*Steroids. Part VIII.** 3 : 5-cyclo*Ergosta*-7 : 9(11) : 22-*trien*-6β-*ol* (i-*Dehydroergosterol*).

By R. W. Rees and C. W. Shoppee.

[Reprint Order No. 5393.]

Dehydroergosteryl toluene-*p*-sulphonate has been converted by methanolysis into 6β-methoxy-3 : 5-*cyclo*ergosta-7 : 9(11) : 22-triene [*i*-dehydroergosteryl methyl ether]. Hydrolysis similarly affords the free alcohol accompanied by dehydroergosterol and a hydrocarbon, the properties of which suggest that it is 3 : 5-*cyclo*ergosta-6 : 8(14) : 9(11) : 22-tetraene.

3 : 5-*cyclo*Ergosta-7 : 9(11) : 22-trien-6β-ol [*i*-dehydroergosterol], on treatment with mineral acid at 15°, reverts to dehydroergosterol; attempts to cause its acetate and *p*-nitrobenzoate to undergo anionotropic rearrangement to a 3 : 5-*cyclo*ergosta-6 : 8 : 22-trien-11ξ-ol were unsuccessful.

The hormones of the adrenal cortex, *e.g.*, corticosterone, cortisone, and cortisol, are characterised by the presence of a substituent oxygen atom at $C_{(11)}$. One route for the partial synthesis of these compounds from naturally occurring steroids devoid of substituents in ring C involves the oxidation of steroid 7 : 9(11)-dienes with sodium dichromate dihydrate, perbenzoic, permonophthalic, performic, or peracetic acid; a second route involves merisation of a steroid 5 : 7 : 9(11)-triene to the 6 : 8(14) : 9(11)-triene, peroxidation, and hydrogenolysis of the 11 : 14-peroxide. It seemed possible that a third route could involve anionotropic rearrangement under appropriate conditions of a suitably 6-sub-

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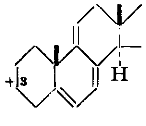
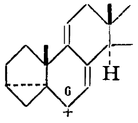
* Part VII, *J.*, 1954, 958.

stituted steroid 7 : 9(11)-diene to yield an 11-substituted steroid 6 : 8-diene, or that electromeric extension of the 3 : 5-*cyclo*steroid rearrangement * might lead directly to such a compound.

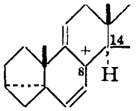
Analogy with cholesterol (Shoppee and Summers, *J.*, 1952, 3361) suggests that application of the 3 : 5-*cyclo*steroid rearrangement to dehydroergosterol should furnish a set of mesomeric carbonium ions (*A*, *B*, *C*, *D*). In the carbonium ion (*B*) there is no adjacent hydrogen atom available for expulsion as a proton, and the sole path of depolarisation is combination with an external anion, *e.g.*, OH^-, at $C_{(6)}$ to yield a 3 : 5-*cyclo*ergosta-7 : 9(11) : 22-trien-6-ol. In the ions (*A*), (*C*), and (*D*), depolarisation can be achieved by co-ordination of an external anion, *e.g.*, OH^-, at $C_{(3)}$, $C_{(8)}$, or $C_{(11)}$, to give in the last case a 3 : 5-*cyclo*ergosta-6 : 8 : 22-trien-11-ol, or by ejection of a proton from $C_{(4)}$, $C_{(14)}$, or $C_{(12)}$, respectively, to give an unsaturated hydrocarbon.



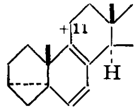
(*A*)



(*B*)

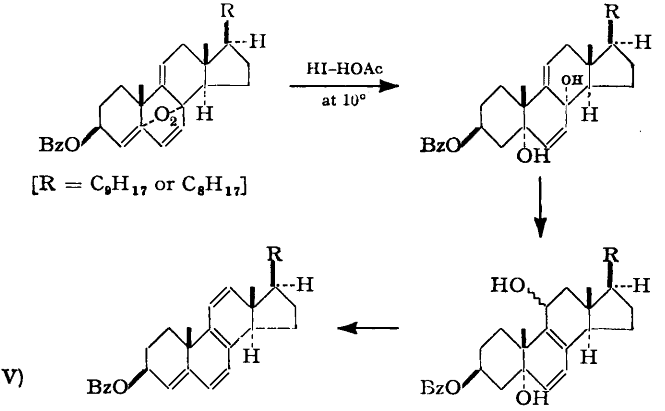


(*C*)



(*D*)

These considerations receive support from the recently reported conversion of the benzoates (I) of dehydroergosterol 5α : 8α-peroxide and of bisdehydrocholesterol 5α : 8α-peroxide, on treatment with hydriodic–acetic acid at 10° by way of labile intermediate 5α : 8α-diols (II) and 5α : 11ξ-diols (III), into ergosta-4 : 6 : 8 : 11 : 22-pentaen-3β-yl benzoate and cholesta-4 : 6 : 8 : 11-tetraen-3β-yl benzoate (IV) respectively (Feit, *Ber.*, 1953, **86**, 1252).



(I) [R = C_9H_{17} or C_8H_{17}]

(II)

(III)

(IV)

Dehydroergosteryl toluene-*p*-sulphonate (V; R = *p*-$C_6H_4Me{\cdot}SO_2$) is extremely unstable but by methanolysis in the presence of potassium acetate affords a 70% yield of a methyl ether, m. p. 53—54°, $[\alpha]_D$ +137°, $\lambda_{max.}$ 248 mμ, log ε 4·1, isomeric with dehydroergosteryl methyl ether (V; R = Me), m. p. 106°, $[\alpha]_D$ +166°, $\lambda_{max.}$ 324 mμ, log ε 4·0 (Heilbron and Simpson, *J.*, 1932, 268); we regard our ether as 3 : 5-*cyclo*ergosta-7 : 9(11) : 22-trien-6β-yl methyl ether (*i*-dehydroergosteryl methyl ether) (VI; R = Me), the β-configuration at $C_{(6)}$ being assigned by analogy with 3 : 5-*cyclo*-cholestan-6β-yl methyl ether (Shoppee and Summers, *loc. cit.*). The ultra-violet absorption characteristics are in good agreement with the values observed for cholest-7 : 9(11)-dien-3β-yl acetate, $\lambda_{max.}$ 245, 243 mμ, log ε 4·1, 4·15 (Dannenberg, *Abh. preuss. Akad. Wiss.*, 1939, **21**, 3; Dorfman, *Chem. Reviews*, 1953, **53**, 47; Fieser and Herz, *J. Amer. Chem. Soc.*, 1953, **75**, 121), and for methyl 3α-acetoxychola-

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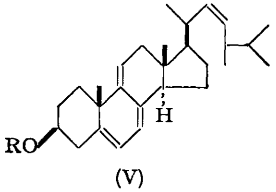
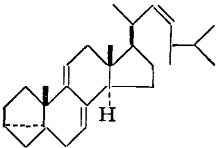
* An investigation of the application of the 3 : 5-*cyclo*steroid rearrangement to ergosterol was abandoned when it was learnt from Professor L. F. Fieser at the Symposium on Steroids at the American Chemical Society Meeting, New York, in September 1951, that such work was already proceeding at Harvard University.

7 : 9(11)-dienoate, $\lambda_{\max.}$ 244·5 mμ, log ε 4·23 (Fieser, Huang, and Babcock, *ibid.*, p. 116), and with the value $\lambda_{\max.}$ 244 mμ calculated by the method devised by Woodward (*ibid.*, 1942, **64**, 72) and extended by Fieser and Fieser ("Natural Products related to Phenanthrene," 3rd Edn., Reinhold, N.Y., 1949). They appear to exclude the structures 3 : 5-*cyclo*ergosta-6:9(11):22-trien-8ξ-yl methyl ether, derived from the cation (*C*), and 3:5-*cyclo*ergosta-6:8:22-trien-11ξ-yl methyl ether derived from the cation (*D*); the position of the ultra-violet absorption maximum in Δ^6-3 : 5-*cyclo*steroids indicates some degree of hyperconjugation (Klotz, *ibid.*, 1944, **66**, 88), producing a bathochromic shift of ~15 mμ (Karrer and Asmis, *Helv. Chim. Acta*, 1952, **35**, 1926; Fieser, Rosen, and Fieser, *J. Amer. Chem. Soc.*, 1952, **74**, 5397), so that for these structures the expected approximate values of $\lambda_{\max.}$ are 210 and 290 mμ. The infra-red absorption spectrum strongly supports the structure (VI; R = Me); a 2% solution in carbon disulphide shows maxima at 1088 (ether link), at 968 (*trans*-CHR=CHR; Δ^{22}), at 848 and 810 (CR_2=CHR; $\Delta^{9(11)}$), and at 1020 and 892 cm.$^{-1}$ (*cyclo*propane ring), whilst a 2% solution in carbon tetrachloride shows additional peaks at 1384 and 1370 cm.$^{-1}$ (*gem*-dimethyl group). By treatment with dilute sulphuric acid in dioxan, the methyl ether (VI; R = Me) undergoes rearrangement to give dehydroergosterol (V; R = H); with hydrogen chloride or bromide in acetic acid, solutions of the methyl ether (VI; R = Me) became green, turning to blue, but no crystalline products could be isolated.



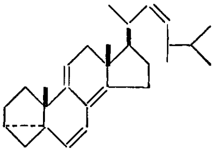
(V)

R = H; m. p. 146°, $[\alpha]_D$ +150°, $\lambda_{\max.}$ 324 mμ, log ε 4·0
R = Ac; m. p. 146°, $[\alpha]_D$ +204°
R = Me; m. p. 106°, $[\alpha]_D$ +166°



(VI)

R = H; m. p. 47°, $[\alpha]_D$ +139°, $\lambda_{\max.}$ 247 mμ, log ε 4·2
R = Ac; m. p. 38°, $[\alpha]_D$ +112°
R = Me; m. p. 53°, $[\alpha]_D$ +137°, $\lambda_{\max.}$ 248 mμ, log ε 4·1



(VII)

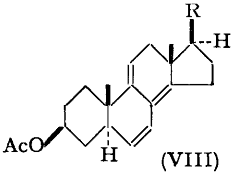
M. p. 102°, $[\alpha]_D$ +81°, $\lambda_{\max.}$ 252 mμ, log ε 4·2

Hydrolysis of dehydroergosteryl toluene-*p*-sulphonate with aqueous acetone in the presence of potassium acetate (cf. Beynon, Heilbron, and Spring, *J.*, 1937, 406) gives dehydroergosterol (V; R = H), an isomeric alcohol, m. p. 47°, $[\alpha]_D$ +139°, $\lambda_{\max.}$ 247 mμ, log ε 4·1, characterised as the acetate, m. p. 36—38°, $[\alpha]_D$ +112°, and a hydrocarbon, $C_{28}H_{40}$, m. p. 102°, $[\alpha]_D$ +81°, $\lambda_{\max.}$ 252 mμ, log ε 4·2.

The position of the ultra-violet absorption maximum at 247 mμ in the new alcohol is again consistent with a 3 : 5-*cyclo*steroid-7 : 9(11) : 22-triene structure (calc. $\lambda_{\max.}$ 244 mμ), derived from the cation (*B*), and appears to exclude the alternative structures 3 : 5-*cyclo*-ergosta-6 : 9(11) : 22-trien-8ξ-ol (calc. $\lambda_{\max.}$ 210 mμ) and 3 : 5-*cyclo*ergosta-6 : 8 : 22-trien-11ξ-ol (calc. $\lambda_{\max.}$ 290 mμ) derived from cations (*C*) and (*D*); we therefore regard the compound as 3 : 5-*cyclo*ergosta-7 : 9(11) : 22-trien-6β-ol (*i*-dehydroergosterol) (VI; R = H). It was stable to hot 2N-methanolic potassium hydroxide, but was rearranged by dilute sulphuric acid in dioxan to dehydroergosterol (V; R = H). With hydrogen chloride or hydrogen bromide in acetic acid a deep green colour was produced and an impure substance, m. p. 100—110°, $\lambda_{\max.}$ 212 mμ, containing bromine (?3β : 8ξ-dibromoergosta-6 : 9(11) : 22-triene) was isolated.

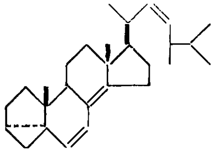
The hydrocarbon, $C_{28}H_{40}$, cannot be ergosta-3 : 5 : 7 : 9(11) : 22-pentaene, which might have been produced by internal depolarisation of the carbonium ion (*A*), because the observed absorption maximum at 252 mμ is much too low for such a structure [calc. $\lambda_{\max.}$ 353 mμ; obs. for the enol acetate of ergosta-4 : 7 : 9(11) : 22-tetraen-3-one, $\lambda_{\max.}$ 355 mμ, log ε 4·24 (Heilbron, Kennedy, Spring, and Swain, *J.*, 1938, 869)]; the alternative 2 : 4 : 6 : 9(11) : 22-pentaene [calc. $\lambda_{\max.}$ 308 mμ; obs. for cholesta-2 : 4 : 6-triene, $\lambda_{\max.}$ 305 mμ, log ε 4·15 (Schmutz, Schaltegger, and Sanz, *Helv. Chim. Acta*, 1951, **34**, 1111)] and -2 : 4 : 6 : 8 : 22-pentaene (calc. $\lambda_{\max.}$ 343 mμ) structures appear likewise to be excluded. Internal depolarisation of the cation (*C*) would furnish 3 : 5-*cyclo*ergosta-6 : 8(14) : 9(11) : 22-

tetraene (VII). The absorption maximum for this cross-conjugated system cannot be calculated, but must lie near the values 243 mμ (log ε 4·08) for cholesta-6 : 8(14) : 9(11)-trien-3β-yl acetate * (VIII; R = C_8H_{17}) observed by Windaus *et al.* (*Annalen*, 1938, **534**, 22; 1942, **552**, 135, 142), and 233 mμ (log ε 4·25) for ergosta-6 : 8(14) : 9(11) : 22-tetraen-3β-yl acetate * (VIII; R = C_9H_{17}) observed by Laubach *et al.* (*J. Amer. Chem. Soc.*, 1953, **75**, 1514). Addition of the increment for hyperconjugation of the *cyclo*propane ring (15 mμ) suggests a value for $\lambda_{max.}$ 248—258 mμ, which corresponds fairly well with the observed maximum at 252 mμ, and is consistent with the maximum reported for 3 : 5-*cyclo*ergosta-6 : 8(14) : 22-triene (IX; $\lambda_{max.}$ 260 mμ) by Fieser, Rosen, and Fieser (*ibid.*, 1952, **74**, 5397) and for 3 : 5-*cyclo*-22a-spirosta-6 : 8(14)-diene (X; $\lambda_{max.}$ 256 mμ) by Djerassi (personal communication). Internal depolarisation of the cation (*D*) would furnish 3 : 5-*cyclo*ergosta-6 : 8 : 11 : 22-tetraene, the absorption maximum of which should lie between that of cholesta-6 : 8 : 11-triene (calc. $\lambda_{max.}$ 303 mμ) and that of cholesta-4 : 6 : 8 : 11-tetraen-3β-ol [calc. $\lambda_{max.}$ 343 mμ; obs. $\lambda_{max.}$ 355 mμ, log ε 4·13 (Windaus *et al.*, *loc. cit.*), of its benzoate (IV; R = C_8H_{17}) [obs. $\lambda_{max.}$ 355 mμ, log ε 4·19 (Feit, *loc. cit.*)], and of ergosta-4 : 6 : 8 : 11 : 22-pentaen-3β-yl benzoate (IV; R = C_9H_{17}) [obs. $\lambda_{max.}$ 355; log ε 4·23 (Feit, *loc. cit.*)]. We therefore regard the hydrocarbon, $C_{28}H_{40}$, as 3 : 5-*cyclo*ergosta-6 : 8(14) : 9(11) : 22-tetraene (VII), despite its anomalous reaction with perbenzoic acid. Although all types of steroid nuclear double bond react with perbenzoic acid, the hydrocarbon on treatment with an excess of perbenzoic acid absorbed only 2 instead of 4 equivalents of oxygen. Difficulty was also encountered in catalytic hydrogenation of the hydrocarbon; hydrogenation with platinum–acetic acid–dioxan stopped completely after 3 mols. had been adsorbed, and the product was still unsaturated towards tetranitromethane. Further hydrogenation with platinum–acetic acid at 70—100°/150 atm. furnished material still unsaturated to tetranitromethane, from which crystalline fractions could not be obtained.



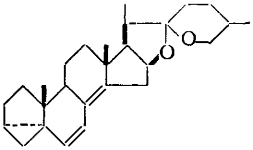
(VIII)

R = C_8H_{17}; m. p. 102°, $\lambda_{max.}$ 243 mμ, log ε 4·08
R = C_9H_{17}; m. p. 151°, $[\alpha]_D$ −94°, $\lambda_{max.}$ 233 mμ, log ε 4·25



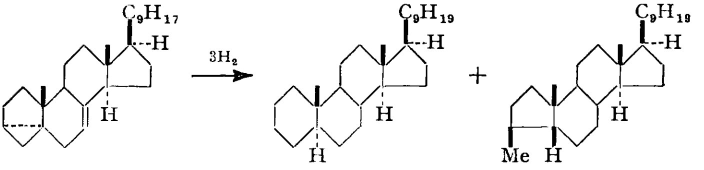
(IX)

M. p. 102°, $[\alpha]_D$ +92°, $\lambda_{max.}$ 260 mμ, log ε 4·4



(X)

M. p. 172°, $[\alpha]_D$ +108°, $\lambda_{max.}$ 256 mμ, log ε 4·3



(XI) (XII) (XIII)

Since hydrogenation of 3 : 5-*cyclo*ergosta-7 : 22-diene (XI) gives a mixture of a little ergostane (XII), m. p. 84°, with much 3β-methyl-A-nor-5β-ergostane (XIII), m. p. 77° (Karrer and Asmis, *Helv. Chim. Acta*, 1952, **35**, 1926), and since steroid 8(14)-double bonds resist hydrogenation—*e.g.*, Bladon *et al.* (*J.*, 1951, 2402), prepared 3β-acetoxyergost-8(14)-ene [" α "-ergostenyl acetate] from 3β-acetoxyergosta-7 : 22-diene by hydrogenation with platinum–acetic acid–ether at 100°/100 atm.—we consider that our product is probably a mixture of the hydrocarbon (XIII) and ergost-8(14)-ene, m. p. 80° (Heilbron, Spring, and Webster, *J.*, 1932, 1705).

Whilst the infra-red spectra of the above non-crystalline fractions showed only a general likeness to that of authentic ergost-8(14)-ene (Bladon *et al.*, *loc. cit.*), nevertheless,

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* These compounds exhibit a secondary maximum at $\lambda_{max.}$ 285 mμ, log ε 3·96 and at $\lambda_{max.}$ 288 mμ, log ε 3·82 respectively.

the hydrocarbon structure (VII) is strongly supported by the infra-red absorption spectrum; a 2% solution of (VII) in carbon disulphide shows maxima at 968 [*trans*-CHR=CHR; Δ^{22}], at 824 and 810 [CR_2=CHR; $\Delta^{9(11)}$], at 764 and 742 [*cis*-CHR=CHR; Δ^{6}], and at 1020 and 884 cm.$^{-1}$ (*cyclo*propane ring), whilst a 2% solution in carbon tetrachloride shows additional peaks at 1382 and 1365 cm.$^{-1}$ (*gem*-dimethyl group).

Mobility in anionotropic systems is promoted (*a*) by catalysis by acids, (*b*) by media of high dielectric constant, and (*c*) by the increasing stability as an anion of the migrating group ($OH < OAc < \cdot O\cdot CO\cdot C_6H_4\cdot NO_2\text{-}p < Hal$) (Burton and Ingold, *J.*, 1928, 904, 1650). The conversion of the 3 : 5-*cyclo*-6β-ol (VI; R = H) into an 11ξ-hydroxy-steroid by catalysis by mineral acid was precluded because the conjugate acid of the former has been shown to revert to dehydroergosterol (V; R = H); we were therefore confined to an examination of the effect of factors (*b*) and (*c*). The 3 : 5-*cyclo*-6β-yl acetate was unchanged when heated with acetic anhydride (dielectric constant 20) or with methyl cyanide (dielectric constant 39); the 3 : 5-*cyclo*-6β-yl *p*-nitrobenzoate was likewise unaffected. The 3 : 5-*cyclo*-6β-yl *p*-nitrobenzoate was also heated with pyridine (dielectric constant 12) at 140° in the presence of added pyridinium *p*-nitrobenzoate (cf. Burton, *J.*, 1934, 1268), but was recovered unaltered. It seems unlikely that conditions suitable for the conversion of a 3 : 5-*cyclo*-steroid-7 : 9(11)-diene-6-ol into an 11ξ-hydroxy-steroid can be devised, but we are investigating the possible anionotropic conversion of other steroid-7 : 9(11)-dien-6-ols into 11ξ-hydroxy-steroids.

EXPERIMENTAL

For general experimental directions, see preceding paper. $[\alpha]_D$ are in $CHCl_3$ unless otherwise stated, whilst ultra-violet absorption spectra were determined in EtOH on a Unicam SP.500 spectrometer with corrected scale and infra-red absorption spectra in CS_2 on a Perkin–Elmer double-beam instrument,

Dehydroergosteryl Toluene-p-*sulphonate.*—Dehydroergosterol (20 g.; dried by azeotropic distillation with benzene), dissolved in dry pyridine (20 c.c.), was treated with a solution of purified toluene-*p*-sulphonyl chloride (20 g.; dried at 20°/0·01 mm.) in dry pyridine (50 c.c.) in an atmosphere of dry nitrogen. The solution was kept at 30—35° for 10 min., left overnight at 10°, and poured into a saturated solution of sodium hydrogen carbonate. After 1 hr., the precipitate was filtered off, washed with water and methanol, and recrystallised from acetone to give *dehydroergosteryl toluene*-p-*sulphonate* (19 g.), m. p. 130° (decomp. with production of a red colour), $[\alpha]_D^{20}$ +170° (*c*, 2·80) * [Found (after drying at 15°/0·02 mm. for 4 hr.): C, 76·9; H, 8·9. $C_{35}H_{48}O_3S$ requires C, 76·6, H, 8·8%] (cf. Buisman and Westerhof, *Rec. Trav. chim.*, 1952, **71**, 925). A similar product was obtained by the procedure described by Karrer and Asmis (*Helv. Chim. Acta*, 1952, **35**, 1926). The toluene-*p*-sulphonate is a white crystalline solid, which rapidly becomes yellow and after some months decomposes to a black tar. It could be chromatographed on neutral aluminium oxide in pentane, elution with pentane giving a specimen, m. p. 140—143° (decomp.), whose m. p. dropped to 130—135° during a few days at room temperature; use of alkaline aluminium oxide in pentane led to decomposition since elution with pentane and benzene–pentane (1 : 19) gave oils, which slowly solidified, and by crystallisation from acetone–methanol gave material, m. p. 100°, probably consisting essentially of 3 : 5-*cyclo*ergosta-6 : 8(14) : 9(11) : 22-tetraene (VII).

3 : 5-cyclo*Ergosta*-7 : 9(11) : 22-*trien*-6β-*yl Methyl Ether* (VI; R = OMe).—Dehydroergosteryl toluene-*p*-sulphonate [m. p. 130° (decomp.); 4 g.] was heated with anhydrous potassium acetate (12 g.; freshly fused) in dry methanol (800 c.c.) for 4 hr. Methanol (400 c.c.) was removed by distillation and then by evaporation at 35°/10 mm.; after addition of water, the product was extracted with ether, and the extract washed with water, dried, and evaporated. The resultant oil (3·3 g.) was chromatographed on aluminium oxide (100 g.) in pentane. Elution with pentane (5 × 300 c.c.) yielded material (total 2·30 g.) which crystallised; by recrystallisation from methanol this gave 3 : 5-cyclo*ergosta*-7 : 9(11) : 22-*trien*-3β-*yl methyl ether*, m. p.

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* It may be useful to record that cholesteryl toluene-*p*-sulphonate has $[\alpha]_D^{15}$ −39° (*c*, 2·20), and to note that 7-dehydrocholesteryl toluene-*p*-sulphonate, m. p. 105° (decomp.) (B, K), has $[\alpha]_D$ −38° (K), whilst ergosteryl toluene-*p*-sulphonate, m. p. 114° (B), 116° (F), 105° (K) (decomp.), has $[\alpha]_D$ −119° (!) (B), −45° (F), −46° (K) [B = Buisman and Westerhof (*loc. cit.*); F = Fieser, Rosen, and Fieser (*J. Amer. Chem. Soc.*, 1952, **74**, 5397); K = Karrer and Asmis (*loc. cit.*)]. The increments in $[M]_D$ for conversion of $\text{-OH} \longrightarrow O\cdot SO_2\cdot C_6H_4Me\text{-}p$ thus appear to increase from zero for cholesterol to +250° for $\Delta^{5:7}$-sterols and to +350° for a $\Delta^{5:7:9(11)}$-sterol.

53—54°, $[\alpha]_D^{20}$ +137° (*c*, 1·97), $\lambda_{max.}$ 248 mμ, log ε 4·1 [Found (after drying at 15°/0·01 mm. for 18 hr.): C, 85·0; H, 10·8; OMe, 8·1. $C_{29}H_{44}O$ requires C, 85·2; H, 10·85; OMe, 7·6%]; the compound gave a positive Rosenheim test (red → intense green), and a positive Tortelli–Jaffé test (intense green). Elution with benzene yielded yellow solid material (228 mg.), giving by crystallisation from acetone an unidentified substance, m. p. 174—175° with decomp. at 180°, $[\alpha]_D$ −7° (*c*, 1·07), $\lambda_{max.}$ 226 mμ, log ε 4·2 (if M = 400) [Found (after drying at 15°/0·01 mm. for 18 hr.): C, 75·65; H, 9·4; OMe, 3·4%].

The methyl ether (270 mg.), dissolved in 90% dioxan (50 c.c.), was treated with 2N-sulphuric acid (0·35 c.c.) at 15° for 15 hr. The product, isolated in the usual way, was chromatographed on aluminium oxide; elution with pentane yielded some oil, but elution with benzene and ether–benzene (1 : 1) furnished dehydroergosterol, m. p. 144°, mixed m. p. 144—146°.

The methyl ether (700 mg.) was treated with acetic acid (100 c.c.) containing 48% hydrobromic acid (10 c.c.) at 15°; the solution at once became dark green, and after being kept overnight contained a yellow precipitate, which was filtered off (m. p. 92—93°). This material, which contained bromine, could not be crystallised satisfactorily from any solvent. The filtrate furnished a brown oil, which was dissolved in benzene–pentane and filtered through aluminium oxide; the resulting yellow oil did not crystallise. It contained bromine, and was refluxed with zinc dust in acetic acid for 1 hr.; chromatography of the reduction product gave only oils (eluted with pentane).

3 : 5-cyclo*Ergosta*-7 : 9(11) : 22-*trien*-6β-*ol* (VI; R = H) *and* 3 : 5-cyclo*Ergosta*-6 : 9(11) : 8(14) : 22-*tetraene* (VII).—Dehydroergosteryl toluene-*p*-sulphonate (4·36 g.) was heated with potassium acetate (10 g.) in aqueous acetone (2 : 1; 375 c.c.) for 6 hr. The product, isolated in the usual way after removal of acetone at 10 mm., was an oil (3·48 g.) which soon crystallised and was chromatographed on aluminium oxide (100 g.) in pentane. Elution with pentane (300 c.c.) yielded crystals (160 mg.) which, recrystallised from acetone, gave 3 : 5-cyclo*ergosta*-6 : 9(11) : 8(14) : 22-*tetraene* (VII) as needles, m. p. 102°, $[\alpha]_D^{20}$ +81° (*c*, 2·00), $\lambda_{max.}$ 252 mμ, log ε 4·2 [Found (after drying at 60°/0·03 mm. for 4 hr.): C, 88·8; H, 10·8. $C_{28}H_{40}$ requires C, 89·3; H, 10·7%]; the hydrocarbon gave a deep orange colour with tetranitromethane, and positive Rosenheim (green) and Tortelli–Jaffé tests. Further elution with pentane (4 × 300 c.c.) gave oils (total 1·41 g.), which slowly solidified and by recrystallisation from acetone–methanol furnished 3 : 5-cyclo*ergosta*-7 : 9(11) : 22-*trien*-6β-*ol* (VI; R = H), m. p. 46—47°, $[\alpha]_D^{15}$ +139° (*c*, 1·107), $\lambda_{max.}$ 247 mμ, log ε 4·2 [Found (after drying at 15°/0·02 mm. for 20 hr.): C, 85·0; H, 10·6. $C_{28}H_{42}O$ requires C, 85·2; H, 10·7%], giving positive Rosenheim (green) and Tortelli–Jaffé tests; it was characterised by preparation (acetic anhydride–pyridine at 15° for 15 hr.) of the *acetate*, which crystallised on cooling in the presence of acetone–methanol, and, recrystallised with some difficulty from methanol at −80°, had m. p. 36—38°, $[\alpha]_D^{15}$ +112° (*c*, 0·61) [Found (after drying at 20°/0·01 mm. for 4 hr.): C, 82·8; H, 10·2. $C_{30}H_{44}O_2$ requires C, 82·5; H, 10·15%], and the p-*nitrobenzoate*, needles (from methanol), m. p. 82—85° [Found: N, 2·7. $C_{35}H_{45}O_4N$ requires N, 2·6%]. Further elution with pentane (2 × 300 c.c.) yielded uncrystallisable material (128 mg.), but use of benzene–pentane mixtures gave dehydroergosterol, m. p. and mixed m. p. 146°, $[\alpha]_D^{15}$ +155° (*c*, 1·40), after recrystallisation from acetone; elution with benzene and with ether also gave dehydroergosterol (total, 1·80 g.). From some experiments, carried out under conditions apparently identical with those described, only 3 : 5-*cyclo*ergosta-6 : 9(11) : 8(14) : 22-tetraene (VII) and dehydroergosterol could be isolated; this inconsistency is to be attributed to variation in the quality of dehydroergosteryl toluene *p*-sulphonate produced in different preparations.

3 : 5-*cyclo*Ergosta-7 : 9(11) : 22-trien-6β-ol (m. p. 46°; 115 mg.) was refluxed with methanolic 2N-potassium hydroxide for 2·5 hr.; cooling, addition of a few drops of water, saturation with carbon dioxide, and vacuum-evaporation gave unchanged material (95 mg.), m. p. 44° after crystallisation from acetone–methanol. The 3 : 5-*cyclo*trien-6β-ol (110 mg.), dissolved in 90% aqueous dioxan (15 c.c.), was treated with 2N-sulphuric acid (0·13 c.c.) at 15° for 24 hr.; the product (95 mg.), isolated in the usual way, was chromatographed on a long column of aluminium oxide (6 g.) prepared in pentane. Elution with pentane (3 × 10 c.c.) gave starting material (8 mg.), m. p. 45°, after crystallisation from acetone–methanol; elution with benzene–pentane mixtures furnished no material, but use of benzene and ether–benzene (1 : 1) gave dehydroergosterol (57 mg.), m. p. 144° after recrystallisation from methanol. The 3 : 5-*cyclo*trien-6β-ol (50 mg.) was dissolved in ether and shaken with 2N-hydrochloric acid but no colour developed and the starting material was recovered; when the 3 : 5-*cyclo*trien-6β-ol (110 mg.) was dissolved in acetic acid (10 c.c.) and treated with concentrated hydrochloric acid (1 c.c.) at 15°, the solution immediately became dark green, but after 24 hr. no crystalline product could be isolated by chromatography. When the

3 : 5-*cyclo*trien-6β-ol (102 mg.) was treated in acetic acid (10 c.c.) with 48% hydrobromic acid (1 c.c.) at 15°, the solution at once became dark green. Next morning, the product was isolated in the usual way as a brown oil (105 mg.) which solidified partially on being rubbed with pentane. The material, dissolved in benzene–pentane (1 : 4), was filtered through a column of aluminium oxide (5 g.), to yield a coloured solid which could not be satisfactorily purified by crystallisation or chromatography. The product, m. p. 100—110°, $\lambda_{max.}$ 212 mμ, contained bromine and gave a negative Rosenheim test.

3 : 5-*cyclo*Ergosta-6 : 9(11) : 8(14) : 22-tetraene (VII) (44·5 mg.) was treated with a chloroform solution (6·0 c.c.) of perbenzoic acid (23 mg./c.c.) for 3 days at 20°; at the end of this period the concentration in a blank experiment was unchanged, and the perbenzoic acid consumed was 33·5 mg. (2·05 mols.). In another experiment with the hydrocarbon (110 mg.) at 0°, the perbenzoic acid consumed was 57 mg. (1·41 mols.).

3 : 5-*cyclo*Ergosta-6 : 9(11) : 8(14) : 22-tetraene (45 mg.), dissolved in pure dry carbon tetrachloride (3 c.c.), by titration with a solution of bromine in carbon tetrachloride (17·2 mg./c.c.) required 5·50 c.c. (9·8 atom-equiv. of Br) to give a faint yellow colour; at 20° the solution rapidly darkened, to give finally a green amorphous precipitate.

3 : 5-*cyclo*Ergosta-6 : 9(11) : 8(14) : 22-tetraene (89 mg.), dissolved in pure dioxan (5 c.c.) and acetic acid (50 c.c.), was hydrogenated with pre-reduced platinum oxide (42 mg.) at 19°. Hydrogenation ceased after 50 min. and no further absorption occurred during 40 min. (16·4 c.c., 2·92 mols.); the product (101 mg.), obtained from the filtered solution by evaporation at 20°/0·1 mm. for 5 hr., could not be caused to crystallise and gave a yellow colour with tetranitromethane–chloroform. Further hydrogenation was attempted with platinum oxide in acetic acid at 70—100°/150 atm. in a Cook autoclave for 5 hr.; the cooled solution was filtered, the filtrate evaporated in a vacuum, and the residue dissolved in purified ethyl acetate. The solution was washed with water, treated with charcoal, dried, filtered through a layer of magnesium sulphate, and evaporated. The residue (84 mg.) still gave a yellow colour with tetranitromethane–chloroform; chromatography on aluminium oxide (3 g.) and elution with pentane and with hexane gave 4 fractions (5 mg.; 42 mg.; 28 mg.; 5 mg.), of which Nos. 2 and 3 failed to crystallise on inoculation with ergost-8(14)-ene although giving a yellow colour with tetranitromethane–chloroform.

Attempted Anionotropic Rearrangement.—3 : 5-*cyclo*Ergosta-7 : 9(11) : 22-trien-6β-yl acetate (VI; R = Ac) (50 mg.) was heated with acetic anhydride (5 c.c.) in a small ampoule at 100° for 5 hr.; the product, obtained by vacuum-evaporation and crystallisation from methanol at −80°, was unchanged (m. p. 35—38°). A similar experiment with methyl cyanide also failed.

3 : 5-*cyclo*Ergosta-7 : 9(11) : 22-trien-6β-yl *p*-nitrobenzoate (60 mg.) was dissolved in pyridine (3 c.c.) containing *p*-nitrobenzoic acid (30 mg.), and the solution heated in a small bomb-tube at 140° for 12 hr. The cooled, dark red solution was evaporated in a vacuum, and the product extracted with ether; the ethereal solution was washed with 2N-hydrochloric acid, water, and sodium hydrogen carbonate solution, dried, and evaporated. The residue by recrystallisation from methanol gave unchanged starting material (26 mg.), m. p. 82—85°. No other crystalline product could be isolated.

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