**833.　*Studies in the Synthesis of Cortisone.　Part XIII.
The Epimeric 3β : 7-Dihydroxyergost-22-en-11-ones.*\***

By J. Elks and G. H. Phillipps.

3β-Acetoxyergost-22-ene-7 : 11-dione is reduced by vigorous treatment
with alcoholic alkali to 3β : 7α-dihydroxyergost-22-en-11-one and, in much
smaller amounts, the 7β-epimer.　The same compounds have been prepared
by Meerwein–Ponndorf reduction of the 7 : 11-diketone, and their structures
have been proved by studies of their optical rotations and of their behaviours
under ionic-elimination conditions.

THE first methods described for the preparation of 3β-acetoxyergost-22-ene-7 : 11-dione (I)
and related 7 : 11-diketones [1] left some doubt as to the configurations of the products at
$C_{(8)}$ and $C_{(9)}$ : compound (I) was, therefore, submitted to the vigorous treatment with
alcoholic potassium hydroxide that is known to epimerise an 8β : 9β-oriented 11-ketone
to the more stable 8β : 9α-compound.[2,3]　After reacetylation of the crude product a 46%
yield was obtained of a pure compound that was not identical with the starting material.
Its formulation as a diacetoxyergostenone followed from elementary analysis, from the
infrared spectrum, and from its conversion into ergost-22-ene-3 : 7 : 11-trione (II), by
alkaline hydrolysis and subsequent chromic oxidation.　The 7-oxo-group, rather than the
11-oxo-group, of the diketone (I) had been reduced since (*a*) the product did not yield a 2 : 4-
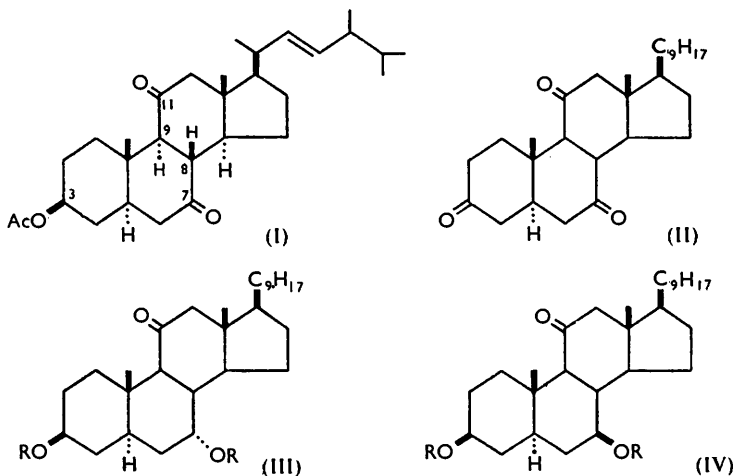


dinitrophenylhydrazone, (*b*) the diacetate differed from 3β : 11α-diacetoxyergost-22-en-7-
one [4] and (*c*) the formation of a diacetate under mild conditions excluded the 3β : 11β-di-
hydroxy-7-oxo-structure.　The dihydroxy-ketone was, therefore, a 3β : 7-dihydroxyergost-
22-en-11-one, and we show below that it was the 7α-hydroxy-isomer (III ; R = H).

* Part XII, *J.*, 1955, 2807.

[1] Rosenkranz and Sondheimer, *Fortschr. Chem. org. Naturstoffe*, 1953, **10**, 274.
[2] Bladon, Henbest, Jones, Lovell, Wood, Woods, Elks, Evans, Hathway, Oughton, and Thomas,
*J.*, 1953, 2921.
[3] Elks, Evans, Robinson, Thomas, and Wyman, *J.*, 1953, 2933.

The treatment of the diketone (I) with alcoholic alkali gave, in addition to the diol (III; R = H), a very small yield of a compound that we show below to be the epimeric 3β : 7β-dihydroxyergost-22-en-11-one (IV; R = H).

Reduction of 3β-acetoxyergost-22-ene-7 : 11-dione (I) by the Meerwein–Ponndorf procedure gave 3β : 7α-dihydroxyergost-22-en-11-one (III; R = H) as a minor product (16% yield). The major product (60% yield) was an isomer, identical with the minor product of the reduction with alcoholic potassium hydroxide; it was oxidised to ergost-22-ene-3 : 7 : 11-trione (II) and was formulated as the epimeric 7β-hydroxy-compound, *i.e.*, (IV; R = H).

The same two compounds were obtained as their acetates, both in very poor yield, by reduction of 3β-hydroxyergost-22-ene-7 : 11-dione with sodium in propan-2-ol and subsequent acetylation. Barnes and Barton [5] have since described the reduction of the diketone (I) with sodium and propanol to a mixture of ergost-22-ene-3β : 7 : 11α-triols; they attributed the 7β-structure to their major product on the basis of its rotation, but this requires correction. Professor Barton writes, " The calculated [M] values recorded by Barnes and Barton are in error; the correct values are −396° and −45° for the 3β : 7α : 11α-triacetoxyergost-22-ene and for the 7β-epimer respectively. The configuration at C$_{(7)}$ of the main sodium–propanol reduction product is therefore 7α, and not 7β as inferred previously."

In the first instance, configurations were assigned to the 7-hydroxy-groups in compounds (III) and (IV) on the basis of their optical rotations (see Table). Of the ΔM values found for our four compounds, three are in good agreement with recorded values; the fourth, that for the 7β-acetoxy-compound, has the right sign but is rather low.

It is now well established [6] that treatment of a 7α-hydroxy-steroid with phosphorus oxychloride and pyridine gives the Δ⁷-olefin, whereas a 7β-hydroxy-steroid is converted into the 7α-chloro-compound under similar conditions. Both of our compounds (III and IV; R = H) were treated in this way; since the free 3-hydroxy-group was expected to interfere, no attempt was made to isolate pure compounds, but the crude products were

*Molecular rotations of the* 3β : 7-*dihydroxyergost-22-en-11-ones and their diacetates.*

| Compound | [M] | ΔM (7-OH) | Standard values * |
|---|---|---|---|
| 3β-Hydroxyergost-22-en-11-one ........................... | +109° † | — | — |
| 3β : 7α-Dihydroxyergost-22-en-11-one (III; R = H) | +52 | −57° | ΔM (7α-OH) −59° |
| 3β : 7β-Dihydroxyergost-22-en-11-one (IV; R = H) | +191 | +82 | ΔM (7β-OH) +110 |

| | | ΔM (7-OAc) | |
|---|---|---|---|
| 3β-Acetoxyergost-22-en-11-one ........................... | +52 † | — | — |
| 3β : 7α-Diacetoxyergost-22-en-11-one (III; R = Ac) | −95 | −147 | ΔM (7α-OAc) −143 |
| 3β : 7β-Diacetoxyergost-22-en-11-one (IV; R = Ac) | +141 | +89 | ΔM (7β-OAc) +208 |

\* Barton and Klyne (*Chem. and Ind.*, 1948, 755). Note that the trivial indices used by these authors for the 7-hydroxy-epimers in the *allo*-series must be interchanged (see, *inter al.*, Heymann and Fieser, *Helv. Chim. Acta*, 1952, **35**, 631; Barton, *J.*, 1949, 2174; Fieser, Fieser, and Chakravarti, *J. Amer. Chem. Soc.*, 1949, **71**, 2226). More recent examples of 7-hydroxy-compounds give figures that agree well with those of Barton and Klyne, with the exception that in the 3β : 17β-diacetoxy-androstane series, the ΔM figures for 7β-hydroxy (+176°) and for 7α-acetoxy (−78°) are anomalous in magnitude, though correct in sign (Heusler and Wettstein, *Helv. Chim. Acta*, 1952, **35**, 284).

† Determined by us.

treated with alumina and their ultraviolet absorptions were then examined. The product from the alcohol (III; R = H) showed a strong peak at 247 mμ ($E_{1\,cm.}^{1\%}$ 202; *cf.* ref. 7), whereas that from the epimer (IV; R = H) showed general absorption only. This confirms the assignments of structure made on the basis of rotation evidence, the absorption

[4] Budziarek, Stevenson, and Spring, *J.*, 1952, 4874; Heusser, Anliker, Eichenberger, and Jeger, *Helv. Chim. Acta*, 1952, **35**, 936.

[5] Barton and Thomas (with, in part, Thomas), *J.*, 1953, 1842; Barton and Klyne, *Chem. and Ind.*, 1948, 755; Heymann and Fieser, *Helv. Chim. Acta*, 1952, **35**, 631; Barton, *J.*, 1949, 2174.

[6] Fieser, Fieser, and Chakravarti, *J. Amer. Chem. Soc.*, 1949, **71**, 2226; Heusler and Wettstein, *Helv. Chim. Acta*, 1952, **35**, 284; Buser, *ibid.*, 1947, **30**, 1379.

[7] Fieser and Fieser, " Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, 3rd Edn., p. 190.

in the product from the 7α-hydroxy-11-ketone (III) being the result, presumably, of dehydration to the 11-oxo-Δ⁷-olefin and migration of the double bond into conjugation.

The reduction of ketones to secondary alcohols by means of alkali alkoxides or alcoholic alkali (which, if the water content is low, exists largely as alkoxide [8]) has been demonstrated in both the steroid [9] and other series [10] (for earlier references see ref. 11); the stereochemistry of the reduction does not, however, appear to have been investigated.

Barton and Rosenfelder [12] have shown that reduction of 3β-acetoxycholestan-7-one with sodium and propan-1-ol gives the 7β(equatorial)- and 7α(axial)-alcohols in the ratio 78 : 22, and this may be taken as an indication of the relative thermodynamic stabilities of the epimeric groups.[13] If the conditions of the reduction of the diketone (I) with alcoholic alkali were sufficiently vigorous to establish a thermodynamic equilibrium at $C_{(7)}$, then the 7β-hydroxy-compound (IV) should predominate in the product. In fact, only 4% of this compound was isolated, whereas the 7α-hydroxy-epimer (III) was obtained in 46% yield. That this was not the result of an equilibration was confirmed when both epimers (III and IV; R = H) were recovered in high yield after being submitted to the conditions used to reduce the diketone (I).

The result, just mentioned, of the reduction of the diketone (I) with alcoholic potassium hydroxide is in striking contrast to the formation of the 7β-hydroxy-epimer (IV) in greatly preponderating amount by the Meerwein–Ponndorf reduction. Although difficult to explain on the earlier view that such hydrogen-transfer processes proceed by a similar mechanism, the difference is explicable on the view [14,15] that the aluminium alkoxides react with carbonyl compounds *via* a cyclic transition state (V), the geometry of which dictates the steric course of the reaction. If reduction by sodium ethoxide occurs as shown in (VI),[15] then, as long as equilibration does not intervene, formation of the axial hydroxy-compound should be favoured, the ethoxide ion having approached from the opposite, less hindered side. This would explain our results and also the formation of 11β-hydroxy-steroids among the products of Wolff–Kishner reduction of 11 : 12-diketones.[16] A further test was made by treating hecogenin acetate (VII; R = Ac, R' = O) with ethanolic potassium hydroxide under the conditions used in the reduction of the diketone (I). The hindrance at $C_{(11)}$ prevented side-reactions, and the product, after removal of a little unchanged ketone, was 60% of *epi*rockogenin (VII; R = H, R' = α-OH) and 40% of rockogenin (VII; R = H, R' = β-OH). This preponderance of the axial 12α-isomer is to be compared with the formation of the 12β-hydroxy-compound as the sole or major product of reduction of hecogenin by hydrogen and a platinum catalyst,[17,18] by sodium and ethanol,[17] or by lithium aluminium hydride.[19]

Dutcher and Wintersteiner [9] have shown that 3-oxo-steroids are reduced by alcoholic sodium ethoxide at 180° to mixtures of the 3α- and 3β-hydroxy-compounds in which the equatorial epimers predominate; this, however, is clearly due to establishment of thermodynamic equilibrium under these conditions.[20]

Perhaps related to these reductions by alcoholic alkali is the recent observation by Djerassi *et al.*[21] that 3-oxo-5α-steroids are reduced by ethanol in presence of aged Raney nickel to mixtures of the 3α- and 3β-hydroxy-compounds in which the former (axial)

[8] Caldin and Long, *J.*, 1954, 3737.
[9] Dutcher and Wintersteiner, *J. Amer. Chem. Soc.*, 1939, **61**, 1992.
[10] Rubin, *ibid.*, 1944, **66**, 2075; Allen, Jones, and van Allen, *J. Org. Chem.*, 1946, **11**, 268.
[11] Hargreaves and Owen, *J.*, 1947, 750.
[12] Barton and Rosenfelder, *J.*, 1951, 1048.
[13] Barton and Robinson, *J.*, 1954, 3045.
[14] Jackman and Macbeth, *J.*, 1952, 3252; Jackman, Macbeth, and Mills, *J.*, 1949, 2641.
[15] Woodward, Wendler, and Brutschy, *J. Amer. Chem. Soc.*, 1945, **67**, 1425; Doering and Aschner, *ibid.*, 1953, **75**, 393.
[16] Wintersteiner and Moore, *J. Biol. Chem.*, 1946, **162**, 725; Djerassi, Ringold, and Rosenkranz, *J. Amer. Chem. Soc.*, 1954, **76**, 5533.
[17] Marker, Wagner, Ulshafer, Wittbecker, Goldsmith, and Ruof, *ibid.*, 1947, **69**, 2167.
[18] Mueller, Norton, Stobaugh, Lin Tsai, and Winniford, *ibid.*, 1953, **75**, 4892.
[19] Hirschmann, Snoddy, Hiskey, and Wendler, *ibid.*, 1954, **76**, 4013; Elks, Phillipps, Taylor, and Wyman, *J.*, 1954, 1739.
[20] Windaus, *Ber.*, 1916, **49**, 1724.
[21] Djerassi, Manson, and Gorman, *J. Amer. Chem. Soc.*, 1955, **77**, 4925.

epimers predominate. A hydrogen-transfer mechanism appeared to be operative in this reaction.

Budziarek, Newbold, Stevenson, and Spring,[22] in preparing the diketone (I) by treatment of 3β-acetoxy-9α : 11α-epoxyergost-22-en-7-one or of 3β : 11α-diacetoxyergosta-8(9) : 22-dien-7-one with strong aqueous-alcoholic potassium hydroxide and subsequent



(V)                    (VI)                    (VII)
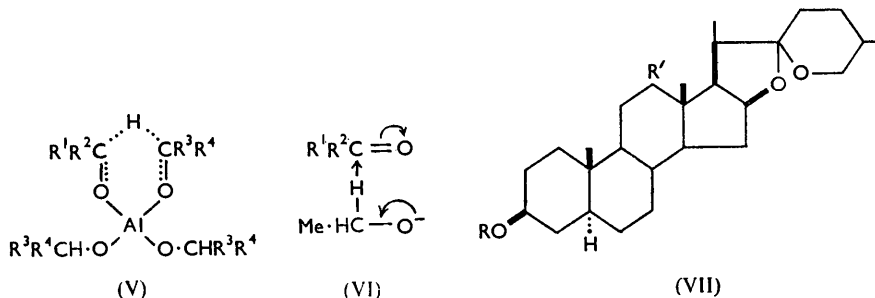
reacetylation, obtained a by-product to which they assigned the empirical formula $C_{32}H_{52}O_5$. The physical constants were similar to those of our 3β : 7α-diacetoxyergost-22-en-11-one (III; R = Ac) and comparison of the melting point and infrared spectrum of our product with those of a sample kindly provided by Prof. F. S. Spring showed them to be identical. The ethoxyl content found by Budziarek *et al.* was presumably due to solvation : the infrared spectrum showed no bands attributable to an ether link.

## EXPERIMENTAL

Rotations were determined on *ca.* 1% solutions in CHCl$_3$, unless otherwise stated. M. p.s were taken on a Kofler block. A Perkin-Elmer model 21 double-beam spectrophotometer equipped with rock-salt optics was used for the determination of infrared spectra.

*Treatment of* 3β-*Acetoxyergost-22-ene-7* : 11-dione *with Alcoholic Potassium Hydroxide.*— A solution of 3β-acetoxyergost-22-ene-7 : 11-dione (10 g.) in absolute alcohol (300 ml.) containing potassium hydroxide (60 g.) was refluxed under nitrogen for 18 hr. · Most of the alcohol was removed under reduced pressure, the residue was diluted with water to 1 l., and the flocculent precipitate was collected, dried, and heated with acetic anhydride (100 ml.) and pyridine (100 ml.) on the steam-bath for 40 min. After removal of reagents under reduced pressure, the gum crystallised from methanol as yellowish needles (4·8 g., 44%), m. p. 173—177°. Further crystallisation from aqueous ethanol or methanol gave 3β : 7α-*diacetoxyergost-22-en-11-one* as colourless needles, m. p. 175—177°, $[\alpha]_D^{20}$ −18·5° (*c* 1·0) (Found : C, 75·1; H, 9·4; Ac, 15·4; EtO, 0·88. $C_{32}H_{50}O_5$ requires C, 74·7; H, 9·8; 2Ac, 16·7; EtO, 0%). The compound showed only general ultraviolet absorption above 220 mμ, and infrared max. (in CS$_2$) at 1740 and 1245 (OAc), 1712 (CO),* and 976 cm.⁻¹ (*trans*-1 : 2-disubstituted ethylene).

The methanol mother-liquors from the first crystallisation of the above compound were evaporated to dryness and the residue was chromatographed on alumina (Peter Spence Grade H ; 180 g.). The first benzene eluates yielded an oil which, on crystallisation from methanol, gave a further 240 mg. (2%) of 3β : 7α-diacetoxyergost-22-en-11-one, m. p. 174—177°, $[\alpha]_D$ −18° (*c* 0·5). Subsequent benzene eluates, on crystallisation from methanol, gave 3β : 7β-diacetoxyergost-22-en-11-one (145 mg., 1·3%), m. p. 171—173°, $[\alpha]_D$ +26° (*c* 0·4), identical (mixed m. p. and infrared spectrum) with material prepared as described below.

The mother-liquors from these crystallisations were evaporated to dryness, and the residue was hydrolysed with boiling alcoholic potassium hydroxide. Crystallisation of the product from methanol gave 260 mg. (2·8%) of 3β : 7β-dihydroxyergost-22-en-11-one, m. p. 224—226°, $[\alpha]_D$ +44° (*c* 0·4), identified by comparison with a sample prepared as described below.

3β : 7α-*Dihydroxyergost-22-en-11-one.*—3β : 7α-Diacetoxyergost-22-en-11-one (1·5 g.) was boiled with a 4% solution of potassium hydroxide in 80% ethanol for 2 hr. Precipitation with water and crystallisation from aqueous methanol gave 3β : 7α-*dihydroxyergost-22-en-11-one* as

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* In Parts XIII—XVIII of this series (this and the following five papers), the infrared structural assignment CO indicates ketone.

²² Budziarek, Newbold, Stevenson, and Spring, *J.*, 1952, 2892.

lustrous plates (1·2 g.), m. p. 197—198°, $[\alpha]_D$ +12·6° ($c$ 0·5) (Found: C, 77·7; H, 10·4. $C_{28}H_{46}O_3$ requires C, 78·1; H, 10·8%), infrared max. (in Nujol) at 3350 (OH), 1690 (CO), and 970 cm.$^{-1}$ (*trans*-1 : 2-disubstituted ethylene).

The dihydroxy-compound, on treatment with acetic anhydride and pyridine, gave the original diacetate.

*Meerwein–Ponndorf Reduction of* 3β-*Acetoxyergost-22-ene-7 : 11-dione.*—The diketone (10 g.) and crushed aluminium *iso*propoxide (10 g.) were heated together in dry propan-2-ol (100 ml.) under an uncooled reflux condenser leading to a cooled distillation condenser. The mixture was refluxed for 1 hr. and the heating was then increased so that propan-2-ol distilled at about 4 drops per min. The volume of the mixture was kept constant by dropwise addition of fresh propan-2-ol. After 6 hr. the reaction was complete, as shown by the absence of acetone from the distillate (dinitrophenylhydrazone test). One-half of the propan-2-ol was removed under reduced pressure and the residual mixture was diluted with ether (*ca.* 1 l.) and shaken with excess of aqueous tartaric acid solution. Some solid which did not dissolve was collected and crystallised from methanol, to give 3β : 7β-*dihydroxyergost-22-en-11-one* as lustrous plates (1·5 g.), m. p. 225—228°, $[\alpha]_D$ +44° ($c$ 0·5) (Found: C, 78·25; H, 10·6. $C_{28}H_{46}O_3$ requires C, 78·1; H, 10·8%), infrared max. (in Nujol) at 3400 (OH), 1688 (CO), and 970 cm.$^{-1}$ (*trans*-1 : 2-disubstituted ethylene).

Removal of solvent from the washed and dried ether solution gave a solid residue which was crystallised from methanol (250 ml.). The first crop (2·8 g.) had m. p. 224—228° and $[\alpha]_D$ +45°, and was identical with the 7β-hydroxy-compound described above. After concentration of the mother-liquors to 100 ml., a second crop (1·8 g., m. p. 210—225°) was obtained which, on recrystallisation, gave a further 1·3 g. of the pure 3β : 7β-dihydroxy-compound (total yield 61%).

The filtrate from the second crop of crystals was diluted with water, and the resulting solid was recrystallised from aqueous methanol, giving fibrous needles (2·3 g.), m. p. *ca.* 180°, which, crystallised from aqueous acetone, gave 3β : 7α-dihydroxyergost-22-en-11-one (1·5 g., 16%), m. p. 198—201 , $[\alpha]_D$ +12·6° ($c$ 0·5), identical with the material obtained as described above.

3β : 7β-*Diacetoxyergost-22-en-11-one.*—3β : 7β-Dihydroxyergost-22-en-11-one (1·0 g.) was warmed on the steam-bath for 1 hr. with acetic anhydride (10 ml.) and pyridine (10 ml.). The solution was poured on ice, and the solid was filtered off, washed with water, and dried. Crystallisation from aqueous methanol gave 3β : 7β-*diacetoxyergost-22-en-11-one* as colourless needles (1·0 g.), m. p. 172—174°, $[\alpha]_D$ +27·5° ($c$ 1·0) (Found: C, 74·6; H, 9·6; Ac, 15·6. $C_{32}H_{50}O_5$ requires C, 74·7; H, 9·8; 2Ac, 16·7%); infrared max. (in $CS_2$) at 1736 and 1240 (OAc), 1710 (CO), and 970 cm.$^{-1}$ (*trans*-1 : 2-disubstituted ethylene).

Hydrolysis of the diacetate with 4% alcoholic potassium hydroxide gave the 3β : 7β-diol in theoretical yield.

3β-*Hydroxyergost-22-ene-7 : 11-dione.*—3β-Acetoxyergost-22-ene-7 : 11-dione (10 g.) was boiled under reflux for 2 hr. in ethanol (300 ml.) containing potassium hydroxide (3·0 g.). Dilution with water gave a flocculent precipitate which crystallised from aqueous alcohol. 3β-*Hydroxyergost-22-ene-7 : 11-dione* separated as needles (7·5 g.), m. p. 194—196°, $[\alpha]_D$ —23° ($c$ 1·0) (Found: C, 78·85; H, 10·7. $C_{28}H_{44}O_3$ requires C, 78·5; H, 10·35%), infrared max. (in Nujol) at 3600 (OH), 1700 (CO), and 970 cm.$^{-1}$ (*trans*-1 : 2-disubstituted ethylene).

Reacetylation with acetic anhydride and pyridine gave material identical with the original acetoxy-compound.

*Ergost-22-ene-3 : 11 : 20-trione.*—(a) *From* 3β-hydroxyergost-22-ene-7 : 11-dione. The diketone (1·0 g.) in acetic acid (75 ml.) was treated with a 2% solution of chromic anhydride in glacial acetic acid (12·0 ml.) and left at room temperature for 18 hr. After addition of a few drops of methanol to destroy excess of chromic acid, the solvent was removed under reduced pressure and the residue was evaporated twice with benzene to remove traces of acetic acid. The residue was then extracted with benzene (3 × 50 ml.), and the benzene solution filtered. The filtrate was reduced to 50 ml. and run on to alumina (acid-washed; 30 g.). Elution with benzene and crystallisation from aqueous methanol gave the 3 : 7 : 11-*trione* as plates, m. p. 187—189°, $[\alpha]_D$ —8° ($c$ 1) (Found: C, 78·8; H, 9·7. $C_{28}H_{42}O_3$ requires C, 78·8; H, 9·9%), infrared max. (in $CS_2$) at 1720—1710 (CO) and 970 cm.$^{-1}$ (*trans*-1 : 2-disubstituted ethylene).

(b) *From* 3β : 7β-dihydroxyergost-22-en-11-one. The dihydroxy-ketone (0·5 g.) in glacial acetic acid (50 ml.) was oxidised by addition of a 2% solution of chromic anhydride in glacial acetic acid (12·0 ml.). Isolated as in (a), ergost-22-ene-3 : 7 : 11-trione (0·3 g.) had m. p. 187—189° and $[\alpha]_D$ —8°; its identity with material prepared as in (a) was established by mixed m. p. and by comparison of infrared spectra.

(c) *From* 3β : 7α-*dihydroxyergost-22-en-11-one.* The dihydroxy-ketone (0·25 g.) in glacial acetic acid (50 ml.) was oxidised by addition of a 2% solution of chromic anhydride in glacial acetic acid (6·0 ml.). Isolated as in (a), ergost-22-ene-3 : 7 : 11-trione had m. p. 187—189° and [α]$_D$ −8°, and was shown to be identical with material prepared as in (a).

*Reduction of* 3β-*Hydroxyergost-22-ene-7* : 11-*dione with Sodium in Propan-2-ol.*—To a solution of 3β-hydroxyergost-22-ene-7 : 11-dione (3·0 g.) in warm propan-2-ol (30 ml.) pieces of sodium (6·0 g.) were gradually added. The mixture was then refluxed for 2 hr., by which time all the sodium had dissolved. After removal of most of the solvent under reduced pressure, water (*ca.* 100 ml.) was added to the residue. The precipitate was dried and heated on the steam-bath for 20 min. with acetic anhydride (25 ml.) and pyridine (25 ml.). After removal of the acetylating mixture under reduced pressure the residue was evaporated twice with methanol and twice with benzene. The gummy residue was chromatographed in benzene on alumina (90 g.; acid-washed; Peter Spence grade "H"). Evaporation of the benzene eluate (200 ml.) left a gum (0·5 g.), which crystallised from aqueous methanol in needles (0·3 g.), m. p. 173—177°, [α]$_D$ −17°. The infrared spectrum and a mixed m. p. determination showed the compound to be 3β : 7α-diacetoxyergost-22-ene-7 : 11-dione. The following 3 : 1-benzene-ether eluate (200 ml.) gave a gum (1·0 g.) which, after three crystallisations from aqueous methanol, yielded needles (0·25 g.), m. p. 173—177° and [α]$_D$ +25°, whose infrared spectrum and mixed m. p. showed the substance to be 3β : 7β-diacetoxyergost-22-ene-7 : 11-dione.

*Treatment of the 7-Hydroxy-compounds with Phosphorus Oxychloride.*—(*a*) 3β : 7α-Dihydroxy-ergost-22-en-11-one (0·5 g.) in dry pyridine (4 ml.) was heated with phosphorus oxychloride (2 ml.) in pyridine (3·5 ml.) for 2 hr. at *ca.* 100°. After being cooled the mixture was diluted to *ca.* 80 ml. with ether and treated with ice (*ca.* 10 g.). The ether solution was washed with sodium hydrogen carbonate solution, water, N-hydrochloric acid, and water, and evaporated. The gummy residue was shaken in light petroleum (50 ml.) with alumina (15 g.; Peter Spence Grade O). After 2 hr., the alumina was filtered off and washed with methanol (3 × 50 ml.). The solvents were removed from the combined petroleum and methanol filtrates under reduced pressure, to leave a gum (0·34 g.), whose ultraviolet spectrum (in EtOH) showed a maximum at 247 mμ ($E_{1\,cm.}^{1\%}$ 202).

(*b*) 3β : 7β-Dihydroxyergost-22-en-11-one (0·5 g.), treated as in (*a*), finally gave a yellow gum (0·39 g.), the ultraviolet spectrum of which showed general absorption only.

*Reduction of Hecogenin Acetate with Alcoholic Potassium Hydroxide.*—Hecogenin acetate (2·0 g.) was boiled under reflux for 18 hr. with potassium hydroxide (12·0 g.) in dry ethanol (60 ml.). The brown solution was poured into water, and the precipitated solid (1·85 g.) was filtered off and boiled under reflux for 1 hr. with Girard reagent P (1·0 g.) in ethanol (40 ml.) containing acetic acid (4·5 ml.); the solution was poured into a solution of sodium hydrogen carbonate (7 g.) in water (*ca.* 300 ml.), and the precipitate was extracted into ether. The extract was washed with water, dried (MgSO$_4$), and evaporated, to leave a solid residue (1·45 g.), m. p. 204—210°. The infrared spectrum and the rotation (−40° in acetone) of this material were consistent with its being a mixture of rockogenin (33%) and *epi*rockogenin (67%).

With acetic anhydride and pyridine at 100° it gave a mixture of rockogenin diacetate and *epi*rockogenin diacetate, [α]$_D$ −33° (*c* 1·19 in acetone) (corresponding to 39% and 61% of the respective isomers [19]), after crystallisation from methanol (Found : C, 72·1; H, 9·4. Calc. for C$_{31}$H$_{48}$O$_6$ : C, 72·05; H, 9·4%). Paper-chromatography of the mixed diols corroborated the above evidence of its constitution (for method, see ref. 23).

The aqueous layer from the Girard separation deposited 0·36 g. of crude hecogenin on acidification.

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[23] Brooks, Hunt, Long, and Mooney, *J.*, in the press.