Maclean and Spring:

Steroids. Part X.\* 7- and 11-Oxo-steroids from 22:23-Dibromo-75:11a-dihydroxyergost-8-en-33-yl Acetate.

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Short treatment of 22:23-dibromo-7 $\xi$ :11 $\alpha$ -dihydroxyergost-8-en-3 $\beta$ -yl acetate (I) with boron trifluoride gives a mixture of the two  $\beta\gamma$ -unsaturated ketones, 22:23-dibromo-7-oxoergost-9(11)-en-3 $\beta$ -yl acetate (II) and 22:23-dibromo-11-oxo-9 $\beta$ -ergost-7-en-3 $\beta$ -yl acetate (III). Oxidation of (II) with osmium tetroxide (followed by acetylation and debromination) gives a product identical with the 3:11-diacetate of 3 $\beta$ :9 $\xi$ :11 $\alpha$ -trihydroxyergost-22-en-7-one (Budziarek, Hamlet, and Spring, J., 1953, 778). It follows that the hydroxyl group at C<sub>(9)</sub> in this and related compounds is  $\alpha$ -orientated.

TREATMENT of 22: 23-dibromo- $9\alpha$ : 11 $\alpha$ -epoxyergost-7-en- $3\beta$ -yl acetate with sulphuric acid gives 22: 23-dibromo- $7\xi$ : 11 $\alpha$ -dihydroxyergost-8-en- $3\beta$ -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- $9\beta$ -ergost-7-en- $3\beta$ -yl acetate (III). Debromination of this by zinc in benzene-ethanol yields 11-oxo- $9\beta$ -ergosta-7: 22-dien- $3\beta$ -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*,



1953, **36**, 398) by short treatment of  $9\alpha$ :  $11\alpha$ -epoxyergost-7-en- $3\beta$ -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- $3\beta$ -yl acetate (II), treatment of which with dilute alkali followed by reacetylation gives the isomeric  $\alpha\beta$ -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 chromato-graphy of the reaction mixture on alumina yields the  $\alpha\beta$ -unsaturated ketones (V) and (IV) in one operation, the  $\beta\gamma$ -unsaturated ketones being isomerised on the column.

\* Part IX, preceding paper.

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Debromination of 22: 23-dibromo-7-oxoergost-9(11)-en-3 $\beta$ -yl acetate (II) by zinc dust in ether-ethanol gives 7-oxoergosta-9(11): 22-dien-3 $\beta$ -yl acetate,  $[\alpha]_D -55^\circ$ , 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-3 $\beta$ -yl acetate,  $[\alpha]_D +20^\circ$ , 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<sub>(8)</sub>. Recently a C<sub>(8)</sub>-epimer of 7: 11-dioxoergost-22-en-3 $\beta$ -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  $[\alpha]_D +20^\circ$  is 7-oxo-8 $\alpha$ -ergosta-9(11): 22-dien-3 $\beta$ -yl acetate (II*a*) and that the isomer of  $[\alpha]_D -55^\circ$  has the normal 8 $\beta$ -configuration.

	$[\alpha]_{\mathbf{D}}$	$[M]_{\mathbf{D}}$
7: 11-Dioxoergost-22-en- $3\beta$ -yl acetate	$-28^{\circ}$	$-132^{\circ}$
7: 11-Dioxo- $8\alpha$ -ergost-22-en- $3\beta$ -yl acetate	+30	+141
$\Delta 8\beta \longrightarrow 8\alpha =$		+273
7-Oxoergosta-9(11) : 22-dien- $3\beta$ -yl acetate	-55	-250
7-Oxo-8 $\alpha$ -ergosta-9(11) : 22-dien-3 $\beta$ -yl acetate	+20	+ 91
$\Delta 8\beta \longrightarrow 8\alpha =$		+341

Oxidation of 22:23-dibromo-7-oxoergost-9(11)-en-3 $\beta$ -yl acetate (II) with perbenzoic acid gives the  $9\alpha$ :  $11\alpha$ -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-8 $\alpha$ -ergosta-9(11) : 22-dien-3 $\beta$ -yl acetate successively with bromine, perbenzoic acid, and zinc dust gives  $9\alpha$  :  $11\alpha$ -epoxy-7-oxoergost-22-en-3 $\beta$ -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  $9\alpha$  :  $11\alpha$ -epoxy-7-oxoergost-22-en-3 $\beta$ -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- $8\alpha$ -ergost-22-en-3 $\beta$ -yl acetate is converted into the more stable  $8\beta$ -epimer. For this reason,  $9\alpha$  :  $11\alpha$ -epoxy-7-oxoergost-22-en-3 $\beta$ -yl acetate is believed to have the normal  $8\beta$ -configuration.

Oxidation of 22: 23-dibromo-7 $\xi: 11\alpha$ -dihydroxyergost-8-en-3 $\beta$ -yl acetate (I) with perbenzoic acid gives 22: 23-dibromo- $8\alpha: 9\alpha$ -epoxy- $7\xi: 11\alpha$ -dihydroxyergostan- $3\beta$ -yl acetate (VII), which with hydrogen bromide in acetic acid gives 22:23-dibromo- $9\xi:11\alpha$ dihydroxy-7-oxoergostan-3β-yl acetate and thence by debromination 9ξ: 11α-dihydroxy-7-oxoergost-22-en-3\beta-yl acetate (Budziarek, Hamlet, and Spring, J., 1953, 778; Budziarek and Spring, *Chem. and Ind.*, 1952, 1102). This compound has been obtained from  $7\xi : 11\alpha$ dihydroxyergosta-8: 22-dien-3 $\beta$ -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  $9\alpha$ :  $11\alpha$ epoxyergosta-7: 22-dien- $3\beta$ -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- $9\xi:11\alpha$ -dihydroxy-7-oxoergost-22-en- $3\beta$ -yl acetate. The last compound is consequently a cis-glycol and the 9-hydroxyl group in this and related compounds is  $\alpha$ -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<sub>30</sub>H<sub>46</sub>O<sub>3</sub>Br<sub>2</sub> 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- $3\beta$ -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- $3\beta$ -yl acetate as rhombic plates, m. p. 231—233°,  $[\alpha]_D - 36^\circ$ ,  $-34^\circ$  (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-3 $\beta$ -yl Acetate.—(a) A solution of 22: 23-dibromo-11-oxo-9 $\beta$ -ergost-7-en-3 $\beta$ -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-8en-3 $\beta$ -yl acetate (70 mg.) which separates from methanol as elongated plates, m. p. 200—201°,  $[\alpha]_{\rm D}$  +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-7 $\xi$ : 11 $\alpha$ -dihydroxyergost-8-en-3 $\beta$ -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  $\times$  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-3 $\beta$ -yl acetate as elongated plates, m. p. 200—203°,  $[\alpha]_{\rm D}$  +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 ( $\varepsilon$  9000). It was undepressed in m. p. when mixed with a specimen described above.

22: 23-Dibromo-7-oxoergost-8-en- $3\beta$ -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- $3\beta$ -yl acetate as plates, m. p. 240—242°,  $[\alpha]_D - 29^\circ$  (c, 0.5) (Found: C, 58.8; H, 7.6%). Light absorption: Max. at 2530 Å ( $\epsilon$  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°,  $[\alpha]_D - 28^\circ$ , prepared as described by Budziarek, Johnson, and Spring (*loc. cit.*).

(b) A solution of 22:23-dibromo-7-oxoergost-9(11)-en-3 $\beta$ -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-3 $\beta$ -yl acetate (150 mg.),  $[\alpha]_{\rm D}$  -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 ( $\epsilon$  9250).

11-Oxo-9 $\beta$ -ergosta-7: 22-dien-3 $\beta$ -yl Acetate.—A solution of 22: 23-dibromo-11-oxo-9 $\beta$ -ergost-7-en-3 $\beta$ -yl acetate (1 g.) in benzene-ethanol (200 ml.; 1:1) was heated under reflux for 3 $\frac{1}{2}$  hr. with zinc dust (3 g.) added portionwise. The product was isolated in the usual manner and crystallised from acetone to give 11-oxo-9 $\beta$ -ergosta-7: 22-dien-3 $\beta$ -yl acetate as hexagonal plates, m. p. 159—161° (600 mg.),  $[\alpha]_{\rm D} - 206°$  (c, 2.55) (Found: C, 79.5; H, 10.1. Calc. for C<sub>30</sub>H<sub>46</sub>O<sub>3</sub>: C, 79.2; H, 10.2%). Bladon *et al.* (*loc. cit.*) give m. p. 159—161°,  $[\alpha]_{\rm D} - 191°$ . 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-3 $\beta$ -yl Acetate.—A solution of 22 : 23-dibromo-7-oxoergost-9(11)en-3 $\beta$ -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-3 $\beta$ -yl acetate was isolated by means of ether and crystallised from acetone as plates (300 mg.), m. p. 177—178°,  $[\alpha]_{\rm D} -55^{\circ}$ (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°,  $[\alpha]_{\rm D} -58^{\circ}$ , and Schoenewaldt et al. (loc. cit.) give m. p. 176— 177°,  $[\alpha]_{\rm D} -43\cdot5^{\circ}$ .

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

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(200 mg.), m. p. 175–177°,  $[\alpha]_D - 45^\circ$  (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 ( $\varepsilon$  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-9a: 11a-epoxy-7-oxoergostan-3 $\beta$ -yl Acetate.—A stirred solution of 22: 23-dibromo-7-oxoergost-9(11)-en-3 $\beta$ -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-9a: 11a-epoxy-7-oxoergostan-3 $\beta$ -yl acetate as plates (3·3 g.), m. p. 228—230°,  $[\alpha]_D - 44^\circ$  (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.)],  $[\alpha]_D - 49^\circ$  (c, 1·1) (Found : C, 57·2; H, 7·4. Calc. for C<sub>30</sub>H<sub>46</sub>O<sub>4</sub>Br<sub>2</sub>: C, 57·1; H, 7·35%). It does not show selective absorption of high intensity above 2200 Å.

 $3\beta: 11\alpha$ -Diacetoxy-22: 23-dibromo- $9\alpha$ -hydroxyergostan-7-one.—A solution of 22: 23-dibromo-7-oxoergost-9(11)-en- $3\beta$ -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 ( $2 \times 150$  c.c.) and then with chloroform  $(2 \times 150$  c.c.). The washed and dried (Na<sub>2</sub>SO<sub>4</sub>) 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  $3\beta$ :  $11\alpha$ -diacetoxy-22: 23-dibromo- $9\alpha$ -hydroxyergostan-7-one (550 mg.) as needles, m. p. 247— $250^{\circ}$  (not raised by further crystallisation) alone or mixed with a specimen prepared as described by Budziarek, Hamlet, and Spring (*loc. cit.*),  $[\alpha]_D - 27^\circ$  (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  $3\beta:11\alpha$ -diacetoxy-22:23-dibromo- $9\alpha$ -hydroxyergostan-7one (300 mg.), m. p. 247–249° alone or mixed with the specimen above,  $[\alpha]_D - 27^\circ$  (c, 2.0) (Found : C, 55.9; H, 7.5%).

 $3\beta: 11\alpha$ -Diacetoxy-9 $\alpha$ -hydroxyergost-22-en-7-one.—A solution of  $3\beta: 11\alpha$ -diacetoxy-22: 23dibromo-9 $\alpha$ -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  $3\beta: 11\alpha$ -diacetoxy-9 $\alpha$ -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.*)],  $[\alpha]_D - 46^\circ$  (*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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