$[\alpha]^{20}D$ −44.6° in water, *c* 1. Using the Kline–Acree[18] modification of the Willstätter–Schudel hypoiodite titration, 0.117 g. of the nonose (assuming quantitative cleavage of 0.156 g. of the phenylhydrazone) consumed 0.879 meq. of iodine; equiv. wt. calcd. 270, found 266 ± 2.

Oxidation of D-*arabino*-L-*galacto*-Nonose.—To a solution of 0.90 g. of D-*arabino*-L-*galacto*-nonose in 50 ml. of water was added 1.12 g. of barium carbonate and 1.5 ml. of bromine. After standing in the dark for 30 hours, the excess bromine was removed by aeration and barium was removed by the addition of a slight excess of dilute sulfuric acid and filtration. The solution then was passed over a small column of Duolite A-4 in the acetate form and concentrated to dryness at reduced pressure. Extraction of the resulting residue with two 100-ml. portions of boiling ethanol, followed by concentration of the extracts, produced 0.42 g. (47%) of nearly pure lactone, m.p. 204–206°. Recrystallization from ethanol yielded pure D-*arabino*-L-*galacto*-nononic γ-lactone, m.p. 205–206°, $[\alpha]^{20}D$ +58.5° in water, *c* 0.5.

Anal. Calcd. for $C_9H_{16}O_9$: C, 40.3; H, 6.01. Found: C, 40.4; H, 6.13.

A solution of 0.154 g. of the above lactone in 3.5 ml. of 0.2 *N* sodium hydroxide was diluted to a volume of 10.0 ml. with water. After 1 hour, the resulting solution of sodium salt (0.177 g.) showed constant $[\alpha]^{20}D$ −4.38°. Rapid passage of the salt solution over Amberlite IR-100, *or* the addition of acetic acid, followed by cooling for several hours, produced crystalline D-*arabino*-L-*galacto*-nononic acid. After recrystallization from a small volume of water, with rapid cooling, the acid showed m.p. 223° and $[\alpha]^{20}D$ +3.7° (constant for 30 minutes) in water, *c* 0.3.

Anal. Calcd. for $C_9H_{18}O_{10}$: C, 37.8; H, 6.34; neut. equiv., 286. Found: C, 37.1; H, 6.51; neut. equiv., 288 ± 2.

Treatment of the above lactone with phenylhydrazine and acetic acid in the usual manner yielded D-*arabino*-L-*galacto*-nononic phenylhydrazide,[3] m.p. 251°.

D-*arabino*-L-*talo*-**Nonose.**—1-Deoxy-1-nitro-D-*arabino*-L-*talo*-nonitol was converted to the corresponding sugar as described above for its epimer, except that in this instance any unchanged deoxynitrononitol remained in solution in the hydrolysis reaction mixture. From 0.32 g. of the deoxynitrononitol there was obtained 0.32 g. (84%) of D-*arabino*-L-*talo*-nonose phenylhydrazone, m.p., without recrystallization, 209–210°.

Anal. Calcd. for $C_{15}H_{24}O_8N_2$: C, 50.0; H, 6.71; N, 7.77. Found: C, 49.8; H, 6.74; N, 7.78.

Cleavage of the phenylhydrazone with benzaldehyde gave the amorphous nonose, $[\alpha]^{20}D$ −11.9° in water, *c* 2.

Quantitative oxidation of the nonose with hypoiodite[18] showed an equivalent weight of 265 ± 2; calculated, 270.

D-*arabino*-L-*talo*-**Nononic γ-Lactone.**—Oxidation of 210 mg. of D-*arabino*-L-*talo*-nonose with bromine, as described above for its epimer, yielded 45 mg. of D-*arabino*-L-*talo*-nononic γ-lactone. After recrystallization from ethanol, the product showed m.p. 184–185° and $[\alpha]^{20}D$ +23.5° in water, *c* 0.4.

Anal. Calcd. for $C_9H_{16}O_9$: C, 40.3; H, 6.01. Found: C, 40.2; H, 6.03.

Fermentation Tests.[15]—The two nonoses were tested separately for fermentability with five different strains of *Saccharomyces cerevisiae* by both the capillary tube method[19] and a manometric method. In the capillary tube tests, neither nonose showed evidence of being fermented when held for as long as 8 days, whereas D-glucose used as a control gave a positive result in 6 hours. In two manometric tests, the following R.Q. values were observed: D-glucose, 2.8 and 2.1; endogenous, 0.62 and 0.59; D-*arabino*-L-*galacto*-nonose, 0.55 and 0.80; D-*arabino*-L-*talo*-nonose, 0.71 and 0.68. It was concluded that neither of the two nonoses is fermentable by *Saccharomyces cerevisiae*.

(18) G. M. Kline and S. F. Acree, *J. Research Natl. Bur. Standards*, **5**, 1063 (1930); *Ind. Eng. Chem., Anal. Ed.*, **2**, 413 (1930).

(19) C. C. Lindegren, *Wallerstein Lab. Communs.*, **19**, 49 (1956).

ST. LOUIS, MO.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CLARK UNIVERSITY, AND THE WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY]

D-Homosteroids. II. Derivatives of 3β-Hydroxy-17a,17a-dimethyl-D-homoandrostan-17-one[1]

BY MILAN USKOKOVIĆ, MARCEL GUT AND RALPH I. DORFMAN

RECEIVED FEBRUARY 19, 1959

3β-Hydroxy-17a,17a-dimethyl-D-homoandrostan-17-one derivatives with halide and with methoxy at carbon 16 were prepared. Proof of the position of the halide is given and some isomerizations and substitutions of these halides are described.

A description of the synthesis of 3β-hydroxy-17a,17a - dimethyl - D - homoandrostan - 17 - one has been given in the preceding paper.[2] We wish now to report the preparation of some α-halo and α-methoxy keto derivatives of that compound.

Treatment of 3β-acetoxy-17a,17a-dimethyl-D-homoandrostan-17-one (I) with one mole of bromine in acetic acid–ether solution gave 3β-acetoxy-16α-bromo-17a,17a-dimethyl-D-homoandrostan-17-one (II). The axial position of the halide was confirmed by its single ultraviolet absorption peak at 322 mμ[3] and also by the absence of a shift of the ketonic absorption in the infrared spectrum.[4] An attempt was made to dehydrobrominate the bromoketone II by refluxing it for 1 hour in collidine or by keeping its dimethylformamide solution for 2 hours at 100°. Instead of the expected α,β-unsaturated ketone the isomeric 16β-bromoketone IV (λ_{max} 281 mμ) was obtained, and the original ketone absorption wave number was shifted from 1705 to 1715 cm.$^{-1}$. The absence of elimination is due to the steric effects of neighboring groups: the 15β (axial) hydrogen is hindered by the angular 18-methyl group and is therefore not available for attack by a base with high steric requirements such as collidine or dimethylformamide, which have to bring about the transelimination of the elements of hydrogen bromide. On the other hand, attack by a base on the sterically available

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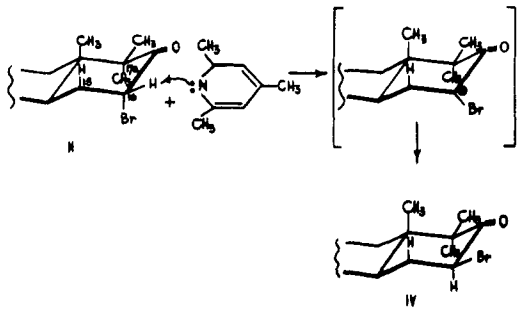
(2) M. Uskoković, M. Gut and R. I. Dorfman, THIS JOURNAL, **81**, 4561 (1959).

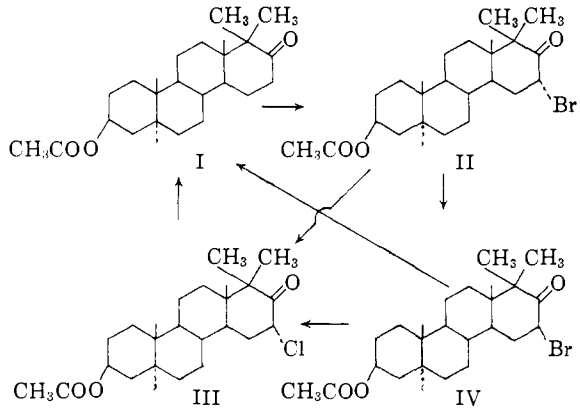
(3) R. C. Cookson, *J. Chem. Soc.*, 282 (1954); R. C. Cookson and S. H. Dandegaonker, *ibid.*, 352 (1955).

(4) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1954); E. G. Gumnis and J. E. Page, *J. Chem. Soc.*, 3847 (1957).

16β (equatorial) hydrogen brings about a transitional 16-carbanion, followed by recombination to the more stable 16β-bromoketone IV. Unbonded repulsion between the 17aα (axial) methyl group and the 16α (axial) bromine will contribute to the speed of isomerization. The steric influence of the



angular 18-methyl group is decisive in the above isomerization. This becomes clear from the fact that the dehydrobromination of 2β-bromolanostanone, in absence of steric hinderance, proceeds smoothly in boiling collidine.[5] That the isomerization does not involve the dissociation of a bromide anion, nor the formation of a bromonium ion or an enol intermediate, follows from the treatment with hot concentrated formic acid, which resulted in the quantitative recovery of the 16α-bromoketone III.[6,7] The reduction of IV with zinc in acetic acid solution gave the original ketone I. The treatment of either the 16α-bromoketone II or the 16β-bromoketone IV with dimethylformamide and lithium chloride gave the 3β-acetoxy-16α-chloro-17a,17a-dimethyl-D-homoandrostan-17-one (III), which in turn could be reduced with zinc in acetic acid to the starting ketone I. The chloroketone

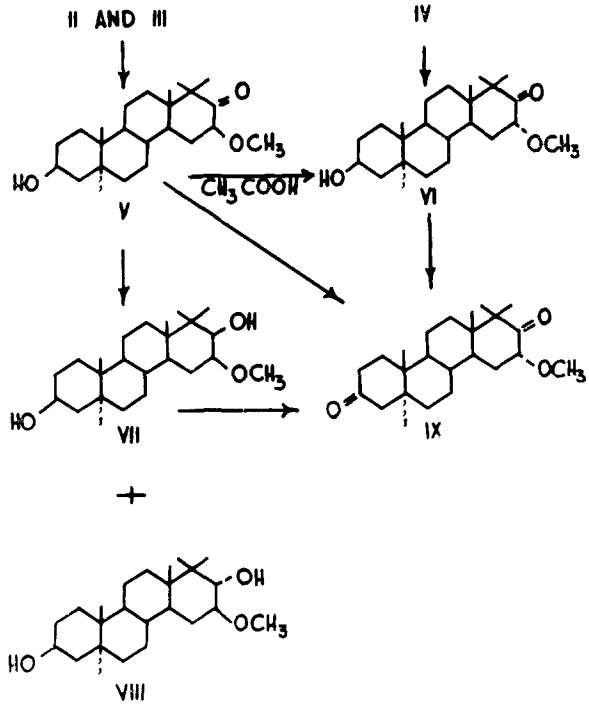


III shows an unexpected ultraviolet absorption maximum at λ_{max} 257 mμ,[3] and a shift of the original ketonic infrared absorption to 1720 cm.$^{-1}$.[4]

The configuration of the chlorine is confirmed by the transformation of III to the 3β-hydroxy-16β-methoxy - 17a,17a - dimethyl - D - homoandrostan-17-one (V), which was also obtained from the 16α-bromoketone II with methoxyl ion in an S_N2 reaction. The 16β-bromoketone IV gave, in the same fashion, the isomeric 16α-methoxyketone VI. Compound V can be isomerized to VI in acetic acid with catalytic amounts of *p*-toluenesulfonic acid for 24 hours at room temperature, very likely through an enol intermediate.

The 16β-methoxy-17-ketone V was reduced with potassium borohydride in methanol, whereby both isomeric 17-hydroxy compounds were obtained. The less polar isomer, possessing the axial 17β-hydroxy group (VII) was eluted first as the major product. The VII was more levorotatory [−32°] than the equatorial 17α-hydroxy derivative (VIII) [−16°] which was eluted as a minor product later on.

The chromic oxide in acetic acid oxidation of the 16β-methoxy-17-ketone (V) and of the 16β-methoxy-17β-hydroxy compound (VIII) gave 16α-methoxy - 17a,17a - dimethyl - D - homoandrostane-3,17-dione (IX), which was also obtained by the oxidation of the 16α-methoxy-17-ketone VI. During oxidation the 16β-methoxy group isomerizes into the 16α-position as described above. The infrared analysis shows a maximum for the 16β-methoxy group at 1110 cm.$^{-1}$ (-C-O-C-) while the maximum for the 16α analog shifts to 1122–1125 cm.$^{-1}$.



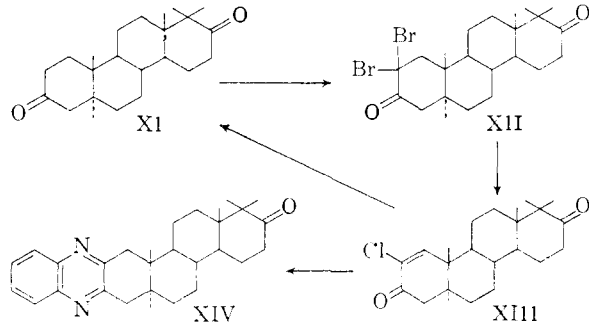
The bromination of 17a,17a-dimethyl-D-homoandrostane-3,17-dione (XI) with two moles of bromine in ether–acetic acid solution gave insoluble 2,2 - dibromo - 17a,17a - dimethyl - D - homoandrostane-3,17-dione (XII), with ultraviolet absorption peaks at λ_{max} 318 and 291 mμ; the infrared absorption maximum of the ketone had shifted from 1712 to 1728 cm.$^{-1}$. The dibromide XII was transformed (heating with dimethylformamide and lithium chloride at 100° for 2 hours) to 2-chloro-17a,17a-dimethyl-D-homoandrost-1-ene-3,17-dione (XIII) with a λ_{max} 247 mμ and ν_{max} 1730 cm.$^{-1}$ (2-chloro-Δ^1 group). The proof of structure of XIII rests in its transformation with

(5) D. H. R. Barton, D. A. Lewis and J. F. McGhie, *ibid.*, 2907 (1957).

(6) B. Ellis, D. Patel and V. Petrow, *ibid.* 800 (1958).

(7) C. W. Shoppee, R. H. Jenkins and G. H. R. Summers, *ibid.*, 3048 (1958).

o-phenylenediamine to its quinoxaline derivative XIV, showing strong ultraviolet absorption maxima at 238 and 322 mμ. Steric hindrance would obviously have prevented *o*-phenylenediamine condensation at carbon 16 and 17. The chloroketone XIII was also reduced with zinc in acetic acid to the diketone XI. The proof that the dibromination



of XI did not take place in ring D rests with an attempt to dibrominate the ketone I. The only product isolated was the monobromoketone II, which, in turn, could not be further brominated.

Experimental[8]

3β-Acetoxy-16α-bromo-17a,17a-dimethyl-D-homoandrostan-17-one (II) from I.—To the ether solution of 374.5 mg. of I was added a few drops of 38% hydrobromic acid in acetic acid, the solution cooled to 0° and then 160 mg. of bromine dissolved in 1 ml. of acetic acid were added dropwise. The disappearance of bromine was instantaneous. After stirring the mixture for 15 minutes, 200 ml. of ether was added, the ether solution washed with 2 *N* sodium carbonate solution and water. Then the organic layer was separated off, dried and evaporated. The residue, recrystallized from methanol, gave II, m.p. 165–166°, with a yield better than 95%, $[\alpha]^{20}D$ −137° (*c* 0.97); ultraviolet absorption λ 322 mμ ε 114; infrared absorption maxima ν_{max} 1705 (>C=O), 1735, 1245 (acetate) 747 (bromine), 1399, 1389, 1377 cm.$^{-1}$ (isopropyl group).

Anal. Calcd. for $C_{24}H_{37}O_3Br$: C, 63.57; H, 8.23; Br, 17.62. Found: C, 63.69; H, 8.27; Br, 16.11 ± 1.6.

3β-Acetoxy-16β-bromo-17a,17a-dimethyl-D-homoandrostan-17-one (IV) from II.—The solution of 300 mg. of II in 10 ml. of freshly distilled *s*-collidine was refluxed for one hour under nitrogen. After cooling, 100 ml. of ether was added and the ether solution was washed with 2 *N* hydrochloric acid and water, dried over anhydrous sodium sulfate and evaporated. The crystalline residue, after recrystallization from methanol, gave 200 mg. of IV, m.p. 250–252°, $[\alpha]^{20}D$ −58° (*c* 0.82); ultraviolet maximum ϵ_{281} 73.5; infrared absorption maxima: ν_{max}: 1715 (>C=O), 1737, 1245 (acetate), 748 (bromine), 1399, 1390, 1365 cm.$^{-1}$ (isopropyl group).

Anal. Calcd. for $C_{24}H_{37}O_3Br$: C, 63.57; H, 8.23; Br, 17.62. Found: C, 63.72; H, 8.26; Br, 16.08.

The same product was also obtained when II was heated in dimethylformamide solution for two hours at 100°, followed by extraction in ether, washing and evaporation.

3β-Acetoxy-16α-chloro-17a,17a-dimethyl-D-homoandrostan-17-one (III) from II or IV.—To the solution of 100 mg. of II (or III) in 10 ml. of dimethylformamide was added 150 mg. of anhydrous lithium chloride and the reaction mixture heated at 100° for two hours. After cooling, the mixture was poured in a large excess of water, extracted with ether, the extract washed with 2 *N* hydrochloride acid and water, dried over anhydrous sodium sulfate and evaporated. The crystalline residue, after recrystallization from methanol, gave III, m.p. 236–239° $[\alpha]^{20}D$ −45° (*c* 1.453); ultraviolet maximum ϵ_{257} 170; infrared absorption maxima: ν_{max} 784 and 1440 (chlorine), 1737 and 1245 (acetate), 1720 (ketone). 1395, 1387, 1365 cm.$^{-1}$ (isopropyl group).

Anal. Calcd. for $C_{24}H_{37}O_3Cl$: C, 70.47; H, 9.12; Cl, 8.67. Found: C, 70.68; H, 9.13; Cl, 8.53.

3β-Acetoxy-17a,17a-dimethyl-D-homoandrostan-17-one (I) from III and from IV.—To the solution of 50 mg. of III in 5 ml. of glacial acetic acid were added 50 mg. of zinc powder and 50 mg. of anhydrous sodium acetate, and the reaction mixture heated for 10 minutes at 100°. The zinc was filtered off, washed with ethyl acetate and to the filtrate was added a large excess of ethyl acetate. This solution was washed with 2 *N* sodium carbonate solution and water, dried and evaporated. The non-crystalline residue was chromatographed and the fractions with 1% ethyl acetate in benzene gave, after recrystallization from acetone, I, m.p. 172–175°, which furnished an infrared spectrum identical with the one obtained from an authentic sample.[2] Compound I was also obtained in the same way from IV.

3β-Hydroxy-16β-methoxy-17a,17a-dimethyl-D-homoandrostan-17-one (V) from III or from II.—The solution of 150 mg. of III in 50 ml. of 5% methanolic potassium hydroxide solution was refluxed under nitrogen for 4 hours and then the mixture was poured into a large excess of water. The suspension was exhaustively extracted with ether, the ether extract washed with water, dried over sodium sulfate and evaporated. The residue was chromatographed and the 10% ethyl acetate–benzene eluates gave, after recrystallization from acetone–hexane, 70 mg. of V, m.p. 200–204°, $[\alpha]^{20}D$ −108° (*c* 1.21); ultraviolet maximum ϵ_{285} 80.3; infrared maxima: ν_{max} 3600 (hydroxyl), 1712 (ketone), 1110 (methoxyl), 1397, 1385, 1368, 1170, 958 cm.$^{-1}$ (isopropyl group).

Anal. Calcd. for $C_{23}H_{38}O_3$: C, 76.19; H, 10.57. Found: C, 75.98; H, 10.50.

The same product (V) was also obtained when the bromoketone II was treated with methanolic potassium hydroxide in exactly the same fashion.

3β-Hydroxy-16α-methoxy-17a,17a-dimethyl-D-homoandrostan-17-one (VI) from IV.—The bromoketone IV was treated with methanolic potassium hydroxide in exactly the same way as described above. The crude product was chromatographed and the fractions with 5% ethyl acetate in benzene, after recrystallization from acetone–hexane, gave VI, m.p. 194–197°. On admixture with V the melting point was depressed to 182–200°, $[\alpha]^{20}D$ −81° (*c* 0.560); ultraviolet maxima ϵ_{290} 44.2; infrared maxima: ν_{max} 3400 (hydroxy), 1720 (ketone), 1125 (methoxyl), 1398, 1385, 1365, 1160, 958 cm.$^{-1}$ (isopropyl group).

Anal. Calcd. for $C_{23}H_{38}O_3$: C, 76.19; H, 10.57. Found: C, 75.62; H, 11.07.

3β-Hydroxy-16α-methoxy-17a,17a-dimethyl-D-homoandrostan-17-one (VI) from V.—The solution of 20 mg. of V in 20 ml. of acetic acid and 1 mg. of *p*-toluenesulfonic acid was shaken for 24 hours at room temperature. Then 100 ml. of methylene chloride was added and the solution washed with 2 *N* sodium carbonate solution and water to neutrality, dried over anhydrous sodium sulfate and evaporated. The crystalline residue was recrystallized from acetone–hexane whereby VI was obtained. It was identical in all respects with the compound described above.

16β-Methoxy-17a,17a-dimethyl-D-homoandrostane-3β,17β-diol (VII) and 16β-Methoxy-17a,17a-dimethyl-D-homoandrostane-3β,17α-diol (VIII) from V.—To the solution of 150 mg. of V in 50 ml. of methanol was added 100 mg. of potassium borohydride and the mixture stirred overnight at room temperature. After evaporating off the methanol in vacuum, the residue was taken up in ethyl acetate, the organic layer washed with water, then dried and finally the solvent evaporated. The residue was chromatographed and the fractions obtained with 10% ethyl acetate–benzene gave after recrystallization from acetone VII, m.p. 214–216°, $[\alpha]^{20}D$ −34.2° (*c* 1.170); infrared absorption maxima ν_{max} 3550 (hydroxyl), 1035 (equatorial 3β-OH), 1000 (17β-OH), 1110 cm.$^{-1}$ (methoxyl).

Anal. Calcd. for $C_{23}H_{40}O_3$: C, 75.77; H, 11.06. Found: C, 75.29; H, 10.91.

(8) All melting points were taken on a Kofler block. Rotations were taken in a 1-dm. tube in chloroform. Ultraviolet absorption spectra were determined in methanol by means of a Cary model 11 MS spectrophotometer. The infrared spectra were obtained from a pressed potassium bromide pellet taken on a Perkin–Elmer model 12C spectrometer. All chromatographic separations were made on Davison Silica Gel mesh 60–200, unless otherwise indicated. The microanalysis were performed by Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

The fraction obtained with 25% ethyl acetate in benzene gave, after recrystallization from acetone, VIII, m.p. 205–208° $[\alpha]^{20}D$ −16° (*c* 10.310); infrared maxima ν_{max} 3500 (hydroxyl), 1045, 1040 (equatorial 3β- and 17α-OH groups), 1103 cm.$^{-1}$ (methoxy group).

Anal. Calcd. for $C_{23}H_{40}O_3$: C, 75.77; H, 11.06. Found: C, 75.91; H, 11.09.

16α-Methoxy-17a,17a-dimethyl-D-homoandrostane-3,-17-dione (IX) from V and VI.—To the solution of 150 mg. of V in 50 ml. of methylene chloride was added the solution of 200 mg. of chromic trioxide in 2 ml. of 80% acetic acid, and the reaction mixture was shaken for 24 hours at room temperature. The excess chromic oxide was reduced with a few drops of saturated aqueous sodium hydrogen sulfite solution and then the methylene chloride solution was washed with water to neutrality, dried and evaporated. The noncrystalline residue was chromatographed and the fractions with 5% ethyl acetate–benzene gave, after recrystallization from ether, 120 mg. of IX, m.p. 216–221° (transformation 195–205°); infrared absorption maxima: ν_{max} 1710 (keto groups), 1400, 1386, 1380, 1335, 1170, 955 (isopropyl group), 1122 cm.$^{-1}$ (methoxy group). The oxidation of VI gave the same product.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.47; H, 10.21.

16α-Methoxy-17a,17a-dimethyl-D-homoandrostane-3,-17-dione (IX) from VII.—The oxidation was carried out in exactly the same way with double the amount of chromic acid solution, and after chromatography and recrystallization, the product was identical with IX, described above.

2,2-Dibromo-17a,17a-dimethyl-D-homoandrostane-3,-17-dione (XII) from XI.—To the solution of 150 mg. of XI[2] in 50 ml. of anhydrous ether was added a few drops of 38% hydrobromic acid in acetic acid, the solution cooled to 0°, and the solution of 0.047 ml. of bromine in 2 ml. of acetic acid was added dropwise under vigorous stirring. After one mole-equivalent of bromine was added, further addition caused the precipitation of dibromide XII. After all the bromine was added, the resulting suspension was stirred for an additional half-hour. The precipitated product was filtered off and washed with ether, m.p. 233–234°, λ_{max} 318 and 291 mμ; infrared absorption maxima: ν_{max} 1728 (3-ketone), 1705 (17-ketone), 1394, 1384, 1379, 1163, 965 (isopropyl group), 762 (bromine).

2-Chloro-17a,17a-dimethyl-D-homoandrost-1-ene-3,17-dione (XIII) from XII.—To the solution of 150 mg. of XII in 10 ml. of dimethylformamide was added 100 mg. of anhydrous lithium chloride and the reaction mixture was then heated for 2 hours at 100°. After cooling, the reaction mixture was poured into a large excess of water, the crystalline precipitate was filtered off, washed with water, and dried. The product was chromatographed and the fractions with 1 and 2% ethyl acetate in benzene gave, after recrystallization from ether, XIII, m.p. 244–248°, λ_{max} 247 mμ; infrared absorption maxima ν_{max} 1730 (3-ketone); 1705 (17-ketone), 797 cm.$^{-1}$ (chlorine).

Anal. Calcd. for $C_{22}H_{31}O_2Cl$: C, 72.80; H, 8.62. Found: C, 72.97; H, 8.62.

17a,17a-Dimethyl-D-homoandrostane-3,17-dione (XI) from XIII.—To the solution of 50 mg. of XIII in 10 ml. of glacial acetic acid was added 50 mg. of zinc powder and the reaction mixture was refluxed for two hours under nitrogen. After cooling, the zinc was filtered off, washed with a large excess of ethyl acetate, then the filtrate was washed with water, 2 *N* sodium hydroxide solution, and again with water, dried over sodium sulfate and evaporated. The noncrystalline residue was chromatographed and the fraction with 1 and 2% ethyl acetate in benzene gave, after recrystallization from methanol, XI, m.p. 202–205°, which had the infrared spectrum identical with the spectrum from authentic material.[2]

Quinoxalo[2,3-b]-17a,17a-dimethyl-D-homoandrostan-17-one (XIV) from XIII.—To the solution of 5 mg. of XIII in 1 ml. of glacial acetic acid was added 2 mg. of *o*-phenylenediamine, and the reaction mixture was refluxed for 2 hours under nitrogen. After cooling, 50 ml. of chloroform was added, the chloroform solution was washed with 2 *N* hydrochloric acid and water, dried over sodium sulfate and evaporated. The residue crystallized from ether, giving XIV, m.p. 230–233°, λ_{max} 238 and 332 mμ.

WORCESTER, MASS.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF SYNTHEX, S. A.]

Steroids. CXXXIII.[1] B-Homo-androstane Derivatives

BY H. J. RINGOLD

RECEIVED JULY 20, 1959

Platinum reduction of the cyanohydrin of 7-ketoandrostane-3β,17β-diol diacetate gave the aminomethyl compound which underwent ring expansion on treatment with nitrous acid. The resultant B-homoketone IV, on Wolff–Kishner reduction, gave B-homoandrostane-3β,17β-diol (Va) oxidized to the dione VII, while selective saponification of V-diacetate followed by oxidation and hydrolysis gave B-homodihydrotestosterone (VI). Biological activities of VI and VII are described.

As a continuation of the investigation in these laboratories of the relationship of structural changes to biological activity in the androgen series it was of interest to prepare an androstane derivative with a seven-membered ring B, a hitherto unknown structure. A-Homo-[2] and D-homo-dihydrotestosterone[3] have been reported, the former exhibiting a very low order of androgenic activity[2] while the latter compound was found to be about as androgenic as dihydrotestosterone.[3] We and others have described the synthesis of 2-[4], 4-[5], 6-[6] and 7-[7] alkyltestosterone derivatives.

This paper presents the synthesis of B-homoandrostane-3β,17β-diol (Va), B-homodihydrotestosterone (VI) and B-homoandrostane-3,17-dione (VII) from Δ^5-androstene-3β,17β-diol diacetate (I) by a straight-forward route.[8] Treatment of I with N-bromosuccinimide in boiling carbon tetrachloride gave the allylic 7-bromo compound which was hydrolyzed to the 7-hydroxy derivative(s) by stirring with alumina and finally con-

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(3) M. W. Goldberg and R. Monnier, *ibid.*, **23**, 376, 840 (1940).

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