[CONTRIBUTION FROM THE INSTITUTO DE QUÍMICA DE LA UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO]

Some Experiments with 16β-Bromo-17α-acetoxy-20-keto Steroids. Synthesis of 16α-17α-Dihydroxy-steroids and Related Compounds[1]

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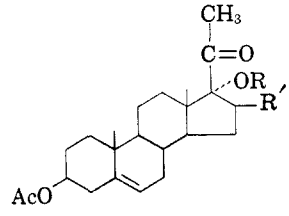
The elimination with zinc of the acetoxyl group and the bromine atom from 16β-bromo-Δ⁵-pregnene-3β,17α-diol-20-one 3,17-diacetate afforded Δ⁵,¹⁶-pregnadien-3β-ol-20-one acetate. Strong alkalies produced the corresponding 16α,17α-epoxide. Acetoxylating reagents and mild bases convert the 16β-bromo-17α-acetoxy-20-keto steroids into the 16α-acetoxy, 17α-hydroxy-20-keto compounds. The hydrolysis products from the above compounds were studied.

The bromohydrins prepared by oxide opening of steroidal 16α,17α-epoxy-20-ketones, are intermediates in the Julian[2] synthesis of 17α-hydroxy steroids which proceeds either by removal of the bromine atom with Raney nickel of by hydrogenolysis in the presence of a palladium catalyst.[3] The elimination of hydrogen bromide from the bromohydrins by mild bases is also known.[2] We have now studied the behavior of such bromohydrins, possessing an acetylated 17α-hydroxyl group towards reducing agents, acetoxylating reagents, and bases. The acetylation of the 17α-hydroxyl group in 16β-bromo-Δ⁵-pregnene-3β, 17α-diol-20-one 3-acetate (Ia) which is strongly hindered, was carried out using a procedure similar to that described by Turner[4] and in this way the diacetate (Ib) was obtained. This product, on refluxing with zinc dust in ethanol, loses both the bromine atom and the acetoxyl group, producing Δ⁵,¹⁶-pregnadien-3β-ol-20-one acetate (II). However, relatively strong bases, such as potassium carbonate, also cause elimination of the bromine atom and the acetyl group, but with formation of the epoxide, 16α,17α-epoxy-Δ⁵-pregnene-3β-ol-20-one (III).

Acetoxylating reagents such as silver acetate or sodium acetate in acetic acid or weak bases like pyridine in ethanol or collidine cause the elimination of the bromine atom in (Ib), with formation of a diacetate $C_{25}H_{36}O_6$, with m.p. 212°, $[\alpha]_D^{20}$ −72°, showing free hydroxyl bands in the infrared. The hydroxyl group is not acetylable under usual conditions (acetic anhydride and pyridine) but only with acetic anhydride in the presence of *p*-toluenesulfonic acid;[4] the substance is recovered unchanged after treatment with the pyridine-chromium trioxide complex.[5]

Recently, Heusler and Wettstein[6] obtained Δ⁵-pregnene-3β,16β,17α-triol-20-one 3,16-diacetate (Ic) by acetolysis of the 16α,17α-epoxide, using a mixture of acetic and sulfuric acids. By saponification or acid hydrolysis of this product they were able to prepare a D-homo derivative which on acetylation furnished a diacetate. We repeated the above experiments and in addition, prepared the triacetate (Id) by acid-catalyzed acetylation of the diacetate (Ic).

It was found that the diacetate (Ic) and triacetate (Id) of the 16β-hydroxy series are completely different from our diacetate m.p. 212° and the corresponding triacetate, but when we carried out the potassium bicarbonate saponification or the acid hydrolysis on our diacetate a D-homo compound was formed which proved to be identical with that obtained by the above mentioned authors. In view of the above results we assign to our substance the structure of Δ⁵-pregnene-3β,16α,17α-triol-20-one 3,16-diacetate (Ie) and the triacetate must have the formula (If).



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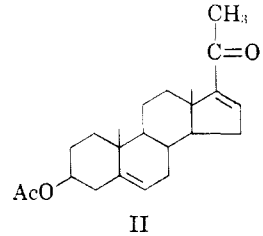
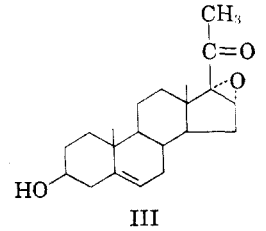


II

a, R = H, R′ = Br (β)
b, R = Ac, R′ = Br (β)
c, R = H, R′ = AcO (β)
d, R = Ac, R′ = AcO (β)
e, R = H, R′ = AcO (α)
f, R = Ac, R′ = AcO (α)



III

It is highly probable that the mechanism of the reaction[7] involves the following steps:

(1) Since the manuscript was written three articles by Cooley, Ellis, Hartley, and Petrow, *J. Chem. Soc.*, 4373, 4377, 4383 (1955), have appeared in which similar grounds are covered.

(2) Julian, Meyer, Karpel, and Ryden, *J. Am. Chem. Soc.*, **71**, 3574 (1949).

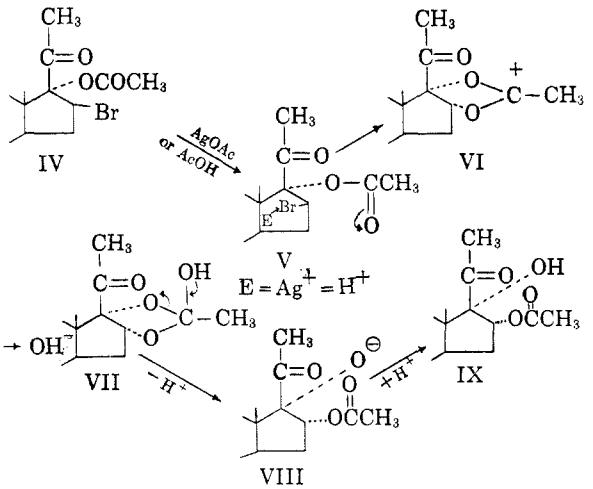
(3) Colton, Nes, van Dorp, Mason, and Kendall, *J. Biol. Chem.*, **194**, 235 (1952).

(4) Turner, *J. Am. Chem. Soc.*, **75**, 3489 (1954).

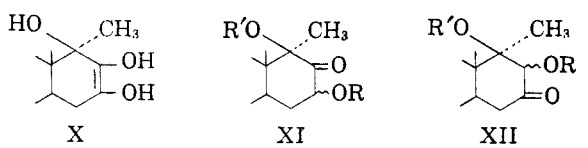
(5) Poos, Arth, Beyler, and Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

(6) Heusler and Wettstein, *Chem. Ber.*, **87**, 1301 (1954).

(7) This mechanism was suggested to us by a referee to whom we are grateful.



From the three possible structures assigned by Heusler and Wettstein[6] to the D-homo compound, XIa and XIIa are the more probable, which can rearrange through the common enolic form X. The 17α-hydroxyl group in XIa or XIIa probably has the β-configuration since Turner[8] has pointed out



X XI XII

a, R = R′ = H
b, R = Ac, R′ = H
c, R = Ac, r′ = Ac

a, R = R′ = H
b, R = Ac, R′ = H
c, R = Ac, R′ = Ac

that the alkali-promoted D-homo rearrangements of 17-hydroxy-20-keto-pregnane derivatives take place with inversion of configuration. Since both the 16α and 16β diacetates produce the same D-homo compound, doubtlessly one of them rearranges *via* the common enol to the more stable configuration.

Inhoffen, Blomeyer, and Brückner[9] have reported the preparation of Δ⁵-pregnene-3β,16α,17α-triol-20-one by osmium tetroxide hydroxylation of 5,6-dibromo-Δ¹⁶-pregnen-3β-ol-20-one acetate and hydrolysis of the osmic ester with sodium sulfite, followed by the addition of zinc dust to regenerate the Δ⁵-double bond. It is likely that under these conditions of D-homo rearrangement takes place, since sodium sulfite affords an alkaline medium strong enough to cause the saponification of the acetyl group and we have seen that the conditions needed for saponification provoke the D-homo rearrangement.

Consequently, we prepared Inhoffen's triol, but it was not identical with the D-homo triol (XIa or XIIa). It was assumed that the zinc dust may have caused the epimerization of the D-homo derivative and this proved to be the case, since Inhoffen's compound was obtained when our 3β, 16α-diacetate (Ie) was saponified in the presence of zinc dust; the diacetate prepared by acetylation of this D-homo compound was also identical in all aspects with that of Inhoffen. The supposed Δ⁵-pregnene-3β,16α,17α-triol-20-one is therefore a D-homo steroid, most probably the 17α-hydroxy epimer of XIa or XIIa. It is pertinent to mention that when the 3β,16β-diacetate (Ic) was saponified in the presence of zinc dust, no epimerization occurred, the D-homo derivative (XIa or XIIa) being obtained directly.

Treatment under drastic conditions with potassium hydroxide of the diacetates Ic, Ie, or the D-homo derivative (XIa or XIIa) afforded the same diketone which was obtained by Inhoffen[9] by strong treatment of the substance produced by hydrolysis of his osmic ester. This preparation was repeated to confirm the results. This diketone obviously is not Δ⁵-pregnen-3β-ol-16,20-dione, but must possess the structure proposed by Sarett[10] who postulated the formation of this diketone by dehydration from the triol (XIIa) *via* XIIIa affording XIV.

The acetylation of 16β-bromo-17α-hydroxy-progesterone (XVa) with acetic anhydride and *p*-toluenesulfonic acid, furnished 16β-bromo-Δ³,⁵-pregnadiene-3,17α-diol-20-one 3,17-diacetate (XVIa). It is well known that acetic anhydride in the presence

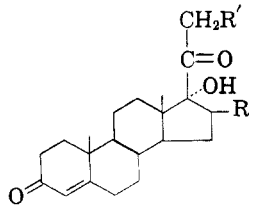
XIII XIV

a, R = H
b, R = Ac

of *p*-toluenesulfonic acid transforms keto groups into the corresponding enol acetates.[11] Treatment of this bromo compound (XVIa) with pyridine in ethanol afforded Δ³,⁵-pregnadiene-3,16α,17α-triol-20-one 3,16-diacetate (XVIb) but if the reaction is carried out with sodium acetate in acetic acid, Δ⁴-pregnene-16α,17α-diol-3,20-dione 16-acetate (XVc) is obtained. The enol acetate (XVIb) could be transformed into the Δ⁴-3-keto compound (XVc), by hydrolysis with *p*-toluenesulfonic acid in methanol or by prolonged refluxing with sodium acetate in acetic acid.

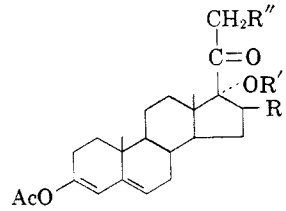
Following the method of Heusler and Wettstein[6] we repeated the preparation of 16β-acetoxy-17α-hydroxy-progesterone (XVd) and of the D-homo derivative (XVIIIa or XIXa) obtained from it by saponification. The 16β-isomer (XVd) proved to be different from our 16α-acetoxy-17α-hydroxy-

(8) Turner, *J. Am. Chem. Soc.*, **75**, 3484 (1953).
(9) Inhoffen, Blomeyer, and Brückner, *Chem. Ber.*, **87**, 593 (1954).
(10) Arth, Poos, and Sarett, *J. Am. Chem. Soc.*, **77**, 3834 (1955) (*footnote* N° 9).
(11) Bedoukian, *J. Am. Chem. Soc.*, **67**, 1430 (1945).



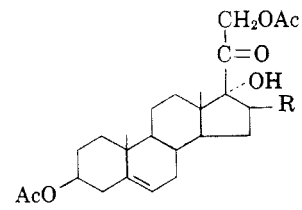
XV

a, R = Br (β) R′ = H
b, R = Br (β) R′ = AcO
c, R = AcO (α) R′ = H
d, R = AcO (β) R′ = H
e, R = AcO (α) R′ = AcO
f, R = AcO (β) R′ = AcO



XVI

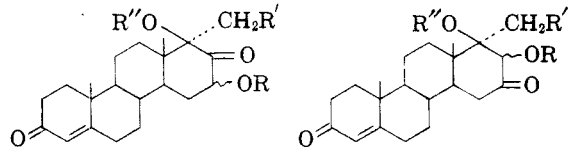
a, R = Br (β) R′ = Ac, R″ = H
b, R = AcO (α) R′ = H, R″ = H
c, R = AcO (α) R′ = H, R″ = AcO



XVII

a, R = Br (β)
b, R = AcO (α)
c, R = AcO(β)

progesterone (XVc) but both substances gave the same D-homo product (XVIIIa or XIXa) on saponification.



XVIII

a, R = H, R′ = H, R″ = H
b, R = Ac, R′ = H, R″ = H
c, R = Ac, R′ = H, R″ = Ac
d, R = H, R′ = OH, R″ = H

XIX

a, R = H, R′ = H, R″ = H
b, R = Ac, R′ = H, R″ = H
c, R = Ac, R′ = H, R″ = Ac
d, R = H, R′ = OH, R″ = H

Inhoffen[9] by selective osmium tetroxide hydroxylation of the Δ^{16}-double bond of $\Delta^{4,16}$-pregnadiene-3,20-dione, prepared a substance to which he assigned the 16α,17α-dihydroxyprogesterone structure. We repeated this experiment and found that it is in fact a D-homo compound identical with that obtained by saponification of the above progesterones (XVc) and (XVd).

The bromohydrin (XVIIa) which resulted from oxide opening of 16α,17α-epoxy-Δ^5-pregnene-3β,21-diol-20-one diacetate[12] with hydrobromic acid, was acetylated with acetic anhydride and *p*-toluenesulfonic acid and without isolation of the acetyl bromohydrin, the crude product was treated with sodium acetate in acetic acid giving Δ^5-pregnene-3β,-16α,17α,21-tetrol-20-one, 3,16,21-triacetate (XVIIb). An alternative procedure was the addition of bromine on the double bond and bromination of the 21 methyl group in the diacetate (Ie), with subsequent treatment with sodium iodide in acetone and acetoxylation by means of potassium acetate.[12,13]

16β-Bromo-Δ^4-pregnene-17α,21-diol-3,20-dione 21-acetate (16β-bromo "S"-21-acetate[12]) was acetylated under the same conditions as used before, and brief treatment with sodium acetate in acetic acid, afforded a mixture of three substances, which were separated by chromatography. The least polar was 16α,17α-epoxy-$\Delta^{3,5}$-pregnadiene-3,21-diol-20-one diacetate (XX). $\Delta^{3,5}$-Pregnadiene-3,16α,17α,21-tetrol-20-one, 3,16,21-triacetate (XVIc) and Δ^4-pregnene-16α,17α,21-triol-3,20-dione 16,21 diacetate (XVe) were isolated from the more polar fractions.

The enol acetate (XX) also was prepared by acetylation of the corresponding Δ^4-3-ketone[2] in the presence of *p*-toluenesulfonic acid and the product proved to be identical with that obtained in the above chromatogram.

The hydroxylation of $\Delta^{4,16}$-pregnadien-21-ol-3,-20-dione acetate[14] with osmium tetroxide and subsequent hydrolysis under mild conditions with sodium sulfite, furnished in low yields the D-homo compound (XVIIId or XIXd). Δ^4-Pregnene-16β,-17α,21-triol-3,20-dione 16,21-diacetate (XVf) was prepared according to Heusler and Wettstein[6] and its alkaline hydrolysis product was identical with the D-homo derivative (XVIIId or XIXd).

The lithium aluminum hydride reduction of the diacetates (Ic) and (Ie) was considered to be of interest, since similar steroidal polyalcohols have been reported to be of biological importance.[15,16] Δ^5-Pregnene-3β,16α,17α,20β-tetrol (XXIa) and the 16β-isomer (XXIb) were prepared and also the corresponding triacetates (XXIc) and (XXId). The lithium aluminum hydride reduction was also carried out with the D-homo derivative (XIa or XIIa) to prove that in the above reductions no D-homo rearrangements had taken place. In this case a different tetrol (XXIIa) was obtained; its triacetate (XXIIb), was prepared and was different from (XXIc or XXId). The hydrogenation of the diacetate (Ie) with Adams catalyst furnished the saturated derivative (XXIII).

In Table I are recorded the molecular rotation

(12) Julian, Meyer, Karpel, and Ryden Waller, *J. Am. Chem. Soc.*, **72**, 5145 (1950).

(13) Rosenkranz, Pataki, Kaufmann, Berlin, and Djerassi, *J. Am. Chem. Soc.*, **72**, 4081 (1950).

(14) Cole and Julian, *J. Org. Chem.*, **19**, 131 (1954).

(15) Hirschmann and Hirschmann, *J. Biol. Chem.*, **157**, 601 (1945).

(16) Hirschmann and Hirschmann, *J. Biol. Chem.*, **184**, 259 (1950).

TABLE I

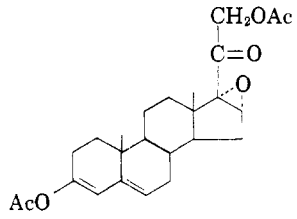
MOLECULAR ROTATION DATA ON STEROIDS

Compounds	$[\alpha]_D$	M_D	ΔM_D
Δ^5-Pregnene-3β,16α,17α-triol-20-one 3,16-diacetate (Ie)	−72	−311	+147
Δ^5-Pregnene-3β,16β,17α-triol-20-one 3,16-diacetate (Ic)	−38	−164	
16α-Acetoxy-17α-hydroxy-progesterone (XVc)	+49	+190	+202
16β-Acetoxy-17α-hydroxy-progesterone (XVd)	+101	+392	
21-Acetate of 16α-acetoxy compound S (XVe)	+44	+196	+246
21-Acetate of 16β-acetoxy compound S (XVf)	+99	+442	
Δ^5-Pregnene-3β,16α,17α,21-tetrol-20-one 3,16,21-triacetate (XVIIb)	−57	−280	+162
Δ^5-Pregnene-3β,16β,17α,21-tetrol-20-one 3,16,21-triacetate (XVIIc)	−24	−118	
Δ^5-Pregnene-3β,16α,17α,20β-tetrol (XXIa)	−89	−311	+216
Δ^5-Pregnene-3β,16β,17α,20β-tetrol (XXIb)	−27	− 95	
Δ^5-Pregnene-3β,16α,17α,20β-tetrol-3,16,20-triacetate (XXIc)	−88	−418	+256
Δ^5-Pregnene-3β,16β,17α-tetrol-3,16,20-triacetate (XXId)	−34	−162	
Δ^5-Pregnene-3β,16α,17α-triol-20-one 3,16,17-triacetate (If)	−74	−351	+114
Δ^5-Pregnene-3β,16β,17α,triol-20-one 3,16,17-triacetate (Id)	−50	−237	

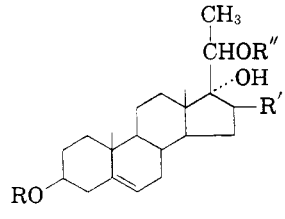
(M_D) values of different pairs of 16α and 16β derivatives. (The rotational values of the 16β isomers are those obtained by Heusler and Wettstein[6].)

It can be seen that in all cases the introduction of the 16α-acetoxy group results in a large negative shift of the M_D, which is in accord with data published earlier.[17]

Acknowledgment. The authors wish to thank Dr. Carl Djerassi of Wayne University for his valuable help in the preparation of this manuscript and Dr. George Rosenkranz of Syntex, S. A., for a generous gift of steroids.

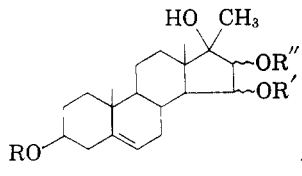


XX



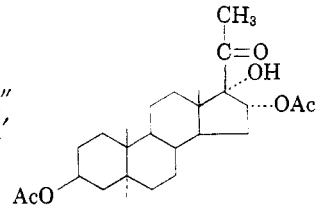
XXI

a, R = H, R′ = OH (α) R″ = H
b, R = H, R′ = OH (β) R″ = H
c, R = Ac, R′ = AcO (α) R″ = Ac
d, R = Ac, R′ = AcO (β) R″ = Ac



XXII

a, R = R′ = R″ = H
b, R = R′ = R″ = Ac



XXIII

EXPERIMENTAL[18]

16β-Bromo-Δ⁵-pregnene-3β,17α-diol-20-one 3-acetate (Ia). A mixture of 16α,17α-epoxy-Δ⁵-pregnen-3β-ol-20-one-acetate (10 g.) in 80 ml. of acetic acid and 10 ml. of a saturated solution of hydrobromic acid in acetic acid was allowed to stand for 30 minutes at room temperature and diluted with ice-water. By crystallization from chloroform-methanol 9.6 g. of the bromohydrin, m.p. 160–162° was obtained. The analytical sample (thick prisms from chloroform-hexane) showed m.p. 174–175°, $[\alpha]_D$ −18°, ν_{max} 1718 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{23}H_{32}BrO_4$: C, 60.92; H, 7.33; Br, 17.62. Found: C, 60.35; H, 7.12; Br, 16.98.

16β-Bromo-Δ⁵-pregnene-3β,17α-diol-20-one diacetate (Ib). To a solution of the bromohydrin (Ia) (8 g.) in 200 ml. of acetic anhydride, 3 g. of *p*-toluenesulfonic acid was added and the mixture was allowed to stand for 20 hours at room temperature. Water then was added and after hydrolysis of the acetic anhydride, the oily precipitate was extracted with ether, and the ethereal extract was washed with sodium carbonate and water. After drying with sodium sulfate, the solution was evaporated *in vacuo*. Crystallization from acetone-hexane furnished 7.5 g., m.p. 150–154° dec. The analytical sample was prepared by repeated crystallization from acetone-hexane, m.p. 156–158° dec. $[\alpha]_D$ −22°, ν_{max} 1736, 1718 cm.$^{-1}$

Anal. Calc'd for $C_{25}H_{35}BrO_5$: C, 60.59; H, 7.11; Br, 16.14. Found: C, 60.84; H, 7.35; Br, 16.28.

Zinc dust reduction of Ib. To a solution of Ib (2 g.) in 120 ml. of ethanol, 10 g. of zinc dust was added. The mixture was refluxed for 3 hours and after filtration of the zinc, the solution was evaporated. Crystallization of the residue from methanol afforded 990 mg. with m.p. 168–172°. The analytical sample showed m.p. 175–177° $[\alpha]_D$ −39°, λ_{max} 238 mμ (log ε 4.08), ν_{max} 1718, 1660 cm.$^{-1}$; it was identified with an authentic specimen by mixture m.p. determination and infrared comparison.

Anal. Calc'd for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.93; H, 9.07.

Potassium carbonate saponification of Ib. A solution of 1 g. of Ib in 40 ml. of methanol was mixed with 1 g. of potas-

(17) Fukushima and Gallagher, *J. Am. Chem. Soc.*, **73**, 196 (1951).

(18) Melting points are uncorrected. Rotations were determined at 20° in chloroform, unless noted otherwise. The infrared spectra were determined in chloroform solution on a Perkin-Elmer model 12C single beam spectrophotometer with sodium chloride prism; we are indebted to Miss Teresa Cárdenas for these measurements and Mrs. P. López for the ultraviolet absorption spectra which were determined in 95% ethanol solution at Syntex, S.A. The elemental analysis were carried on by Dr. Franz Pascher, Bonn, Germany.

sium carbonate in 8 ml. of water and refluxed for 1 hour. Then it was concentrated to a small volume and diluted with water, and the precipitate was extracted with ether and the ethereal extract washed with water. After concentration there crystallized 540 mg. of needles (m.p. 188–189°) which were identified with an authentic specimen of 16α,17α-epoxy-Δ⁵-pregnen-3β-ol-20-one by mixture m.p. and infrared comparison.

Δ⁵-PREGNENE-3β,16α,17α-TRIOL-20-ONE 3,16-DIACETATE (Ie)

(*a*) *With sodium acetate.* A solution in acetic acid (150 ml.) of 2 g. of the acetyl bromohydrin (Ib) and 6 g. of anhydrous sodium acetate was refluxed for 3 hours, then diluted with water, and the precipitate was isolated with ether in the usual way. By crystallization from ether-hexane, long needles (1.32 g.) were formed, m.p. 212°. From the mother liquors 250 mg. were obtained m.p. 204–208°, $[\alpha]_D$ −72°, ν_{max} 1736, 1718, 1700 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39. Found: C, 69.33; H, 8.52.

(*b*) *With silver acetate.* When the above experiment was carried out using silver acetate (2 g.) and heating for 4 hours on the steam-bath with mechanical stirring, 1.69 g. was obtained with m.p. 207–209°. This product was identified with the above substance through a mixture m.p. determination and infrared comparison.

(*c*) *With pyridine.* A solution of Ib (500 mg.) and 2 ml. of pyridine in 20 ml. ethanol was refluxed for 2 hours, then diluted with water and the precipitate was collected and washed with water. Crystallization from acetone-hexane afforded the diacetate (Ie) (220 mg.) m.p. 205–206°.

(*d*) *With collidine.* A solution of Ib (3 g.) in 15 ml. of collidine was refluxed for 1 hour; collidine hydrobromide began to precipitate after a few minutes. It was filtered and washed with ether (yield 1.1 g.) and more ether was added. After successive washings with diluted hydrochloric acid and water the ethereal extract was concentrated, yielding 1.82 g. m.p. 208–209°, $[\alpha]_D$ −71°. This product gave no depression in mixture m.p. with the products obtained by the other methods and the infrared spectrum was identical.

When 300 mg. of the diacetate (Ie) in 5 ml. of anhydrous pyridine was treated with a mixture of 5 ml. of pyridine and 300 mg. of chromium trioxide and allowed to stand at room temperature overnight, the diacetate (Ie) was recovered unchanged.

The diacetate (Ie) also was recovered unchanged after heating for 1 hour at the steam bath with pyridine and acetic anhydride.

Δ⁵-Pregnene-3β,16α,17α-triol-20-one triacetate (If). The diacetate (Ie) (200 mg.) and 100 mg. of *p*-toluenesulfonic acid were dissolved in 8 ml. of acetic anhydride and allowed to stand for 16 hours at room temperature. Addition of water, isolation with ether in the usual way, and crystallization from methanol, furnished 170 mg. of small plates, m.p. 209–210°; the analytical sample showed m.p. 214–216° (from methanol), $[\alpha]_D$ −74°, ν_{max} 1736, 1700 cm.$^{-1}$.

Anal. Calc'd for $C_{27}H_{38}O_7$: C, 68.33; H, 8.07. Found: C, 68.54; H, 8.03.

Δ⁵-Pregnene-3β,16β,17α-triol-20-one 3,16-diacetate (Ic). Following the method described by Heusler and Wettstein[6] we prepared this diacetate in approximately the same yield; in our hands the product exhibited m.p. 174–175°, $[\alpha]_D$ −35°, ν_{max} 1736, 1700 cm.$^{-1}$ and free hydroxyl band (the infrared spectrum proved to be different from that of our 16α isomer (Ie) [reported[6] m.p. 169–171°, $[\alpha]_D^{26}$ −38° ($CHCl_3$)].

Δ⁵-Pregnene-3β,16β,17α-triol-20-one triacetate (Id). The diacetate (Ic) (175 mg.) was acetylated with 50 mg. of *p*-toluenesulfonic acid in 5 ml. of acetic anhydride. By crystallization from ether-hexane 90 mg. were obtained, m.p. 203–204°, ν_{max} 1736, 1700 cm.$^{-1}$ (the mixture m.p. with the 16α isomer (If) gave a depression and the infrared spectra of the two isomers were different.

Anal. Calc'd for $C_{27}H_{38}O_7$: C, 68.33; H, 8.07. Found: C, 68.13; H, 8.00.

D-Homo compound (XIa or XIIa) *from the diacetate* (Ie). (*a*). *With potassium bicarbonate.* A solution containing 1 g. of diacetate (Ie), 1.5 g. of potassium bicarbonate, 100 ml. of methanol, and 20 ml. of water was refluxed for 1 hour, then concentrated to a small volume and diluted with water. The precipitate was collected and washed with water. Crystallization from acetone-ether furnished 250 mg. of small needles, m.p. 240–242°; the analytical sample (from methanol-ether) exhibited m.p. 243–244°, $[\alpha]_D$ −63° ν_{max} 1700 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.13; H, 9.04.

The saponification of the diacetate (Ie) (1.5 g.) with 1 g. of potassium carbonate afforded 490 mg. of D-homo compound (XIa or XIIa), m.p. 233–237°, recrystallized from acetone-ether to m.p. 238–240°.

(*b*). *Hydrolysis with hydrochloric acid.* One gram of the diacetate (Ie) with 8 ml. of hydrochloric acid in 100 ml. of methanol was heated on the water-bath for 2 hours. After concentration to a small volume, the solution was diluted with water and extracted with ethyl acetate. The organic layer was thoroughly washed with water and evaporated. The residue was crystallized from acetone-ether, yielding 470 mg. m.p. 230–235°; several crystallizations from acetone-ether afforded small needles, m.p. 235–238°. This product gave no depression on admixture with the D-homo compounds obtained on alkaline hydrolysis and the infrared spectrum was identical.

Diacetate of the D-homo compound (XIb or XIIb). The D-homo triol (200 mg.) (XIa or XIIa) in 2 ml. of pyridine and 2 ml. of acetic anhydride was heated 1 hour in the steam-bath, and the mixture was diluted with water and the precipitate collected. Crystallization from acetone furnished 100 mg. with m.p. 245–250°. The analytical sample exhibited m.p. 253–254° (from acetone-ether), $[\alpha]_D$ −55°, ν_{max} 1736, 1700 cm.$^{-1}$

Anal. Calc'd for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39. Found: C, 69.53; H, 8.32.

Triacetate of the D-homo compound (XIc or XIIc).[19] The acetylation of the D-homo derivative (XIa or XIIa) (120 mg.) was carried out with 10 ml. of acetic anhydride and 50 mg. of *p*-toluenesulfonic acid (m.p. 195–197° from ether-hexane). The analytical sample exhibited m.p. 203–204° (small brilliant plates), $[\alpha]_D$ −26°, ν_{max} 1736, 1718 cm.$^{-1}$

Anal. Calc'd for $C_{27}H_{38}O_7$: C, 68.33; H, 8.07. Found: C, 68.69; H, 8.36.

The saponification of 1.2 g. of the diacetate (Ic) with 1 g. of potassium carbonate yielded 515 mg., m.p. 233–238° (from methanol-ether). One crystallization from the same solvent, gave m.p. 237–238° $[\alpha]_D$ −65°. This D-homo derivative gave no depression on mixture m.p. with the products obtained by hydrolysis of the diacetate (Ie). The infrared spectra were also identical; [reported[6] m.p. 235–237°, $[\alpha]_D^{26}$ −63° ($CHCl_3$)].

The diacetate prepared by us showed m.p. 250–255° (from acetone-hexane). [Reported[6] m.p. 242–244°, $[\alpha]_D$ −34° ($CHCl_3$)]. [Inhoffen[9] also prepared this diacetate m.p. 232–234°, $[\alpha]_D$ −38.5° ($CHCl_3$)]. This diacetate proved to be identical with that obtained above in all its physical constants.

The same triacetate (XIc or XIIc) was obtained on acetylation of the diacetate (XIb or XIIb).

Saponification of the diacetate (Ie) *in the presence of zinc dust.* To a solution of the diacetate (Ie) (350 mg.) in 50 ml. of methanol, 2 g. of zinc dust and 300 mg. of potassium

(19) K. Heusler and A. Wettstein describe a triacetate obtained by acetylation with acetic anhydride and pyridine of the D-homo derivative (XIa or XIIa) with m.p. 157°

carbonate in 5 ml. of water were added. The mixture was refluxed 2 hours with mechanical stirring and then the zinc was filtered; the solution was concentrated to a small volume and diluted with water. The precipitate was collected and washed with water. Crystallization from methanol-ether yielded 210 mg. with m.p. 238–239°. Repeated crystallization from methanol-ether raised the m.p. to 245–248°, $[\alpha]_D$ −65° (ethanol), ν_{max} (mull) 1700 cm.$^{-1}$ and free hydroxyl band.

The diacetate showed m.p. 172–174° (from ether-hexane), $[\alpha]_D$ −93°, ν_{max} 1736, 1700 cm.$^{-1}$ and free hydroxyl band.

We repeated the selective hydroxylation of the Δ^{16} double bond in $\Delta^{5,16}$-pregnadien-3β-ol-20-one acetate following the method described by Inhoffen.[9] In our hands the hydrolysis product of the osmic ester showed m.p. 242–245°, $[\alpha]_D$ −62° (ethanol). This D-homo triol gave no depression on mixture m.p. and the infrared spectrum was identical with that of the D-homo compound obtained above. The diacetate exhibited m.p. 173–174° and proved to be identical with the above diacetate by mixture m.p. and infrared comparison [reported[9] m.p. 170–171°, $[\alpha]_D$ −98.8 ($CHCl_3$)].

When 400 mg. of the diacetate (Ic) were saponified in the presence of zinc dust, following the same procedure as above only 110 mg. of the D-homo triol (XIa or XIIa), m.p. 239–241° was obtained (identified by mixture m.p. and infrared comparison with an authentic specimen).

17a-Methyl-D-homo-Δ^5-androsten-3β-ol-16,17-dione (XIV). The diacetate (Ie) (1 g.) was refluxed for 3 hours in a solution of 8 g. of potassium hydroxide in 100 ml. of methanol. The solution was concentrated to a small volume, diluted with water, acidified, and extracted. By addition of hexane 530 mg. crystallized, m.p. 170–176°. Several recrystallizations from methanol afforded 390 mg. m.p. 192–193° $[\alpha]_D$ −54°, λ_{max} 276 mμ (log ε 3.97), ν_{max} 1650 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.16; H, 9.15.

Inhoffen's triol[9] (150 mg.) furnished 100 mg. of the diketone, m.p. 190–192°, $[\alpha]_D$ −52°. It proved to be identical with the above product by mixture m.p. and infrared comparison (reported[9] m.p. 186–187°, λ_{max} 277 mμ; ε 9,120). Similar treatment of the diacetate (Ic) or the D-homo compound (XIa or XIIa) yielded diketones identical in all aspects with the above products.

The diacetate (XIIIb) in our hands, exhibited m.p. 204–206°, $[\alpha]_D$ −64°, λ_{max} 244 mμ (log ε 4.08), ν_{max} 1750, 1718, 1675 cm.$^{-1}$ (reported[9] m.p. 197–198°, $[\alpha]_D$ −68.4°, λ_{max} 244 mμ; ε 11,230).

Anal. Calc'd for $C_{25}H_{34}O_5$: C, 72.43; H, 8.27. Found: C, 72.09; H, 8.15.

16β-Bromo-17α-hydroxyprogesterone (XVa).[20] 16α,17α-Epoxyprogesterone (12 g.) was transformed into the bromohydrin with hydrobromic acid in acetic acid as in the preparation of Ia. Crystallization from chloroform-hexane yielded thick prisms (14.5 g.), m.p. 190° dec. The analytical sample (from acetone-hexane) showed m.p. 193–195° (began to decompose at 186°), $[\alpha]_D$ +92°, λ_{max} 240–242, 300 mμ (log ε 4.24, 2.07) ν_{max} 1718, 1700, 1660 cm.$^{-1}$, and free hydroxyl band.

Anal. Calc'd for $C_{21}H_{29}BrO_3$: C, 61.59; H, 7.13. Found: C, 62.05; H, 7.21.

16β-Bromo-$\Delta^{3,5}$-pregnadiene-3,17α-diol-20-one diacetate (XVIa). The bromohydrin (XVa) (10 g.) was acetylated in 130 ml. of acetic anhydride and 2 g. of *p*-toluenesulfonic acid as in the preparation of Ib. Crystallization from ether-hexane furnished 8.9 g. of brilliant prismatic needles, m.p. 134–135° dec. The analytical sample exhibited m.p. 145–148° dec., $[\alpha]_D$ −74°, λ_{max} 234 mμ (log ε 4.30), ν_{max} 1736 cm.$^{-1}$

(20) This product was prepared by Julian[1] but was not characterized.

Anal. Calc'd for $C_{25}H_{33}BrO_5$: C, 60.83; H, 6.73; Br, 16.21. Found: C, 61.08; H, 7.01; Br, 16.22.

$\Delta^{3,5}$-Pregnadiene-3,16α,17α-triol-20-one diacetate (XVIb). The enol-acetate (XVIa) (2 g.) was refluxed with 10 ml. of pyridine in 100 ml. of ethanol for 6 hours. The product was isolated as in the above experiment and recrystallized from acetone-ether, m.p. 195–197°, yield 1.23 g.; the analytical sample showed m.p. 199–200° (small plates from acetone-ether), positive tetranitromethane test, $[\alpha]_D$ −128°, λ_{max} 234 mμ (log ε 4.31), ν_{max} 1736, 1700 cm.$^{-1}$, and free hydroxyl band.

Anal. Calc'd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.81; H, 7.96.

16α-Acetoxy-17α-hydroxyprogesterone (XVc). The enol-acetate (XVIa) (4 g.) was refluxed with 8 g. of anhydrous sodium acetate in 120 ml. of acetic acid for 6 hours, then diluted with water and the precipitate was collected and washed thoroughly with water; crystallization from acetone-hexane afforded 2.9 g. of long prismatic needles, m.p, 174–176°; recrystallization raised the m.p. to 175–177°. $[\alpha]_D$ +49°, λ_{max} 240 mμ (log ε 4.20), ν_{max} 1736, 1700, 1660 cm.$^{-1}$, and free hydroxyl band.

Anal. Calc'd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.31; H, 8.36.

16α-Acetoxy-17α-hydroxyprogesterone (XVc). The enol acetate (XVIb) (800 mg.) and 2 g. of anhydrous sodium acetate in 40 ml. of acetic acid were refluxed for 12 hours. Crystallization from acetone-ether afforded 200 mg., m.p. 171–173° and 200 mg., m.p. 165–168° from the mother liquors. $[\alpha]_D$ +49.6°, λ_{max} 240 mμ (log ε 4.20) identified by the standard methods with the product obtained before.

The hydrolysis of (XVIb) (200 mg.) with 100 mg. of *p*-toluenesulfonic acid in 10 ml. of methanol with refluxing 2 hours followed by addition of water and extraction with ether, furnished 90 mg. of (XVc) m.p. 167–169° (from acetone-ether). Further crystallization raised the m.p. to 175–177°, $[\alpha]_D$ +47° identified also by the standard methods with the products obtained before.

D-Homo compound (XVIIIa or XIXa) *from* (XVc). A mixture of (XVc) (3.4 g.), 100 ml. of methanol, 2 g. of potassium carbonate, and 10 ml. of water was refluxed for 1 hour; the solution was concentrated to a small volume, diluted with water, and extracted with ethyl acetate. The organic layer was washed, dried, and concentrated, and by addition of ether 1.02 g. of small needles crystallized, m.p. 220–222°. Further crystallization from acetone-ether raised the m.p. to 227–228°, $[\alpha]_D$ +86°, λ_{max} 240 mμ (log ε 4.23), ν_{max} 1700, 1660 cm.$^{-1}$, and free hydroxyl band.

Anal. Calc'd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.49; H, 8.65.

The *monoacetate* (XVIIIb or XIXb) was obtained by heating 15 minutes on the steam bath the D-homo compound (XVIIIa or XIXa) (200 mg.) with a mixture of 1 ml. of acetic anhydride and 1 ml. of pyridine. After dilution with water, the precipitate was filtered and crystallized from acetone-ether, yielding 130 mg. m.p. 217–218°, $[\alpha]_D$ +75°, ν_{max} 1730, 1700, 1660 cm.$^{-1}$, and free hydroxyl band.

Anal. Calc'd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.07; H, 8.46.

The *diacetate* (XVIIIc or XIXc) (prepared in the same way, only the heating was prolonged to two hours) exhibited m.p. 200–203° (from acetone-ether), $[\alpha]_D$ +89°, λ_{max} 238 mμ (log ε 4.30), ν_{max} 1736, 1718, 1660 cm.$^{-1}$

Anal. Calc'd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 70.38; H, 7.90.

16β-Acetoxy-17α-hydroxyprogesterone (XVd). This substance was prepared by the method of Heusler and Wettstein[6] with m.p. 185–186° (acetone-hexane), $[\alpha]_D$ +87°, λ_{max} 240 mμ (log ε 4.21), ν_{max} 1736, 1718, 1660 cm.$^{-1}$, and free hydroxyl band. (Reported m.p. 183–184°, $[\alpha]_D$ +101° ($CHCl_3$), λ_{max} 242 mμ (ε 16,600).) M.p. depression on admixture with the 16α hydroxy isomer (XVc) and the infrared spectra are different.

The D-homo product of saponification was obtained by the

method of the Swiss authors[6] and exhibited m.p. 221–223°; it was identified by the standard methods with the D-homo derivative (XVIIIa or XIXa) obtained on saponification of the 16α-hydroxy isomer (XVc).

The product of hydroxylation with osmium tetroxide of $\Delta^{4,16}$-pregnadiene-3,20-dione was prepared following Inhoffen's procedure; it showed m.p. 223–225°, $[\alpha]_D$ +98°, and was identified with the above D-homo derivatives by mixture m.p. and infrared comparison.

16β-Bromo-Δ⁵-pregnene-3β,17α,21-triol-20-one 3,21-diacetate (XVIIa). 16α,17α-Epoxy-Δ⁵-pregnene-3β,21-diol-20-one diacetate[2] (2.73 g.) was transformed into the bromohydrin as before. Crystallization from ether-hexane afforded 2.72 g. of small prisms, m.p. 135–140° dec. The analytical sample exhibited m.p. 173–175° dec. (needles from acetone-hexane), $[\alpha]_D$ −56.7°, ν_{max} 1736 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{25}H_{35}BrO_6$: C, 58.70; H, 6.89; Br, 15.62. Found: C, 58.95; H, 6.88; Br, 15.65.

Δ⁵-Pregnene-3β,16α,17α,21-tetrol-20-one 3,16,21-triacetate (XVIIb). (*a*) *From* (XVIIa). The bromohydrin (XVIIa) (2.1 g.) and 100 mg. of *p*-toluenesulfonic acid were dissolved in 40 ml. of acetic anhydride. The mixture was heated 2 hours at 70° and left at room temperature overnight and then was poured into water, extracted with ether, and the ethereal extract was washed with sodium carbonate solution and water. The oily acetyl bromohydrin and 5 g. of anhydrous sodium acetate were dissolved in 50 ml. of acetic acid and refluxed 1.5 hours. The mixture then was diluted with water and extracted with ether and the ethereal extract was washed with sodium carbonate and water. The residue obtained after evaporation, crystallized from benzene-hexane, yielding 625 mg., m.p. 208–210°. The analytical sample exhibited m.p. 210–212° (long needles from methanol), $[\alpha]_D$ −57°, ν_{max} 1736 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{27}H_{38}O_8$: C, 66.10; H, 7.88. Found: C, 66.18; H, 7.86.

(*b*) *From* Ie. The diacetate (Ie) (1 g.) in 30 ml. of glacial acetic acid with a few drops of saturated solution of hydrobromic acid in acetic acid was brominated by adding dropwise a solution of 700 mg. of bromine in 10 ml. of acetic acid. The solution was left standing for 1 hour at room temperature and diluted with water and extracted with ether. The residue, left after removal of the solvent, and 1.1 g. of sodium iodide were dissolved in acetone (100 ml.) and refluxed for 1 hour; then 10 g. of potassium acetate (freshly prepared by neutralization of potassium bicarbonate with acetic acid) was added and the refluxing was continued 6 hours. The mixture was diluted with water and extracted with ether. Crystallization from ether-hexane furnished needles (400 mg.) m.p. 194–196°: several crystallizations from methanol raised the m.p. to 208–210°, $[\alpha]_D$ −57°, identified with the above product by the standard methods.

Δ³,⁵-Pregnadiene-3,16α,17α,21-tetrol-20-one 3,16,21-triacetate (XVIc), *Δ⁴-pregnene-16α,17α,21-triol-3,20-dione 16,21-diacetate* (XVe) *and 16α,17α-epoxy-Δ³,⁵-pregnadiene-3,21-diol-20-one diacetate* (XX). 16β-Bromo-compound "S"-acetate[21] (XVb) (1.8 g.) was acetylated in 100 ml. of acetic anhydride with 200 mg. of *p*-toluenesulfonic acid under the same conditions used for the bromohydrin (XVIIa). The oily residue was acetoxylated also in the same way as used for (XVIIa). The oily product was chromatographed on 50 g. of alumina (previously washed with ethyl acetate). The fractions which were eluted with benzene-hexane 1:1, with benzene-ether 1:1, 1:2, 1:3, and with ether, crystallized.

The fractions eluted with benzene-hexane 1:1 were combined and recrystallized from acetone-hexane, yielding 200 mg. of 16α,17α-epoxy-Δ³,⁵-pregnadiene-3,21-diol-20-dione diacetate (XX) m.p. 183–185°, positive test with tetranitro methane, $[\alpha]_D$ −33°, λ_{max} 234 mμ (log ε 4.26), ν_{max} 1736, 1718 cm.$^{-1}$.

(21) Obtained by oxide opening of 16α-17α-epoxy-21-acetoxy progesterone (see ref. 12).

Anal. Calc'd for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C, 69.92; H, 7.61.

This substance was identical with a product prepared by acetylation (in the presence of *p*-toluenesulfonic acid) of 16α,17α-epoxy-21-acetoxy-progesterone[2] (250 mg.). Crystallization from acetone-hexane furnished 140 mg. of needles, m.p. 184–186°, $[\alpha]_D$ −36°.

The crystalline fractions eluted with benzene-ether 1:1, 1:2, and 1:3 were combined and recrystallized from acetone-hexane, yielding XVIc in small prisms, m.p. 170–172° (80 mg.) positive test with tetranitromethane, $[\alpha]_D$ −93°, λ_{max} 234 mμ (log ε 4.29), ν_{max} 1736 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{27}H_{36}O_8$: C, 66.37; H, 7.43. Found: C, 66.10; H, 7.44.

The fractions eluted with ether, after several recrystallizations from acetone-ether, yielded XVe in small needles (40 mg.) m.p. 200–202°, $[\alpha]_D$ +44°, λ_{max} 240 mμ (log ε 4.19), ν_{max} 1736, 1700, 1660 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{25}H_{34}O_7$: C, 67.24; H, 7.67. Found: C, 67.27; H, 7.74.

D-Homo compound (XVIIId or XIXd) *prepared by selective hydroxylation of Δ⁴,¹⁶-pregnadien-21-ol-3,20-dione-acetate*[22] *with osmium tetroxide.* Δ⁴,¹⁶-Pregnadien-21-ol-3,20-dione acetate (3.48 g.) was dissolved in 400 ml. of anhydrous ether and 2.4 g. of osmium tetroxide was added. The solution was permitted to stand for 4 days, then the black precipitate (5 g.) was collected and dissolved in 300 ml. of ethanol followed by the addition of 30 g. of sodium sulfite in 300 ml. of water. Nitrogen was bubbled in and the flask was stoppered; the mixture was agitated 40 hours at room temperature, filtered through Celite, diluted with water, and extracted 3 times with ethyl acetate. The combined extracts were washed with water, dried, and evaporated. The oily residue crystallized on addition of ether, 150 mg., m.p. 218–220°. The analytical sample exhibited m.p. 228–230° (small prisms from methanol-ether), $[\alpha]_D$ +82° (ethanol), λ_{max} 240 mμ (log ε 4.23), ν_{max} 1718, 1670 cm.$^{-1}$ and free hydroxyl band.

16β-Acetoxy-compound S-acetate (XVf) was prepared using the method reported by Heusler and Wettstein,[6] m.p. 168–170°, $[\alpha]_D$ +101°, λ_{max} 240, 294 mμ (log ε 4.24, 2.24), ν_{max} 1736, 1700, 1660 cm.$^{-1}$, and free hydroxyl band. (Reported m.p. 167–168°, $[\alpha]_D$ +99° ($CHCl_3$), λ_{max} 241 mμ; ε 17,000.)

The saponification of this substance was also carried out under the conditions described[6] and the product had m.p. 227–229°, $[\alpha]_D$ +88° (ethanol) [reported m.p. 225–227° dec., $[\alpha]_D$ +101° (chloroform-ethanol), λ_{max} 241 mμ (ε 16,800)]. This substance was identified with the hydroxylation product of Δ⁴,¹⁶-pregnadien-21-ol-3,20-dione-acetate by the standard methods.

Δ⁵-Pregnene-3β,16α,17α,20β-tetrol (XXIa). The diacetate (Ie) (1.5 g.) in 40 ml. of anhydrous tetrahydrofuran was added slowly to a slurry of lithium aluminum hydride (500 mg.) in 30 ml. of the same solvent. When the addition was completed, the mixture was refluxed 30 minutes. The excess of lithium aluminum hydride, was decomposed with a few drops of ethyl acetate and 5 ml. of a saturated solution of sodium sulfate were added followed by anhydrous sodium sulfate. The solution was filtered and evaporated. Crystallization from acetone-ether afforded 690 mg. m.p. 267–270°. The analytical sample showed m.p. 298–300°, $[\alpha]_D$ −89° (ethanol).

Anal. Calc'd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 72.53; H, 9.83.

The *triacetate* (XXIc) showed m.p. 212–213° (from acetone-hexane fluffy needles), $[\alpha]_D$ −88°, ν_{max} 1736 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Found: C, 68.33; H, 8.83.

Δ⁵-Pregnene-3β,16β,17α,20β-tetrol (XXIb). The reduction

(22) This substance was prepared by the method of Cole and Julian (Ref. 14).

of 500 mg. of Ic in 50 ml. of tetrahydrofuran with 400 mg. of lithium aluminum hydride was carried out in the same way as above. Crystallization from acetone-ether, yielded 200 mg. m.p. 245–248°, $[\alpha]_D$ −27° (ethanol).

Anal. Calc'd for $C_{21}H_{34}O_4.H_2O$: C, 68.44; H, 9.85. Found: C, 68.79; H, 9.83.

The *triacetate* (XXId) exhibited m.p. 228° (small prisms from acetone-hexane), $[\alpha]_D$ −34°, ν_{max} 1736 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Found: C, 67.52; H, 8.79.

17a-Methyl-D-homo-Δ⁵-androstene-3β,16ζ,17aζ-tetrol (XXIIa). The D-homocompound (XIa or XIIa) (700 mg.) was reduced with lithium aluminum hydride (300 mg.) in 100 ml. of tetrahydrofuran as above. Crystallization from methanol-ether furnished 325 mg. of prisms, m.p. 300–302°. The analytical sample showed m.p. 310–312° (methanol-ether), $[\alpha]_D$ −50° (ethanol).

Anal. Calc'd for $C_{27}H_{40}O_7$: C, 71.96; H, 9.78. Found: C, 71.77; H, 9.89.

The *triacetate* (XXIIb) showed m.p. 231–232° (acetone-ether), $[\alpha]_D$ −55°, ν_{max} 1736 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{27}H_{46}O_7$: C, 68.04; H, 8.46. Found: C, 67.93; H, 8.45.

Allopregnane-3β,16α,17α-triol-20-one 3,16-diacetate (XXIII). The diacetate (Ie) (2 g.) in 100 ml. of glacial acetic acid was hydrogenated in the presence of 200 mg. of Adams catalyst (prehydrogenated) until 1 mole of hydrogen was absorbed. The catalyst was filtered and the solution was diluted with water and extracted with ether.

Crystallization from ether-hexane furnished 1.15 g. of needles, m.p. 159–162°. The analytical sample showed m.p. 161–163° (from acetone-hexane), $[\alpha]_D$ −33°, ν_{max} 1736, 1718, 1700 cm.$^{-1}$ and free hydroxyl band.

Anal. Calc'd for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81. Found: C, 69.47; H, 8.88.

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