Steroids of Unnatural Configuration. Part XII.[1] Hydroxylation of 5β-Lumist-2-ene

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Hydroxylation of 5β-lumist-2-ene leads to the four stereoisomeric 5β-lumistane-2,3-diols, the i.r. spectra of which show the expected variation with conformational type.

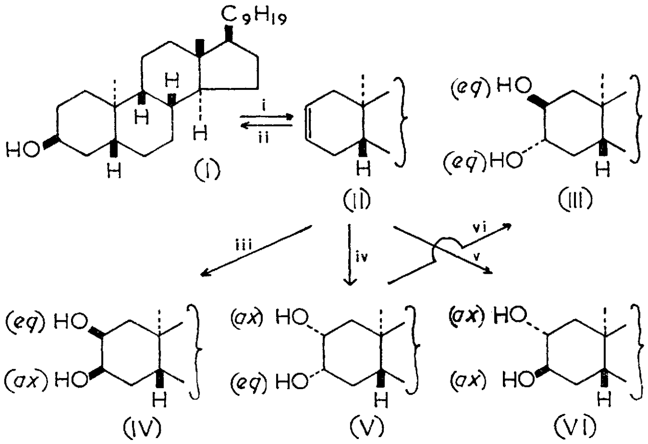
THIS work arose from an investigation involving the hydroxylation of various cholestenes and a spectrometric examination of the resulting vicinal diols.[2] Our object in it was to study the application of the preparative methods to a 10α-methyl olefin (II), and then to see whether the diol's spectra would follow the normal pattern.

Treatment of the toluene-*p*-sulphonate of 5β-lumistan-3β-ol (I) [3] with active alumina [4] gave an olefin for which the Δ^2-structure (II) was established by oxidation to the corresponding 2,3-seco-diacid.[3] Reaction of the olefin with perbenzoic acid afforded an epoxide (not isolated) which was reduced with lithium aluminium hydride to the original alcohol (I), thus showing that epoxidation occurs at the β-face. With this established, the standard hydroxylation procedures (see Scheme) were used with 5β-lumist-2-ene; reasoning along the previous lines [2] leads to the configurational assignments embodied in the diols' structures.

In a stereochemical sense the behaviour is, as expected, the ' reverse ' of that exhibited by 5α-cholest-2-ene. The i.r. spectra agree well with the characteristics of different conformational types:[2] of the three diols in which intramolecular bonding occurs, the Δν value is bigger for the *eq–ax* compounds (IV) and (V)

Hydroxy-group stretching bands of diols [dilute solutions in carbon tetrachloride were examined in 1 cm. cells as described previously;[2] values of $\nu_{max.}$, $\Delta\nu_{\frac{1}{2}}$ (half-intensity band width), and $\Delta\nu$ (' free ' minus bonded OH frequency) are in cm.$^{-1}$, and ε_{max} in mole^{-1} l. cm.$^{-1}$].

	' Free ' OH			Bonded OH			
Diol	$\nu_{max.}$	$\varepsilon_{max.}$	$\Delta\nu_{\frac{1}{2}}$	$\nu_{max.}$	$\varepsilon_{max.}$	$\Delta\nu_{\frac{1}{2}}$	$\Delta\nu$
(VI)	3629	124	24				
(IV)	3628	61	32	3583	61	48	45
(V)	3630	71	25	3583	62	48	47
(III)	3631	63	23	3600	74	38	31



SCHEME

Reagents: i, Tosylate + Al_2O_3; ii, BzO_2H, then $LiAlH_4$; iii, OsO_4; iv, I_2–AcOAg in moist AcOH, then $LiAlH_4$; v, AcO_2H, then KOH; vi, EtONa–EtOH at 175°

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[1] Part XI, K. D. Bingham, G. D. Meakins, and J. Wicha, preceding paper.

[2] C. W. Davey, E. L. McGinnis, J. M. McKeown, G. D. Meakins, M. W. Pemberton, and R. N. Young, *J. Chem. Soc.*, 1968, 2674.

[3] J. Castells, G. A. Fletcher, E. R. H. Jones, G. D. Meakins, and R. Swindells, *J. Chem. Soc.*, 1960, 2627.

[4] G. H. Douglas, P. S. Ellington, G. D. Meakins, and R. Swindells, *J. Chem. Soc.*, 1959, 1720.

than for the *eq–eq* isomer (III), and only in the last diol is the ε value of the bonded band greater than that of the absorption of the free hydroxy-group.

EXPERIMENTAL

For general directions see ref. 2.

Compound (I) was obtained as previously[3] from 5β-lumista-7,22-dien-3β-ol,[5] which was conveniently prepared in the present work as follows. Freshly cut lithium (5 g.) was added during 10 min. to a stirred solution of lumisteryl dinitrobenzoate[3] (15 g.) in dry ether–liquid ammonia (1 : 1; 1·1 l.). After a further 15 min. dry ethanol (150 ml.) was added dropwise, the mixture was worked up, and the product was chromatographed on neutral deactivated alumina (500 g.). Light petroleum eluted a mixture of olefins (1 g.). Light petroleum–ether (4 : 1) eluted 5β-lumista-7,22-dien-3β-ol (7·7 g.), m.p. 140—142°.

5β-*Lumist*-2-*ene* (II).—Treatment of 5β-lumistan-3β-ol[3] (I) (2 g.) in dry pyridine (20 ml.) with toluene-*p*-sulphonyl chloride (2 g.) at −6° for 48 hr. gave 5β-*lumistan*-3β-*yl toluene*-p-*sulphonate* (2·1 g.), m.p. 126—128° (from ethanol), $[\alpha]_D$ −20° (*c* 0·6) (Found: C, 75·7; H, 10·05; S, 5·35. $C_{35}H_{56}O_3S$ requires C, 75·6; H, 10·1; S, 5·7%). Contact with Grade H alumina for 18 hr.[4] afforded material which was chromatographed on neutral alumina (100 g.). Light petroleum (b.p. 30—40°) eluted 5β-*lumist*-2-*ene* (860 mg.), m.p. 64—66° (from methanol), $[\alpha]_D$ −14° (*c* 1·1) (Found: C, 87·3; H, 12·7. $C_{28}H_{48}$ requires C, 87·4; H, 12·6%), $\nu_{max.}$ 754 and 670 cm.$^{-1}$.

A solution of the olefin (50 mg.) and perbenzoic acid (42 mg.) in chloroform (10 ml.) was kept at 20° for 2 hr., diluted with benzene (10 ml.), and filtered through neutral deactivated alumina (25 g.). The product, the i.r. spectrum of which did not show olefinic or ketonic absorption, was dissolved in ether and heated under reflux for 1 hr. with lithium aluminium hydride (25 mg.) to give 5β-lumistan-3β-ol[3] (20 mg.), m.p. and mixed m.p. 125—127°.

Chromium trioxide (400 mg.) in water–acetic acid (1 : 10; 5·5 ml.) was added during 1 hr. to a stirred solution of 5β-lumist-2-ene (200 mg.) in acetic acid (8 ml.) at 60°. Work-up after a further 3 hr. afforded 2,3-seco-5β-lumistane-2,3-dioic acid (88 mg.), m.p. 222—225°, identified by comparison with authentic material.[3]

5β-*Lumistane*-2,3-*diols*.—The product obtained from 5β-lumist-2-ene (450 mg.) and osmium tetroxide (500 mg.) in the usual way[2] was chromatographed on deactivated alumina (35 g.). Benzene–ether (3 : 1) eluted 5β-*lumistane*-2β,3β-*diol* (IV) (312 mg.), m.p. 172—174° (from methanol), $[\alpha]_D$ +26° (*c* 1·3) (Found: C, 80·3; H, 12·0. $C_{28}H_{50}O_2$ requires C, 80·3; H, 12·0%).

5β-Lumist-2-ene (230 mg.) was used in the Woodward sequence at 20° under the conditions described earlier,[6] and the product was chromatographed on deactivated alumina (40 g.). Light petroleum eluted 5β-lumist-2-ene (116 mg.). Benzene–ether (1 : 3) eluted 5β-*lumistane*-2α,3α-*diol* (V) (55 mg.), m.p. 151—153° (from aqueous methanol), $[\alpha]_D$ +4° (*c* 0·7) (Found: C, 80·2; H, 11·8%). This diol (50 mg.) was heated for 36 hr. at 175° with a solution made from sodium (2·1 g.) and dry ethanol (55 ml.), and the product was chromatographed on deactivated alumina (10 g.). Ether–methanol (9 : 1) eluted 5β-*lumistane*-2β,3α-*diol* (III) (26 mg.), m.p. 189—192° (from acetone), $[\alpha]_D$ +4° (*c* 0·7) (Found: C, 79·95; H, 11·9%).

5β-Lumist-2-ene (500 mg.) in acetic acid was treated with hydrogen peroxide, and the product was hydrolysed with potassium hydroxide (as described previously[2] for 5β-cholest-3-ene). Chromatography on deactivated alumina (35 g.) gave 5β-*lumistane*-2α,3β-*diol* (VI) [299 mg.; eluted with benzene–ether (1 : 1)], m.p. 189—190° (from methanol), $[\alpha]_D$ −3° (*c* 1·5) (Found: C, 80·3; H, 11·95%).

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[6] P. S. Ellington, D. G. Hey, and G. D. Meakins, *J. Chem. Soc.* (*C*), 1966, 1327.