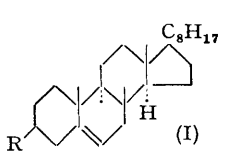
16. *Some Basic Steroid Derivatives.*

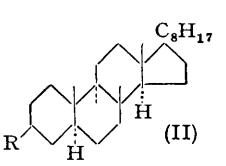
By Douglas P. Dodgson and Robert D. Haworth.

As the amœbicidal properties of conessine might have been associated with the steroidal structure of the alkaloid, a number of basic steroid derivatives have been prepared, but none of their pharmacological activities appears to be greater than that of conessine.

Many compounds, chiefly tertiary diamines and certain alkaloids, *e.g.*, emetine, have been used or suggested as amœbicidal agents, but as a result of the lack of a suitable *in vivo* technique, many of the compounds previously tested gave high activity *in vitro* which did not necessarily correspond to their activity *in vivo*. A more suitable method for a preliminary evaluation of activity *in vivo* has however recently been developed (Jones, *Ann. Trop. Med. Parasit.*, 1946, **40**, 130; *Brit. J. Pharmacol.*, 1947, **2**, 217). It has long been known that extract of *Holarrhena antidysenterica* is valuable in the treatment of amœbic dysentery, and the activity of conessine, the major alkaloidal constituent of the extract, has been confirmed by the new technique referred to above. In view of the established steroid nature of conessine it was decided to prepare a number of basic steroid derivatives and the following compounds, none of which are sufficiently active to be effective in low doses, have been tested as amœbicidal agents: 3β-dimethylaminocholest-5-ene (I; R = NMe_2), 3β-dimethylaminocholestane (II; R = NMe_2), 3β-2′-diethylaminoethylaminocholest-5-ene (I; R = $NH{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$), 3β-(*N*-2-diethylaminoethyl-*N*-methylamino)cholest-5-ene (I; R = $NMe{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$), 23-amino-3α : 7α : 12α-trihydroxynorcholane (III; R = OH, R′ = NH_2), 23-dimethylamino-3α : 7α : 12α-trihydroxynorcholane (III; R = OH, R′ = NMe_2), methyl 3ξ-dimethylamino-7α : 12α-dihydroxycholanate* (III; R = NMe_2, R′ = CO_2Me), 3ξ : 23-bisdimethylamino-7α : 12α-dihydroxynorcholane (III; R = R′ = NMe_2), 3ξ : 17ξ-bisdimethylaminoandrostane (IV).



(I)



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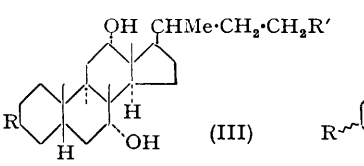

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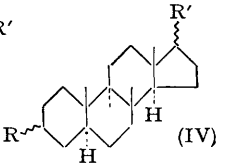

(IV)

3β-Dimethylaminocholest-5-ene (I; R = NMe_2) was prepared by heating cholesteryl chloride with methanolic dimethylamine at 180°, with dimethylamine hydriodide as catalyst, and reduction with hydrogen in presence of palladium–charcoal in acetic acid solution gave 3β-dimethylaminocholestane (II; R = NMe_2). This base was also obtained by reducing 3-oximinocholestane (Fujii and Matsukawa, *J. Pharm. Soc. Japan*, 1936, **56**, 642) with sodium and amyl alcohol to 3β-aminocholestane, which was methylated by

* The symbol ξ in names, and the wavy bond in formulae, signify linkages of uncertain configuration (cf. *Chem. and Ind.*, 1951, June 23rd, p. SN7).

heating it with formaldehyde and formic acid. The intermediate 3β-aminocholestane (II; R = NH_2) obtained by reducing the oximino-compound was the major constituent of a mixture which was acetylated and separated into two acetamido-derivatives melting at 245—246° and 213° respectively; the former, on hydrolysis with acids gave the 3β-amino-derivative which had m. p. 106—120°. This amine, probably a component of the mixture isolated by Windaus and Adamla (*Ber.*, 1911, **44**, 3051), gave, in spite of the wide melting range, high yields of pure derivatives on acetylation or methylation.

3β-2′-Diethylaminoethylaminocholest-5-ene (I; R = $NH{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$), prepared by the action of 2-diethylaminoethylamine on cholesteryl chloride or preferably on the toluene-*p*-sulphonate, partly decomposed during attempted distillation to cholest-3 : 5-diene and 2-diethylaminoethylamine. It gave a sparingly soluble hydrochloride and a characteristic dipicrate from either of which the base was regenerated in a crystalline form, m. p. 64°. Methylation of the base with formaldehyde and formic acid yielded 3β-(*N*-2-diethylaminoethyl-*N*-methylamino)cholest-5-ene (I; R = $NMe{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$), as an oil which was characterised as the dihydrochloride, m. p. 280°, and the dipicrate, m. p. 243—245°.

Whilst a detailed study of the stereochemistry of these basic cholestenes and cholestanes has not been possible, it is suggested that the compounds have the 3β-configuration in agreement with Shoppee's conclusions (*J.*, 1946, 1147) concerning replacement reaction at $C_{(3)}$ in Δ^5-steroids. 3β-Aminocholestane like cholestan-3β-ol gives a digitonin complex quite readily and, although this reaction is not understood, the analogy is attractive; it is interesting in this connection to record that 3β-acetamidocholestane and 3β-dimethylaminocholestane do not give adducts with digitonin. The lævorotations observed with the 3β-dimethylamino-, 3β-2′-diethylaminoethylamino- and 3β-(*N*-2′-diethylaminoethyl-*N*-methylamino)cholest-5-enes are consistent with the lævorotation of cholesterol, and the reduction of the first compound to the dextrorotatory 3β-dimethylaminocholestane is not only reminiscent of the change in optical properties which accompanies the reduction of cholesterol to cholestan-3-ol, but the molecular rotation difference of −226° is in excellent quantitative agreement.

23-Dimethylamino-3α : 7α : 12α-trihydroxynorcholane (III; R = OH, R′ = NMe_2) was prepared by methylating with formaldehyde and formic acid the corresponding 23-amino-compound (III; R = OH, R′ = NH_2) obtained from cholic azide (Caldwell, *J. Amer. Chem. Soc.*, 1938, **60**, 991). Oppenauer oxidation with aluminium *tert.*-butoxide gave a dihydroxy-keto-derivative which is considered to be 23-dimethylamino-7α : 12α-dihydroxy-3-ketonorcholane by analogy with the preferential attack of the 3-hydroxy-group during similar oxidation of methyl cholate (Kuwada and Norimo, *Bull. Chem. Soc. Japan*, 1942, **17**, 147). The conversion of this keto tertiary amine into 3ξ : 23-bisdimethylamino-7α : 12α-dihydroxynorcholane (III; R = R′ = NMe_2) by oximation of the 3-keto-group and subsequent reduction and methylation was successful, although the oximation proved difficult in practice and only a few milligrams of the dihydrochloride of the amine were obtained by this method; an alternative procedure gave improved yields. 7α : 12α-Dihydroxy-3-ketocholanic acid was oximated and reduced to 3ξ-amino-7α : 12α-dihydroxycholanic acid as described by Jones, Smith, and Webb (*J.*, 1949, 2164). The primary amine was then methylated with formaldehyde, to methyl 3ξ-dimethylamino-7α : 12α-dihydroxycholanate, which was converted *via* the hydrazide and azide into 23-amino-3ξ-dimethylamino-7α : 12α-dihydroxynorcholane (III; R = NMe_2, R′ = NH_2) which was isolated as the dihydrochloride. Methylation with formaldehyde gave 3ξ : 23-bisdimethylamino-7α : 12α-dihydroxynorcholane (III; R = R′ = NMe_2) which was also isolated as the dihydrochloride, identical with the dihydrochloride prepared as outlined above.

3ξ : 17ξ-Bisdimethylaminoandrostane (IV; R = R′ = NMe_2) was obtained from 3 : 17-bishydroxyaminoandrostane (Ruzicka, Meister, and Prelog, *Helv. Chim. Acta*, 1947, **30**, 867) by reduction to the 3ξ : 17ξ-diamine (IV; R = R′ = NH_2) which was characterised as its ditoluene-*p*-sulphonate and as 3ξ : 17ξ-diacetamidoandrostane (IV; R = R′ = NHAc), and when methylated with formaldehyde in the usual manner gave 3ξ : 17ξ-bisdimethylaminoandrostane (IV; R = R′ = NMe_2), m. p. 101—102°.

Experimental

3β-*Dimethylaminocholest-5-ene* (I; R = NMe_2).—Cholesteryl chloride was prepared in 80% yield by the method of Daughenbaugh and Allison (*J. Amer. Chem. Soc.*, 1929, **51**, 3665) but with light petroleum (b. p. 40—60°) instead of pyridine as solvent. During preliminary experiments it was found that the action of warm thionyl chloride on cholesterol gave a compound, $C_{27}H_{46}Cl_2$, m. p. 118°, probably identical with 3 : 5-dichlorocholestane obtained previously by Mauthner (*Monatsh.*, 1906, **27**, 305, 421) by the action of hydrogen chloride on cholesterol or cholesteryl chloride.

Cholesteryl chloride (3 g.), 50% methanolic dimethylamine (20 c.c.), and dimethylamine hydriodide (0·6 g.) were heated for 18 hours at 180°. Hydrogen chloride was passed into a washed and dried ethereal extract of the product, and the gelatinous water-insoluble hydrochloride was collected, crystallised from methanol, and basified. 3β-*Dimethylaminocholest-5-ene* (I; R = NMe_2) separated from ether in long prisms (0·3 g.), m. p. 151°, $[\alpha]_D^{20}$ −31·5° ± 1·0° (*c*, 0·5 in chloroform) (Found: C, 84·2; H, 12·2. $C_{29}H_{51}N$ requires C, 84·2; H, 12·4%). 3β-Methoxycholest-5-ene, m. p. 83°, was isolated from the non-basic portion from the reaction, but attempts to improve the yields of the base (I; R = NMe_2) by using non-polar solvents or excess of dimethylamine as solvent failed and considerable quantities of cholesteryl chloride were recovered.*

3β-*Aminocholestane* (II; R = NH_2).—Cholesterol was converted into cholestan-3β-ol and cholestan-3-one as described in *Org. Synth.*, XVII, pp. 43, 45. 3-Hydroxyaminocholestane, prepared in ethanol, separated from ethyl acetate in colourless needles, m. p. 196°, $[\alpha]_D^{20}$ +38° (*c*, 0·25 in chloroform) (Found: C, 80·4; H, 12·0. Calc. for $C_{27}H_{47}ON$: C, 80·7; H, 11·8%). Fujii and Matsukawa (*loc. cit.*) give m. p. 187° (decomp.). The oxime (1 g.) in amyl alcohol (70 c.c.) was reduced by gradual addition of sodium (6 g.) during 2—3 hours to the boiling solution. The alcohol was washed with water and removed under reduced pressure, and the residue was taken up in ether. The hydrochlorides precipitated by hydrogen chloride were collected and basified, and the amine mixture, m. p. 90—120°, was recovered. Acetylation by boiling acetic anhydride (1 c.c.) in ether (10 c.c.) gave 3β-*acetamidocholestane*, which crystallised from alcohol in hexagonal plates, m. p. 245—246°, $[\alpha]_D^{20}$ +12° (*c*, 0·2 in chloroform) (Found, after drying for 8 hours at 100° at 0·5 mm.: C, 81·3; H, 11·8. $C_{29}H_{51}ON$ requires C, 81·0; H, 12·0%). The mother-liquors yielded an *isomer*, which separated from ether in slender needles, m. p. 213° (Found, after drying for 8 hours at 100° at 0·001 mm.: C, 81·5; H, 11·6%), but the quantity available was too small for further examination. 3β-Acetamidocholestane (0·25 g.) was heated under reflux in ethanol (210 c.c.) and concentrated hydrochloric acid (140 c.c.) for 24 hours, then evaporated to dryness, and the basified product was isolated with ether. 3β-*Aminocholestane* (II; R = NH_2) separated from ethyl alcohol in colourless needles, m. p. 106—120°, which adhere to solvent (Found, after drying at 100° and 0·001 mm.: C, 83·4; H, 12·5. $C_{27}H_{49}N$ requires C, 83·7; H, 12·7%) and readily give a precipitate with digitonin.

3β-*Dimethylaminocholestane* (II; R = NMe_2).—(*a*) 3β-Dimethylaminocholest-5-ene (0·25 g.) in acetic acid (3 c.c.) was rapidly reduced with hydrogen in presence of palladium–charcoal (0·4 g.), and the product was isolated with ether. (*b*) 3β-Aminocholestane (60 mg.; m. p. 90—120°) was heated for 3 hours on a water-bath with 90% formic acid (1·25 c.c.) and 40% formaldehyde (1 c.c.). Traces of unchanged primary amine were removed by addition of ethanol (1 c.c.), concentrated hydrochloric acid (0·5 c.c.), and sodium nitrite (20 mg.), and after 1 hour the product was taken up in ether and precipitated as the water-insoluble hydrochloride, and the base recovered. 3β-*Dimethylaminocholestane* (II; R = NMe_2), prepared by either method, crystallised from ether in long prisms, m. p. 106°, $[\alpha]_D^{20}$ +23° ± 2·0° (*c*, 1·75 in chloroform) (Found, after drying at room temperature at 1 mm. for 3 hours: C, 83·9; H, 12·9. $C_{29}H_{53}N$ requires C, 83·8; H, 12·9%). This tertiary amine does not give a precipitate with digitonin.

3β-(2-*Diethylaminoethylamino*)*cholest-5-ene* (II; R = $NH{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$).—(*a*) Cholesteryl chloride (2 g.), 2-diethylaminoethylamine (10·6 c.c.), and hydrogen iodide (1·2 g.) were heated at 145° for 18 hours (*b*) Cholesteryl toluene-*p*-sulphonate (Wallis, Fernholz, and Gephart, *J. Amer. Chem. Soc.*, 1937, **59**, 137) (20 g.), 2-diethylaminoethylamine (100 c.c.), and toluene-*p*-sulphonic acid (16 g.) were refluxed for 18 hours.

The mixture, from experiments (*a*) or (*b*), was basified and extracted with ether and evaporated, and unchanged 2-diethylaminoethylamine was removed under reduced pressure.

* Considerably increased yields of (I; R = NMe_2) have been obtained by the action of dimethylamine on cholesteryl toluene-*p*-sulphonate. These results will be reported later.

The residue was taken up in ether, and the hydrochloride, precipitated with dry hydrogen chloride, crystallised with difficulty from methanol–acetone in needles, m. p. 255—265°, and for subsequent stages was obtained sufficently pure by dissolving the crude salt in a minimum of methyl alcohol and reprecipitating it with ether. The crude *base*, obtained in yields of 25 and 70% by method (*a*) and (*b*) respectively, was recovered from the hydrochloride and crystallised from acetone in colourless needles, m. p. 64°, $[\alpha]_D^{20}$ −18° (*c*, 0·9 in ethanol) (Found: C, 81·6; H, 12·0. $C_{33}H_{60}N_2$ requres C, 81·8; H, 12·5%). The *dipicrate*, prepared in methyl alcohol, crystallised from acetic acid in yellow prisms, m. p. 224—226° (Found: C, 57·6; H, 6·8. $C_{33}H_{60}N_2,2C_6H_3O_7N_3$ requires C, 57·3; H, 7·1%), and gave the base (I; R = $NH{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$), m. p. 64°, on treatment with sodium hydroxide.

3β-(N-2-*Diethylaminoethyl*-N-*methylamino*)*cholest*-5-*ene* (I; R = $NMe{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$).—The base described above (1 g.) was heated on a water-bath for 2 hours with 90% formic acid (5 c.c.) and 40% formaldehyde (3 c.c.). After basification, the product was isolated with ether, and the *dihydrochloride* precipitated and collected; it crystallised from methyl alcohol in colourless needles, m. p. 280° (decomp.), $[\alpha]_D^{20}$ −12° (*c*, 0·5 in methyl alcohol) (Found: C, 70·9; H, 11·0. $C_{34}H_{62}N_2,2HCl$ requires C, 71·4; H, 11·3%). The *dipicrate* separated from acetic acid in yellow needles, m. p. 243—245° (decomp.) (Found: C, 58·0; H, 7·1. $C_{34}H_{62}N_2,2C_6H_3O_7N_3$ requires C, 57·7; H, 7·2%).

23-*Dimethylamino*-3α : 7α : 12α-*trihydroxynorcholane* (III; R′ = OH, R′ = NMe_2).—Methyl cholate (Reichstein and Grand, *Helv. Chim. Acta*, 1945, **28**, 344), b. p. 280° (bath-temp.)/0·001 mm., was converted *via* cholic hydrazide and azide (Bondi and Muller, *Z. physiol. Chem.*, 1906, **47**, 499) into 23-amino-3α : 7α : 12α-trihydroxynorcholane (Caldwell, *loc. cit.*), m. p. 185—186°, b. p. 260—270° (bath-temp.)/0·001 mm., $[\alpha]_D^{20}$ +50° (*c*, 0·5 in ethyl alcohol) (Found: C, 72·4; H, 10·8. Calc. for $C_{23}H_{41}O_3N$: C, 72·8; H, 10·8%). This primary amine (10 g.) was heated on a water-bath for 3 hours with 90% formic acid (12·5 c.c.) and 40% formaldehyde (10 c.c.). The product was evaporated under reduced pressure, dissolved in N-hydrochloric acid (400 c.c.), and treated with N-sodium nitrite (100 c.c.). After 1 hour the solution was rendered alkaline and the 23-*dimethylamino*-3α : 7α : 12α-*trihydroxynorcholane* (III; R = OH, R′ = NMe_2), isolated with ether, separated in cubic crystals, which melted about 130°, resolidified at 140°, and finally melted at 165—166°, $[\alpha]_D^{20}$ +46° (*c*, 0·5 in ethyl alcohol) (Found, after drying at 120°/2 mm. for 2 hours: C, 73·2; H, 10·7. $C_{25}H_{45}O_3N$ requires C, 73·7; H, 11·1%). This tertiary amine (III; R = OH, R′ = NMe_2) had b. p. 250—260°/0·005 mm. and gave a *hydrochloride* which crystallised from methyl alcohol–acetone in needles, m. p. 295—296° (Found: C, 67·4; H, 10·5. $C_{25}H_{46}O_3NCl$ requires C, 67·6; H, 10·4%).

23-*Dimethylamino*-7α : 12α-*dihydroxy*-3-*ketonorcholane*.—23-Dimethylamino-3α : 7α : 12α-trihydroxynorcholane (III; R = OH, R′ = NMe_2) (5 g.), aluminium *tert.*-butoxide (6·0 g.), benzene (150 c.c.), and acetone (50 c.c.) were refluxed for 24 hours. The mixture was cooled, decomposed with water, and extracted with ether, and the extract washed with N-hydrochloric acid (2 × 50 c.c.). The acid washings were made alkaline and the liberated base, isolated with ether, crystallised from acetone; 23-*dimethylamino*-7α : 12α-*dihydroxy*-3-*ketonorcholane* (3·9 g.) was obtained as colourless needles, m. p. 180—181° (Found: C, 73·6; H, 10·5. $C_{25}H_{43}O_3N$ requires C, 74·0; H, 10·7%). The *hydrochloride* separated from methyl alcohol–acetone in colourless needles, m. p. 271—273° (Found: C, 67·4; H, 10·2; Cl, 7·6. $C_{25}H_{44}O_3NCl$ requires C, 67·9; H, 10·1; Cl, 8·0%). The 2 : 4-*dinitrophenylhydrazone hydrochloride*, prepared in methyl alcohol containing concentrated hydrochloric acid (2 equivs.), separated from methyl alcohol in clusters of orange needles, m. p. 230—233° (Found: C, 59·5; H, 8·0. $C_{31}H_{48}O_6N_5Cl$ requires C, 59·8; H, 7·8%).

3ξ-*Amino*-23-*dimethylamino*-7α : 12α-*dihydroxynorcholane* (III; R = NH_2, R′ = NMe_2).—23-Dimethylamino-7α : 12α-dihydroxy-3-ketonorcholane (1 g.), sodium acetate (1 g.), and hydroxylamine hydrochloride (0·8 g.) were refluxed in ethyl alcohol for 24 hours. The mixture was neutralised, and the crude oxime, m. p. 125—150° (10 mg.), isolated with ether, was dissolved in amyl alcohol (35 c.c.) and reduced with sodium (2 g.). After addition of dilute hydrochloric acid, the mixture was evaporated to dryness under reduced pressure and the residue made alkaline and extracted with ether. 3ξ-Amino-23-dimethylamino-7α : 12α-dihydroxynorcholane was obtained as a pale yellow oil, b. p. 240—250° (bath-temp.)/0·001 mm., which gave a *dihydrochloride* as colourless needles, m. p. 319—323° (Found: Cl, 14·6. $C_{25}H_{48}O_2N_2Cl_2$ requires Cl, 14·8%), from methyl alcohol–acetone.

Methyl 3ξ-*Dimethylamino*-7α : 12α-*dihydroxycholanate* (III; R = NMe_2, R′ = CO_2Me).—3ξ-Amino-7α : 12α-dihydroxycholanic acid hydrochloride (5 g.), prepared as described by Jones,

Webb, and Smith (*loc. cit.*), was refluxed for 1½ hours with 90% formic acid (6 c.c.) and 40% formaldehyde (5 c.c.). Methyl alcoholic hydrogen chloride (10 c.c. of 1%) was repeatedly added to the solution which was evaporated until the formaldehyde was eliminated. A further 30 c.c. of the methyl-alcoholic hydrogen chloride was added and after 1 hour's refluxing dilute sodium hydrogen carbonate solution was added and the product isolated with ether. Concentration of the *moist* ethereal solution gave *methyl* 3ξ-*dimethylamino*-7α : 12α-*dihydroxycholanate* as long prisms (3·5 g.), m. p. 70—80° [Found, after drying at 100°/0·3 mm. (loss in wt., 4·6%) : C, 72·0; H, 10·8. $C_{27}H_{47}O_4N$ requires C, 72·2; H, 10·6%]. The *hydrochloride* separated from methyl alcohol–acetone in long feathery needles, m. p. >360° (Found, after drying for 12 hours at 100°/0·5 mm. over P_2O_5 : C, 66·5; H, 10·4; Cl, 7·4. $C_{27}H_{48}O_4NCl$ requires C, 66·7; H, 10·0; Cl, 7·3%).

23-*Amino*-3ξ-*dimethylamino*-7α : 12α-*dihydroxynorcholane* (III; R = NMe_2, R′ = NH_2).—Methyl 3ξ-dimethylamino-7α : 12α-dihydroxycholanate (2·5 g.) was heated on a water-bath for 48 hours with 90% hydrazine (12·5 c.c.) and ethyl alcohol (12·5 c.c.). The mixture was evaporated to dryness under reduced pressure and the residual hydrazide, dissolved in concentrated hydrochloric acid (2 c.c.) and ice (30 g.), was stirred at 0° for 1 hour with sodium nitrite (0·6 g.) and neutralised with sodium hydroxide. The crude azide was collected and decomposed by warming for ½ hour with acetic acid (12 c.c.) and water (6 c.c.). The base (III; R = NMe_2, R′ = NH_2), liberated by addition of sodium hydroxide and isolated with ether, was an oil, which yielded a *dihydrochloride* (1·1 g.), crystallising from methyl alcohol and acetone in needles, m. p. 326—330° (decomp.) (Found : Cl, 14·6. $C_{25}H_{48}O_2N_2Cl_2$ requires Cl, 14·8%).

3ξ : 23-*Bisdimethylamino*-7α : 12α-*dihydroxynorcholane* (III; R = R′ = NMe_2).—23-Amino-3ξ-dimethylamino-7α : 12α-dihydroxynorcholane dihydrochloride (0·8 g.) was heated for 2 hours with sodium hydrogen carbonate (0·32 g.), 90% formic acid (3 c.c.), and 40% formaldehyde (2·5 c.c.). The mixture was repeatedly evaporated to dryness under reduced pressure with 1% methyl-alcoholic hydrogen chloride and then rendered alkaline with sodium hydroxide, and the base, isolated with ether, yielded a dihydrochloride which crystallised from methyl alcohol–acetone in small hygroscopic prisms, m. p. 315—318° (Found : Cl, 13·9. $C_{27}H_{52}O_2N_2Cl_2$ requires Cl, 14·0%)

3ξ : 17ξ-*Diaminoandrostane* (III; R = R′ = NH_2).—3 : 17-Bishydroxyaminoandrostane (2 g.), m. p. 271—273° (from ethyl alcohol), $[\alpha]_D^{20}$ +60° (*c*, 0·15 in chloroform) (Found : C, 71·7; H, 9·1. Calc. for $C_{19}H_{30}O_2N_2$: C, 71·7; H, 9·4%), was reduced by sodium (11 g.) in boiling amyl alcohol (200 c.c.). After 2—3 hours the solution was acidified, the solvent removed under reduced pressure, the residue basified and extracted with ether and the crude dihydrochloride (2·1 g.) precipitated. The base, obtained from the dihydrochloride (0·2 g.), was taken up in ether (50 c.c.), dried, and mixed with acetic anhydride (0·3 c.c.). After 1 hour, 3ξ : 7ξ-*diacetamidoandrostane* (V; R = R′ = NHAc) separated and crystallised from aqueous ethyl alcohol in prisms, m. p. 300° (Found : C, 73·8; H, 10·1. $C_{23}H_{38}O_2N_2$ requires C, 73·8; H, 10·2%). A further sample of the crude base (IV; R = R′ = NH_2) was mixed in ether with toluene-*p*-sulphonic acid; the *ditoluene*-p-*sulphonate* crystallised from methyl alcohol–acetone in small needles, m. p. >360° (Found : C, 62·1; H, 7·6. $C_{19}H_{34}N_2,2C_7H_8O_3S$ requires C, 62·5; H, 7·9%).

3ξ : 17ξ-*Bisdimethylaminoandrostane* (IV; R = R′ = NMe_2).—Crude 3ξ : 17ξ-diaminoandrostane (1·5 g.) was heated for 2 hours with 90% formic acid (4 c.c.) and 40% formaldehyde (3 c.c.), and the mixture evaporated to dryness, basified, and extracted with ether. Removal of the ether gave an oil, b. p. 200°/0·001 mm., which separated from methyl alcohol in leaflets (1·0 g.), m. p. 101—102° (Found : C, 79·2; H, 12·0. $C_{23}H_{42}N_2$ requires C, 79·8; H, 12·2%). The *ditoluene*-p-*sulphonate*, prepared in ether, separated from methyl alcohol–acetone in short rods, m. p. 270—272°, $[\alpha]_D^{20}$ +8° (*c*, 0·2 in ethyl alcohol) (Found : C, 64·2; H, 8·5. $C_{23}H_{42}N_2,2C_7H_8O_3S$ requires C, 64·4; H, 8·4%). The *dihydrochloride* was very soluble in water and separated from methyl alcohol–acetone in prisms, m. p. 360°; it sublimes at 250°/0·5 mm. (Found : C, 66·2; H, 10·8. $C_{23}H_{42}N_2,2HCl$ requires C, 65·9; H, 10·5%).

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