the ether was treated with Girard reagent T and the ketonic material separated. Distillation of the latter afforded 7.0 g. of oil, b.p. 148–155° (0.1 mm.), $[\alpha]^{23}D$ +68° (*c* 3.48), together with considerable distillation residue which formed a brittle glass on cooling. Analysis of the distillate gave the values: C, 81.27, 81.14; H, 9.22, 9.06.

Following the separation of VIII semicarbazone the methanolic mother liquor deposited on long standing a second crop of crystalline material containing some resin. This crystallized from methanol in needles, m.p. 96–96.5°, $[\alpha]^{29}D$ +245° (*c* 2.36), after drying at room temperature. The analysis of this material (C, 68.98, 68.77; H, 7.79, 7.93) indicated it to be a bromo hydrocarbon, $C_{20}H_{27-29}Br$. Since the material gave no immediate color with tetranitromethane it was assumed to be essentially non-olefinic in character.

SHREWSBURY, MASS.

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

Steroids. XLVII.[1] Synthesis of Steroidal Hormone Analogs Hydroxylated at C-2[2]

BY FRANZ SONDHEIMER, ST. KAUFMANN, J. ROMO, H. MARTINEZ AND G. ROSENKRANZ

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Testosterone acetate (I) on reaction with lead tetraacetate yields two isomeric substances, shown to be 2β-hydroxytestosterone diacetate (II) and 2α-hydroxytestosterone diacetate (III). On mild alkaline saponification both of these isomers give 2α-hydroxytestosterone (IV), a substance which may be reacetylated to the diacetate III. Both II and III on reduction with zinc regenerate testosterone acetate, although III does so only very slowly. Two of the substances obtained previously by Ehrhart, Ruschig and Aumüller from progesterone and lead tetra-acetate are shown to be 2α-hydroxydesoxycorticosterone diacetate (XVI) and 2α-hydroxyprogesterone (XIIIb). The interesting observation has been made that 6-bromotestosterone acetate (V) on acetolysis yields the above-mentioned 2α-acetoxy isomer III. Similarly it is shown that the acetolysis product of 6-bromo- and 6-chloro-Δ^4-cholesten-3-one (VIIIa,b), formulated by Rivett and Wallis as 6α-acetoxy-Δ^4-cholesten-3-one (IX), is in fact the 2α-acetoxy isomer (VII). Taking advantage of this novel rearrangement, progesterone (XI) is converted *via* the 6-bromo compound (XII) to 2α-acetoxyprogesterone (XIIIa) and thence 2α-hydroxyprogesterone (XIIIb), and desoxycorticosterone acetate (XIV) *via* the amorphous 6-bromo compound (XV) to 2α-hydroxydesoxycorticosterone diacetate (XVI).

Steroidal hormones bearing an oxygen substituent at the C-11 position have become of considerable importance within the last few years. It is of interest to prepare hormone analogs oxygenated elsewhere in the molecule in order to investigate their biological activity. In this communication we describe the synthesis of several such analogs with a hydroxyl grouping at the C-2 position.

The only method hitherto described for preparing a Δ^4-2-ol-3-one (as the acetate) involves the reaction of a Δ^4-3-one with lead tetraacetate.[3] With Δ^4-cholesten-3-one it was rigidly established[3a] that reaction had taken place at the C-2 position, to yield Δ^4-cholesten-2ξ-ol-3-one acetate, through conversion of the product by hydrogenation, saponification and oxidation to 2,3-secocholestane-2,3-dioic acid. The configuration of the 2-acetoxy grouping was not established. The reaction of progesterone with lead tetra-acetate was shown to lead to a complex mixture of substances,[3b,c] and will be discussed further below.

We have carried out the lead tetra-acetate reaction with testosterone acetate (I), and have observed that two isomeric products, each containing one more acetoxy grouping than the starting material, could be isolated. The one with m.p. 202–203°, $[\alpha]^{20}D$ −68°,[4] was obtained in 25% yield and that with m.p. 212–213°, $[\alpha]^{20}D$ +68° in 17% yield. When either of these substances was hydrolyzed under mild conditions (potassium bicarbonate) the identical saponification product was formed, which on re-acetylation yielded the latter (dextrorotatory) of the initial products. These facts indicate that the two substances formed in the lead tetra-acetate reaction bear the extra acetoxy groupings at the same position, but in different configurations.[5] *Ab initio*, attack of the reagent might have occurred at C-2 or C-6, but the isomer pair cannot possess the epimeric 6-acetoxy structures, since 6β-hydroxytestosterone diacetate with completely different properties (m.p. 132–133°, $[\alpha]^{20}D$ +26°; free glycol, m.p. 216–218°, $[\alpha]^{20}D$ +34°) recently has been prepared in these laboratories.[10b] It follows that the pair must be represented by the epimeric 2-acetoxy formulations II and III, and this is in agreement with the 2-acetoxy structure demonstrated by Seebeck and Reichstein[3a] for the product from Δ^4-cholesten-3-one and lead tetraacetate. It can clearly be seen by inspection of Stewart–Hirschfelder models that the 2α-structure III is the less hindered of these, and since the 2β-acetoxy grouping in II is adjacent to a carbonyl function, it is capable of being inverted under the basic conditions of the saponification step to the more stable 2α-ol-3-one structure IV. It therefore follows that the "labile" levorotatory tetraacetate product is Δ^4-androstene-2β,17β-diol-3-one (2β-hydroxytestosterone) diacetate (II), the "stable" dextrorotatory product is Δ^4-androstene-2α,17β-diol-3-one (2α-hydroxytestosterone) diacetate (III), and that either on saponification yields Δ^4-androstene-2α,17β-diol-3-one (2α-hydroxytestosterone) (IV). The correctness of the

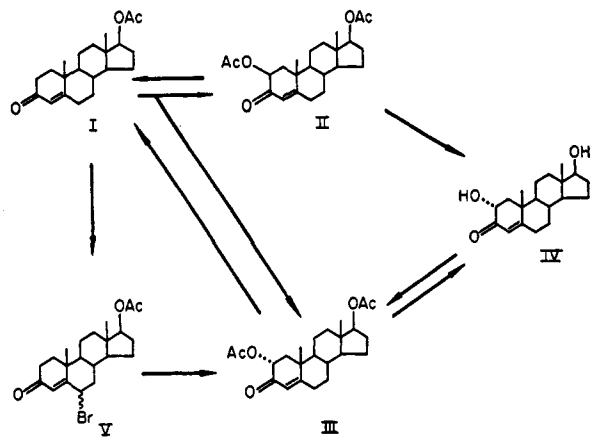
(1) Part XLVI, O. Mancera, G. Rosenkranz and F. Sondheimer, *J. Chem. Soc.*, 2189 (1953).

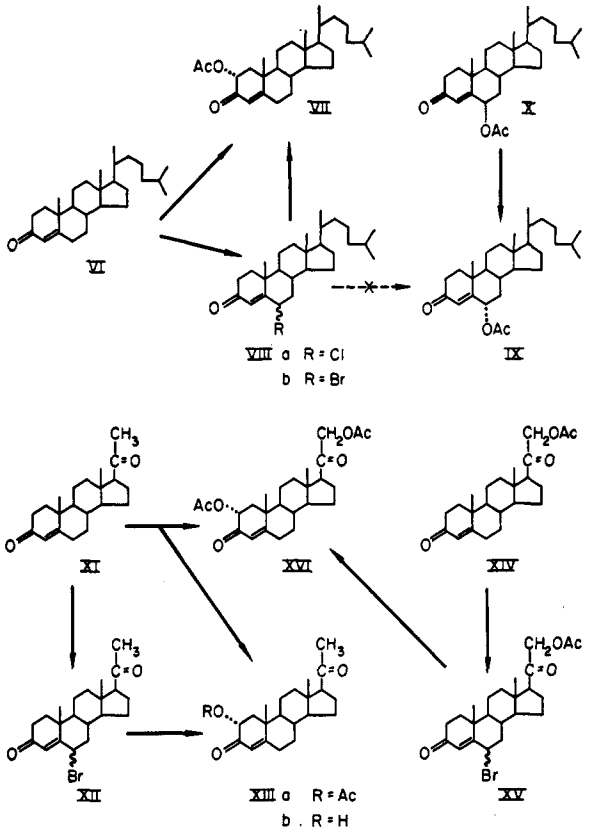
(2) Part of the work described in this paper forms the basis of U. S. Patent 2,602,803.

(3) Reaction with Δ^4-cholesten-3-one: (a) E. Seebeck and T. Reichstein, *Helv. Chim. Acta*, **27**, 948 (1944). Reaction with progesterone; (b) G. Ehrhart, H. Ruschig, and W. Aumüller, *Angew. Chem.*, **52**, 363 (1939); *Ber.*, **72**, 2035 (1939); (c) T. Reichstein and C. Montigel, *Helv. Chim. Acta*, **22**, 1212 (1939).

(4) All rotations were determined in chloroform solution, unless indicated otherwise.

(5) The alternative formulation of the two substances as *positional* isomers (at C-2 and C-6) is ruled out, since the shift of a hydroxyl group during the saponification step which would have to be postulated for one of the isomers is not likely to occur under the *alkaline* conditions employed.





structural assignments of the first two of these compounds is supported by the fact that the former is less strongly absorbed on alumina than is the latter, as would be expected in view of the less planar shape of II compared with III. The M_D increment for introduction of the 2β-acetoxy grouping into testosterone acetate is $-581°$, while that for introduction of the 2α-acetoxy grouping is $-53°$.[6] It may be noted that the corresponding M_D increase in Seebeck and Reichstein's Δ^4-cholesten-2ξ-ol-3-one acetate over that in Δ^4-cholesten-3-one is $-50°$, and it clearly follows that Reichstein's product must have the 2α-configuration, as in VII.

The above described 2β-hydroxytestosterone diacetate II was smoothly reduced to testosterone acetate on short treatment with zinc in acetic acid at room temperature. This reaction, which is analogous to the reductive removal of the acetoxy groupings in the similarly constituted *trans*-1-acetoxy-2-keto-10-methyl-$\Delta^{3,6}$-hexahydronaphthalene[7] and 12α-bromo-Δ^{16}-pregnene-3α,21-diol-11,20-dione 21-monoacetate,[8] provides confirmation that no gross rearrangement had occurred in the lead tetraacetate reaction leading to II. It is interesting to note that zinc de-acetylation at C-2 proceeded much more readily with the 2β-isomer II than with the 2α-isomer III (*cf.* Experimental section).

As was just mentioned, the reaction of progesterone with lead tetraacetate has been studied previously,[3b,c] the aim being the preparation of desoxycorticosterone acetate (XIV). It was shown by Reichstein and Montigel[3c] that this latter substance was indeed formed, although only in *ca.* 3% yield. Ehrhart, Ruschig and Aumüller[3b] isolated in addition a diacetoxyprogesterone by direct crystallization of the reaction mixture, and two different monohydroxyprogesterones, one with $[\alpha]^{20}D$ +186 ± 19° (EtOH) and one with $[\alpha]^{20}D$ +40° (EtOH), by mild base saponification of the total product. We have now been able to assign structures to two of the three products obtained by the German workers. In our hands the reaction product from progesterone and lead tetraacetate by direct crystallization furnished a diacetoxyprogesterone with properties in fairly good agreement with that of Ehrhart, *et al.*,[3b] which proved to be identical with a specimen of 2α-hydroxydesoxycorticosterone diacetate (XVI) prepared by a method to be described below. Bis-acetoxylation of progesterone had therefore occurred at the 2α- and 21-positions. The monohydroxyprogesterone with $[\alpha]^{20}D$ +186° of the German investigators we believe to be 2α-hydroxyprogesterone (XIIIb), since its properties, as well as those of its acetate, are in reasonably good agreement with those of a sample of XIIIb described below. The structure of the other hydroxyprogesterone of Ehrhart, *et al.*, remains obscure. The 2β-hydroxy formulation is unlikely, since it has been shown above that both 2β- and 2α-acetoxytestosterone acetate on mild basic hydrolysis give 2α-hydroxytestosterone (IV). Nor can the substance be formulated as the known 6α- or 6β-hydroxyprogesterone[9,10] as there is no correspondence in properties, and the 17α-hydroxyprogesterone and 17β-hydroxyisoprogesterone structures are excluded for the same reason.

The lead tetraacetate method of preparing 2-acetoxy-Δ^4-3-ketones suffers from the disadvantage that with more complex steroids the reagent may cause attack of the side-chain. We have now found an alternative method which does not suffer from this defect, although the yields leave something to be desired.

During an investigation on the synthesis of 6-hydroxy-Δ^4-3-ketones we had occasion to study the

(6) The optical rotations (in chloroform) for various hormones, needed for calculating molecular rotation differences, were determined in these laboratories: testosterone acetate, $[\alpha]^{20}D$ +96°; free testosterone, $[\alpha]^{20}D$ +109°; progesterone, $[\alpha]^{20}D$ +204°; desoxycorticosterone acetate, $[\alpha]^{20}D$ +186°.

(7) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, THIS JOURNAL, **73**, 2403 (1951); **74**, 4223 (1952).

(8) W. R. Nes and H. L. Mason, *ibid.*, **73**, 4765 (1951).

(9) C. P. Balant and M. Ehrenstein, *J. Org. Chem.*, **17**, 1587 (1952).

(10) (a) F. Sondheimer and G. Rosenkranz, *Experientia*, **9**, 62 (1953); (b) *idem.*, *J. Chem. Soc.*, in press.

reaction of 6-bromotestosterone acetate (V) (prepared[11] from testosterone acetate with N-bromosuccinimide[12]) with potassium acetate in acetic acid. In analogy to a similar reaction reported by Rivett and Wallis[13] in the cholestane series, 6α-hydroxytestosterone diacetate was expected as the product. In fact the substance obtained in *ca.* 12% yield proved to be identical with the above described "stable" isomer formed from testosterone acetate and lead tetraacetate, *viz.*, 2α-hydroxytestosterone diacetate (III). It appears that during the acetolysis reaction a rearrangement from the C-6 to the C-2 position had taken place. This seems to be the first example of this type of shift, although rearrangement of bromine in the opposite sense has been observed before.[14] By analogy the formulation of the acetolysis product (m.p. 139–139.5°, $[\alpha]^{26}D$ +62°) of 6-chloro (VIIIa) or 6-bromo-Δ^4-cholesten-3-one (VIIIb) as 6α-acetoxy-Δ^4-cholesten-3-one (IX) by Rivett and Wallis[13] was made doubtful. Indeed in another connection we had prepared the latter substance by isomerization of 6β-acetoxy-Δ^4-cholesten-3-one (X)[10b,15] with hydrogen chloride in chloroform containing alcohol (*cf.* Ehrenstein, *et al.*,[9,16] for similar isomerizations in other series), and its properties (m.p. 106–107°, $[\alpha]^{20}D$ +82°) showed that it was different from the product of Rivett and Wallis. On the other hand, the properties of the latter are in good agreement with those of the above-mentioned 2α-acetoxy-Δ^4-cholesten-3-one (VII) (m.p. 141–142°, $[\alpha]^{15}D$ +65.5°) prepared by Seebeck and Reichstein,[3a] and it is clear that in the cholestane series a similar rearrangement from C-6 to C-2 had taken place.[17]

In a similar fashion progesterone (XI) and desoxycorticosterone acetate (XIV) were converted by reaction with N-bromosuccinimide to the corresponding 6-bromo compounds XII and XV, and thence by acetolysis to 2α-acetoxyprogesterone (XIIIa) and 2α-hydroxydesoxycorticosterone diacetate (XVI), respectively. That these latter substances really possess the 2α-acetoxy structures was confirmed by calculation of molecular rotation differences. In XIIIa the M_D contribution of the 2α-acetoxy grouping[6] is −31° and in XVI it is −30°, values in reasonably good agreement with −53° in the testosterone acetate and −50° in the Δ^4-cholesten-3-one series (*vide supra*). Moreover, the 6α-acetoxy and 6β-acetoxy derivatives both of progesterone[9,10,18] and of desoxycorticosterone acetate[10b,16,19] have been described and differ markedly in properties from those of XIIIa and XVI. Mild saponification of 2α-acetoxyprogesterone (XIIIa) led to 2α-hydroxyprogesterone (XIIIb).

Experimental[20]

Reaction of Testosterone Acetate with Lead Tetraacetate (Preparation of II and III).—A solution of testosterone acetate (100 g.) and lead tetraacetate (150 g.) in glacial acetic acid (1.5 l.) was heated at 100° for 2.5 hours. The solid product obtained by addition of water was collected by filtration. Two crystallizations from methanol followed by two crystallizations from ethyl acetate furnished 29.8 g. (25%) of 2β-hydroxytestosterone diacetate (II) as well-formed prisms with m.p. 202–203°, $[\alpha]D$ −68°, λ_{max} 242 mμ, log ε 4.23, $\nu_{max}^{CHCl_3}$ 1736 and 1682 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.22; H, 8.36.

The combined mother liquors from the crystallization of II were chromatographed on a column of ethyl acetate-washed alumina. The fractions eluted with benzene–hexane proved to be low-melting mixtures of the two isomers, difficult to separate by crystallization. The further fractions eluted with benzene and benzene–ether on crystallization from ethyl acetate furnished 20.3 g. (17%) of 2α-hydroxytestosterone diacetate (III) as large prisms with m.p. 212–213°, $[\alpha]^{20}D$ +68°, λ_{max} 240 mμ, log ε 4.24, $\nu_{max}^{CHCl_3}$ 1736 and 1684 cm.$^{-1}$. There was a strong depression in m.p. on admixture with II.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.42; H, 8.39.

2α-Hydroxytestosterone (IV). (a) By Saponification of the 2β-Acetoxy Isomer II.—A solution of 5.0 g. of II in 200 cc. of methanol was heated under reflux with 5 g. of potassium bicarbonate in 50 cc. of water for 4 hours. Crystallization of the product from acetone–hexane provided 2.4 g. of 2α-hydroxytestosterone, m.p. 161–162°, $[\alpha]^{20}D$ +120°, λ_{max} 242 mμ, log ε 4.24, $\nu_{max}^{CHCl_3}$ 1670 cm.$^{-1}$ and free hydroxyl band.

Anal. Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.08; H, 8.98.

(b) By Saponification of the 2α-Acetoxy Isomer III.—Saponification of III with potassium bicarbonate as described for the 2β-isomer furnished 2α-hydroxytestosterone, m.p. 160–161°, $[\alpha]^{20}D$ +118°, in similar yield to that obtained in (a). Identity was established by mixture melting point determination and comparison of infrared spectra.

Acetylation of 2α-hydroxytestosterone, as obtained under (a) or (b), with acetic anhydride and pyridine (steam-bath, 1 hour) yielded the diacetate III (identified by mixture melting point and infrared spectrum) in nearly quantitative yield.

Testosterone Acetate (I). (a) By Zinc Reduction of 2β-Hydroxytestosterone Diacetate (II).—A mixture of 1 g. of zinc dust and 500 mg. of II in 10 cc. of glacial acetic acid and 3 cc. of water was stirred at room temperature for 10 minutes. The filtered solution was evaporated almost to dryness, diluted with water and extracted with chloroform. The zinc residue was extracted several times with boiling chloroform, the combined chloroform solutions were washed with sodium bicarbonate, dried and evaporated. Crystallization of the residue from acetone–hexane furnished 305 mg. (72%) of testosterone acetate, m.p. 134–139°, raised to 139–141° after one further crystallization. Identity with an authentic specimen was established through mixture melting point and infrared spectrum.

(11) C. Meystre and A. Wettstein, *Experientia*, **2**, 408 (1946); C. Djerassi, G. Rosenkranz, J. Romo, S. Kaufmann and J. Pataki, THIS JOURNAL, **72**, 4534 (1950).

(12) That bromination of a Δ^4-3-ketone with N-bromosuccinimide yields the 6-bromo compound has been well established (footnote 11). We have obtained further evidence of the correctness of the structure of 6-bromotestosterone acetate (V) through conversion by reaction with hydrochloric acid (*cf.* H. Reich and A. Lardon, *Helv. Chim. Acta*, **29**, 671 (1946)) to androstan-17β-ol-3,6-dione, identified with a sample prepared by an independent method.[10b]

(13) D. E. A. Rivett and E. S. Wallis, *J. Org. Chem.*, **15**, 35 (1950).

(14) *Cf.* H. H. Inhoffen and G. Zühlsdorff, *Ber.*, **76**, 233 (1943).

(15) *Inter al.*, B. Ellis and V. A. Petrow, *J. Chem. Soc.*, 1078 (1939).

(16) P. T. Herzig and M. Ehrenstein, *J. Org. Chem.*, **16**, 1050 (1951).

(17) Professor L. F. Fieser of Harvard University has informed us that he has independently prepared 6α-acetoxy-Δ^4-cholesten-3-one [(a) L. F. Fieser, THIS JOURNAL, **75**, 4377 (1953)] and shown that the product of Rivett and Wallis is the 2α-acetoxy isomer. It was therefore decided to publish our results in the same issue of THIS JOURNAL [*cf.* (b) L. F. Fieser and M. A. Romero, *ibid.*, **75**, 4716 (1953)].

(18) M. Ehrenstein and T. O. Stevens, *J. Org. Chem.*, **5**, 318 (1940); **6**, 908 (1941).

(19) S. H. Eppstein, P. D. Meister, D. H. Peterson, H. C. Murray, H. M. Leigh, D. A. Lyttle, L. M. Reineke and A. Weintraub, THIS JOURNAL, **75**, 408 (1953).

(20) Melting points are uncorrected. Rotations were measured in chloroform and ultraviolet absorption spectra in 95% ethanol solution, unless specified otherwise. Infrared spectra were obtained with a Perkin–Elmer model 12C single beam spectrophotometer with sodium chloride prism. We are indebted to Srta. Paquita Revaque for these measurements and to Srta. Amparo Barba for the microanalyses.

(b) **By Zinc Reduction of 2α-Hydroxytestosterone Diacetate (III).**—The reduction was carried out with 500 mg. of III, 1 g. of zinc dust, 10 cc. of acetic acid and 3 cc. of water as described under (a). By direct crystallization of the product from ether–hexane, 230 mg. (46%) of crude starting material with m.p. 203–208° was obtained. Chromatographic purification of the mother liquors on alumina then yielded 15 mg. (3.5%) of testosterone acetate, identified in the usual way.

Androstan-17β-ol-3,6-dione from 6-Bromotestosterone Acetate (V).—A solution of 2.5 g. of 6-bromotestosterone acetate (V)[11] in 80 cc. of methanol containing 3.2 cc. of concentrated hydrochloric acid was boiled under reflux for 3 hours. Addition of water, extraction with ether and crystallization of the product from chloroform–hexane furnished 1.05 g. of androstan-1-β-ol-3,6-dione, m.p. 235–236°, $[\alpha]^{20}D$ +9°, no appreciable absorption in the ultraviolet, $\nu_{max}^{CHCl_3}$ 1700 cm.$^{-1}$ and free hydroxyl band.

Anal. Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.74; H. 9.04.

The substance was identical with an authentic specimen[10b] as evidenced by mixture melting point and infrared comparison.

2α-Hydroxytestosterone Diacetate (III) from 6-Bromotestosterone Acetate (V).—A solution of 2.5 g. of 6-bromotestosterone acetate (V)[11] in 70 cc. of glacial acetic acid was heated under reflux with 10 g. of anhydrous potassium acetate for 4 hours. Dilution with water, extraction with ether and crystallization of the product from ether–hexane furnished 1.18 g. of a halogen-free product with m.p. 175–180°. Repeated recrystallization from acetone–hexane led to 0.29 g. of 2α-hydroxytestosterone diacetate (III), m.p. 209–212°, $[\alpha]^{20}D$ +66°, λ_{max} 240 mμ, log ε 4.23.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.36; H, 8.08.

Identity with the previously described material was established through mixture melting point and infrared comparison.

6α-Acetoxy-Δ^4-cholesten-3-one (IX).—This substance was prepared from the 6β-isomer X[10b,15] by isomerization with hydrogen chloride in chloroform containing alcohol (method of Ehrenstein, *et al.*[9,16]). The experimental procedure was almost exactly that which Professor L. F. Fieser subsequently informed us he had employed.[17a] It was obtained in 60% yield, and crystallized from methanol as prisms, m.p. 106–107°, $[\alpha]^{20}D$ +82°, λ_{max} 236 mμ, log ε 4.22, $\nu_{max}^{CHCl_3}$ 1736 and 1670 cm.$^{-1}$. (Fieser[17a] gives m.p. 103–104°, $[\alpha]^{22}D$ +76°, λ_{max} 238 mμ, log ε 4.20.)

Anal. Calcd. for $C_{29}H_{46}O_3$: C, 78.68; H, 10.48. Found: C, 78.59; H, 10.69.

Δ^4-Cholesten-6α-ol-3-one was obtained by saponification of IX with potassium bicarbonate in refluxing aqueous methanol. After crystallization from acetone–hexane it showed m.p. 159–160°, $[\alpha]^{20}D$ +82°, λ_{max} 240 mμ, log ε 4.21, $\nu_{max}^{CHCl_3}$ 1668 cm.$^{-1}$ and free hydroxyl band. (Fieser[17a] gives: m.p. 155–156.5°, $[\alpha]^{23}D$ +81°, λ_{max} 240 mμ, log ε 4.23.)

Anal. Calcd. for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.98; H, 11.19.

6-Bromoprogesterone (XII).—A solution of 10 g. of progesterone in 300 cc. of carbon tetrachloride was concentrated by distillation to *ca.* 250 cc. to remove moisture. N-Bromosuccinimide (6 g.) was added and the mixture heated under reflux for 1 hour. Filtration, evaporation of the solvent and trituration of the residue with hexane yielded 5.1 g. of 6-bromoprogesterone (XII), m.p. 139–142° dec. Crystallization from acetone–hexane led to the analytical sample with m.p. 143–145° dec., $[\alpha]^{20}D$ +77°, λ_{max} 248 mμ, log ε 4.22 $\nu_{max}^{CHCl_3}$ 1700 and 1670 cm.$^{-1}$.

Anal. Calcd. for $C_{21}H_{29}O_2Br$: C, 64.10; H, 7.42; Br, 20.33. Found: C, 64.31; H, 7.61; Br, 20.84.

2α-Acetoxyprogesterone (XIIIa).—This compound was obtained by heating under reflux 2 g. of 6-bromoprogesterone and 8 g. of anhydrous potassium acetate in 50 cc. of glacial acetic acid for 4 hours. After crystallization from acetone–hexane it weighed 0.36 g. and exhibited m.p. 197–198°, $[\alpha]^{20}D$ +164°, λ_{max} 240 mμ, log ε 4.24, $\nu_{max}^{CHCl_3}$ 1736, 1700 and 1684 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 73.81; H, 8.48.

Free 2α-hydroxyprogesterone (XIIIb), m.p. 182–183°, $[\alpha]^{20}D$ +199° (EtOH), λ_{max} 242 mμ, log ε 4.22, was obtained by saponification with potassium bicarbonate in boiling aqueous methanol, and recrystallizing from acetone–hexane. (Ehrhart, *et al.*,[3b] give m.p. 185°, $[\alpha]D$ +186 ± 19° (EtOH) for a hydroxyprogesterone of unknown structure, and m.p. 198° for its acetate.)

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.12; H, 9.26.

2α-Hydroxydesoxycorticosterone Diacetate (XVI).—Desoxycorticosterone acetate (3 g.) was brominated at C-6 through being refluxed with 1.8 g. of N-bromosuccinimide in 170 cc. of dry carbon tetrachloride for 10 minutes, a photospot lamp (GE No. RSP 2) being used for heating and illumination. The succinimide was removed by filtration, the filtrate was evaporated to dryness, and the amorphous residue was directly heated under reflux with 12 g. of anhydrous potassium acetate in 60 cc. of glacial acetic acid for 4 hours. Chromatographic purification of the product on ethyl acetate washed alumina and crystallization of the fractions eluted with benzene–hexane from acetone–hexane furnished 0.21 g. of 2α-hydroxydesoxycorticosterone diacetate (XVI) with m.p. 194–195°, $[\alpha]^{20}D$ +154°, λ_{max} 240 mμ log ε 4.22, $\nu_{max}^{CHCl_3}$ 1736, 1700 and 1686 cm.$^{-1}$.

Anal. Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.92; H, 8.09.

Progesterone on reaction with lead tetraacetate[3b,c] in our hands yielded a diacetoxyprogesterone, m.p. 195–196°, $[\alpha]^{20}D$ +157° (Ehrhart, Ruschig and Aumüller[3b] give m.p. 198°, $[\alpha]^{20}D$ +165° (EtOH)), which proved to be identical with the above described 2α-hydroxydesoxycorticosterone diacetate (XVI), as evidenced by mixture melting point determination and comparison of infrared spectra.

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