reaction mixtures still contained appreciable amounts of unchanged starting materials (R_f 0.12) but showed a fairly strong spot with R_f 0.42 due presumably to IX with a weak spot of R_f 0.82, attributed to X. After 5 hours, the intensities of the spots corresponding to IX and X had increased at the expense of the slowest-travelling spot. After 19 hours, only traces of the starting material and the cyclic phosphate IX remained, X being the major product of reaction. In these experiments some simple hydrolysis of the starting material also occurred as judged by the appearance of a weak spot corresponding to free D-ribose.

Synthetic[54] Ribofuranose 1-Phosphate.—After 19 hours this substance was largely unchanged, except for some simple hydrolysis to free ribose.

Hydrolysis of Ribose Phosphates.—In 0.1 *N* perchloric and 0.1 *N* hydrochloric acids, no difference in the rates of the hydrolysis of the synthetic and the enzymatic samples of ribofuranose 1-phosphate could be detected. However, in 0.01 *N* hydrochloric acid at 20° the synthetic ester was found to be slightly more stable (curves I and II, Fig. 1). Synthetic ribopyranose 1-phosphate (curve III) was much more stable than either of the above esters. In 0.1 *N* hydrochloric acid at 20° the extent of hydrolysis of this ester was as follows: 32.5% in 2 hours, 50% in 4 hours and 75% in 9 hours. Curve IV shows the relative stability of the product X of reaction (22 hours) of ribose α-1-phosphate (VIII) with D.C.C. Of the total amount of phosphate present in the reaction mixture, 10.8% had appeared as inorganic phosphate[20] and is to be ascribed to the hydrolysis of VIII prior to the formation of X.

The ribofuranose 1-phosphates and ribopyranose 1-phosphate were separately heated in 0.5 *N* sodium hydroxide at 80° for 1 hour in polyethylene tubes. In no case could any inorganic phosphate be detected[20] after this treatment. Paper chromatography, after neutralization of the solutions showed the presence of intact phosphate esters. These neutralized solutions were then treated briefly with acid and the expected free ribose and inorganic phosphate identified by paper chromatography.

(54) Synthetic ribopyranose 1-phosphate has been found to undergo the reaction sequence of the type (VIII → X). The dependence of the process of cyclization in pyranose 1-phosphates upon the conformations of the phosphate and the adjacent hydroxyl groups will be discussed in a forthcoming communication.

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF SYNTEX S. A.]

Steroids. LXXIII.[1a] The Direct Oppenauer Oxidation of Steroidal Formate Esters. A New Synthesis of 17α-Hydroxyprogesterone[1b]

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It is shown that steroidal Δ^5-3β-ol formates are oxidized directly by the Oppenauer method to the corresponding Δ^4-3-ketones. Δ^5-Pregnene-3β,17α-diol-20-one 3-formate (IVa) was prepared from 16α,17α-oxido-Δ^5-pregnen-3β-ol-20-one acetate (Ia) by hydrogen bromide addition, hydrogenation over a palladium–calcium carbonate catalyst, saponification and formylation, or more simply from free 16α,17α-oxido-Δ^5-pregnen-3β-ol-20-one (Ib) by hydrogen bromide addition, hydrogenation over a palladium–charcoal catalyst and formylation. Acetylation of IVa at C-17 gave Δ^5-pregnene-3β,17α-diol-20-one 3-formate 17-acetate (IVb), which on Oppenauer oxidation yielded 17α-acetoxyprogesterone (V), saponified to 17α-hydroxyprogesterone (VI). Another example of the formate protection procedure in the androstane series is described, which leads from dehydroisoandrosterone formate (VIIb) to testosterone acetate (IXa) and propionate (IXb).

In the course of an investigation aimed at finding new routes to certain of the adrenal hormones from readily available starting materials, we were faced with the problem of protecting 3β-hydroxy-Δ^5-steroids at C-3 in such a way that operations could be carried out on the side chain, while permitting the necessary Δ^4-3-one system to be formed subsequently in a simple fashion. It was found that this objective could be achieved readily through protection at C-3 by means of the formate esters.

Such Δ^5-3β-ol formates were shown to be stable toward a number of reagents used to modify the side chain, such as acetic anhydride and *p*-toluenesulfonic acid (for C-17 acetylation of 17α-hydroxypregnan-20-one derivatives), bromine, followed successively by sodium iodide and potassium acetate (for introduction of the 21-acetoxy group into 17α-hydroxypregnan-20-ones) and to sodium borohydride in non-alcoholic solvents (for reduction of 17-ketoandrostanes).[2] Moreover, once the necessary reactions have been carried out in the side chain, we found that the Δ^5-3β-ol formate grouping may then be oxidized by the Oppenauer method directly in one step to the required Δ^4-3-one. In the present paper a new and convenient synthesis of 17α-hydroxyprogesterone (VI) by use of the formate protection procedure is described, as well as another application in the androstane series. In the subsequent paper[3] the method is used for syntheses of Reichstein's substance S and related compounds.

The 3-formate (IVa) of Δ^5-pregnene-3β,17α-diol-20-one (IIIb) is a key intermediate both for the synthesis of 17α-hydroxyprogesterone and of substance S, but unfortunately the previously described syntheses of IIIb[4] are either involved or proceed in rather poor yield. Two syntheses of IVa were therefore worked out which employ 16α,17α-oxido-Δ^5-pregnen-3β-ol-20-one (Ib) (obtainable in high yield by alkaline hydrogen peroxide treatment[5] of $\Delta^{5,16}$-pregnadien-3β-ol-20-one acetate, the degradation product of diosgenin) as starting ma-

(1a) Paper LXXII, F. Neumann, O. Mancera, G. Rosenkranz and F. Sondheimer, THIS JOURNAL, **77**, 5676 (1955).

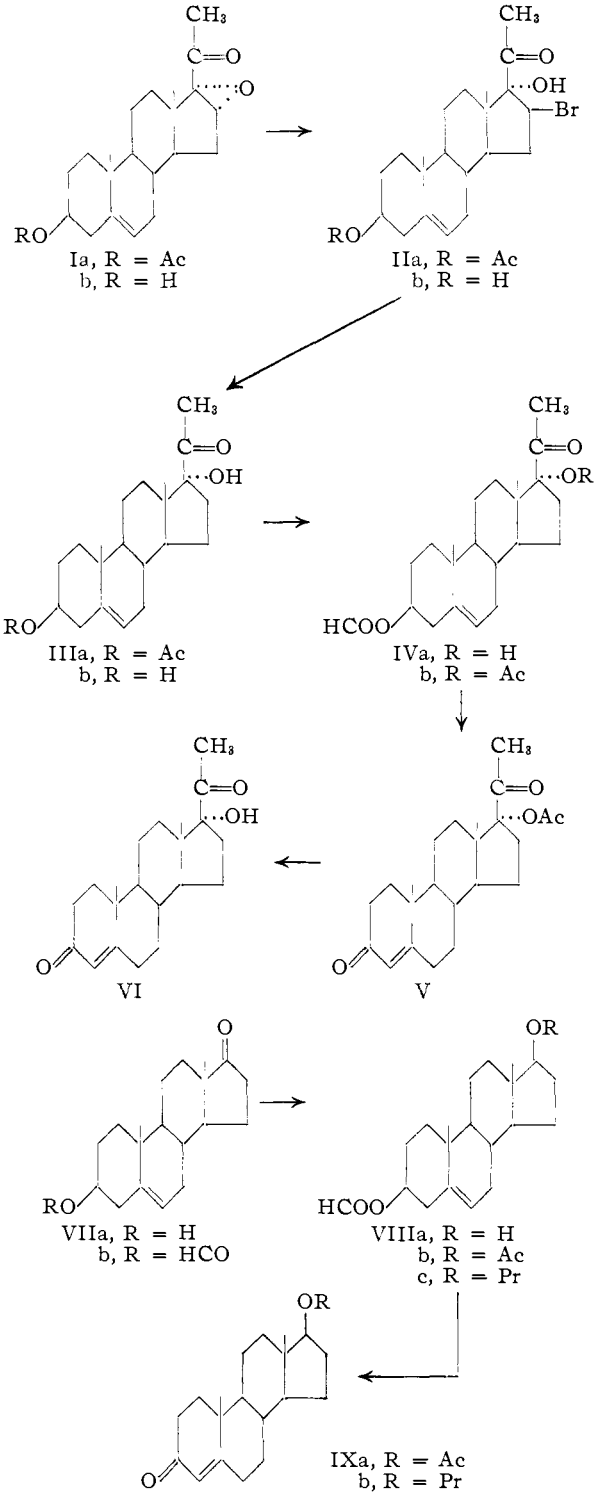
(1b) The major part of the work described in this paper forms the basis of Mexican Patent Application No. 34216 (Aug. 2, 1952), No. 35342 (Jan. 13, 1953) and No. 36949 (Aug. 18, 1953).

(2) Furthermore H. Hirschmann, F. B. Hirschmann and G. L. Farrell (*ibid.*, **75**, 4862 (1953)) have shown that formates of Δ^5-3β-ols are stable toward lead tetraacetate in acetic acid (for introduction of the 21-acetoxy group into pregnan-20-ones).

(3) H. J. Ringold, G. Rosenkranz and F. Sondheimer, *ibid.*, **78**, 820 (1956).

(4) (a) H. G. Fuchs and T. Reichstein, *Helv. Chim. Acta*, **24**, 804 (1941); (b) P. Hegner and T. Reichstein, *ibid.*, **24**, 828 (1941); (c) P. L. Julian, E. W. Meyer and I. Ryden, THIS JOURNAL, **72**, 367 (1950).

(5) P. L. Julian, E. W. Meyer, W. J. Karpel and I. R. Waller *ibid.*, **72**, 5145 (1950).



terial and which are satisfactory as regards yield and ease of operation. The first synthesis involved acetylation of Ib,[5] followed by treatment of the resulting Ia with hydrogen bromide in glacial acetic acid, whereby the bromohydrin IIa was obtained, which on hydrogenolysis over a 2% palladium–calcium carbonate catalyst (the Kendall[6a] modification of the Julian[5,6b] 17α-hydroxyl introduction) gave Δ^5-pregnene-3β,17α-diol-20-one 3-acetate (IIIa).[7] Saponification with potassium carbonate produced Δ^5-pregnene-3β,17α-diol-20-one (IIIb)[4] in an over-all yield from Ia of 83%; IIIb was then transformed to the 3-formate IVa (88%) by means of 85% formic acid at 60–70°.[8]

This route to IVa is somewhat involved, necessitating both an acetylation and a subsequent saponification step. Furthermore, for large-scale operation, the fact that the reduction step was rather slow (24–48 hours) and needed a relatively large amount of catalyst to proceed to completion (Pd: steroid ratio = 1:17) was a disadvantage. As a result of a detailed investigation aimed at simplifying the above synthesis, the following improved process was worked out. Free 16α,17α-oxido-Δ^5-pregnen-3β-ol-20-one (Ib)[5] on reaction in methylene dichloride solution with hydrogen bromide in acetic acid produced the bromohydrin IIb containing only a small percentage of the acetate IIa. This product was reduced very readily on being shaken in hydrogen over a 5% palladium–charcoal catalyst in methanol solution in the presence of slightly over one equivalent of ammonium acetate, which reacts with the liberated hydrogen bromide and thus prevents the reduction of the Δ^5-double bond which occurs in the absence of ammonium acetate. Under these conditions hydrogenolysis was complete in 1–2 hours by use of a Pd:steroid ratio of 1:200. The methanolic hydrogenation mixture was then heated with potassium carbonate to saponify the 3-acetate present and the very insoluble Δ^5-pregnane-3β,17α-diol-20-one (IIIb) was removed together with the catalyst. At this stage pure IIIb may be obtained by extraction, *e.g.*, with hot pyridine. However, for the preparation of the 3-formate IVa, the catalyst–steroid mixture is best heated directly with formic acid and by this method IVa may be obtained readily on the kilogram scale in an over-all yield from Ib of 76%.

The next step in the synthesis of 17α-hydroxyprogesterone involved protection of the 17α-hydroxy group of IVa through acetylation by means of acetic anhydride and *p*-toluenesulfonic acid.[9,10] This reaction produced Δ^5-pregnane-3β,17α-diol-20-one 3-formate 17-acetate (IVb) in about 90% yield, no ester interchange with the formate grouping being observed. Direct Oppenauer oxidation[11] of the mixed diester IVb by means of aluminum isopropoxide in a mixture of boiling cyclohexanone and

(6) (a) F. B. Colton, W. R. Nes, D. A. van Dorp, H. L. Mason and E. C. Kendall, *J. Biol. Chem.*, **194**, 235 (1952); (b) P. L. Julian, E. W. Meyer, W. J. Karpel and I. Ryden, THIS JOURNAL, **71**, 3574 (1949).

(7) A. Ercoli and P. de Ruggeri (ref. 13) have now reported that the reduction of the bromohydrin IIa with Raney nickel (*cf* ref. 5 and 6b) gives only a poor yield of Δ^5-pregnene-3β,17α-diol-20-one 3-acetate (IIIa). The Italian workers successfully employed the corresponding iodohydrin (see ref. 13).

(8) *Cf.* L. F. Fieser and S. Rajagopalan, THIS JOURNAL, **71**, 3938 1949).

(9) Huang-Minlon, E. Wilson, N. L. Wendler and M. Tishler, *ibid.*, **74**, 5394 (1952).

(10) R. B. Turner, *ibid.*, **75**, 3489 (1953).

(11) R. B. Turner (ref. 10) has shown that the 17α-acetoxy-20-ketopregnane side-chain is stable toward Oppenauer conditions, by oxidizing Δ^5-pregnene-3β,17α-diol-20-one 17-monoacetate (obtained from Δ^5-pregnene-3β,17α-diol-20-one (IIIb) by successive diacetylation and partial saponification at C-3) to 17α-acetoxyprogesterone (V). We had independently carried out this series of transformations but find that the above-described synthesis of V from IIIb *via* the formate IVb is superior in detail.

xylene[12] proceeded smoothly and furnished 86% of 17α-acetoxyprogesterone (V).[10,11] Finally, saponification with potassium hydroxide in boiling aqueous methanol gave 17α-hydroxyprogesterone (VI) (91%). The over-all yield of this substance from 16α,17α-oxido-Δ⁵-pregnen-3β-ol-20-one (Ib) was 53% and this synthesis of VI compares favorably with the others described recently[4c,7,10,13] which employ Ib as starting material.

17-Hydroxyprogesterone has recently become of interest since its esters have been shown to possess long acting progestational activity.[14] Such esters may be obtained[9,10] by the esterification of 17α-hydroxyprogesterone (VI), but our synthetic route to the latter is ideally suited for their direct preparation since they are formed from Δ⁵-pregnene-3β,17α-diol-20-one 3-formate (IVa) through C-17 acylation with the corresponding acid anhydride followed by Oppenauer oxidation.[15]

Another example of the utility of the formate protection procedure is provided by a new route to testosterone esters from dehydroisoandrosterone (Δ⁵-androsten-3β-ol-17-one) (VIIa). The latter was converted to the formate VIIb in the usual way and the 17-keto group of VIIb was then reduced at room temperature with sodium borohydride in aqueous tetrahydrofuran. This treatment caused no hydrolysis of the ester grouping and resulted in Δ⁵-androstene-3β,17β-diol 3-monoformate (VIIIa). The 17-acetate VIIIb and 17-propionate VIIIc were prepared by treatment of VIIIa with the appropriate anhydride in the presence of *p*-toluenesulfonic acid. Lastly, Oppenauer oxidation of the mixed diesters VIIIb and VIIIc under the conditions indicated above produced testosterone acetate (IXa) and propionate (IXb), respectively.

Experimental[16]

Δ⁵-Pregnene-3β,17α-diol-20-one 3-Acetate (IIIa).—A solution of hydrogen bromide in glacial acetic acid (215 cc., 32% w./v.) was added during 10 minutes to a stirred suspension of 107 g. of 16α,17α-oxido-Δ⁵-pregnen-3β-ol-20-one acetate (Ib)[5] in 1.1 l. of glacial acetic acid, the internal temperature being kept at 18° by ice-cooling. A homogeneous solution resulted a few minutes after the end of the addition, followed shortly thereafter by partial crystallization of the bromohydrin. After a reaction time of 25 minutes at 18°, the mixture was poured into 7 l. of water, the crude bromohydrin IIa was collected, thoroughly washed with water and air-dried for 24 hours at room temperature. The product then still had a moisture content of 25–30% but was satisfactory for the hydrogenation step.

The total crude bromohydrin was suspended in 5 l. of 96% ethanol (previously distilled over Raney nickel) together with 400 g. of a 2% palladium–calcium carbonate catalyst. The mixture was then shaken in hydrogen (20 lb. pressure) at 25° until uptake of gas ceased (*ca.* 40 hours). During the course of the hydrogenation, the reaction vessel was flushed several times with fresh hydrogen to remove liberated carbon dioxide. The suspension was heated to boiling, the catalyst was removed and washed thoroughly with boiling ethanol. The combined filtrates were concentrated to 500 cc., cooled in ice and the resulting precipitate was collected. This procedure produced 91.0 g. of Δ⁵-pregnene-3β,17α-diol-20-one 3-acetate (IIIa) with m.p. 223–227°, [α]D −74°, −39° (dioxane). Another 0.5 g. with m.p. 222–227° (total yield, 85%) was obtained from the mother liquors. A sample after crystallization from ethyl acetate showed m.p. 232–234°, [α]D −40° (dioxane); reported m.p. 232–234°,[4c] [α]^{15}D −41° (dioxane).[4b]

Δ⁵-Pregnene-3β,17α-diol-20-one (IIIb).—A suspension of 50 g. of the acetate IIIa with m.p. 223–227° in 3 l. of methanol was treated with a solution of 50 g. of potassium carbonate in 300 cc. of water, the mixture was boiled under reflux for 1 hour and then cooled in ice. The resulting Δ⁵-pregnene-3β,17α-diol-20-one (IIIb) was collected. It weighed 38.4 g. and showed m.p. 270–272°, [α]D −36° (dioxane); reported: m.p. 265°,[4c] 271–273°,[4b] [α]^{15}D −37° (dioxane).[4b] The mother liquors after neutralization with acetic acid and concentration furnished another 5.1 g. with m.p. 261–265° (total yield 98%).

Δ⁵-Pregnene-3β,17α-diol-20-one 3-Formate (IVa). (a) From Isolated Δ⁵-Pregnene-3β,17α-diol-20-one (IIIb).—A suspension of 90 g. of IIIb in 2.3 l. of 85% formic acid was stirred for 2 hours at 70°. A homogeneous solution did not result at any time but a change of crystal form was noted. The mixture was cooled in ice and the formate IVa was collected. It weighed 81.0 g. (83%) and showed m.p. 203–207°. A sample was crystallized from acetone and then exhibited m.p. 207–209°, [α]D −86°.

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.53; H, 9.06.

The formic acid mother liquors were concentrated under reduced pressure to 100 cc., water was added and the precipitate was collected and saponified with boiling methanolic potassium hydroxide (300 cc., 2%, 1 hour). In this way 4.9 g. (5.4%) of IIIb with m.p. 266–269° was recovered.

(b) Directly from 16α,17α-Oxido-Δ⁵-pregnen-3β-ol-20-one (Ia).—A solution of hydrogen bromide in acetic acid (180 cc., 32% w./v.) was added during 5 minutes to an ice-cooled and stirred solution of 265 g. of the oxide Ia[5] in 2 l. of methylene dichloride and 140 cc. of acetic acid, initially at 20°. Twenty minutes after the end of the addition the temperature had dropped to 10° and a mixture of 1.2 kg. of ice and 1.2 kg. of water was added with vigorous agitation. The resulting precipitate was collected, washed with 250 cc. of methylene dichloride (precooled to 0°) and dried *in vacuo* at 35°. The resulting bromohydrin IIb (300 g., 91%) showed m.p. 190–195°, [α]D −25°, and was shown by chromatographic analysis to contain a small percentage of the 3-acetate.

A mixture of 250 g. of the crude bromohydrin IIb, 60 g. of ammonium acetate (Baker C.P.) and 25 g. of a 5% palladium–charcoal catalyst (American Platinum Works) in 4.5 l. of methanol was shaken in hydrogen at 570 mm. and 25° for 90 minutes, by which time uptake of gas had ceased. The suspension was then boiled for 1 hour with 60 g. of potassium carbonate in 500 cc. of water, neutralized with acetic acid, concentrated to 1 l. and cooled in ice. The resulting mixture of catalyst and Δ⁵-pregnene-3β,17α-diol-20-one (IIIb) was dried at 90° and weighed 321 g. The very insoluble diol IIIb may be separated readily by extraction with hot pyridine followed by crystallization from the same solvent. However, for the preparation of the formate IVa, the mixture was heated to 60° with 3 l. of 85% formic acid and stirred at this temperature for 2 hours. The suspension was then concentrated under reduced pressure at 40° to 1.5 l., ice-cooled, the solid was collected and washed first with cold formic acid and finally with water. Drying at 90°, separation of steroid from catalyst through extraction with hot acetone followed by crystallization from this solvent produced 182.5 g. (76% over-all from Ia) of Δ⁵-preg-

(12) While this solvent was necessary for complete oxidation at the atmospheric pressure (*ca.* 570 mm.) of Mexico City, experiments carried out elsewhere indicate that the lower boiling toluene is satisfactory at sea level.

(13) Since completion of this work (ref. 1b) A. Ercoli and P. de Ruggeri (*Gazz. chim. ital.*, **84**, 479 (1954)) have described syntheses both of Δ⁵-pregnene-3β,17α-diol-20-one (IIIb) and of 17α-hydroxyprogesterone (VI) from 16α,17α-oxido-Δ⁵-pregnen-3β-ol-20-one (Ib) *via* the 16,17-iodohydrins. We have successfully reproduced their over-all yields, which are very similar to those reported in the present paper but have found that the preparation and handling of the 16,17-iodohydrins on the large-scale present considerable difficulties.

(14) K. Junkmann, *Arch. exp. Pathol. Pharmakol.*, **223**, 244 (1954); M. E. Davis and G. L. Wied, *J. Clin. Endocrinol. Metabolism*, **15**, 923 (1955).

(15) E. Batres, R. Gomez, G. Rosenkranz and F. Sondheimer, THIS JOURNAL, No. LXXVI.

(16) Melting points are uncorrected. Rotations were determined (at 20°) in chloroform and ultraviolet absorption spectra in 95% ethanol solution, unless noted otherwise. We should like to thank Mrs. P. Lopez and Miss M. T. Cardenas for these determinations and Mrs. A. Gonzalez for the microanalyses.

nene-3β,17α-diol-20-one 3-formate (IVa), m.p. 203–206°, $[\alpha]_D$ −86°, identified with the above described compound through mixture m.p. determination and infrared comparison.

Δ^5-Pregnene-3β,17α-diol-20-one 3-Formate 17-Acetate (IVb).—A mixture of 100 g. of the formate IVa, 2.5 g. of *p*-toluenesulfonic acid hydrate and 400 cc. of acetic anhydride was heated with stirring at 80° for 30 minutes, allowed to stand at room temperature for 2 hours and finally overnight at 0°. The diester IVb was collected, washed first with a little cold acetic anhydride and then with hot water. The dried product weighed 99.5 g. (89%) and showed m.p. 192–196°. The analytical sample was obtained through crystallization from acetone and exhibited m.p. 198–200°, $[\alpha]_D$ −75°.

Anal. Calcd. for $C_{24}H_{34}O_5$: C, 71.61; H, 8.51. Found: C, 71.88; H, 8.50.

17α-Acetoxyprogesterone (V).—The diester IVb (51 g., m.p. 192–196°) was dissolved in 1.4 l. of commercial xylene[12] and 510 cc. of cyclohexanone and the solution was distilled (250 cc. of distillate collected) to remove moisture. Aluminum isopropoxide (51 g.) dissolved in 210 cc. of xylene was added during 5 minutes to the slowly distilling solution and distillation was then continued for an additional 45 minutes (further 210 cc. of distillate collected). The mixture was cooled rapidly, a mixture of ice and water was added and the solvents were removed through steam distillation. The resulting solid was collected by filtration on Celite and dried. Extraction with hot acetone, followed by crystallization from this solvent, furnished 40.7 g. (86%) of 17α-acetoxyprogesterone with m.p. 240–243°, $[\alpha]_D$ +70°. A further purified sample showed m.p. 245–247°, $[\alpha]_D$ +73°, +54° (dioxane); reported[10] m.p. 243–244.5°, $[\alpha]_D$ +56° (dioxane).

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 73.96; H, 8.84.

17α-Hydroxyprogesterone (VI).—A solution of 17.5 g. of potassium hydroxide in 20 cc. of water and 250 cc. of methanol was added during 30 minutes to a boiling solution of 100 g. of 17α-acetoxyprogesterone (V) in 3 l. of methanol, in an atmosphere of nitrogen. Boiling was continued for a further 2 hours and the solution was then cooled, neutralized with acetic acid and concentrated under reduced pressure to 100 cc. Addition of water, followed by crystallization of the precipitated solid from acetone–hexane, produced 81 g. (91%) of 17α-hydroxyprogesterone (VI) with m.p. 220–222°, $[\alpha]_D$ +95°, +105° (acetone), $\lambda_{max.}$ 240 mμ, log ϵ 4.23; reported m.p. 220–222°,[17] $[\alpha]_D$ +97°,[4c] +103° (acetone).[17] No depression in m.p. was observed on admixture with a sample prepared by another method[15] which had been identified with the natural hormone.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.22; H, 9.26.

(17) G. Rosenkranz, J. Pataki, S. Kaufmann, J. Berlin and C. Djerassi, THIS JOURNAL, **72**, 4081 (1950).

Δ^5-Androsten-3β-ol-17-one Formate (VIIb).—A suspension of 20 g. of dehydroisoandrosterone (VIIa) in 220 cc. of 85% formic acid was heated at 60° with stirring for 1 hour. Water was then added, the precipitated crude formate VIIb was collected, washed well with water and dried. It weighed 20.5 g. (93%) and showed m.p. 138–144°. Crystallization from acetone–pentane produced the analytical sample, m.p. 144–146°, $[\alpha]_D$ −8°.

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 76.10; H, 9.23.

Δ^5-Androstene-3β,17α-diol 3-Monoformate (VIIIa).—A solution of 50 mg. of sodium borohydride in 0.4 cc. of water was added to 1.0 g. of the formate VIIb dissolved in 40 cc. of tetrahydrofuran. After 3 hours at room temperature the excess reagent was destroyed by addition of a few drops of formic acid and the solution was evaporated under reduced pressure almost to dryness. Water was added to the residue and the solid was collected to furnish 0.98 g. (97%) of the crude diol monoformate VIIIa with m.p. 162–167°. One crystallization from acetone–hexane produced 0.72 g. of the analytically pure compound, m.p. 170–172°, $[\alpha]_D$ −55°.

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.18; H, 9.40.

Δ^5-Androstene-3β,17β-diol 3-Formate 17-Acetate (VIIIb).—A solution of 300 mg. of the monoformate VIIIa and 100 mg. of *p*-toluenesulfonic acid hydride in 3 cc. of acetic anhydride was allowed to stand for 14 hours at room temperature. The precipitated diester VIIIb (110 mg., m.p. 143–148°) was collected and the mother liquors were poured into aqueous sodium acetate solution. Crystallization of the resulting precipitate from hexane produced another 150 mg. (total yield 77%) of VIIIb with m.p. 142–147°. The analytical sample showed m.p. 146–148°, 149–151° (Kofler), $[\alpha]_D$ −70°.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.10; H, 9.33.

Δ^5-Androstene-3β,17β-diol 3-Formate 17-Propionate (VIIIc).—This compound was prepared from VIIIa as described above for the acetate VIIIb, propionic anhydride being substituted for acetic anhydride. It exhibited m.p. 109–111°, $[\alpha]_D$ −65°.

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.56; H, 8.96.

Testosterone Acetate (IXa) and Propionate (IXb).—Oppenauer oxidation of 0.5 g. of the mixed diester VIIIb exactly as described above for the diester IVb produced 0.25 g. (55%) of testosterone acetate (IXa) with m.p. 140–142°, identified with an authentic specimen by mixture m.p. determination and infrared comparison. Similarly, Oppenauer oxidation of 0.5 g. of the diester VIIIc yielded 0.21 g. of testosterone propionate (IXb) with m.p. 119–121°, identified with an authentic sample.

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