aqueous methanol was refluxed for 18 hours. The cloudy solution was filtered while hot, then concentrated until turbid, cooled, 50 ml. of water added, and the solids collected by filtration; yield 1.95 g., $\lambda_{max.}^{EtOH}$ 19,680 at 240 mμ. The infrared spectrum indicated the loss of the 21-acetate and substantial replacement of hydrazone groups by oxime group.

Anal. Calcd. for $C_{21}H_{30}O_5N_2$: N, 7.18. Found: N, 8.61.

(B).—A mixture of 9.18 g. of cortisone acetate 3-monosemicarbazone, 2.78 g. of hydroxylamine hydrochloride, 3.28 g. of sodium acetate, 45 ml. of acetic acid and 275 ml. of methanol was refluxed for 15 hours. The methanol was removed by distillation, the residue poured into water and the precipitated solid removed by filtration; yield 6.8 g. (72%), m.p. 165–175° dec., $\lambda_{max.}^{EtOH}$ 20,900 at 240 mμ. Its infrared spectrum was identical with that of authentic cortisone acetate 3,20-bis-oxime (IIIc).

Anal. Calcd. for $C_{23}H_{26}O_6N_2$: N, 6.49. Found: N, 6.76.

BLOOMFIELD, NEW JERSEY

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

Steroids. LXXVII.[1] Synthesis and Reactions of 16β-Oxygenated Pregnan-20-one Derivatives

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Oxidation of $\Delta^{5,16}$-pregnadien-3β-ol-20-one acetate (I) with alkaline hydrogen peroxide has been shown to give 16β,17β-oxido-17-iso-Δ^5-pregnen-3β-ol-20-one acetate (IIIa) in low yield in addition to 16α,17α-oxido-Δ^5-pregnen-3β-ol-20-one acetate (II). The β-oxide IIIa adds hydrogen bromide with the formation of 17α-bromo-Δ^5-pregnene-3β,16β-diol-20-one 3-monoacetate (V), identical with the product obtained from $\Delta^{5,16}$-pregnadien-3β-ol-20-one acetate (I) by successive addition of bromine to the Δ^5-double bond, addition of hypobromous acid to the Δ^{16}-double bond and treatment with sodium iodide (I → VI → VII → V). The bromohydrin V on treatment with potassium hydroxide and reacetylation gives back the β-oxide IIIa, whereas catalytic hydrogenation over a palladium–charcoal catalyst produces Δ^5-pregnene-3β,16β-diol-20-one 3-monoacetate (VIIIa), which can be dehydrated to $\Delta^{5,16}$-pregnadien-3β-ol-20-one (I). Lithium aluminum hydride reduction and subsequent acetylation of Δ^5-pregnene-3β,16β-diol-20-one 3-monoacetate (VIIIa) gives Δ^5-pregnene-3β,16β,20β-triol triacetate (IXb), identical with the acetylated lithium aluminum hydride reduction product of the "diosone" XI derived from diosgenin X. Catalytic hydrogenation of the triacetate IXb yields the known allopregnane-3β,16β,20β-triol triacetate (XII) and the stereochemical configuration of the various 16β-oxygenated pregnan-20-one derivatives is therefore fixed.

16β-Hydroxylated pregnan-20-one derivatives such as Δ^5-pregnene-3β,16β-diol-20-one 3-monoacetate (VIIIa) are of interest since their 16-γ-methyl-δ-acetoxyvalerates are the so-called "diosones" (*e.g.*, XI), which are important intermediates in the industrial conversion of steroidal sapogenins (*e.g.*, diosgenin, X) to the adrenal and the sex hormones. In contrast to the 16α-hydroxypregnan-20-ones which may be obtained by several chemical methods[3] as well as by microbiological means,[4] only one synthetic route to 16β-hydroxypregnan-20-ones (unsubstituted at C-17) has been described.[5] This route proceeds from the corresponding Δ^{16}-pregnen-20-one by addition of hypobromous acid to yield the 16β-hydroxy-17α-bromopregnan-20-one, followed by debromination with zinc.[5,6] The stereochemistry at C-16 and C-17 of the resulting 16β-hydroxypregnan-20-one was not, however, rigidly established.

We first became interested in this subject when investigating the oxidation of $\Delta^{5,16}$-pregnadien-3β-ol-20-one acetate (I) with alkaline hydrogen peroxide. This reaction is known[7] to produce an oxide in about 95% yield, shown to be the 16α,17α-oxide II by its subsequent reactions. The formation of this isomer is in accord with the known predominant α-attack of steroidal 16(17)- and 17(20)-double bonds.[8] We have now isolated a by-product in 1–2% yield, for which the 16β,17β-oxide structure IIIa (16β,17β-oxido-17-iso-Δ^5-pregnen-3β-ol-20-one acetate) was first proposed on the basis of the elemental analysis, the infrared spectrum and the comparatively high negative rotation which was expected for a 17-isopregnane derivative.[8a] This formulation for the substance was subsequently proved to be correct through its further transformations (*vide infra*). Although by-products derived by β-attack of 17-ketoandrostanes (containing a 17-("20")-double bond) have been isolated,[9] the above appears to be the first recorded instance of the formation of a product derived by β-attack of a steroid with a 16(17)-double bond.

The reaction of 16α,17α-oxido-Δ^5-pregnen-3β-ol-20-one acetate (II) with hydrogen bromide in acetic acid is known[10] to yield 16β-bromo-Δ^5-pregnene-3β,17α-diol-20-one 3-monoacetate (IV) by opening of the oxide ring in such wise as to produce the new substituents in the quasi-axial configura-

(1) Paper LXXVI, E. Batres, R. Gómez, G. Rosenkranz and F. Sondheimer, *J. Org. Chem.*, **21**, 240 (1956).

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(3) H. Hirschmann, F. B. Hirschmann and J. W. Corcoran, *Federation Proc.*, **12**, 218 (1953); *J. Org. Chem.*, **20**, 572 (1955); H. Hirschmann, F. B. Hirschmann and G. L. Farrel, THIS JOURNAL, **75**, 4862 (1953); W. Cole and P. L. Julian, *J. Org. Chem.*, **19**, 131 (1954); S. Bernstein, M. Heller and S. M. Stolar, THIS JOURNAL, **76**, 5674 (1954).

(4) D. Perlman, E. Titus and J. Fried, *ibid.*, **74**, 2126 (1952); E. Vischer, J. Schmidlin and A. Wettstein, *Helv. Chim. Acta*, **37**, 321 (1954).

(5) G. Gansau, Doctorate Thesis, Technische Universität, Berlin-Charlottenburg, 1952. ADDED IN PROOF.—S. Bernstein, M. Heller and S. M. Stolar (THIS JOURNAL, **77**, 5327 (1955)) have now described another route to such compounds.

(6) In addition, syntheses of 16β,17α-dihydroxypregnan-20-ones have been described recently (a) by H. H. Inhoffen, F. Blomeyer and K. Brückner [*Ber.*, **87**, 593 (1954)] and (b) by K. Heusler and A. Wettstein [*ibid.*, **87**, 1301 (1954)].

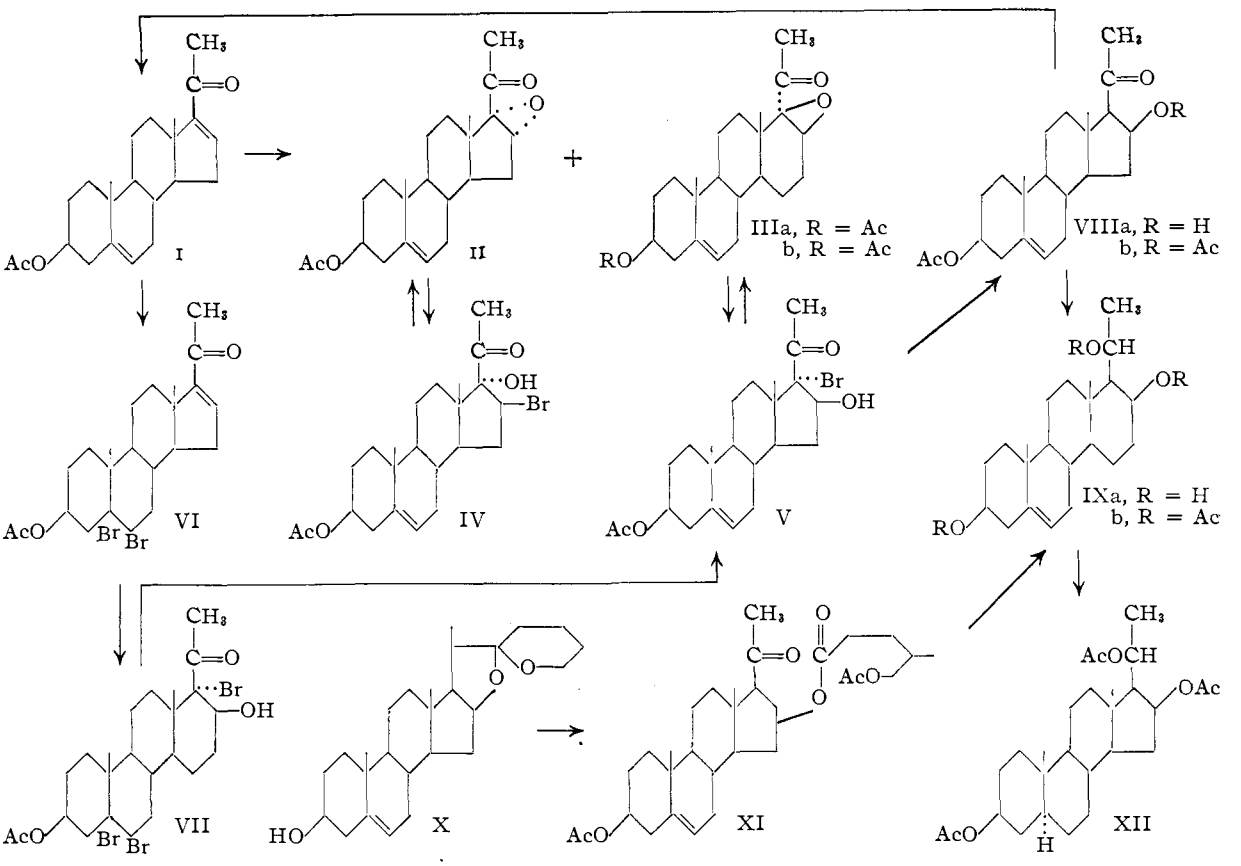
(7) P. L. Julian, E. W. Meyer, W. J. Karpel and I. R. Waller, THIS JOURNAL, **72**, 5145 (1950).

(8) L. F. Fieser, *Experientia*, **6**, 312 (1950).

(8a) *Cf.* A. Butenandt and L. Mamoli, *Ber.*, **68**, 1847 (1935); A. Butenandt and G. Fleischer, *ibid.*, **70**, 96 (1937).

(9) L. Ruzicka and H. Kägi, *Helv. Chim. Acta*, **19**, 842 (1936); K. Miescher and W. Klarer, *ibid.*, **22**, 962 (1939).

(10) *Cf.* H. J. Ringold, B. Löken, G. Rosenkranz and F. Sondheimer THIS JOURNAL, **78**, 816 (1956).



tion. The 16β,17β-oxide IIIa has now been shown also to produce a bromohydrin with hydrogen bromide in acetic acid, to which we similarly assign the structure 17α-bromo-Δ⁵-pregnene-3β,-16β-diol-20-one 3-monoacetate (V) with the substituents at C-16 and C-17 in the quasi-axial configuration. Whereas we have found the 16β-bromo-17α-hydroxy compound IV to be reconverted readily to the α-oxide II on being heated with pyridine at 90°, the 16β-hydroxy-17α-bromo compound V was recovered unchanged under these conditions. By heating with potassium hydroxide in aqueous methanol, however, the bromohydrin V smoothly lost the elements of hydrogen bromide and produced 16β,17β-oxido-Δ⁵-isopregnen-3β-ol-20-one (IIIb); on acetylation the corresponding acetate IIIa was obtained from which the bromohydrin V had been derived.

Gansau[5] has shown that the reaction of Δ⁴,¹⁶-pregnadiene-3,20-dione with N-bromoacetamide in aqueous acetone results in the addition of hypobromous acid to the Δ¹⁶-double bond with formation of a bromohydrin to which the structure 17α-bromo-Δ⁴-pregnen-16β-ol-3,20-dione was assigned. The corresponding reaction with Δ⁵,¹⁶-pregnadien-3β-ol-20-one acetate (I) required the protection of the Δ⁵-double bond as the 5,6-dibromide VI,[6a] which with N-bromoacetamide in aqueous acetone smoothly produced 5,6,17-tribromopregnane-3β,-16β-diol-20-one 3-monoacetate (VII). The Δ⁵-double bond was regenerated by treatment of the last-mentioned substance with sodium iodide in acetone. This procedure yielded 17α-bromo-Δ⁵-pregnene-3β,16β-diol-20-one 3-monoacetate (V), which proved to be identical in every respect with the bromohydrin V derived from the 16β,17β-oxide IIIa.

In order to obtain Δ⁵-pregnene-3β,16β-diol-20-one 3-monoacetate (VIIIa) it was necessary to remove the bromo grouping from the bromohydrin V. This debromination was best effected through hydrogenation in methanol solution over a 5% palladium–charcoal catalyst in the presence of ammonium acetate (to prevent reduction of the Δ⁵-double bond), as had been the corresponding 16β-bromo-17α-hydroxy isomer IV.[10] By this means Δ⁵-pregnene-3β,16β-diol-20-one 3-monoacetate (VIIIa), further characterized as the diacetate VIIIb, was obtained in 92% yield. That no gross rearrangement had occurred in the reduction step was shown through chromatography of the diacetate VIIIb on alkaline alumina, when the expected β-elimination took place[11] and Δ⁵,¹⁶-pregnadien-3β-ol-20-one acetate (I) was produced. The corresponding conversion of the 3-monoacetate VIIIb to I did not occur with alumina, but could be brought about through heating with acetic acid and hydrochloric acid.

The debromination of 17α-bromo-Δ⁴-pregnen-16β-ol-3,20-dione to Δ⁴-pregnen-16β-ol-3,20-dione (corresponding to our conversion of V to VIIIa) had been carried out by Gansau[5] in about 20% yield by means of zinc dust.[12] The 16β-hydroxypregnane rather than the 16β-hydroxyisopregnane

(11) *Cf.* G. P. Mueller, R. E. Stobaugh and R. S. Winniford, THIS JOURNAL, **75**, 4888 (1953).

(12) In accord with this, we have found the reduction of V to VIIIa with zinc dust to proceed only in low yield.

structure was favored by the German author on the basis of molecular rotation differences and the assumption was made that no inversion occurred in the reduction step. Since the "vicinal action" of the 16β-hydroxy group is unknown and the assumption regarding the retention of configuration is not necessarily justified, we felt it desirable to provide additional evidence for the stereochemistry assigned to the debromination product VIIIa through its identification with a known compound.[13] This was achieved through reduction of VIIIa with lithium aluminum hydride. The Δ⁵-pregnene-3,16,20-triol thus obtained gave a triacetate which was identical with a sample prepared by the lithium aluminum hydride reduction and subsequent acetylation of Δ⁵-pregnene-3β,16β-diol-20-one 3-acetate 16-γ-methyl-δ-acetoxyvalerate ("diosone") (XI).[14] Moreover, catalytic hydrogenation of the Δ⁵-double bond of the triacetate produced a compound, identified with a substance shown by Hirschmann, *et al.*,[15] to be allopregnane-3β,16β,20β-triol triacetate (XII). The triol obtained by the lithium aluminum hydride reduction of VIIIa and XI is therefore Δ⁵-pregnene-3β,16β,20β-triol (IXa) and the Δ⁵-pregnene-3β,16β-diol-20-one 3-monoacetate structure for VIIIa is rigidly established. This in turn provides final evidence for the 16β-hydroxy-17α-bromo structure for the bromohydrin V and the 16β,17β-oxido structure for the oxide IIIa.

Acknowledgments.—We would like to express our thanks to Dr. H. Hirschmann of the Department of Medicine, Western Reserve University, for interesting correspondence and for carrying out the identification of our allopregnane-3β,16β,20β-triol triacetate (XII) and to Dr. G. Gansau for providing us with a copy of the thesis mentioned in footnote 5.

Experimental[16]

16β,17β-Oxido-17-iso-Δ⁵-pregnen-3β-ol-20-one Acetate (IIIa). (a) As By-product in the Hydrogen Peroxide Oxidation of Δ⁵,¹⁶-Pregnadien-3β-ol-20-one Acetate (I).—The oxidation of Δ⁵,¹⁶-pregnadien-3β-ol-20-one acetate (I) with alkaline hydrogen peroxide was carried out as described by Julian, *et al.*[5] The total product was acetylated (acetic anhydride–pyridine, 1 hour at 90°) and the isolated product was triturated with hexane at room temperature. The insoluble material, obtained in 90–95% yield, was almost pure 16α,17α-oxido-Δ⁵-pregnen-3β-ol-20-one acetate (II) with m.p. 156–158°, $[\alpha]_D$ −10°.

The hexane washings were evaporated to small volume and allowed to stand for several weeks at room temperature. In this way a precipitate with m.p. 130–134°, $[\alpha]_D$ −45°, separated, which was chromatographed on acid-washed alumina. Hexane eluted first some of the α-oxide II and then material with m.p. *ca.* 140°. The latter was rechromatographed on alumina and the fractions with m.p. above 165°, eluted with hexane, were crystallized from methylene chloride–methanol. This procedure produced in 1–2% yield the β-oxide IIIa with m.p. 176–178°, $[\alpha]_D$ −108°, no high-intensity absorption in the ultraviolet.

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 74.00; H, 8.66.

(b) **From 17α-Bromo-Δ⁵-pregnene-3β,16β-diol-20-one 3-Monoacetate (V).**—A solution of 3.5 g. of potassium hydroxide in 5 cc. of water and 20 cc. of methanol was added to a suspension of 10 g. of the bromohydrin V (described below) in 100 cc. of methanol and the mixture was boiled under reflux for 1 hour. Water was added and the product was isolated with methylene chloride in the usual way. Crystallization from methylene chloride–methanol furnished 6.1 g. of the β-oxide IIIb with m.p. 143–145°, $[\alpha]_D$ −110°. Acetylation of this material with pyridine and acetic anhydride (1 hour at 90°) and subsequent crystallization from methylene chloride–methanol produced 6.4 g. (78% overall) of the β-oxide acetate IIIa with m.p. 175–177°, $[\alpha]_D$ −109°. The m.p. was undepressed on admixture with a sample prepared by method a.

16β,17β-Oxido-17-iso-Δ⁵-pregnen-3β-ol-20-one (IIIb).—A solution containing 2 g. of the β-oxide acetate IIIa (obtained by method a), 0.5 g. of potassium hydroxide, 1 cc. of water and 25 cc. of methanol was boiled under reflux for 1 hour. Acidification with acetic acid, evaporation to small volume and addition of water gave a precipitate which on crystallization from methylene chloride–methanol yielded 1.62 g. (91%) of the β-oxide IIIb with m.p. 147–148°, $[\alpha]_D$ −112°. The m.p. was undepressed on admixture with the sample of IIIb described above, obtained by base treatment of the bromohydrin V.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.37; H, 9.13.

5,6,17-Tribromopregnane-3β,16β-diol-20-one 3-Monoacetate (VII).—Δ⁵,¹⁶-Pregnadien-3β-ol-20-one acetate (I) was converted to the 5,6-dibromide VI (m.p. 122–124°, $[\alpha]_D$ −52°), as described by Inhoffen, *et al.*[6a] N-Bromoacetamide (170 g., freshly crystallized from chloroform) was added to a stirred solution of 170 g. of the dibromide VI in 7.2 l. of acetone and 720 cc. of water at room temperature. The resulting clear solution was allowed to stand for 16 hours, another 50 g. of N-bromoacetamide was added and the solution was allowed to stand another 24 hours. At this stage an aliquot on being worked up no longer showed any high intensity absorption in the ultraviolet. Water (15 l.) was therefore added and the mixture was extracted several times with methylene chloride. The organic extract was washed with water, dried and evaporated almost to dryness under reduced pressure. Addition of methanol and cooling produced 84 g. (42%) of the tribromo compound VII with m.p. 151–153°. A further purified sample showed m.p. 156–157.5°, $[\alpha]_D$ −42°, no high-intensity absorption in the ultraviolet.

Anal. Calcd. for $C_{23}H_{35}O_3Br_3$: C, 45.05; H, 5.42; Br, 39.09. Found: C, 45.01; H, 5.70; Br, 38.93.

17α-Bromo-Δ⁵-pregnene-3β,16β-diol-20-one 3-Monoacetate (V). (a) From 5,6,17-Tribromopregnane-3β,16β-diol-20-one 3-Monoacetate (VII).—Sodium iodide (56 g.) was added to a stirred suspension of 41.5 g. of the tribromo compound VII in 500 cc. of acetone, at room temperature. Stirring was continued for another 15 minutes and the mixture was then set aside overnight. An aqueous concentrated sodium thiosulfate solution was added until disappearance of the brown iodine color. The clear almost colorless solution was poured into 2.5 l. of water, whereby an oil separated which soon solidified. The precipitate was collected, dried and crystallized from aqueous methanol. In this way 26.8 g. (87%) of the bromohydrin V with m.p. 156–158° was obtained. A further purified specimen showed m.p. 158–159°, $[\alpha]_D$ −44°.

Anal. Calcd. for $C_{23}H_{35}O_4Br$: C, 60.93; H, 7.33; Br, 17.62. Found: C, 60.91; H, 7.38; Br, 17.55.

(b) **From 16β,17β-Oxido-17-iso-Δ⁵-pregnen-3β-ol-20-one Acetate (IIIa).**—Glacial acetic acid (15 cc.) was saturated

(13) An indication that the debromination product VIIIa had the 16β-hydroxypregnane structure as has the "diosone" XI (*cf.* ref. 15) was provided by the fact that VIIIa and its diacetate VIIIb underwent dehydration with hot aqueous acetic acid at almost identical rates as did the "diosone" XI (see Experimental Section).

(14) The triacetate is probably also identical with the Δ⁵-pregnene-3,16,20-triol triacetate obtained by R. E. Marker, D. L. Turner, R. B. Wagner, P. R. Ulshafer, H. M. Crooks and E. L. Wittle, THIS JOURNAL, **63**, 774 (1941)] by Meerwein-Ponndorf reduction and subsequent acetylation of the "diosone" XI.

(15) H. Hirschmann, F. B. Hirschmann and M. A. Daus, *J. Biol. Chem.*, **178**, 751 (1949). The substance had been obtained by these workers both by a repetition of Marker's degradation of tigogenin, involving preparation of the "diosone," catalytic hydrogenation over a platinum catalyst, saponification and acetylation (Marker, *et al.*, ref. 14) and also by a series of reactions involving the urinary steroid allopregnane-3β,16α,20β-triol.

(16) Melting points are uncorrected. Unless noted otherwise, rotations were determined at 20° in chloroform and ultraviolet absorption spectra in 95% ethanol solution. We are grateful to Mrs. P. López and Miss M. T. Cárdenas for these measurements and to Mrs. A. González for the microanalyses.

with hydrogen bromide at 0° and this solution was added to a stirred suspension of 10 g. of the β-oxide IIIa in 65 cc. of glacial acetic acid. At the end of the addition the temperature had reached 33° and was kept there by slight warming for 40 minutes. The solution was then allowed to stand at room temperature for 1 hour and was poured into 1 l. of iced water. The precipitate was collected, washed with a little 80% aqueous methanol (to remove some oil adhering to the crystals) and dried. Crystallization from aqueous methanol furnished 7.5 g. (62%) of the bromohydrin V with m.p. 154–156°, $[\alpha]_D$ −43°. The m.p. was undepressed on admixture with a specimen prepared by method a.

Δ⁵-Pregnene-3β,16β-diol-20-one 3-Monoacetate (VIIIa) from 17α-Bromo-Δ⁵-pregnene-3β,16β-diol-20-one 3-Monoacetate (V). (a) **By Catalytic Hydrogenation.**—A mixture containing 11 g. of the bromohydrin V and 2.8 g. of ammonium acetate in 250 cc. of methanol was shaken in hydrogen over 5 g. of a 5% palladium–charcoal catalyst at 22° and 2 atmospheres pressure. After 30 minutes, the uptake of hydrogen ceased and the catalyst was removed and washed with 50 cc. of methanol. Distilled water (100 cc.) was gradually added to the filtrate, which was then cooled in ice. This procedure caused the precipitation of 8.4 g. (92.5%) of the diol monoacetate VIIIa with m.p. 156–158°. Crystallization from methylene chloride–hexane yielded the analytical specimen with m.p. 160–161°, $[\alpha]_D$ +24°, $[\alpha]_D$ −25° (dioxane).

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.63; H, 9.19.

(b) **By Zinc Reduction.**—Zinc dust (25 g.) was added during 1 hour to a stirred solution of 10 g. of the bromohydrin V and 25 g. of sodium acetate in 600 cc. of glacial acetic acid, the internal temperature being maintained between 15 and 19° by occasional cooling. The mixture was then stirred at room temperature for a further 2 hours, the excess metal was removed and the filtrate was poured into 6 l. of iced water. The mixture was left at 0° overnight and the precipitate was then collected, washed well with water and dried. Successive crystallizations from aqueous methanol and from methylene chloride–hexane furnished 2.6 g. (31%) of the diol monoacetate VIIIa with m.p. 158–160°, $[\alpha]_D$ +25°, $[\alpha]_D$ −24° (dioxane). The m.p. was raised to 160–161° on further crystallization and was undepressed on admixture with a sample prepared by method a.

Δ⁵-Pregnene-3β,16β-diol-20-one Diacetate (VIIIb).—The monoacetate VIIIa was acetylated with acetic anhydride and pyridine for 24 hours at room temperature, in the usual way. After being crystallized from methylene chloride–methanol, the diacetate VIIIb showed m.p. 165–166°, $[\alpha]_D$ −26°, $[\alpha]_D$ −24° (dioxane).

Anal. Calcd. for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71. Found: C, 72.17; H, 8.88.

Δ⁵,¹⁶-Pregnadien-3β-ol-20-one Acetate (I) from Δ⁵-Pregnene-3β,16β-diol-20-one 3-Monoacetate (VIIIa) and Diacetate (VIIIb) (with O. Mancera).—The diacetate VIIIb (0.5 g.) was slowly chromatographed on 50 g. of alkaline alumina. The solid fractions eluted with hexane–benzene and benzene weighed 0.42 g. and showed λ_{max} 240 mμ, log ε 3.90. Crystallization from acetone–hexane furnished 0.28 g. (65%) of Δ⁵,¹⁶-pregnadien-3β-ol-20-one acetate (I) with m.p. 173–175°, $[\alpha]_D$ −38°, λ_{max} 240 mμ, log ε 3.98. The m.p. was undepressed on admixture with an authentic sample with m.p. 175–177°, $[\alpha]_D$ −40°, λ_{max} 240 mμ, log ε 3.97.

The monoacetate VIIIa suffered no dehydration with alkaline alumina. This reaction was brought about by heating a solution containing 0.5 g. of VIIIa, 12 cc. of acetic acid, 2 cc. of water and 1 drop of concentrated hydrochloric acid for 3 hours on the steam-bath. The solution was diluted with water, cooled and the precipitate was collected. Crystallization from methylene chloride furnished 0.15 g. (32%) of the diene I with m.p. 172–174°, λ_{max} 240 mμ, log ε 3.96, undepressed in m.p. on admixture with an authentic sample.

The "diosone" XI (0.1 g.) was heated with 8 cc. of glacial acetic acid and 2 cc. of water for 3 hours on the steam-bath. Isolation in the usual way gave a product, the ultraviolet absorption spectrum of which showed the diene I to have been formed in 51% yield. Similar treatment of the diacetate VIIIb gave 48% of I and the monoacetate VIIIa gave 46% of I.

Δ⁵-Pregnene-3β,16β,20β-triol Triacetate (IXb). (a) **From Δ⁵-Pregnene-3β,16β-diol-20-one 3-Monoacetate (VIIIa).**—A solution of 8.5 g. of the 3-monoacetate VIIIa in 150 cc. of dry ether was gradually added to 8.5 g. of lithium aluminum hydride in 250 cc. of ether and the mixture was boiled under reflux for 2 hours. Water was added cautiously to destroy the excess hydride and then excess dilute hydrochloric acid. The precipitate which had separated at the interface was collected, washed well with water and dried. It was then boiled with 3 l. of acetone for 30 minutes, when 4.55 g. (60%) of the exceedingly insoluble 3β,16β,20β-triol IXa with m.p. 283–285° remained out of solution. No attempt was made to isolate the corresponding 3β,16β,20α-triol which was probably present in the ether and acetone extracts.

It was found difficult to purify the above triol IXa due to its extreme insolubility and 3.5 g. was therefore heated with 35 cc. of pyridine and 10 cc. of acetic anhydride on the steam-bath, with stirring. Solution occurred after 1 hour and water was added after a further 30 minutes heating. The mixture was stirred to effect hydrolysis of the anhydride, the solid was collected, washed with water and crystallized from aqueous methanol. The resulting triacetate IXb (3.81 g.) showed m.p. 147–148°, $[\alpha]_D$ +2.5°; reported[14] m.p. 143°.

Anal. Calcd. for $C_{27}H_{40}O_6$: C, 70.40; H, 8.75. Found: C, 70.06; H, 8.70.

(b) **From Δ⁵-Pregnene-3β,16β-diol-20-one 3-Acetate 16-γ-Methyl-δ-acetoxyvalerate ("Diosone") (XI).**—The lithium aluminum hydride reduction of 8.5 g. of the "diosone" XI was carried out exactly as described under (a) for the corresponding 3-monoacetate VIIIa. The crude 3β,16β,-20β-triol IXa, which remained insoluble in boiling acetone, weighed 4.1 g. and showed m.p. 262–266°.

The above 3β,16β,20β-triol IXa with m.p. 262–266° (3.5 g.) on acetylation as described under (a) produced 3.05 g. of the triacetate IXb with m.p. 147–148°, $[\alpha]_D$ +2.2°. The m.p. was undepressed on admixture with the compound prepared by method a and both substances showed absolutely identical infrared spectra in potassium bromide suspension (Baird double beam recording spectrophotometer).[17]

Δ⁵-Pregnene-3β,16β,20β-triol (IXa).—Potassium hydroxide (1 g.) in 2 cc. of water was added to a solution of 1 g. of the triacetate IXb in 50 cc. of methanol and the solution was boiled under reflux for 1 hour. The precipitate was collected and washed well with hot methanol and water. The resulting pure triol IXa (0.65 g., 90%) showed m.p. 288–290°. The rotation could not be measured due to the extreme insolubility of the substance; reported[14] m.p. 281–285°.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.19; H, 10.13.

Allopregnane-3β,16β,20β-triol Triacetate (XII).—A solution of 0.45 g. of Δ⁵-pregnene-3β,16β,20β-triol triacetate (IXb) in 10 cc. of glacial acetic acid was shaken in hydrogen over 0.1 g. of a prereduced platinum catalyst at 22° and 592 mm. After 20 minutes 1.01 equivalents of hydrogen had been absorbed and uptake stopped. The catalyst was removed and the filtrate was diluted with water. The precipitate was collected, washed with water, dried and crystallized from methylene chloride–hexane. The allopregnane-3β,16β,20β-triol triacetate XII thus produced weighed 0.41 g. (91%) and showed m.p. 164–165°, $[\alpha]_D$ +46°, $[\alpha]_D$ +49° (ethanol); reported[15] m.p. 164–166°, $[\alpha]^{25}_D$ +48° (ethanol). Identity with an authentic sample of allopregnane-3β,16β,20β-triol triacetate[15] was kindly demonstrated by Dr. H. Hirschmann through mixed m.p. determination and infrared comparison.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.10; H, 9.15. Found: C, 69.90; H, 9.23.

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(17) We are indebted to Professor C. Djerassi of Wayne University for the infrared spectra.