585. *Studies in the Synthesis of Cortisone. Part II.* A New Synthesis of 3β-Acetoxyergost-22-en-11-one.*

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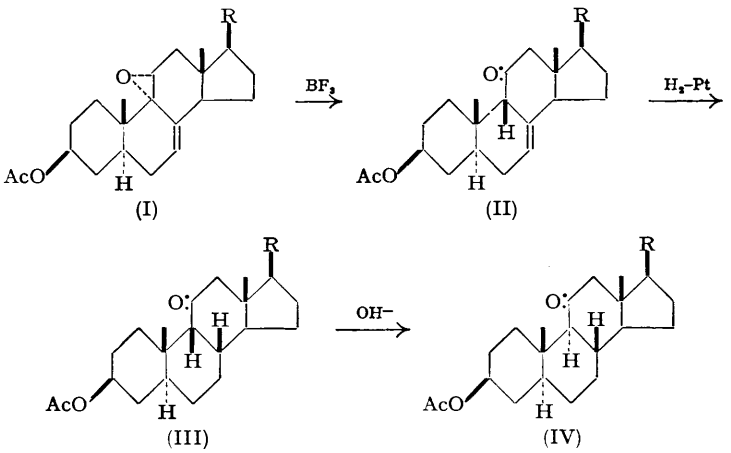
Ergosteryl-D acetate 22 : 23-dibromide or dichloride has been converted into 3β-acetoxyergost-22-en-11-one by the route to 11-keto-steroids described in the previous paper.

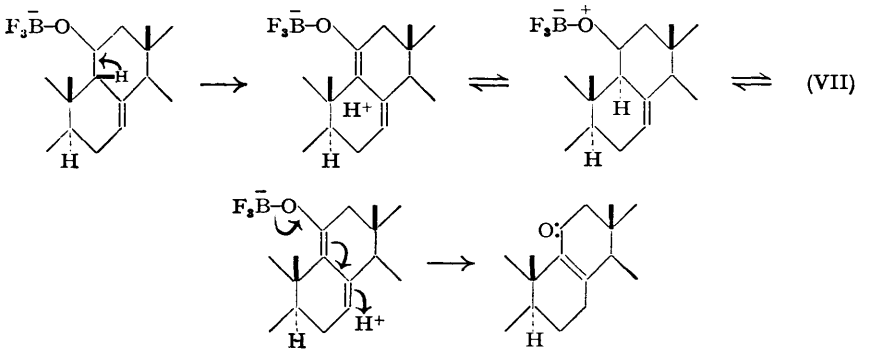
In Part I * of this series a new method has been described for introducing an 11-keto-group into *allo*steroids. This may be illustrated as follows :



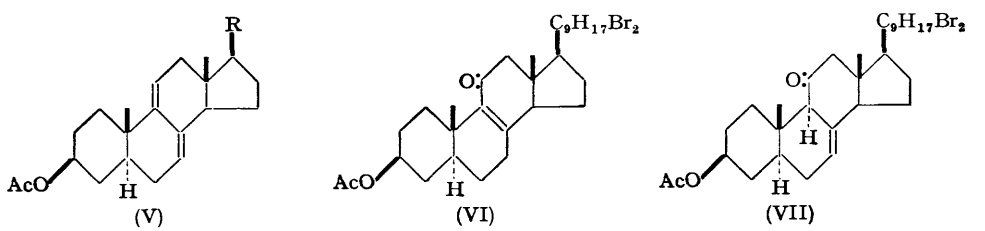
The present paper describes the extension of this route to include the preparation of 3β-acetoxyergost-22-en-11-one (IV; R = C_9H_{17}), a key intermediate in the synthesis of cortisone from ergosterol (cf. Chamberlin, Ruyle, Erickson, Chemerda, Aliminosa, Erickson, Sita, and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 2396; Chemerda, Chamberlin, Wilson, and Tishler, *ibid.*, p. 4053; Rosenkranz, Djerassi, Yashin, and Pataki, *Nature*, 1951, **168**, 28; Pataki, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 5615). Owing to the rather similar reduction rates of the 7 : 8- and 22 : 23-double bonds in (II; R = C_9H_{17}), this compound could not be converted directly into 3β-acetoxy-9β-ergost-22-en-11-one (III; R = C_9H_{17}) by selective hydrogenation (see Part I). However, the possibility of protecting the side-chain double bond during this stage as its dibromo-derivative was suggested by the observations of Budziarek, Johnson, and Spring (*J.*, 1953, 534) that such bromine atoms are stable under hydrogenation conditions but are easily removed, with restoration of the 22 : 23-double bond, by the use of zinc.

* Part I, preceding paper.

Since 3β-acetoxy-22 : 23-dibromo-9β-ergost-7-en-11-one (II; R = $C_9H_{17}Br_2$) could not be obtained by direct addition to the Δ^{22}-compound, owing to the ease with which nuclear bromination occurred even at −50°, attention was turned to the rearrangement of 3β-acetoxy-22 : 23-dibromo-9α : 11α-epoxyergost-7-ene (I; R = $C_9H_{17}Br_2$). Preparation of this epoxide from the diene (V; R = $C_9H_{17}Br_2$) and its conversion into 3β-acetoxy-22 : 23-dibromoergost-8(9)-en-11-one (VI), by means of boron trifluoride in benzene, have already been described (Budziarek, Johnson, and Spring, *J.*, 1952, 3410). Parallel with the observations recorded in Part I, we found that by using either a different solvent or a much shorter reaction time this rearrangement could be stopped at the required intermediate βγ-unsaturated ketone (II; R = $C_9H_{17}Br_2$). Thus, in acetone, ethyl acetate, or ether rearrangement was slow (owing to co-ordination of the solvent with boron trifluoride), and the βγ-unsaturated ketone separated from solution in good yield. However, this method was limited in scale by the poor solubility of the epoxide in such solvents. In benzene or toluene, rearrangement was very rapid; since the solution remained homogeneous, it was necessary to stop the reaction at the optimum time by addition of pyridine. With 5% solutions of the epoxide at room temperature, the optimum reaction time was only *ca.* 15 sec., but in toluene at −35° an 80% yield was obtained after 15 min. Reaction beyond the optimum time resulted in lower yields through the formation, first, of the 9α-isomer (VII) and then of the 11-keto-$\Delta^{8(9)}$-compound (VI). It thus appears that the rearrangement of 3β-acetoxy-22 : 23-dibromo-9β-ergost-7-en-11-one to the conjugated unsaturated ketone (VI) involves, as its first stage, inversion of configuration at $C_{(9)}$ (cf. chart).



Hydrogenation of (II; R = $C_9H_{17}Br_2$) to (III; R = $C_9H_{17}Br_2$) presented difficulties not met in the examples described in the previous paper. The poor solubility of the βγ-unsaturated ketone in acetic acid necessitated the addition of chloroform or dioxan, and platinum-catalysed hydrogenation in such solvent mixtures was found to be appreciably slower than



that of, for instance, (II; R = C_9H_{17}) in acetic acid alone. Further, a considerable proportion of the material was isomerised to the 11-keto-$\Delta^{8(9)}$-compound. Debromination of (III; R = $C_9H_{17}Br_2$) with zinc readily yielded 3β-acetoxy-9β-ergost-22-en-11-one (III; R = C_9H_{17}), and evidence that this still retained the 9β-configuration was provided by reduction to 3β-acetoxy-9β-ergostan-11-one (III; R = C_9H_{19}), identical with the compound obtained by hydrogenation of (II; R = C_9H_{17}) (cf. Part I).

Returning now to the hydrogenation of (II; R = $C_9H_{17}Br_2$), further investigation

showed that no advantage could be gained by working at higher temperatures (70—100°) in neutral or acidic media, or by adding sodium acetate or catalytic amounts of hydrochloric acid, since these modifications tended to favour isomerisation irrespective of the catalyst used (*viz.*, platinum, palladium–carbon, or Raney nickel). However, a substantial improvement in yield was obtained by hydrogenation at elevated pressure, perhaps because the rate of hydrogenation is more influenced by the concentration of hydrogen on the catalyst surface than is the rate of isomerisation. The reduction product obtained by this method was best purified after debromination; α-dihydroergosteryl acetate was obtained as a by-product (see Experimental section). Thus, platinum-catalysed hydrogenation of (II; R = $C_9H_{17}Br_2$) at 100 atmospheres pressure in chloroform–acetic acid with subsequent debromination gave 3β-acetoxy-9β-ergost-22-en-11-one in 70—74% yield.

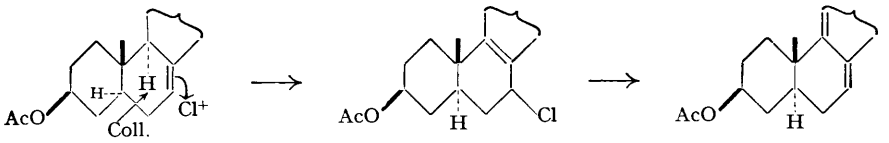
Clearly there was less isomerisation if hydrogenation was rapid. If, then, the slowness of hydrogenation at atmospheric pressure was in some measure caused by poisoning of the catalyst by traces of hydrogen bromide (derived by hydrogenation of the side-chain halogens), it might be advantageous to use the corresponding dichloro-compound (II; R=$C_9H_{17}Cl_2$). 3β-Acetoxy-22 : 23-dichloro-9α : 11α-epoxyergost-7-ene (I; R = $C_9H_{17}Cl_2$), required in the preparation of (II; R = $C_9H_{17}Cl_2$), was obtained by selective oxidation of 3β-acetoxy-22 : 23-dichloroergosta-7 : 9(11)-diene (V; R = $C_9H_{17}Cl_2$). We have now devised a more direct method for preparing this diene than that described by Anderson, Stevenson, and Spring (*J.*, 1952, 2901). Treatment of α-dihydroergosteryl acetate with chlorine at −20° to +20° gave only a poor (isolated) yield of the desired dichloride, but a marked improvement was obtained on adding collidine (or pyridine) to the mixture before chlorination. Adding the base after the chlorine was ineffective. Some illustrative results are summarised in Table 1,

TABLE 1.

Reaction conditions	Properties of crude total product $[\alpha]_D$ (*c*, 2·0)	7 : 9(11)-Diene (%) *
No addition of collidine	−66°	49
Collidine (2 mols.) added after chlorine	−57	48
Collidine (7 mols.) added	+ 5	82
Collidine (2·2 mols.) added	+ 9	84
Collidine (0·75 mol.) added	0	82

* Based on ε = 19,000 at 242 mμ for pure diene (see Experimental).

the yields of the crude diene being assessed from light-absorption data; purification was wasteful. Collidine did not prevent subsequent addition of hydrogen chloride to the 7 : 9(11)-diene system. A convenient explanation of its action is that it removes the potential proton at $C_{(9)}$ *at the same time* as the original 7(8)-ethylenic linkage is attacked by Cl^+, *viz.*:



Rearrangement of 3β-acetoxy-22 : 23-dichloro-9α : 11α-epoxyergost-7-ene to 3β-acetoxy-22 : 23-dichloro-9β-ergost-7-en-11-one (II; R = $C_9H_{17}Cl_2$) proceeded normally in ether. With a platinum catalyst in acetic acid, the uptake of hydrogen by the latter compound was high (*ca.* 2 mols.), hydrogenolysis of the 11-keto-group occurring to a considerable extent, and of the halogen atoms to some extent. When the reaction was stopped after uptake of 1 mol., there was some indication of incomplete reduction of the 7 : 8-double bond. The required compound, 3β-acetoxy-22 : 23-dichloro-9β-ergostan-11-one (III; R = $C_9H_{17}Cl_2$) was best obtained, although in poor yield, by platinum-catalysed hydrogenation in ethyl acetate. Modifying the conditions of hydrogenation, as for the dibromo-compound, was not a substantial improvement. Dehalogenation of (III; R = $C_9H_{17}Cl_2$) with zinc in acetic acid required more vigorous conditions than that of the bromo-compound; in spite of this, there was no indication of epimerisation, and 3β-acetoxy-9β-ergost-22-en-11-one was obtained, identical with the product described earlier.

Finally, prolonged treatment of the 11-keto-Δ^{22}-9β-stanol (III; R = C_9H_{17}) with hot ethanolic potassium hydroxide, with subsequent reacetylation, gave in excellent yield the required 3β-acetoxyergost-22-en-11-one (IV; R = C_9H_{17}), identical with authentic material (cf. Heusser, Kurath, Dällenbach, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106). Of the two routes to this compound examined, the first, involving the use of 22 : 23-dibromo-compounds, is by far the better and appears to offer a useful alternative to those already described (cf., *inter alia*, *idem*, *ibid.*; Chamberlin *et al.*, *loc. cit.*; Schoenewaldt, Turnbull, Chamberlin, Reinhold, Erickson, Ruyle, Chemerda, and Tishler, *J. Amer. Chem. Soc.*, 1952, **74**, 2696).

TABLE 2.

Compound	$[M]_D$ 9β-	9α-	$\Delta[M]_D$ 9β ⟶ 9α
IX; R = H, R′ = C_9H_{17}	+ 90°	+ 55°	− 35°
IX; R = H, R′ = $C_9H_{17}Br_2$	+185	+110 †	− 75
IX; R = H, R′ = $C_9H_{17}Cl_2$	+170	+ 95 †	− 75
IX; R = H, R′ = C_9H_{19} *	+195	+150	− 45
IX; R = OH, R′ = C_9H_{19} *	+415	+115	−300
IX; R = OH, R′ = CHMe·CO_2Me *	+365	+ 80	−285
IX; R = OH, R′ = $COCH_3$ *	+700	+310	−390
VIII; R = H, R′ = C_9H_{17} *	−865	+115	+970
VIII; R = H, R′ = $C_9H_{17}Br_2$	−750	+ 80	+830
VIII; R = OAc, R′ = C_9H_{17} *	−250	+430	+680

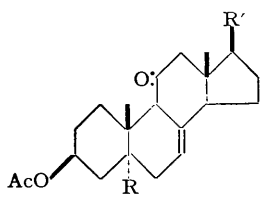
* Part I, *loc. cit.* † Obtained by addition of the necessary halogen to (IV; R = C_9H_{17}).

TABLE 3. *Absorption maxima* (*cm.*$^{-1}$), *in* CS_2.

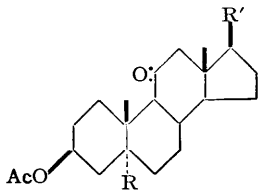
Compound	9α-Isomer Acetyl	9α-Isomer Ketone	9β-Isomer Acetyl	9β-Isomer Ketone
VIII; R = H, R′ = C_9H_{17}	1735	1710	1736	1725
VIII; R = H, R′ = $C_9H_{17}Br_2$	1736	1718	1737	1726
IX; R = H, R′ = C_9H_{17} (C.S. nos.: 9α-, C.S. 49; 9β-, C.S. 50 *)	1731	1706	1734	1712
IX; R = H, R′ = C_9H_{19}	1735	1715	1735	1720
IX; R = H, R′ = $C_9H_{17}Br_2$	1732	1708	1736	1715
IX; R = H, R′ = $C_9H_{17}Cl_2$	1730	1705	1737	1716

* Spectra thus marked have been deposited at the Chemical Society. Photocopies may be obtained from the General Secretary. In such requests the C.S. number must be cited.

Tables 2 and 3 show that regular changes in molecular rotation and infra-red absorption accompany epimerisation at $C_{(9)}$. Thus, inversion at $C_{(9)}$ (β⟶α) in (IX; R = H) leads to a small negative change in molecular rotation (Table 2). The strong vicinal effect of a hydroxy-group at $C_{(5)}$ is apparent from the marked increase in magnitude of the Δ value for compounds (IX; R = OH); a 7 : 8-ethylenic linkage, as in (VIII), increases the Δ value and changes its sign. It is proposed, in a later paper, to show that the molecular-rotation difference is also influenced by the nature of the side-chain.



(VIII)



(IX)

Compared with the corresponding natural isomers, the 9β-compounds (VIII; R = H) and (IX; R = H) show a characteristic displacement of the carbonyl band in the infra-red towards the higher wave-numbers (Table 3), leading to a less well-defined resolution of the acetyl and carbonyl bands.

EXPERIMENTAL

Unless otherwise specified, optical measurements were determined on chloroform solutions (*c*, 0·9—1·2) at room temperature. Other general experimental directions are given in *J.*, 1953, 2918).

3β-*Acetoxy*-22 : 23-*dibromo*-9β-*ergost*-7-*en*-11-*one* (II; R = $C_9H_{17}Br_2$).—(*a*) A solution of

3β-acetoxy-22 : 23-dibromo-9α : 11α-epoxyergost-7-ene (Budziarek, *et al.*, *J.*, 1952, 3410) (50 g.) in toluene (1·5 l.) was concentrated to 1 l. at atmospheric pressure. With exclusion of moisture, the solution was treated with freshly distilled boron trifluoride–ether complex (10 ml.; 1 mol.) for 15 min. at −35°. Pyridine (20 ml.) was then added to the solution, which, after warming to room temperature, was washed successively with water, aqueous sodium hydrogen carbonate, and water, and concentrated *in vacuo* to 200 ml.; on addition of ethanol (1 l.) and cooling in the refrigerator, needles (41 g., 82%) separated with m. p. 195—197°, $[\alpha]_D$ −120°. Crystallisation from benzene afforded the 11-*ketone* as needles, m. p. 196—198°, $[\alpha]_D$ −123° (Found: C, 58·6; H, 7·65. $C_{30}H_{46}O_3Br_2$ requires C, 58·65; H, 7·55%). The compound showed no selective absorption of high intensity above 220 mμ. Infra-red spectrum (in CS_2): peaks at 1737 and 1240 (acetate), 1726 (11-ketone), 1656, 821, and 805 cm.$^{-1}$ (trisubstituted nuclear double bond).

The mother-liquors were evaporated to dryness *in vacuo*; crystallisation of the residue from ethyl acetate gave 3β-*acetoxy*-22 : 23-*dibromoergost*-7-*en*-11-*one* (VII) as plates, m. p. 217—219°, $[\alpha]_D$ −13° (Found: C, 58·65; H, 7·7%). This showed no selective absorption of high intensity above 220 mμ. Infra-red spectrum (in CS_2): peaks at 1736 and 1238 (acetate) and 1718 cm.$^{-1}$ (11-ketone).

(*b*) Freshly distilled boron trifluoride–ether complex (2 ml.; 1 mol.) was added to a solution of the 9α : 11α-epoxide (10 g.) in dry ether (500 ml.), the solution then being kept at 0° for 18 hr.; the 9β-compound (7·8 g., 78%) separated as needles, m. p. 193—196°, $[\alpha]_D$ −118°.

Hydrogenation of 3β-*Acetoxy*-22 : 23-*dibromo*-9β-*ergost*-7-*en*-11-*one*.—(a) *At atmospheric pressure.* A solution of the above βγ-unsaturated ketone (5 g.) in chloroform–acetic acid (1 : 1; 20 ml.) was shaken with Adams catalyst (2 g.) under hydrogen until 1 mol. of hydrogen was absorbed (*ca.* 1 hr.). Isolation with ether followed by crystallisation from ethyl acetate gave 3β-*acetoxy*-22 : 23-*dibromo*-9β-*ergostan*-11-*one* (III; R = $C_9H_{17}Br_2$) (2·17 g., 54%) as laths, m. p. 226—230° (decomp.), $[\alpha]_D$ +30° (Found: C, 58·6; H, 7·95. $C_{30}H_{48}O_3Br_2$ requires C, 58·45; H, 7·85%). Infra-red spectrum (in CS_2): peaks at 1736 and 1242 (acetate) and 1715 cm.$^{-1}$ (11-ketone).

The second crop from the above crystallisation had $\lambda_{max.}$ 252 mμ ($E^{1\%}_{1cm}$ 135) in EtOH. Hydrogenation of (II; R = $C_9H_{17}Br_2$) under the above conditions, but on a larger scale (17 g.), gave the saturated dibromo-ketone in 30% yield.

Debromination. Zinc dust (10 g.) was added, during 1 hr., to a stirred solution of the foregoing ketone (2 g.) in chloroform (40 ml.) and acetic acid (80 ml.), at <50°. After being stirred for a further hour at room temperature, the solution was filtered and diluted with water. Isolation with chloroform, followed by crystallisation from chloroform–methanol, gave 3β-*acetoxy*-9β-*ergost*-22-*en*-11-*one* (III; R = C_9H_{17}) (1·2 g., 81%) as plates, m. p. 170—173°, $[\alpha]_D$ +20° (Found: C, 78·9; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). Infra-red spectrum (in CS_2): peaks at 1734 and 1240 (acetate), 1712 (11-ketone), and 970 cm.$^{-1}$ (Δ^{22}).

(b) *At elevated pressure.* The 9β-unconjugated ketone (37·5 g.) in chloroform–acetic acid (1 : 1; 670 ml.) was shaken with Adams's catalyst (3·35 g.) under hydrogen at 100 atm. for 30 min. The solution was filtered and treated with zinc dust (50 g.) as described above. Isolation with chloroform, followed by crystallisation from methanol–chloroform, gave 3β-acetoxy-9β-ergost-22-en-11-one (20·7 g., 74%) as plates, m. p. 170—174°, $[\alpha]_D$ +18·5°.

It was not always possible to purify the 11-ketone by crystallisation alone, without undue wastage; in such instances chromatography was used. Crude material (7 g.) [prepared as above from 10 g. of (III; R = $C_9H_{17}Br_2$)] was adsorbed on alumina (P. Spence, Grade 0, 180 g.); the first fractions obtained on elution with light petroleum–benzene (3 : 1; 2 × 100 ml.) had $[\alpha]_D$ <+15°—these were discarded. Material obtained by elution with light petroleum–benzene (3 : 1; 300 ml.) and benzene (300 ml.) was crystallised from chloroform–methanol to give the 11-ketone (5·2 g., 70%) as plates, m. p. 167—169°, $[\alpha]_D$ +20°. Repeated crystallisation from methanol of the combined fractions with $[\alpha]_D$ <+15° (see above) gave α-dihydroergosteryl acetate as plates, m. p. 174—178°, $[\alpha]_D$ −18·5° (Found: C, 82·25; H, 11·05. Calc. for $C_{30}H_{48}O_2$: C, 81·8; H, 11·0%). Barton and Cox (*J.*, 1948, 1354) give m. p. 181°, $[\alpha]_D$ −19°, −20°. On admixture with authentic material the m. p. was not depressed. The corresponding alcohol had m. p. 170—174°, $[\alpha]_D$ −18° (Found: C, 84·3; H, 11·5. Calc. for $C_{28}H_{46}O$: C, 84·35; H, 11·6%) (*idem*, *ibid.*, give m. p. 176°, $[\alpha]_D$ −19°). Admixture with authentic material did not depress the m. p.

3β-*Acetoxy*-9β-*ergostan*-11-*one* (III; R = C_9H_{19}).—3β-Acetoxy-9β-ergost-22-en-11-one (100 mg.) was hydrogenated with prereduced Adams catalyst (30 mg.) in acetic acid (100 ml.). One mol. of hydrogen was absorbed. Isolation with ether followed by crystallisation from methanol gave the 11-ketone (45 mg.) as rods, m. p. and mixed m. p. 151—152°, $[\alpha]_D$ +45° (cf. Part I).

3β-*Acetoxyergost*-22-*en*-11-*one* (IV; R = C_9H_{17}).—A solution of the 9β-isomer (2 g.) and potassium hydroxide (20 g.) in ethanol (150 ml.) was heated under reflux for 18 hr. The product was isolated with ether and reacetylated with acetic anhydride (24 ml.) and pyridine (20 ml.) at 100° for 1 hr. Crystallisation from methanol gave the 11-ketone (1·69 g., 85%) as needles, m. p. 124—125°, $[\alpha]_D$ +12° (Found: C, 78·8; H, 10·5. Calc. for $C_{30}H_{48}O_3$: C, 78·9; H, 10·6%). Admixture with an authentic sample did not depress the m. p. (cf. Heusser *et al.*, *loc. cit.*, who record m. p. 125—126°, $[\alpha]_D$ +12·5°). The infra-red spectrum was identical with that of authentic material.

Addition of water to the mother-liquors from the above crystallisation gave further 11-ketone (90 mg., 4·6%) with m. p. 119—123°, $[\alpha]_D$ +11·8°.

3β-*Acetoxy*-22 : 23-*dibromoergostan*-11-*one* (IV; R = $C_9H_{17}Br_2$).—Bromine (1·55 g., 1·1 mols.) in chloroform (6 ml.) was added dropwise to 3β-acetoxyergost-22-en-11-one (4 g.) in chloroform (20 ml.); rapid decolorisation ensued. On addition of methanol (100 ml.) and cooling to 0°, needles (1·2 g.) separated with m. p. 225—231°; $[\alpha]_D$ +16·7°. Crystallisation from ethanol gave the 11-*ketone* 22 : 23-*dibromide* as needles, m. p. 233—236°, $[\alpha]_D$ +18·5° (Found: C, 58·2; H, 7·9. $C_{30}H_{48}O_3Br_2$ requires C, 58·4; H, 7·85%). Infra-red spectrum (in CS_2): bands at 1732 and 1242 (acetate), and 1708 cm.$^{-1}$ (11-ketone).

3β-*Acetoxy*-22 : 23-*dichloroergosta*-7 : 9(11)-*diene* (V; R = $C_9H_{17}Cl_2$).—To α-dihydroergosteryl acetate (10 g.) in carbon tetrachloride (150 ml.) and redistilled collidine (6 ml.) at 0°, chlorine (4 g.) in carbon tetrachloride (500 ml.) was added slowly with stirring. The mixture was left at room temperature with stirring, for 1 hr., and then washed successively with 2N-hydrochloric acid and water. Removal of the carbon tetrachloride by distillation on the steam-bath at atmospheric pressure, followed by crystallisation of the residue from chloroform–methanol, gave needles (6·3 g., 55%), m. p. 204—207° (decomp.), $[\alpha]_D$ +33° (*c*, 1·94). Recrystallisation from chloroform–methanol afforded the 7 : 9(11)-diene as needles, m. p. 227—229° (decomp.), $[\alpha]_D$ +45° (*c*, 2) (Found: C, 70·6; H, 9·05; Cl, 14·0. Calc. for $C_{30}H_{46}O_2Cl_2$: C, 70·7; H, 9·1; Cl, 13·9%). Light absorption: Max. at 242 (ε = 19,000) and 235 mμ (ε = 17,000). Anderson *et al.*, *loc. cit.*, record m. p. 235—237°, $[\alpha]_D$ +44°.

The corresponding *alcohol*, prepared from the acetate with potassium hydroxide in methanol–dioxan, crystallised from chloroform–methanol in blades, m. p. 210—212° (decomp.), $[\alpha]_D$ +37·4° (*c*, 1·4) (Found: Cl, 15·2. $C_{28}H_{44}OCl_2$ requires Cl, 15·3%). Light absorption: Max. at 243 (ε = 20,000) and 235 mμ (ε = 18,300).

Treatment of 3β-*Acetoxy*-22 : 23-*dichloroergosta*-7 : 9 (11)-*diene with Hydrogen Chloride*.—The diene (330 mg.) in carbon tetrachloride (22 ml.) containing hydrogen chloride (55 mg.), was stirred for 30 min. at 0°. The solvent was evaporated *in vacuo*, leaving a solid, m. p. 225—227° (decomp.) (undepressed on admixture with starting material), $[\alpha]_D$ +41°. Light absorption: Max. at 242 (ε = 18,900) and 235 mμ (ε = 17,000).

3β-*Acetoxy*-22 : 23-*dichloro*-9α : 11α-*epoxyergost*-7-*ene*.—An ethereal solution of monoperphthalic acid (40 ml. containing 1·3 equivs. of available oxygen) was added to a cooled solution of 3β-acetoxy-22 : 23-dichloroergosta-7 : 9(11)-diene (10·5 g.) in chloroform (freshly distilled over anhyd. K_2CO_3; 100 ml.) at such a rate that the temperature did not exceed −5°. After being left for 2 hr. at 0°, the mixture was washed successively with aqueous sodium hydrogen carbonate, dilute aqueous ferrous sulphate, and water. The solution was then dried ($MgSO_4$) and evaporated to dryness *in vacuo*. The residue was triturated with hot acetone (30 ml.), cooled, and filtered off. The *epoxide* (7·4 g., 68%) melted at 191—197° and had $[\alpha]_D$ −14°. Crystallisation from ethyl acetate gave the compound as needles, m. p. 204—208°, $[\alpha]_D$ −18·5° (Found: C, 68·5; H, 8·6. $C_{30}H_{46}O_3Cl_2$ requires C, 68·55; H, 8·8%). Infra-red spectrum (in Nujol): bands at 1730 and 1240 (acetate) and 1652 and 833 cm.$^{-1}$ (trisubstituted ethylene).

3β-*Acetoxy*-22 : 23-*dichloro*-9β-*ergost*-7-*en*-11-*one* (II; R = $C_9H_{17}Cl_2$).—Freshly distilled boron trifluoride–ether complex (1·3 ml., 1 mol.) was added to 3β-acetoxy-22 : 23-dichloro-9α : 11α-epoxyergost-7-ene (5·25 g.) in dry ether (500 ml.), the solution then being kept at 0° for 18 hr. The 11-*ketone dichloride* (2·9 g., 55%) separated as needles, m. p. 217—222°, $[\alpha]_D$ −134° (Found: C, 68·4; H, 8·5. $C_{30}H_{46}O_3Cl_2$ requires C, 68·55; H, 8·8%). The compound showed no significant absorption above 220 mμ. Infra-red spectrum (in CS_2): bands at 1738 and 1240 (acetate), 1726 (11-ketone), 1657, 820, and 808 cm.$^{-1}$ (associated with trisubstituted nuclear double bond). The ethereal filtrate was washed successively with water, sodium hydrogen carbonate solution, and water, and evaporated until solid began to separate; the crystals were collected and crystallised from ethyl acetate, to give the 11-ketone dichloride (1·08 g., 20·6%), $[\alpha]_D$ −122°.

3β-*Acetoxy*-22 : 23-*dichloro*-9β-*ergostan*-11-*one* (III; R = $C_9H_{17}Cl_2$).—The foregoing ketone (2·63 g.) in ethyl acetate (250 ml.) was hydrogenated in the presence of prereduced Adams catalyst (500 mg.), 2·2 mols. of hydrogen being absorbed in 65 min. Filtration, evaporation of the solvent, and repeated crystallisation of the residue from methanol gave the 11-*ketone dichloride* (650 mg., 25%) as plates, m. p. 248—252°, $[\alpha]_D$ +32° (Found : C, 68·4; H, 9·1; Cl, 13·1. $C_{30}H_{48}O_3Cl_2$ requires C, 68·3; H, 9·1; Cl, 13·45%). Infra-red spectrum (in CS_2) : bands at 1737 and 1240 (acetate), and 1716 cm.$^{-1}$ (11-ketone).

Dechlorination. Zinc dust (5 g.) was added during 1 hr. to a solution of the above ketone (570 mg.) in refluxing acetic acid (50 ml.), and heating was continued for 4 hr. Isolation with chloroform and crystallisation from methanol gave 3β-acetoxy-9β-ergost-22-en-11-one (340 mg., 74%), identical in a mixed m. p. determination and infra-red spectrum with a specimen prepared by the alternative route described above.

3β-*Acetoxy*-22 : 23-*dichloroergostan*-11-*one* (IV; R = $C_9H_{17}Cl_2$).—Chlorine (2 g., 3 mols.) in carbon tetrachloride (150 ml.) was added dropwise to 3β-acetoxyergost-22-en-11-one (5 g.) in pyridine (250 ml.) and carbon tetrachloride (150 ml.) at 0°. After 1 hr. at room temperature, the solution was washed with 2N-hydrochloric acid and water. Evaporation *in vacuo* followed by crystallisation from methanol–chloroform gave the 11-*ketone dichloride* as needles, m. p. 212—215°, $[\alpha]_D$ +18° (Found : C, 68·2; H, 9·1; Cl, 13·2. $C_{30}H_{48}O_3Cl_2$ requires C, 68·3; H, 9·1; Cl, 13·45%). Infra-red spectrum (in CS_2) : bands at 1730 and 1240 (acetate), and 1705 cm.$^{-1}$ (11-ketone).

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