geneous on paper chromatography in solvents A and D with R_{Ad} 1.51 and 1.60, respectively.

Anal. Calcd. for $C_{16}H_{19}N_5O_2$: C, 61.3; H, 6.11; N, 22.4. Found: C, 61.9; H, 6.48; N, 22.2.

2,2'-[p-(2,4-Diacetamido-6-ethyl-5-pyrimidinyl)phenylimino]diethanol (XXIII). To a cold (0°) solution of 0.45 g. (1.44 mmoles) of the *p*-aminophenylpyrimidine (XXIV) in 2.5 ml. of 50% aqueous acetic acid was added 0.50 g. (11.0 mmoles) of ethylene oxide and the solution was kept at 0° for 15 hr., then was evaporated to dryness *in vacuo* at 40°. The residue was dissolved in 10 ml. of chloroform, the chloroform was washed with 5 ml. of saturated aqueous sodium bicarbonate solution and the bicarbonate wash back-extracted with 5 ml. of chloroform. The chloroform extracts were combined, dried over magnesium sulfate, filtered, and the filtrate evaporated *in vacuo* to leave 0.42 g. (73%) of a white glas ; $\lambda_{max(\mu)}^{film}$ 3.0–3.1 (OH, NH), 5.90 (amide C=O), 6.30 (pyrimidine ring, amide NH), 9.55 (C—OH), 12.25 (*p*-disubstituted benzene). The crude product was hydrolyzed to diaminopyrimidine (XX) as described above.

2,4-Diamino-5-{p-[bis(2-chloroethyl)amino]phenyl}-6-ethylpyrimidine dihydrochloride (XXI). A stirred suspension of 0.500 g. (1.27 mmoles) of the bis(2-hydroxyethyl)amine dihydrochloride (XX) in 10 ml. of thionyl chloride was heated at 65–70° for 35 min., then was evaporated *in vacuo* (bath temperature 20–25°), leaving a dark solid residue. The residue was triturated with 4 ml. of cold absolute ethanol, yielding 0.450 g. of undissolved solid whose infrared spectrum and paper chromatogram showed it to contain a small amount of starting hydroxy compound (XX). The solid was largely dissolved in 20 ml. of absolute ethanol at room temperature by vigorous stirring and the solution was freed of 0.018 g. of XX by filtration. Ethanolic hydrogen chloride (10 ml. of a solution saturated at 10°) was added to the filtrate, which was then evaporated *in vacuo* (bath at 25°), affording 0.35 g. (70%) of tan solid which decomposed in the range 260–280° but did not melt. Its infrared spectrum was identical with that of the analytical sample. The analytical sample, obtained by washing the product with cold ethanolic hydrogen chloride and drying over phosphorus pentoxide at room temperature, had $\lambda_{max(\mu)}^{Nujol}$ 3.02, 3.10 and 3.18 (NH), 4.21–4.60 (NH^+), 6.10 and 6.13 (pyrimidine ring), 11.31 (*p*-disubstituted benzene); there was no C—OH absorption in the 9.5–9.8 μ region. On paper chromatography in solvent E, the product moved as a single spot with R_{Ad} 2.90, easily distinguished from XX (R_{Ad} 1.03).

Anal. Calcd. for $C_{16}H_{21}Cl_2N_5 \cdot 2HCl$: C, 45.0; H, 5.43; Cl, 33.2; N, 16.3. Found: C, 45.0; H, 5.07; Cl, 33.2; N, 16.3.

Compound XXI lost hydrogen chloride on heating and a sample dried at 100° showed the following analysis:

Found: C, 45.9; H, 5.89; Cl, 31.4; N, 16.3.

Acknowledgment. The authors are indebted to Dr. Peter Lim and his group for infrared interpretations and paper chromatography and to Mr. O. P. Crews and his group for the large-scale preparation of intermediates.

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[CONTRIBUTION FROM THE ORGANIC CHEMISTRY DEPARTMENT, RESEARCH DIVISION, ABBOTT LABORATORIES]

Lactones Derived from 17β-Hydroxyandrostan-16β-ylacetic Acids[1]

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The condensation of 3β-hydroxy-17-oxo-5-androstene with glyoxylic acid gave rise to 3β-hydroxy-17-oxo-5-androsten-16-ylidenacetic acid. The latter served as the intermediate to prepare 3β,17β-dihydroxy-5-androsten-16β-ylacetic acid lactone and its saturated analog. These lactones were converted in turn to 17β-hydroxy-3-oxo-4-androsten-16β-ylacetic acid lactone, 17β-hydroxy-3-oxo-5α-androstan-16β-ylacetic acid lactone, and 17β-hydroxy-3-oxo-1,4-androstadien-16β-ylacetic acid lactone.

As part of a study of new ring D substituted steroids, it became desirable to make some of the lactones having a two-carbon side chain at position 16. This series was approached by condensation of the available 3β-hydroxy-17-oxo-5-androstene (I) with glyoxylic acid to obtain the desired 3β-hydroxy-17-oxo-5-androsten-16-ylidenacetic acid (IIa) in good yield. The recently described method of Newman, Sagar, and Cochrane[2] for this type of glyoxylic acid condensation was used. The new compound IIa was further characterized by preparing the corresponding acetate IIb, the methyl ester IIc, and the acetate methyl ester IId.

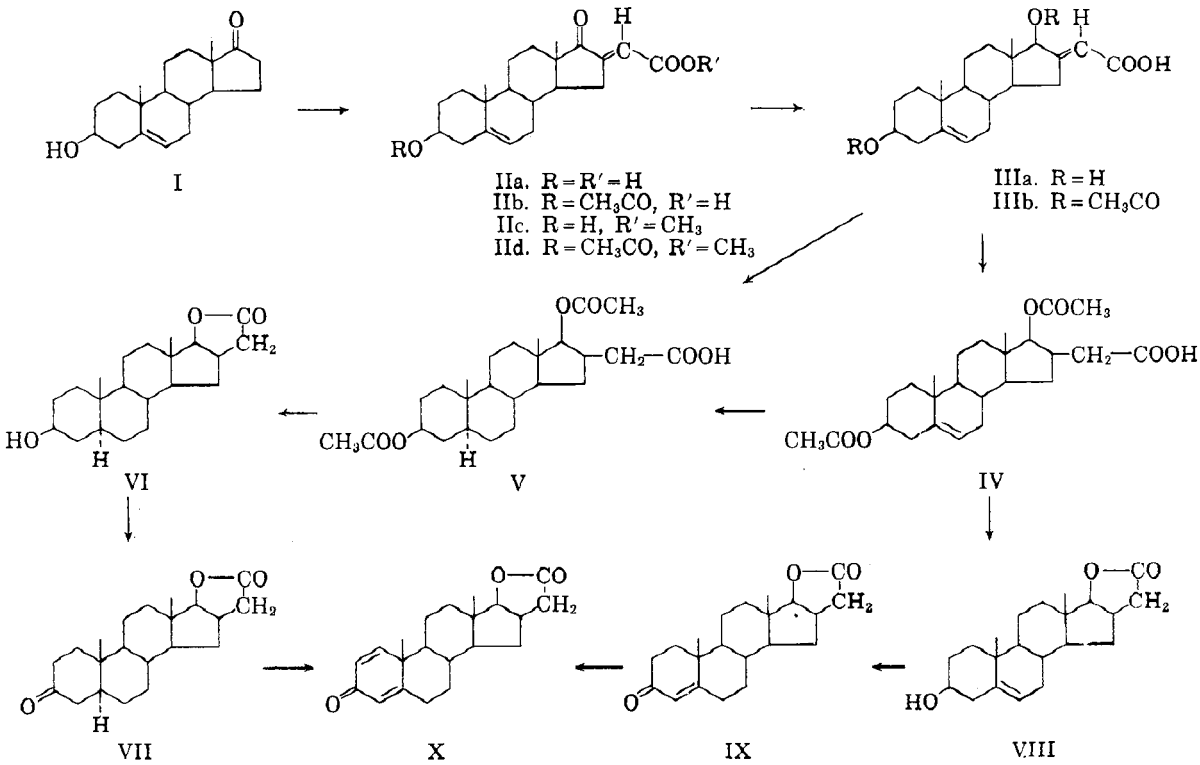
The reduction of IIa with sodium borohydride afforded 3β,17β-dihydroxy-5-androsten-16-ylidenacetic acid (IIIa), and the latter (IIIa) was converted into the diacetate IIIb. In accordance with established principles, the newly formed hydroxy group on C-17 of IIIa was assigned the β-position. The side chain at C-16 of II lay in the general plane of the molecule and for that reason was not expected to interfere with the attack of the reducing agent from the less hindered α-side.[3]

Partial hydrogenation of IIIb led to the isolation of 3β,17β-diacetoxy-5-androsten-16β-ylacetic acid (IV), while complete hydrogenation gave 3β,17β-diacetoxy-5α-androstan-16β-ylacetic acid (V). The reduction of IV gave V as expected. After the treatment of IV or V with potassium hydroxide and subsequently hydrochloric acid, the 3β,17β-dihydroxy-5-androsten-16β-ylacetic acid lactone (VIII) and the 3β,17β-dihydroxy-5α-androstan-16β-ylacetic acid lactone (VI), respectively, were obtained.

(1) This paper was presented at the 138th National Meeting of the American Chemical Society in New York, N. Y., September 11–16, 1960; Abstracts of Papers 14-0.

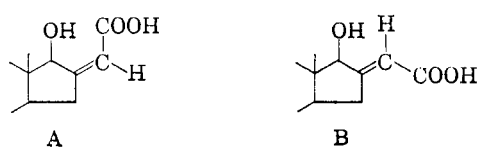
(2) M. S. Newman, W. C. Sagar, and C. C. Cochrane, *J. Org. Chem.*, 23, 1832 (1958).

(3) L. F. Fieser, *Experientia*, 6, 312 (1950); for a similar example see F. A. Kincl and M. García, *Chem. Ber.*, 92, 595 (1959); F. Neumann, O. Mancera, G. Rosenkranz, and F. Sondheimer, *J. Am. Chem. Soc.*, 77, 5676 (1955).



A study of molecular models demonstrated that the α-side of IIIb was less hindered sterically than the β-side, and thus the reduction of IIIb would lead predominantly to the β-oriented side chain at C-16 in IV and V.[3] This assignment was confirmed when the ease of lactone formations (IV→VIII, and V→VI) was observed. These facile lactone formations could only be expected if both substituents on C-16 and C-17 were on the same side of the molecule.

Lactone formation from IIIa might be expected if the carboxylic acid group were *cis* with respect to C-17 as shown by partial structure A but not if it were *trans* as indicated by B. It was of interest to note that IIIa was isolated in the form of the free acid. The fact that no lactone was formed allows the tentative assignment of the *trans* configuration to IIIa. This assignment of *trans* configuration also applies to the related structures II and III.



When VI was oxidized in a two phase system,[4] the desired 17β-hydroxy-3-oxo-5α-androstan-16β-ylacetic acid lactone (VII) was obtained. The oxidation of VIII under acidic conditions[5] led to the isolation of 17β-hydroxy-3-oxo-4-androsten-16β-ylacetic acid lactone (IX). From the latter (IX) 17β-hydroxy-3-oxo-1,4-androstadien-16β-ylacetic acid lactone (X) was prepared by selenium dioxide dehydrogenation.[6] The lactone X was also obtained from 17β-hydroxy-3-oxo-5α-androstan-16β-ylacetic acid lactone (VII) by bromination followed by elimination of the elements of hydrogen bromide according to the procedure of Joly, Warnant, Nominé, and Bertin.[7]

(4) W. F. Bruce, *Org. Syntheses*, **Coll. Vol. II**, 139 (1943).

(5) P. L. Julian, W. Cole, A. Magnani, and E. W. Meyer, *J. Am. Chem. Soc.*, **67**, 1728 (1945).

EXPERIMENTAL[8-12]

3-β-Hydroxy-17-oxo-5-androsten-16-ylidenacetic acid (IIa). The general procedure of Newman, Sagar, and Cochrane[2] was followed. To a cooled suspension of 17.12 g. of trisodium periodate (para), partly dissolved in 1.6 ml. of

(6) *Cf.*, J. S. Baran, *J. Am. Chem. Soc.*, **80**, 1687 (1958).

(7) R. Joly, J. Warnant, G. Nominé, and D. Bertin, *Bull. soc. chim. France*, 366 (1958). P. Wieland, K. Heusler, and A. Wettstein, *Helv. Chim. Acta*, **43**, 523 (1960).

(8) The melting points were determined on a Fisher-Johns melting point apparatus and are not further corrected. The optical rotations were determined in a 1 dm. tube in chloroform solution at 25° except where noted otherwise. The values have a limit of error of ±5°.

(9) We wish to thank Mr. Elmer Shelberg and his staff for microanalyses.

(10) The infrared spectra were recorded on a Perkin-Elmer Infrared Spectrophotometer Model 21 using 0.2*M* chloroform solutions or 0.02*M* potassium bromide pellets. We are indebted to Mr. William Washburn and his associates for the recording and interpretation of the infrared spectra.

(11) We wish to thank Mr. Frank Chadde for the recording of the ultraviolet spectra.

(12) In the catalytic reductions we had the assistance of Messrs. M. Freifelder and George Stone, to both of whom we express our thanks.

concd. sulfuric acid and 96 ml. of water, was added 12 g. of *d*-tartaric acid in 15 ml. of water. After 5 min. the ice bath was removed and the mixture was shaken mechanically for 25 min. at room temperature. 3β-Hydroxy-17-oxo-5-androstene (I) (23.04 g.), 12 g. of sodium hydroxide in 216 ml. of water, and 200 ml. of methanol were added in sequence. Stirring at room temperature was continued overnight. After heating the reaction mixture for 1 hr. at 80°, the solution was diluted with 700 ml. of ice and water, and the resulting slurry was extracted with ether. The ether solution was washed with 2*N* sodium hydroxide solution and water. The dried ether solution was evaporated to leave a residue of 2.14 g. of crude starting material.

The alkaline layer was acidified and the resulting precipitate was filtered and washed with water. The compound was recrystallized from methanol-water to give 21.82 g. (79%) of IIa, m.p. 239–241°. The substance was not changed by sublimation at 200° and 0.2 mm.

A sample was recrystallized for analysis, m.p. 241–242°; $[\alpha]_D$ −94° (*c*, 0.66); $\lambda_{max}^{CH_3OH}$ 239 mμ (ε 12,700); λ_{max}^{KBr} 2.95 μ, 3.6–3.9 μ, 5.85 μ, 6.1 μ, 12.4 μ.

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.23; H, 8.19; O, 18.58. Found: C, 73.29; H, 8.25; O, 18.78.

3β-Acetoxy-17-oxo-5-androsten-16-ylidenacetic acid (IIb). A solution of 5 g. of the above keto acid IIa in 30 ml. of pyridine and 15 ml. of acetic anhydride was allowed to stand at room temperature overnight. Following the addition of 15 ml. of water to the reaction mixture, the latter was warmed on the steam bath for 1 hr. The cooled solution was poured upon a mixture of ice and dilute hydrochloric acid, and the resulting slurry was extracted with ether. The ether layer was washed with 10% hydrochloric acid and water and dried over anhydrous magnesium sulfate. After evaporation of the solvent, 5.3 g. of the crude acetate IIb was obtained. The product was recrystallized from methanol to yield 4.54 g. (81%) of IIb, m.p. 265–267°.

A sample was further purified for analysis, m.p. 271–273°; $[\alpha]_D$ −105° (*c*, 1.22); $\lambda_{max}^{CH_3OH}$ 239 mμ (ε 11,970); λ_{max}^{KBr} 3.2–3.9 μ, 5.75–5.85 μ, 5.95 μ, 8.1 μ.

Anal. Calcd. for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82; O, 20.70. Found: C, 71.51; H, 7.90; O, 20.56.

3β-Hydroxy-17-oxo-5-androsten-16-ylidenacetic acid methyl ester (IIc). The general procedure of Lorette and Brown[13] was followed. A mixture of 7.5 g. of the keto acid IIa in 75 ml. of methanol, 2 ml. of concd. hydrochloric acid and 7.5 ml. of 2,2-dimethoxypropane was warmed to 50°. Three 7.5-ml. portions of 2,2-dimethoxypropane were added at intervals of 1 hr. The reaction mixture was kept at 50° overnight. The solvent was removed under reduced pressure and the resulting solid was recrystallized from acetone-petroleum ether (b.p. 90–100°) to give 6.2 g. (79%) of IIc, m.p. 140–141°.

The analytical sample had a melting point of 141–142°; $[\alpha]_D$ −87° (*c*, 1.30).

Anal. Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.86; H, 8.65.

3β-Acetoxy-17-oxo-5-androsten-16-ylidenacetic acid methyl ester (IId). The above methyl ester IIc (3.20 g.) was acetylated with pyridine–acetic anhydride in the usual manner. The resulting compound was recrystallized from methanol-water to give 2.905 g. (81%) of IId, m.p. 147–148°.

The analytical sample had a melting point of 148–149°; $[\alpha]_D$ −101° (*c*, 1.17).

Anal. Calcd. for $C_{24}H_{32}O_5$: C, 71.97; H, 8.05. Found: C, 71.97; H, 8.05.

3β,17β-Dihydroxy-5-androsten-16-ylidenacetic acid (IIIa). To the cold solution of 25.5 g. of 3β-hydroxy-17-oxo-5-androsten-16-ylidenacetic acid (IIa) in 1200 ml. of methanol, 10.2 g. of sodium borohydride in 35 ml. of water was added from a dropping funnel. The latter was rinsed once with 10 ml. of water. The reaction mixture was kept for 30 min. in an ice bath, was allowed to reach room temperature during a period of 1 hr. and was then refluxed for 30 min. The addition of 240 ml. of a 25% sodium hydroxide solution was followed by the evaporation of most of the methanol under reduced pressure. The resulting slurry was acidified with dilute hydrochloric acid; the residue was filtered and washed with several small portions of water. The crude product was dried at 75° under vacuum and recrystallized from methanol. A first crop of 19.201 g. of IIIa, m.p. 310–312° dec., was obtained. Upon concentration of the mother liquors, a second crop of 2.737 g., m.p. 309–311° dec., was isolated. The yield was 85%.

Recrystallization gave an analytical sample, m.p. 311–312° (capillary, dec.); $[\alpha]_D$ −157° (*c*, 0.38 in dioxane); $\lambda_{max}^{CH_3OH}$ 220 mμ (ε 12,500);[14] λ_{max}^{KBr} 2.95 μ, 3.6–4.0 μ, 5.88 μ, 6.06 μ, 12.35 μ.

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.76; H, 8.87.

3β,17β-Diacetoxy-5-androsten-16-ylidenacetic acid (IIIb). The solution of 27.92 g. of 3β,17β-dihydroxy-5-androsten-16-ylidenacetic acid (IIIa) in 180 ml. of anhydrous pyridine and 90 ml. of acetic anhydride was allowed to stand at room temperature overnight. After the careful addition of 90 ml. of water to the reaction mixture, it was warmed on the steam bath for 2 hr. The cooled solution was poured into 1600 ml. of ice cold water; the residue was filtered and washed with several portions of water. The compound was recrystallized from methanol-water to give a first crop of 32.98 g. (95%) of IIIb, m.p. 209–211°. A second crop of 0.973 g., m.p. 175–180°, was not satisfactory for further use.

An analytical sample melted at 210–212°; $[\alpha]_D$ −136° (*c*, 1.12); λ_{max}^{KBr} 3.1–4.0 μ, 5.70 μ, 5.80 μ, 6.04 μ, 8.15 μ, 12.3 μ.

Anal. Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96; O, 22.30. Found: C, 70.02; H, 8.12; O, 22.04.

3β,17β-Diacetoxy-5-androsten-16β-ylacetic acid (IV). The solution of 8.62 g. of 3β,17β-diacetoxy-5-androsten-16-ylidenacetic acid (IIIb) in 150 ml. of glacial acetic acid was reduced over a 2% ratio of platinum oxide. The reduction was stopped after 110–120% of the calculated amount of hydrogen was absorbed. The catalyst was separated by filtration and the solvent evaporated from the resulting clear solution. The crystalline residue was recrystallized twice from acetone-petroleum ether to yield 4.186 g. (48%) of IV, m.p. 251–253°. Upon concentration of the mother liquors, an additional 1.464 g. of crystalline material, m.p. 220–226°, was obtained.

The analytical sample had a melting point of 252–253°; $[\alpha]_D$ −50° (*c*, 0.93). The ultraviolet spectrum did not show a maximum at 220 mμ. λ_{max}^{KBr} 3.1–3.8 μ, 5.77 μ, 5.88 μ, 8.0–8.1 μ, 12.3 μ, 12.5 μ.

Anal. Calcd. for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39; O, 22.19. Found: C, 69.44; H, 8.57; O, 22.18.

3β,17β-Diacetoxy-5α-androstan-16β-ylacetic acid (V). A solution of 4.31 g. of 3β,17β-diacetoxy-5-androsten-16-ylidenacetic acid (IIIb) in 150 ml. of glacial acetic acid was hydrogenated over a 10% ratio of platinum oxide. The catalyst was separated by filtration and the solvent removed from the filtrate under reduced pressure. The crystalline residue was recrystallized twice from methanol-water to give 2.85 g. (65%) of V, m.p. 242–244°. After concentration of the mother liquors, 1.158 g. of material melting at 165–179° was obtained.

Purification for analysis gave a sample with a melting point of 243–244°; $[\alpha]_D$ −1° (*c*, 1.24); λ_{max}^{KBr} 3.1–3.8 μ, 5.75 μ, 5.85 μ, 8.0–8.1 μ.

Anal. Calcd. for $C_{25}H_{38}O_6$: C, 69.09; H, 8.82. Found: C, 69.38; H, 8.93.

The above compound V was obtained in 80% yield after the complete reduction of IV. Further reduction of the second crops from the preparation of IV yielded the saturated product V in 40–60% yield.

(13) N. B. Lorette and J. H. Brown, Jr., *J. Org. Chem.*, 24, 261 (1959).

(14) *Cf.*, A. T. Nielsen, *J. Org. Chem.*, **22**, 1539 (1957).

3β,17β-Dihydroxy-5α-androstan-16β-ylacetic acid lactone (VI). A solution of 2.76 g. of 3β,17β-diacetoxy-5α-androstan-16β-ylacetic acid (V) and 3.19 g. of potassium hydroxide pellets in 120 ml. of methanol and 12 ml. of water was heated under reflux on the steam bath for 2 hr. The solution was diluted with 400 ml. of water and then concentrated under vacuum to approximately 180 ml. After the addition of 440 ml. of water, the warm slurry was acidified with 300 ml. of 10% hydrochloric acid. The suspension was warmed on the steam bath for 15 min. The solution was cooled and the solid was separated by filtration, washed with several small amounts of water, and dried overnight at 75° under vacuum. The crude product was recrystallized from acetone to give a first crop of 1.565 g. (74%) of VI, m.p. 233–235°. A second crop of 0.180 g., m.p. 229–231°, was obtained after further concentration of the mother liquors.

The analytical sample had a melting point of 236–237°; $[\alpha]_D$ +22° (*c*, 1.23); $\lambda_{max}^{CHCl_3}$ 2.76 μ, 2.89 μ, 5.67 μ, 8.53 μ.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.71; O, 14.44. Found: C, 75.98; H, 9.68; O, 14.55.

17β-Hydroxy-3-oxo-5α-androstan-16β-ylacetic acid lactone (VII). To the cooled solution of 4.62 g. of sodium dichromate, 6.3 ml. of concd. sulfuric acid and 3.4 ml. of acetic acid in 20 ml. of water was added dropwise with vigorous stirring the warm solution of 2.90 g. of 3β,17β-dihydroxy-5α-androstan-16β-ylacetic acid lactone (VI) in 155 ml. of benzene according to the general procedure of Bruce.[4] The mixture was stirred at room temperature for 20 hr. The aqueous phase was separated and extracted twice with benzene. The organic solution was washed with water, dried, and the solvent removed to leave 2.73 g. of a colorless crystalline residue. This was recrystallized from acetone to give 2.091 g. (72%) of VII, m.p. 222–224°. From the mother liquors a second crop of 0.363 g., m.p. 217–221°, was isolated.

An analytical sample had a melting point of 223–225°; $[\alpha]_D$ +48° (*c*, 1.05); $\lambda_{max}^{CHCl_3}$ 5.66 μ, 5.85 μ, 8.53 μ.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.33; H, 9.15. Found: C, 76.36; H, 9.38.

3β,17β-Dihydroxy-5-androsten-16β-ylacetic acid lactone (VIII). A solution of 3.00 g. of 3β,17β-diacetoxy-5-androsten-16β-ylacetic acid (IV) and 3.75 g. of potassium hydroxide pellets in 130 ml. of methanol and 13 ml. of water was refluxed on the steam bath for 2 hr. The reaction mixture was diluted with 350 ml. of water and concentrated to approximately 180 ml. The resulting slurry was diluted with 500 ml. of water, and 340 ml. of 10% hydrochloric acid was added. The precipitate was filtered, washed with several small amounts of water, and dried at 75° under vacuum overnight. The material was then recrystallized from acetone to give a first crop of 1.888 g. (82%) of VIII, m.p. 236–239°. A second crop of 0.312 g., m.p. 226–228°, was isolated from the mother liquors.

The analytical sample melted at 237–239°; $[\alpha]_D$ −38° (*c*, 1.07); $\lambda_{max}^{CHCl_3}$ 2.76 μ, 2.87 μ, 5.66 μ, 8.53 μ, 12.37 μ.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.33; H, 9.15. Found: C, 76.44; H, 9.22.

17β-Hydroxy-3-oxo-4-androsten-16β-ylacetic acid lactone (IX). The solution of 1.80 g. of 3β,17β-dihydroxy-5-androsten-16β-ylacetic acid lactone (VIII) in 80 ml. of glacial acetic acid was treated successively with 0.80 g. of bromine in 8 ml. of acetic acid, 0.73 g. of chromic anhydride in 1.5 ml. of water and 11 ml. of acetic acid for 2 hr. Chromous chloride solution (70 ml., 1*N*) was added and the solution allowed to stand under nitrogen for 2 hr.[5] The reaction mixture was diluted with 700 ml. of distilled water; the precipitate was separated by filtration and washed with several small portions of water. The product was dried at 55° under vacuum overnight and recrystallized from acetone to yield 1.15 g. (64%) of the desired lactone IX, m.p. 250–252°.

The analytical sample melted at 251–253° and showed $[\alpha]_D$ +113° (*c*, 1.34); $\lambda_{max}^{CH_3OH}$ 240 mμ (ε 16,200); $\lambda_{max}^{CHCl_3}$ 5.65 μ, 5.99 μ, 6.17 μ, 8.53 μ, 11.54 μ.

Anal. Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.76; H, 8.67.

17β-Hydroxy-3-oxo-1,4-androstadien-16β-ylacetic acid lactone (X). *(A) From 17β-hydroxy-3-oxo-4-androsten-16β-ylacetic acid lactone* (IX). The mixture of 2 g. of IX, 0.80 g. of freshly sublimed selenium dioxide and 0.4 ml. of glacial acetic acid in 40 ml. of *t*-butyl alcohol was refluxed with stirring for 5 hr.[6] After the addition of 0.25 g. more selenium dioxide, stirring and refluxing were continued for 18 hr. The reaction mixture was allowed to cool and the residue was removed by filtration. The solid was washed with a total of 30 ml. of *t*-butyl alcohol and discarded. The combined filtrates were evaporated to dryness under reduced pressure, and the residue (2.475 g.) was dissolved in 200 ml. of methylene chloride. The turbid solution was filtered, the filtrate was washed with 10% hydrochloric acid and water. The resulting yellow methylene chloride solution was dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the solution evaporated to leave a residue of 2.242 g. of crude material which was further purified by chromatography on 100 g. of silica gel. The ether-acetone (9:1) eluates gave, after evaporation of the solvent, a total of 1.018 g. of partly crystalline material. Two recrystallizations from acetone–petroleum ether produced 0.478 g. of yellow crystals, m.p. 231–233°. Upon further concentration of the mother liquors, a second crop of the same compound amounting to 0.315 g., m.p. 229–231°, was isolated. The yield amounts to 40%.

A small sample of the first crop was sublimed under high vacuum at 180–210° and then recrystallized three times from acetone-petroleum ether. This analytical sample had the following physical constants: m.p. 238–239°; $[\alpha]_D$ +29° (*c*, 1.28); $\lambda_{max}^{CH_3OH}$ 243 mμ (ε 16,000); $\lambda_{max}^{CHCl_3}$ 5.65 μ, 6.00 μ, 6.15 μ, 6.22 μ, 8.53 μ, 11.24 μ.

Anal. Calcd. for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.36; H, 7.91.

(B) From 17β-hydroxy-3-oxo-5α-androstan-16β-ylacetic acid lactone (VII). Two grams of VII was dissolved in 30 ml. of glacial acetic acid and treated with 3.04 g. of 30% hydrogen bromide in acetic acid and then with 2.092 g. of bromine in 8 ml. of acetic acid with stirring at about 15° for 5 min. Stirring of the reaction mixture at room temperature was continued for 15 min. After addition of 250 ml. of water, the precipitate was collected on a filter and washed with small amounts of water. The material was dissolved in benzene and the solution was washed with water. The benzene was evaporated under reduced pressure at about 40°. The crystalline residue of crude dibromide was dissolved in 25 ml. of *N,N*-dimethylformamide and added to a stirred suspension of 3.02 g. of lithium bromide and 3.02 g. of lithium carbonate in 45 ml. of *N,N*-dimethylformamide at 95°, under nitrogen, and the mixture was stirred overnight.[7] The cooled reaction mixture was diluted with 200 ml. of water and 50 ml. of 2*N* hydrochloric acid and then extracted with three 150-ml. portions of methylene chloride. The organic phase was washed neutral with water, dried, and concentrated to give 1.775 g. of crystalline residue, which was purified by chromatography on 90 g. of silica. From the ether-acetone (9:1) eluates a total of 1.236 g. of X was obtained. Recrystallization from acetone–petroleum ether gave 1.002 g., m.p. 237–239°. A second crop of 0.205 g., m.p. 235–237°, was obtained from the mother liquors to bring the yield to 61%. Further purification by sublimation and recrystallization gave a sample, m.p. 239–240°; $[\alpha]_D$ +24° (*c*, 1.03); $\lambda_{max}^{CH_3OH}$ 243 mμ (ε 16,000); $\lambda_{max}^{CHCl_3}$ 5.65 μ, 6.00 μ, 6.15 μ, 6.22 μ, 8.53 μ, 11.24 μ.

Anal. Calcd. for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.49; H, 8.09.

The products from preparation A and B are identical.

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