[CONTRIBUTION FROM THE LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY]

$\Delta^{5,7}$-STEROIDS. VI. THE PREPARATION OF $\Delta^{5,7}$-STEROIDAL HORMONES[1, 2]

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The utility of the NBS[3] (Wohl-Ziegler) method, followed by dehydrobromination, for the preparation of $\Delta^{5,7}$-steroids from Δ^5-steroids is now well established. It was of interest to us to extend this reaction to compounds of the so-called "hormone" type, *i.e.* compounds in which the C_{17}-substituents are oxygen, hydroxyl, acetyl, and the like. In this publication we wish to report on the preparation of a number of such $\Delta^{5,7}$-steroids.

Dehydroisoandrosterone acetate (I) was brominated with NBS in the usual manner (1) of this laboratory to afford 7α-bromo-Δ^5-androstene-3β-ol-17-one acetate (II)[4] which on being refluxed with *s*-collidine in xylene gave $\Delta^{5,7}$-androstadiene-3β-ol-17-one acetate (III), 28% yield from I. III, in turn, was hydrolyzed with alcoholic potash to give the free steroid, $\Delta^{5,7}$-androstadiene-3β-ol-17-one (IV). Acetylation of IV in the usual manner gave back III, identical with the material prepared directly from I. Benzoylation of IV gave VII which was identical with the material prepared from dehydroisoandrosterone benzoate (V) *via* NBS bromination and dehydrobromination. Hydrolysis of VII, likewise, gave IV. The intermediate bromobenzoate (VI) was not isolated and characterized as was the case with the acetate derivative (II).

Δ^5-Androstene-3β,17β-diol diacetate (VIII) was similarly brominated and dehydrobrominated to give $\Delta^{5,7}$-androstadiene-3β,17β-diol diacetate (XIV).[5] Hydrolysis of XIV with alcoholic potash gave the free steroid, $\Delta^{5,7}$-androstadiene-3β,17β-diol (XII). Acetylation gave back XIV, identical with the diacetate prepared from the Δ^5-diacetate, and benzoylation gave the dibenzoate (XVI). The diol (XII) was prepared also in the following manner. Δ^5-Androstene-3β,17β-diol-3-acetate-17-benzoate (IX)[6] was converted to the $\Delta^{5,7}$-

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[1] Presented in part before the Organic Group at the third annual meeting of the North Jersey Section, American Chemical Society, Newark, N. J., January 8, 1951.

[2] Paper V. Bernstein and Sax, *J. Org. Chem.*, **16,** 685 (1951).

[3] NBS = N-Bromosuccinimide.

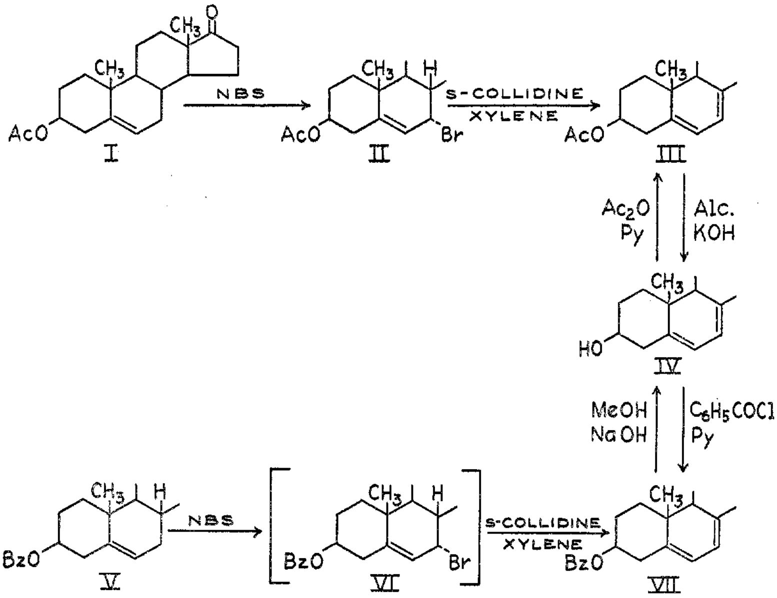
[4] The assignment of the α-configuration for the bromine atom at the C_7-position follows that of Bide, Henbest, Jones, and Wilkinson, *J. Chem. Soc.*, 1788 (1948), and that of Fieser, *Experientia*, **6,** 312 (1950).

[5] Butenandt, Hausmann, and Paland, *Ber.*, **71,** 1316 (1938) have prepared $\Delta^{5,7}$-androstadiene-3β,17β-diol, m.p. 212°, its acetate, m.p. 132° $[\alpha]_D^{23}$ +41° (alc.), and benzoate, m.p. 217–218°, by the classical Windaus method [Windaus, Lettré, and Schenck, *Ann.*, **520,** 98 (1935)]. However, there are several divergent physical constants between their results and those reported herein (see Experimental).

[6] Fukushima, Lieberman, and Praetz, *J. Am. Chem. Soc.*, **72,** 5205 (1950) have recently reported the preparation of 7-bromo-Δ^5-androstene-3β,17β-diol-3-acetate-17-benzoate by benzoyl peroxide catalyzed bromination with NBS of the Δ^5-steroid (IX) in carbon tetrachloride. Dehydrobromination of the bromocompound to give XV was not reported.

3-acetate-17-benzoate (XV), which on partial hydrolysis according to the method of Levy and Kapp (2) gave the $\Delta^{5,7}$-17-benzoate (XIII). Acetylation of XIII gave back XV. Further hydrolysis of XIII with methanolic potash gave the diol (XII).

FLOWSHEET I



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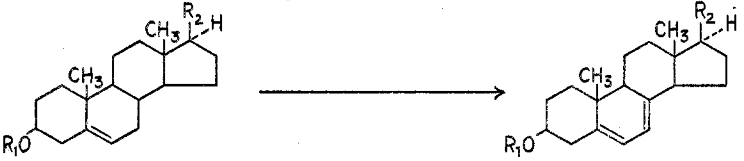

VIII $R_1 = Ac$, $R_2 = OAc$
IX $R_1 = Ac$, $R_2 = OBz$
X $R_1 = Ac$, $R_2 = COCH_3$
XI $R_1 = Ac$, $R_2 = COCH_2OAc$

XII $R_1 = H$, $R_2 = OH$
XIII $R_1 = H$, $R_2 = OBz$
XIV $R_1 = Ac$, $R_2 = OAc$
XV $R_1 = Ac$, $R_2 = OBz$
XVI $R_1 = Bz$, $R_2 = OBz$
XVII $R_1 = H$, $R_2 = COCH_3$
XVIII $R_1 = Ac$, $R_2 = COCH_3$
XIX $R_1 = Bz$, $R_2 = COCH_3$
XX $R_1 = H$, $R_2 = COCH_2OH$
XXI $R_1 = Ac$, $R_2 = COCH_2OAc$
XXII $R_1 = Bz$, $R_2 = COCH_2OBz$

The following additional $\Delta^{5,7}$-steroids were prepared and characterized: $\Delta^{5,7}$-pregnadiene-3β-ol-20-one (XVII), acetate (XVIII) (20% yield from X), and benzoate (XIX); and $\Delta^{5,7}$-pregnadiene-3β,21-diol-20-one (XX), diacetate (XXI) (15% yield from XI), and dibenzoate (XXII).

In the preparation of the $\Delta^{5,7}$-steroids reported herein no attempt was made to investigate the possible multiplicity of the bromination products. Also no attempt was made to isolate the expected dehydrobromination by-products, namely, the $\Delta^{4,6}$-steroids. The isolation and characterization of the $\Delta^{4,6}$-steroids has been set aside for future work.

Transformation products of these interesting $\Delta^{5,7}$-steroids will be the subject matter of future publications from this laboratory.

EXPERIMENTAL

Absorption spectra. All spectra were determined with a Beckman quartz spectrophotometer (National Technical Laboratories, South Pasadena, California), and were determined, unless otherwise stated, in commercial absolute alcohol.

Melting points. All m.p.'s are uncorrected, and were determined with uncalibrated Anschütz thermometers (total immersion). Many of the m.p.'s were dependent on the rate of heating and on the temperature of the bath at which the sample was inserted; generally, the sample was inserted in the bath about 5–10° below its anticipated m.p. With some of the compounds consistent m.p.'s were difficult to obtain due most probably to solvation.

Optical rotations. The sample was dissolved in chloroform (unless otherwise stated) to make a 2-ml. solution, and the rotation was determined in a 1-dcm. semi-micro tube.

Petroleum ether. The petroleum ether fraction used was b.p. 64–66° (unless otherwise stated) and was purified with conc'd sulfuric acid and potassium permanganate.

All reactions and distillations were carried out in a nitrogen atmosphere.

7α-Bromo-Δ^5-androstene-3β-ol-17-one acetate (II). A mixture of 3.3 g. (0.01 M) of dehydroisoandrosterone acetate (I) and 2.15 g. (0.012 M) of NBS in 50 ml. of carbon tetrachloride and 75 ml. of petroleum ether was refluxed and irradiated for 5 minutes by the heat and light of a photospot lamp (Type RSP-2, General Electric Company). The mixture was immediately cooled and filtered. The succinimide was washed with carbon tetrachloride, m.p. 98–122°, wt. 1.16 g. (calc'd wt. 1.19 g.). The filtrate was evaporated *in vacuo*, and the temperature of distillation was maintained at room temperature and below. During the evaporation crystals separated. Petroleum ether was added to the residue and the white crystals were removed, wt. 2.54 g., m.p. 112° d. Four recrystallizations to constant m.p. from benzene-petroleum ether gave 1.33 g. of needles, m.p. 154.5–155° d. From the mother liquors there were obtained two additional fractions, wt. 0.85 g., m.p. 155° d. and 0.31 g., m.p. 153° d. 61% yield.

An aliquot of the main fraction was recrystallized further from benzene-petroleum ether, m.p. 155°d., $[\alpha]_D^{20} -260.2°$, $]\alpha]_{Hg}^{20} -313.6°$ (20.6 mg., $\alpha_D -2.68°$, $\alpha_{Hg} -3.23°$) · α_{Hg}/α_D 1.21; $[M]_D -1064$.

Anal. Calc'd for $C_{21}H_{29}BrO_3$ (409.36): C, 61.61; H, 7.14; Br, 19.52.

Found: C, 61.60; H, 7.35; Br, 19.49.

$\Delta^{5,7}$-Androstadiene-3β-ol-17-one acetate (III). *A.* A mixture of 1.12 g. of 7α-bromo-Δ^5-androstene-3β-ol-17-one acetate (II) and 1.5 ml. of *s*-collidine[7] in 35 ml. of xylene was refluxed for 15 minutes, cooled, and filtered. The filtrate was evaporated *in vacuo* and afforded an oily residue. Treatment with petroleum ether gave crystals which were separated, wt.

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[7] No systematic study has been made on the influence of the number of molar equivalents of *s*-collidine in the dehydrobromination of 7α-bromocompounds. It is our belief, after surveying the results in the experimental part, that the best yields may be obtained with a 1.2–1.5:1 molar ratio of *s*-collidine to the bromocompound.

0.64 g., m.p. 122–128°, $\lambda_{\max}$ 239, 270.5, 281, and 292 mμ, ϵ 5,300, 5,800, 6,200, and 3,400 resp. The mother liquor was evaporated, and gave from dilute methanol 0.15 g., m.p. 133–142°, $\lambda_{\max}$ 239, 271, 281, and 292–293 mμ, ϵ 7,400, 7,850, 8,200, and 4800 resp.

Both fractions were recrystallized from dilute methanol and were combined. Recrystallization from dilute methanol gave 0.20 g. of pure III, m.p. 155.5–158.5°, $\lambda_{\max}$ 271, 281, and 293 mμ; ϵ 10,600, 11,200, and 6,300 resp.

B. A mixture of 3.3 g. (0.01 M) of dehydroisoandrosterone acetate and 2.14 g. (0.012 M) of NBS in 50 ml. of carbon tetrachloride and 75 ml. of petroleum ether was refluxed and irradiated for 5 minutes by the heat and light of a photospot lamp. To the still refluxing mixture was added 7.5 ml. of freshly distilled *s*-collidine; the mixture was cooled and filtered. The filtrate was evaporated *in vacuo*, and the residue was refluxed for 15 minutes with 125 ml. of xylene, cooled, and filtered. The filtrate was evaporated *in vacuo* and afforded an oily residue. Methanol was added, and then removed *in vacuo*. This gave a mixture of oil and solid. Crystallization from dilute methanol gave 1.93 g., m.p. 131–142°, $\lambda_{\max}$ 239, 271, 281, and 293 mμ; ϵ 5,750, 7,000, 7,400, and 4,260. Recrystallization from dilute methanol, petroleum ether, and dilute methanol gave 0.91 g., m.p. 154–157° with slight previous softening; 28% yield.

An aliquot of this material was further recrystallized from petroleum ether, m.p. 155.5–158°; $\lambda_{\max}$ 271, 281, and 293 mμ; ϵ 10,000, 10,530, and 6,050 resp.; $[\alpha]_{\text{D}}^{26} -92.9°$, $[\alpha]_{\text{Hg}}^{26} -117.2°$ (9.9 mg., $\alpha_{\text{D}} -0.46°$, $\alpha_{\text{Hg}} -0.58°$) $\alpha_{\text{Hg}}/\alpha_{\text{D}}$ 1.26; $[\text{M}]_{\text{D}}$ −305.

Anal. Calc'd for $C_{21}H_{28}O_3$(328.43): C, 76.79; H, 8.59.

Found: C, 76.55; H, 8.54.

In another run by essentially the same technique there was obtained material of m.p. 158–161° (with slight previous softening), $\lambda_{\max}$ 271, 281, and 293 mμ; ϵ 10,500, 11,000, and 6,200 resp.

C. The $\Delta^{5,7}$-steroid (IV) (0.1 g.) in 10 ml. of acetic anhydride was refluxed for ½ hour. The excess anhydride was removed *in vacuo*, and the residue was recrystallized successively from methanol, dilute methanol, and petroleum ether (b.p. 67–70°), m.p. 158–160.5° (after resolidification, initial melt at 151.5–153.5°), $\lambda_{\max}$ 271, 281, and 292 mμ; ϵ 11,300, 11,850, 6,700 resp.

$\Delta^{5,7}$-Androstadiene-3β-ol-17-one (IV). *A.* A solution of 500 mg. of $\Delta^{5,7}$ androstadiene-3β-ol-17-one acetate (III) in 30 ml. of 5% alcoholic potash was allowed to stand at room temperature overnight. Addition of water gave a precipitate, and the mixture was allowed to stand at room temperature for 1.5 hours. The free steroid (IV) was collected and washed with water and dilute methanol, wt. 0.45 g., m.p. 172–185°; $\lambda_{\max}$ 271, 281.5, and 293.5 mμ; ϵ 8,850, 9,450, and 5,280 resp. The product was recrystallized from dilute methanol and benzene-petroleum ether, wt. 0.21 g., m.p. 187–189°, $\lambda_{\max}$ 271, 281.5, and 293 mμ; ϵ 10,410, 10,900, and 6,250 resp. $[\alpha]_{\text{Hg}}^{27} -159.7°$ (13.15 mg., chloroform, $\alpha_{\text{D}} -1.05°$); $[\alpha]_{\text{Hg}}^{27} -130.7°$, $[\alpha]_{\text{Hg}}^{27} -154.3°$ (12.7 mg., abs. alc., $\alpha_{\text{D}} -0.83°$, $\alpha_{\text{Hg}} -0.98°$); $\alpha_{\text{Hg}}/\alpha_{\text{D}}$ 1.18 (abs. alc.); $[\text{M}]_{\text{D}}$ −374.

Anal. Calc'd for $C_{19}H_{26}O_2$ (286.40): C, 79.68; H, 9.15.

Found: C, 79.89; H, 9.40.

B. A mixture of 0.40 g. of $\Delta^{5,7}$-benzoate (VII), 0.1 g. of sodium hydroxide, and 10 ml. of methanol was refluxed for 1 hour. The product was worked up in benzene and gave 0.32 g., m.p. 180–184°. Two recrystallizations from benzene-petroleum ether gave 0.22 g., m.p. 186–189°.

$\Delta^{5,7}$-Androstadiene-3β-ol-17-one benzoate (VII). A mixture of 3.92 g. (0.01 M) of dehydroisoandrosterone benzoate (V) and 2.14 g. (0.012 M) of NBS in 50 ml. of carbon tetrachloride and 25 ml. of petroleum ether was reacted and dehydrobrominated with 5 ml. of *s*-collidine in 50 ml. of xylene in the usual manner. Three recrystallizations from benzene-acetone gave 0.40 g. of pure VII, m.p. 253–256° d., $\lambda_{\max}^{1\%\text{CA}}$[8] 229, 271, 281, and 293 mμ; ϵ 13,500, 12,600, 12,800,

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[8] 1% CA = 1% chloroform-absolute alcohol, *i.e.* the weighed sample was dissolved in 1 ml. of reagent chloroform and this solution was rapidly diluted to 100 ml. with commercial absolute alcohol.

and 7,000 resp. $[\alpha]_D^{26}$ −64.9°, $[\alpha]_{Hg}^{26}$ −82.0° (18.3 mg., α_D −0.59°, α_{Hg} −0.75°); α_{Hg}/α_D 1.27; $[M]_D$ −253.

Anal. Calc'd for $C_{26}H_{30}O_3$(390.50): C, 79.96; H, 7.74.
Found: C, 80.00; H, 7.92.

The mother liquors were triangularly recrystallized from benzene-acetone, and from acetone-methanol, and gave 3 fractions in order of increasing solubility, wt. 0.26 g., m.p. 210–239° d.; wt. 0.5 g., m.p. 183–190°; and wt. 0.34 g., m.p. 183–184° (dark melt). This last or most soluble fraction consisted principally of $\Delta^{4,6}$-androstadiene-3β-ol-17-one benzoate as indicated by the ultraviolet absorption spectrum, λ_{max} 238–239, 270, 281, and 292–293 mμ; ε 29,400, 4,150, 3,890 and 1,770 resp.

Anal. Found: C, 80.30; H, 8.00.

$\Delta^{5,7}$-Androstadiene-3β,17β-diol diacetate (XIV). *A.* Δ^5-Androstene-3β,17β-diol diacetate (VIII) (3.48 g., 0.0093 M) in 50 ml. of carbon tetrachloride and 75 ml. of petroleum ether was brominated with 1.99 g. (0.0112 M) of NBS, and dehydrobrominated with 7.5 ml. of *s*-collidine in 100 ml. of xylene in the usual manner. The crude product, oily crystals, was recrystallized from dilute methanol, wt. 2.18 g., m.p. 100°, cloudy melt, λ_{max} 239, 271, 281, and 292–293 mμ; ε 8,950, 6,790, 6,900, and 4,100. Recrystallization from methanol, followed by dilute methanol gave 0.65 g. of XIV, m.p. 132–134°, λ_{max} 270–271, 281, and 292–292.5 mμ, ε 10,800, 11,300, and 6,400, resp. $[\alpha]_D^{31}$ −135.8°, $[\alpha]_{Hg}^{31}$ −172.1° (21.5 mg., α_D −1.46°, α_{Hg} −1.85°) α_{Hg}/α_D 1.27; $[M]_D$ −505, 19% yield.

Anal. Calc'd for $C_{23}H_{32}O_4$(372.49): C, 74.16; H, 8.66.
Found: C, 74.24; H, 8.73.

B. In another run which was carried out as above (A) with 3.74 g. (0.01 M) of VIII and 2.14 g. (0.012 M) of NBS, the dehydrobromination was performed with 2 ml. of *s*-collidine in 50 ml. of xylene. The product was worked up in xylene, and the extract was washed with dilute acetic acid and saturated saline. The dried solution was treated with Norit and filtered through Celite. Evaporation gave oily crystals which were recrystallized from dilute methanol and dilute acetone, wt. 1.02 g., m.p. 132–135°, 27% yield.

C. The $\Delta^{5,7}$-diol (XII) (0.5 g.) was acetylated with acetic anhydride and pyridine in the usual manner, and recrystallization of the diacetate (XIV) from dilute acetone gave 0.30 g., m.p. 135–136.5°.

$\Delta^{5,7}$-Androstadiene-3β,17β-diol-3-acetate-17-benzoate (XV). *A.* Δ^5-Androstene-3β,17β-diol-3-acetate-17-benzoate (4.39 g., 0.0101 M) in 65 ml. of carbon tetrachloride and 25 ml. of petroleum ether was brominated in the usual manner with 2.14 g. (0.012 M) of NBS. The dehydrobromination was performed with 1.75 ml. of *s*-collidine in 100 ml. of xylene. The product was worked up in xylene-ether. The extract was washed with dilute acetic acid, sodium bicarbonate solution and water, dried with magnesium sulfate, treated with Norit and filtered through Celite. Evaporation *in vacuo* gave a yellow residue which, when crystallized from methanol, gave yellow gummy crystals. Recrystallization from acetone-methanol gave 1.48 g., pale yellow crystals, m.p. 138–160°, λ_{max} 229–230, 270.5, 282, and 292–293 mμ; ε 14,400, 9,550, 10,000, and 5,750 resp. (79% pure, 26–27% yield). Several recrystallizations from acetone-methanol, and treatment with Norit gave 0.65 g. of white needles, m.p. 168.5–171°, λ_{max} 228.5, 270.5, 281, and 292.5 mμ; ε 14,850, 12,450, 12,700, and 7,000 resp., $[\alpha]_D^{29}$ −44.7°, $[\alpha]_{Hg}^{29}$ −60.7° (17.45 mg., α_D −0.39°, α_{Hg} −0.53°) α_{Hg}/α_D 1.36; $[M]_D$ −194.

Anal. Calc'd for $C_{28}H_{34}O_4$(434.55): C, 77.39; H, 7.89.
Found: C, 77.48; H, 8.14.

B. $\Delta^{5,7}$-Androstadiene-3β,17β-diol-17-benzoate (XIII) (48 mg.) in 1 ml. of pyridine was acetylated in the usual manner with 0.25 ml. of acetic anhydride. Recrystallization of the crude product from acetone-methanol gave 42.1 mg. of XV, m.p. 167.5–169.8°, λ_{max} 229, 271, 281, and 292.5 mμ; ε 14,850, 12,400, 12,800, and 6,800 resp.

Anal. Found: C, 77.17; H, 8.11.

$\Delta^{5,7}$-Androstadiene-3β,17β-diol-17-benzoate (XIII). Compound XV (0.5 g.) in 5 ml. of methanol and 5 ml. of methylene chloride was treated with 0.58 ml. of a 1.7 *N* methanolic potash solution. The mixture was allowed to stand at +3 to +5° overnight. During this time the product crystallized. Dilute acetic acid was added and the long, silky needles were

washed with water. Additional product was obtained by working up the mother liquor in methylene chloride. Evaporation of the methylene chloride, and treatment of the residue with methanol gave a second crop of crystals. Both fractions were combined and recrystallized from methanol and acetone, wt. 0.21 g., m.p. 201–204.5° d., λ_{max} 229, 271, 281, and 292–293 mμ; ϵ 12,300, 10,800, 11,150, and 5,600. $[\alpha]_D^{27}$ −91.7°, $[\alpha]_{Hg}^{27}$ −123°, (10.25 mg., α_D −0.47°, α_{Hg} −0.63°) α_{Hg}/α_D 1.34, $[M]_D$ −359.

An additional 0.1 g. of XIII was obtained from the mother liquors, m.p. 197–202° d.

Anal. Calc'd for $C_{26}H_{32}O_3$ (392.52): C, 79.55; H, 8.22.

Found: C, 79.19; H, 8.44.

$\Delta^{5,7}$-*Androstadiene-3β,17β-diol* (XII). *A.* $\Delta^{5,7}$-diacetate (XIV) (4.7 g.) in 30 ml. of alcohol was treated with 55 ml. of 5% alcoholic potash, and the mixture was refluxed for ½ hour, cooled in an ice-alcohol bath, and filtered. This gave 3.8 g. (?) of crude diol (XII). The product was recrystallized from alcohol, wt. 2.6 g., m.p. 223–226°. An additional 0.8 g. was obtained from the mother liquors, m.p. 220–224°. λ_{max} 271, 281.5, and 293 mμ; ϵ 11,200, 11,750, and 6,800 resp. $[\alpha]_D^{30}$ −204.9°, $[\alpha]_{Hg}^{30}$ −266.0° (28.8 mg., pyridine, α_D −2.95°, α_{Hg} −3.83°) α_{Hg}/α_D 1.30 (pyridine); $[M]_D$ −590.

Anal. Calc'd for $C_{19}H_{28}O_2$ (288.41): C, 79.12; H, 9.78.

Found: C, 79.11; H, 10.29.

B. Compound XIII (120 mg.) was refluxed for ½ hour with 11 ml. of 2.5% methanolic potash. Addition of ice-water gave crystals which were collected. Several recrystallizations from dilute alcohol gave XII, m.p. 224–225.5°, λ_{max} 271, 281, and 293 mμ; ϵ 10,500, 11,000, and 6,150 resp. $[\alpha]_D^{27}$ −209.4°, $[\alpha]_{Hg}^{27}$ −271.7° (10.6 mg., pyridine, α_D −1.11°, α_{Hg} −1.44°) α_{Hg}/α_D 1.30 (pyridine); $[M]_D$ −603.

$\Delta^{5,7}$-*Androstadiene-3β,17β-diol dibenzoate* (XVI). $\Delta^{5,7}$-diol (XII) (0.30 g.) was benzoylated in the usual manner. Recrystallization from benzene-acetone, and acetone gave 0.29 g. of XVI, m.p. 230.5–232.5°, $\lambda_{max}^{1\% CA}$ 229, 271, 281, and 293 mμ; ϵ 25,900, 14,000, 14,200, and 7,250 resp. $[\alpha]_D^{30}$ −32.5°, $[\alpha]_{Hg}^{30}$ −49.3° (19.05 mg., α_D −0.31°, α_{Hg} −0.47°) α_{Hg}/α_D 1.52; $[M]_D$ −161.

Anal. Calc'd for $C_{33}H_{36}O_4$ (496.62): C, 79.81; H, 7.31.

Found: C, 79.94; H, 7.36.

$\Delta^{5,7}$-*Pregnadiene-3β-ol-20-one acetate* (XVIII). *A.* Δ^5-Pregnene-3β-ol-20-one acetate (X) (1.08 g., 0.003 M) in 15 ml. of carbon tetrachloride and 25 ml. of petroleum ether was brominated in the usual manner with 0.64 g. (0.0036 M) of NBS. Dehydrobromination with 1 ml. of *s*-collidine in 25 ml. of xylene afforded crude XVIII. Treatment with methanol gave 0.19 g., m.p. 155–158°, λ_{max} 272, 282, and 294 mμ; ϵ 10,400, 11,050, and 6,700 resp. Addition of water to the mother liquor gave 0.10 g., m.p. 139–148°, λ_{max} 272, 282, and 293–294 mμ; ϵ 8,100, 8,570, and 5,230 resp. The main fraction of crystals was recrystallized from dilute methanol, wt. 0.13 g., m.p. 161–164°, λ_{max} 272, 282, and 294 mμ; ϵ 10,700, 11,300, and 6,790 resp., $[\alpha]_D^{31}$ −33.5°, $[\alpha]_{Hg}^{31}$ −41.9° (23.85 mg., α_D −0.40°, α_{Hg} −0.50°) α_{Hg}/α_D 1.25; $[M]_D$ −119.

Anal. Calc'd for $C_{23}H_{32}O_3$ (356.49): C, 77.49; H, 9.05.

Found: C, 77.61; H, 9.26.

B. In a run with 7.16 g. (0.02 M) of X, 4.28 g. (0.024 M) of NBS, 50 ml. of carbon tetrachloride, and 50 ml. of petroleum ether, 3.2 ml. of *s*-collidine, and 75 ml. xylene there was obtained 1.47 g., m.p. 165–168°; 20–21% yield.

C. The acetate (XVIII) collected from a number of runs was recrystallized several times from acetone-methanol, m.p. 166–168°, λ_{max} 271.5, 282, and 293.5 mμ; ϵ 11,580, 12,200, and 7,100 resp. $[\alpha]_D^{28}$ −26.7°, $[\alpha]_{Hg}^{23}$ −35.1° (50.1 mg., α_D −0.67°, α_{Hg} −0.88°) α_{Hg}/α_D 1.31; $[M]_D$ −95.

D. A mixture of 90 mg. of $\Delta^{5,7}$-pregnadiene-3β-ol-20-one (XVII) in 10 ml. of acetic anhydride was refluxed for 15 minutes. The excess acetic anhydride was removed *in vacuo*, the residue was dissolved in acetone, and the solution was concentrated with simultaneous addition of petroleum ether. This afforded 42 mg. of XVIII, m.p. 165–167°. Recrystallization from acetone-petroleum ether gave 35.5 mg., m.p. 165.5–167.5°, λ_{max} 271.5, 282, and 293.5 mμ; ϵ 11,350, 11,950, and 7,100 resp. $[\alpha]_D^{29}$ −32.8°, $[\alpha]_{Hg}^{29}$ −39.0° (9.75 mg., α_D −0.16°, α_{Hg} −0.19°) α_{Hg}/α_D 1.19; $[M]_D$ −117.

Anal. Found: C, 77.82; H, 9.28.

In another run, 1.0 g. of XVII gave 0.67 g., m.p. 167–169°, λ_{max} 271–271.5, 282, and 294 mμ; ϵ 10,900, 11,600, and 6,750 resp.

Acetylation of XVII with acetic anhydride and boron trifluoride etherate gave XVIII, m.p. 167–169°.

$\Delta^{5,7}$-Pregnadiene-3β-ol-20-one (XVII). Compound XVIII (0.31 g.) in 10 ml. of methanol was treated with 0.25 g. of potassium carbonate in 1 ml. of water, the mixture was refluxed for 2 hours. Water was added, the mixture was cooled, and XVII was collected, wt. 0.27 g., m.p. 225–229°. Recrystallization from methanol and dilute methanol gave 0.20 g., m.p. 228–230°, $\lambda_{max}^{1\%CA}$ 272, 282.5, and 294 mμ; ϵ 11,500, 12,100, and 7,400 resp. $[\alpha]_D^{29}$ −79.3°, $[\alpha]_{Hg}^{29}$ −101.7° (17.9 mg., α_D −0.71°, α_{Hg} −0.91°) α_{Hg}/α_D 1.28; $[M]_D$ −249.

Anal. Calc'd for $C_{21}H_{30}O_2$ (314.45): C, 80.21; H, 9.62.

Found: C, 80.19; H, 9.94.

XVII was also obtained by refluxing for 2 hours a mixture of 5.3 g. of the acetate (XVIII), 2.0 g. of potassium carbonate, 1.5 g. of potassium bicarbonate, and 75 ml. of methanol; m.p. 227–229°.

$\Delta^{5,7}$-Pregnadiene-3β-ol-20-one benzoate (XIX). $\Delta^{5,7}$-Pregnadiene-3β-ol-20-one (70 mg.) was benzoylated in the usual manner. Recrystallization from dilute acetic acid, and from acetone-methanol gave pure XIX, m.p. 227–229°, $\lambda_{max}^{1\%CA}$ 229, 272, 282, and 293.5 mμ; ϵ 13,000, 12,350, 12,700, and 7,225 resp. $[\alpha]_D^{25}$ −6.9°, $[\alpha]_{Hg}^{25}$ −9.5° (37.8 mg., α_D −0.13°, α_{Hg} −0.18°) α_{Hg}/α_D 1.38; $[M]_D$ −29.

Anal. Calc'd for $C_{23}H_{34}O_3$ (418.55): C, 80.34; H, 8.19.

Found: C, 80.33; H, 8.44.

$\Delta^{5,7}$-Pregnadiene-3β,21-diol-20-one diacetate (XXI). *A.* Δ^5-Pregnene-3β,21-diol-20-one diacetate (XI) (2.07 g., 0.005 M) in 50 ml. of carbon tetrachloride and 25 ml. of petroleum ether was brominated in the usual manner with 1.07 g. (0.006 M) of NBS. The dehydrobromination was carried out with 2 ml. of *s*-collidine in 50 ml. of xylene. The product was worked up in xylene which on evaporation afforded a viscous oil. It was dissolved in methanol and the resulting solution, when worked, gave crystals, wt. 0.27 g., m.p. 119–130°. Two recrystallizations from methanol gave 60 mg., m.p. 141–142.5°, λ_{max} 272, 282, and 294 mμ; ϵ 10,500, 11,300, and 6,740 resp. One further recrystallization from methanol gave 43 mg., m.p. 141–142°, λ_{max} 272, 282, and 294 mμ; ϵ 10,400, 11,100, and 6,450 resp., $[\alpha]_D^{28}$ −8.5° (18.8 mg., α_D −0.08°); $[M]_D$ −35.

Anal. Calc'd for $C_{25}H_{34}O_5$ (414.52): C, 72.43; H, 8.27.

Found: C, 72.49; H, 8.58.

B. Two runs each of 8.32 g. of XI, 4.28 g. of NBS, 125 ml. of carbon tetrachloride, and 25 ml. of petroleum ether were combined after the bromination and the dehydrobromination was carried out with 10 ml. of *s*-collidine in 100 ml. of xylene. The product was worked up in xylene-benzene and gave an oil which was crystallized from methanol. Recrystallization from methanol gave 2.49 g. of XXI, m.p. 142–146°, λ_{max} 272, 282, and 294 mμ; ϵ 10,300, 10,950, and 6,450 resp., 15% yield.

C. A solution of 20 mg. of $\Delta^{5,7}$-pregnadiene-3β,21-diol-20-one (XX) in 1 ml. of pyridine was acetylated at room temperature with 0.2 ml. of acetic anhydride. Recrystallization from methanol gave pure XXI, m.p. 142–143°.

$\Delta^{5,7}$-Pregnadiene-3β,21-diol-20-one (XX). *A.* The $\Delta^{5,7}$-diacetate (XXI) (0.5 g.) in 65 ml. of methanol was treated with 300 mg. of potassium carbonate and 500 mg. of potassium bicarbonate in 10 ml. of water. This gave a precipitate which dissolved on the addition of 20 ml. of acetone. The cleared solution was allowed to stand at room temperature overnight, neutralized with acetic acid, and evaporated *in vacuo*. Water was added, and the product was worked up in ether. The extract was washed with sodium bicarbonate solution and water, dried, and evaporated *in vacuo*. The crystalline residue was recrystallized from methanol, wt. 150 mg., m.p. 197–207°. Further recrystallization from methanol gave pure XX, m.p. 205–207°, λ_{max} 272, 282, and 294 mμ; ϵ 11,400, 11,950, and 7,180 resp., $[\alpha]_D^{27.5}$ −80.0° (16.5 mg., α_D −0.66°); $[M]_D$ −264.

Anal. Calc'd for $C_{21}H_{30}O_3$ (330.45): C, 76.32; H, 9.15.

Found: C, 75.99; H, 9.20.

B. Compound XXI (0.5 g.) in 20 ml. of methanol was treated with 0.4 g. of potassium carbonate in 2 ml. of water, and the mixture was refluxed for 2 hours. Addition of water with cooling gave 0.35 g., m.p. 180–193° with slight decomposition. Recrystallization from methanol, ethyl acetate, and methanol gave pure XX, m.p. 207–209.5°, λ_{max} 272, 282, and 294 mμ; ϵ 11,950, 12,600, and 7,600 resp. $[\alpha]_D^{29}$ $-82.1°$ (19 mg., α_D $-0.78°$); $[M]_D$ -270.

$\Delta^{5,7}$-Pregnadiene-3β,21-diol-20-one dibenzoate (XXII). A solution of 40 mg. of $\Delta^{5,7}$-diol (XIX) in 1 ml. of pyridine was benzoylated in the usual manner with 0.2 ml. of benzoyl chloride. Recrystallization from methanol gave pure XXII, m.p. 175–178° (inserted in m.p. bath at 168°), λ_{max} 229, 272, 282, and 294 mμ; ϵ 31,800, 13,400, 13,850 and 7,460 resp.

Anal. Calc'd for $C_{35}H_{38}O_5$ (538.65): C, 78.04; H, 7.11.
Found: C, 78.04; H, 7.79.

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SUMMARY

$\Delta^{5,7}$-Androstadiene-3β-ol-17-one, $\Delta^{5,7}$-androstadiene-3β,17β-diol, $\Delta^{5,7}$-pregnadiene-3β-ol-20-one, and $\Delta^{5,7}$-pregnadiene-3β, 21-diol-20-one have been prepared and characterized.

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