159. *Steroids. Part VII.* Reactions of 22 : 23-Dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl Acetate.*

By RICHARD BUDZIAREK, J. C. HAMLET, and F. S. SPRING.

The dibromide named in the title has been converted into 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (III) and thence into 22 : 23-dibromo-8α : 9α-epoxy-7 : 11-diketoergostan-3β-yl acetate (VIII) and 22 : 23-dibromo-9ξ : 11α-dihydroxy-7-ketoergostan-3β-yl acetate (X). The behaviour of the last compound with alkali has been examined. With dilute alkali simple hydrolysis of the 3β-acetoxy-group occurs, but, with stronger alkali, dehydration also occurs with formation of 22 : 23-dibromo-3β : 11α-dihydroxyergost-8-en-7-one (XVI).

TREATMENT of ergosteryl-D acetate 22 : 23-dibromide with one molar proportion of perbenzoic acid gives 22 : 23-dibromo-9α : 11α-epoxyergost-7-en-3β-yl acetate, which with sulphuric acid under defined conditions gives 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (I) (Budziarek, Johnson, and Spring, *J.*, 1952, 3410). The present paper describes some reactions of the triol monoacetate (I).

Oxidation of (I) with perbenzoic acid gives, in excellent yield, 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (III) debromination of which with zinc dust in ether–methanol gives the known 8α : 9α-epoxy-7ξ : 11α-dihydroxyergost-22-en-3β-yl acetate (VI) (Heusser, Anliker, Eichenberger, and Jeger, *Helv. Chim. Acta*, 1952, **35**, 936). The dibromide (III) was further characterised by acetylation to 3β : 7ξ : 11α-triacetoxy-22 : 23-dibromo-8α : 9α-epoxyergostane (IV), debromination of which gave the known 3β : 7ξ : 11α-triacetoxy-8α : 9α-epoxyergost-22-ene (VII) (Heusser *et al.*, *loc. cit.*; Budziarek, Johnson, and Spring, *loc. cit.*), and by alkaline hydrolysis to 22 : 23-dibromo-8α : 9α-epoxyergostane-3β : 7ξ : 11α-triol (II), debromination of which gives 8α : 9α-epoxyergost-22-ene-3β : 7ξ : 11α-triol (V). Chromic acid oxidises the 22 : 23-dibromo-monoacetate (III) to 22 : 23-dibromo-8α : 9α-epoxy-7 : 11-diketoergostan-3β-yl acetate (VIII), previously obtained similarly from 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (I) (Budziarek *et al.*, *loc. cit.*).

Aqueous hydrogen bromide in acetic acid (cf. Heusser *et al.*, *loc. cit.*) converts the saturated dibromo-acetate epoxide (III) into 22 : 23-dibromo-9ξ : 11α-dihydroxyergostan-7-one (X), debromination of which gives 9ξ : 11α-dihydroxy-7-ketoergost-22-en-3β-yl acetate (XIII), also obtained by Anderson, Budziarek, Newbold, Stevenson, and Spring (*Chem. and Ind.*, 1951, 1035) on treatment of 9α : 11α-epoxyergosta-7 : 22-dien-3β-yl acetate successively with one mol. of bromine, excess of perbenzoic acid, and zinc and acetic acid. Budziarek, Newbold, Stevenson, and Spring (*J.*, 1952, 2892) ascribed the β-orientation to the 9-hydroxyl group in (XIII), the two hydroxyl groups being considered as *trans*-orientated with respect to each other " since they almost certainly originate by a hydrolytic cleavage of a 9α : 11α-oxide intermediate." This argument does not now appear satisfactory since the instability of 9α : 11α-epoxyergosta-7 : 22-dien-3β-yl acetate and of 22 : 23-dibromo-9α : 11α-epoxyergost-7-en-3β-yl acetate to traces of mineral acid results in the addition of bromine being accompanied by hydrolytic rearrangement to give, in part, 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (Budziarek, Johnson, and Spring, *loc. cit.*) which may thus be the precursor of 3β-acetoxy-9ξ : 11α-dihydroxyergost-22-en-7-one in the reaction sequence described by Budziarek, Newbold, *et al.* (*loc. cit.*) (cf. Heusser *et al.*, *loc. cit.*). This view was strengthened when 9ξ : 11α-dihydroxy-7-ketoergost-22-en-3β-yl acetate (XIII) was obtained in high yield from 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (III) by means of zinc and acetic acid. There is therefore no valid reason for assuming the β-configuration for the $C_{(9)}$-hydroxyl group in (XIII) and its derivatives.

22 : 23-Dibromo-9ξ : 11α-dihydroxy-7-ketoergostan-3β-yl acetate (X) was characterised by alkaline hydrolysis to the 3β : 9ξ : 11α-triol (IX) and as the 3β : 11α-diacetate (XI),

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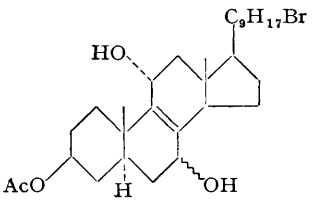
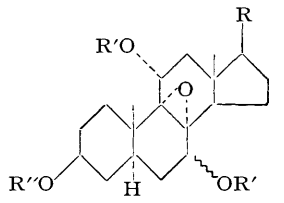
which were debrominated to the respective 22-unsaturated compounds (XII) and (XIV); the last compound has been obtained by a different route by Budziarek, Newbold, *et al.* (*loc. cit.*).

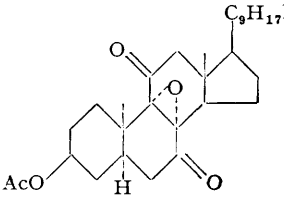
Although 22 : 23-dibromo-9α : 11α-dihydroxy-7-ketoergostan-3β-yl acetate is hydrolysed



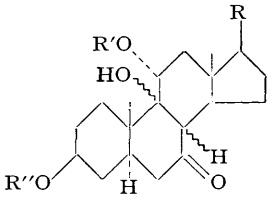
(I)



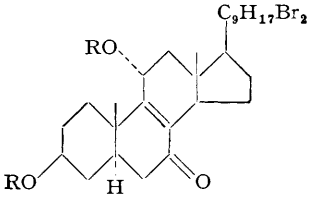
(II) R = $C_9H_{17}Br_2$, R′ = R″ = H
(III) R = $C_9H_{17}Br_2$, R′ = H, R″ = Ac
(IV) R = $C_9H_{17}Br_2$, R′ = R″ = Ac
(V) R = C_9H_{17}, R′ = R″ = H
(VI) R = C_9H_{17}, R′ = H, R″ = Ac
(VII) R = C_9H_{17}, R′ = R″ = Ac



(VIII)



(IX) R = $C_9H_{17}Br_2$, R′ = R″ = H
(X) R = $C_9H_{17}Br_2$, R′ = H, R″ = Ac
(XI) R = $C_9H_{17}Br_2$, R′ = R″ = Ac
(XII) R = C_9H_{17}, R′ = R″ = H
(XIII) R = C_9H_{17}, R′ = H, R″ = Ac
(XIV) R = C_9H_{17}, R′ = R″ = Ac



(XV) R = Ac
(XVI) R = H

by 1% alcoholic potassium hydroxide to the 3β : 9ξ : 11α-triol (IX), treatment with 10% methanolic potassium hydroxide gives 22 : 23-dibromo-3β : 11α-dihydroxyergost-8-en-7-one (XVI), which is also obtained by treatment of 22 : 23-dibromo-3β : 9ξ : 11α-trihydroxyergostan-7-one (IX) with 10% alkali.

Experimental

M. p.s are corrected. Specific rotations were determined in chloroform solution in a 1-dm. tube at 18—20°. Ultra-violet absorption spectra were measured in absolute ethanol solution with a Unicam SP. 500 spectrophotometer.

22 : 23-*Dibromo*-8α : 9α-*epoxy*-7ξ : 11α-*dihydroxyergostan*-3β-*yl Acetate*.—A solution of perbenzoic acid in chloroform (5%; 1·1 mol.) was added slowly with stirring at 0° to a suspension of 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (15 g.) in chloroform (150 c.c.), and the mixture kept at room temperature for 4 hours; dissolution was then complete. The mixture was washed with water, sodium hydrogen carbonate solution, and water, dried ($MgSO_4$) and evaporated under reduced pressure. Two crystallisations from acetone gave 22 : 23-*dibromo*-8α : 9α-*epoxy*-7ξ : 11α-*dihydroxyergostan*-3β-*yl acetate* (12 g.) as needles, m. p. 245—246°, $[\alpha]_D$ +16°, +15° (*c*, 2·0, 1·6) (Found: C, 55·3; H, 7·7. $C_{30}H_{48}O_5Br_2$ requires C, 55·6; H, 7·5%).

3β : 7ξ : 11α-*Triacetoxy*-22 : 23-*dibromo*-8α : 9α-*epoxyergostane*.—22 : 23-Dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (700 mg.) was heated in pyridine (5 c.c.) and acetic anhydride (5 c.c.) on the steam-bath for 3 hours. The *triacetate*, isolated by means of ether, separated from methanol–chloroform as prismatic needles (740 mg.), m. p. (after three crystallisations) 220—221°, $[\alpha]_D$ +4°, +4° (*c*, 1·0, 4·0) (Found: C, 55·4; H, 7·3. $C_{34}H_{52}O_7Br_2$ requires C, 55·7; H, 7·2%).

3β : 7ξ : 11α-*Triacetoxy*-8α : 9α-*epoxyergost*-22-*ene*.—A solution of 3β : 7ξ-11α-triacetoxy-22 : 23-dibromo-8α : 9α-epoxyergostane (400 mg.) in ether–methanol (1 : 1; 100 c.c.) was refluxed with zinc dust (4 g.) added portionwise during 3 hours. Filtration and concentration

gave prisms (300 mg.), m. p. 160—162°. Two recrystallisations from methanol gave 3β : 7ξ : 11α-triacetoxy-8α : 9α-epoxyergost-22-ene as prisms, m. p. 165—166°, $[\alpha]_D$ +3° (*c*, 3·0) (Found: C, 71·6; H, 9·3. Calc. for $C_{34}H_{52}O_7$: C, 71·3; H, 9·15%). Heusser, Anliker, Eichenberger, and Jeger (*loc. cit.*) give m. p. 158—159°, $[\alpha]_D$ +6°.

8α : 9α-*Epoxy*-7ξ : 11α-*dihydroxyergost*-22-*en*-3β-*yl Acetate*.—A solution of 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (500 mg.) in ether–methanol (1 : 1; 100 c.c.) was similarly reduced with zinc. Addition of a few drops of water to the concentrated filtrate gave the product (340 mg.), which after four recrystallisations from aqueous methanol formed needles, m. p. 130—131° (unchanged after prolonged drying at 100°/10^{-3} mm.), $[\alpha]_D$ +19°, +18° (*c* 1·3, 1·2) (Found: C, 73·5; H, 10·0. Calc. for $C_{30}H_{48}O_5$: C, 73·7; H, 9·9%). Heusser *et al.* (*loc. cit.*) give m. p. 147—148°, $[\alpha]_D$ +16°.

Pyridine–acetic anhydride converted the triol monoacetate into the triacetate, m. p. and mixed m. p. 164·5—166°, $[\alpha]_D$ +2° (*c*, 2·9).

22 : 23-*Dibromo*-8α : 9α-*epoxyergostane*-3β : 7ξ : 11α-*triol*.—(*a*) 22 : 23-Dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (700 mg.) in methanolic potassium hydroxide (2%; 50 c.c.) was heated under reflux for 2 hours. The solution was diluted with water, and the solid collected (very sparingly soluble in ether), and washed with water until the filtrate was neutral to litmus. After drying, the *triol* crystallised from acetone as needles (550 mg.), m. p. 235—237°, raised by two further crystallisations from acetone to 241—242°, $[\alpha]_D$ +29° (*c*, 0·5) (Found: C, 55·7; H, 7·75. $C_{28}H_{46}O_4Br_2$ requires C, 55·45; H, 7·65%).

(*b*) 3β : 7ξ : 11α-Triacetoxy-22 : 23-dibromo-8α : 9α-epoxyergostane (100 mg.) in methanolic potassium hydroxide (2%; 50 c.c.) and benzene (2 c.c.) was heated under reflux for 2 hours. Crystallisation of the product from acetone gave the same triol (60 mg.) as needles, m. p. and mixed m. p. 239—240°, $[\alpha]_D$ +27° (*c*, 0·4).

Pyridine–acetic anhydride converted the triol into 3β : 7ξ : 11α-triacetoxy-22 : 23-dibromo-8α : 9α-epoxyergostane, needles (from methanol–chloroform), $[\alpha]_D$ +4° (*c*, 2·8), m. p. 220—221° alone or mixed with the specimen described above.

8α : 9α-*Epoxyergost*-22-*ene*-3β : 7ξ : 11α-*triol*.—(*a*) 8α : 9α-Epoxy-7ξ : 11α-dihydroxyergost-22-en-3β-yl acetate (300 mg.) in methanolic potassium hydroxide (1%; 60 c.c.) was heated under reflux for 2 hours. The unsaturated *triol*, isolated by means of ether, separated from acetone in needles (250 mg.), m. p. 160—163°, raised by three recrystallisations from acetone to 166—167°; $[\alpha]_D$ was +32° (*c*, 1·0) (Found: C, 74·9; H, 10·5. $C_{28}H_{46}O_4$ requires C, 75·3; H, 10·4%).

(*b*) 22 : 23-Dibromo-8α : 9α-epoxyergostane-3β : 7ξ : 11α-triol (250 mg.) in ether–methanol (1 : 1; 60 c.c.) was heated under reflux with zinc dust added portionwise during 3 hours. Filtration and concentration gave the unsaturated triol (170 mg.), which on recrystallisation from acetone had m. p. and mixed m. p. 166—167°, $[\alpha]_D$ +31° (*c*, 0·9).

(*c*) 3β : 7ξ : 11α-Triacetoxy-8α : 9α-epoxyergost-22-ene (100 mg.) in methanolic potassium hydroxide (2%; 40 c.c.) was heated under reflux for 2 hours. The product, isolated by means of ether, crystallised from acetone as needles (60 mg.), m. p. 165—166°, $[\alpha]_D$ +30° (*c*, 0·8), undepressed in m. p. when mixed with the specimens described above.

Acetylation (pyridine–acetic anhydride) of the unsaturated triol gave 3β : 7ξ : 11α-triacetoxy-8α : 9α-epoxyergost-22-ene as prisms (from methanol) $[\alpha]_D$ +3° (*c*, 2·7), m. p. 164—166° alone or mixed with the specimen described above.

22 : 23-*Dibromo*-8α : 9α-*epoxy*-7 : 11-*diketoergostan*-3β-*yl Acetate* [with Dr. G. T. Newbold].—A solution of 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (216 mg.) in acetic acid (15 c.c.) was treated with a solution of chromium trioxide in acetic acid (11·7 c.c.; 0·145N) added during 1½ hours with stirring at room temperature. Next morning the solution was heated at 45—50° for 30 minutes, treated with methanol, evaporated to small bulk under reduced pressure, and diluted with water. 22 : 23-Dibromo-8α : 9α-epoxy-7 : 11-diketoergostan-3β-yl acetate, isolated by means of ether, crystallised from methanol–chloroform as flat needles (160 mg.), m. p. 210—212°, $[\alpha]_D$ −43° (*c*, 1·0) (Found: C, 55·9; H, 7·2. Calc. for $C_{30}H_{44}O_5Br_2$: C, 55·9; H, 6·9%). It was undepressed in m. p. when mixed with a specimen prepared by Budziarek, Johnson, and Spring (*loc. cit.*).

22 : 23-*Dibromo*-9ξ : 11α-*dihydroxy*-7-*ketoergostan*-3β-*yl Acetate*.—A solution of 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (5 g.) in acetic acid (40 c.c.) was treated with aqueous hydrogen bromide (48%; 1·5 c.c.) at room temperature and the mixture kept for 1 hour. The crystalline solid which separated from the blue solution was collected, washed successively with a little acetic acid and methanol, and dried (4·2 g.; m. p. 246—248°). Three recrystallisations from acetone gave 22 : 23-*dibromo*-9ξ : 11α-*dihydroxy*-7-*ketoergostan*-3β-*yl*

acetate (X) as hexagonal prisms, m. p. 250—251°, $[\alpha]_D$ −36°, −35° (*c*, 2·5, 2·1) (Found : C, 55·6; H, 7·6. $C_{30}H_{48}O_5Br_2$ requires C, 55·6; H, 7·5%).

9ξ : 11α-*Dihydroxy*-7-*ketoergost*-22-*en*-3β-*yl Acetate*.—(*a*) The acetate (X) in ether–methanol (1 : 1) was heated under reflux with zinc dust for 4 hours. The product, isolated in the usual manner, was 9ξ : 11α-dihydroxy-7-ketoergost-22-en-3β-yl acetate (yield, quantitative) which separated from methanol as rectangular plates, $[\alpha]_D$ −69°, −67·5° (*c*, 1·0, 0·8), m. p. 267—269°, alone or mixed with the specimen described by Budziarek, Newbold, Stevenson, and Spring (*loc. cit.*) (Found : C, 74·0; H, 10·1. Calc. for $C_{30}H_{48}O_5$: C, 73·7; H, 9·9%).

(*b*) When 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (400 mg.) in acetic acid (30 c.c.) was treated as above (zinc dust, 4 g.), the same product (210 mg.) was obtained having m. p. and mixed m. p. 267—269°, $[\alpha]_D$ −67° (*c*, 0·9).

3β : 9ξ : 11α-*Trihydroxyergost*-22-*en*-7-*one*.—Hydrolysis of 3β-acetoxy-9ξ : 11α-dihydroxyergost-22-en-7-one (100 mg.) with 2% methanolic potassium hydroxide (30 c.c.) gave 3β : 9ξ : 11α-*trihydroxyergost*-22-*en*-7-*one* (70 mg.) which separated from acetone (or methanol) as needles, m. p. 258—259°, $[\alpha]_D$ −71° (*c*, 1·1) (Found : C, 75·2; H, 10·4. $C_{28}H_{46}O_4$ requires C, 75·3; H, 10·4%).

3β : 11α-*Diacetoxy*-22 : 23-*dibromo*-9ξ-*hydroxyergostan*-7-*one*.—22 : 23-Dibromo-9ξ : 11α-dihydroxy-7-ketoergostan-3β-yl acetate (400 mg.) in pyridine (20 c.c.) and acetic anhydride (10 c.c.) was heated on the steam-bath for 3 hours. The solid separating from the cooled mixture was washed with methanol and dried (330 mg.; m. p. 256—257°). After two recrystallisations from acetone (or methanol–chloroform), 3β : 11α-*diacetoxy*-22 : 23-*dibromo*-9ξ-*hydroxyergostan*-7-*one* was obtained as needles, m. p. 259—260°, $[\alpha]_D$ −29°, −27° (*c*, 1·6, 0·9) (Found : C, 55·65; H, 7·5. $C_{32}H_{50}O_6Br_2$ requires C, 55·65; H, 7·3%).

3β : 11α-*Diacetoxy*-9ξ-*hydroxyergost*-22-*en*-7-*one*.—(*a*) 3β : 11α-Diacetoxy-22 : 23-dibromo-9ξ-hydroxyergostan-7-one (150 mg.) was debrominated by heating its solution in ether–methanol (1 : 2; 100 c.c.) with zinc dust (2 g.) for 4 hours under reflux. The product, isolated in the usual manner, crystallised from methanol to yield 3β : 11α-diacetoxy-9ξ-hydroxyergost-22-en-7-one (100 mg.) as needles, m. p. 194—196°, $[\alpha]_D$ −43° (*c*, 1·0), undepressed in m. p. when mixed with the specimen described by Budziarek, Newbold, *et al.* (*loc. cit.*) (Found : C, 72·6; H, 9·6. Calc. for $C_{32}H_{50}O_6$: C, 72·4; H, 9·5%).

(*b*) 3β : 9ξ : 11α-Trihydroxyergost-22-en-7-one with pyridine and acetic anhydride gave the same 3β : 11α-diacetate as needles (from methanol), m. p. and mixed m. p. 193—195°, $[\alpha]_D$ −42° (*c*, 0·8).

22 : 23-*Dibromo*-3β : 9ξ : 11α-*trihydroxyergostan*-7-*one*.—(*a*) 22 : 23-Dibromo-9ξ : 11α-dihydroxy-7-ketoergostan-3β-yl acetate (300 mg.) was heated in methanolic potassium hydroxide (1%; 200 c.c.) under reflux for 2 hours. 22 : 23-*Dibromo*-3β : 9ξ : 11α-*trihydroxyergostan*-7-*one*, isolated in the usual manner (250 mg.; m. p. 258—260°), crystallised from acetone as needles, m. p. 262—263°, $[\alpha]_D$ −45°, −42° (*c*, 0·25, 0·3) (Found, after drying in high vacuum over P_2O_5 at 100° for 7 days: C, 54·0, 54·1; H, 7·75, 7·9. $C_{28}H_{46}O_4Br_2,H_2O$ requires C, 53·9; H, 7·75%). It is sparingly soluble in chloroform and separates as thick, elongated plates from methanol–chloroform.

Acetylation of the triol with pyridine and acetic anhydride gave the 3β : 11α-diacetate (quantitative yield) as needles (from acetone), m. p. and mixed m. p. 259—260°, $[\alpha]_D$ −28° (*c*, 0·8) (Found : C, 55·6; H, 7·6%).

Debromination of the triol by refluxing its solution in methanol with zinc dust for 4 hours gave, in quantitative yield, 3β : 9ξ : 11α-trihydroxyergost-22-en-7-one which separated from methanol as flat needles, m. p. and mixed m. p. 257—259°, $[\alpha]_D$ −70° (*c*, 0·7).

(*b*) A solution of 22 : 23-dibromo-9ξ : 11α-dihydroxy-7-ketoergostan-3β-yl acetate (300 mg.) in dry acetone (200 c.c.) was treated with a stream of dry hydrogen chloride for 30 minutes at 18° and then kept at room temperature for 2 days. The solvent was removed under reduced pressure and the product isolated by means of ether. Crystallisation from acetone (or methanol) gave 3β : 9ξ : 11α-trihydroxy-22 : 23-dibromoergostan-7-one as plates, m. p. 258—259°, $[\alpha]_D$ −43° (*c*, 0·2) (Found : C, 54·1; H, 7·9%). It does not exhibit selective absorption of high intensity above 2000 Å and the m. p. of a mixture with the specimen described under (*a*) was undepressed.

3β : 11α-*Diacetoxy*-22 : 23 : *dibromoergost*-8-*en*-7-*one*.—22 : 23-Dibromo-3β : 9ξ : 11α-trihydroxyergostan-7-one (150 mg.) in 10% methanolic potassium hydroxide (50 c.c.) was refluxed for 18 hours. The product, isolated by means of ether, was acetylated by warm pyridine and acetic anhydride (1 hr.). The acetylated product, isolated by means of ether, crystallised from methanol giving 3β : 11α-diacetoxy-22 : 23-dibromoergost-8-en-7-one as needles (70 mg.),

m. p. 158—160°, $[\alpha]_D$ +18° (*c*, 0·8) (Found: C, 57·3; H, 7·5. Calc. for $C_{32}H_{48}O_5Br_2$: C, 57·1; H, 7·2%). Light absorption: Max. at 2520 Å (ε = 9000). It was undepressed in m. p. when mixed with the specimen described by Budziarek, Stevenson, and Spring, *J.*, 1952, 4874.

22 : 23-*Dibromo*-3β : 11α-*dihydroxyergost*-8-*en*-7-*one*.—22 : 23-Dibromo-9α : 11α-dihydroxy-7-ketoergostan-3β-yl acetate (200 mg.) in methanolic potassium hydroxide (10%; 100 c.c.) was heated under reflux for 18 hours. The product, isolated by ether and crystallised four times from methanol, yielded 22 : 23-dibromo-3β : 11α-dihydroxyergost-8-en-7-one (120 mg.) as needles, m. p. 228—230°, $[\alpha]_D$ +4° (*c*, 1·8) (Found: C, 57·3; H, 7·6. Calc. for $C_{28}H_{44}O_3Br_2$: C, 57·1; H, 7·5%). Light absorption: Max. at 2520 Å (ε = 8000). The m. p. of a mixture with the specimen described by Budziarek, Stevenson, and Spring (*loc. cit.*) was undepressed.

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