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# Steroidal Sapogenins. XXVIII.[2] Conversion of Steroidal Sapogenins to $\Delta^{16}$-20-Keto-pregnenes[3]

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The three-step conversion of steroidal sapogenins (I) to $\Delta^{16}$-20-ketopregnenes (VII) has been systematically studied. Treatment of I with acetic anhydride gave pseudosapogenin (II) in high yield. Oxidation of II with $CrO_3$ or $H_2O_2$ gave the oxidation intermediates III and smaller quantities of VII, 16,17-$\alpha$-epoxides (X), and some unidentified products. Alkaline hydrolysis of pure III with *t*-butyl alcohol–potassium hydroxide proceeded quantitatively. This reagent had no effect on pure compounds of type VII with or without a C-12 carbonyl. This paper presents complete physical properties of a number of type VII compounds prepared from various sapogenins and of their $C_{16-17}$-saturated analogs.

Pregnene and allopregnene derivatives with the $\Delta^{16}$-20-keto moiety and saturated analogs are excellent sources for the preparation of cortisone or cortisone analogs.[4–6] This paper presents the results of studies leading to improved procedures for the preparation of these compounds from steroidal sapogenins. In addition a complete description of the physical properties of these compounds is presented. Many of the compounds described were first prepared by Marker and co-workers,[7a–c] although in most cases only melting points were given. The methods subsequently presented by other workers[8a–d] as well as the procedures described herein are fundamentally only variants of Marker's procedures. These involve essentially a three-step process as shown in Fig. 1. In the standard sequence a sapogenin (I) is treated with acetic anhydride to give the pseudosapogenin acetate (IIa) which is oxidized with $CrO_3$ to the intermediate V. V can be treated in a variety of ways to yield the desired $\Delta^{16}$-20-ketopregnene (VII). In addition VII can be obtained by oxidation of dihydropseudosapogenin (III)[7b] or the equivalent dihy-

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(2) Paper XXVII, M. E. Wall and H. A. Walens, This Journal, **77**, 5661 (1955).

(3) A preliminary announcement of these researches has been presented previously; M. E. Wall, H. E. Kenney, H. W. Jones and E. S. Rothman, Fifth Meeting-in-Miniature, Philadelphia Section A.C.S. Jan. 29, 1953, Abstracts of Papers, p. 10.

(4) A. Wettstein, *Experientia*, **10**, 397 (1954).

(5) G. Rosenkranz and F Sondheimer, *Progr. Chem. Org. Natur. Prod.*, **10**, 274 (1953).

(6) C. W. Shoppee, *Ann. Rev. Biochem.*, **22**, 261 (1953).

(7) (a) R. E. Marker, *et al.*, This Journal, **62**, 3350 (1940); (b) **69**, 2167 (1947); (c) **64**, 468 (1942).

(8) (a) C. Djerassi, J. Romo and G. Rosenkranz, *J. Org. Chem.*, **16**, 754 (1951); (b) D. H. Gould, H. Staeudle and E. B. Hershberg, This Journal, **74**, 3685 (1952); (c) G. P. Mueller, R. E. Stobaugh and R. S. Winniford, *ibid.*, **75**, 4888 (1953); (d) W. G. Dauben and G. J. Fonken, *ibid.*, **76**, 4618 (1954).

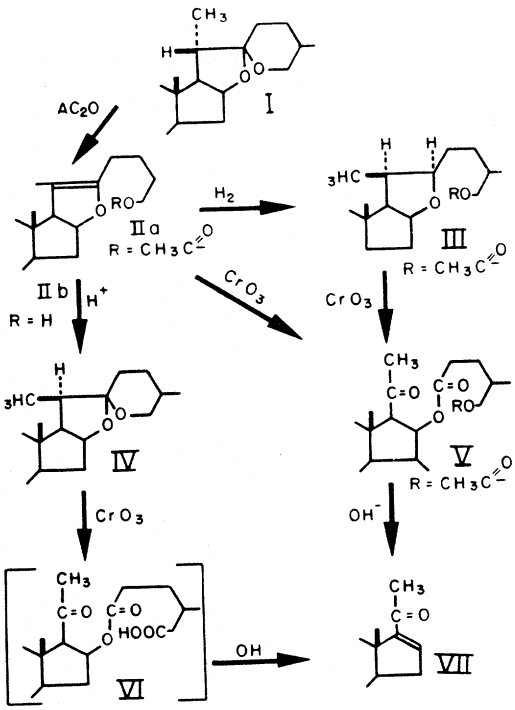


Fig. 1.

dro-20-isosapogenin[9a,b] or 20-isosapogenin (IV).[9a,b]

We have studied each phase of the three-step conversion of I to VII. Gould, Staeudle and Hershberg[8b] have shown that use of strong Lewis acids such as aluminum chloride in conjunction with acetic anhydride permitted conversion of I to IIa at reflux temperatures and thus eliminated the use of sealed vessels and 200° temperatures as well as shortening the reaction time. In our hands, the yields of IIa by this procedure were inferior to those obtained by the original Marker procedure.[7a,b] However, a somewhat similar procedure published by Dauben and Fonken[8d] utilizing pyridine hydrochloride as the Lewis acid has given us excellent results with a wide variety of sapogenins including the reputedly difficult 12-ketosapogenins.[10] Use of pyridine and acetyl chloride, an alternative procedure described by Dauben and Fonken,[8d] was satisfactory for diosgenin but gave undesirable side reactions with hecogenin, and we failed to obtain pseudohecogenin diacetate. From the researches of Gould, Staeudle and Hershberg[8b] and of Dauben and Fonken[8d] we reasoned that a salt of a weak base and strong acid such as ammonium chloride could be used in a similar fashion. Refluxing equimolar proportions of diosgenin or hecogenin and ammonium chloride in acetic anhydride led to conversion of these sapogenins to the corresponding pseudosapogenin acetates.

The oxidation of pseudosapogenins was studied using pure pseudodiosgenin, pseudohecogenin and pseudosarsasapogenin diacetates. The oxidants studied were $CrO_3$ in acetic acid containing sodium acetate[8b] and to a lesser extent $H_2O_2$ in acetic acid.[7c,8c] Although the oxidation product V was usually the major product, other components also were present. For example $CrO_3$ oxidation of pseudodiosgenin diacetate followed by chromatography on the mild adsorbent Florisil gave "diosone" in the initial hexane eluents. Further elution with solvents of increasing polarity yielded oily mixtures which contained, in addition to "diosone," products with free hydroxyl, C-20 carbonyl, conjugated carbonyl, and carbonyl of unknown nature. Whereas subsequent alkaline cleavage of the initial "diosone" fractions resulted in excellent yields of 5,16-pregnadien-3β-ol-20-one (VIII), similar treatment of the later impure fractions gave much lower recovery of the desired product, VIII. Similar results were obtained with other oxidation intermediates, tigone and hecone. In some cases the formation of products other than the desired oxidation intermediate V occurred to a considerable extent and thus constituted a major cause for reduced yields of VII.

The observations of Fukushima and Gallagher[11] which indicated that treatment of $\Delta^{16}$-20-keto-pregnenes such as VII with methanolic potassium hydroxide resulted in formation of 16-methoxyl derivatives, impelled us to study carefully the third step of the reaction sequence. We found that use of primary or secondary alcohols with a variety of strong or weak bases or with hydrochloric acid always gave mixtures of VII and products containing C-20 unconjugated carbonyl. Use of *t*-butyl alcohol containing potassium hydroxide[3] resulted in formation of the desired $\Delta^{16}$-20-ketopregnenes in excellent yields. Thus crystalline "tigone," allopregnane-3β,16β-diol-20-one 3-acetate, 16-(δ-acetoxy-γ-methyl valerate) treated at 30° for three hours with the above reagent was converted quantitatively to 16-allopregnen-3β-ol-20-one. Purified "diosone" and "hecone" (non-crystalline) also were converted to the corresponding $\Delta^{16}$-20-ketopregnenes in about 90% yield.

In the course of non-isolation experiments in which hecogenin was converted to 16-allopregnen-3β-ol-12,20-dione 3-acetate (IX) we were able to isolate a small quantity of 16α,17α-epoxyallopregnan-3β-ol-12,20-dione 3-acetate (X). When these non-isolation runs were conducted with $H_2O_2$ as the oxidant,[8c] the over-all yield of pregnene IX averaged about 40% whereas in similar experiments with a separate epoxidation step, the yield of the epoxide X averaged 60%. This indirectly indicated that somewhere along the sequence some epoxide was being formed prior to the final $H_2O_2$ epoxidation. Recently, Mueller and Norton[12] have stated that $\Delta^{16}$-12,20-ketopregnenes form 16,17-α-epoxides when treated with alcohols containing potassium hydroxide in the presence of air. In the absence of air they stated that addition of alcohol to the 16,17-double bond took place. Earlier, Moore and Wittle[13] on treating the oxidation intermediate derived from pseudokammogenin with alcoholic potassium hydroxide in the presence of air obtained converse results, *i.e.*, formation of 16-methoxy or 16-ethoxy derivatives. On treating the $\Delta^{16}$-12,20-

(9) (a) M. E. Wall, C. R. Eddy and S. Serota, THIS JOURNAL, **76**, 2849 (1954); (b) **77**, 1230 (1955).

(10) R. B. Wagner, J. A. Moore and R. F. Forker, *ibid.*, **72**, 1856 (1950).

(11) D. K. Fukushima and T. F. Gallagher, *ibid.*, **73**, 196 (1951).

(12) G. P. Mueller and L. L. Norton, *ibid.*, **77**, 143 (1955).

(13) J. A. Moore and E. L. Wittle, *ibid.*, **74**, 6287 (1952).

allopregnene (IX) with *t*-butyl alcohol and potassium hydroxide both in the presence and absence of air we recovered only starting material. Accordingly, we believe that the 16,17-$\alpha$-epoxide X found in our experiments was formed during the oxidation of pseudohecogenin to "hecone." It will be recalled that crude "hecone" contained some admixture of material with conjugated carbonyl indicating the presence of the $\Delta^{16}$-12,20-ketopregnene (IX).[14] Since we have shown that the oxide X was not formed from allopregnene IX in the presence of alkaline *t*-butyl alcohol, it is probable that IX present in crude "hecone" was partially converted to X by oxidant *prior to alkaline cleavage*.

The yield in the conversion of I to VII has varied with the starting sapogenin. Diosgenin was the best, being converted to 5,16-pregnadien-3$\beta$-ol-20-one in 91.5% yield (ultraviolet assay) and 78% yield based on crystalline product isolated. Conversion of other sapogenins to VII proceeded less favorably, averaging 50–60% by assay and 35–50% by isolation.

Finally, we wish to mention briefly the ultraviolet and infrared absorption spectra[15] of the 16-dehydropregnenes. With the exception of 12-keto derivatives, these steroids exhibited the typical ultraviolet maximum at 239 m$\mu$, log $\epsilon$ 3.96–4.00, and in the infrared an absorption peak in the region of 1665–1670 cm.$^{-1}$ characteristic of $\Delta^{16}$-20-ketones.[16] In the case of 16-dehydro-12,20-ketones we found, in agreement with previous workers[8c] that a hypsochromic shift to 227–228 m$\mu$, log $\epsilon$ 3.89, occurred in the ultraviolet. We observed also an equally characteristic shift[8c] to 1680 cm.$^{-1}$ in the infrared. The infrared absorption spectra of both $\Delta^{16}$-20- and $\Delta^{16}$-12,20-ketopregnenes exhibited at least five similar and characteristic absorption bands in the fingerprint region between 1000–650 cm.$^{-1}$. These bands were relatively weak and were due probably to the conjugated $\Delta^{16}$-20-keto moiety since they disappeared on saturation of the double bond.

## Experimental

Melting points were obtained on a Kofler micro hot-stage. Optical rotations were determined in chloroform. Ultraviolet absorption spectra were taken in methanol solution with a Cary recording spectrophotometer. Infrared absorption spectra were for the most part obtained in $CS_2$ solution, concentration 3–10 g. per liter, with a Perkin–Elmer model 21 spectrophotometer.

**Preparation of $\Delta^{16}$-20-Ketopregnenes. A. Standard Procedure, Preparation of 5,16-Pregnadien-3$\beta$-ol-20-one (VIII).**—Ten grams of diosgenin acetate and 20 ml. of acetic anhydride were heated at 195° for 18 hours in a sealed tube. After cooling, the tube was opened, 4 ml. of water added, and the mixture warmed on the steam-bath. To the resultant crude acetic acid solution were added an additional 100 ml. of glacial acetic acid and 2.5 g. of sodium acetate. The solution was cooled to 15° and with continual stirring 4 g. of chromic oxide in 15 ml. of 80% acetic acid–20 ml. of water were added over a period of 15 minutes. The mixture then was allowed to stand one hour at 22°. Two volumes of water were added and the crude "diosone" repeatedly extracted with ether. The ethereal extracts were washed with water, the aqueous washes re-extracted, and the combined ethereal extracts evaporated to a sirup. The sirup was dissolved in 200 ml. of *t*-butyl alcohol and any residual acetic acid present neutralized with concentrated aqueous potassium hydroxide. To the neutral *t*-butyl alcohol solution was added 10 g. of potassium hydroxide in 12 ml. of water. The mixture was agitated vigorously at 30° for three hours, diluted with water and extracted with ether. The ethereal solution containing VIII was washed until neutral and dried over anhydrous sodium sulfate. The solvent was removed on the steam-bath. The crude, dry VIII weighed 7.01 g., m.p. 197–203, 89.5% pure by ultraviolet assay. Hence, the crude sample contained 6.28 g. of VIII for an over-all yield of 91.5%. One crystallization from acetone gave plates, m.p. 203–205°, with ultraviolet and infrared absorption curves nearly identical to those prepared from a reference sample. The purified product weighed 5.39 g., yield calculated on this basis 78%. Several recrystallizations from acetone gave plates, m.p. 210–212°, $[\alpha]^{25}D$ −32°, $\lambda_{max.}$ 239 m$\mu$, log $\epsilon$ 3.96 (lit.[17] m.p. 212–214°).

**VIII Acetate.**—Acetylation of VIII in pyridine–acetic anhydride at room temperature followed by the usual work-up gave VIII acetate as rods from methanol, m.p. 171–173°, $[\alpha]^{25}D$ −35°, $\nu_{max}^{CS_2}$ 1735, 1668 (both ±5) and weak bands near 965, 925, 900, 838, 825, 820, 710, 665, 650 cm.$^{-1}$.

The above procedure is a general one and has been applied to the conversion of all types of steroidal sapogenins to $\Delta^{16}$-20-ketopregnenes, although yields were generally lower than with diosgenin. A second method exemplifies the use of pyridine hydrochloride.[8d]

**B. Use of Pyridine Hydrochloride. Preparation of 16-allopregnen-3$\beta$-ol-12,20-dione Acetate (IX Acetate).**—Hecogenin acetate, 200 g., acetic anhydride, 1 l., and pyridine hydrochloride, 48.4 g., were refluxed for five hours, cooled and excess acetic anhydride decomposed by cautiously adding 180 ml. of water. Using proportional quantities of solvents and reagents, oxidation and alkaline cleavage were conducted as described previously. The crude product was acetylated and chromatographed on 1 kg. of Florisil. Elution with benzene removed an oily sirup. Elution with chloroform gave 98 g. of crude IX acetate, m.p. 162–172°, which after several crystallizations from ether gave 62 g. (40%) of plates, m.p. 179–180°, $[\alpha]^{25}D$ +125°, $\lambda_{max.}$ 227 m$\mu$, log $\epsilon$ 3.89, $\nu_{max}^{CS_2}$ 1735, 1710, 1680 (all ±5), weak bands near 970, 920, 900, 825, 710, 670 and 645 cm.$^{-1}$ (lit.[8c] gives m.p. 178–181°, $[\alpha]^{27}D$ +128°, $\lambda_{max.}$ 227–228 m$\mu$, log $\epsilon$ 3.87). Further elution with ether containing 2% ethanol gave considerable quantities of a colorless glass containing free hydroxyl. Re-acetylation of this product led to isolation of **16$\alpha$,17$\alpha$-epoxyallopregnane-3$\beta$-ol-12,20-dione acetate (X)**, m.p. 229–231°, with infrared spectrum identical to an authentic specimen.

Method B has been applied to all types of sapogenins and was especially convenient for large scale runs. Similar use of pyridine–acetyl chloride for conversion of I to IIa was not universally applicable. Thus in agreement with Dauben and Fonken[8d] we found diosgenin could be converted to pseudodiosgenin diacetate. However, we observed that when the method was applied to hecogenin, no pseudohecogenin diacetate could be obtained.

**Use of Ammonium Chloride.**—Optimal conditions have not been worked out. The following experiments indicate the potentialities of the method. Hecogenin acetate, 2.0 g., and 0.35 g. of ammonium chloride were refluxed with 10 ml. of acetic anhydride for five hours. After cooling, the solution was poured into water forming a pale yellow gum. The infrared spectrum of this crude product was similar to that of authentic pseudohecogenin diacetate. The crude product was dissolved in benzene and passed through a Florisil column. Crystallization of the benzene eluates from hexane gave tablets, m.p. 93–95° (lit.[8c] gives m.p. 92–94°). Treatment in a similar manner of 10.0 g. of diosgenin acetate gave 5 g. of pseudodiosgenin diacetate.

**Effect of $CrO_3$ Oxidation on Pseudosapogenin Acetates.**—In a typical experiment 10 g. of pseudodiosgenin diacetate,

(14) Gould, Staeudle and Hershberg, ref. 8, noted the presence of a similar constituent in crude "diosone" and ascribed its presence to hydrolysis of the acid sensitive 16$\beta$-ester under the acidic conditions of the oxidation.

(15) A catalog of the infrared absorption curves of the various 16-dehydropregnenes will be published elsewhere.

(16) R. N. Jones, P. Humphries and K. Dobriner, THIS JOURNAL, 71, 241 (1949).

(17) R. E. Marker, T. Tsukamoto and D. L. Turner, *ibid*, 62, 2525 (1940).

m.p. 98–100°, were oxidized with $CrO_3$ by method A. The crude "diosone" was chromatographed on Florisil. Elution with hexane–benzene (1–1) gave 7.1 g. of a pale yellow oil (A). The infrared spectrum of fraction A was in accord with the structure of "diosone": no absorption in the 3600 cm.$^{-1}$ region, characteristic strong ester band near 1735 cm.$^{-1}$ and a partially resolved band near 1710 cm.$^{-1}$ due to C-20 carbonyl. Further elution with benzene, chloroform and benzene–ethanol (1–1), gave oils. The infrared spectrum of these all showed a band near 3540 cm.$^{-1}$ (unknown hydroxyl, not 3β which comes at 3620 cm.$^{-1}$), a weak to moderate strength band near 1775 cm.$^{-1}$ (unknown carbonyl, lactone?), a strong ester band 1735 cm.$^{-1}$, a partially resolved C-20 carbonyl band near 1710 cm.$^{-1}$ and a weak to moderate band near 1667 cm.$^{-1}$ ($\Delta^{16}$-20-ketone). These later fractions were combined as B, 4.1 g. Alkaline cleavage of A and B gave, respectively, 4.0 and 0.9 g. of 16-pregnen-3β-ol-20-one (VIII), the respective yields based on "diosone" being 92 and 35%. Similar results were obtained during the oxidation of pseudohecogenin and pseudosarsasapogenin diacetates.

**$H_2O_2$ Oxidation.**—Crude pseudohecogenin diacetate obtained by method B was oxidized with $H_2O_2$–acetic acid exactly as described by Mueller, *et al.*[8c] As in the previous $CrO_3$ oxidation the yield of crystalline IX acetate was 40%. However, when the crude IX acetate *prior* to crystallization was converted to epoxide X,[8c] the yield of crystalline X was 60% (based on hecogenin acetate), indicating that crude IX acetate contained a considerable quantity of X.

**Effect of *t*-Butyl Alcohol–Potassium Hydroxide on $\Delta^{16}$-20-ketopregnenes.**—One hundred mg. of 5,16-pregnadien-3β-ol-20-one acetate (VIII acetate) was refluxed two hours in 5 ml. of *t*-butyl alcohol containing 100 mg. of potassium hydroxide and 0.2 ml. of water. After the usual ethereal extraction, the product was acetylated in pyridine–acetic anhydride. The mixture was diluted with water and filtered. The crystalline insoluble fraction was crystallized once from methanol, m.p. 166–169°, infrared spectrum identical to an authentic sample of VIII acetate. IX acetate, 50 mg., was stirred vigorously at 25° for three hours in the *presence of air* with 15 ml. of *t*-butyl alcohol containing 50 mg. of potassium hydroxide and 1 ml. of water. A duplicate experiment was conducted in a *nitrogen* atmosphere. After the usual workup, the infrared spectra of both samples indicated that the compounds were unchanged except for hydrolysis of the 3β-acetate. Crystallization from Skellysolve C–acetone gave for the first time crystalline **16-allopregnen-3β-ol-12,20-dione** as plates, m.p. 194–197°, $[\alpha]^{25}D$ +142°, $\lambda_{max.}$ 227 mμ, log ε 3.89, $\nu_{max}^{CS_2}$ 1717, 1683 cm.$^{-1}$, weak bands near 980, 910, 895, 825, 715, 710 and 645 cm.$^{-1}$.

**16-Allopregnen-3β-ol-20-one (XI).**—Crude pseudotigogenin diacetate was prepared by method A and catalytically hydrogenated.[18] The crude dihydropseudotigogenin diacetate thus obtained was oxidized to give "tigone." After chromatography on Florisil, the purified "tigone" was obtained as an oil which slowly crystallized from pentane, m.p. 102–104°, $[\alpha]^{25}D$ +10.5°, (lit.[19] gives m.p. 101–102°). Crystalline tigone, 1.22 g., was given the usual *t*-butyl alcohol–potassium hydroxide cleavage. The crude product weighed 0.82 g., m.p. 196–200°, 90% XI by ultraviolet absorption assay corresponding to 0.73 g. of XI, yield 100% based on "tigone"). Crystallization from acetone gave 0.67 g. of plates, m.p. 200–203°, which on further crystallization gave m.p. 201–203°, $[\alpha]^{25}D$ +31° (lit.[20] gives m.p. 202–204°).

**XI Acetate.**—Crude XI was prepared from 10 g. of tigogenin acetate without isolation by method A. The crude product was acetylated, taken up in hexane–benzene (1–1) and passed through a Florisil column; yield after one recrystallization from methanol, 3.9 g. (50%), m.p. 158–162°. After several recrystallizations from methanol, the analytical sample was obtained as rods, m.p. 164–166° (lit.[20] gives m.p. 162–164°), $[\alpha]^{25}D$ +45°, $\lambda_{max}$ 239 mμ, log ε 3.96, $\nu_{max}^{CS_2}$ 1735, 1665 (both ±5), weak bands near 975, 922, 905, 820, 710, 670, 650 cm.$^{-1}$.

**16-Pregnen-3β-ol-20-one Acetate (XII Acetate).**—In the same manner as described above, smilagenin acetate gave a 55% yield of XII acetate, m.p. 138–141°. The analytical sample crystallized from methanol as plates, m.p. 141–143° (lit.[21] gives m.p. 144–146°), $[\alpha]^{25}D$ +41°, $\lambda_{max.}$ 239 mμ, log ε 3.96, $\nu_{max}^{CS_2}$ 1735, 1665 (±5), weak bands near 965, 925, 900, 825, 820, 710, 665, 650 cm.$^{-1}$. Hydrolysis of XII acetate in *t*-butyl alcohol–potassium hydroxide gave XII, plates from methanol, m.p. 186–188° (lit.[21] gives m.p. 188–190°), $[\alpha]^{25}D$ +49°).

**16-Allopregnene-2α-3β-diol-20-one 2,3-Diacetate (XIII Acetate).**—In the same manner described above, gitogenin diacetate gave a 42% yield of XII acetate, rods from methanol, m.p. 184–186° (compound previously undescribed), $[\alpha]^{25}D$ −17°, $\lambda_{max.}$ 239 mμ, log ε 3.98. Saponification of XIII acetate in *t*-butyl alcohol gave XIII, m.p. 228–229° (lit.[7b] gives m.p. 228–230°), $[\alpha]^{25}D$ +31°.

**16-Pregnene-2β,3β-diol-20-one 2,3-Diacetate (XIV Diacetate).**—Markogenin diacetate was converted to XIV acetate by method B, then proceeding as above, yield 30%, as rods from aqueous acetone, m.p. 145–147, $[\alpha]^{25}D$ +26°, $\nu_{max}^{CS_2}$ 1735, 1665 (±5), weak bands near 975, 945, 910, 825, 815 and 710 cm.$^{-1}$. Saponification in the usual manner gave XIV, plates from acetone, m.p. 196–198°, $[\alpha]^{25}D$ +28°, $\lambda_{max.}$ 239 mμ, log ε 3.92.

**5,16-Pregnadiene-2α,3β-diol-20-one 2,3-Diacetate (XV Acetate).**—Yuccagenin diacetate was converted to XV acetate by method A followed by acetylation and chromatography. The product gave rods from methanol, m.p. 189–191° (lit.[7b] gives m.p. 178–181°), $[\alpha]^{25}D$ −78°, log ε 3.94. Saponification gave XV, plates from ethyl acetate, m.p. 226–228°, $[\alpha]^{25}D$ −22°.

**Pregnan-3β-ol-20-one (XVI).**—Catalytic hydrogenation of XII with palladium–barium sulfate or palladium–charcoal in the usual manner[7b] gave XVI, rods from ethanol–pentane, m.p. 145–147° (lit.[22] gives m.p. 149°), $[\alpha]^{25}D$ +73°, $\nu_{max}^{CHCl_3}$ 1700 cm.$^{-1}$ ± 5. Acetylation gave XVI acetate as rods from methanol, m.p. 116–118°, $[\alpha]^{25}D$ +83° (lit.[22] gives m.p. 121°).

**Allopregnan-3β-ol-20-one (XVII).**—Hydrogenation of XI gave XVII, plates from methanol, m.p. 194–196° (lit.[20] gives 192–194°), $[\alpha]^{25}D$ +79°, $\nu_{max}^{CHCl_3}$ 1700 cm.$^{-1}$ ± 5. The XVII acetate was obtained as plates from methanol, m.p. 144–146° (lit.[20] gives m.p. 145°), $[\alpha]^{25}D$ +69°.

**5-Pregnen-3β-ol-20-one (XVIII).**—Hydrogenation of VIII gave XVIII as rods from ether, m.p. 188–190° (lit.[23] gives m.p. 188–190°). Acetylation of XVIII gave the acetate, rods from pentane–ethanol, m.p. 145–147°, $[\alpha]^{25}D$ +11° (lit.[23] gives m.p. 149–151°), $\nu_{max}^{CS_2}$ 1735, 1700 cm.$^{-1}$ (both ±5).

**Allopregnan-3β-ol-12,20-dione (XIX).**—Hydrogenation of IX gave XIX as rods from ether, m.p. 192–193°, $[\alpha]^{25}D$ +146°, $\nu_{max}^{CHCl_3}$ 1710–1700 cm.$^{-1}$ ±5 (broad single band). The acetate was obtained as rods from methanol, m.p. 192–193°, $[\alpha]^{25}D$ +137° (lit.[8c] gives m.p. 189–190°, $[\alpha]^{29}D$ +139°).

**Allopregnane-2α,3β-diol-20-one (XX).**—Hydrogenation of XIII gave XX, rods from methanol, m.p. 233–235° (lit.[7b] gives m.p. 238–240°), $[\alpha]^{25}D$ +71°. The diacetate was obtained as plates from acetone, m.p. 191–193°, $[\alpha]^{25}D$ −25°.

**5-Pregnene-2α,3β-diol-20-one 2,3-Diacetate (XXI Diacetate).**—Hydrogenation of XV diacetate gave XXI diacetate as plates from methanol, m.p. 193–195° (lit.[7b] gives m.p. 189–192°), $[\alpha]^{25}D$ −24°, $\nu_{max}^{CS_2}$ 1735, 1700 cm.$^{-1}$ (both ±5).

**Pregnane-2β,3β-diol-20-one 2,3-Diacetate (XXII Diacetate).**—Hydrogenation of XIV diacetate gave XXII diacetate, plates from methanol, m.p. 128–129°, $[\alpha]^{25}D$ +79°, $\nu_{max}^{CS_2}$ 1735, 1700 cm.$^{-1}$ (both ±5).

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(18) R. E Marker and E. Rohrmann, THIS JOURNAL, **62**, 521 (1940).

(19) R. E. Marker, *et al.*, *ibid.*, **63**, 774 (1941).

(20) R. E. Marker and D. L. Turner, *ibid.*, **62**, 3005 (1940).

(21) R. E. Marker and E. Rohrmann, *ibid.*, **62**, 523 (1940).

(22) R. E. Marker, O. Kamm and E. L. Wittle, *ibid.*, **59**, 1841 (1937).

(23) R. E. Marker and J. Krueger, *ibid.*, **62**, 3349 (1940).