Some Oxidation Products of Ergosta-7 : 14 : 22-trien-3β-yl Acetate (Ergosterol B_3 Acetate).

By D. H. R. Barton and G. F. Laws.

[Reprint Order No. 4635.]

Photo-oxidation of ergosta-7 : 14 : 22-trien-3β-yl acetate (I; R = Ac) affords 7α : 8α-epoxy-15-oxo-14ξ-ergost-22-en-3β-yl acetate, 7α-hydroxy-15-oxo- and 15ξ-hydroxy-7-oxo-ergosta-8(14) : 22-dien-3β-yl acetate, and a hydroperoxide or peroxide the constitution of which has not been fully eludicated.* The structures assigned are based on an extensive series of further transformations.

Chromic acid oxidation of (I; R = Ac) affords 7 : 15-dioxoergosta-8(14) : 22-dien-3β-yl acetate, reduced by zinc dust and acetic acid to a mixture of 7 : 15-dioxo-8β : 14α- and -8α : 14β-ergost-22-en-3β-yl acetate. On catalytic hydrogenation followed by Clemmensen reduction both diketones give ergostan-3β-yl acetate.

Treatment of (I; R = Ac) with perphthalic acid affords, amongst other products, ergosta-8(14) : 22-diene-3β : 7ξ : 15ξ-triol 3-acetate 7-(hydrogen phthalate) which is smoothly transformed by acid into 15-oxoergosta-8(14) : 22-dien-3β-yl acetate. Reduction of the last product with lithium and liquid ammonia gives 3β-hydroxyergost-22-en-15-one, whence a number of derivatives has been obtained. The corresponding 15-oxocholestan-3β-yl acetate and derivatives have also been prepared.

The bearing of these observations on the relative stabilities of stereoisomeric steroids and on molecular-rotation correlations is briefly discussed.

The importance now assumed by the smooth photo-oxidation of steroidal homoannular dienes (Bergmann, and McLean, *Chem. Reviews*, 1941, **28**, 367; Jones, Henbest, *et al.*, *J.*, 1952, 4883, 4890, 4894; Laubach, Schreiber, Agnello, Lightfoot, and Brunings, *J. Amer. Chem. Soc.*, 1953, **75**, 1514) has led us to examine the applicability of this technique to comparable heteroannular systems, with potential cortisone syntheses in mind. In brief, we have found that, amongst readily available steroidal heteroannular dienes, only ergosta-7 : 14 : 22-trien-3β-yl acetate (ergosterol B_3 acetate) (and presumably its 7 : 14-dienic

analogues) is subject to smooth photochemical oxidation. Characterisation of the products has led us to a more extensive investigation of ergosta-7 : 14 : 22-trien-3β-ol.

Photo-oxidation of ergosta-7 : 14 : 22-trien-3β-yl acetate (I; R = Ac) gave a complex mixture of products resolved by chromatography into four homogeneous compounds. The most easily eluted was shown to be 7α : 8α-epoxy-15-oxo-14ξ-ergost-22-en-3β-yl acetate (II; R = Ac) on the following evidence. The ultra-violet absorption indicated the presence of a saturated ketone group, which was shown to be contained in a five-membered ring by the infra-red spectrum [bands at 1744 (five-ring ketone), 1736 and 1240 cm.$^{-1}$ (acetate)]. The infra-red spectrum also disclosed bands at 1302 and 896 cm.$^{-1}$ due to an epoxide grouping, and at 968 cm.$^{-1}$ due to the *trans*-ethylenic linkage in the side chain. The compound could not be acetylated or oxidised under mild conditions. Hydrogenation under acid conditions gave ergost-8(14)-en-3β-yl acetate (III; R = Ac). These observations are consistent with formula (II; R = Ac) and its correctness was confirmed by treatment with methanolic potassium hydroxide, followed by re-acetylation, which gave 15-oxoergosta-8(14) : 22-diene-3β : 7α-diol diacetate (IV; R = R′ = Ac) (see below). The formation of a comparable epoxy-ketone in the photo-oxidation of cholesta-2 : 4-diene has also been observed (Werner Bergmann, personal communication; Conca and Bergmann, *J. Org. Chem.*, 1953, **18,** 1104).

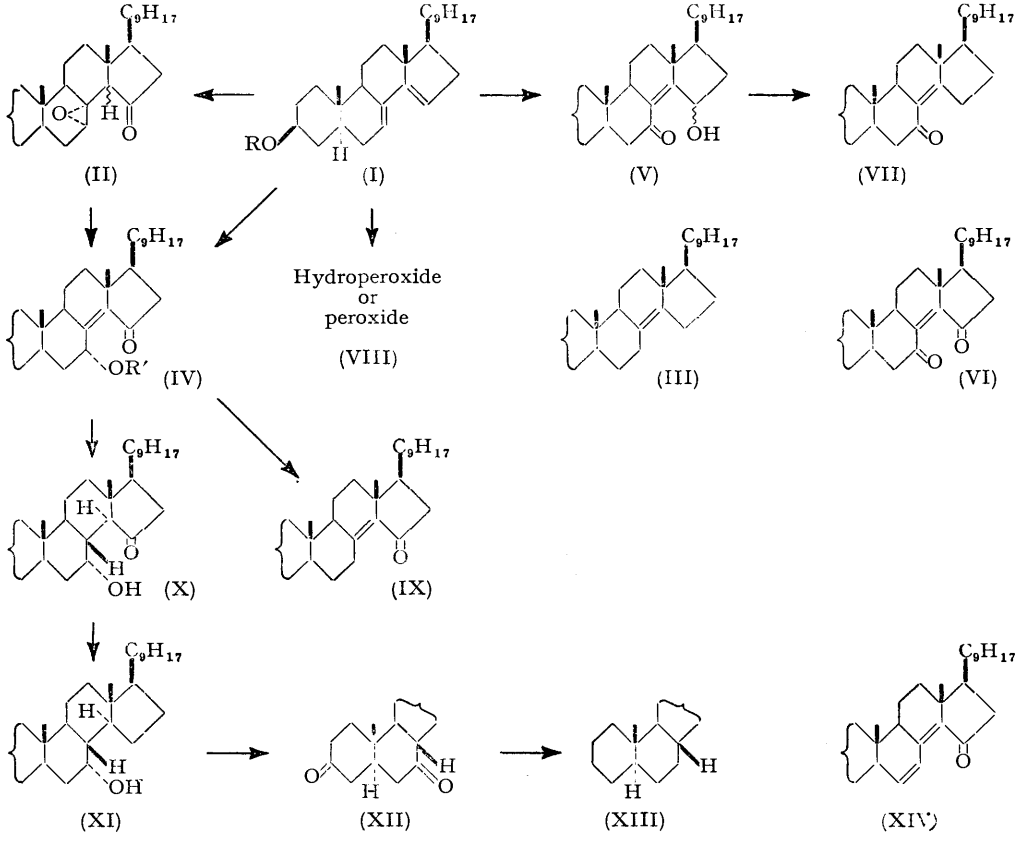
The second most easily eluted product of the photo-oxidation was shown to be 15ξ-hydroxy-7-oxoergosta-8(14) : 22-dien-3β-yl acetate (V; R = Ac). The evidence for the constitution of this compound is as follows. The ultra-violet absorption revealed the presence of an αβ-unsaturated ketone group. The infra-red spectrum [bands at 1666 (αβ-unsaturated carbonyl in a six-membered ring), 1736 and 1234 cm.$^{-1}$ (acetate)] confirmed this, and further indicated a hydroxyl group (band at 3430 cm.$^{-1}$). The presence of the latter was shown chemically by base-catalysed acetylation to give a diacetate, and by chromic acid oxidation to 7 : 15-dioxoergosta-8(14) : 22-dien-3β-yl acetate (VI; R = Ac) (see below). Hydrogenation under acid conditions gave ergost-8(14)-en-3β-yl acetate (III; R = Ac). The characterisation of the secondary hydroxyl group as contained in CO·C:C·CH(OH), and a final confirmation of structure, were secured by reduction with zinc dust and acetic acid, which gave 7-oxoergosta-8(14) : 22-dien-3β-yl acetate (VII; R = Ac) (Heusser, Saucy, Anliker, and Jeger, *Helv. Chim. Acta*, 1952, **35**, 2090) [infra-red bands (in Nujol) at 1740 (acetate) and 1670 cm.$^{-1}$ (αβ-unsaturated ketone in a six-membered ring)].

The third product of photo-oxidation was identified as a hydroperoxide or peroxide (VIII), the constitution of which has not been elucidated.

The compound eluted last in the chromatogram was shown to be 7α-hydroxy-15-oxo-ergosta-8(14) : 22-dien-3β-yl acetate (IV; R = Ac, R′ = H) on the following evidence. The ultra-violet absorption showed the presence of an αβ-unsaturated ketone group. The infra-red spectrum [bands at 1708 (αβ-unsaturated CO in a five-membered ring), 1736 and 1244 cm.$^{-1}$ (acetate)] confirmed this, and further indicated a hydroxyl group (band at 3460 cm.$^{-1}$). The latter was shown to be secondary, (*a*) by acetylation to a diacetate (IV; R = R′ = Ac) and (*b*) by chromic acid oxidation to 7 : 15-dioxoergosta-8(14) : 22-dien-3β-yl acetate (VI; R = Ac) (see below). Hydrogenation under acid conditions afforded ergost-8(14)-en-3β-yl acetate (III; R = Ac). The secondary hydroxyl group was shown to be contained in CO·C:C·CH(OH) by reduction with zinc dust and acetic acid, which furnished 15-oxoergosta-8(14) : 22-dien-3β-yl acetate (IX; R = Ac). The ultra-violet and infra-red [bands at 1734 and 1235 (acetate), 1703 (αβ-unsaturated CO in a five-membered ring), and 967 cm.$^{-1}$ (*trans*-ethylenic linkage)] absorption spectra confirmed the formulation of the latter. As expected, catalytic hydrogenation in acetic acid gave ergost-8(14)-en-3β-yl acetate (III; R = Ac).

The configuration of the hydroxyl group at $C_{(7)}$ was established in the following way. Reduction with lithium and liquid ammonia (cf. Birch, *J.*, 1944, 430 and subsequent papers; Sondheimer, Yashin, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 2696; Schoenewaldt, Turnbull, Chamberlin, Reinhold, Erickson, Ruyle, Chemerda, and Tishler, *ibid.*, p. 2696) followed by re-acetylation under mild conditions gave a monoacetate shown by the reactions outlined in the sequel to be 15-oxoergost-22-ene-3β : 7α-diol 3-acetate

(X; R = Ac). Wolff–Kishner reduction of the latter furnished ergost-22-ene-3β : 7α-diol (XI; R = H). Oxidation of the diol by chromic acid afforded ergost-22-ene-3 : 7-dione (XII), the stability of which to attempted alkaline epimerisation at $C_{(8)}$ was demonstrated. Wolff–Kishner reduction of the diketone gave ergost-22-ene (XIII), isolated and identified as the dibromide (Barton, Cox, and Holness, *J.*, 1949, 1771). These experiments show that the configurations at $C_{(8)}$ and $C_{(14)}$ in (X) and in (XI) are β and α respectively. Further



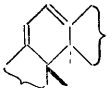
evidence on this point is presented later in connection with the chemistry of 15-oxoergosta-8(14) : 22-dien-3β-yl acetate. The molecular rotation observed for ergost-22-ene-3 : 7-dione was −195°, in excellent agreement with the calculated value of −200° [based on the known molecular rotation of ergost-22-ene (Barton, Cox, and Holness, *loc. cit.*) and calculated from the standard tables of Barton and Klyne (*Chem. and Ind.*, 1948, 755); other calculated molecular rotations in the present paper are, unless specified to the contrary, obtained in the same way]. The observed molecular rotation for ergost-22-ene-3β : 7α-diol (XI; R = H) was −100°; the calculated value for the 7α-diol is −99° in good agreement, whereas for the analogous 7β-compound it would be +70°. Similarly the observed $[M]_D$ for 15-oxoergosta-3β : 7α-diol was +19°. The calculated $[M]_D$'s for 7α- and 7β-compounds [the 15-oxo-contribution being assumed as +89° (see below)] are −10° and +159° respectively.

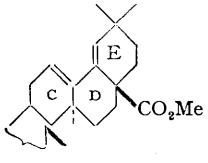
The assignment of the α-configuration at $C_{(7)}$ was confirmed as follows. Treatment of ergost-22-ene-3β : 7α-diol with pyridine–acetic anhydride gave the 3β-acetate. With pyridine–phosphorus oxychloride this lost water smoothly to furnish ergosta-7 : 22-dien-3β-yl acetate, this ready elimination being best explained by placing the hydroxyl at $C_{(7)}$ in the α(polar)-configuration (cf. Barton and Rosenfelder, *J.*, 1951, 1048). A 7β-hydroxyl (equatorial and *cis* relative to the $C_{(8)}$β-H) would have reacted to give a chloro-compound (cf. Fieser, Fieser, and Chakravarti, *J. Amer. Chem. Soc.*, 1949, **71**, 2226).

On digestion with methanolic hydrochloric acid (cf. Romo, Stork, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 2918; Lemin, Rosenkranz, and Djerassi, *ibid.*, 1953, **75**, 1745) 7α-hydroxy-15-oxoergosta-8(14) : 22-dien-3β-yl acetate afforded, after reacetylation, 15-oxoergosta-6 : 8(14) : 22-trien-3β-yl acetate (XIV; R = Ac). The constitution assigned is based on the proved structure of the precursor and on the ultra-violet absorption spectrum [$\lambda_{max.}$ 297 mμ; the calculated maximum according to Fieser, and Fieser ("Natural Products Related to Phenanthrene," Reinhold Publ. Corpn., 1949, p. 184), is 295 mμ].

In the steroid series homoannular dienes are readily converted into peroxides. We find that, of steroidal heteroannular dienes, only the *cisoid* 7 : 14-system reacts readily [3 : 5-, 7 : 9(11)-, and 8 : 14-dienes do not react]. Clearly it is the *cisoid* nature of the diene which is of dominant importance, as in the comparable reactions with maleic anhydride. However, not all *cisoid* dienes are subject to ready photochemical oxidation: α- and β-amyra-10 : 12-dienyl acetate (XV) do not react readily, nor does methyl olea-12 : 18-dienolate acetate (XVI) (Barton and Brooks, *J.*, 1951, 257). The resistance to photochemical oxidation shown by these *cisoid* dienes parallels their resistance to reaction with maleic anhydride and must be ascribed to their hindered nature.

The susceptibility of ergosta-7 : 14 : 22-trien-3β-yl acetate to oxidation by chromic acid has been examined. Oxidation with 4·4 equivalents gave (IV; R = Ac, R′ = H). Oxidation with 10 equivalents afforded 7 : 15-dioxoergosta-8(14) : 22-dien-3β-yl acetate (VI; R = Ac) as major product, together with some (IV; R = Ac, R′ = H). The constitution assigned to the 7 : 15-diketone is based on the established structure of the precursor and on the following considerations. The ultra-violet absorption [$\lambda_{max.}$ 259 mμ (ε 11,200)] is consistent with an ene-1 : 4-dione system. The infra-red spectrum showed bands at 1732 and 1234 (acetate), 1700 (αβ-unsaturated CO in a five-membered ring), 1645 (αβ-unsaturated CO in a six-membered ring) and at 970 cm.$^{-1}$ (*trans*-ethylenic linkage).* It reacted smoothly with hydrazine to give a pyridazine derivative. As expected of an ene-1 : 4-dione structure, the 8(14)-ethylenic linkage was readily reduced by zinc dust and

(XV) 



(XVI)

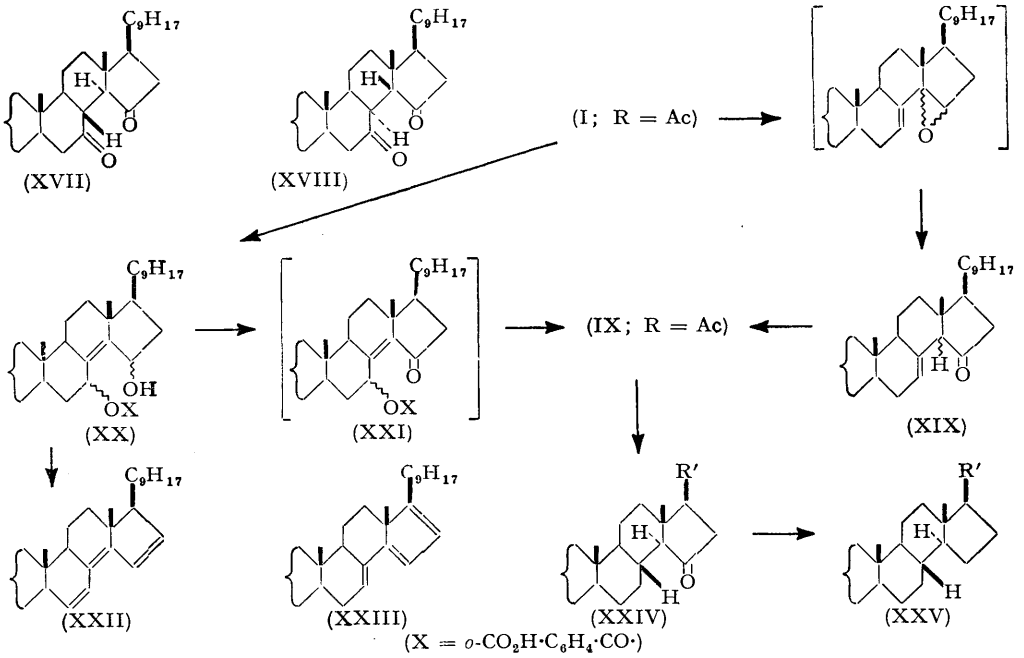
acetic acid. Two diketones were produced, both of which had the $C_{(8)}$- and $C_{(14)}$-hydrogen atoms *trans* to each other as judged by the selenium dioxide test (Barnes and Barton, *J.*, 1953, 1419). The higher-melting diketone, produced in minor amount, was readily isomerised to the lower-melting compound by treatment with methanolic potassium hydroxide followed by reacetylation. The lower-melting diketone was recovered unchanged under the same conditions. Reduction of *both* diketones by palladium-catalysed hydrogenation (to saturate the side-chain ethylenic linkage) followed by application of the Clemmensen method gave ergostan-3β-yl acetate. Thus the more stable (lower-melting) diketone is the 8β : 14α-compound (XVII; R = Ac) and the isomer probably has the 8α : 14β-configuration (XVIII; R = Ac). 7 : 15-Dioxo-8β : 14α-ergost-22-en-3β-yl acetate showed bands at 1738 (five-ring ketone), 1738 and 1240 (acetate), 1710 (six-ring ketone), and 965 cm.$^{-1}$ (*trans*-ethylenic linkage). The 8α : 14β-isomer showed bands at 1748 (five-ring ketone), 1738 and 1240 (acetate), 1720 (six-ring ketone), and 968 cm.$^{-1}$ (*trans*-ethylenic linkage). The spectra are thus in accord with the assigned constitutions.

The action of perphthalic acid on ergosta-7 : 14 : 22-trien-3β-yl acetate has afforded

* Although we regard the homogeneity and constitution of the 7 : 15-dioxoergosta-8(14) : 22-dien-3β-yl acetate described herein as established, it does not correspond in absorption spectrum or in expected molecular rotation with the compound regarded as 7 : 15-dioxoergost-8(14)-en-3β-yl acetate by Stavely and Bollenback (*J. Amer. Chem. Soc.*, 1943, **65**, 1285). The discrepancy might have been resolved if our compound had been contaminated with 15-oxoergosta-8(14) : 22-dien-3β-yl acetate, but work summarised in the Experimental section excludes this. The ultra-violet absorption spectra of the two pyridazine derivatives are, however, in good agreement.

results of interest. The triene rapidly reacted with one mol. of the per-acid. Treatment of the crude product with boron trifluoride in benzene furnished, according to the duration of the reaction, either 15-oxo-14ξ-ergost-7 : 22-dien-3β-yl acetate (XIX; R = Ac) or 15-oxoergost-8(14) : 22-dien-3β-yl acetate (IX; R = Ac). The βγ-unsaturated ketone was converted into the αβ-unsaturated isomer (IX; R = Ac) on treatment with ethanolic hydrochloric acid followed by reacetylation. The constitution assigned to (XIX; R = Ac) is based on the method of formation, the ultra-violet absorption spectrum [$\lambda_{max.}$ 293 mμ (ε 75)], the infra-red spectrum [bands at 1737 (superimposed acetate and five-ring ketone), 1238 (acetate), 972 (*trans*-ethylenic linkage), and 825 cm.$^{-1}$ (triply substituted ethylenic linkage)], and the conversion into (IX; R = Ac).

The two unsaturated ketones mentioned above are not obtained in good yield. The major product of the reaction with perphthalic acid is an unsaturated hydrogen phthalate, conveniently isolated as the sodium salt. This ester has been assigned the constitution (XX; R = Ac) on the following evidence. Oxidation by chromic acid gave an unsaturated ketone (XXI; R = Ac), not isolated in a state of purity, but reduced by zinc dust and acetic acid to (IX; R = Ac). On melting, (XX; R = Ac) decomposed to give a conjugated triene formulated as (XXII; R = Ac) on the basis of its absorption spectrum [$\lambda_{max.}$ 282 mμ; the calculated maximum according to Fieser and Fieser (*op. cit.*) is 274 mμ], its strongly positive tetranitromethane test, and the mode of preparation. The alternative

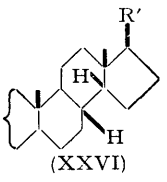


structure (XXIII) is excluded by the calculated $\lambda_{max.}$ (313 mμ) thereof and by the fact that the triene obtained did not react readily with maleic anhydride. Treatment of the sodium salt of (XX; R = Ac) with ethanolic hydrochloric acid followed by re-acetylation furnished (IX; R = Ac). The non-acidic fraction of the original perphthalic oxidation treated in the same way likewise afforded (IX; R = Ac). The total yield of the latter, based on ergosta-7 : 14 : 22-trien-3β-yl acetate, was 65%.

Reduction of (IX; R = Ac) by lithium and liquid ammonia gave 3β-hydroxyergost-22-en-15-one (XXIV; R = H, R′ = C_9H_{17}). In agreement with the assigned constitution this showed bands at 3620 (hydroxyl), 1738 (five-ring ketone), and 968 cm.$^{-1}$ (*trans*-ethylenic linkage). The 15-oxostanols thus become readily accessible compounds.* 3β-Hydroxy-

* Dr. J. Fried of the Squibb Institute for Medical Research has kindly informed us that 15-oxygenated steroids have also been isolated in his laboratory as microbiological oxidation products.

ergost-22-en-15-one was characterised as the acetate and benzoate. Wolff–Kishner reduction afforded ergost-22-en-3β-ol (XXV; R = Ac, R′ = C_9H_{17}) (Barton, Cox, and Holness, *loc. cit.*), further identified by conversion into the benzoate. Alkaline hydrolysis of the 3β-acetoxyergost-22-en-15-one, even under such drastic conditions as refluxing with 20% (w/v) ethanolic potassium hydroxide, failed to provoke inversion at $C_{(14)}$ and from this fact, as well as from the course of the Wolff–Kishner reduction, we conclude that the C–D-ring junction in saturated steroids is more stable in the *trans*- than in the *cis*(XXVI)-configuration. The assignment of the 14α-configuration in 15-oxoergost-22-en-3β-yl acetate is also supported by the molecular-rotation contribution (see Table) of the keto-group, which is +89°. For a 14β-configuration a contribution of *ca.* −425° would have been expected (Klyne, *J.*, 1952, 2916). Catalytic hydrogenation of 15-oxoergost-22-en-3β-yl acetate afforded 15-oxoergostan-3β-yl acetate (XXIV; R = Ac, R′ = C_9H_{19}) further characterised by alkaline hydrolysis to the alcohol and by benzoylation of the latter. The acetate showed bands at 1735 (acetate and five-ring ketone) and 1240 cm.$^{-1}$ (acetate); the band for the *trans*-ethylenic linkage was absent. Wolff–Kishner reduction of 3β-hydroxyergostan-15-one gave ergostan-3β-ol (XXV; R = H, R′ = C_9H_{19}).



(XXVI)

In collaboration with Dr. C. S. Barnes (see Barnes, Barton, and Laws, *Chem. and Ind.*, 1953, 616) some analogous experiments have been carried out in the cholestanol series. 15-Oxocholest-8(14)-en-3β-yl acetate was reduced by lithium and liquid ammonia to 3β-hydroxycholestan-15-one (XXIV; R = H, R′ = C_8H_{17}), characterised as the acetate, benzoate, and 2 : 4-dinitrophenylhydrazone. Wolff–Kishner reduction, as expected, gave cholestan-3β-ol (XXVI; R = H, R′ = C_8H_{17}), further characterised as the acetate. On one occasion reduction with lithium and liquid ammonia gave a saturated diol, characterised as the diacetate and dibenzoate. This is formulated as cholestan-3β : 15(?)α-diol, the α-configuration being probable because the method of preparation is such as to afford the more stable equatorial hydroxyl group (with respect to ring c) at $C_{(15)}$ (Barton, *Experientia*, 1950, **6**, 316; *J.*, 1953, 1027).

Interesting molecular-rotation data are disclosed in the Table. They show that the 15-keto-group exerts no " vicinal action " on simple acylation reactions at $C_{(3)}$ and that it has only a small effect on the Δ value for side-chain reduction. Both these observations are in accord with our previous studies in this field (Barton and Cox, *J.*, 1948, 783; Barton, Cox, and Holness, *loc. cit.*; Barton and Brooks, *J. Amer. Chem. Soc.*, 1950, **72**, 1633; Barton and Holness, *ibid.*, p. 3274).

15-Oxo-derivative of	$[M]_D$ Alcohol	Acetate	Benzoate	Δ_1	Δ_2	Ref.
			Standard values :	−29°	+ 5°	1
Ergost-22-en-3β-ol	+ 46°	+ 14° *	+ 57°	−32	+11	2
Ergostan-3β-ol	+163	+133	+179	−30	+16	2
	Δ +117	+119	+122	Standard Δ = + 103°		3
Cholestan-3β-ol	+182	+163	+197	−19	+15	2

* This value, coupled with the $[M]_D$ of −75° recorded by Barton, Cox, and Holness (*loc. cit.*) for ergost-22-en-3β-yl acetate, gives an $[M]_D$ contribution of +89° for a 15-keto-group. If the $[M]_D$'s of ergostan-3β-yl acetate (+27°; see Barton and Cox, *J.*, 1948, 1354) and of 15-oxoergostan-3β-yl acetate are used, then the $[M]_D$ contribution is +106°.

Refs.: 1, Barton and Cox, *J.*, 1948, 783; 2, Experimental section, this paper; 3, Barton, Cox, and Holness, *loc. cit.*

Experimental

For general experimental detail see *J.*, 1952, 2339. $[\alpha]_D$ were measured in $CHCl_3$, ultra-violet absorption spectra in EtOH. Infra-red spectra were kindly determined by Messrs. Glaxo Laboratories Ltd. in carbon disulphide solution and by Dr. H. M. E. Cardwell and Dr. F. B. Strauss (Oxford). The latter spectra will be reported in detail elsewhere.

Ergosta-7 : 14 : 22-*trien*-3β-*yl Acetate* (I; R = Ac).—Prepared by Barton and Brooks's method (*J.*, 1951, 257) in 35% overall yield (based on ergosterol), this had m. p. 140—141°,

$[\alpha]_D$ −221° (*c*, 2·1). In order to obtain this yield consistently it is advantageous to add 3—5% of pyridine to the (washed) chloroform solution before evaporation *in vacuo*. Otherwise chlorine-containing impurities (hydrochlorides) evolve hydrogen chloride and thus diminish the yield.

Photo-oxidation of Ergosta-7 : 14 : 22-trien-3β-yl Acetate.—(i) *Apparatus.* The solution undergoing oxidation was contained in a Pyrex glass tube (3 × 60 cm.) fitted at the lower end with a sintered-glass gas-distribution plate. The tube was held vertically and irradiated along its length by a " natural " fluorescent light (20 w; 2 ft. long) in the presence of a stream of oxygen.

(ii) *Selection of sensitising dye.* A solution of the triene (100 mg.) in absolute ethanol (300 ml.) was irradiated in the presence of dye (12—14 mg.) and oxygen. The change in position and intensity of the absorption maxima characteristic of the parent triene and/or its oxidation products was observed. In the ultra-violet measurements the appropriate blank solutions containing dissolved dye were, of course, employed. The annexed Table refers to changes produced after 16—18 hr. irradiation. Since erythrosin B appeared to be more efficient than other dyes it was used for the preparative work.

Dye	Colour	Final $\lambda_{max.}$ (mμ)	Decrease (%) in ε
Tetrabromo-(R)-fluorescein (eosin)	Red-yellow	253	58
Tetrabromo-(R)-tetrachloro-(P)-fluorescein (phloxine)	Red	253	58
Tetraiodo-(R)-fluorescein (erythrosin B)	Red	253	62
Tri-iodo-(R)-fluorescein (erythrosin A)	Red	252	50
Tetrachloro-(P)-tetraiodo-(R)-fluorescein (rose-bengal)	Red	252	61
Chlorophyll	Green	253	54
Di-iodo-(R)-dimethyl-(R)-fluorescein	Orange	243	0
Dibromo-(R)-dimethyl-(R)-fluorescein	Orange	243	0
Thionine and cyanine blue	Blue	243	0

(iii) *Typical preparative experiment.* The triene (1·0 g.) in absolute ethanol (300 ml.) containing dissolved erythrosin B (45 mg.) was irradiated overnight in a stream of oxygen. The alcohol was removed *in vacuo* and the residue dissolved in light petroleum (b. p. 40—60°) and chromatographed. Elution as indicated in detail in the sequel gave 7α : 8α-epoxy-15-oxo-14ξ-ergost-22-en-3β-yl acetate (180 mg.), 15ξ-hydroxy-7-oxoergosta-8(14) : 22-dien-3β-yl acetate (220 mg.), the hydroperoxide or peroxide (160 mg.), and 7α-hydroxy-15-oxoergosta-8(14) : 22-dien-3β-yl acetate (180 mg.).

The products of irradiation in methanol were the same as in ethanol. Further irradiation of the hydroperoxide or peroxide gave back unchanged starting material and none of the other products of reaction.

7α : 8α-Epoxy-15-oxo-14ξ-ergost-22-en-3β-yl Acetate (II; R = Ac).—This *compound*, eluted with light petroleum and crystallised from methanol as plates, had m. p. 189—190°, $[\alpha]_D$ −53° (*c*, 1·1), $\lambda_{max.}$ 300 mμ (ε 50) (Found: C, 76·7; H, 9·7. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·85%). The acetate (50 mg.) in " AnalaR " acetic acid (10 ml.) was hydrogenated overnight in presence of a platinum catalyst at room temperature. Working up in the usual way afforded ergost-8(14)-en-3β-yl acetate, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ ±0° (*c*, 2·0)}. The acetate (100 mg.) in " AnalaR " acetic acid (10 ml.) was unchanged by chromium trioxide (20 mg.) in the same solvent at room temperature overnight.

15ξ-Hydroxy-7-oxoergosta-8(14) : 22-dien-3β-yl Acetate (V; R = Ac).—This *compound*, eluted with benzene and crystallised from light petroleum as needles, had m. p. 159°, $[\alpha]_D$ −48° (*c*, 2·0), $\lambda_{max.}$ 258 mμ (ε 9500) (Found: C, 76·4; H, 9·7. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·85%). Catalytic hydrogenation as above afforded ergost-8(14)-en-3β-yl acetate, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ ±0° (*c*, 2·0)}.

The acetate (120 mg.) was refluxed with a 5% solution of anhydrous sodium acetate in acetic anhydride (10 ml.) for 1 hr. Chromatography and crystallisation from aqueous methanol afforded 3β : 15ξ-*diacetoxyergosta*-8(14) : 22-*dien*-7-*one*, m. p. 91—92°, $[\alpha]_D$ −97° (*c*, 2·2), $\lambda_{max.}$ 257 mμ (ε 10,000) (Found: C, 75·4; H, 9·7. $C_{32}H_{48}O_5$ requires C, 74·9; H, 9·45%).

The monoacetate (220 mg.) in acetic acid (30 ml.) was refluxed with zinc dust (500 mg.) for 1 hr. The product, crystallised as needles from light petroleum (b. p. 60—80°), gave 7-oxoergosta-8(14) : 22-dien-3β-yl acetate, m. p. 152°, $[\alpha]_D$ −93° (*c*, 2·2), $\lambda_{max.}$ 262 mμ (ε 10,700) (Found: C, 79·4; H, 10·2. Calc. for $C_{30}H_{46}O_3$: C, 79·25; H, 10·2%). Heusser, Saucy, Anliker, and Jeger (*Helv. Chim. Acta*, 1952, **35**, 2090) reported m. p. 154—155° (corr.), $[\alpha]_D$ −75°, $\lambda_{max.}$ 262 mμ (ε 9100).

The Hydroperoxide or Peroxide (VIII).—This compound, eluted with 4 : 1 benzene–ether and crystallised from light petroleum (b. p. 60—80°) as needles, had m. p. 164—165° (decomp.),

$[\alpha]_D$ −34° (*c*, 2·1), no selective absorption in the ultra-violet above 210 mμ (Found : C, 71·8, 71·6; H, 9·1, 9·3%).

7α-*Hydroxy*-15-*oxoergosta*-8(14) : 22-*dien*-3β-*yl Acetate* (IV; R = Ac, R′ = H).—This *compound*, eluted with 4 : 1 benzene–ether and crystallised from light petroleum (b. p. 60—80°) as needles, had m. p. 180—181°, $[\alpha]_D$ −5° (*c*, 1·8), $\lambda_{max.}$ 253 mμ (ε 12,600) (Found : C, 76·5; H, 9·7. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·85%). Acetylation with pyridine–acetic anhydride overnight at room temperature gave a mixture, separated by chromatography, of unchanged starting material and 3β : 7α-*diacetoxyergosta*-8(14) : 22-*dien*-15-*one*. Recrystallised from light petroleum (b. p. 40—60°), the latter had m. p. 150—151°, $[\alpha]_D$ +18° (*c*, 2·3), $\lambda_{max.}$ 251 mμ (ε 12,600) (Found : C, 74·5; H, 9·3. $C_{32}H_{48}O_5$ requires C, 74·95; H, 9·45%). Hydrogenation of the monoacetate in acetic acid in presence of platinum afforded ergost-8(14)-en-3β-yl acetate, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ ±0° (*c*, 2·1)}.

7α-Hydroxy-15-oxoergosta-8(14) : 22-dien-3β-yl acetate (200 mg.) in acetic acid (25 ml.) was refluxed with zinc dust (1·0 g.) for 1 hr. Recrystallisation of the product from light petroleum (b. p. 60—80°) afforded 15-*oxoergosta*-8(14) : 22-*dien*-3β-*yl acetate* as needles, m. p. 179—180°, $[\alpha]_D$ +66° (*c*, 3·3), $\lambda_{max.}$ 259 mμ (ε 15,700) (Found : C, 79·0; H, 10·0. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%). Hydrogenation in acetic acid in presence of platinum gave ergost-8(14)-en-3β-yl acetate, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ ±0° (*c*, 2·0)}.

7α : 8α-Epoxy-15-oxoergost-22-en-3β-yl acetate (see above) (100 mg.) in methanol (25 ml.) and aqueous potassium hydroxide (1 ml.; 5%) was heated under reflux until there was no further increase in the intensity of the absorption maximum at 251 mμ (2 hr.). The product, after reacetylation with pyridine–acetic anhydride at room temperature and crystallisation from light petroleum (b. p. 40—60°), was 3β : 7α-diacetoxyergosta-8(14) : 22-dien-15-one, identified by m. p., mixed m. p., and absorption spectrum [$\lambda_{max.}$ 251 mμ (ε 11,200)].

3β-*Acetoxy*-7α-*hydroxyergost*-22-*en*-15-*one* (X; R = Ac).—7α-Hydroxy-15-oxoergosta-8(14) : 22-dien-3β-yl acetate (300 mg.) in anhydrous ether (30 ml.) was added with stirring to a solution of lithium (200 mg.) in dry liquid ammonia (50 ml.) at −80°. Anhydrous ether (15 ml.) was added and the solution stirred for a further 20 min. Working up in the usual way, acetylation with pyridine–acetic anhydride at room temperature, and crystallisation from light petroleum (b. p. 60—80°), gave 3β-*acetoxy*-7α-*hydroxyergost*-22-*en*-15-*one* as long needles, m. p. 183°, $[\alpha]_D$ +4° (*c*, 1·4) (Found : C, 76·2; H, 9·95. $C_{30}H_{48}O_4$ requires C, 76·25; H, 10·25%).

Ergost-22-*ene*-3β : 7α-*diol* (XI; R = H) *and its Derivatives*.—The foregoing monoacetate (200 mg.) in absolute ethanol (1 ml.) was added to a solution of sodium (200 mg.) in absolute ethanol (2 ml.) and later also hydrazine hydrate (99%; 1 ml.). The mixture was heated in a sealed tube at 180° overnight. Crystallisation of the product from benzene–light petroleum (b. p. 60—80°) afforded *ergost*-22-*ene*-3β : 7α-*diol* as plates, m. p. 193°, $[\alpha]_D$ −24° (*c*, 2·0) (Found : C, 80·3; H, 11·3. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%). The diol (40 mg.) was treated with pyridine–acetic anhydride overnight at room temperature. The product, crystallised from aqueous methanol (28 mg.), had m. p. 120°, $[\alpha]_D$ −27° (*c*, 1·1). It must be the 3β-monoacetate (calculated $[M]_D$ for monoacetate −128°; for diacetate −212°; observed −124°). This was confirmed as follows. The monoacetate (28 mg.) in dry pyridine (1 ml.) and redistilled phosphorus oxychloride (0·5 ml.) was heated on the steam-bath for 30 min. The product, crystallised from chloroform–methanol, gave ergosta-7 : 22-dien-3β-yl acetate, identified by m. p. and mixed m. p.

Ergost-22-ene-3β : 7α-diol (200 mg.) in "AnalaR" acetic acid (5 ml.) was treated with chromium trioxide (70 mg.) in aqueous acetic acid (80%; 2 ml.) at room temperature overnight. Chromatography over alumina and crystallisation of the product from light petroleum (b. p. 60—80°) afforded *ergost*-22-*ene*-3 : 7-*dione* as plates, m. p. 202—203°, $[\alpha]_D$ −47° (*c*, 1·9) (Found : C, 81·25; H, 10·6. $C_{28}H_{44}O_2$ requires C, 81·5; H, 10·75%). The diketone (7 mg.) was refluxed with 10% methanolic potassium hydroxide for 45 min. It was recovered unchanged {m. p., mixed m. p., and rotation, $[\alpha]_D$ −43° (*c*, 0·5)}.

The diketone (66 mg.) in absolute ethanol (1 ml.) was subjected to Wolff–Kishner reduction as detailed above. The product (44 mg.) was dissolved in carbon tetrachloride (0·57 ml.) containing the theoretical amount of bromine (17 mg.) and left overnight at room temperature. Crystallisation from acetone gave ergost-22-ene dibromide, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ ±0° (*c*, 0·4)}. For the authentic specimen of the dibromide (Barton, Cox, and Holness, *loc. cit.*) we now find $[\alpha]_D$ +2° (*c*, 1·3).

15-*Oxoergosta*-6 : 8(14) : 22-*trien*-3β-*yl Acetate* (XIV; R = Ac).—7α-Hydroxy-15-oxoergosta-8(14) : 22-dien-3β-yl acetate (90 mg.) in methanol (15 ml.) and concentrated aqueous hydrochloric acid (1 ml.) was heated under reflux for 8 hr. (no further change in the ultra-violet

absorption spectrum). The product was reacetylated and chromatographed, to give 15-*oxo-ergosta*-6 : 8(14) : 22-*trien*-3β-*yl acetate*, plates (from methanol), m. p. 198—199°, $[\alpha]_D$ −35° (*c*, 1·5), $\lambda_{max.}$ 297 mμ (ε 20,400) (Found: C, 79·1; H, 9·7. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%).

Chromic Acid Oxidation of Ergosta-7 : 14 : 22-*trien*-3β-*yl Acetate*.—(a) *With* 4·4 *equivs. of oxidant.* To ergosta-7 : 14 : 22-trien-3β-yl acetate (5 g.) in " AnalaR " acetic acid (250 ml.) and " AnalaR " benzene (250 ml.) at 0° chromium trioxide (2 g.) in " AnalaR " acetic acid (120 ml.) containing a little water was added with good stirring during 30 min. The solution was left at 0° overnight. Working up in the usual way, chromatography of the product over alumina (elution with 4 : 1 benzene–ether) and recrystallisation from light petroleum (b. p. 60—80°) afforded 7α-hydroxy-15-oxoergosta-8(14) : 22-dien-3β-yl acetate (750 mg.), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +4° (*c*, 1·4)}, and absorption spectrum [$\lambda_{max.}$ 252 mμ (ε 12,800)].

(b) *With* 10 *equivs. of oxidant.* To ergosta-7 : 14 : 22-trien-3β-yl acetate (10 g.) in " AnalaR " acetic acid (150 ml.) and " AnalaR " benzene (250 ml.) at 0° chromium trioxide (7·5 g.) in " AnalaR " acetic acid (100 ml.) containing a little water was added with good stirring during 2 hr. The solution was left at 0° overnight. Working up in the usual way and crystallisation from methanol and then from light petroleum (b. p. 60—80°) gave 7 : 15-*dioxoergosta*-8(14) : 22-*dien*-3β-*yl acetate* (VI; R = Ac) (1·45 g.) as long needles m. p. 180—181°, $[\alpha]_D$ +36° (*c*, 2·3), $\lambda_{max.}$ 259 mμ (ε 11,300) (Found: C, 76·9; H, 9·3. $C_{30}H_{44}O_4$ requires C, 76·9; H, 9·45%). Chromatography of the mother-liquors afforded a further 0·75 g. of the diketone as well as 7α-hydroxy-15-oxoergosta-8(14) : 22-dien-3β-yl acetate (0·39 g.), identified by m. p., mixed m. p., rotation, and absorption spectrum.

7 : 15-Dioxoergosta-8(14) : 22-dien-3β-yl acetate was also obtained by chromic acid oxidation (3·0 equivs.) of 7α-hydroxy-15-oxoergosta-8(14) : 22-dien-3β-yl acetate and of 15ξ-hydroxy-7-oxoergosta-8(14) : 22-dien-3β-yl acetate. In each case it was identified by m. p., mixed m. p., and absorption spectrum.

In order to confirm the 8(14)-ene-7 : 15-dione structure a quantitative zinc dust reduction was carried out. 7 : 15-Dioxoergosta-8(14) : 22-dien-3β-yl acetate (100 mg.) in " AnalaR " acetic acid (10 ml.) was stirred with zinc dust (1 g.) at room temperature. The ultra-violet absorption maximum at 259 mμ was determined from time to time on an aliquot portion. The following results were obtained (*t*, in hr.): $t = \frac{1}{2}$, ε 2900; $t = 2$, ε 1800; $t = 4$, ε 1000; $t = 5$, ε 800. Under the same (quantitative) conditions 15-oxoergosta-8(14) : 22-dien-3β-yl acetate was unaffected at room temperature and under reflux.

7 : 15-Dioxoergosta-8(14) : 22-dien-3β-yl acetate (150 mg.) was treated with hydrazine as directed by Stavely and Bollenback (*J. Amer. Chem. Soc.*, 1943, **65**, 1285). The resulting *pyridazine*, recrystallised from light petroleum (b. p. 60—80°) as needles, had m. p. 250° (with charring), $\lambda_{max.}$ 261 mμ (ε 2100) (Found: C, 77·65; H, 9·7; N, 6·1. $C_{30}H_{44}O_2N_2$ requires C, 77·55; H, 9·55; N, 6·05%).

Action of Perphthalic Acid on Ergosta-7 : 14 : 22-*trien*-3β-*yl Acetate*.—(i) *Conversion into* 15-*oxoergosta*-7 : 22-*dien*-3β-*yl acetate*. Ergosta-7 : 14 : 22-trien-3β-yl acetate (4·4 g.) in anhydrous ether (120 ml.) was treated at 0° with perphthalic acid (2 mols.) in anhydrous ether (80 ml.). After 5½ hr. (consumption of 1·1 mols. of per-acid) the solution was washed with 2% aqueous sodium hydroxide and then with water. Evaporation of the ethereal solution *in vacuo* furnished a gum. This was dried azeotropically with benzene, dissolved in dry benzene (150 ml.), and treated with freshly distilled boron trifluoride–ether complex (3 ml.) overnight at room temperature. Working up in the usual way and chromatography over alumina [elution with 3 : 1 light petroleum (b. p. 40—60°)–benzene] afforded 15-*oxoergosta*-7 : 22-*dien*-3β-*yl acetate* (XIX; R = Ac) (400 mg.). Recrystallised from light petroleum this had m. p. 148—149°, $[\alpha]_D$ −39° (*c*, 2·7), $\lambda_{max.}$ 293 mμ (ε 75) (Found: C, 78·7; H, 10·0. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%). When the reaction was repeated, but the benzene solution was left for 2 days, 15-oxoergosta-8(14) : 22-dien-3β-yl acetate (20 mg. from 300 mg. of triene) was obtained.

15-Oxoergosta-7 : 22-dien-3β-yl acetate (500 mg.) in ethanol (28 ml.) containing concentrated aqueous hydrochloric acid (2 ml.) was left at room temperature. A maximum at 258 mμ due to the conjugated ketone developed. When this had reached a maximum (3 days) the mixture was worked up and the product reacetylated. Recrystallisation from light petroleum (b. p. 60—80°) furnished 15-oxoergosta-8(14) : 22-dien-3β-yl acetate (270 mg.), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +66° (*c*, 2·0)}, and absorption spectrum [$\lambda_{max.}$ 258 mμ (ε 15,600)].

(ii) *Isolation of the hydrogen phthalate and related transformations.* Ergosta-7 : 14 : 22-trien-3β-yl acetate (26·4 g.) in anhydrous ether (720 ml.) was treated at 0° with perphthalic acid (2 mols.) as above. The ethereal solution was washed with 2% aqueous sodium hydroxide.

The resulting ethereal solution was then shaken with saturated ammonium sulphate solution (500 ml.), whereupon a copious white precipitate of ergosta-8(14) : 22-diene-3β : 7ξ : 15ξ-triol 3-acetate 15-(sodium phthalate) separated. This was washed with anhydrous ether and with water and dried (23·3 g.). The residual ethereal layer was washed with water and evaporated *in vacuo*, to give a gum (15·6 g.). The sodium salt and the gum were treated separately as indicated below.

The sodium salt (22 g.) was heated under reflux in methanol (2·2 l.) and concentrated aqueous hydrochloric acid (44 ml.) until there was no further increase in the maximum at 260 mμ (1 hr.). Working up in the usual way, reacetylation of the product, and crystallisation from light petroleum (b. p. 60—80°) gave 15-oxoergosta-8(14) : 22-dien-3β-yl acetate (9·5 g.), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +68° (*c*, 2·2)}.

The gum (15 g.) in methanol (200 ml.) with addition of concentrated aqueous hydrochloric acid (10 ml.) was heated under reflux for 1 hr. Working up and reacetylation as above gave 15-oxoergosta-8(14) : 22-dien-3β-yl acetate (4·0 g.), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +68° (*c*, 2·0)}. A further 4·3 g. of slightly less pure ketone was isolated from combined mother-liquors.

The sodium salt (500 mg.) in aqueous ethanol was acidified with dilute hydrochloric acid. Crystallisation of the product from aqueous methanol afforded the corresponding *acid* as needles of indefinite m. p. [softens at 110°, m. p. (decomp.) at about 120°, resolidification at about 140°, m. p. (decomp. and charring) at 190°], $[\alpha]_D$ −91° (*c*, 3·4), $\lambda_{max.}$ 275 mμ (ε 1400) [cf. phthalic acid, $\lambda_{max.}$ 275 mμ (ε 1200)] (Found, on material dried *in vacuo* at room temperature : C, 71·9; H, 8·5. $C_{38}H_{52}O_7,CH_3{\cdot}OH$ requires C, 71·75; H, 8·65%).

The sodium salt (540 mg.) in " AnalaR " acetic acid (15 ml.) was treated with chromium trioxide (150 mg.) in acetic acid (15 ml.) containing a little water and left overnight at room temperature. After being worked up in the usual way, the resulting gum in " AnalaR " acetic acid (20 ml.) was refluxed with zinc dust (1·0 g.) for 1 hr. The product, recrystallised from light petroleum (b. p. 60—80°), furnished 15-oxoergosta-8(14) : 22-dien-3β-yl acetate (150 mg.), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +68° (*c*, 3·4)}, and absorption spectrum [$\lambda_{max.}$ 259 mμ (ε 15,400)].

Ergosta-6 : 8(14) : 15 : 22-*tetraen*-3β-*yl Acetate* (XXII; R = Ac).—The hydrogen phthalate (see above) (200 mg.) was heated *in vacuo* for 1 hr. at 90°. The resulting clear yellow melt was dissolved in ether and washed with dilute sodium hydroxide solution and water. After removal of the ether *in vacuo* and filtration in benzene solution through alumina, the product was crystallised (needles) from methanol, to give *ergosta*-6 : 8(14) : 15 : 22-*tetraen*-3β-*yl acetate*, m. p. 159—165°, $[\alpha]_D$ −104° (*c*, 1·2), $\lambda_{max.}$ 231 and 282 mμ (ε 16,100 and 8500 respectively) (Found : C, 82·3, 82·9; H, 10·1, 10·2. $C_{30}H_{44}O_2$ requires C, 82·5; H, 10·15%). The tetraene (21 mg.) in dry benzene (2 ml.) containing redistilled maleic anhydride (13 mg.) was refluxed for 4 hr. Working up gave unchanged tetraene, identified by m. p., mixed m. p., absorption spectrum, and rotation.

7 : 15-*Dioxo*-8β : 14α- *and* -8α : 14β-*ergost*-22-*en*-3β-*yl Acetate*.—7 : 15-Dioxoergosta-8(14) : 22-dien-3β-yl acetate (see above) (1·36 g.) in " AnalaR " acetic acid (75 ml.) was heated under reflux with portionwise addition of zinc dust (5 g.) during 45 min. Crystallisation of the product as plates from methanol afforded 7 : 15-*dioxo*-8(?α) : 14(?β)-*ergost*-22-*en*-3β-*yl acetate* (XVIII; R = Ac) (210 mg.), m. p. 243°, $[\alpha]_D$ −27° (*c*, 2·3) (Found : C, 76·7; H, 9·9. $C_{30}H_{46}O_4$ requires C, 76·55; H, 9·85%). Chromatography (40 fractions) of the product from the mother-liquors of these crystallisations over alumina (elution with 1 : 1 carbon tetrachloride–benzene) gave 7 : 15-*dioxo*-8β : 14α-*ergost*-22-*en*-3β-*yl acetate* (XVII; R = Ac), as needles from light petroleum (b. p. 40—60°), m. p. 126—127°, $[\alpha]_D$ −65° (*c*, 2·1) (Found : C, 76·1; H, 9·65%). Both diketones (50 mg.) were refluxed with 5% methanolic potassium hydroxide for 1 hr., reacetylated, and chromatographed over alumina. The lower-melting diketone was recovered unchanged (m. p. and mixed m. p.) but the higher-melting diketone was isomerised to the lower-melting isomer, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ −65° (*c*, 1·7)}. Both diketones (5 mg.) in ethanol (5 ml.) were refluxed with a large excess (50 mg.) of selenium dioxide for 30 min. There was no deposition of selenium and the products showed no selective absorption above 220 mμ (ε < 500).

Both 7 : 15-diketones (120 mg.) were separately hydrogenated in ethyl acetate (15 ml.) in presence of 5% palladised calcium carbonate during 30 min. After removal of the catalyst and solvent the separate reaction products were dissolved in " AnalaR " acetic acid (30 ml.) and reduced under reflux (1 hr.) by addition of amalgamated zinc (5 g.) and concentrated hydrochloric acid (4 ml.). Working up in the usual way afforded in both cases ergostan-3β-yl acetate,

identified by m. p., mixed m. p., and rotation. The identities were confirmed by hydrolysis to ergostanol (m. p. and mixed m. p.) and by benzoylation of the latter (m. p. and mixed m. p. with authentic benzoate).

3β-*Hydroxyergost-22-en-15-one and its Derivatives.*—To metallic lithium (450 mg.) in anhydrous liquid ammonia (150 ml.) at −80°, there was added with vigorous stirring 15-oxo-ergosta-8(14) : 22-dien-3β-yl acetate (1·0 g.) in dry ether (200 ml.) during 10 min. After a further 10 min.' stirring, the excess of lithium was destroyed by the addition of a little *tert.*-butanol in ether. Working up in the usual way and repeated recrystallisation of the product from methanol afforded 3β-*hydroxyergost-22-en-15-one* as plates, m. p. 180—181°, $[\alpha]_D$ +11° (*c*, 3·1) (Found : C, 81·3; H, 11·6. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%). This with pyridine–acetic anhydride overnight at room temperature afforded the corresponding *acetate*, m. p. 176—177° (from methanol), $[\alpha]_D$ +3° (*c*, 1·6) (Found : C, 78·8; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). The homogeneity of the acetate was confirmed by chromatography. Alkaline hydrolysis with 10% (w/v) methanolic potassium hydroxide and with 20% (w/v) ethanolic potassium hydroxide, both under reflux for 1 hr., gave back 3β-hydroxyergost-22-en-15-one with physical constants (m. p., mixed m. p., and rotation) as recorded above.

Treatment of 3β-hydroxyergost-22-en-15-one with pyridine–benzoyl chloride furnished the *benzoate*, long needles (from chloroform–methanol), m. p. 194—195°, $[\alpha]_D$ +11° (*c*, 2·7) (Found : C, 81·3; H, 9·7. $C_{35}H_{50}O_3$ requires C, 81·05; H, 9·7%).

3β-*Hydroxyergostan-15-one and its Derivatives.*—Hydrogenation of 15-oxoergost-22-en-3β-yl acetate in ethyl acetate for 2 hr. (5% palladised calcium carbonate) afforded 15-*oxoergostan*-3β-*yl acetate*, needles [from light petroleum (b. p. 60—80°], m. p. 173—174°, $[\alpha]_D$ +29° (*c*, 2·0) (Found : C, 78·3; H, 10·7. $C_{30}H_{50}O_3$ requires, C, 78·55; H, 11·0%). The same compound was obtained by catalytic hydrogenation of the unsaturated 15-oxo-acetate over platinum in acetic acid overnight, followed by treatment with a little chromic acid (to convert any 15-hydroxy-compound into 15-ketone).

Alkaline hydrolysis of the saturated acetate furnished 3β-*hydroxyergostan-15-one*. Recrystallised from methanol and then from light petroleum (b. p. 60—80°), this had m. p. 189—190°, $[\alpha]_D$ +39° (*c*, 2·3) (Found : C, 80·85; H, 12·0. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%). Treatment with pyridine–benzoyl chloride afforded the *benzoate*, needles [from light petroleum (b. p. 60—80°)], m. p. 173°, $[\alpha]_D$ +34° (*c*, 1·9) (Found : C, 81·2; H, 10·25. $C_{35}H_{52}O_3$ requires C, 80·7; H, 10·05%).

3β-*Hydroxycholestan-15-one and its Derivatives* [with C. S. BARNES].—Commerical 7-dehydrocholesterol (Messrs. Glaxo Laboratories Ltd.) (10 g.) was acetylated and the acetate (8·5 g.) treated with hydrogen chloride in chloroform in the usual way (cf. Barton and Brooks, *loc. cit.*). Crystallisation from chloroform–methanol gave a fraction (3 g.), enriched in cholesta-7 : 14-dien-3β-yl acetate, of m. p. 77—79°, $[\alpha]_D$ −126° (*c*, 1·86), $\lambda_{max.}$ 244 mμ (ε 11,500). This fraction was treated with perphthalic acid and the resulting (whole) product was digested with methanolic hydrochloric acid as in the preparation of 3β-hydroxyergosta-8(14) : 22-dien-15-one (see above). The crude αβ-unsaturated ketone was acetylated and then chromatographed over alumina (15 fractions). Elution with benzene–light petroleum (b. p. 40—60°) (1 : 6 to 2 : 3) gave 15-oxocholest-8(14)-en-3β-yl acetate (600 mg.), m. p. 134—135° (from chloroform–methanol), $[\alpha]_D$ +116° (*c*, 1·18), $\lambda_{max.}$ 260 mμ (ε 14,500). The physical constants are in excellent agreement with those given by Wintersteiner and Moore (*J. Amer. Chem. Soc.*, 1943, **65**, 1513).

15-Oxocholest-8(14)-en-3β-yl acetate (500 mg.) in anhydrous ether (50 ml.) was added with stirring to a solution of lithium (250 mg.) in liquid ammonia (100 ml.). The mixture was stirred for 5 min. and then *tert.*-butanol (20 ml.) was added and the solution stirred until decolorisation was complete. Crystallisation of the product from methanol gave 3β-*hydroxycholestan-15-one*, m. p. (slow heating) 174—175°, $[\alpha]_D$ +47° (*c*, 0·87) (Found : C, 80·35; H, 11·2. $C_{27}H_{46}O_2$ requires C, 80·55; H, 11·5%). Acetylation afforded the *acetate*, m. p. 141—143° (from methanol), $[\alpha]_D$ +38° (*c*, 0·90) (Found : C, 78·0; H, 11·2. $C_{29}H_{48}O_3$ requires C, 78·3; H, 10·9%), and benzoylation gave the *benzoate*, m. p. 148—149° (from methanol), $[\alpha]_D$ +40° (*c*, 0·86) (Found : C, 80·5; H, 10·4. $C_{34}H_{50}O_3$ requires C, 80·6; H, 9·95%). The 2 : 4-*dinitrophenylhydrazone*, prepared in the usual way, had m. p. 214—216° (from methanol; slow heating) (Found : N, 9·6. $C_{33}H_{50}O_5N_4$ requires N, 9·6%).

On one occasion reduction of 15-oxocholest-8(14)-en-3β-yl acetate (2 g.) as described above gave a gelatinous product. Acetylation and crystallisation from chloroform–methanol afforded the highly crystalline 3β : 15(?α)-*diacetoxycholestane* (900 mg.), m. p. 145—147°, $[\alpha]_D$ +50° (*c*, 1·99) (Found : C, 76·05; H, 10·75. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%). Alkaline hydrolysis and benzoylation afforded the corresponding *dibenzoate*, m. p. 191—192° (from

chloroform–methanol), $[\alpha]_D$ +75° (*c*, 1·16), $\lambda_{max.}$ 230, 273, and 280 mμ (ε 30,000, 1800, and 1500 respectively) (Found: C, 80·7; H, 9·25. $C_{41}H_{56}O_4$ requires C, 80·35; H, 9·2%).

Wolff–Kishner Reduction of 15-*Oxo-compounds.*—3β-Hydroxyergost-22-en-15-one (see above) (70 mg.) in absolute ethanol (1 ml.) was added to a solution of sodium (100 mg.) in absolute ethanol (2 ml.) and hydrazine hydrate (99%; 1 ml.) and heated in a sealed tube at 180° overnight. Crystallisation of the product from methanol gave ergost-22-en-3β-ol, m. p. 152°, $[\alpha]_D$ −10° (*c*, 1·9), undepressed in m. p. on admixture with an authentic specimen (Barton, Cox, and Holness, *J.*, 1949, 1771) of the same m. p. and rotation. The identity was confirmed by conversion into the benzoate, m. p. 143—144° (from chloroform–methanol), $[\alpha]_D$ −5° (*c*, 2·3), undepressed in m. p. on admixture with an authentic specimen of corresponding m. p. and rotation (Barton, Cox, and Holness, *loc. cit.*).

3β-Hydroxyergostan-15-one (50 mg.) was subjected to Wolff–Kishner reduction as above. Crystallisation of the product from chloroform–methanol gave ergostan-3β-ol, identified by m. p. mixed m. p., and rotation {$[\alpha]_D$ +15° (*c*, 1·7)}.

[With C. S. BARNES.] 3β-Hydroxycholestan-15-one (100 mg.) was subjected to Wolff–Kishner reduction as above. Crystallisation of the product from methanol afforded cholestan-3β-ol, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +24° (*c*, 1·43)}. Acetylation gave cholestan-3β-yl acetate, likewise identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +13° (*c*, 2·02)}.

We thank the Government Grants Committee of the Royal Society, the Central Research Fund of London University, and Imperial Chemical Industries Limited for financial assistance. One of us (G. F. L.) is indebted to the Nuffield Foundation and to the D.S.I.R. for maintenance grants. We are grateful to Messrs. Glaxo Laboratories Limited for gifts of chemicals. We thank Dr. J. Weiss (Newcastle) for helpful discussions on the mechanism of photochemical oxidation.

BIRKBECK COLLEGE, LONDON, W.C.1. [*Received, September 5th*, 1953.]