acetate started to crystallize after 10 minutes, and was precipitated completely by addition of water. After crystallization from acetone it had m.p. 235–238°, $[\alpha]D$ +178° (acetone), λ_{max} 238 mμ, log ε 4.16, $\lambda_{max}^{CHCl_3}$ 1736, 1700 and 1660 cm.$^{-1}$ and free hydroxyl band. Identity was established by mixture melting point determination and infrared comparison.

Δ^4-Pregnene-11α,17α,21-triol-3,20-dione (XII).—A solution of 35 mg. of the trihydroxyprogesterone monoacetate Xb in 4 cc. of methanol was hydrolyzed with 35 mg. of potassium bicarbonate in 1 cc. of water for 48 hours at room temperature.[22] Water was added and the product was extracted with chloroform. It was crystallized from acetone–ether, and then had m.p. 215–218°, $[\alpha]^{20}D$ +110° (EtOH), λ_{max} 242 mμ, log ε 4.24, λ_{max}^{mull} 1700 and 1660 cm.$^{-1}$ and free hydroxyl band; reported for the microbiological product[6c]: m.p. 217–219°, $[\alpha]^{20}D$ +117° (EtOH).

Anal. Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.37; H, 8.14.

A sample obtained by an independent route[18] had m.p. 209–211° and 216–219° (polymorphic forms), $[\alpha]^{20}D$ +112° (EtOH), and there was no depression in melting point on admixture.

(22) *Cf.* T. Reichstein and J. v. Euw, *Helv. Chim. Acta*, **21**, 1183 (1938).

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

Steroids. XLII. Steroidal Sapogenins. XXVI.[1] The Chemical Reduction of Δ^8-11-Keto and of Saturated 11-Keto Steroids. A New Approach to 11-Keto and 11α-Hydroxy Steroids[2]

BY FRANZ SONDHEIMER, O. MANCERA, G. ROSENKRANZ AND CARL DJERASSI[3]

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Δ^8-22a-5α-Spirosten-3β-ol-11-one propionate (I) was reduced by means of lithium in liquid ammonia to 22a-5α-spirostan-3β-ol-11-one (IIa), thus providing a new route to cortisone. When the reduction of I with lithium in ammonia was carried out in the presence of alcohol, 22a-5α-spirostan-3β,11α-diol (IIIa) resulted. The latter reducing conditions smoothly converted saturated 11-keto steroids to the corresponding 11α-hydroxy compounds. Thus IIa yielded IIIa, pregnan-3α-ol-11,-20-dione 20-ethylene ketal (VI) led to pregnane-3α,11α-diol-20-one 20-ethylene ketal (VII), and cortisone 3,20-diethylene ketal (X) gave the corresponding 11α-hydroxy compound XI; the latter was converted by treatment with *p*-toluenesulfonic acid and acetone to Δ^4-pregnene-11α,17α,21-triol-3,20-dione (XIIa), the 11-epimer of Kendall's compound F.

All the methods so far reported for the chemical introduction of an 11-keto or hydroxy group into ring C unsubstituted steroids[4] have proceeded *via* a $\Delta^{7,9(11)}$-diene, and thence *via* a derivative bearing oxygen substituents at C-7 as well as at C-11, from which the substituent at C-7 had to be removed subsequently. We now wish to describe the details[2] of a new method for effecting 11-oxygenation, which we have applied to the preparation of 22a-5α-spirostan-3β-ol-11-one (II) and 22α-5α-spirostane-3β,11α-diol (III), which proceeds directly from the $\Delta^{7,9(11)}$-diene to the 11-oxygenated derivative, no additional group being introduced at C-7. This method both with regards to the number of steps (seven from the Δ^5-3-ol, "diosgenin" in this case, or three from the $\Delta^{7,9(11)}$-diene) and overall yield appears to be superior to the other methods that have been published[4,5] for the chemical introduction of a C-11 oxygen function into $\Delta^{7,9(11)}$-dienes. Furthermore, in view of previously recorded transformations[6] the present work constitutes an alternate route to cortisone.

The starting point for the present method was Δ^8-22a-5α-spirosten-3β-ol-11-one propionate (I), which may easily be obtained in good yield from $\Delta^{7,9(11)}$ - 22a - 5α - spirostadien - 3β - ol[7] propionate through treatment with one mole of perbenzoic or permonophthalic acid, followed by rearrangement of the 9,11-oxide with boron trifluoride.[2] The saturation of the double bond in I was first carried out by means of catalytic hydrogenation. These experiments, as was anticipated, did not lead to the 11-keto steroid with the "natural" B/C ring junction (8β,9α), but gave rise to a series of interesting "abnormal" derivatives which are being investigated further.[8]

We next turned our attention to the chemical reduction of the Δ^8-11-one I, since this type of reduction might well lead to the most stable of the four possible dihydro products, *i.e.*, to the 8β,9α-compound (possessing the "natural" configuration) rather than the 8α,9β-isomer. Some of the usual

(1) (a) Steroids. XLI. J. Romo, G. Rosenkranz, C. Djerassi and F. Sondheimer, THIS JOURNAL, **75**, 1277 (1953). (b) Steroidal Sapogenins. XXV. H. Martinez, H. J. Ringold, G. Rosenkranz and C. Djerassi, *ibid.*, **75**, 239 (1953).

(2) This paper is to be regarded as "Introduction of the 11-Keto and 11α-Hydroxy Groups into Ring C Unsubstituted Steroids (Part 7)." A preliminary announcement of part of this work has been published (F. Sondheimer, R. Yashin, G. Rosenkranz and C. Djerassi, *ibid.*, **74**, 2696 (1952)).

(3) Department of Chemistry, Wayne University, Detroit 1, Michigan.

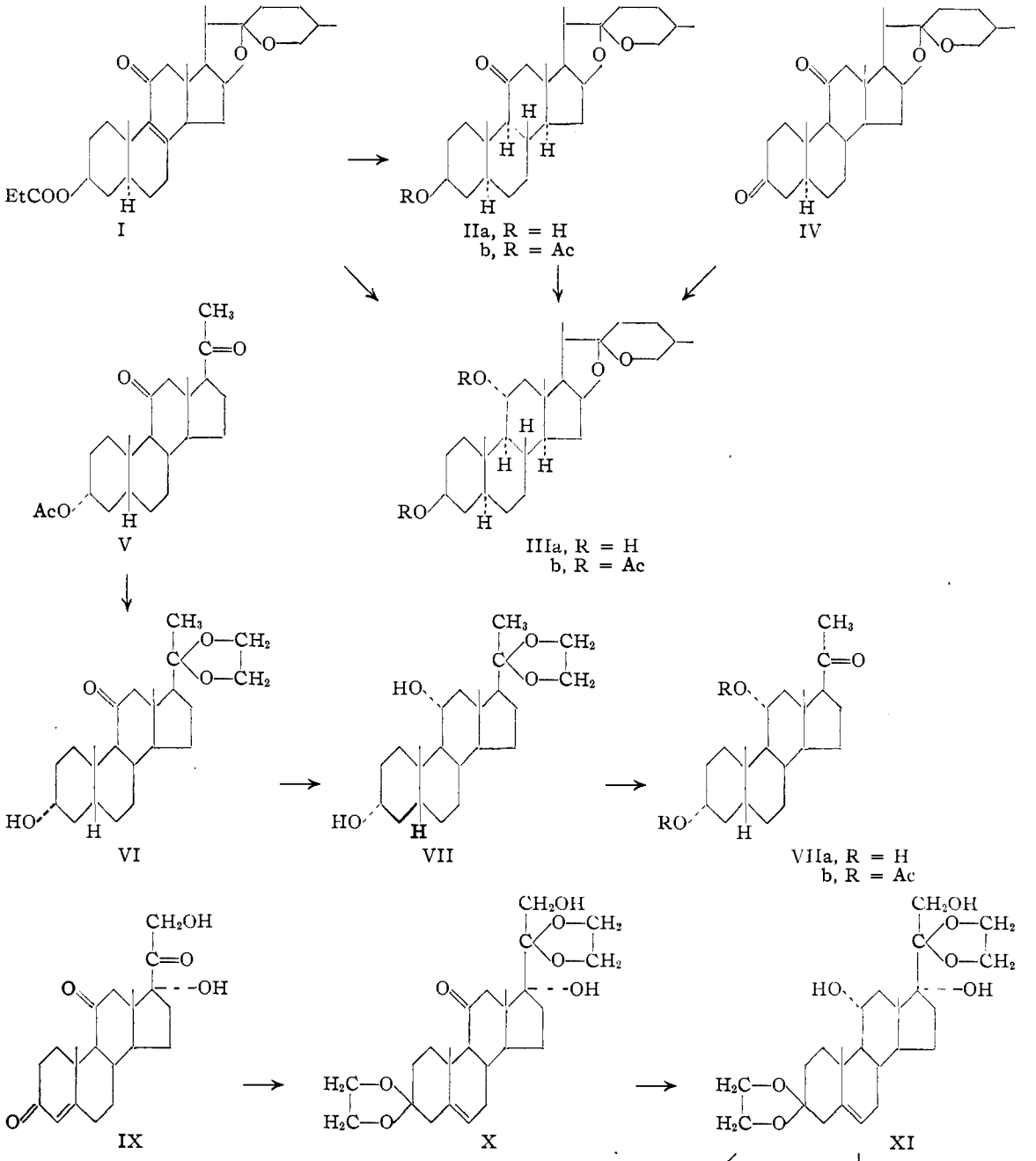
(4) For recent reviews see L. Velluz, A. Petit and J. Mathieu, *Bull. soc. chim.*, 1 (1952); A. J. Birch, *Ann. Repts. on Progress Chem. (Chem. Soc. London)*, **48**, 204 (1951).

(5) At the same time that the preliminary announcement of this work appeared (footnote 2), E. Schoenewaldt, L. Turnbull, E. M. Chamberlin, D. Reinhold, A. E. Erickson, W. V. Ruyle, J. M. Chemerda and M. Tishler (THIS JOURNAL, **74**, 2696 (1952)), independently described a method for introducing an 11-keto group both in the ergostane and in the spirostane series, which appears to be identical with ours.

(6) (a) E. M. Chamberlin, W. V. Ruyle, A. E. Erickson, J. M. Chemerda, L. M. Aliminosa, R. L. Erickson, G. E. Sita and M. Tishler, *ibid.*, **73**, 2396 (1951); (b) C. Djerassi, E. Batres, J. Romo and G. Rosenkranz, *ibid.*, **74**, 3634 (1952); (c) J. M. Chemerda, E. M. Chamberlin E. H. Wilson and M. Tishler, *ibid.*, **73**, 4052 (1951); (d) G. Rosenkranz, J. Pataki and C. Djerassi, *ibid.*, **73**, 4055 (1951); (e) G. Rosenkranz, C. Djerassi, R. Yashin and J. Pataki, *Nature*, **168**, 28 (1951).

(7) G. Rosenkranz, J. Romo, E. Batres and C. Djerassi, *J. Org. Chem.*, **16**, 298 (1951).

(8) An account of these hydrogenation experiments, together with the experimental details for preparing I from $\Delta^{7,9(11)}$-22a-5α-spirostadien-3β-ol, will be published separately. (C. Djerassi, W. Frick, G. Rosenkranz and F. Sondheimer, THIS JOURNAL, in press).



conditions for effecting chemical reductions (metal–alcohol and metal–acid combinations) were investigated, but although saturation of the unsaturated linkage took place, only intractable mixtures resulted. This may well have been due to partial isomerization at C-14 *via* the $\Delta^{9(11)8,(14)}$-enol, since the Δ^8-11-ketone I has been shown to be easily invertable at this center through boiling with 5% ethanolic potassium hydroxide.[2] When the reduction of I was carried out by means of sodium in liquid ammonia, the desired 22α-5α-spirostan-3β-ol-11-one (IIa) could be isolated in small yield. This result was not improved by substituting calcium for sodium, but when lithium in liquid ammonia was employed, the 11-ketone IIa was obtained in 61% yield. That this compound really possessed the "natural" B/C ring junction was established by direct comparison with an authentic sample.[9] This result not only completes a new path to cortisone, but unequivocally proves the

(9) (a) C. Djerassi, H. J. Ringold and G. Rosenkranz, THIS JOURNAL, **73**, 5513 (1951); (b) C. Djerassi, E. Batres, M. Velasco and G. Rosenkranz, *ibid.*, **74**, 1712 (1952).

Δ^8-11-keto structure for I and hence the 9,11-oxido formulation for its precursor.

When the reduction of I was performed with lithium in liquid ammonia *in the presence of alcohol*, a compound was obtained in 58% yield, which seemed to contain two more hydrogen atoms than IIa, which did not show a ketone band in the infrared spectrum, and which formed a diacetate. It was suspected that this substance was the known[9b] 22a-5α-spirostane-3β,11α-diol (IIIa), and this was confirmed through comparison of the free compound and of the diacetate IIIb with authentic specimens. It was thought most likely that the reaction leading from the Δ^8-11-ketone I to IIIa proceeded *via* the 11-ketone IIa (since this was the product when no alcohol was present) and that IIa was further reduced to the 11α-hydroxy compound IIIa by the lithium–alcohol–ammonia combination. This indeed seemed to be the case, for when the authentic 11-ketone IIa was treated under these very conditions, the 11α-hydroxy compound IIIa was obtained in practically quantitative yield. Similarly 22a-5α-spirostane-3,11-dione (IV)[9] was reduced under these conditions both at C-3 and C-11 again to yield the 3β,11α-diol IIIa, further characterized as the diacetate IIIb.[10] This reduction of an 11-ketone to the 11α-hydroxy compound is in marked contrast to the formation of the 11β-hydroxy group through reduction with lithium aluminum hydride,[9b,11,15] lithium borohydride,[12] sodium borohydride[13] and through catalytic hydrogenation.[14]

This convenient and novel method for converting 11-ketones to the corresponding 11α-hydroxy compounds is of considerable utility at the present time, since a general program is under way in these laboratories aimed at synthesizing the 11α-hydroxy analogs of the various adrenal hormones. Thus, when pregnan-3α-ol-11,20-dione 20-ethylene ketal (VI)[15] (prepared from pregnan-3α-ol-11,20-dione acetate (V)) was treated with the lithium–alcohol–ammonia combination, and the corresponding 11α-hydroxy compound VII so produced was treated in acetone solution with *p*-toluenesulfonic acid to effect cleavage of the ketal function, pregnane-3α,11α-diol-20-one (VIIIa) was obtained in 94% yield. The diacetate (VIIIb) of this compound, which may also be obtained from 11α-acetoxyprogesterone through hydrogenation to pregnan-11α-ol-3,20-dione acetate, followed by preferential reduction at C-3 with sodium borohydride and acetylation,[16] has served as starting material for a synthesis of Δ^4-pregnene-11α,21-diol-3,20-dione, the 11-epimer of corticosterone.[17] The successful lithium–alcohol–ammonia reduction of the 11-ketone to the 11α-hydroxy compound in this series demonstrates that the reaction is applicable to 11-ketones of the 5β (normal) series as well as to those of the 5α (allo) series.

Another example of the utility of the above described reduction procedure is to be found in a simple conversion of Δ^4-pregnene-17α,21-diol-3,11,-20-trione (cortisone) (IX) to Δ^4-pregnene-11α,17α,-21-triol-3,20-dione (XIIa), the 11-epimer of Kendall's compound F. The 3,20-diethylene ketal (X) of cortisone on reduction with lithium in liquid ammonia containing alcohol was converted in 96% yield to the corresponding 11α-hydroxy compound XI. When the latter was treated with *p*-toluenesulfonic acid in acetone solution at room temperature, only the ketal grouping at C-3 was attacked, and the 20-ethylene ketal XIII was obtained. On boiling the acetone solution, both ketal groupings were cleaved, and the desired triol XIIa was obtained in 73% yield. It exhibited properties in good agreement with those reported for this compound obtained by the microbiological oxidation of Reichstein's substance S,[18] and proved to be identical with a sample synthesized by an alternative method[1a]; it was further characterized as its 11,21-diacetate XIIb.[1a,18,19]

Experimental[20]

22a-5α-Spirostan-3β-ol-11-one (IIa).—A solution of 4.84 g. of Δ^8-22a-5α-spirosten-3β-ol-11-one propionate (I)[2] in 40 cc. of dry dioxane and 40 cc. of dry ether was added in a thin stream to a stirred solution of 0.21 g. of lithium metal in 200 cc. of liquid ammonia. The blue solution decolorized after *ca.* 85% of the steroid solution had been added. After the end of the addition lithium metal was added in small pieces to the solution, until a blue color persisted (*ca.* 40 mg. required), and 5 g. of solid ammonium chloride was then added. The ammonia was allowed to evaporate, water and chloroform were added to the residue, and the organic layer was washed with dilute hydrochloric acid, sodium carbonate solution and water, dried and evaporated. The solid residue (λ_{max} 254 mμ, log ϵ 2.81) was refluxed with 4 g. of potassium hydroxide in 40 cc. of methanol for 1 hour, since in a previous experiment chromatography had shown this material not to have been completely saponified at C-3 by the ammonia. Addition of water gave 4.21 g. of material with m.p. 168–179°, which on chromatographic purification and crystallization from acetone–hexane yielded 2.62 g. (61%) of 22a-5α-spirostan-3β-ol-11-one (IIa) with m.p. 223–225°, $[\alpha]^{20}D$ −29°, no appreciable absorption in the ultraviolet, $\lambda_{max}^{CHCl_3}$ 1700 cm.$^{-1}$ and free hydroxyl band; reported[9b]: m.p. 223–225°, $[\alpha]^{20}D$ −30°.

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.30; H, 9.83. Found: C, 75.61; H, 10.08.

The compound was identified with an authentic sample

(10) After these experiments had been completed, two reports appeared (H. Heusser, R. Anliker and O. Jeger, *Helv. Chim. Acta*, **35**, 1537 (1952); H. L. Herzog, E. P. Oliveto, M. A. Jevnik and E. B. Hershberg, THIS JOURNAL, **74**, 4470 (1952)), describing the chemical reduction of other 11-keto steroids, both in the 5α and in the 5β series, to the corresponding 11α-hydroxy compounds by means of sodium in boiling propanol.

(11) *Inter al.* L. H. Sarett, M. Feurer and K. Folkers, *ibid.*, **73**, 1777 (1951).

(12) *Inter al.* N. L. Wendler, Huang-Minlon and M. Tishler, *ibid.*, **73**, 3818 (1951).

(13) H. Heymann and L. F. Fieser, *ibid.*, **73**, 5252 (1951).

(14) *Cf.* J. von Euw and T. Reichstein, *Helv. Chim. Acta*, **30**, 305 (1947).

(15) G. Rosenkranz, J. Pataki and C. Djerassi, *J. Org. Chem.*, **17**, 290 (1952).

(16) O. Mancera, H. J. Ringold, C. Djerassi, G. Rosenkranz and F. Sondheimer, THIS JOURNAL, **75**, 1286 (1953) (Steroids XLIII).

(17) O. Mancera, G. Rosenkranz, C. Djerassi and F. Sondheimer, *ibid.*, in press.

(18) J. Fried, R. W. Thoma, J. R. Gerke, J. E. Herz, M. N. Donin and D. Perlman, *ibid.*, **74**, 3962 (1952).

(19) (a) J. Romo, A. Zaffaroni, J. Hendrichs, G. Rosenkranz, C. Djerassi and F. Sondheimer, *Chemistry and Industry*, 783, 834 (1952); (b) H. L. Herzog, E. P. Oliveto, M. A. Jevnik and E. B. Hershberg, THIS JOURNAL, **74**, 4470 (1952).

(20) Melting points are uncorrected. Unless noted otherwise, rotations were determined in chloroform and ultraviolet absorption spectra in 95% ethanol solution. We are grateful to Srta. Paquita Revaque for these measurements as well as for the infrared spectra, which were measured on a Perkin–Elmer model 12C spectrometer with sodium chloride prism. Thanks are due to Srta. Amparo Barba and staff for microanalyses.

through mixture melting point determination and infrared comparison.

The 3-acetate IIb (pyridine–acetic anhydride, steam-bath, 1 hour) crystallized from chloroform–hexane, and exhibited, m.p. 223–227°, $[\alpha]^{20}D$ −41°, $\lambda_{max}^{CHCl_3}$ 1724 and 1704 cm.$^{-1}$. It proved to be identical (mixture melting point, infrared spectrum) with an authentic specimen; reported: m.p. 222–223°, $[\alpha]^{20}D$ −32°[9b]; m.p. 224–229°, $[\alpha]D$ −39.4°.[8a].

22a-5α-Spirostane-3β,11α-diol (IIIa) from Δ^8-22a-5α-Spirosten-3β-ol-11-one Propionate (I).—A solution of 0.50 g. of the Δ^8-11-one (I)[9] in 20 cc. of ether was added to a stirred solution of 6 cc. of methanol[21] in 250 cc. of liquid ammonia. Lithium metal (0.50 g.) was added in small pieces over *ca.* 15 minutes (the blue color which appeared after the addition of each piece was discharged a few seconds later). Ammonium chloride (8 g.) was then added and the product was isolated as in the previous experiment; it weighed 0.45 g. and exhibited no absorption in the ultraviolet. Saponification was completed through refluxing for 1 hour with 0.5 g. of potassium hydroxide in 10 cc. of methanol. Chromatographic purification of the product and crystallization from methanol or hexane furnished 0.26 g. (58%) of the 3β,11α-diol (IIIa) with m.p. 218–220°, $[\alpha]^{20}D$ −78°, $\lambda_{max}^{CHCl_3}$ free hydroxyl band only, identified by direct comparison (mixture melting point, infrared spectrum) with an authentic specimen: reported,[9b] m.p. 217–218°, $[\alpha]^{20}D$ −69°.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25. Found: C, 75.16; H, 10.34.

The diacetate IIIb on crystallization from acetone–hexane had m.p. 174–176°, $[\alpha]^{20}D$ −79°, $\lambda_{max}^{CHCl_3}$ 1724 cm.$^{-1}$; reported[9b]: m.p. 175–177°, $[\alpha]^{20}D$ −84°. Identity with an authentic sample was established in the usual way.

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72.06; H, 9.36. Found: C, 72.26; H, 9.45.

When ethanol was employed instead of methanol in the reduction procedure, identical results were obtained.

22a-5α-Spirostane-3β,11α-diol (IIIa) from 22a-5α-Spirostan-3β-ol-11-one (IIa).—The reduction of 1.00 g. of the 3β-ol-11-one (IIa) in 10 cc. of dioxane (added to 100 cc. of liquid ammonia containing 10 cc. of methanol) with 0.5 g. of lithium was carried out as above, the metal being added during 5 minutes. Addition of 5 g. of ammonium chloride, evaporation of the ammonia and addition of water furnished 0.97 g. of the diol IIIa with m.p. 212–215°, $[\alpha]D$ −76°, raised on one crystallization from ether to m.p. 217–219°. Identity with an authentic specimen was established in the usual manner.

The diacetate IIIb had m.p. 173–176°, $[\alpha]^{20}D$ −76° and was identified by comparison with an authentic specimen.

22a-5α-Spirostane-3β,11α-diol (IIIa) from 22a-5α-Spirostane-3,11-dione (IV).—The reduction was carried out as described for the previous experiment with 1.5 g. of the dione (IV)[9] in 10 cc. of dioxane, 150 cc. of liquid ammonia, 15 cc. of methanol, 1.5 g. of lithium and 15 g. of ammonium chloride. After the ammonia had been evaporated, water was added and the precipitate collected. The diol IIIa weighed 1.45 g. (96%), and had m.p. 210–215°, $[\alpha]^{20}D$ −77°, raised on one crystallization to 215–218°. Identity with an authentic specimen was established in the usual way.

The diacetate IIIb had m.p. 172–174°, $[\alpha]^{20}D$ −78° and was identical with an authentic specimen.

Pregnane-3α,11α-diol-20-one 20-Ethylene Ketal (VII).—Pregnan-3α-ol-11,20-dione 20-ethylene ketal (VI) was prepared from pregnan-3α-ol-11,20-dione acetate (V) in 80% yield as described by Rosenkranz, Pataki and Djerassi.[15] A solution of 1 g. of (VI) in 30 cc. of ether was added to 100 cc. of liquid ammonia containing 5 cc. of methanol. The solution was then treated with 0.5 g. of lithium metal followed by 5 g. of ammonium chloride as described above. Evaporation of ammonia, addition of water to the residue, extraction with ether and concentration of the ether solution to *ca.* 50 cc. caused the precipitation of 0.86 g. (86%) of VII with m.p. 193–197°. Crystallization from acetone–hexane yielded the analytical sample with m.p. 199–200°, $[\alpha]^{20}D$ +16°, $\lambda_{max}^{CHCl_3}$ free hydroxyl band only.

Anal. Calcd. for $C_{23}H_{38}O_4$: C, 72.97; H, 10.12. Found: C, 73.21; H, 10.36.

(21) *Cf.* A. L. Wilds, Abstracts, p. 20M, American Chemical Society Meeting, New York, September, 1951.

Pregnane-3α,11α-diol-20-one (VIIIa).—The preceding ketal VII (0.74 g.) in 50 cc. of acetone was treated with 75 mg. of *p*-toluenesulfonic acid, and the solution was allowed to stand at room temperature for 24 hours. Addition of water and extraction with chloroform yielded 0.65 g. (99%) of the 20-ketone VIIIa with m.p. 169–175°, raised by further crystallization from acetone–hexane to m.p. 178–179°, $[\alpha]^{20}D$ +88°, $\lambda_{max}^{CHCl_3}$ 1700 cm.$^{-1}$ and free hydroxyl band.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.43; H, 10.20.

In a preparative experiment, in which the intermediate ketal VII was not purified, 4.0 g. of VI yielded 3.34 g. (94%) of VIIIa with m.p. 172–175°.

Acetylation of VIIIa with acetic anhydride–pyridine (1 hour, steam-bath) yielded the 3,11-diacetate VIIIb with m.p. 142–144°, $[\alpha]^{20}D$ +61°, $\lambda_{max}^{CHCl_3}$ 1720 and 1700 cm.$^{-1}$, identified by comparison with a sample prepared by an independent method.[16,22]

Δ^5-Pregnene-11α,17α,21-triol-3,20-dione 3,20-Diethylene Ketal (XI).—Δ^5-Pregnene-17α,21-diol-3,11,20-trione 3,20-diethylene ketal (cortisone diketal) (X) (0.30 g., m.p. 235–239°) in 5 cc. of dioxane was added to 3 cc. of methanol and 50 cc. of liquid ammonia, and the solution was treated successively with 0.25 g. of lithium and 3 g. of ammonium chloride in the usual way. Evaporation of ammonia and addition of water yielded 0.29 g. (96%) of the 11α-ol XI with m.p. 295–300°, raised on crystallization from chloroform–hexane to 298–301°, no appreciable absorption in the ultraviolet, λ_{max}^{nujol} free hydroxyl band only.

Anal. Calcd. for $C_{25}H_{38}O_7$: C, 66.64; H, 8.50. Found: C, 66.87; H, 8.81.

Δ^4-Pregnene-11α,17α,21-triol-3,20-dione 20-Ethylene Ketal (XIII).—The aforementioned diketal XI (0.30 g.) was allowed to stand with 50 mg. of *p*-toluenesulfonic acid in 100 cc. of acetone for 24 hours at room temperature with occasional shaking; the insoluble diketal slowly went into solution as reaction proceeded. The solution was concentrated to 30 cc. *in vacuo*, cooled in ice, and the precipitate was collected. The monoketal XIII weighed 0.17 g. (63%) and showed m.p. 270–275°, raised on crystallization from methanol to m.p. 287–290°, $[\alpha]D$ + 55° (EtOH), λ_{max} 240 mμ, log ε 4.24, λ_{max}^{nujol} 1668 cm.$^{-1}$ and free hydroxyl band.

Anal. Calcd. for $C_{23}H_{34}O_6$: C, 67.95; H, 8.43. Found: C, 68.11; H, 8.33.

Δ^4-Pregnene-11α,17α,21-triol-3,20-dione (XIIa).—The diketal XI (0.29 g.) and 50 mg. of *p*-toluenesulfonic acid were refluxed overnight with 100 cc. of acetone at 580 mm. (if the reaction is worked up at this stage, some of the monoketal XIII can still be isolated), another 50 mg. of *p*-toluenesulfonic acid was added and refluxing was continued for another 5 hours. The solution was evaporated to dryness *in vacuo*, water and chloroform were added, the organic layer was washed with sodium bicarbonate solution and water, dried and evaporated. Crystallization of the residue from acetone–hexane yielded 0.17 g. (73%) of the 3,20-dione XIIa with m.p. 200–205°, raised on further crystallization from this solvent pair to constant m.p. 209–211°, $[\alpha]^{20}D$ +112° (EtOH), λ_{max} 242 mμ, log ε 4.24, λ_{max}^{mull} 1700 and 1660 cm.$^{-1}$ and free hydroxyl band. One further crystallization in the presence of a seed of a sample (m.p. 215–218°) obtained by a different route[18a] gave material with m.p. 216–219°, probably a different polymorphic form. Reported for the microbiological product[18]: m.p. 217–219°, $[\alpha]^{20}D$ +117° (EtOH); for the synthetic product[18a]: m.p. 215–218°, $[\alpha]^{20}D$ +110° (EtOH). Identity with samples obtained by either method[23] was established through mixture melting point determination and infrared comparison.

The 11,21-diacetate XIIb was crystallized from acetone–hexane and had m.p. 222–224°; it was identical with a specimen (m.p. 221–223°) obtained by an independent method[18a,19a] as evidenced by mixture melting point determination and infrared comparison.

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(22) This substance, as well as the free diol VIIIa, was first prepared by W. P. Long, C. W. Marshall and T. F. Gallagher, *J. Biol. Chem.*, **165**, 197 (1946) by degradation of 3α,11α-dihydroxycholanic acid.

(23) We would like to thank Dr. A. Zaffaroni of our Biochemistry Department for providing a sample of the microbiological product.