565. *Steroids of Unnatural Configuration. Part V.*[1] *Preparation of Lumistanol A from an Oxidation Product of Lumisteryl Acetate.*

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

3β-Acetoxy-5β-hydroxylumista-7,22-dien-6-one (II), an oxidation product of lumisteryl acetate, has been converted into the acetate of lumistanol A, one of the hexahydro-derivatives of lumisterol. This work provides further evidence for the formulation of lumistanol A as 5β-lumistan-3β-ol (VIII; R = H).

In previous work structure (II) was established[1] for the acetoxy-hydroxy-ketone[2] obtained by oxidising lumisteryl acetate (I; R = Ac) with chromic acid, and lumistanol A, one of the hexahydro-derivatives of lumisterol (I; R = H), was shown[3] to have structure (VIII; R = H). The conversion of the acetoxy-hydroxy-ketone (II) into lumistanyl A acetate (VIII; R = Ac) by the route described below links the oxidation and reduction products of lumisterol and provides further proof that lumistanol A has the 5β,8β-configuration.

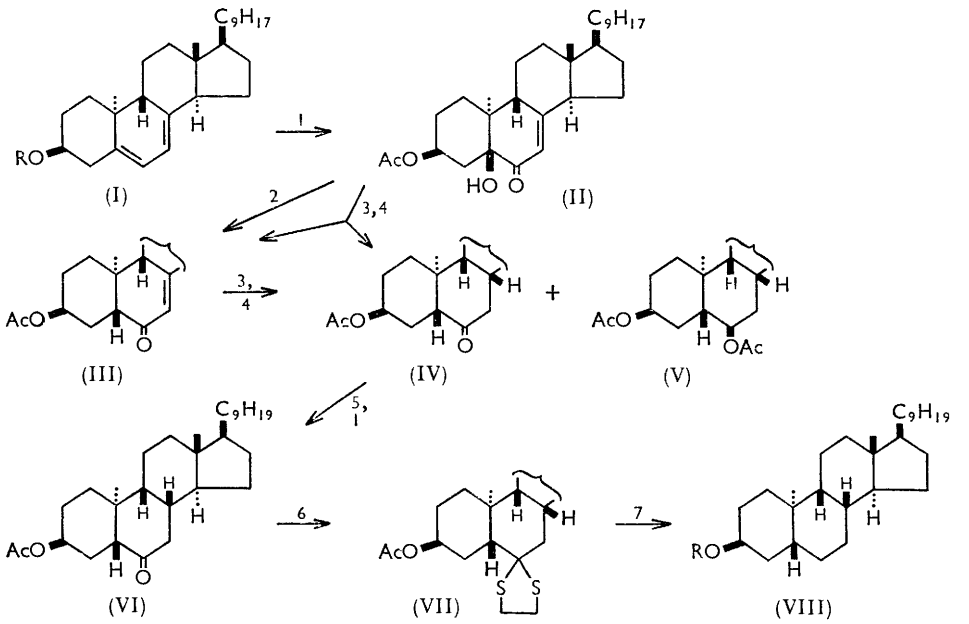
The 5-hydroxyl group of the acetoxy-hydroxy-ketone (II) was removed by reduction with zinc in boiling acetic acid to give the conjugated acetoxy-ketone (III). Lithium in ammonia reduced the latter to a mixture which after acetylation was resolved into the non-conjugated acetoxy-ketone (IV) and the diacetate (V). By direct reduction of the acetoxy-hydroxy-ketone (II), followed by acetylation, a mixture of the conjugated acetoxy-ketone (III) and the non-conjugated acetoxy-ketone (IV) was obtained. (The proportions of the products formed in these dissolving-metal reductions depended on the experimental conditions.)

Hydrogenation of the side-chain double bond in the non-conjugated acetoxy-ketone (IV) was accompanied by partial reduction of the 6-oxo-group, but after mild oxidation the saturated acetoxy-ketone (VI) was isolated in good yield. Wolff–Kishner reduction of this ketone led to intractable oils, and the 6-oxo-group was removed *via* the dithioketal (VII) (conveniently formed in the presence of the boron trifluoride–ether complex[4]) which was desulphurised to lumistanyl A acetate (VIII; R = Ac).

The light absorption of the intermediates (III)—(VII) confirmed the nature of their functional groups: stereochemical features were deduced as follows. Reduction of the 7,8-double bond in the conjugated acetoxy-ketones (II) and (III) by lithium in ammonia will give[5] the more stable 8β-configuration of the non-conjugated acetoxy-ketone (IV) (both 8α,5α- and 8α,5β-structures require one ring to be in the boat form[3]). The acetoxy-ketone (IV) was recovered unchanged after treatment with boiling methanolic potassium

[1] Part IV, preceding paper
[2] Burawoy, *J.*, 1937, 409.
[3] Part II, *J.*, 1960, 2627.
[4] Fieser, *J. Amer. Chem. Soc.*, 1954, **76**, 1945.
[5] Barton and Robinson, *J.*, 1954, 3045.

hydroxide and reacetylation, and therefore has the more stable configuration at $C_{(5)}$. Although both 8β,5α- and 8β,5β-structures correspond to all-chair forms, the 8β,5β-structure (*trans*-A/B-ring fusion) (IV) containing one less skew interaction is preferred. The 6-acetoxy-group in the diacetate (V) is assigned the β-configuration since this leads to an equatorial conformation for the group.



Reagents: 1, CrO_3–$COMe_2$. 2, Zn–AcOH. 3, Li–NH_3. 4, Ac_2O–C_5H_5N. 5, H_2–Pt–EtOAc. 6, $HS{\cdot}[CH_2]_2{\cdot}SH$–$BF_3$. 7, Raney Ni–EtOH.

Experimental

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

3β-*Acetoxy*-5β-*lumista*-7,22-*dien*-6-*one* (III). Zinc dust (20 g.) was added in portions during 1 hr. to a refluxing solution of 3β-acetoxy-5β-hydroxylumista-7,22-dien-6-one (II) (2·5 g.) [1] in acetic acid (150 c.c.). After filtration and evaporation at 15 mm. the residue was extracted with ether. The material so obtained crystallised from methanol to give the *acetoxy-ketone* (1·1 g.), m. p. 125—127°, $[\alpha]_D$ +14° (*c* 0·5) (Found: C, 79·4; H, 10·0. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%), $\lambda_{max.}$ 2440 Å (ε 15,800), $\nu_{max.}$ 1740, 1675 (conjugated 6-oxo-group), and 1234 cm.$^{-1}$.

Reductions by Lithium in Ammonia.—(a) *Of* 3β-*acetoxy*-5β-*hydroxylumista*-7,22-*dien*-6-*one* (II). Lithium (500 mg.) was added in portions to a stirred solution of the acetoxy-hydroxy-ketone (1 g.) in dry ether (100 c.c.) and liquid ammonia (250 c.c.). Stirring was continued until a blue colour persisted and then for a further 30 min. Solid ammonium chloride was added and the material so obtained was treated with acetic anhydride (5 c.c.)–pyridine (5 c.c.) at 20° for 24 hr. The acetylated product was chromatographed on deactivated alumina (100 g.). Elution with light petroleum–benzene (1 : 1) gave 3β-*acetoxy*-5β-*lumist*-22-*en*-6-*one* (IV) (190 mg.), needles (from methanol), m. p. 135—137°, $[\alpha]_D$ −41° (*c* 0·7) (Found: C, 78·7; H, 10·5. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%), no ultraviolet absorption near 2500 Å, $\nu_{max.}$ 1739, 1712 (non-conjugated 6-oxo-group), 1242, and 1017 cm.$^{-1}$.

Benzene eluted 3β-acetoxy-5β-lumista-7,22-dien-6-one (III) (270 mg.), m. p. 124—126°, identified by mixed m. p. and comparison of infrared spectra with authentic material.

(b) *Of* 3β-*acetoxy*-5β-*lumista*-7,22-*dien*-6-*one* (III). The acetoxy-ketone (800 mg.) in dry ether (50 c.c.) was added rapidly to a stirred solution of lithium (800 mg.) in liquid ammonia (250 c.c.). Ammonium chloride was added after 10 min., and the products were isolated and acetylated as in the preceding experiment. The material so obtained was chromatographed

on deactivated alumina (70 g.). Light petroleum–benzene (9 : 1) eluted 3β,6β-*diacetoxy*-5β-*lumist*-22-*ene* (V) (190 mg.) which crystallised from methanol as needles, m. p. 114—116°, $[\alpha]_D$ −15° (*c* 0·7) (Found: C, 76·95; H, 10·7. $C_{32}H_{52}O_4$ requires C, 76·75; H, 10·5%), $\nu_{max.}$ 1743 and 1245 cm.$^{-1}$.

Elution with light petroleum–benzene (4 : 1) gave 3β-acetoxy-5β-lumist-22-en-6-one (IV) (340 mg.), m. p. 135—137°, identified by mixed m. p. and comparison of infrared spectra with authentic material. The acetoxy-ketone (50 mg.) was refluxed under nitrogen for 2 hr. with 5% methanolic potassium hydroxide. The material obtained by dilution with water and extraction with ether was acetylated at 20°, to give starting material (30 mg.), m. p. and mixed m. p. 134—136°, $[\alpha]_D$ −39° (*c* 0·8).

3β-*Acetoxy*-5β-*lumistan*-6-*one* (VI).—A solution of the above acetoxy-ketone (IV) (100 mg.) in ethyl acetate (10 c.c.) was shaken in hydrogen with Adams catalyst (100 mg.) for 30 min., filtered, and evaporated. The material so obtained (only weak absorption for a 6-oxo-group at 1713 cm.$^{-1}$) was dissolved in acetone (10 c.c.) and treated with 8N-chromic acid (0·5 c.c.) at 20° for 1 min. Dilution with water and extraction with ether afforded 3β-*acetoxy*-5β-*lumistan*-6-*one* (50 mg.), m. p. 95—97° after crystallisation from methanol, $[\alpha]_D$ −25° (*c* 0·8) (Found: C, 78·4; H, 10·7. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%), $\nu_{max.}$ 1742, 1713, and 1245 cm.$^{-1}$.

5β-*Lumistan*-3β-*yl Acetate* (*Lumistanyl A acetate*) (VIII; R = Ac).—A solution of 3β-acetoxy-5β-lumistan-6-one (40 mg.) in ethane-1,2-dithiol (0·4 c.c.) was treated with the boron trifluoride–ether complex (0·4 c.c.) at 20°. After 15 min. aqueous potassium hydrogen carbonate was added and the mixture was extracted with ether. The material so obtained crystallised from a small volume of methanol to give the dithioketal (VII) (not analysed), m. p. 134—136°, $\nu_{max.}$ 1734, 1245, and 1017 cm.$^{-1}$. This compound was refluxed in ethanol (50 c.c.) with Raney nickel (2 c.c. of slurry under ethanol) for 12 hr. Filtration and evaporation of the solution gave 5β-lumistan-3β-yl acetate (28 mg.), cubes (from ethanol), m. p. 81—83°, $[\alpha]_D$ +6° (*c* 0·4), $\nu_{max.}$ 1733, 1247, and 1231 (complex acetate band) cm.$^{-1}$, identified by mixed m. p. and comparison of infrared spectra with that of authentic material.[3] A mixture of this product and 3β-acetoxy-5α-lumistane,[3] which has a simple acetate band at 1241 cm.$^{-1}$, melted at 60—70°.

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The University, Manchester, 13.
The Dyson Perrins Laboratory, Oxford University. [*Received, January 8th*, 1960.]