905. 3 : 5-cyclo*Ergosta*-7 : 22-*dien*-6β-*ol* *and* 3 : 5-cyclo*Ergosta*-7 : 9(11) : 22-*trien*-6β-*ol*.

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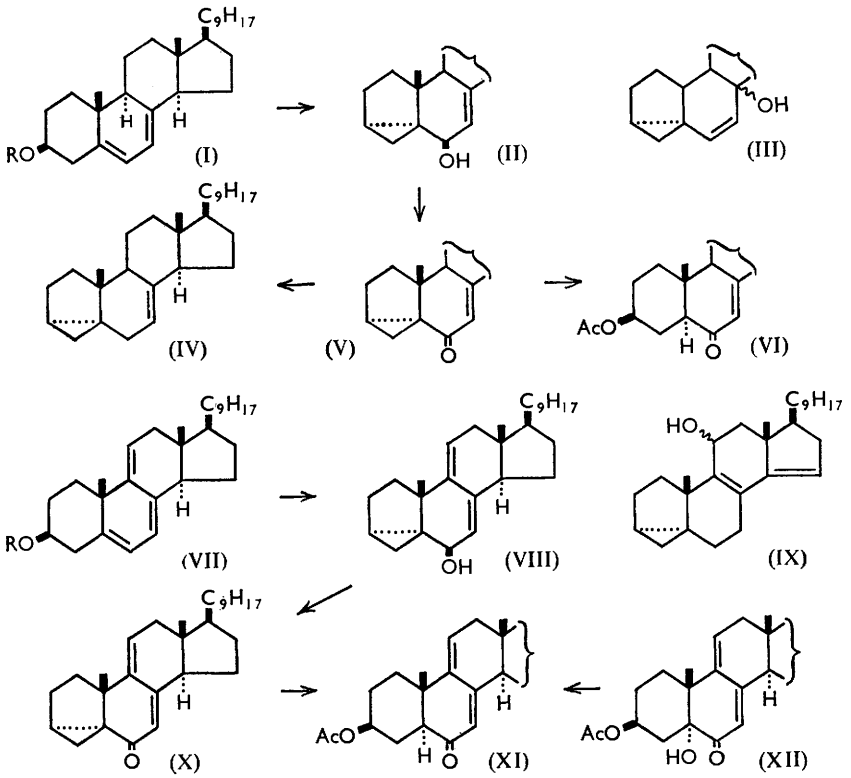
Chemical evidence confirming the correctness of the formulations of the compounds in the title given by Nes and Steele [1] is presented.

It is generally accepted that the formation of 6-substituted 3 : 5-*cyclo*-steroids by solvolysis of 3β-substituted Δ^5-steroids in buffered media involves the participation at position 3 of the π-electrons of the Δ^5-double bond. Nes and Steele [1] recently showed that in the 3 : 5-*cyclo*steroid rearrangement of 3β-substituted steroidal 5 : 7-dienes and 5 : 7 : 9(11)-trienes the same 1 : 3-interaction (homoallylic participation) occurs and that there is no



significant participation at position 3 by the 7 : 8- and the 9 : 11-double bond. Consequently, here also the main products are 6-substituted compounds and not the alternative products of anionotropic rearrangement. Thus ergosteryl toluene-*p*-sulphonate (I; R = $C_6H_4Me{\cdot}SO_2$) and dehydroergosteryl toluene-*p*-sulphonate (VII; R = $C_6H_4Me{\cdot}SO_2$) on hydrolysis in boiling aqueous acetone containing potassium acetate [2,3] or potassium hydrogen carbonate [1] yield 3 : 5-*cyclo*ergosta-7 : 22-dien-6β-ol (II) and 3 : 5-*cyclo*ergosta-7 : 9(11) : 22-trien-6β-ol (VIII) respectively, and not 3 : 5-*cyclo*ergosta-6 : 22-dien-8ξ-ol (III) and, for example, 3 : 5-*cyclo*ergosta-8(9) : 14 : 22-trien-11ξ-ol (IX), a possibility suggested by Nes and Shoppee.[3] We now describe some chemical and physical evidence which confirms the correctness of Nes and Steele's [1] formulations.

[1] Nes and Steele, *J. Org. Chem.*, 1957, **22**, 1457.
[2] Rees and Shoppee, *J.*, 1954, 3422; Nes, *J. Amer. Chem. Soc.*, 1956, **78**, 193.
[3] Nes and Shoppee, *J.*, 1957, 93.

3 : 5-*cyclo*Ergosta-7 : 22-dien-6β-ol (II) on oxidation with manganese dioxide in chloroform at 55° or chromium trioxide in pyridine at room temperature gave 3 : 5-*cyclo*ergosta-7 : 22-dien-6-one (V). The characteristic behaviour of allylic alcohols to the former reagent [4] and the demonstrated stability of the *cyclo*propane ring of 3 : 5-*cyclo*stanols to the latter reagent,[5] together with the ultraviolet absorption maximum at 249 mμ and the infrared carbonyl absorption maximum at 1642 cm.$^{-1}$, are in agreement with this structure. Chromium trioxide in pyridine also oxidises allylic alcohols to αβ-unsaturated ketones,[6] *e.g.*, 3β-acetoxyergosta-7 : 22-diene-5 : 6β-diol (cerevisteryl monoacetate) is smoothly converted into 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one also prepared by oxidation with manganese dioxide.[7] Wolff–Kishner reduction of the ketone (V) yielded 3 : 5-*cyclo*ergosta-7 : 22-diene (IV) identical with the product obtained by Karrer and Asmis [8] by reduction of the diene ester (I; R = $C_6H_4Me{\cdot}SO_2$) with lithium aluminium hydride. Acid-catalysed hydration of the ketone (V) in acetic acid containing sulphuric acid, followed by acetylation, gave 3β-acetoxyergosta-7 : 22-dien-6-one [9] (VI) (cf. the similar treatment of 3 : 5-*cyclo*cholestan-6-one [10]).

The same sequence of reactions has been applied to 3 : 5-*cyclo*ergosta-7 : 9(11) : 22-trien-6β-ol (VIII). Oxidation by chromium trioxide in pyridine gave 3 : 5-*cyclo*-7 : 9(11) : 22-trien-6-one (X), which showed infrared absorption maxima at 1658 and 1616 cm.$^{-1}$ and an ultraviolet absorption maximum at 298 mμ consistent with the presence of a dienone system. Acid-catalysed hydration of this product yielded 3β-acetoxyergosta-7 : 9(11) : 22-trien-6-one (XI) identical with the product of reduction of 3β-acetoxy-5-hydroxyergosta-7 : 9(11) : 22-trien-6-one [11] (XII) with zinc and acetic acid.

The β-configuration of the 6-hydroxyl group in the products (II) and (VIII) is assumed by analogy; [12] supporting evidence from the infrared spectra of numerous 3 : 5-*cyclo*-steroid derivatives will be presented later.[6]

Experimental

Ultraviolet and infrared spectra were determined with a Cary recording spectrometer and a Grubb-Parsons GS2 double-beam grating spectrometer respectively, the solvent being alcohol and carbon tetrachloride. $[\alpha]_D$ are in chloroform.

3 : 5-*cyclo*Ergosta-7 : 22-dien-6β-ol was prepared by Nes and Steele's method [1] and purified by chromatography on neutral aluminium oxide. Elution with pentane and pentane–benzene gave a little 3 : 5-*cyclo*ergosta-6 : 8(14) : 22-triene, m. p. 103°, $[\alpha]_D$ +95° (*c* 1·1), $\lambda_{max.}$ 262 mμ (log ε 4·4); use of ether furnished 3 : 5-*cyclo*ergosta-7 : 22-dien-6β-ol, m. p. 131—133°, $[\alpha]_D$ −12° (*c* 0·8), after crystallisation from acetone, and of chloroform gave ergosterol, m. p. 163—165°.

3 : 5-cyclo*Ergosta*-7 : 22-*dien*-6-*one*.—(*a*) 3 : 5-*cyclo*Ergosta-7 : 22-dien-6β-ol (700 mg.) in pyridine (7 ml.) was treated with chromium trioxide (700 mg.) in pyridine (7 ml.) and left overnight. After dilution with ether the solution was filtered and the filtrate washed several times with water, dried (Na_2SO_4), and evaporated. The crystalline product crystallised from ether, to give 3 : 5-cyclo*ergosta*-7 : 22-*dien*-6-*one* as plates, m. p. 168—169°, $[\alpha]_D$ +43° (*c* 1·25). $\lambda_{max.}$ 249 mμ (log ε 4·13), $\nu_{max.}$ 1642 cm.$^{-1}$ [Found (after drying at 50°/0·05 mm. for 12 hr.): C, 85·3; H, 10·6. $C_{28}H_{42}O$ requires C, 85·2; H, 10·7%].

(*b*) 3 : 5-*cyclo*Ergosta-7 : 22-dien-6β-ol (150 mg.) in chloroform (50 ml.) was shaken at 55° for 5 hr. with activated manganese dioxide (3·5 g.). Filtration of the solution through neutral

[4] Amendolla, Rosenkranz, and Sondheimer, *J.*, 1954, 1226.
[5] Burn, Ellis, Petrow, Stuart-Webb, and Williamson, *J.*, 1957, 4092.
[6] Summers, unpublished work.
[7] Blears and Shoppee, *Chem. and Ind.*, 1953, 947.
[8] Karrer and Asmis, *Helv. Chim. Acta*, 1952, **35**, 1926.
[9] Barton and Robinson, *J.*, 1954, 3045.
[10] Ladenburg, Chakravorty, and Wallis, *J. Amer. Chem. Soc.*, 1939, **61**, 3483.
[11] Zürcher, Heusser, Jeger, and Geistlich, *Helv. Chim. Acta*, 1954, **37**, 1562.
[12] Shoppee and Summers, *J.*, 1952, 3361; Evans and Summers, *J.*, 1957, 906.

aluminium oxide followed by removal of the chloroform gave 3 : 5-*cyclo*ergosta-7 : 22-dien-6-one, m. p. and mixed m. p. 166—168° (from ether).

3β-*Acetoxy*-5α-*hydroxyergosta*-7 : 22-*dien*-6-*one*.—Cerevisteryl monoacetate (50 mg.) in pyridine (1 ml.) was treated with chromium trioxide (59 mg.) in pyridine (1 ml.) and the mixture left overnight. Working up in the usual way gave a solid (39 mg.) which on crystallisation from acetone gave 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one, m. p. and mixed m. p. 268—269°, $[\alpha]_D$ −5° (*c* 0·4).

3β-*Acetoxyergosta*-7 : 22-*dien*-6-*one*.—3 : 5-*cyclo*Ergosta-7 : 22-dien-6-one (500 mg.) in acetic acid (100 ml.) was refluxed with 5N-sulphuric acid (25 ml.) for 2 hr., then poured into water, which was extracted with ether. The extract was washed with water and saturated sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated. The oily product was treated with acetic anhydride and pyridine overnight. The acetate (460 mg.) was chromatographed on aluminium oxide (15 g.). Elution with pentane–benzene (1 : 1) gave 3β-acetoxyergosta-7 : 22-dien-6-one (345 mg.) which from acetone formed needles, m. p. 185°, $[\alpha]_D$ −15° (*c* 1·1), $\nu_{max.}$ 1733 and 1675 cm.$^{-1}$, undepressed in m. p. on admixture with a specimen prepared by Barton and Robinson's method.[9]

3 : 5-cyclo*Ergosta*-7 : 22-*diene*.—Wolff–Kishner reduction of 3 : 5-*cyclo*ergosta-7 : 22-dien-6-one (250 mg.) in the usual way gave an oil (180 mg.) which on filtration in pentane through aluminium oxide and crystallisation from ether–methanol gave 3 : 5-*cyclo*ergosta-7 : 22-diene, m. p. 102—104°, identical (infrared spectrum) with a specimen obtained by Karrer and Asmis's procedure.[8]

3 : 5-cyclo*Ergosta*-7 : 9(11) : 22-*trien*-6β-*ol*.—This [1] was purified by filtration in ether through neutral aluminium oxide and crystallised from acetone as needles, m. p. 126°, $[\alpha]_D$ +129°, $\lambda_{max.}$ 247 mμ (log ε 4·19).

With methyl iodide and silver oxide (reflux for 8 hr.) it gave an oil which crystallised only on being seeded with 3 : 5-*cyclo*ergosta-7 : 9(11) : 22-trien-6β-yl methyl ether,[2] m. p. 56°. The infrared spectra of the specimens were identical.

3 : 5-cyclo*Ergosta*-7 : 9(11) : 22-*trien*-6-*one*.—3 : 5-*cyclo*Ergosta-7 : 9(11) : 22-trien-6β-ol (310 mg.) in pyridine (3 ml.) was treated with chromium trioxide (310 mg.) in pyridine (3 ml.) and left overnight. Working up as described above gave a solid which from ethyl acetate and ether gave 3 : 5-cyclo*ergosta*-7 : 9(11) : 22-*trien*-6-*one*, m. p. 152—154°, $[\alpha]_D$ +212° (*c* 1·56), $\lambda_{max.}$ 298 mμ (log ε 4·10), $\nu_{max.}$ 1658 and 1616 cm.$^{-1}$ [Found (after drying at 50°/0·05 mm. for 12 hr.): C, 85·3; H, 10·45. $C_{28}H_{40}O$ requires C, 85·7; H, 10·3%].

3β-*Acetoxyergosta*-7 : 9(11) : 22-*trien*-6-*one*.—(*a*) A solution of 3 : 5-*cyclo*ergosta-7 : 9(11) : 22-trien-6-one (1 g.) in acetic acid (200 ml.) containing 5N-sulphuric acid (50 ml.) was refluxed for 2 hr. Working up in the usual way, followed by acetylation of the product with acetic anhydride in pyridine, gave a red oil which was chromatographed on aluminium oxide (30 g.). Elution with pentane–benzene (9 : 1) gave an oil which on crystallisation from methanol gave 3β-*acetoxyergosta*-7 : 9(11) : 22-*trien*-6-*one*, m. p. 142—148°, $[\alpha]_D$ −36° (*c* 1·75), $\lambda_{max.}$ 293·5 mμ (log ε 4·75), $\nu_{max.}$ 1238, 1667, and 1739 cm.$^{-1}$ [Found (after drying at 50°/0·05 mm. for 12 hr.): C, 79·35; H, 9·3. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%].

(*b*) 3β-Acetoxy-5-hydroxyergosta-7 : 9(11) : 22-trien-6-one,[11] m. p. 239—242° (250 mg.), in acetic acid (30 ml.) was refluxed for 1 hr. with portion-wise addition of zinc dust (2 g.). Chromatography of the product on aluminium oxide (8 g.) and elution with pentane–benzene (9 : 1) gave 3β-acetoxyergosta-7 : 9(11) : 22-trien-6-one, m. p. 144—146° identical with the above specimen.

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