410. *Studies in the Steroid Group. Part LX.* Reduction of Ergosterol Epidioxide.*

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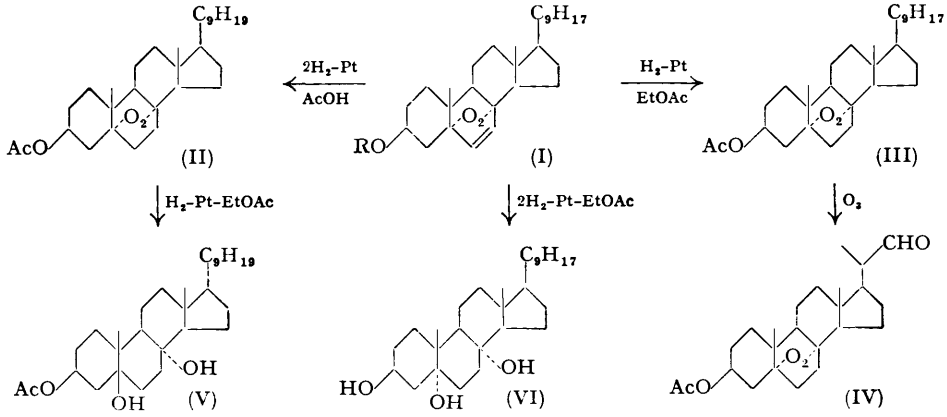
As with dehydroergosterol epidioxide, hydrogenation of ergosterol epidioxide in the presence of platinum catalysts first leads to reduction of the Δ^6-bond. Further reduction takes place readily causing either saturation of the Δ^{22}-bond or fission of the epidioxide bridge (to furnish 5α : 8α-diols), depending on the experimental conditions. Dehydration of these 5α : 8α-diols yields 5α-hydroxy-Δ^7-compounds and 5α : 8α-epoxides; the properties of the latter are compared with those of the $\Delta^{9(11)}$-analogues described in the previous paper.

In Part LVI of this series (*J.*, 1952, 4883) the course of hydrogenation of 9 : 11-dehydroergosterol epidioxide under various conditions was reported. The present paper describes a comparative study of the reduction of ergosterol epidioxide. The only previous work on the hydrogenation of this compound was by Windaus, Bergmann, and Lüttringhaus (*Annalen*, 1929, **472**, 195) who described the formation of an " ergostenediol-I " when the epidioxide was reduced in ethanol in the presence of a palladium catalyst. Alternatively, zinc–alkali reduction of the epidioxide was shown to yield a triol [now known to be ergosta-6 : 22-diene-3β : 5α : 8α-triol (IX)], which afforded the same ergostenediol on catalytic hydrogenation. Müller suggested later (*Z. physiol. Chem.*, 1935, **231**, 75) that this ergostenediol-I might be an ergost-8(14)-ene-3 : 5-diol; the correct structure is discussed below.

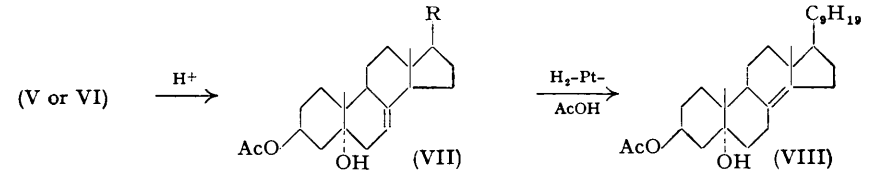


The acetate (I; R = Ac) of ergosterol epidioxide was prepared from ergosteryl acetate by slight modification of the original method of Windaus and Brunken (*Annalen*, 1928, **460**, 225). [In the formulæ the epidioxide bridge is depicted as being in an α-configuration because of the readiness of acetylation of derived 5-hydroxy-steroids (cf. Part LVI), and for a further reason discussed below.] Hydrogenation of (I; R = Ac) in acetic acid with Adams catalyst resulted in the rapid uptake of two mols. of hydrogen, to give the fully saturated epidioxide (II), whereas reduction in neutral solution employing a catalyst derived from a hydrated platinic oxide (cf. Part LVI) afforded a dihydro-compound (III) —these results very closely paralleled those obtained with dehydroergosterol epidioxide. The structure of the dihydro-compound (III) was confirmed by ozonolysis to the aldehyde (IV), together with the corresponding acid.

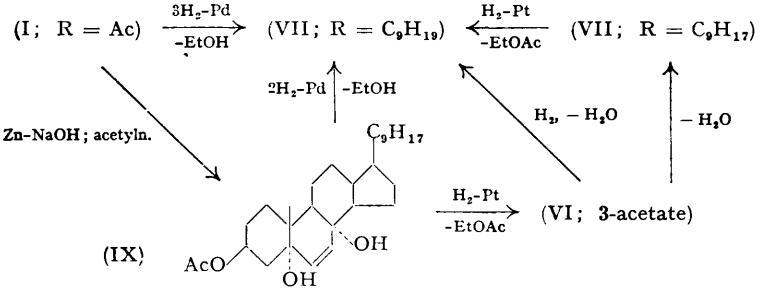
Further hydrogenation of the tetrahydro-acetate (II) in concentrated ethyl acetate solution with Adams catalyst resulted in the uptake of one mol., to produce the 5α : 8α-diol (V)—a behaviour analogous to that observed in the 9 : 11-dehydro-series, except that

* Part LIX, preceding paper.

this saturated glycol was somewhat more soluble and separated only in 60% yield. Hydrogenation of (I; R = Ac) under these conditions gave only a negligible precipitate of the Δ^{22}-5α : 8α-diol (although a good yield of $\Delta^{9(11):22}$-5α : 8α-diol was obtained in the dehydro-series). This side-chain unsaturated diol could be isolated after such experiments by chromatography, but its preparation was best effected by hydrogenating ergosterol epidioxide itself in concentrated ethyl acetate solution, the sparingly soluble triol (VI) then separating rapidly in good yield.



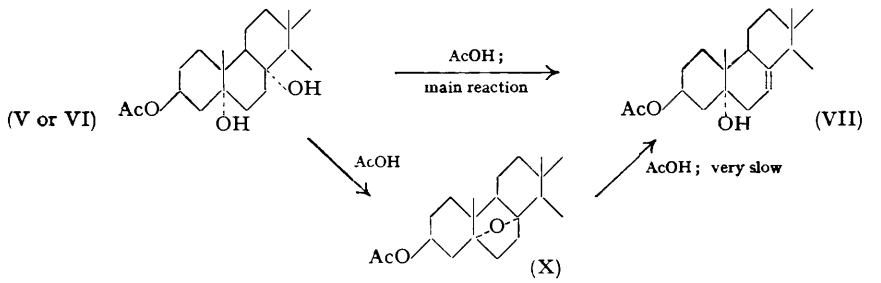
These 5α : 8α-glycols were very readily dehydrated by dilute mineral acids, to yield 5α-hydroxy-Δ^7-steroids (VII; R = C_9H_{17} or C_9H_{19}) (cf. the dehydration of 8α-hydroxy-Δ^9-compounds to 7 : 9-dienes, Part LVI). The structure (VII) was confirmed by (*a*) acetylation to 3β : 5α-diacetates, and (*b*) the infra-red and ultra-violet absorption due to the Δ^7-bond (cf. Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402; Bladon, Henbest, and Wood, *J.*, 1952, 2737). Further, these Δ^7-compounds were converted in high yield into the known $\Delta^{8(14)}$-steroid (VIII) (cf. Part LVI) when shaken in acetic acid with platinum and hydrogen. (Dr. D. H. R. Barton has kindly informed us that the 5-hydroxy-$\Delta^{7:22}$-compound is also obtained by lithium aluminium hydride reduction of ergosterol epidioxide.) The conditions employed for the dehydration of the 8α-hydroxyl group in the 5 : 8-diols are those favouring *trans*-elimination, and thus a kinetically controlled dehydration takes place towards $C_{(7)}$ with loss of the 7β-hydrogen atom, and not towards the $C_{(14)}$ (α-H) (or possibly $C_{(9)}$) position to give a thermodynamically more stable compound. The reaction thus provides further proof for the α-configurations of the 8-hydroxyl group and hence of the epidioxide bridge in compounds (I)—(IV).



As soon as the $\Delta^{8(14)}$-compound (VIII) became available (Part LVI) it was clear that, contrary to Müller's suggestion (*loc. cit.*), the much higher-melting "ergostenediol-I" could not have this structure. The physical constants recorded by the earlier workers were in good agreement with those of the Δ^7-compound (VII; R = C_9H_{19}), and their identity was confirmed on repetition of the Windaus' preparations of the diol. The Windaus reactions, as mentioned earlier, involve hydrogenation either of ergosterol epidioxide ($3H_2$ uptake) or of the $\Delta^{6:22}$-5 : 8-diol (IX) ($2H_2$ uptake), and no doubt proceed *via* a diol (V) or (VI) saturated in ring B; this diol is then dehydrated to a Δ^7-compound in contact with the (acidic) hydrogen adsorbed on the palladium catalyst. However, by use of a platinum catalyst and ethyl acetate as solvent selective reduction of the 6 : 7-bond in (IX) can be achieved, to give the nuclear-saturated glycol (VI). The relationships that have now been established are depicted in the accompanying scheme.

Dehydration of $\Delta^{9(11)}$-5α : 8α-glycols to the corresponding 5α : 8α-epoxides in high yield by 5% acetic acid in boiling acetone has been described in the previous paper. However, when the 5 : 8-diols (V) or (VI) were similarly treated, 80% of the starting material was

recovered together with about 15% of the 5-hydroxy-Δ^7-steroid (VII) and 5% of the 5α : 8α-epoxide (X). Longer reaction times resulted in the dehydration of larger proportions of diol, but the ratio of (VII) to (X) remained approximately constant. These experiments indicated that (VII) and (X) were being formed from the diol by two competing reactions, and that the rate of isomerisation of (X) to the Δ^7-compound must be slow relative to the dehydration reactions. Actually it was found, by separate experiment, that the 5 : 8-oxide was only very slowly isomerised in the acetic acid–acetone medium, although slightly more rapidly in acetic acid alone. Treatment of the oxide with dilute mineral acid rapidly yielded (VII).



Further reactions in the 9 : 11-dehydro-series established that, although the formation of the 5 : 8-oxide corresponding to (X) was the main reaction (in acetic acid–acetone), direct dehydration of the 5 : 8-diol to a 5-hydroxy-7 : 9-diene corresponding to (VII) also took place to a small extent. Conjugated diene was formed more rapidly from the diol than from the $\Delta^{9(11)}$-5 : 8-oxide under the same conditions.

It was evident that each of the three reactions just considered proceeded more rapidly with the Δ^9-compounds than with the nuclear saturated analogues. This is doubtless due to the greater case of fission of the allylic $C_{(8)}$–oxygen bond which has to be broken in each of the reactions of the $\Delta^{9(11)}$-compounds. Dehydration of the 5 : 8-glycols to 5-hydroxy-Δ^7(or $\Delta^{7:9}$)-steroids, catalysed by mineral acid, no doubt proceeds partly *via* the 5 : 8-oxides (similar proportions formed as with acetic acid), but of course further rapid isomerisation occurs under these conditions.

Although perhydrophenanthrene compounds with *trans-anti-cis*-configurations at the ring junctions can readily adopt chair conformations in each ring (cf. Johnson, *Experientia*, 1951, **7**, 315), in the nuclear-saturated 5α : 8α-diol (V) or (VI) the additional *trans*-fused ring D will force either ring B or ring C into a boat conformation. Of these alternatives, the former (*i.e.*, ring B boat, rings A and C chair) appears the more likely, as there is much steric interference between the two angular methyl groups attached to $C_{(10)}$ and $C_{(13)}$ in the other conformation. When ring B is in the boat form, the conformation of the 5 : 8-glycols is that of the ergosterol epidioxide or the 6 : 7-dihydroergosterol epidioxide from which they are derived; in each case the molecule seems relatively unstrained. The 5- and the 8-hydroxyl group are found to be quite close to each other, and thus favourably arranged for forming 5 : 8-oxides. However, in this conformation, the 8α-hydroxyl group is also seem to be polar (with respect to ring B) and coplanar with the 7β-hydrogen atom, thus facilitating dehydration to Δ^7-compounds under acidic conditions, and this becomes the main direction of reaction in the nuclear-saturated compounds. The conformation of steroids with an 8α-substituent (in particular, 3β-acetoxy-8α-ergostan-11-one) will be discussed further in another paper.

Experimental

General experimental directions are given in the previous paper.

3β-Acetoxy-5α : 8α-epidioxyergosta-6 : 22-diene (Ergosteryl Acetate Epidioxide) (I; R = Ac).—Ergosteryl acetate (20 g.) was dissolved in absolute ethanol (3 l.) together with eosin (150 mg.), and the solution was irradiated and heated under reflux by means of a 300-w tungsten-filament lamp placed beneath the flask, while oxygen was bubbled through the solution continuously. Irradiation was stopped when the solution ceased to show a maximum at 2800 Å (about 24 hr.). The product crystallised as plates (10 g.), m. p. 193—200°, when the solution was concentrated

to a small bulk. Two further recrystallisations from chloroform–ethanol gave the epidioxide as flat needles, (8·5 g.), m. p. 199—206°, $[\alpha]_D$ −19° (*c*, 1·0) (Windaus and Brunken, *loc. cit.*, give m. p. 202°, $[\alpha]_D$ −18°). Hydrolysis of the acetate (5·0 g.) with boiling 5% methanolic potassium hydroxide (300 c.c.) for 10 min. gave ergosterol epidioxide, stout needles (4·0 g.) (from ethanol), m. p. 181—185°, $[\alpha]_D$ −36° (*c*, 0·9) (Windaus and Brunken record m. p. 178°, $[\alpha]_D$ −36°).

3β-*Acetoxy*-5α : 8α-*epidioxyergostane* (II).—Ergosteryl acetate epidioxide (1 g.) was shaken in acetic acid (100 c.c.) with hydrogen and prereduced Adams catalyst (50 mg.) until 2 mols. of hydrogen had been absorbed. The solution was filtered and evaporated to dryness under reduced pressure and the residue chromatographed on deactivated alumina (100 g.). Elution with light petroleum–benzene (3 : 1) yielded crystals (0·6 g.), m. p. 185—198°, which gave 3β-*acetoxy*-5α : 8α-*epidioxyergostane* as plates (from methanol) (0·37 g.), m. p. 204—209°, $[\alpha]_D$ −89° (*c*, 1·1) (Found: C, 76·1; H, 10·55. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%). The compound showed no ultra-violet light absorption. Elution with benzene gave a fraction (250 mg.), m. p. 200—225°, which on recrystallisation from methanol afforded 3β-*acetoxyergost*-7-*en*-5α-*ol* (VII; R = C_9H_{19}) as plates, m. p. 224—229°, $[\alpha]_D$ +20° (*c*, 1·0) (Found: C, 78·7; H, 11·1. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). Light absorption: ε_{2050} 7200; ε_{2100} 4500 (under the same conditions γ-ergostenol exhibited ε_{2050} 6700 and ε_{2100} 4800). This Δ^7-compound is the 3-acetate of "ergostendiol I" (see below); Windaus, Bergmann, and Lüttringhaus (*loc. cit.*) give m. p. 227°, $[\alpha]_D$ +14·7°. Alkaline hydrolysis of (II) gave, after crystallisation from methanol, 5α : 8α-*epidioxyergostan*-3β-*ol* as fine needles, m. p. 175—177°, $[\alpha]_D$ −104° (*c*, 0·75) (Found: C, 77·75; H, 10·9. $C_{28}H_{48}O_3$ requires C, 77·7; H, 11·2%).

Ergost-7-*ene*-3β : 5α-*diol and its Diacetate*.—Prepared by hydrolysis of the 3β-acetate, this *diol* crystallised from ethyl acetate as plates, m. p. 232—240°, $[\alpha]_D$ +16° (*c*, 0·94) (Found: C, 80·6; H, 11·5. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%). This corresponds to "ergostendiol I" (see also below), for which Windaus, Bergmann, and Lüttringhaus record m. p. 234°, $[\alpha]_D$ +14·7°.

3β-Acetoxyergost-7-en-5α-ol (0·5 g.) was heated in chloroform (11·3 c.c.) with acetyl chloride (3·8 c.c.) and dimethylaniline (5·8 c.c.) under reflux for 20 hr. After evaporation to dryness under reduced pressure, the residue was worked up with ether and water. The material extracted by ether was chromatographed on deactivated alumina (50 g.). Elution with benzene–light petroleum (2 : 3) yielded a gum from which the *diacetate* was obtained by crystallisation from methanol as flat needles (280 mg.), m. p. 127·5—129·5°, $[\alpha]_D$ +68° (*c*, 1·0) (Found: C, 76·8; H, 10·35. $C_{32}H_{52}O_4$ requires C, 76·75; H, 10·45%).

3β-*Acetoxyergostane*-5α : 8α-*diol* (V).—3β-Acetoxy-5α : 8α-epidioxyergostane (1 g.) in ethyl acetate (50 c.c.) was shaken in hydrogen with prereduced Adams catalyst (100 mg.). Absorption of hydrogen almost ceased at 43 c.c. (1 mol = 49 c.c.), and the hydrogenation was interrupted. The solution was warmed to redissolve some precipitated 5α : 8α-diol, filtered, and evaporated to dryness under reduced pressure. The residue was chromatographed on deactivated alumina (100 g.), giving 3 principal fractions: (*a*) light petroleum–benzene (3 : 1) eluted starting material (150 mg.), m. p. 205—207°, $[\alpha]_D$ −85° (*c*, 0·6); (*b*) benzene afforded plates (50 mg.), m. p. 224—228°, $[\alpha]_D$ +20° (*c*, 0·7), which gave no m. p. depression on admixture with 3β-acetoxyergost-7-en-5α-ol; (*c*) methanol–ether (1 : 9) gave 3β-*acetoxyergostane*-5α : 8α-*diol* (700 mg.), which crystallised from methanol, containing a little pyridine, as fine needles, m. p. 170—200° (decomp.), $[\alpha]_D$ −43° (*c*, 0·72) (Found: C, 75·3; H, 11·0. $C_{30}H_{52}O_4$ requires C, 75·6; H, 11·0%). The substance showed no ultra-violet light absorption.

Hydrolysis of the 5 : 8-diol 3-acetate with alkali, followed by isolation with ether and crystallisation from methanol, gave *ergostane*-3β : 5α : 8α-*triol*, m. p. 170—180°, $[\alpha]_D$ −50° (*c*, 0·63) (Found: C, 77·05; H, 11·65. $C_{28}H_{50}O_3$ requires C, 77·35; H, 11·6%).

3β-*Acetoxy*-5α : 8α-*epoxyergostane* (X; C_9H_{19} side chain).—3β-Acetoxyergostane-5α : 8α-diol (400 mg.) was heated with 5% acetic acid in acetone (100 c.c.) under reflux for 6 hr. After dilution with water the product was isolated with ether. It was added in the minimum of benzene to deactivated alumina (40 g.). The column was eluted as follows: (*a*) light petroleum (b. p. 60—80°) gave a gum (100 mg.) which, on crystallisation from methanol containing a trace of pyridine, gave the 5α : 8α-*epoxide* as needles (60 mg.), m. p. 99—101°, $[\alpha]_D$ −3° (*c*, 0·5) (Found: C, 78·2; H, 11·0. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%) (the substance showed no ultra-violet light absorption); (*b*) benzene afforded a fraction (260 mg.) giving 3β-acetoxyergost-7-en-5α-ol, m. p. 220—225° (from methanol), $[\alpha]_D$ +18° (*c*, 0·9); (*c*) methanol–ether (1 : 9) eluted 50 mg. of gum which crystallised from methanol to give unchanged 5α : 8α-diol as needles, m. p. 160—190° (decomp.).

Relative Stabilities of 3β-*Acetoxy*-5α : 8α-*epoxyergostane and* 3β-*Acetoxy*-5α : 8α-*epoxyergost-*

9(11)-*ene towards Acetic Acid.*—(i) 3β-Acetoxy-5α : 8α-epoxyergostane (35 mg.) was heated under reflux with 5% acetic acid in acetone (10 c.c.) for periods up to 16 hr. The steroid was then recovered with ether in the usual way and chromatographed on 5 g. of deactivated alumina. The material was recovered unchanged (m. p. 98—99°).

The saturated 5α : 8α-epoxide (33 mg.) was dissolved in glacial acetic acid (10 c.c.) and kept overnight at 20°. The product was worked up with ether and chromatographed on 5 g. of deactivated alumina. Two fractions were eluted: (*a*) benzene–light petroleum (1 : 4) gave the epoxide as a gum (28 mg.), which crystallised as needles, m. p. 97—100°; (*b*) ether–methanol (9 : 1) gave a solid (4 mg.), m. p. 190—208°, which crystallised from ethyl acetate as flakes, m. p. 210—220°, corresponding to the Δ^7-5α-hydroxy-compound. The conversion into the Δ^7-isomer in this experiment is thus of the order of 12—15%.

(ii) 3β-Acetoxy-5α : 8α-epoxyergost-9(11)-ene was treated with 5% acetic acid in acetone, as in the experiments with the saturated 5α : 8α-epoxide. The product was isolated with ether, and the conversion into $\Delta^{7:9(11)}$-diene estimated by light-absorption measurements. The results after varying reaction times were as follows [ε being assumed to be 16,000 at 2420 Å for the pure 5α-hydroxy-7 : 9(11)-diene] :

Time (hr.)	ε_{2420}	Conversion (%)	Time (hr.)	ε_{2420}	Conversion (%)
2	—	—	16	1300	*ca.* 8
4½	450	2—3	14 in AcOH at 20°	3000	*ca.* 20

3β-Acetoxyergost-9-ene-5α : 8α-diol (115 mg., shown by ultra-violet measurements to be free from 7 : 9-diene) was heated under reflux with 5% acetic acid in acetone (10 c.c.) for 1 hr. Isolation with ether followed by chromatography afforded the 5 : 8-oxide fraction (100 mg.) (eluted with light petroleum, and obtained pure by crystallisation from methanol, cf. previous paper). Further elution with ether gave a semi-solid product (14 mg.; ε 9000, corresponding to 8% of 7 : 9-diene), which on crystallisation gave plates, m. p. 210—220°.

3β-*Acetoxyergost-7-en-5α-ol* (VII; R = C_9H_{19}) *from* 3β-*Acetoxy-5α : 8α-epoxyergostane.*—The epoxide (50 mg.) was dissolved in methanol (5 c.c.) and a trace of concentrated hydrochloric acid added. Agitation produced an immediate precipitate of minute plates which on recrystallisation from methanol gave flat needles (20 mg.), m. p. and mixed m. p. 224—227°, $[\alpha]_D$ +18° (*c*, 0·6).

Ergost-22-ene-3β : 5α : 8α-triol (VI).—Ergosterol epidioxide (1 g.) in the minimum volume of ethyl acetate was shaken in hydrogen with prereduced Adams catalyst (100 mg.). A dense white precipitate of the triol, in the form of fine needles, quickly began to separate, the uptake of hydrogen becoming gradually slower until it had virtually ceased after 93 c.c. (2 mols. = 99 c.c.). The product was removed by filtration, washed with a little ethyl acetate, and dried (yield, 850 mg.; m. p. 182—192°). This material without further purification was in general used for the preparation of the 5α : 8α-epoxide (see below). A sample, crystallised twice from methanol containing a trace of pyridine, gave the *triol* as flat needles, m. p. 202—215°, $[\alpha]_D$ −65° (*c*, 0·67) (Found: C, 77·9; H, 11·5. $C_{28}H_{48}O_3$ requires C, 77·7; H, 11·2%). No ultra-violet-light absorption could be detected.

Dehydration of Ergost-22-ene-3β : 5α : 8α-triol in Mineral Acid to give Ergosta-7 : 22-diene-3β : 5α-diol.—The triol (200 mg.) was dissolved in the minimum volume of methanol and a trace of hydrochloric acid added to the cooled solution. The *diol*, precipitated as platelets (140 mg.), m. p. 220—230°, recrystallised from *iso*propyl alcohol as plates (50 mg.), m. p. 227—234°, $[\alpha]_D$ +1° (*c*, 0·5) (Found: C, 80·55; H, 10·8. $C_{28}H_{46}O_2$ requires C, 81·05; H, 11·2%). Acetic anhydride–pyridine at 20° gave 3β-*acetoxyergosta-7 : 22-dien-5α-ol* (VII; R = C_9H_{17}) (flat needles from ethyl acetate), m. p. 228—233°, $[\alpha]_D$ +2° (*c*, 0·7) (Found: C, 78·7; H, 10·45. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). Acetylation of the monoacetate by acetyl chloride–dimethylaniline yielded 3β : 5α-diacetoxyergosta-7 : 22-diene, which after chromatography and recrystallisation from methanol formed needles, m. p. 158·5—161°, $[\alpha]_D$ +51° (*c*, 0·6) (Found: C, 77·2; H, 10·15. $C_{32}H_{50}O_4$ requires C, 77·0; H, 10·1%).

3β-*Acetoxyergost-7-en-5α-ol and -8(14)-ene* (VIII) *from* 3β-*Acetoxyergosta-7 : 22-dien-5α-ol.*—The diene (400 mg.) was dissolved in ethyl acetate (150 c.c.) and shaken in hydrogen with Adams catalyst (50 mg.) until no further uptake of hydrogen occurred. The solution was filtered and evaporated until the product separated as plates, m. p. 215—225°. Recrystallisation from ethyl acetate gave 3β-acetoxyergost-7-en-5α-ol as plates (100 mg.), m. p. and mixed m. p. 224—228°, $[\alpha]_D$ +16° (*c*, 1·0).

A solution of the diene (200 mg.) in acetic acid (25 c.c.) was shaken with hydrogen in the

presence of Adams catalyst (50 mg.) for 9 hr.; 1 mol. of hydrogen was rapidly absorbed, the shaking being prolonged in order to achieve complete isomerisation of the nuclear double bond. Recrystallisation of the product from methanol gave 3β-acetoxyergost-8(14)-en-5α-ol (VIII), m. p. and mixed m. p. with an authentic sample, 160—163°, $[\alpha]_D$ −1·5° (*c*, 0·78).

3β-*Acetoxy*-5α : 8α-*epoxyergost*-22-*ene* (X; C_9H_{17} side chain).—Ergost-22-ene-3β : 5α : 8α-triol (2·0 g.) was heated under reflux for 6 hr. with 5% acetic acid in acetone (400 c.c.). The product, isolated with ether, was acetylated by treatment overnight in pyridine (20 c.c.) with acetic anhydride (10 c.c.) at 20°. The product was isolated with ether and passed in benzene solution on to deactivated alumina (200 g.). Elution with light petroleum–benzene (4 : 1) yielded fractions: (*a*) (100 mg.) which crystallised from methanol as fine needles, m. p. 112—114·5°, $[\alpha]_D$ +25° (*c*, 0·98) (this material remains unidentified); (*b*) a gum (100 mg.) from which, on crystallisation from methanol, 3β-*acetoxy*-5α : 8α-*epoxyergost*-22-*ene* was obtained as needles (60 mg.), m. p. 133—136°, $[\alpha]_D$ −35° (*c*, 1·0) (Found: C, 78·6; H, 10·45. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). Further elution with light petroleum–benzene (1 : 1) afforded crystals (630 mg.) which, after 3 crystallisations from ethyl acetate, gave 3β-acetoxyergosta-7 : 22-dien-5α-ol as platelets (100 mg.), m. p. (and mixed m. p.) 222—230°, $[\alpha]_D$ +2° (*c*, 1·0). Finally, methanol–ether (1 : 9) eluted a gum (1·2 g.) from which 3β-*acetoxyergost*-22-*ene*-5α : 8α-*diol* was obtained as small needles (from methanol), m. p. 190—195° (becoming lower on recrystallisation), $[\alpha]_D$ −61·5° (*c*, 0·75) (Found: C, 76·1; H, 10·7. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%).

3β-*Acetoxyergost*-22-*ene*-5α : 8α-*diol from Ergosta*-6 : 22-*diene*-3β : 5α : 8α-*triol* (IX) ("*Ergostadiene-triol* I").—Ergosta-6 : 22-diene-3β : 5α : 8α-triol was prepared in 60% yield, as described by Windaus *et al.* (*Annalen*, 1928, **465**, 148; 1929, **472**, 195) by treatment of ergosteryl acetate epidioxide with zinc and alkali. It had m. p. 215—225°, $[\alpha]_D$ −15° (*c*, 0·3) (the above authors give m. p. 227°, $[\alpha]_D$ −13·7°) (Found: C, 77·75; H, 10·9. Calc. for $C_{28}H_{46}O_3$: C, 78·1; H, 10·75%). The triol (300 mg.) was acetylated by treatment overnight with pyridine and acetic anhydride, and the crude product, after working up *via* ether, was shaken in hydrogen with prereduced Adams catalyst (50 mg.) and ethyl acetate (70 c.c.). Absorption of 17 c.c. of hydrogen (1 mol.) was rapid, the rate then slackening. The hydrogenation was interrupted at this point, the catalyst removed, and the solution evaporated to dryness under reduced pressure. The residue was passed in benzene on to deactivated alumina (40 g.) from which further washing with benzene eluted 70 mg. of solid (presumed 5α-hydroxy-Δ^7-material) which was discarded. The remainder of the material was recovered from the column by elution with methanol–ether (1 : 4), giving a solid (270 mg.), which after two recrystallisations from methanol gave 3β-acetoxyergost-22-ene-5α : 8α-diol as needles (60 mg.), m. p. 165—180°, $[\alpha]_D$ −61° (*c*, 0·6). The compound showed no lowering of m. p. on being mixed with an authentic sample (previous experiment) of similar m. p. (168—185°).

3β-*Acetoxyergosta*-7 : 22-*dien*-5α-*ol from* 3β-*Acetoxy*-5α : 8α-*epoxyergost*-22-*ene*.—The Δ^{22}-5α : 8α-epoxide (50 mg.) was dissolved in methanol (2 c.c.), and a trace of hydrochloric acid added. A precipitate of minute needles, m. p. 200—220°, was produced. Two recrystallisations from ethyl acetate gave 3β-acetoxyergosta-7 : 22-dien-5α-ol as small, flat needles, m. p. and mixed m. p. 222—230°, $[\alpha]_D$ +3° (*c*, 0·54).

3β-*Acetoxyergost*-7-*en*-5α-*ol from Ergosteryl Acetate Epidioxide*.—Ergosteryl acetate epidioxide (500 mg.) (in ethanol) was shaken with palladium black in hydrogen until 3 mols. had been absorbed. After filtration, the solution was evaporated to dryness. Chromatography of the residue on deactivated alumina (50 g.) gave a solid (250 mg.), m. p. 212—219°, eluted with benzene, which, after two recrystallisations from *iso*propyl alcohol, yielded 3β-acetoxyergost-7-en-5α-ol, m. p. and mixed m. p. 225—229°, $[\alpha]_D$ +18° (*c*, 1·0).

Ergost-22-*ene*-3β : 5α : 8α-*triol from* 5α : 8α-*Epidioxyergost*-22-*en*-3β-*ol*.—The sterol (1 g.; see next experiment) was shaken in the minimum amount of ethyl acetate with prereduced Adams catalyst (50 mg.) in hydrogen. The uptake almost ceased after the absorption of 1 mol. by which time the greater part of the triol (0·8 g.) had been precipitated as fine needles, m. p. 180—185°. Recrystallisation from methanol–pyridine gave material, m. p. 195—202°, $[\alpha]_D$ −67° (*c*, 1·0), showing no m. p. depression on admixture with an authentic sample, m. p. 202—215°.

3β-*Acetoxy*-5α : 8α-*epidioxyergost*-22-*ene* (III).—Ergosteryl acetate epidioxide (5·0 g.) was shaken in ethyl acetate (300 c.c.) in hydrogen together with prereduced yellow, hydrated platinum oxide (50 mg.) until 1·2 mols. of hydrogen had been absorbed. The catalyst was removed, the solution evaporated under reduced pressure, and the residue chromatographed on alumina (300 g.). Elution with benzene gave the *dihydro-acetate* (3·0 g.), plates (from ethanol) (2·3 g.), m. p. 209—215°, $[\alpha]_D$ −121° (*c*, 1·1) (Found: C, 75·95; H, 10·25. $C_{30}H_{48}O_4$ requires

C, 76·2; H, 10·25%). Hydrolysis of this in the usual manner afforded 5α : 8α-*epidioxyergost*-22-*en*-3β-*ol*, matted needles (from methanol), m. p. 175—177°, $[\alpha]_D$ −137° (*c*, 1·4) (Found : C, 77·85; H, 10·8. $C_{28}H_{46}O_3$ requires C, 78·1; H, 10·75%).

3β-*Acetoxy*-5α : 8α-*epidioxybisnorcholan*-22-*al* (IV) *and Methyl* 3β-*Acetoxy*-5α : 8α-*epidioxybisnorcholanate*.—3β-Acetoxy-5α : 8α-epidioxyergost-22-ene (2·0 g.) was dissolved in ethyl acetate (100 c.c.) and cooled to −65°. A saturated solution of ozone in ethyl acetate at −70° was added until a blue colour persisted. The solution, after having attained room temperature, was shaken with ferrous sulphate solution until no further ozone reaction (starch–iodide) was obtained. The solution was washed free from iron salts and shaken with cold aqueous 2% potassium hydroxide to extract acids (see below). The ethyl acetate solution was washed until alkali-free, dried, and evaporated to dryness under reduced pressure. The residue (1·8 g.) was passed in benzene on to deactivated alumina (100 g.). Elution with benzene afforded solid (800 mg.), m. p. 170—190°. Several recrystallisations from *iso*propyl ether gave 3β-*acetoxy*-5α : 8α-*epidioxybisnorcholan*-22-*al* as triangular plates (200 mg.), m. p. 189—199° (decomp.), $[\alpha]_D$ −113° (*c*, 1·0) (Found : C, 71·05; H, 8·85. $C_{24}H_{36}O_5$ requires C, 71·25; H, 9·0%). This gave a yellow gelatinous 2 : 4-dinitrophenylhydrazone.

The alkaline extract was acidified and the precipitated acid taken up in ether. The ethereal layer was evaporated to dryness under reduced pressure, affording a solid (300 mg.), which was crystallised once from ethyl acetate. The acid and ethereal diazomethane gave the *methyl* ester, plates (50 mg.) (from methanol), m. p. 190—195°, $[\alpha]_D$ −120° (*c*, 1·0) (Found : C, 68·85; H, 8·95. $C_{25}H_{38}O_6$ requires C, 69·1; H, 8·8%).

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