Steroids. Part X. 7- and 11-Oxo-steroids from 22 : 23-Dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl Acetate.*

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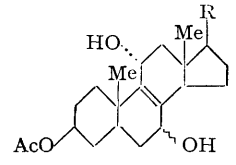
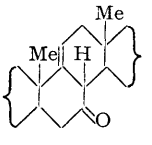
Short treatment of 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (I) with boron trifluoride gives a mixture of the two βγ-unsaturated ketones, 22 : 23-dibromo-7-oxoergost-9(11)-en-3β-yl acetate (II) and 22 : 23-dibromo-11-oxo-9β-ergost-7-en-3β-yl acetate (III). Oxidation of (II) with osmium tetroxide (followed by acetylation and debromination) gives a product identical with the 3 : 11-diacetate of 3β : 9ξ : 11α-trihydroxyergost-22-en-7-one (Budziarek, Hamlet, and Spring, *J.*, 1953, 778). It follows that the hydroxyl group at $C_{(9)}$ in this and related compounds is α-orientated.

TREATMENT of 22 : 23-dibromo-9α : 11α-epoxyergost-7-en-3β-yl acetate with sulphuric acid gives 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (I) (Budziarek, Johnson, and Spring, *J.*, 1952, 3410). Treatment of (I) with the boron trifluoride–ether complex in absolute benzene for a short time gives two isomeric non-conjugated unsaturated ketones. One of these is 22 : 23-dibromo-11-oxo-9β-ergost-7-en-3β-yl acetate (III). Debromination of this by zinc in benzene–ethanol yields 11-oxo-9β-ergosta-7 : 22-dien-3β-yl acetate, previously prepared (Bladon, Henbest, Jones, Lovell, Wood, Woods, Evans, Elks, Hathway, Oughton, and Thomas, *J.*, 1953, 2921; Heusler and Wettstein, *Helv. Chim. Acta*,



(I)



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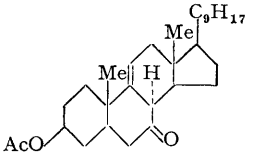
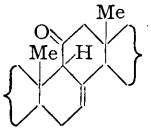


(II*a*)



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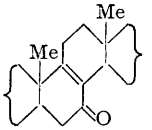
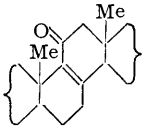


(IV)



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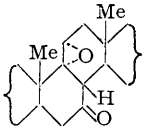

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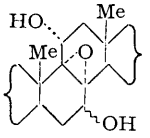
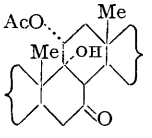


(VII)



(VIII)

(R = $C_9H_{17}Br_2$)

1953, **36,** 398) by short treatment of 9α : 11α-epoxyergost-7-en-3β-yl acetate with boron trifluoride. Filtration of a solution of (III) through a column of alumina converts it into the conjugated isomer (V) described by Budziarek, Johnson, and Spring (*loc. cit.*). The second (major) product of the reaction of (I) with boron trifluoride is 22 : 23-dibromo-7-oxoergost-9(11)-en-3β-yl acetate (II), treatment of which with dilute alkali followed by reacetylation gives the isomeric αβ-unsaturated ketone (IV) previously obtained by a different method (Budziarek, Johnson, and Spring, *loc. cit.*). Treatment of the triol monoacetate (I) with boron trifluoride for a short time followed directly by chromatography of the reaction mixture on alumina yields the αβ-unsaturated ketones (V) and (IV) in one operation, the βγ-unsaturated ketones being isomerised on the column.

* Part IX, preceding paper.

Debromination of 22 : 23-dibromo-7-oxoergost-9(11)-en-3β-yl acetate (II) by zinc dust in ether–ethanol gives 7-oxoergosta-9(11) : 22-dien-3β-yl acetate, $[\alpha]_D$ −55°, identical with the product obtained by a different method by Heusser, Anliker, Eichenberger, and Jeger (*Helv. Chim. Acta*, 1952, **35**, 936; cf. Schoenewaldt, Turnbull, Chamberlin, Reinhold, Erickson, Ruyle, Chemerda, and Tishler, *J. Amer. Chem. Soc.*, 1952, **74**, 2696). The compound differs from 7-oxoergosta-9(11) : 22-dien-3β-yl acetate, $[\alpha]_D$ +20°, described by Budziarek, Stevenson, and Spring (*J.*, 1952, 4874; Budziarek, Newbold, Stevenson, and Spring, *J.*, 1952, 2892) who concluded that the two isomers differ in orientation around $C_{(8)}$. Recently a $C_{(8)}$-epimer of 7 : 11-dioxoergost-22-en-3β-yl acetate has been described (Budziarek and Spring, *J.*, 1953, 956) and a comparison of the molecular-rotation relation of the two diketones with those of the two unsaturated ketones supports the original view and suggests that the isomer of $[\alpha]_D$ +20° is 7-oxo-8α-ergosta-9(11) : 22-dien-3β-yl acetate (II*a*) and that the isomer of $[\alpha]_D$ −55° has the normal 8β-configuration.

	$[\alpha]_D$	$[M]_D$
7 : 11-Dioxoergost-22-en-3β-yl acetate	−28°	−132°
7 : 11-Dioxo-8α-ergost-22-en-3β-yl acetate	+30	+141
Δ8β ⟶ 8α =		+273
7-Oxoergosta-9(11) : 22-dien-3β-yl acetate	−55	−250
7-Oxo-8α-ergosta-9(11) : 22-dien-3β-yl acetate	+20	+ 91
Δ8β ⟶ 8α =		+341

Oxidation of 22 : 23-dibromo-7-oxoergost-9(11)-en-3β-yl acetate (II) with perbenzoic acid gives the 9α : 11α-epoxide (VI) previously obtained by oxidation of ergosteryl-D acetate 22 : 23-dibromide with hydrogen peroxide (Anderson, Stevenson, and Spring, *J.*, 1952, 2901).

Treatment of 7-oxo-8α-ergosta-9(11) : 22-dien-3β-yl acetate successively with bromine, perbenzoic acid, and zinc dust gives 9α : 11α-epoxy-7-oxoergost-22-en-3β-yl acetate (as VI, but R = C_9H_{17}) (Budziarek, Newbold, Stevenson, and Spring, *loc. cit.*) which is also obtained from the dibromide by debromination; one of these reactions must have involved inversion at $C_{(8)}$. This probably occurred in the latter and not in the former case since, although 9α : 11α-epoxy-7-oxoergost-22-en-3β-yl acetate is very sensitive to alkali (Budziarek, Stevenson, and Spring, *loc. cit.*), it is recovered unchanged after treatment with acetic acid, or with hydrogen bromide in acetic acid under which conditions 7 : 11-dioxo-8α-ergost-22-en-3β-yl acetate is converted into the more stable 8β-epimer. For this reason, 9α : 11α-epoxy-7-oxoergost-22-en-3β-yl acetate is believed to have the normal 8β-configuration.

Oxidation of 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (I) with perbenzoic acid gives 22 : 23-dibromo-8α : 9α-epoxy-7ξ : 11α-dihydroxyergostan-3β-yl acetate (VII), which with hydrogen bromide in acetic acid gives 22 : 23-dibromo-9ξ : 11α-dihydroxy-7-oxoergostan-3β-yl acetate and thence by debromination 9ξ : 11α-dihydroxy-7-oxoergost-22-en-3β-yl acetate (Budziarek, Hamlet, and Spring, *J.*, 1953, 778; Budziarek and Spring, *Chem. and Ind.*, 1952, 1102). This compound has been obtained from 7ξ : 11α-dihydroxyergosta-8 : 22-dien-3β-yl acetate (as I, but R = C_9H_{17}) under similar conditions by Heusser, Anliker, Eichenberger, and Jeger (*Helv. Chim. Acta*, 1952, **35**, 936) and by Budziarek, Newbold, Stevenson, and Spring (*J.*, 1952, 2892) by treatment of 9α : 11α-epoxyergosta-7 : 22-dien-3β-yl acetate successively with 1 mol. of bromine, excess of perbenzoic acid, and zinc. The configuration of the 9-hydroxyl group in these compounds has now been established. Oxidation of (II) with osmium tetroxide followed by acetylation of the product gives a diacetate (VIII) identical with that obtained by acetylation of 22 : 23-dibromo-9ξ : 11α-dihydroxy-7-oxoergost-22-en-3β-yl acetate. The last compound is consequently a *cis*-glycol and the 9-hydroxyl group in this and related compounds is α-oriented.

Experimental

M. p.s are corrected. Specific rotations were determined in $CHCl_3$ in a 1-dm. tube at approx. 15°. Ultra-violet absorption spectra were measured in EtOH, with a Unicam SP. 500 spectrophotometer. For chromatography, activated alumina (Grade II) and light petroleum (b. p. 60—80°) were employed.

22 : 23-*Dibromo*-11-*oxo*-9β-*ergost*-7-*en*-3β-*yl Acetate*.—A suspension of 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate (500 mg.) in benzene (100 ml.) was shaken with boron trifluoride–ether complex (1 ml.). After 12 min., dissolution was complete; the mixture was diluted with ether and the product isolated in the usual manner. Twelve crystallisations of the product from acetone yielded 22 : 23-*dibromo*-11-*oxo*-9β-*ergost*-7-*en*-3β-*yl* acetate as needles (25 mg.), m. p. 200—203°, $[\alpha]_D$ −118° (*c*, 0·5) (Found: C, 58·9; H, 7·85. $C_{30}H_{46}O_3Br_2$ requires C, 58·6; H, 7·55%). It does not show selective absorption of high intensity above 2200 Å.

22 : 23-*Dibromo*-7-*oxoergost*-9(11)-*en*-3β-*yl Acetate*.—The combined mother-liquors from the first eight crystallisations of the foregoing compound were concentrated. A crop of plates (400 mg.; m. p. 231—233°) was obtained, two recrystallisations of which from acetone gave 22 : 23-*dibromo*-7-*oxoergost*-9(11)-*en*-3β-*yl acetate* as rhombic plates, m. p. 231—233°, $[\alpha]_D$ −36°, −34° (*c*, 2·2, 1·8) (Found: C, 58·85; H, 7·7%). It gives a pale yellow colour with tetranitromethane in chloroform and does not show selective absorption of high intensity above 2200 Å.

22 : 23-*Dibromo*-11-*oxoergost*-8-*en*-3β-*yl Acetate*.—(*a*) A solution of 22 : 23-dibromo-11-oxo-9β-ergost-7-en-3β-yl acetate (100 mg.) in benzene (25 ml.) was filtered through a column of alumina (8 × 2 cm.). Elution with benzene (300 ml.) gave 22 : 23-dibromo-11-oxoergost-8-en-3β-yl acetate (70 mg.) which separates from methanol as elongated plates, m. p. 200—201°, $[\alpha]_D$ +98° (*c*, 1·0). It does not give a colour with tetranitromethane in chloroform and a mixture with a specimen prepared according to Budziarek, Johnson, and Spring (*loc. cit.*) was undepressed in m. p.

(*b*) A suspension of 22 : 23-dibromo-7ξ : 11α-dihydroxyergost-8-en-3β-yl acetate in benzene was treated with boron trifluoride–ether complex as described above. A solution of the product in benzene–light petroleum (50 ml.; 1 : 4) was filtered through alumina (15 × 2 cm.). Elution with benzene (350 ml.) gave a fraction (100 mg.) which, after five crystallisations from methanol, gave 22 : 23-dibromo-11-oxoergost-8-en-3β-yl acetate as elongated plates, m. p. 200—203°, $[\alpha]_D$ +96° (*c*, 1·0) (Found: C, 58·8; H, 7·7%). It does not give a colour with tetranitromethane in chloroform. Light absorption: Max. at 2540 Å (ε 9000). It was undepressed in m. p. when mixed with a specimen described above.

22 : 23-*Dibromo*-7-*oxoergost*-8-*en*-3β-*yl Acetate*.—(*a*) Continued washing of the alumina column described in (*a*) above with ether (300 ml.) gave a fraction (260 mg.) which separated from methanol–chloroform to give 22 : 23-dibromo-7-oxoergost-8-en-3β-yl acetate as plates, m. p. 240—242°, $[\alpha]_D$ −29° (*c*, 0·5) (Found: C, 58·8; H, 7·6%). Light absorption: Max. at 2530 Å (ε 9000). It does not give a colour with tetranitromethane in chloroform. It is undepressed in m. p. when mixed with a specimen, m. p. 240—242°, $[\alpha]_D$ −28°, prepared as described by Budziarek, Johnson, and Spring (*loc. cit.*).

(*b*) A solution of 22 : 23-dibromo-7-oxoergost-9(11)-en-3β-yl acetate (170 mg.) in 2% aqueous-methanolic potassium hydroxide (50 ml.) was heated under reflux for 2 hr., and the product acetylated by hot pyridine and acetic anhydride for 3 hr. The acetylated product crystallised from methanol–chloroform, to yield 22 : 23-dibromo-7-oxoergost-8-en-3β-yl acetate (150 mg.), $[\alpha]_D$ −28° (*c*, 2·0), m. p. 239—241° undepressed when mixed with the specimen described above (Found: C, 58·6; H, 7·6%). Light absorption: Max. at 2520 Å (ε 9250).

11-*Oxo*-9β-*ergosta*-7 : 22-*dien*-3β-*yl Acetate*.—A solution of 22 : 23-dibromo-11-oxo-9β-ergost-7-en-3β-yl acetate (1 g.) in benzene–ethanol (200 ml.; 1 : 1) was heated under reflux for 3½ hr. with zinc dust (3 g.) added portionwise. The product was isolated in the usual manner and crystallised from acetone to give 11-oxo-9β-ergosta-7 : 22-dien-3β-yl acetate as hexagonal plates, m. p. 159—161° (600 mg.), $[\alpha]_D$ −206° (*c*, 2·55) (Found: C, 79·5; H, 10·1. Calc. for $C_{30}H_{46}O_3$: C, 79·2; H, 10·2%). Bladon *et al.* (*loc. cit.*) give m. p. 159—161°, $[\alpha]_D$ −191°. It gives a pale yellow colour with tetranitromethane in chloroform and does not show selective absorption of high intensity above 2200 Å.

7-*Oxoergosta*-9(11) : 22-*dien*-3β-*yl Acetate*.—A solution of 22 : 23-dibromo-7-oxoergost-9(11)-en-3β-yl acetate (500 mg.) in ethanol–ether (50 ml., 1 : 1) was heated under reflux for 3 hr. with zinc dust (2 g.) added portionwise. 7-Oxoergosta-9(11) : 22-dien-3β-yl acetate was isolated by means of ether and crystallised from acetone as plates (300 mg.), m. p. 177—178°, $[\alpha]_D$ −55° (*c*, 1·3) (Found: C, 79·4; H, 10·2%). It gives a pale yellow colour with tetranitromethane in chloroform and shows no selective light absorption of high intensity above 2200 Å. Heusser *et al.* (*loc. cit.*) give m. p. 176—177°, $[\alpha]_D$ −58°, and Schoenewaldt *et al.* (*loc. cit.*) give m. p. 176—177°, $[\alpha]_D$ −43·5°.

3β-*Hydroxyergosta*-8 : 22-*dien*-7-*one*.—A solution of 7-oxoergosta-9(11) : 22-dien-3β-yl acetate (300 mg.) in 3% aqueous-methanolic potassium hydroxide (50 ml.) was heated under reflux for 2 hr. The product, 3β-hydroxyergosta-8 : 22-dien-7-one, crystallised from methanol as plates

(200 mg.), m. p. 175—177°, $[\alpha]_D$ −45° (*c*, 1·0) (Found : C, 81·4; H, 10·7. Calc. for $C_{28}H_{44}O_2$: C, 81·5; H, 10·75%). Light absorption : Max. at 2560 Å (ε 9000). It gives a pale yellow colour with tetranitromethane in chloroform and was undepressed in m. p. when mixed with a specimen prepared as described by Schoenewaldt *et al.* (*loc. cit.*).

22 : 23-*Dibromo*-9α : 11α-*epoxy*-7-*oxoergostan*-3β-*yl Acetate*.—A stirred solution of 22 : 23-dibromo-7-oxoergost-9(11)-en-3β-yl acetate (4·35 g.) in chloroform (50 ml.) was treated dropwise with perbenzoic acid (1·1 mols.) in chloroform (14 ml.) during 3 hr. at 0°. The solution was kept at 0° overnight and the product isolated in the usual manner. Crystallisation from methanol–chloroform gave 22 : 23-dibromo-9α : 11α-epoxy-7-oxoergostan-3β-yl acetate as plates (3·3 g.), m. p. 228—230°, $[\alpha]_D$ −44° (*c*, 2·5). Two crystallisations from acetone gave elongated needles, m. p. 222—224° [either alone or mixed with a specimen prepared according to Anderson *et al.* (*loc. cit.*)], $[\alpha]_D$ −49° (*c*, 1·1) (Found : C, 57·2; H, 7·4. Calc. for $C_{30}H_{46}O_4Br_2$: C, 57·1; H, 7·35%). It does not show selective absorption of high intensity above 2200 Å.

3β : 11α-*Diacetoxy*-22 : 23-*dibromo*-9α-*hydroxyergostan*-7-*one*.—A solution of 22 : 23-dibromo-7-oxoergost-9(11)-en-3β-yl acetate (1·0 g.) in ether–benzene (50 c.c.; 4 : 1) and pyridine (0·74 c.c.) was treated with osmium tetroxide (1·0 g.); a brown colour rapidly developed. After 5 days at room temperature, the mixture was evaporated under reduced pressure and the residue refluxed for 5 hr. with a solution of sodium sulphite (5 g.) in aqueous ethanol (100 c.c.; 50%). The mixture was concentrated under reduced pressure, acidified (Congo-red) with dilute hydrochloric acid, and extracted with ether (2 × 150 c.c.) and then with chloroform (2 × 150 c.c.). The washed and dried (Na_2SO_4) chloroform extract was evaporated and the residue treated with acetic anhydride–pyridine at room temperature overnight. The acetylated product crystallised from chloroform–methanol to give 3β : 11α-diacetoxy-22 : 23-dibromo-9α-hydroxyergostan-7-one (550 mg.) as needles, m. p. 247—250° (not raised by further crystallisation) alone or mixed with a specimen prepared as described by Budziarek, Hamlet, and Spring (*loc. cit.*), $[\alpha]_D$ −27° (*c*, 1·0) (Found : C, 55·95; H, 7·4. Calc. for $C_{32}H_{50}O_6Br_2$: C, 55·65; H, 7·3%). The substance showed no high-intensity light absorption above 2200 Å and gave no colour with tetranitromethane in chloroform. Budziarek, Hamlet, and Spring give m. p. 259—260°, $[\alpha]_D$ −29°, −27°; the m. p. is dependent upon the rate of heating. The material extracted by means of ether was acetylated and the acetate purified by chromatography on alumina to give 3β : 11α-diacetoxy-22 : 23-dibromo-9α-hydroxyergostan-7-one (300 mg.), m. p. 247—249° alone or mixed with the specimen above, $[\alpha]_D$ −27° (*c*, 2·0) (Found : C, 55·9; H, 7·5%).

3β : 11α-*Diacetoxy*-9α-*hydroxyergost*-22-*en*-7-*one*.—A solution of 3β : 11α-diacetoxy-22 : 23-dibromo-9α-hydroxyergostan-7-one (200 mg.) in methanol–benzene (50 c.c.; 1 : 1) was refluxed with zinc dust (3·0 g.) activated by ammonium chloride added during 4 hr. The product, isolated by means of ether, was 3β : 11α-diacetoxy-9α-hydroxyergost-22-en-7-one (120 mg.), separating from aqueous acetone as needles, m. p. 193—195° [alone or mixed with a specimen (m. p. 194—196°) prepared by Budziarek, Hamlet, and Spring (*loc. cit.*)], $[\alpha]_D$ −46° (*c*, 1·0) [lit., −43° (*c*, 1·0)] (Found : C, 72·6; H, 9·8. Calc. for $C_{32}H_{50}O_6$: C, 72·4; H, 9·5%).

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