*Steroids. Part IX.** 22 : 23-*Dichloroergosta*-7 : 9(11)-*dien*-3β-*yl Acetate* (*Ergosteryl-D Acetate* 22 : 23-*Dichloride*).

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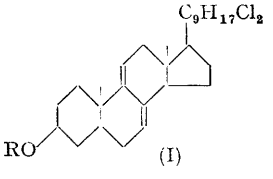
The conversion of ergosteryl-D acetate 22 : 23-dichloride into 11-oxygenated derivatives is described.

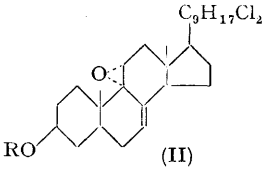
Treatment of 5α : 6-dihydroergosteryl acetate † with bromine gives an unstable tetrabromoergostenyl acetate, treatment of which with sodium iodide yields ergosteryl-D acetate 22 : 23-dibromide. Treatment of 5α : 6-dihydroergosteryl acetate with chlorine gives in low yield a mixture of tetrachloroergostenyl acetates I and II of which the former is converted by sodium iodide into ergosteryl-D acetate 22 : 23-dichloride (I; R = Ac) (Anderson, Stevenson, and Spring, *J.*, 1952, 2901). The present paper is mainly concerned with an examination of the reactions of ergosteryl-D acetate 22 : 23-dichloride.

Partial dehalogenation of tetrachloroergostenyl acetate II by zinc dust in ether–ethanol gives 22 : 23-dichloroergosta-7 : 14-dien-3β-yl acetate (ergosteryl-B_3 acetate 22 : 23-dichloride), further dehalogenation of which by zinc dust and acetic acid gives ergosteryl-B_3 acetate.

Dehalogenation of ergosteryl-D acetate 22 : 23-dichloride by zinc dust and acetic acid gives ergosteryl-D acetate. The elimination of chlorine from the dichloride is more difficult than the removal of bromine from the dibromide. In the latter case conversion into ergosteryl-D acetate is complete after short treatment with zinc dust in ether–ethanol, conditions which do not effect ergosteryl-D acetate 22 : 23-dichloride. Alkaline hydrolysis of the dichloride merely removes the acetyl group, giving (I; R = H).



(I)



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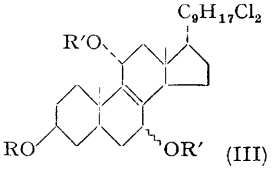

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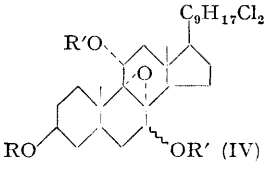

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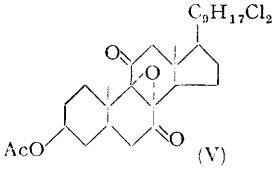

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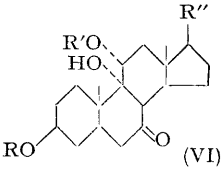

(VI)

Oxidation of ergosteryl-D acetate 22 : 23-dichloride (I) with 1 mol. of perbenzoic acid gives 22 : 23-dichloro-9α : 11α-epoxyergost-7-en-3β-yl acetate (II; R = Ac), characterised by alkaline hydrolysis to the alcohol (II; R = H). The structure allocated to the epoxide is based on analogy, including a consideration of molecular-rotation differences. Rearrangement of (II; R = Ac) by mineral acid yields 22 : 23-dichloro-7ξ : 11α-dihydroxyergost-8-en-β-yl acetate (III; R = Ac, R′ = H), characterised as the triacetate (III; R = R′ = Ac) and by alkaline hydrolysis to the triol (III; R = R′ = H). Perbenzoic acid oxidises 22 : 23-dichloro-7ξ : 11α-dihydroxyergost-8-ene-3β-yl acetate to 22 : 23-dichloro-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (IV; R = Ac, R′ = H), which affords normally the triol (IV; R = R′ = H) and the triacetate (IV; R = R′ = Ac).

Oxidation of the monoacetate (IV; R = Ac, R′ = H) with chromic acid yields 22 : 23-dichloro-8α : 9α-epoxy-7 : 11-dioxoergostan-3β-yl acetate (V), the structure of which was confirmed by its conversion into 7 : 11-dioxoergost-22-en-3β-yl acetate (Budziarek, Newbold, Stevenson, and Spring, *J.*, 1952, 2892) by zinc dust and acetic acid.

On treatment with mineral acid, 22 : 23-dichloro-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (IV; R = Ac, R′ = H) undergoes the arrangement

* Part VIII, *J.*, 1953, 956. † Frequently termed " 5-dihydroergosteryl acetate."

observed for 8α : 9α-epoxy-7ξ : 11α-dihydroxyergost-22-en-3β-yl acetate (Heusser, Anliker, Eichenberger, and Jeger, *Helv. Chim. Acta*, 1952, **35**, 936) and 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (Budziarek, Hamlet, and Spring, *J.*, 1953, 778). The product, 3β-acetoxy-22 : 23-dichloro-9α : 11α-dihydroxyergostan-7-one (VI; R = Ac, R′ = H, R″ = $C_9H_{17}Cl_2$), was identified by its smooth transformation into the known 3β-acetoxy-9α : 11α-dihydroxyergost-22-en-7-one on dechlorination with zinc dust.

The α-orientation of the $C_{(9)}$-hydroxyl group in this and related compounds has been established by Maclean and Spring (see following paper).

Experimental

M. p.s are corrected; specific rotations were measured in chloroform solution (unless otherwise specified) in a 1-dm. tube at 16—18°, and ultra-violet absorption spectra in absolute ethanol.

22 : 23-*Dichloroergosta*-7 : 14-*dien*-3β-*yl Acetate*.—A solution of tetrachloroergostenyl acetate II (385 mg.; $[\alpha]_D$ −257°) in ether (40 c.c.) and ethanol (60 c.c.) was heated under reflux with zinc dust (2 g.) for 2 hr. The product was isolated by means of ether. Crystallisation from chloroform–methanol gave in low yield 22 : 23-*dichloroergosta*-7 : 14-*dien*-3β-*yl acetate*, m. p. 206—209°, $[\alpha]_D$ −173°, −169° (*c*, 1·8, 1·4) (Found: C, 70·5; H, 9·2; Cl, 14·2. $C_{30}H_{46}O_2Cl_2$ requires C, 70·7; H, 9·1; Cl, 13·9%). Light absorption: Max. at 2420 Å (ε 10,000).

Ergosta-7 : 14 : 22-*trien*-3β-*yl Acetate* (*Ergosteryl-B*$_3$ *Acetate*).—A solution of 22 : 23-dichloroergosta-7 : 14-dien-3β-yl acetate (35 mg.) in glacial acetic acid was heated with zinc dust (200 mg.) on the steam-bath for 1 hr. The product, isolated in the usual manner, after many crystallisations from aqueous methanol, gave ergosteryl-B_3 acetate as fine needles, m. p. 132—134°, $[\alpha]_D$ −218° (*c*, 0·3), undepressed in m. p. when mixed with a specimen, m. p. 138—140°, prepared as described by Barton and Brooks (*J.*, 1951, 277). Light absorption: Max. at 2420 Å (ε 8800).

22 : 23-*Dichloroergosta*-7 : 9(11)-*dien*-3β-*ol*.—A solution of ergosteryl-D acetate 22 : 23-dichloride (430 mg.; m. p. 235—237°, $[\alpha]_D$ −44°) in benzene (5 c.c.) and aqueous-methanolic potassium hydroxide (3%; 85 c.c.) was refluxed for 6 hr. The product was isolated by means of ether and crystallised from aqueous acetone, to give 22 : 23-*dichloroergosta*-7 : 9(11)-*dien*-3β-*ol* as needles, m. p. 215—216°, $[\alpha]_D$ +33·5° (*c*, 1·4) (Found: C, 69·5; H, 9·8; Cl, 14·0. $C_{28}H_{44}OCl_2,H_2O$ requires C, 69·3; H, 9·55; Cl, 14·6%). Light absorption: Max. at 2370 (ε 16,200), 2440 (ε 17,700), and 2520 Å (ε 12,500).

22 : 23-*Dichloro*-9α : 11α-*epoxyergost*-7-*en*-3β-*yl Acetate*.—22 : 23-Dichloroergosta-7 : 9(11)-dien-3β-yl acetate (1 g.) in dry chloroform (22·5 c.c.) was treated at 0° with perbenzoic acid (1·3 mols.) in chloroform (6 c.c.) with stirring during 2½ hr. and kept at 0° for 4 hr. The product (1 g.), isolated in the usual manner, was repeatedly crystallised from acetone, to give 22 : 23-*dichloro*-9α : 11α-*epoxyergost*-7-*en*-3β-*yl acetate* as prismatic needles, m. p. 220—221° (decomp.), $[\alpha]_D$ −34°, −34·3° (*c*, 1·1) (Found: C, 68·7; H, 9·1. $C_{30}H_{46}O_3Cl_2$ requires C, 68·55; H, 8·8%). Light absorption: ε_{2080} 3150, ε_{2150} 1600, ε_{2200} 300. The compound gives a light yellow colour with tetranitromethane in chloroform.

Hydrolysis of the acetate for 2½ hr. by boiling 3% ethanolic potassium hydroxide gave 22 : 23-*dichloro*-9α : 11α-*epoxyergost*-7-*en*-3β-*ol* which separates from acetone as prismatic needles, m. p. 221—223°, $[\alpha]_D$ −37° (*c*, 0·6) (Found: C, 69·8; H, 9·3. $C_{28}H_{44}O_2Cl_2$ requires C, 69·6; H, 9·2%). Light absorption: ε_{2060} 5800, ε_{2140} 2100, ε_{2200} 300.

22 : 23-*Dichloro*-7ξ : 11α-*dihydroxyergost*-8-*en*-3β-*yl Acetate*.—22 : 23-Dichloro-9α : 11α-epoxyergost-7-en-3β-yl acetate (3·85 g.) in tetrahydrofuran (40 c.c.) was treated with aqueous sulphuric acid (2N; 1·5 c.c.). The mixture was kept at 16° for 4 hr. and the solid (1·6 g.) collected and washed with chloroform. From the mother-liquor a further crop (0·17 g.) separated after 1 hr. The combined crops were crystallised from pyridine, to give 22 : 23-*dichloro*-7ξ : 11α-*dihydroxyergost*-8-*en*-3β-*yl acetate* as fine needles, m. p. 237—239° (decomp.), $[\alpha]_D$ +74°, +70° (*c*, 0·27, 0·28 in pyridine) (Found: C, 66·3; H, 9·1. $C_{30}H_{48}O_4Cl_2$ requires C, 66·3; H, 8·9%). Light absorption: ε_{2120} 7300, ε_{2150} 6900, ε_{2200} 4600.

22 : 23-*Dichloroergost*-8-*ene*-3β : 7ξ : 11α-*triol* was obtained by refluxing the monoacetate with 3% ethanolic potassium hydroxide for 6½ hr. It separates from aqueous pyridine as rectangular plates, m. p. 225—226° (decomp.), $[\alpha]_D$ +135°, +128° (*c*, 0·2 in pyridine) (Found: C, 67·1; H, 9·4. $C_{28}H_{46}O_3Cl_2$ requires C, 67·05; H, 9·2%). Light absorption: ε_{2120} 6400, ε_{2150} 6000, ε_{2200} 3800.

Acetylation of the monoacetate with pyridine and acetic anhydride gave the *triacetate* which separates from aqueous acetone as needles, m. p. 151—153°, $[\alpha]_D$ +102°, +101° (*c*, 0·77, 0·62) (Found: C, 65·0; H, 8·3. $C_{34}H_{52}O_6Cl_2$ requires C, 65·05; H, 8·4%). Light absorption: ε_{2100} 11,300, ε_{2150} 9650, ε_{2200} 6700.

22 : 23-*Dichloro*-8α : 9α-*epoxy*-7ξ : 11α-*dihydroxyergostan*-3β-*yl Acetate*.—Perbenzoic acid (1·2 mols.) in chloroform (10 c.c.) was added to a suspension of 22 : 23-dichloro-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (1·34 g.) in chloroform (35 c.c.) and the mixture kept at 16° for 4 hr.; dissolution was then complete. The product, isolated in the usual manner and crystallised from acetone, gave 22 : 23-*dichloro*-8α : 9α-*epoxy*-7ξ : 11α-*dihydroxyergostan*-3β-*yl acetate* as prisms, m. p. 277—279° (decomp.), $[\alpha]_D$ +21°, +20° (*c*, 0·87, 1·0) (Found: C, 64·6; H, 8·7. $C_{30}H_{48}O_5Cl_2$ requires C, 64·4; H, 8·6%).

22 : 23-*Dichloro*-8α : 9α-*epoxyergostane*-3β : 7ξ : 11α-*triol* was obtained by refluxing the monoacetate with 3% ethanolic potassium hydroxide containing a little benzene for 3 hr. It separates from aqueous methanol as needles, m. p. 271—273° (decomp.), $[\alpha]_D$ +30°, +28° (*c*, 0·7, 0·5) (Found: C, 65·3; H, 9·0. $C_{28}H_{46}O_4Cl_2$ requires C, 65·0; H, 8·95%).

22 : 23-*Dichloro*-8α : 9α-*epoxy*-3β : 7ξ : 11α-*triacetoxyergostane*, obtained by treatment of the monoacetate with pyridine and acetic anhydride, separates from aqueous acetone as needles, m. p. 212—214°, $[\alpha]_D$ +7°, +5° (*c*, 0·6, 1·1) (Found: C, 63·5; H, 8·4. $C_{34}H_{52}O_7Cl_2$ requires C, 63·4; H, 8·1%).

22 : 23-*Dichloro*-8α : 9α-*epoxy*-7 : 11-*dioxoergostan*-3β-*yl Acetate*.—22 : 23-Dichloro-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (230 mg.) in glacial acetic acid (25 c.c.) was treated with a solution of chromic anhydride in acetic acid (N; 2·1 ml.) during 1½ hr. The solution was stirred for 1 hr., and kept overnight at room temperature and then at 45—50° for 30 min. The product (230 mg.) was isolated by means of ether and crystallised from methanol–chloroform, to give 22 : 23-*dichloro*-8α : 9α-*epoxy*-7 : 11-*dioxoergostan*-3β-*yl acetate* as needles, m. p. 223—224° (decomp.), $[\alpha]_D$ −53·4°, −53° (*c*, 0·7, 0·7) (Found: C, 64·7; H, 8·1. $C_{30}H_{44}O_5Cl_2$ requires C, 64·85; H, 8·0%).

7 : 11-*Dioxoergost*-22-*en*-3β-*yl Acetate*.—A solution of 22 : 23-dichloro-8α : 9α-epoxy-7 : 11-dioxoergostan-3β-yl acetate (110 mg.) in glacial acetic acid (15 c.c.) was heated on the steam-bath with zinc dust (1 g.), added portionwise during 3 hr. The product was isolated by means of ether and crystallised from methanol, to give 7 : 11-dioxoergost-22-en-3β-yl acetate as needles, m. p. 196—198°, $[\alpha]_D$ −29° (*c*, 0·6) (Found: C, 76·4; H, 9·4. Calc. for $C_{30}H_{46}O_4$: C, 76·55; H, 9·85%). A mixture with a specimen prepared as described by Budziarek *et al.* (*loc. cit.*) was undepressed in m. p.

3β-*Acetoxy*-22 : 23-*dichloro*-9α : 11α-*dihydroxyergostan*-7-*one*.—A solution of 22 : 23-dichloro-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (350 mg.) in acetic acid (5·5 c.c.) was treated with hydrobromic acid (48%; 0·5 ml.). The crystalline solid (225 mg.) separating from the blue solution was collected after 30 min., washed, and crystallised from acetone, to give 3β-*acetoxy*-22 : 23-*dichloro*-9α : 11α-*dihydroxyergostan*-7-*one* as prisms, m. p. 285—286° (decomp.), $[\alpha]_D$ −42° (*c*, 0·85) (Found: C, 64·6; H, 8·7. $C_{30}H_{48}O_5Cl_2$ requires C, 64·4; H, 8·6%).

3β-*Acetoxy*-9α : 11α-*dihydroxyergost*-22-*en*-7-*one*.—A solution of 3β-acetoxy-22 : 23-dichloro-9α : 11α-dihydroxyergostan-7-one (150 mg.) in glacial acetic acid (50 c.c.) was heated for 4 hr. on the steam-bath with zinc dust (2 g.). Isolation of the product with ether gave 3β-acetoxy-9α : 11α-dihydroxyergost-22-en-7-one as rectangular plates (140 mg.) (from methanol), m. p. 267—269°, $[\alpha]_D$ −67° (*c*, 0·7) (Found: C, 73·7; H, 10·0. Calc. for $C_{30}H_{48}O_5$: C, 73·7; H, 9·9%). A mixture with the specimen prepared as described by Budziarek, Hamlet, and Spring (*loc. cit.*) was undepressed in m. p.

22 : 23-*Dichloro*-3β : 9α : 11α-*trihydroxyergostan*-7-*one* was obtained from the monoacetate by refluxing its solution in aqueous-ethanolic potassium hydroxide (1%) containing a little benzene for 1½ hr. It separates from chloroform–methanol as plates, m. p. 286—287° (decomp.), $[\alpha]_D$ −49°, −50° (*c*, 0·3 in pyridine) (Found: C, 63·3; H, 9·2. $C_{28}H_{46}O_4Cl_2$,MeOH requires C, 63·4; H, 9·2%).

Acetylation of the monoacetate by acetic anhydride and pyridine on the steam-bath for 3 hr. gave 3β : 11α-*diacetoxy*-22 : 23-*dichloro*-9α-*hydroxyergostan*-7-*one* which separates from methanol–chloroform as needles, m. p. 292—293° (decomp.), $[\alpha]_D$ −36°, −34° (*c*, 0·6) (Found: C, 64·1; H, 8·6. $C_{32}H_{50}O_6Cl_2$ requires C, 63·9; H, 8·4%).

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