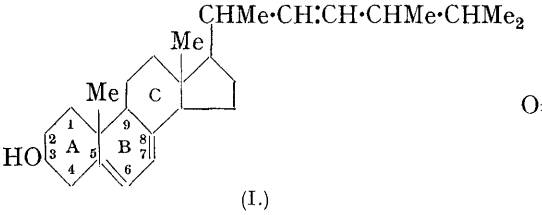
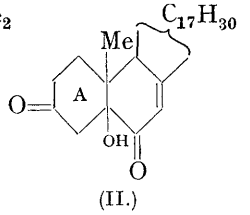
## 87. *Studies in the Sterol Group. Part XXX. The Oxidation of Ergosterol, Ergosteryl Acetate, and Lumisteryl Acetate with Chromic Anhydride.*

By A. Burawoy.

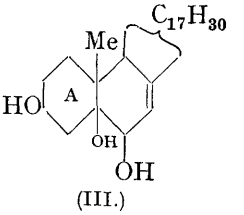
Although previous attempts to oxidise ergosterol (I) by means of chromic anhydride proved unsatisfactory (Reindel, *Annalen*, 1929, **466**, 136), reinvestigation of the reaction has shown that even under relatively drastic conditions a fair yield of ergostadiene-3 : 6-dion-5-ol (II) can be isolated. It is identical with that previously obtained by the oxidation of ergostadiene-3 : 5 : 6-triols-I and -II (III) (Heilbron, Morrison, and Simpson, J., 1933, 302; Dunn, Heilbron, Phipers, Samant, and Spring, J., 1934, 1576) and, as anticipated, it exhibits the characteristic selective absorption of an αβ-unsaturated ketone.




(I.)



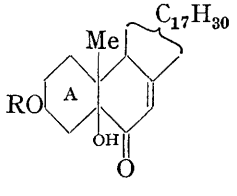

(II.)

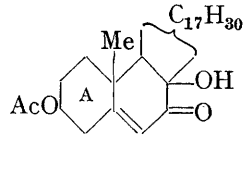



(III.)

Oxidation of ergosteryl acetate with the same reagent gives a neutral compound, $C_{30}H_{46}O_4$, m. p. 264°, which also exhibits the absorption spectrum of an αβ-unsaturated ketone. The Zerewitinoff method established the presence of one hydroxyl group, which is tertiary, since the compound is recovered unchanged after treatment with acetic anhydride. This fact clearly suggests that the compound is 3-*acetoxyergostadien*-6-*on*-5-*ol* (IV, R = Ac). An attempt to confirm this structure by converting the compound into the known ergostadiene-3 : 6-dion-5-ol (II) was unsuccessful, since on hydrolysis a mixture of acid and neutral products was obtained from which (IV, R = H) could not be isolated. That (IV) correctly represents the structure of the oxidation product was demonstrated by its reduction with aluminium *iso*propoxide, whereby ergostadiene-3 : 5 : 6-triol-II (III) was obtained, identical with that prepared by the oxidation of ergosterol with perbenzoic acid (Windaus and Lüttringhaus, *Annalen*, 1930, **481**, 127).

(IV.)




(V.)

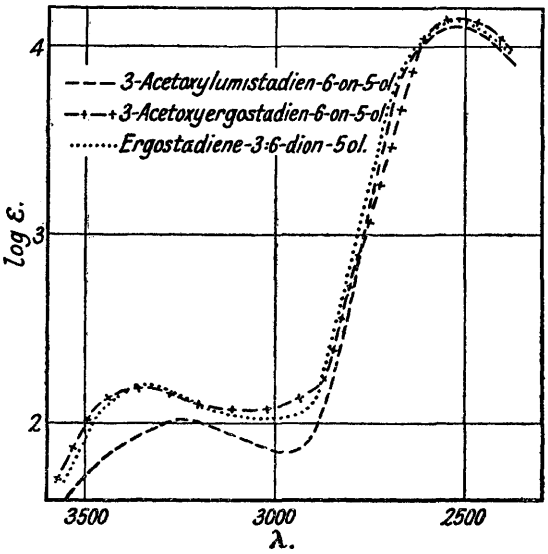
In Part XXI (Heilbron, Spring, and Stewart, J., 1935, 1221) it was suggested that lumisterol differs from ergosterol only in the orientation of one or more of the asymmetric centres. Proof of the correctness of this view is to be found in the parallel behaviour of ergosteryl and lumisteryl acetates on oxidation with chromic acid. From the latter a 3-*acetoxylumi-*

*stadienonol* is obtained which exhibits the typical absorption spectrum of an αβ-unsaturated ketone. That the hydroxyl group is tertiary and attached to a carbon atom adjacent to the carbonyl group is shown by the fact that oxidation of the lumistadienetriol-II monoacetate of Dimroth (*Ber.*, 1936, **69**, 1123) gives the same 3-acetoxylumistadienonol. Lumistadienetriol-II is, however, a stereoisomeride of lumistadienetriol-I (Heilbron, Moffet, and Spring, following paper), which has been shown to contain a tertiary-secondary α-glycol system in addition to the $C_3$-hydroxyl group (Heilbron, Spring, and Stewart, *loc. cit.*).

The characterisation of the primary products of oxidation of both ergosteryl and lumisteryl acetates not only establishes the identity of the conjugated system in the two sterols, but also confirms that this is located at $C_5$–$C_6$ and $C_7$–$C_8$. The conjugated ethenoid system of the two sterols must be in either ring B or ring C (Inhoffen, *Annalen*, 1932, **494**, 116); of the four possible arrangements of the unsaturated system in these two rings, only the one indicated will allow of the formation of a hydroxy-αβ-unsaturated ketone in which the introduced hydroxyl group is tertiary and attached to a carbon atom adjacent to the carbonyl group. The constitution of the oxidation product from ergosteryl acetate has been shown to be (IV). The structure of 3-acetoxylumistadienonol, however, may be represented by either (IV) or (V); the decision between these structures is in favour of the former, since the absorption spectra of this compound and of 3-acetoxyergostadien-6-on-5-ol exhibit a band of high intensity at 2520 A. In contrast, sterol derivatives containing the chromophore of (V), such as 7-ketocholesteryl acetate, 7-ketositosteryl acetate, and 7-keto-$\Delta^5$-cholestene,* are all characterised by a high-intensity band at 2350—2370 A.

## Experimental.

*Ergostadiene*-3 : 6-*dion*-5-*ol*.—The oxidation was effected by addition of a solution of chromic acid (8·5 g.) in 90% acetic acid (55 c.c.) to ergosteryl acetate (10 g.) in acetic acid (300 c.c.) at 50°, the mixture being mechanically stirred. After 5 minutes the homogeneous solution was largely diluted with water, the precipitate filtered off, crystallised from alcohol, and recrystallised from benzene–alcohol, ergostadiene-3 : 6-dion-5-ol being obtained as plates, m. p. 249° (decomp.) either alone or in admixture with a specimen prepared by the method of Dunn, Heilbron, Phipers, Samant, and Spring (*loc. cit.*); yield, 20%. Identity of the two specimens was confirmed by a comparison of the corresponding oximes, m. p. 232—233°, either alone or in admixture; $[\alpha]_D^{20°}$ + 20° ($l$ = 1, $c$ = 1·16 in chloroform).




The absorption spectrum of chloroform solutions is shown in the figure: maxima, (*a*) 2520 A., ε = 13,450; (*b*) 3325 A., ε = 160.

3-*Acetoxyergostadien*-6-*on*-5-*ol*.—A suspension of ergosteryl acetate (10 g.) in acetic acid (200 c.c.) was treated with a solution of chromic acid (6·5 g.) in 80% acetic acid (24 c.c.), at 45°, the temperature rising to 80°. After 30 mins.' stirring, methyl alcohol (3 c.c.) was added, and the reaction mixture diluted with water. The solid separating was collected and crystallised successively from ethyl acetate, benzene, and ethyl acetate, from which 3-*acetoxyergostadien*-6-*on*-5-*ol* separated in plates (yield 25%), m. p. 264° (decomp.), $[\alpha]_D^{21°}$ − 4·7° ($l$ = 2, $c$ = 0·90 in chloroform) (Found: C, 76·5; H, 9·7. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·8%); it does not give a semicarbazone. The absorption spectrum (chloroform solution) is shown in the figure: maxima, (*a*) 2515 A., ε = 13,570; (*b*) 3330 A., ε = 155.

* In contrast to this observation, Lettré and Inhoffen ("Über Sterine, Gallensäuren u.s.w.," p. 34) state that 7-keto-$\Delta^5$-cholestene exhibits a maximum at 2480—2540 A.; this we cannot substantiate.

*Active hydrogen determination* (Zerewitinoff method). 15·76 Mg. of 3-acetoxyergostadien-6-on-5-ol evolved 0·84 c.c. of methane at 16° and 0·89 c.c. at 95°, corresponding to 1·12 and 1·18 atoms of active hydrogen per mole respectively.

*Reduction of 3-Acetoxyergostadien-6-on-5-ol.*—A solution of 3-acetoxyergostadien-6-on-5-ol (2·5 g.) and aluminium *iso*propoxide (10 g.) in *iso*propyl alcohol (400 c.c.) was heated under reflux for 52 hours. The mixture was concentrated to half bulk, diluted with water, and extracted with ether. The residue obtained by removal of the ether was repeatedly crystallised from ethyl acetate, from which the triol separated as prisms, m. p. 240°, undepressed on admixture with ergostadiene-3 : 5 : 6-triol-II. The triol does not exhibit selective absorption above 2400 A. (Found : C, 78·5; H, 10·8. Calc. for $C_{28}H_{46}O_3$ : C, 78·1; H, 10·8%). The diacetate, prepared by refluxing the triol with acetic anhydride, separated from alcohol in prisms, m. p. 182° either alone or in admixture with ergostadiene-3 : 5 : 6-triol-II diacetate (Found : C, 75·0; H, 9·8. Calc. for $C_{32}H_{50}O_5$ : C, 74·7; H, 9·8%).

*3-Acetoxylumistadien-6-on-5-ol.*—(a) A solution of lumisteryl acetate (9·5 g.) in acetic acid (200 c.c.) was oxidised at 45° with chromic acid (6·5 g.) in 80% acetic acid (60 c.c.) with mechanical stirring for 30 minutes. The solution was precipitated with water, extracted with ether, the ether removed, and the residue taken up in hot methyl alchol. The oil separating on cooling was isolated by decantation, and crystallisation effected from the same solvent, from which *3-acetoxylumistadien-6-on-5-ol* separated in prisms, m. p. 177—178°, $[\alpha]_D^{19°}$ + 11·7° ($l$ = 1, $c$ = 2·05 in chloroform) (Found : C, 76·5; H, 9·8. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·8%); yield, 15%. Light absorption in chloroform solution (see figure) : maxima, (*a*) 2515 A., $\varepsilon$ = 13,130; (*b*) 3230 A., $\varepsilon$ = 105.

(b) A solution of lumistadiene-3 : 5 : 6-triol monoacetate (1·9 g.) in acetic acid (30 c.c.) was treated with chromic acid (0·45 g.) in 80% acetic acid (22 c.c.) at room temperature, the mixture being mechanically stirred for 2 hours. After the addition of water, the separated solid was collected and crystallised from methyl alcohol, 3-acetoxylumistadien-6-on-5-ol (0·9 g.) being obtained in prisms, m. p. 177—178°, $[\alpha]_D^{19°}$ + 12·3° ($l$ = 1, $c$ = 1·78 in chloroform), identical with the preparation described under (a).

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