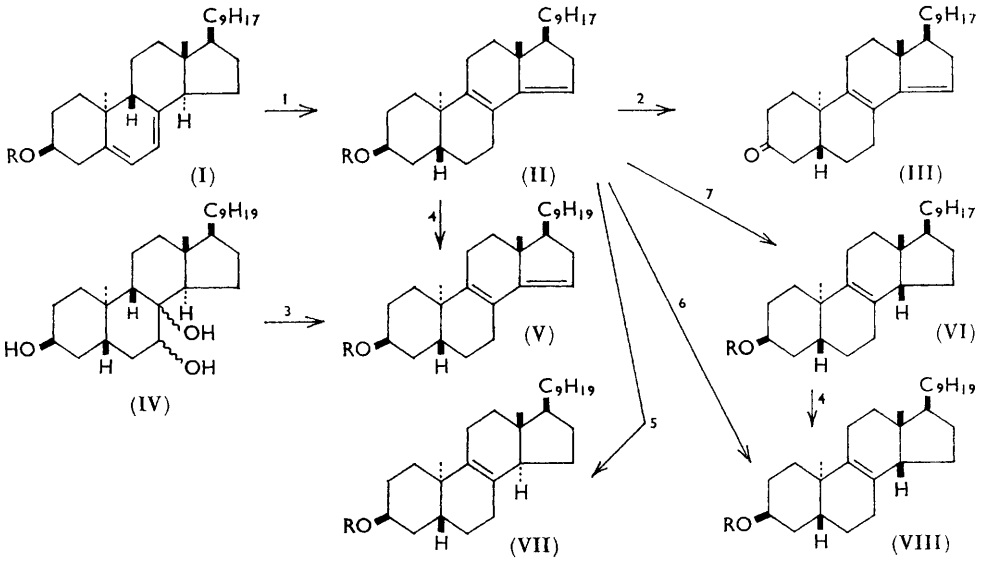
Treatment of lumisterol (I; R = H) or its acetate (I; R = Ac) in chloroform with hydrogen chloride at −10° gave isolumisterol (II; R = H) or its acetate (II; R = Ac) in 85% yield. This result is similar to that observed with 7-dehydrocholesteryl acetate, and appears to be less complex than the reported isomerisation of ergosterol to mixtures of the ergosterol-B isomers.[7] Isolumisterol was purified by the sequence used throughout this work, *viz.*, conversion into the 3,5-dinitrobenzoate, purification of the ester followed by hydrolysis on alkaline alumina,[8] acetylation, crystallisation, and then hydrolysis of the acetate. The marked decrease in rotation which occurs in the formation of isolumisterol [ΔM_D (lumisterol — isolumisterol) = 1240°] is not paralleled in the conversion of ergosterol into any of the ergosterols-B. The ultraviolet absorption of isolumisterol and its derivatives, maxima at 2420 (ε ~21,000) and 2490 Å (ε ~22,000), denotes the presence of a transoid conjugated diene system and is similar to that reported for cholesta-8,14-dien-3β-yl acetate.[7]

Hydrogenation of isolumisteryl acetate in ethyl acetate reduced only the side-chain

[4] Cavill and Solomon, *J.*, 1955, 4426.
[5] Stich, Rotzler, and Reichstein, *Helv. Chim. Acta*, 1959, **42**, 1480.
[6] Ellington and Meakins, *J.*, 1960, 697.
[7] Fieser and Fieser, "Steroids," Reinhold Publ. Co., New York, 1959, pp. 115 *et seq.*
[8] Castells and Fletcher, *J.*, 1956, 3245.

double bond, as shown by the ultraviolet absorption of the product (V; R = Ac): the corresponding alcohol (V; R = H) was later obtained as the minor product in the dehydration of the 3,7,8-triol (IV).[9] In the hydrogenation of isolumisteryl acetate in acetic acid the tetrahydro-acetate (VII; R = Ac) was formed quickly, but when the reaction was allowed to continue for 24 hours an isomeric tetrahydro-acetate (VIII; R = Ac) was obtained. Reduction of isolumisterol with sodium or lithium and ethanol in liquid ammonia gave a dihydro-compound (VI; R = H) containing isolated double bonds, which was hydrogenated in ethyl acetate solution to the tetrahydro-compound (VIII; R = H).

Both the tetrahydro-compounds [(VII) and (VIII); R = H] possess 8,9-double bonds as shown by the osmium tetroxide–lead tetra-acetate sequence (see Table) and their spectrographic properties recorded in the Experimental section. The configurations at



Reagents: 1, HCl in $CHCl_3$. 2, CrO_3 in COMe. 3, H_2SO_4 in MeOH. 4, H_2–Pt in EtOAc. 5, H_2–Pt in AcOH (20 min.). 6, H_2–Pt in AcOH (24 hr.). 7, Na or Li–NH_3–EtOH.

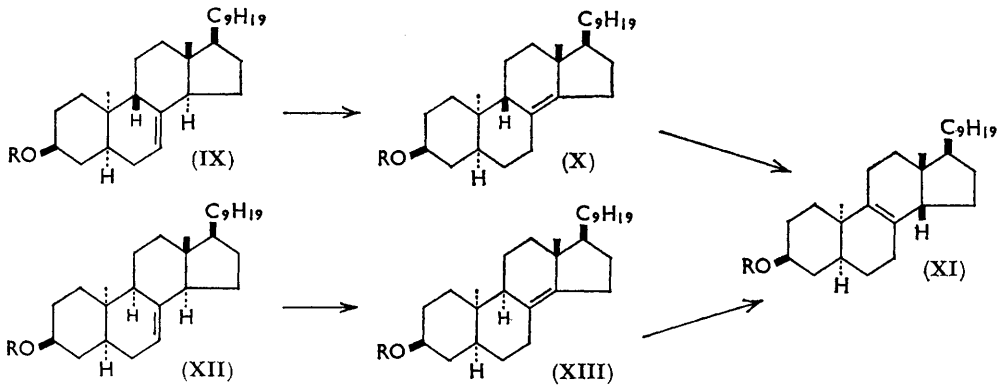
position 14 [α in (VII) and β in (VI) and (VIII)] are those expected from the preparative methods used: shielding of the β-face of isolumisteryl acetate (II; R = Ac) by the 13β-methyl group is the dominant feature in the hydrogenation of the 14,15-double bond, while reduction of the conjugated diene system by dissolving metals is expected to give the more stable *cis*-C/D-ring junction. (The higher stability of the *cis*-fusion in this system depends on the presence of the 8,9-double bond which prevents conformational effects arising in rings A and B [10] from being transmitted to the C/D-ring system.)

The results so far establish the presence of an 8,14-diene system in isolumisterol, and to investigate the remaining uncertainty (the configuration at position 5) the isomerisation with acids of various Δ^7-derivatives of lumisterol was studied. It was hoped that the 7,8-double bond could be moved to the 8,9-position, the appropriate derivatives of lumisterol thus affording the reduction products of isolumisterol. The usual method for such isomerisations, passing hydrogen chloride into a solution of the steroid in chloroform and allowing the reaction to proceed at certain temperatures for various times, is inconvenient for investigating reactions in which more than one product is formed. In

[9] Part II, *J.*, 1960, 2627.
[10] Dreiding, *Chem. and Ind.*, 1954, 1419.

the present work hydrobromic acid in acetic acid, a readily standardised and commercially available reagent, was used, and the reactions were followed polarimetrically.

With the *cis*-A/B-Δ^7-tetrahydro-compounds [(IX) and (XII); R = Ac, derived from lumisterol and 9α-lumisterol (pyrocalciferol), respectively] [11,12] the rotations (see Fig. 1)



Reagent: HBr in $CHCl_3$–AcOH (various times).

showed initial rapid changes, these being in opposite directions in the two cases, followed by a gradual approach to a common $[\alpha]_D$ value of −30°. Isolation and investigation of the products involved showed that the 7,8-double bonds in compounds [(IX) and (XII); R = Ac)] were moved first to the 8,14-position [compounds (X) and (XIII); R = Ac] and

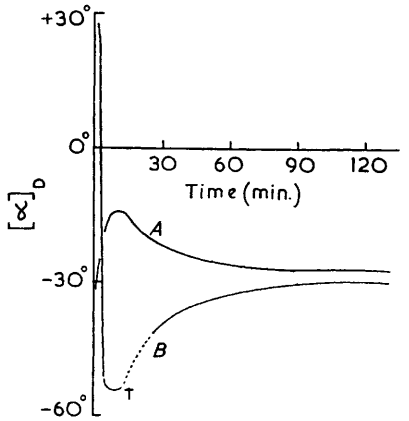


FIG. 1. Isomerisation of (A) 5α-lumist-7-en-3β-yl acetate (IX; R = Ac) and (B) 5α,9α-lumist-7-en-3β-yl acetate (XII; R = Ac) with HBr in $CHCl_3$–AcOH. † More HBr was added at this point.

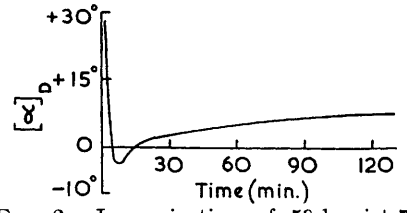


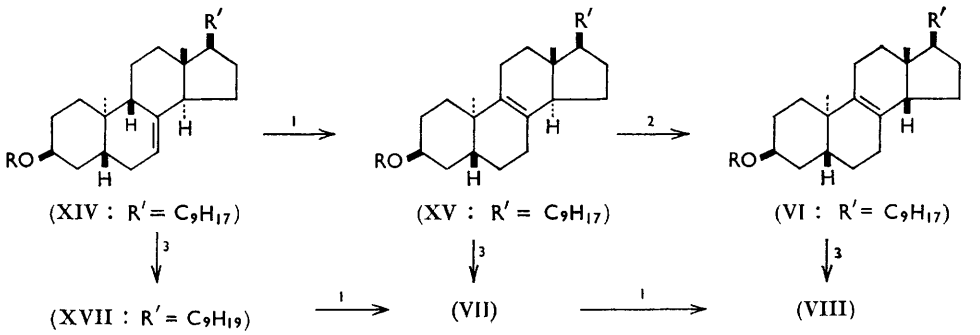
FIG. 2. Isomerisation of 5β-lumist-7-en-3β-yl acetate (XVII; R = Ac) with HBr in $CHCl_3$–AcOH.

then to the 8,9-position [compound (XI); R = Ac]. The 5α-orientations previously established [11,12] for the two Δ^7-compounds, (IX) and (XII), will also apply to the common product of isomerisation (XI; R = Ac): the fact that the product was not identical with either of the Δ^8-tetrahydro-derivatives of isolumisterol, (VII) and (VIII), indicated that the latter have the 5β-configuration.

[11] Part III, *J.*, 1960, 2785.
[12] Part VII, preceding paper.

The isomerisations of the *trans*-A/B-Δ^7-compounds [(XIV) and (XVII); R = Ac] [11] by hydrobromic acid were complex, and only the salient features will be described. With the tetrahydro-compound (XVII; R = Ac), a typical rotation curve for which is shown in Fig. 2, the first product was the 14α-Δ^8-compound (VII; R = Ac, $[\alpha]_D$ −50°), and after a longer time the 14β-Δ^8-compound (VIII; R = Ac, $[\alpha]_D$ −12°) was obtained. Comparison of the rotations of these compounds with the values of the solutions from which they were isolated showed that at least one more isomer, with positive rotation, was present. Isomerisation of the dihydro-compound (XIV; R = Ac) gave, as first product, the 14α-Δ^8-dihydro-isomer (XV; R = Ac), which was hydrogenated in ethyl acetate to the corresponding tetrahydro-compound (VII; R = Ac). Continuation of the isomerisation was complicated by the occurrence of an undesirable side reaction (possibly attack on the side-chain double bond). However, the side reaction appeared to be inhibited by the presence of acetic anhydride, and a prolonged isomerisation carried out in this way afforded the 14β-Δ^8-dihydro-isomer (VI; R = Ac) corresponding to the 14β-tetrahydro-compound (VIII; R = Ac).

The 5β-configuration thus established for the derivatives of isolumisterol is confirmed by the preparation of the diene (V; R = H) from both isolumisteryl acetate (II; R = Ac) and the *trans*-A/B-triol (IV),[9] and completes the structural investigation in this series. The reasoning is, of course, based on the assumption that isolumisterol is formed without



Reagents: 1, HBr in $CHCl_3$–AcOH (various times). 2, HBr in $CHCl_3$–AcOH–Ac_2O. 3, H_2–Pt in EtOAc.

rearrangement of the steroid nucleus. Skeletal rearrangement in the formation of isolumisterol would require that similar changes occur in the dehydration of triol (IV) and, more importantly, in the isomerisation of the Δ^7-derivatives of lumisterol. One of the isomerisation products, the *cis*-A/B-$\Delta^{8(14)}$-compound (XIII; R = Ac), can be hydrogenated in the presence of hydrochloric acid to a hexahydro-9α-lumisterol containing the unaltered steroid nucleus: in the absence of mineral acids the reduction does not occur.[12] Thus, the $\Delta^{8(14)}$-compound (XIII; R = Ac) has a normal steroid nucleus which is not changed by an operation in the presence of acids. It appears likely, therefore, that the later isomerisation product (XI; R = Ac) is similarly constituted, and if this is so all the compounds described here must retain the unaltered steroid nucleus.

With steroids of natural configuration containing the *trans*-A/B-ring fusion isomerisation with acids causes the 7,8-double bond to migrate to the 8,14- and the 14,15-position, the details depending on the particular case considered. When a *cis*-A/B-ring junction is present the position is less clear, but in certain derivatives of cholenic acid the movement of the 7,8-double bond appears to be similar.[13] In contrast with this, the 7,8-double bond of 10α-methyl steroids is isomerised to the 8,14- and the 8,9-position, the Δ^8-14β-compound being the most stable of the isomers under the conditions used. The Δ^8-14β-compound in the unnatural series is in this respect the counterpart of the Δ^{14}-isomer in the natural compounds.*

[13] Ref. 7, pp. 114, 279, 426.

Experimental

For general directions see *J.*, 1958, 2156. Acetates and 3,5-dinitrobenzoates are described in the sections headed by the name of the parent alcohol. The ultraviolet absorption of compounds [(VII), (X), and (XI); R = H] were obtained as described in ref. 6.

The Osmium Tetroxide–Lead Tetra-acetate Sequence.—A solution of the stenol (15 mg.) and benzyl chloride (0·1 c.c.) in dioxan (0·5 c.c., distilled from sodium) was heated at 100° with powdered potassium hydroxide (250 mg.) for 15 min. The mixture was evaporated, finally at 100°/0·1 mm., diluted with water, and extracted with light petroleum. The light petroleum extract was dried, filtered through deactivated alumina (2 g.), and evaporated. The benzyl ether so obtained and osmium tetroxide (25 mg.) were dissolved in dry ether (3 c.c.) containing pyridine (0·1 c.c.), and the solution was refluxed for 1 hr. and then evaporated at 100°/15 mm. Tetrahydrofuran (5 c.c.) was added, and the solution so obtained was refluxed with lithium aluminium hydride (200 mg.) for 30 min. After addition of ethyl acetate and then water the mixture was extracted with ether. Evaporation, finally at 100°/15 mm., afforded the benzyl dihydroxy-ether, which was dissolved in glacial acetic acid (1 c.c.) containing t-butyl alcohol (0·1 c.c.) and treated with lead tetra-acetate (25 mg.). After 12 hr. at 20° the solution was evaporated at 100°/0·1 mm., water was added, and the mixture extracted with ether. The dried ether solution was filtered through deactivated alumina (3 g.) and evaporated, finally at 100°/15 mm. The residue was dissolved in carbon disulphide (5 c.c.) and the solution evaporated. The dicarbonyl compound so obtained was dissolved in carbon disulphide (1 c.c.), and an infrared spectrum of the solution contained in an 0·5 mm. cell was recorded.

In most cases the infrared spectra of the intermediates, the benzyl ether, and the benzyl dihydroxy-ether, were examined, the sequence being continued with recovered materials. In several cases the reactions with osmium tetroxide were repeated, the solutions being kept at 20° for 6 days. This procedure gave higher yields of the osmate esters, and obviated the necessity for benzylating the 3-hydroxyl group. To obtain a reasonable yield of osmate ester from 3β-benzyloxy-5α-ergost-8(14)-ene a period of 40 days was required, extra quantities of osmium tetroxide (~5 mg.) being added every 5 days.

5β-*Lumista*-8,14,22-*trien*-3β-*ol* (*Isolumisterol*) (II; R = H).—Dry hydrogen chloride was passed through a solution of lumisterol (2 g.) in chloroform (40 c.c.) at −10° for 1 hr. Removal of solvent and crystallisation of the residue from methanol gave a product (1·7 g.), m. p. 139—140°, $[\alpha]_D$ −120° (*c* 1·0). Treatment with 3,5-dinitrobenzoyl chloride in pyridine at 20° gave 5β-*lumista*-8,14,22-*trien*-3β-*yl* 3,5-*dinitrobenzoate* (2·1 g.), m. p. 165—166° (needles from ethyl acetate–ethanol), $[\alpha]_D$ −27° (*c* 1·3) (Found: C, 71·0; H, 7·9. $C_{35}H_{46}N_2O_6$ requires C, 71·2; H, 7·85%). Hydrolysis with alkaline alumina [8] and treatment of the product with acetic anhydride in pyridine at 20° gave 5β-lumista-8,14,22-trien-3β-yl acetate (II; R = Ac), m. p. 129—130° (from acetone–methanol), $[\alpha]_D$ −98° (*c* 0·9), $\lambda_{max.}$ 2420 (ε 20,800) and 2490 Å (ε 22,200), $\nu_{max.}$ 1736, 1254, and 1237 (OAc), 973 (22,23-C:C), and 794 cm.$^{-1}$ (14,15-C:C) (lit.,[1] m. p. 128°). This acetate was also obtained by isomerising lumisteryl acetate as described above for lumisterol.

Hydrolysis of the acetate afforded 5β-lumista-8,14,22-trien-3β-ol (II; R = H), m. p. 140—142° (from methanol), $[\alpha]_D$ −121° (*c* 0·8), $\lambda_{max.}$ 2420 (ε 21,000) and 2490 Å (ε 22,500), $\nu_{max.}$ 3625 and 1004 (OH), 982 (22,23-C:C), and 794 cm.$^{-1}$ (14,15-C:C) (lit.,[1] m. p. 138°, $[\alpha]_D$ −125°, $\lambda_{max.}$ 2480—2500 Å).

Oxidation of the preceding alcohol in acetone with 8N-chromic acid gave 5β-*lumista*-8,14,22-*trien*-3-*one* (III), m. p. 179—181° (from methanol), $[\alpha]_D$ −110° (*c* 0·6) (Found: C, 85·15; H, 11·0. $C_{28}H_{42}O$ requires C, 85·2; H, 10·8%), $\lambda_{max.}$ 2420 (ε 20,500) and 2490 Å (ε 21,900), $\nu_{max.}$ 1715 (ketone), 970, and 795 cm.$^{-1}$.

Reduction of 5β-*Lumista*-8,14,22-*trien*-3β-*yl Acetate* (II; R = Ac).—(*a*) *With platinum in ethyl acetate.* The acetate (0·2 g.) in ethyl acetate (13 c.c.) was shaken in hydrogen with Adams catalyst (50 mg.) at 20° for 20 min. Filtration and evaporation of the solution gave 5β-*lumista*-8,14-*dien*-3β-*yl* acetate (V; R = Ac), m. p. 110—111° (from acetone–methanol), $[\alpha]_D$ −85° (*c* 0·7) (Found: C, 82·0; H, 11·1. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%), $\lambda_{max.}$ 2420 (ε 20,400) and 2490 Å (ε 21,000), $\nu_{max.}$ 1739, 1253, and 1236 (OAc), and 797 cm.$^{-1}$ (14,15-C:C). Hydrolysis of the acetate with alkaline alumina [12] gave 5β-*lumista*-8,14-*dien*-3β-*ol* (V; R = H), m. p. 133—134°, $[\alpha]_D$ −102° (*c* 1·1) (Found: C, 84·5; H, 11·9. $C_{28}H_{46}O$ requires C, 84·4; H, 11·6%), $\lambda_{max.}$ 2420 (ε 21,000) and 2490 Å (ε 21,600), $\nu_{max.}$ 3630, 1010 (OH), and 798 cm.$^{-1}$. The formation of this compound from the triol (IV) is described in Part II.[9]

(*b*) *With platinum in acetic acid.* The acetate (0·6 g.) in acetic acid (50 c.c.) was hydrogenated over Adams catalyst (0·2 g.) for 20 min. at 20°. The product was thrice crystallised from ethanol to give 5β-*lumist*-8-*en*-3β-*yl acetate* (VII; R = Ac) (0·23 g.), m. p. 136—139°, $[\alpha]_D$ −47° (*c* 0·9) (Found: C, 81·4; H, 11·7. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%), $\nu_{max.}$ 1738, 1255, 1243, and 1229 cm.$^{-1}$ (OAc). Hydrolysis gave 5β-*lumist*-8-*en*-3β-*ol* (VII; R = H), m. p. 139—141° (needles from ethanol), $[\alpha]_D$ −58° (*c* 1·3) (Found: C, 83·8; H, 12·2. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%), $\nu_{max.}$ 3610 and 1009 cm.$^{-1}$ (OH), $\lambda_{max.}$ 1960 Å (ε 8800), ε_{2100} 3500.

Hydrogenation of 5β-lumista-8,14,22-trien-3β-yl acetate (0·6 g.) in acetic acid (50 c.c.) over Adams catalyst (0·4 g.) was carried out for 24 hr. at 20°. Filtration, evaporation of the solution, and four crystallisations of the product from ethanol gave 5β,14β-lumist-8-en-3β-yl acetate (VIII; R = Ac) (0·21 g.), m. p. 93—95°, $[\alpha]_D$ −12° (*c* 0·6), identified by mixed m. p. and comparison of infrared spectra with an authentic specimen described below.

5β,14β-*Lumista*-8,22-*dien*-3β-*ol* (VI; R = H).—Sodium (1 g.) was added to a stirred solution of 5β-lumista-8,14,22-trien-3β-ol (1 g.) in ether (60 c.c.) and liquid ammonia (60 c.c.). After 30 min. ethanol was added slowly and the mixture worked up in the usual way. The product was treated with 3,5-dinitrobenzoyl chloride in pyridine, to give 5β,14β-lumista-8,22-dien-3β-yl 3,5-dinitrobenzoate (0·6 g.), m. p. 135—137° (from ethyl acetate–ethanol). Hydrolysis of the ester with alkaline alumina [8] afforded 5β,14β-*lumista*-8,22-*dien*-3β-*ol* (VI; R = H), m. p. 128—130° (needles from acetone–methanol), $[\alpha]_D$ −5° (*c* 0·9) (Found: C, 84·5; H, 10·75. $C_{28}H_{46}O$ requires C, 84·35; H, 11·6%), $\nu_{max.}$ 3606, 1011 (OH), and 981 cm.$^{-1}$ (22,23-C:C). The *acetate* (VI; R = Ac) had m. p. 110—111° (from ethanol), $[\alpha]_D$ +2° (*c* 1·2) (Found: C, 81·7; H, 10·9. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%), $\nu_{max.}$ 1738, 1256, and 1240 (OAc), and 977 cm.$^{-1}$.

Reduction of 5β-lumista-8,14,22-trien-3β-ol (1 g.) in ether–liquid ammonia with lithium (0·7 g.) and subsequent treatment as described above gave 5β,14β-lumista-8,22-dien-3β-yl 3,5-dinitrobenzoate (0·65 g.), m. p. 134—137°.

5β,14β-*Lumist*-8-*en*-3β-*ol* (VIII; R = H).—A solution of 5β,14β-lumista-8,22-dien-3β-ol (1 g.) in ethyl acetate (50 c.c.) was shaken in hydrogen with Adams catalyst (0·4 g.) for 15 min. at 20°. Standard manipulation gave 5β,14β-*lumist*-8-*en*-3β-*ol* (0·82 g.), m. p. 131—132° (from ethanol–methanol), $[\alpha]_D$ −11° (*c* 1·0) (Found: C, 83·7; H, 12·0. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%), $\nu_{max.}$ 3615 and 1005 cm.$^{-1}$ (OH), ε_{2100} 3600. The *acetate* (VIII; R = Ac) had m. p. 94—95° (from ethanol), $[\alpha]_D$ −12° (*c* 0·9) (Found: C, 81·6; H, 11·5. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

Isomerisation of Δ^7-*Compounds with Hydrobromic Acid.*—In the following sections hydrobromic acid solution refers to a 50% w/v solution of hydrobromic acid in acetic acid. The chloroform used was washed several times with aqueous sodium hydroxide, then with water, and dried ($CaCl_2$). The acetic acid used was obtained by distilling glacial acetic acid from potassium permanganate. All the reactions were carried out at the room temperature.

(*a*) *Isomerisation of* 5α-*lumist*-7-*en*-3β-*yl acetate* (IX; R = Ac). Hydrobromic acid solution (1 c.c.) was added to a solution of the acetate [11] (5 g.) in chloroform (120 c.c.) and acetic acid (80 c.c.). The rotation of the solution reached a maximum ($[\alpha]_D$ −16°, see Fig. 1) after about 10 min. After a further 10 min., when the $[\alpha]_D$ value was −20°, water was added and the mixture extracted with ether. The ether solution was washed with water, aqueous sodium carbonate, and then water, dried, and evaporated. The material so obtained was hydrolysed with 5% ethanolic potassium hydroxide, and the product chromatographed on deactivated alumina (400 g.). Elution with benzene gave several fractions with negative rotations which were discarded. Further elution with benzene afforded fractions with positive rotations which were combined to give an oil (1·22 g., $[\alpha]_D$ +17°). Treatment of the oil in pyridine with 3,5-dinitrobenzoyl chloride yielded 5α-*lumist*-8(14)-*en*-3β-*yl* 3,5-*dinitrobenzoate* (1·13 g.), m. p. 188—189° (from ethyl acetate–ethanol), $[\alpha]_D$ −10° (*c* 1·1) (Found: C, 70·5; H, 8·8; N, 4·7%).

Hydrolysis of the ester on alkaline alumina gave 5α-*lumist*-8(14)-*en*-3β-*ol* (X; R = H), m. p. 101—103° (from ethanol), $[\alpha]_D$ +20° (*c* 1·2) (Found: C, 83·6; H, 11·9. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%), $\nu_{max.}$ 3610 and 1039 cm.$^{-1}$ (OH), $\lambda_{max.}$ 2030 Å (ε 11,800), ε_{2100} 10,000. Acetylation of this alcohol gave an oil, $[\alpha]_D$ −5°.

When a solution of 5α-lumist-7-en-3β-yl acetate (1 g.) in chloroform (24 c.c.) and acetic acid (16 c.c.) containing hydrogen bromide solution (0·4 c.c.) was kept for 24 hr., the $[\alpha]_D$ value reached a steady figure of −27°. Dilution with water and extraction with ether gave 5α,14β-*lumist*-8-*en*-3β-*yl acetate* (XI; R = Ac) (640 mg.), m. p. 100—102° (from ethanol), $[\alpha]_D$ −28° (*c* 1·0) (Found: C, 81·45; H, 11·35. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). The

corresponding *alcohol* (XI; R = H) had m. p. 114—116° (from ethanol), $[\alpha]_D$ −11° (*c* 0·8) (Found: C, 83·75; H, 12·4. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%), $\nu_{max.}$ 3620 and 1036 cm.$^{-1}$ (OH), $\lambda_{max.}$ 1960 Å (ε 9000), ε_{2100} 3500.

(*b*) *Isomerisation of 5α,9α-lumist-7-en-3β-yl acetate* (XII; R = Ac). Hydrobromic acid solution (0·2 c.c.) was added to a solution of 5α,9α-lumist-7-en-3β-yl acetate [12] (200 mg.) in chloroform (12 c.c.) and acetic acid (8 c.c.). In the first 3 min. the $[\alpha]_D$ value (initially +47°) changed rapidly to a figure of −55°. After a further 2 min. ($[\alpha]_D$ −56°) the mixture was worked up in the usual way and afforded 5α,9α-lumist-8(14)-en-3β-yl acetate (XIII; R = Ac) (60 mg.), m. p. 146—148° (from ethanol), $[\alpha]_D$ −68° (*c* 0·8), identified by mixed m. p. and comparison of infrared spectra with an authentic specimen.[12] This acetate was converted into the corresponding 3,5-dinitrobenzoate, m. p. 143—145° (from ethyl acetate–ethanol), which did not depress the m. p. of an authentic specimen.[12] The alcohol (XIII; R = H) [12] had m. p. 140—143°, $[\alpha]_D$ −61° (*c* 0·9), ε_{2100} 10,200.

When a solution of 5α,9α-lumist-7-en-3β-yl acetate (200 mg.) in chloroform (12 c.c.) and acetic acid (8 c.c.) containing hydrobromic acid solution (0·2 c.c.), prepared as described above, was kept the rotation changed only slowly after the first 10 min. Addition of more hydrobromic acid (1 c.c.) caused the rotation to increase gradually (as shown in Fig. 1) and after 2 hr. a constant $[\alpha]_D$ value of −26° was reached. The product isolated after 24 hr. was 5α,14β-lumist-8-en-3β-yl acetate (XI; R = Ac), m. p. 97—100°, $[\alpha]_D$ −27° (*c* 0·9), identified by mixed m. p. and comparison of infrared spectra with an authentic specimen.

(*c*) *Isomerisation of 5β-lumist-7-en-3β-yl acetate* (XVII; R = Ac). Hydrobromic acid solution (0·4 c.c.) was added to a solution of 5β-lumist-7-en-3β-yl acetate [11] (250 mg.) in chloroform (6 c.c.) and acetic acid (4 c.c.). After 4 min. ($[\alpha]_D$ −4°, see Fig. 2) the mixture was worked up, giving 5β-lumist-8-en-3β-yl acetate (VII; R = Ac) (50 mg.), m. p. 134—137° after four crystallisations from ethanol, $[\alpha]_D$ −48° (*c* 0·9), identified by comparison with an authentic specimen.

In another experiment the reaction was stopped after 15 min. ($[\alpha]_D$ +1°). The product (50 mg.), m. p. 93—94° after four crystallisations from ethanol, $[\alpha]_D$ −12° (*c* 1·4), was identified as 5β,14β-lumist-8-en-3β-yl acetate (VIII; R = Ac) by comparison with authentic material.

(*d*) *Isomerisation of 5β-lumista-7,22-dien-3β-yl acetate* (XIV; R = Ac). Hydrobromic acid solution (0·04 c.c.) was added to a solution of the acetate [11] (250 mg.) in chloroform (6 c.c.) and acetic acid (4 c.c.). After 10 min. ($[\alpha]_D$ −21°) the mixture was worked up, giving *5β-lumist-8,22-dien-3β-yl acetate* (XV; R = Ac) (70 mg.), m. p. 162—164° (after two crystallisations from ethanol and recrystallisation from ethyl acetate), $[\alpha]_D$ −52°, (*c* 1·5) (Found: C, 82·25; H, 11·2. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%), $\nu_{max.}$ 1737, 1255, 1242, 1231 (OAc), and 970 cm.$^{-1}$ (22,23-C:C). Hydrolysis afforded the *alcohol* (XV; R = H), m. p. 145—148° (needles from ethanol), $[\alpha]_D$ −61° (*c* 0·9) (Found: C, 84·0; H, 11·55. $C_{28}H_{46}O$ requires C, 84·35; H, 11·6%), $\nu_{max.}$ 3620, 1011, and 971 cm.$^{-1}$.

Hydrogenation of the acetate (XV; R = Ac) (150 mg.) in ethyl acetate (15 c.c.) with Adams catalyst (80 mg.) for 1 hr. at 20° gave 5β-lumist-8-en-3β-yl acetate (VII; R = Ac) (93 mg.), m. p. 134—136°, $[\alpha]_D$ −45° (*c* 0·9).

When hydrobromic acid solution (5 c.c.) was added to a solution of 5β-lumista-7,22-dien-3β-yl acetate (XIV; R = Ac) (1 g.) in chloroform (34 c.c.), acetic acid (16·5 c.c.), and acetic anhydride (5 c.c.), the $[\alpha]_D$ value (initially +21°) fell to a minimal figure of −19° after 50 min., and then increased gradually, giving a constant figure of +10° after about 30 hr. The product isolated after 48 hr. was 5β,14β-lumista-8,22-dien-3β-yl acetate (VI; R = Ac) (0·54 g.), m. p. 108—110° (from ethanol), $[\alpha]_D$ +2° (*c* 1·0), identified by comparison with an authentic specimen.

Hydrolysis of the acetate afforded the corresponding alcohol (VI; R = H), m. p. 127—129°, $[\alpha]_D$ −5° (*c* 1·0), identical with authentic material.

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