788. *Studies in the Synthesis of Cortisone. Part III.* The Degradation of the Ergosterol Side Chain.*

By A. F. B. Cameron, J. S. Hunt, J. F. Oughton, P. A. Wilkinson, and B. M. Wilson.

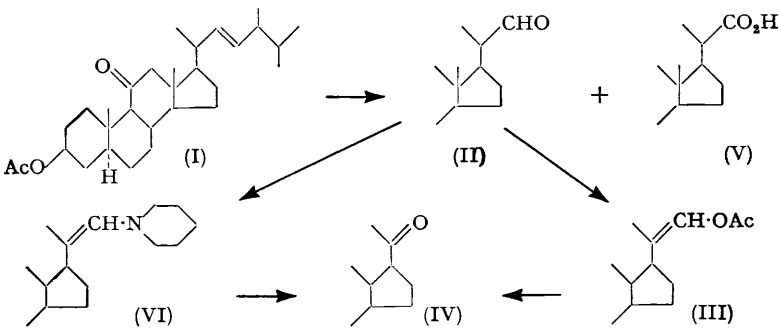
The route to cortisone from 3β-acetoxyergost-22-en-11-one, as described in Part II, has been extended through 3β-acetoxy-11-oxobisnor*allo*cholanal and 3β : 22-diacetoxy-11-oxobisnor*allo*chol-20(22)-en-11-one to 3β-acetoxy-*allo*pregnane-11 : 20-dione. The corresponding 9β-compounds are also described.

The introduction of an 11-keto-group into *allo*-steroids and the preparation of 3β-acetoxyergost-22-en-11-one (I*a*) from ergosteryl-D acetate 22 : 23-dibromide or -dichloride were described in Parts I and II of this series.* This paper deals with the degradation of the side chain of 3β-acetoxyergost-22-en-11-one (I*a*) and its 9-epimer (I*b*) and extends the proposed synthesis of cortisone to the corresponding 3β-acetoxy*allo*pregnane-11 : 20-diones (IV*a* and *b*) (Stork, Romo, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1951, **73**, 3546; Chamberlin, Ruyle, Erickson, Chemerda, Aliminosa, Erickson, Sita, and Tishler, *ibid.*, p. 2396; Djerassi, Batres, Romo, and Rosenkranz, *ibid.*, 1952, **74**, 3634).

Ozonolysis of the $C_{(22)}$-double bond of 3β-acetoxyergost-22-en-11-one (I*a*) should give 3β-acetoxy-11-oxobisnor*allo*cholanic acid (V*a*) or 3β-acetoxy-11-oxobisnor*allo*cholanal (II*a*), depending on the reaction conditions (cf. Chamberlin *et al.*, *loc. cit.*; Bladon, Henbest, Jones, Wood, and Woods, *J.*, 1952, 4890; Levin *et al.*, Amer. Chem. Soc., 120th Meeting, Abs., 1951, 6L). Barbier–Wieland degradation of the methyl ester of (V*a*) has already

* Parts I and II, *J.*, 1953, 2921, 2933.

been reported (Chamberlin *et al.*, *loc. cit.*). The alternative route, *via* the aldehyde (II*a*) and enol-acetate (III*a*) (cf. Bladon *et al.*, *loc. cit.*), would lead to the required ketone (IV*a*) in fewer stages and appeared more attractive provided that good yields could be achieved.



Series (*a*), 9α-H. Series (*b*), 9β-H.

Acetic acid was found to be the most suitable solvent for the formation of the ozonide of (I*a*), since the aldehyde (II*a*) could be obtained in 85—90% crude yield by rapid reduction by an excess of fresh zinc powder. Ozonolysis in ethyl acetate, methanol, or methylene chloride, followed by reduction with ferrous sulphate (Bladon *et al.*, *loc. cit.*) or alkaline sodium dithionite solutions, gave inferior results. The chief by-product was the bisnor*allo*cholanic acid (V*a*), its amount depending on the experimental conditions. This acid was obtained in 66% yield by treatment of the ozonide in acetic acid with permanganate (cf. Part I). Similar ozonolysis of 3β-hydroxyergost-22-en-11-one produced 3β-hydroxy-11-oxobisnor*allo*cholanal and the corresponding acid in yields similar to those in the 3β-acetoxy-series. The sensitivity of the ozonide solution to excess of ozone limited the amount that could be used: formation of the bisnor*allo*cholanic acid, which was slow at the beginning of ozonisation, became faster with increasing concentration of ozonide; and if more than 1·05 mols. of ozone were used the yield of aldehyde was lowered, whereas a large excess of ozone gave a good yield of acid but little or no aldehyde. A method was therefore devised for estimating the end of the ozonisation, since the output of the ozoniser was not sufficiently reliable (see Experimental section). Oxidation could not be limited by carrying it out in ethyl acetate at −70° (cf. Bladon *et al.*, *loc. cit.*), and use of a continuous flow through a packed column (to reduce time of contact) surprisingly increased the yield of acid. The aldehyde itself was very susceptible to oxidation in solution during the working up; although no reactive oxygen could be found in a freshly decomposed ozonide solution containing the aldehyde, the presence of reactive oxygen was again apparent after about 5 minutes' contact with the atmosphere, oxidation evidently proceeding *via* the peracid (Linstead, *Ann. Reports*, 1937, **34**, 234).

With potassium acetate in acetic anhydride 3β-acetoxy-11-oxobisnor*allo*cholanal (cf. Levin *et al.*, *loc. cit.*; Bergmann and Stevens, *J. Org. Chem.*, 1948, **13**, 10; Heyl and Herr, *J. Amer. Chem. Soc.*, 1950, **72**, 2617) gave 3β : 22-diacetoxybisnor*allo*chol-20(22)-en-11-one (III*a*) in 60—70% yield. The 11-keto-group is not attacked by this procedure. The reaction is particularly sensitive to alterations in the relative amounts of acetic acid and potassium acetate. When the 3β-hydroxy-aldehyde was used, with the normal quantity of catalyst, the extra acetic acid produced by the easier acetylation at position 3 had to be removed before appreciable enol acetylation at $C_{(22)}$ took place, but this difficulty could be overcome, at the expense of quality of product, by using a larger amount of catalyst. Pyridine, and *iso*propenyl acetate, with the 3β-acetoxy-aldehyde (II*a*) gave inferior yields of (III*a*) and boron trifluoride–ether complex or perchloric acid yielded only the aldehyde diacetate.

Ozonolysis of (III*a*) produced the required 3β-acetoxy*allo*pregnane-11 : 20-dione (IV*a*) in 94% yield. The high yield and good quality of the product depended on the presence of 1·5—5% of water in the acetic acid during ozonisation. Water added after ozonisation but before reductive decomposition with zinc dust gave a poorer yield of

(IV*a*), similar to that obtained by the use of anhydrous acetic acid throughout. The ozonide gave correct titration values after being kept for several hours in acetic acid solution and appeared to be comparatively stable to excess of ozone.

The same reactions were carried out in the 9β-series (see Part II), starting from 3β-acetoxy-9β-ergost-22-en-11-one (I*b*), with similar results. The 3β-acetoxy-9β-*allo*pregnane-11 : 20-dione (IV*b*) was converted into the corresponding 9α-compound (IV*a*) by refluxing with alcoholic alkali, followed by mild acetylation (cf. Part I). The yield was only 18%, presumably owing to isomerisation at $C_{(17)}$ (cf. Part I).

The characteristic shift of the carbonyl peaks in the infra-red toward higher wave numbers exhibited by the 9β-isomers is shown in the Table (cf. Part II), which also shows

	$[M]_D$		$\Delta[M]_D$	Infra-red CO band (cm.$^{-1}$)	
	9β	9α	9β ⟶ 9α	9α	9β
(I)	+ 90°	+ 55°	− 35°	1708	1715
(II)	+130	+107	− 23	1708	1712
(III)	+392	+ 99	−293	1708	1718
(IV)	+491	+322	−169	1712 *	1712 *
(V)	+117	+ 65	− 52	1708	1718

* In this compound the separate carbonyl bands are unresolved, so the shift in wave number is masked.

that the molecular rotation difference $\Delta[M]_D$ becomes much more negative as the centre of unsaturation in the side chain approaches the nucleus.

The formation of enamines of aldehydes was described by Herr and Heyl (*J. Amer. Chem. Soc.*, 1952, **74**, 3627; 1953, **75**, 1918) while this work was in progress, and it was thought that this might be a possible alternative procedure to enol acetylation of the aldehyde. The aldehyde (II*a*) formed the 22-piperidino-derivative (VI) under the conditions described, but the yield and purity of the crude product were inferior to those of the enol acetate (III*a*) and the pure compound was less stable. Ozonisation in methylene chloride at room temperature, followed by reductive decomposition, gave 3β-acetoxy-*allo*pregnane-11 : 20-dione in comparatively low yield.

Experimental

For determination of optical rotation chloroform solutions were used. Carbon disulphide was the solvent in determinations of the infra-red spectra. Materials for micro-analysis, but not for other determinations, were dried at 100°/*ca.* 0·5 mm. for 2 hr. Other general experimental directions were given in Part I.

3β-*Acetoxy*-11-*oxobisnor*allo*cholanal* (II*a*).—Ozonised oxygen (300 l./hr. containing *ca.* 0·03 g. of ozone/l.) was passed through a vigorously stirred solution of 3β-acetoxyergost-22-en-11-one (I*a*) (100 g., 0·22 mole) in glacial acetic acid (1 l.) until 10·5 g. (0·22 mole) had been absorbed. The variation in the output of the ozoniser over long periods of time rendered calculations of reaction time unreliable; the end of the reaction was confirmed by finding the time interval between (i) the addition of 1 ml. of standard sodium thiosulphate solution to a potassium iodide solution through which the exit gases were passing and (ii) the reappearance of the iodine colour. When this interval became small (*i.e.*, much ozone escaped unchanged) and coincided with a predetermined value, reaction was stopped. Very efficient stirring to break up the gas stream and a baffle to prevent the formation of a vortex were essential for reliability of the end-point. The temperature was kept at 15—20° by cooling. With continued stirring, zinc dust (*ca.* 120 g.) was added during 15 min., and ice was added to the bath to check the rapid rise in temperature. When decomposition was complete (starch–iodide paper), the remaining solids were filtered off and washed with acetic acid, and the combined filtrates were evaporated to dryness under reduced pressure. The residue was dissolved in ether and washed with N-sodium hydroxide until free from steroid acid. After washing with water and drying (Na_2SO_4), evaporation of the ethereal solution yielded crude 3β-*acetoxy*-11-*oxobisnor*allo*cholanal* (76 g., 89%), m. p. 130—133°, $[\alpha]_D^{20}$ +21°.

A specimen of the aldehyde (4·9 g.) in 1 : 1 light petroleum–benzene, chromatographed on acid-washed alumina (Brockmann grade II—III) (150 g.), gave first a gum and then a crystalline solid (2·11 g.). Recrystallisation from aqueous methanol gave the aldehyde as plates (2·0 g.), m. p. 135—140°, $[\alpha]_D^{20}$ +27·5° (*c*, 1·16) (Found : C, 74·25; H, 9·5. $C_{24}H_{36}O_4$ requires C, 74·2;

H, 9·3%). $\nu_{max.}$ 1730—1740 and 2680 (aldehyde), 1730—1740 and 1242 (acetate), and 1708 cm.$^{-1}$ (unconjugated carbonyl). The *semicarbazone* formed colourless needles (from acetic acid), m. p. 214—217° (Found: C, 67·4; H, 8·7; N, 9·6. $C_{25}H_{39}O_4N_3$ requires C, 67·4; H, 8·8; N, 9·4%), $\lambda_{max.}$ 230 mμ (ε 12,700 in EtOH).

The crude aldehyde (5 g.) in anhydrous methanol was treated with a stream of dry hydrogen chloride for 2 min. After being refluxed for 15 min. the solution deposited crystals on cooling (3·4 g.). Recrystallisation from methanol gave 3β-*acetoxy*-22 : 22-*dimethoxybisnor*allo*cholan*-11-*one* (2·8 g.), m. p. 183—185°, $[\alpha]_D^{20}$ +28° (*c*, 1·068) (Found: C, 71·95; H, 9·9. $C_{26}H_{42}O_5$ requires C, 71·85; H, 9·7%). 2N-Sulphuric acid was added to a solution of the above dimethyl-3β-acetoxy-acetal (2·4 g.) in methanol (50 ml.) until precipitation commenced. The solution was refluxed for 3 hr. and poured into water and the precipitate isolated by means of ether. Crystallisation from aqueous methanol afforded 3β-*hydroxy*-11-*oxobisnor*allo*cholanal* (1·2 g.), m. p. 147—150°, $[\alpha]_D^{28}$ +34° (Found: C, 75·8; H, 9·8. $C_{22}H_{34}O_3$ requires C, 76·3; H, 9·9%).

3β-*Acetoxy*-11-*oxobisnor*allo*cholanic Acid* (V*a*).—The alkaline extracts from the aldehyde preparation were combined and acidified, and the precipitate was filtered off, washed, and dried (10·0 g.; m. p. 192—195°). Recrystallisation from aqueous acetone yielded colourless needles of 3β-*acetoxy*-11-*oxobisnor*allo*cholanic acid*, m. p. 196—198°, $[\alpha]_D^{23}$ +16° (*c*, 1·05) (Found: C, 71·1; H, 9·1. $C_{24}H_{36}O_5$ requires C, 71·25; H, 9·0%). $\nu_{max.}$ 1712 and 1266 (carboxyl) and 1708 cm.$^{-1}$ (unconjugated carbonyl). (The product from the alkaline extracts contained varying proportions of 3β-hydroxy-compound according to the length of time the extracts had been allowed to stand.)

The acetoxy-acid was obtained in 66% yield by decomposing the ozonide solution in acetic acid with aqueous potassium permanganate and agitating it with a stream of air for 50 min. Alkaline hydrolysis of the 3β-acetoxy-acid in methanol gave the 3β-*hydroxy*-11-*oxobisnor*allo*cholanic acid* as colourless needles (from chloroform–methanol), m. p. 258—260°, $[\alpha]_D^{23}$ +29° (*c*, 1·07) (Found: C, 73·15; H, 9·5. $C_{22}H_{34}O_4$ requires C, 72·9; H, 9·5%). By the action of ethereal diazomethane on the 3β-acetoxy-acid colourless rhombs of its methyl ester were obtained, m. p. 190—192° (from methanol), $[\alpha]_D^{29}$ +26° (*c*, 1·172) {Chamberlin *et al.*, *loc. cit.*, give m. p. 191—194°, $[\alpha]_D$ +24° (in $CHCl_3$)} (Found: C, 71·95; H, 9·2. Calc. for $C_{25}H_{38}O_5$: C, 71·7; H, 9·15%). The *methyl* 3β-*hydroxy*-ester, similarly prepared, formed plates, m. p. 165—168°, $[\alpha]_D^{29}$ +44° from aqueous methanol (Found: C, 73·3; H, 9·5. $C_{23}H_{36}O_4$ requires C, 73·4; H, 9·7%).

3β : 22-*Diacetoxybisnor*allo*chol*-20(22)-*en*-11-*one* (III*a*).—3β-Acetoxy-11-oxobisnor*allo*-cholanal (128 g.; m. p. 130—133°) in acetic anhydride (200 ml.) containing anhydrous potassium acetate (2·0 g.) was refluxed for 12 hr. and then evaporated to dryness under reduced pressure. The crystalline residue, recrystallised from methanol (500 ml.), gave 3β : 22-*diacetoxybisnor*-allo*chol*-20(22)-*en*-11-*one* as needles (101 g.), m. p. 155—159°. A sample, recrystallised from methanol, showed m. p. 160—163°, $[\alpha]_D^{23}$ +23° (Found: C, 72·6; H, 8·8. $C_{26}H_{38}O_5$ requires C, 72·5; H, 8·9%), $\nu_{max.}$ 1754 and 1216 (enol acetate), 1733 and 1240 (acetate), and 1708 cm.$^{-1}$ (unconjugated carbonyl).

3β-Hydroxy-11-oxobisnor*allo*cholanal (38 g.) in acetic anhydride (76 ml.), containing potassium acetate (0·75 g.), was refluxed for 30 min. The acetic acid was then fractionated off through a 6″ packed column until 50 ml. of distillate had collected. Acetic anhydride (50 ml.) was added to the reaction mixture and refluxing was continued for 10 hr. Removal of the solvent and crystallisation gave 3β : 22-diacetoxybisnor*allo*chol-20(22)-en-11-one (26·9 g.), m. p. 162—166°.

The following experiments were made with the 3β-acetoxy-aldehyde. (*a*) With *iso*propenyl acetate in place of potassium acetate as catalyst in acetic anhydride the aldehyde was recovered unchanged. (*b*) With pyridine, the yield of the enol acetate was only 50%. (*c*) With boron trifluoride–ether complex (50 drops) added to the aldehyde (10·0 g.) in acetic anhydride (50 ml.), a black tar was obtained after storage at room temperature overnight. Crystallisation of the tar from aqueous methanol, after treatment with charcoal, gave 3β : 22 : 22-*triacetoxybisnor*-allo*cholan*-11-*one* (4·7 g.) as colourless rhombs, m. p. 160—162°, $[\alpha]_D^{24}$ +9° (*c*, 1·0) (Found: C, 68·3; H, 8·55. $C_{28}H_{42}O_7$ requires C, 68·5; H, 8·6%), $\nu_{max.}$ 1760 and 1202 (probably due to aldehyde diacetate group), 1728 and 1240 (acetate), and 1780 cm.$^{-1}$ (unconjugated carbonyl). (*d*) The 3β-hydroxy-aldehyde (2·5 g.) in dry carbon tetrachloride (45 ml.) containing acetic anhydride (5 ml.) and perchloric acid (2 drops; 50% solution) was kept at room temperature for 2 hr. After washing of the solution with water and evaporation, the remaining black tar was treated in acetone with charcoal and crystallised from methanol, to give almost colourless crystals of the aldehyde diacetate, m. p. 157—159°, with an infra-red spectrum identical with

that of the product from (*c*). The same material was obtained from the 3β-acetoxy-aldehyde and perchloric acid.

3β-*Acetoxy*allo*pregnane*-11 : 20-*dione* (IV*a*).—3β : 22-Diacetoxybisnor*allo*chol-20(22)-en-11-one (56·5 g.), suspended in acetic acid (280 ml.) containing water (5%), was stirred vigorously while a stream of ozonised oxygen (200 l./hr., containing 0·04 g. of ozone/l.) was passed through. The temperature was kept at 15—20° by cooling. Provided stirring was sufficiently vigorous, absorption of ozone in this reaction was substantially quantitative. The end-point coincided with the detection of large quantities of ozone in the exit gases and the reaction was then stopped. Zinc dust (30 g.) was then added during 5 min. while stirring and external cooling (with added ice) were continued. When a negative test for ozonide was obtained (10—15 min.) the solid was filtered off and washed with acetic acid, and the combined filtrates were evaporated to dryness under reduced pressure. The crystalline residue was recrystallised from aqueous methanol, to yield 3β-acetoxy*allo*pregnane-11 : 20-dione (44·5 g.), m. p. 139—140°. A further 1·8 g. of the diketone were recovered from the mother-liquors of the crystallisation, *via* the semicarbazone (total yield 94%). A sample recrystallised from aqueous methanol had m. p. 141—142°, $[\alpha]_D^{20}$ +88° (*c*, 1·0) (Stork *et al.*, *loc. cit.*, give m. p. 143—144°, $[\alpha]_D^{20}$ +89°; Chamberlin *et al.*, *loc. cit.*, give m. p. 141—143°, $[\alpha]_D^{20}$ +88°) (Found : C, 73·7; H, 9·05. Calc. for $C_{23}H_{34}O_4$: C, 73·8; H, 9·15%), $\nu_{max.}$ 1730 and 1240 (acetyl) and 1712 cm.$^{-1}$ (unconjugated carbonyl). The 20-*semicarbazone* crystallised as needles (from aqueous acetic acid), m. p. 256—260° (decomp.) (Found : C, 66·8; H, 8·6; N, 9·8. $C_{24}H_{37}O_4N_3$ requires C, 66·7; H, 8·6; N, 9·8%). Formation and hydrolysis of the semicarbazone were used for recovery of small amounts of the diketone which failed to crystallise from mother-liquors. For the hydrolysis, the semicarbazone (6·0 g.), suspended in hot acetic acid (30 ml.), was treated with pyruvic acid (8·0 ml.; 40%) in water (15 ml.) containing sodium acetate trihydrate (0·4 g.). The suspension cleared when heated for 5 min. on the water-bath and after a further 5 min. water was added until the solution was cloudy. On cooling, needles of the diketone (3·5 g.) were obtained, having m. p. 140—141°, $[\alpha]_D^{20}$ +86° (*c*, 0·94). Hydrolysis in methanolic potassium hydroxide gave the 3β-hydroxy-diketone as needles, m. p. 188—190°, $[\alpha]_D^{20}$ +109° (*c*, 0·12) (Stork *et al.*, *loc. cit.*, give m. p. 192—194°, $[\alpha]_D^{20}$ +99°) (Found : C, 75·7; H, 9·75. Calc. for $C_{21}H_{32}O_3$: C, 75·9; H, 9·7%).

3β-*Acetoxy*-11-*oxo*-9β-*bisnor*allo*cholanal* (II*b*).—This was prepared from 3β-acetoxy-9β-ergost-22-en-11-one (5 g.) by the process used for the 9α-compound. Recrystallisation of the colourless crystalline product (4·1 g.) from aqueous methanol and then from light petroleum gave needles of 3β-*acetoxy*-11-*oxo*-9β-*bisnor*allo*cholanal* (1·04 g.), m. p. 148—152°, $[\alpha]_D^{23}$ +34° (*c*, 1·04) (Found : C, 74·4; H, 9·2. $C_{24}H_{36}O_4$ requires C, 74·2; H, 9·3%), $\nu_{max.}$ 2680 (aldehyde), 1737 and 1242 (acetate), and 1712 cm.$^{-1}$ (unconjugated carbonyl).

3β-*Acetoxy*-11-*oxo*-9β-*bisnor*allo*cholanic Acid* (V*b*).—The alkaline extracts from the above aldehyde preparation were acidified and the precipitated acid crystallised from aqueous acetone (yield, 0·19 g.). 3β-*Acetoxy*-11-*oxo*-9β-*bisnor*allo*cholanic acid* formed needles (from light petroleum), m. p. 200—202°, $[\alpha]_D^{22}$ +29° (*c*, 1·054) (Found : C, 71·3; H, 8·6. $C_{24}H_{36}O_5$ requires C, 71·25; H, 8·9%), $\nu_{max.}$ 1712 and 1270 (carboxyl) and 1718 cm.$^{-1}$ (unconjugated carboxyl). Its *methyl* ester, prepared by diazomethane, formed needles (from aqueous acetone), m. p. 154—157°, $[\alpha]_D^{24}$ +38·4° (*c*, 1·04) (Found : C, 71·8; H, 9·4. $C_{25}H_{38}O_5$ requires C, 71·7; H, 9·15%).

3β : 22-*Diacetoxy*-9β-*bisnor*allo*chol*-20(22)-*en*-11-*one* (III*b*).—3β-Acetoxy-11-oxo-9β-bisnor-*allo*cholanal (5·8 g.) in acetic anhydride (50 ml.) containing anhydrous potassium acetate (0·1 g.) was refluxed for 6 hr. After evaporation under reduced pressure 3β : 22-*diacetoxy*-9β-*bisnor*allo*chol*-20(22)-*en*-11-*one* (5·5 g.) crystallised from methanol as needles, m. p. 174—176°, $[\alpha]_D^{20}$ +91° (Found : C, 72·7; H, 8·8. $C_{26}H_{38}O_5$ requires C, 72·5; H, 8·9%), $\nu_{max.}$ 1756 and 1212 (enol acetate), 1738 and 1245 (acetate), and 1718 cm.$^{-1}$ (unconjugated carbonyl).

3β-*Acetoxy*-9β-allo*pregnane*-11 : 20-*dione* (IV*b*).—3β : 22-Diacetoxy-9β-bisnor*allo*chol-20(22)-en-11-one (5·0 g.) in acetic acid (120 ml.) was treated with ozone as for the 9α-isomer. Evaporation of the solvent gave 3β-*acetoxy*-9β-allo*pregnane*-11 : 20-*dione* (3·3 g.), which formed needles, m. p. 175—178° (from ether–light petroleum), $[\alpha]_D^{24}$ +131° (*c*, 0·89) (Found : C, 73·7; H, 9·1. $C_{23}H_{34}O_4$ requires C, 73·8; H, 9·15%), $\nu_{max.}$ 1740 and 1240 (acetate) and 1712 cm.$^{-1}$ (unconjugated carbonyl). The 20-*semicarbazone* was obtained from aqueous acetic acid as needles, m. p. 262° (decomp.) (Found : C, 67·0; H, 8·7; N, 9·7. $C_{24}H_{37}O_4N_3$ requires C, 66·7; H, 8·6; N, 9·8%).

3β-*Acetoxy*allo*pregnane*-11 : 20-*dione from the Corresponding* 9β-*Isomer*.—3β-Acetoxy-9β-*allo*pregnane-11 : 20-dione (500 mg.) in methyl alcohol (20 ml.) containing water (2 ml.) and potassium hydroxide (4·0 g.) was refluxed in a stream of nitrogen for 6 hr. Ethyl acetate was

then added and the solution washed with water, dried, and evaporated to a gum. Reacetylation by boiling acetic anhydride (1 hr.) gave a gum, which on crystallisation from methanol gave needles of 3β-acetoxy*allo*pregnane-11 : 20-dione (91 mg.), m. p. and mixed m. p. 140—141°. The infra-red spectrum was identical with that of an authentic specimen.

3β-*Acetoxy*-22-*piperidinobisnor*allo*chol*-20(22)-*en*-11-*one* (VI).—3β-Acetoxy-11-oxobisnor*allo*cholanal (10·0 g.) in dry, thiophen-free benzene (100 ml.) was refluxed with freshly distilled piperidine (2·42 g.) for 4 hr. under an azeotropic-distillation head. No further water appeared to be collecting after this time and the solution was evaporated under reduced pressure to a yellow oil. Crystallisation from methanol gave a yellow solid (5·24 g.), m. p. 100—110°. Two further crystallisations from methanol gave 3β-*acetoxy*-22-*piperidinobisnor*allo*chol*-20(22)-*en*-11-*one* as colourless needles (2·62 g.), m. p. 120—123°, $[\alpha]_D^{20}$ +7° (*c*, 0·68) (Found : C, 76·1; H, 9·8; N, 3·1%. $C_{29}H_{45}O_3N$ requires C, 76·4; H, 9·95; N, 3·1%), $\nu_{max.}$ 1730 and 1235 (acetate), 1705 (carbonyl), 842 and 822 cm.$^{-1}$ (trisubstituted double bond), and 1646 cm.$^{-1}$.

3β-*Acetoxy*allo*pregnane*-11 : 20-*dione from* 3β-*Acetoxy*-22-*piperidinobisnor*allo*chol*-20(22)-*en*-11-*one*.—A stream of ozonised oxygen was passed into a solution of 3β-acetoxy-22-piperidinobisnor*allo*chol-20(22)-en-11-one (2·0 g.) in methylene chloride (100 ml.) at room temperature until reaction ceased. The methylene chloride was then removed in stages under reduced pressure, being replaced gradually by acetic acid. Zinc dust was then added; decomposition of the ozonide was rapidly complete. The solution was evaporated to dryness, and the residue, in ethyl acetate, washed with 5% sodium carbonate solution and water, dried, and evaporated. Crystallisation from methanol gave 3β-acetoxy*allo*pregnane-11 : 20-dione (410 mg.), m. p. and mixed m. p. 140—141°, $[\alpha]_D^{20}$ +86°. The infra-red spectrum was identical with that of an authentic specimen.

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RESEARCH AND DEVELOPMENT DIVISION, GLAXO LABORATORIES, LTD.,
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