2,4-Diamino-5-nitro-6-methylpyrimidine.—A solution of 15.0 g. of 2,4-dichloro-5-nitro-6-methylpyrimidine[16] in 50 ml. of ethanol was added to 150 ml. of 95% ethanol previously saturated with dry ammonia. The solution was heated to boiling while aerated with a continuous stream of ammonia for a period of one-half hour. The solution was then cooled, filtered, and the precipitate repeatedly washed with cold water to remove the ammonium chloride; yield of light tan product 10 g. (82%), m.p. 235° dec.

4-Amino-2-diethylamino-5-formylaminopyrimidine.—Eight grams of 4-amino-2-diethylamino-5-nitropyrimidine,[3] m.p. 110°, was dissolved in 100 ml. of absolute methanol, 2–3 g. of Raney nickel catalyst added and the solution hydrogenated at a pressure of 10 lb./sq. in. for 5 hours. The solution was then filtered and evaporated to dryness. To the residue was added 25 ml. of 90% formic acid and the solution refluxed gently for 15 minutes; the excess formic acid was then evaporated and the residue redissolved in 50 ml. of hot slightly ammoniacal solution. Upon cooling a crude yield of 5.1 g. of dark brown material was deposited. The crude material was then boiled with 200 ml. of water which left a small amount of dark, gummy residue; the aqueous solution was clarified by boiling with Norit. The cooled filtrate yielded 2.9 g. (36.7%) of white crystals, m.p. 175–177°. Recrystallization from ethanol–water mixture gave a product, m.p. 177–179°.

Anal. Calcd. for $C_9H_{15}N_5O$: N, 33.5. Found: N, 33.7.

CORVALLIS, OREGON

[CONTRIBUTION FROM THE CHEMICAL AND BIOCHEMICAL RESEARCH DIVISIONS OF SCHERING CORPORATION]

11-Oxygenated Steroids. I. Partial Syntheses of 11-Ketotestosterone and of Adrenosterone

BY HERSHEL L. HERZOG, MARGARET A. JEVNIK, PRESTON L. PERLMAN, ARTHUR NOBILE AND E. B. HERSHBERG

RECEIVED AUGUST 11, 1952

A new partial synthesis of adrenosterone is described. Adrenosterone has been converted by two independent methods to 11-ketotestosterone.

Adrenosterone (I) (Reichstein's Substance G) is one of the "inactive" companion cortical steroids which were isolated from cortical extracts by Reichstein.[1,2] No processes have been described for its preparation other than chromic acid or alkaline cleavage of the side chain of cortical steroids, which have been used to make small amounts in the process of proving their structures.[2,3]

A five-step synthesis of adrenosterone is outlined in formulas II–VI, and from I the closely related 11-ketotestosterone (VII) has been prepared for the first time. The 17-carbonyl of I has been reduced biochemically with yeast to form VII, whose structure was established by the somewhat longer independent synthesis shown in formulas VIII–XI, from V.

Pregnan-3α,17α-diol-11,20-dione (II) is available from desoxycholic acid,[4,5] and its 20-carbonyl group was hydrogenated selectively with Adams platinum catalyst in methanol to which a trace of pyridine had been added in order to inhibit the reduction of the 11-carbonyl group. The triol III was isolated only as a crude mixture which was then oxidized with lead tetraacetate in acetic acid to etiocholan-3α-ol-11,17-dione (IV).[3a] The oxidation of IV with N-bromoacetamide[6] (NBA) in aqueous acetone gave etiocholan-3,11,17-trione (V).[7] Alternately V was obtained by the reduction of II with sodium borohydride[8] to give the tetrol (IIIa), which was then cleaved at the 17-position with lead tetraacetate to etiocholan-3α,11β-diol-17-one (IVa)[9] followed by oxidation to the triketone (V) with N-bromoacetamide. Bromination of V in acetic acid followed by dehydrobromination–semicarbazone formation introduced the C-4 double bond. Adrenosterone (I) was then regenerated from its semicarbazone with pyruvic acid.[10] The over-all yield of I through II and III was 33%.

Adrenosterone was converted into 11-ketotestosterone (VII) by the highly specific yeast reduction.[11] This method of reduction attacks neither the 3-keto-Δ^4-system nor the 11-carbonyl group. The structure of VII was established by an independent synthesis.

The trione V was converted to the corresponding 3-dioxolane (VIII) by refluxing in benzene with one mole of ethylene glycol in the presence of *p*-toluenesulfonic acid. The resulting mixture of starting material, 3-dioxolane and 3,17-bisdioxolane was separated chromatographically.[12] Catalytic reduction of VIII in the presence of a trace of pyridine afforded etiocholan-17β-ol-3,11-dione 3-dioxolane (IX), which was hydrolyzed to etiocholan-17β-ol-3,11-dione (X), with an over-all yield from VIII to X of 69%. Bromination of X and dehydrobromination of the bromide (XI) gave 11-ketotestosterone (VII), identical with the product from yeast reduction of adrenosterone (I).

(1) T. Reichstein, *Helv. Chim. Acta*, **19**, 29 (1936).

(2) (a) T. Reichstein, *ibid.*, **19**, 223 (1936); (b) T. Reichstein, *ibid.*, **19**, 1107 (1936).

(3) (a) L. H. Sarett, *J. Biol. Chem.*, **162**, 601 (1946); (b) H. L. Mason, C. S. Myers and E. C. Kendall, *ibid.*, **116**, 267 (1936); (c) H. L. Mason, *ibid.*, **124**, 475 (1938).

(4) L. H. Sarett, THIS JOURNAL, **70**, 1454 (1948).

(5) T. H. Kritchevsky, D. L. Garmaise and T. F. Gallagher, *ibid.*, **74**, 483 (1952).

(6) L. F. Fieser and S. Rajagopalan, *ibid.*, **72**, 5530 (1950); L. H. Sarett, *ibid.*, **71**, 1165 (1949).

(7) S. Lieberman and K. Dobriner, *J. Biol. Chem.*, **166**, 773 (1946).

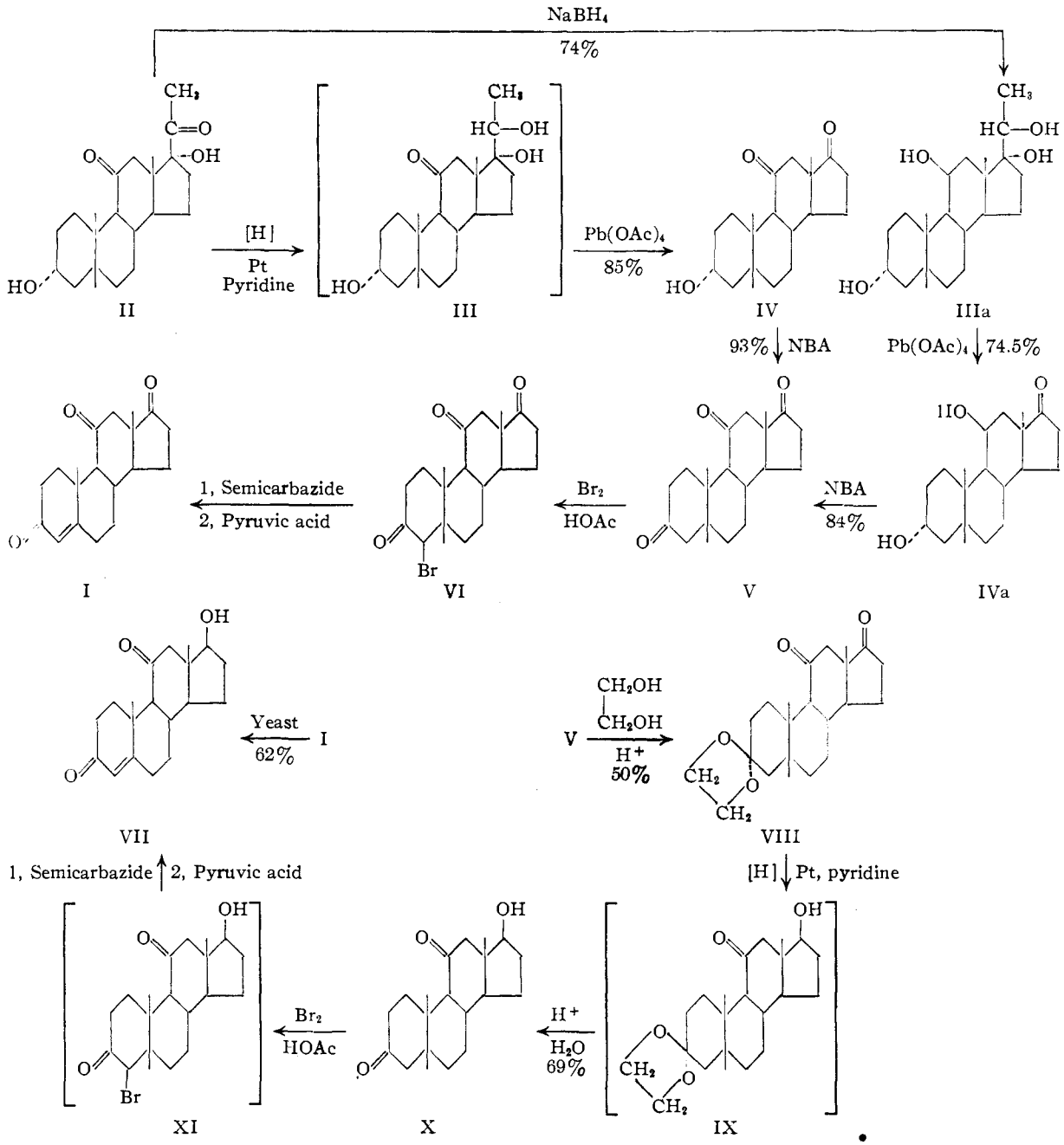
(8) *Cf.* N. L. Wendler, Huang-Minlon and M. Tishler, THIS JOURNAL, **73**, 3818 (1951); H. Heymann and L. F. Fieser, *ibid.*, **73**, 5252 (1951).

(9) L. H. Sarett, *J. Biol. Chem.*, **173**, 185 (1948).

(10) B. A. Koechlin, T. H. Kritchevsky and T. F. Gallagher, *ibid.*, **184**, 393 (1950); E. B. Hershberg, *J. Org. Chem.*, **13**, 542 (1948); V. R. Mattox and E. C. Kendall, *J. Biol. Chem.*, **188**, 287 (1951).

(11) L. Mamoli and A. Vercellone, *Ber.*, **70**, 470 (1937).

(12) H. Koster and H. H. Inhoffen, U. S. Patent 2,302,636 (Nov. 17, 1942).



Experimental[13,14]

Etiocholan-3α-ol-11,17-dione (IV).—To a solution of 10 g. (0.0286 mole) of pregnan-3α,17α-diol-11,20-dione (II)[4,5] in 100 ml. of absolute methanol containing one drop of pyridine was added 2.0 g. of Adams catalyst and the resulting mixture was hydrogenated at atmospheric pressure and room temperature until absorption of hydrogen ceased. It was found convenient to allow the reaction to proceed overnight since uptake of the last portion of hydrogen was quite slow. The catalyst was removed by filtration and the solution was evaporated to dryness on the steam-bath.

A solution of the residual oil in 100 ml. of glacial acetic acid was treated with an acetic solution of 14.1 g. of lead tetraacetate (Arapahoe Chemicals, Inc., Boulder, Colo.; contains 85–90% of active material, 0.0286 mole assuming 90% basis) at room temperature and the resulting solution was allowed to stand overnight. Several volumes of water was added to the reaction mixture and the solution was extracted thoroughly with methylene chloride. The methylene chloride extracts were washed with water and aqueous sodium carbonate and dried over magnesium sulfate. Concentration of the dry solution to a small volume followed by dilution with anhydrous ether and cooling resulted in the precipitation of 7.1 g. of etiocholan-3α-ol-11,17-dione (IV), m.p. 186–187°. A second crop of 0.4 g., m.p. 180–183°, was obtained on concentration of the mother liquor, resulting in a total yield of 85%, $[\alpha]^{26}D$ +138.3° (1% in acetone).

Anal. Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.10; H, 9.29.

The semicarbazone of IV prepared in the usual way melted at 271–272° dec., after crystallization from methanol–water solution.

Anal. Calcd. for $C_{20}H_{31}O_3N_3$: N, 11.62. Found: N, 11.40.

(13) All melting points are corrected.

(14) The authors are indebted to Mr. Edwin Conner, Mrs. Thomas Barrella, Mrs. Raymond McEntire and Miss Joan Mustachio of this Laboratory for the microanalyses and optical data, and to Dr. William Tarpley, Miss Cecelia Vitiello and Miss Betty Blasko for the measurement and interpretation of the infrared spectra.

Etiocholan-3,11,17-trione (V) from IV.—A solution of 14.36 g. (0.0472 mole) of IV in 276 ml. of acetone was diluted with 69 ml. of water and to this solution was added 19.00 g. (0.138 mole) of N-bromoacetamide (NBA). The mixture was shaken at room temperature until the NBA had dissolved completely and was then allowed to stand in the dark at 5–10° for two hours. The orange solution which resulted was poured into an aqueous sodium sulfite solution, containing 35 g. of sodium sulfite, to discharge the color. After thorough extraction of the reaction mixture with methylene chloride the combined extracts were washed with water and dried over magnesium sulfate. Evaporation of the dried solution gave a colorless oil, which crystallized as prisms on trituration with ether. A first crop of 11.24 g. (78.8%) of etiocholan-3,11,17-trione (V), m.p. 133–135°, was obtained. Successive concentrations of the mother liquor gave a total of 2.09 g. as second and third crops, m.p. 131–134°, resulting in a total yield of 93.5%. A sample of V recrystallized from ether melted at 135–136°, $[\alpha]^{23}D$ +150.8° (1% in acetone). Lieberman and Dobriner[7] reported V, m.p. 132–133°, $[\alpha]^{18}D$ +148.5 ± 1° (1.018% in ethanol).

Pregnan-3α,11β,17α,20-tetrol (IIIa).—Solutions of 5.0 g. of II in 75 ml. of methanol and 5.0 g. of sodium borohydride in 15 ml. of water were combined and allowed to stand at room temperature for 43 hours. Removal of the bulk of the methanol by distillation *in vacuo* resulted in the crystallization of 3.75 g. (74%) of pregnan-3α,11β,17α,20-tetrol, m.p. 275–282°, as needles. A sample recrystallized from methanol–water melted at 274–277°.

Anal. Calcd. for $C_{21}H_{36}O_4$: C, 71.55; H, 10.29. Found: C, 71.59; H, 10.63.

Etiocholan-3α,11β-diol-17-one (IVa).—To a solution of 2.0 g. (0.00565 mole) of IIIa in 150 ml. of acetic acid was added 5.0 g. (0.0113 mole) of 85–90% lead tetraacetate in 100 ml. of glacial acetic acid and the reaction mixture was allowed to stand overnight at room temperature. The reaction mixture was diluted with four volumes of water and extracted thoroughly with methylene chloride. The extracts were washed neutral with water and aqueous sodium carbonate and dried over magnesium sulfate. Evaporation of the dried solution left a solid residue which upon crystallization from aqueous methanol yielded 1.30 g. (74.5%) of IVa, m.p. 233–238°. Recrystallization from aqueous methanol raised the m.p. 237–238.6°, $[\alpha]^{26}D$ +104.1° (1% in dioxane). Sarett[9] reported IVa, m.p. 237.5–239°.

Anal. Calcd. for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.70; H, 9.57.

Etiocholan-3,11,17-trione (V) from IVa.—To a solution of 13.41 g. (0.044 mole) of IVa in 545 ml. of acetone, 175 ml. of methanol and 108 ml. of water was added 24.4 g. (0.176 mole) of NBA. After all the NBA had dissolved with shaking at room temperature, the reaction mixture was placed in the dark at 5–10° for three hours. The orange solution was then treated exactly as described in the preparation of V from IV; yield of V, 11.17 g. (84%) in two crops, m.p. 132–134°. Admixture with a sample of V from IV did not result in any depression of melting point.

4-Bromoetiocholan-3,11,17-trione (VI).—To a solution of 3.0 g. (0.00994 mole) of V in 30 ml. of glacial acetic acid containing 0.5 ml. of 0.28 *N* hydrogen bromide in glacial acetic acid was added dropwise, at room temperature with efficient mechanical agitation, 1.67 g. (0.0104 mole) of bromine in 20 ml. of glacial acetic acid at such a rate that the color of the solution discharged immediately following the admission of each portion of the bromine solution. The solution was stirred for five minutes following completion of the addition and was then diluted with 700 ml. of water and extracted thoroughly with methylene chloride. The extracts were washed neutral with water and aqueous sodium carbonate, dried over magnesium sulfate and concentrated carefully *in vacuo*. Trituration of the oily residue with ether caused the crystallization of 3.42 g. (90.4%) of VI as colorless prisms, m.p. 182–183° dec. A second crop of 0.06 g., m.p. 181–182° dec., was obtained on concentration of the mother liquor. Recrystallization of VI from acetic acid–water raised the melting point to 186–187° dec., $[\alpha]^{21}D$ +139.1° (1% in acetone).

Anal. Calcd. for $C_{19}H_{25}O_3Br$: Br, 20.96. Found: Br, 20.95.

Adrenosterone (I).—To 13 g. (0.0341 mole) of VI suspended in 100 ml. of glacial acetic acid under an atmosphere of carbon dioxide at room temperature was added rapidly, with mechanical agitation, a solution of 9.4 g. (0.0844 mole) of semicarbazide hydrochloride and 6.7 g. (0.0844 mole) of sodium acetate in 30 ml. of acetic acid and 26 ml. of water. The colorless solution quickly turned yellow-green and the color discharged slowly as the reaction went to completion. Ten minutes after this addition 41 ml. of 1 *N* sodium acetate was added and the stirring was continued for 20 minutes. Then the carbon dioxide atmosphere was discontinued and 19.7 g. of pyruvic acid (91%) was added. The resulting solution was refluxed for ten minutes, cooled, diluted with 2 l. of water and allowed to stand overnight. The precipitate which formed was removed by filtration and the filtrate was extracted thoroughly with methylene chloride. The methylene chloride extracts were washed with water and aqueous sodium carbonate and dried over magnesium sulfate. The aforementioned precipitate was recrystallized from ethanol and the purified substance was added to the methylene chloride solution. After the bulk of the solvent was removed by distillation the remaining solution was passed through a chromatographic column containing 120 g. of Florisil. Following thorough elution of the column with methylene chloride the combined eluates were evaporated to dryness leaving 8.07 g. of crude product. Recrystallization from acetone–hexane afforded 4.59 g. (45%) of adrenosterone (I), m.p. 212–216°, $[\alpha]^{21}D$ +270.1° (1% in acetone), ϵ_{238} 14.4 × 10^3 (95% ethanol). A second crop of 0.30 g. of I, m.p. 202–212°, was obtained by concentration of the mother liquor. Recrystallization of the first crop from absolute ethanol raised the m.p. to 218.5–220°, $[\alpha]^{28}D$ +271.3° (2.4% in acetone); ϵ_{238} 15.1 × 10^3 (95% ethanol). Sarett[3a] reports I, m.p. 222–224°, $[\alpha]^{25}D$ +281° (acetone), ϵ_{239} 13.8 × 10^3. Reichstein reports I, m.p. 222–224°,[2b] $[\alpha]^{20}D$ +262 ± 3° (ethanol).[1]

Etiocholan-3,11,17-trione 3-Dioxolane (VIII).—To a refluxing solution of 0.42 ml. of ethylene glycol and 0.2 g. of *p*-toluenesulfonic acid in 150 ml. of C.P. benzene was added 2.0 g. of V. During the succeeding one-half hour reflux period water was removed continuously by azeotropic distillation. The solution was then cooled, washed with 10% aqueous sodium carbonate, dried over magnesium sulfate and evaporated to dryness. It is necessary that the benzene be removed completely for the succeeding chromatography to be successful. The residue was dissolved in hexane and chromatographed on 40 g. of Florisil. Approximately 11% of etiocholan-3,11,17-trione 3,17-bisdioxolane[15] was recovered from the hexane eluates. Elution with hexane–ether containing between 1 and 10% ether yielded VIII. Recrystallization from heptane gave 1.15 g. (50%), m.p. 169–172°. An additional recrystallization raised the m.p. to 171–172.5°, $[\alpha]^{25}D$ +130.0° (1% in acetone).

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.62; H, 8.61.

Elution of the column with ether, following the recovery of VIII, gave 20.5% of unreacted V.

Etiocholan-17β-ol-3,11-dione (X).—To a solution of 0.50 g. of VIII in 100 ml. of absolute methanol containing one drop of pyridine was added 0.2 g. of Adams platinum catalyst and the resulting mixture was hydrogenated at atmospheric pressure and room temperature until absorption of hydrogen stopped. It was found convenient to allow the reaction to proceed overnight. The catalyst was removed by filtration and the filtrate was concentrated to a small volume. To the residual solution 100 ml. of acetone and 2 ml. of concentrated hydrochloric acid were added and the resulting mixture was refluxed for two hours. The cooled reaction mixture was diluted with water and extracted with methylene chloride. The combined extracts were washed neutral with water, dried over magnesium sulfate and concentrated. The residual oil was crystallized from ether–hexane, yielding 0.30 g. (69%) of X, m.p. 160–163°. Recrystallization from the same solvent pair raised the m.p. to 165–165.5°, $[\alpha]^{25}D$ +65.6° (1% in acetone).

Anal. Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.33; H, 9.67.

11-Ketotestosterone (VII). A. From the Biochemical Reduction of Adrenosterone (I).—To a solution of 200 g. of sucrose in 1.5 l. of tap water contained in a 2-l. Fernbach flask was added 0.45 g. of adrenosterone. The resulting

(15) H. Herzog, *et al.*, THIS JOURNAL, **75**, 269 (1953).

suspension was autoclaved at 15 lb. pressure (120°) for 45 minutes. To the cooled solution was then added 100 ml. of ethanol and 100 g. of Fleischmann bakers' yeast. The *p*H of the reaction mixture was adjusted to 4.5–5.0 by the addition of dilute sulfuric acid, the yeast cell mass was dispersed and mechanical agitation, sufficiently slow so that anaerobic conditions were maintained, was commenced and continued for 48 hours. Hourly adjustment of the *p*H of the medium to 4.5–5.0 by the addition of dilute ammonium hydroxide was carried on during the first 12 hours. Subsequently *p*H determination and adjustment was made every eight hours.

At the end of the reaction period the mixture was centrifuged for one hour and the supernatant liquid was separated. The remaining cell mass was extracted by refluxing for one-half hour with two 1-l. portions of methanol. The combined methanolic extracts and supernatant liquid were concentrated *in vacuo* to 200 ml. and 400 ml. of water was added. The aqueous solution was then extracted three times with ethylene dichloride, and the combined ethylene dichloride extracts were washed neutral and dried. The solvent was removed *in vacuo* and the residue was crystallized from acetone–hexane solution; yield 0.28 g. (62%), m.p. 177–180°, $[\alpha]^{25}D$ +182.4° (1% in acetone).

B. **Bromination and Dehydrobromination of Etiocholan-17β-ol-3,11-dione (X).**—To a solution of 0.61 g. (0.002 mole) of X in 20 ml. of glacial acetic acid containing one drop of 0.28 *N* hydrogen bromide in acetic acid was added, dropwise, with mechanical stirring, 0.33 g. of bromine in 10 ml. of glacial acetic acid at such a rate that the color of the bromine solution was discharged as fast as it was added. Stirring was continued for five minutes, whereupon the reaction mixture was diluted with water and extracted with methylene chloride. The combined methylene chloride extracts were washed neutral with water and aqueous sodium carbonate and dried over magnesium sulfate.

The dried solution was evaporated to dryness and the residual oil was taken up in 30 ml. of glacial acetic acid. To the stirred solution, under a carbon dioxide atmosphere, was added a solution of 0.28 g. of semicarbazide hydrochloride and 0.20 g. of sodium acetate in 2 ml. of water and 2 ml. of acetic acid. After ten minutes 2.4 ml. of 1 *N* sodium acetate in acetic acid was added and stirring was continued for ten minutes. Then the stirring and carbon dioxide atmosphere were discontinued, 0.58 g. of pyruvic acid (91%) in 1 ml. of water and 3 ml. of acetic acid was added and the resulting solution was refluxed for ten minutes. The solution was cooled to room temperature, diluted with water and extracted with methylene chloride. After the methylene chloride extracts were washed neutral with aqueous sodium carbonate they were dried over magnesium sulfate and concentrated to about 40 ml. The resulting solution was then chromatographed on Florisil (15 g.) and the column was eluted first with methylene chloride and thereafter with methylene chloride containing 1% of methanol. All the crystalline fractions (0.43 g.) were combined and recrystallized from acetone–hexane, yielding 0.26 g. (43%) of VII, m.p. 177–180°. A sample recrystallized for analysis melted at 181–182.4°, $[\alpha]^{25}D$ +177.8° (1% in acetone), ϵ_{238} 14.4 × 10^3 (ethanol).

Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.31; H, 8.52.

Mixture melting point of samples from A and B showed no depression.

BLOOMFIELD, N. J.

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF SCHERING CORP.]

11-Oxygenated Steroids. II. The Reduction of 11-Carbonyl to 11α-Hydroxyl in the Etiocholane Series

BY HERSHEL L. HERZOG, MARGARET A. JEVNIK AND E. B. HERSHBERG

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Reduction with sodium and propanol-1 has been shown to convert 11-carbonyl to 11α-hydroxyl and 17-carbonyl to 17β-hydroxyl in several etiocholane derivatives. The 11α-hydroxyl group is shown to resist oxidation by N-bromoacetamide in aqueous acetone under conditions where the 3α- and 17β-hydroxyl groups are oxidized to the corresponding carbonyl groups.

The reduction of 11-ketosteroids to 11β-hydroxysteroids has been effected by catalytic hydrogenation using a platinum catalyst in acetic acid,[1,2] by lithium aluminum hydride,[3] by lithium borohydride[4] and by sodium borohydride.[5]

No satisfactory, general method has been described whereby an 11-ketosteroid can be converted to an 11α-hydroxysteroid.[6,6a] Comparatively few 11α-hydroxysteroids are known; among these are sarmentogenin and its degradation products,[7] the products derived from the Wolff–Kishner reductions of 11-(α and β)-hydroxy-12-ketocholanic acid[8–10] and 12β-hydroxy-11-ketocholanic acid[8,11,12] and the 11α-hydroxyallopregnanes and derived steroids prepared by Djerassi and co-workers[13] from $\Delta^{7,9(11)}$-allopregnadien-3β-ol-20-one acetate by performic acid oxidation, followed by alkaline rearrangement of the resulting 9α,11α-epoxide.[13a]

(1) A. Lardon and T. Reichstein, *Helv. Chim. Acta*, **26**, 586 (1943).

(2) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, N. Y., 1949, p. 655.

(3) L. H. Sarett, M. Feurer and K. Folkers, THIS JOURNAL, **73**, 1777 (1951).

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

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

(6) F. Sondheimer, R. Yashin, G. Rosenkranz and C. Djerassi in a recent communication (*ibid.*, **74**, 2696 (1952)) noted that the carbonyl group and the double bond conjugated with it in Δ^8-22-isoallospirosten-3β-ol-11-one propionate are both reduced to yield the saturated 11α-ol with the aid of lithium, liquid ammonia and alcohol.

(6a) NOTE ADDED IN PROOF.—Following the submission of the preliminary communication describing part of this work (H. L. Herzog, E. P. Oliveto, M. A. Jevnik and E. B. Hershberg, THIS JOURNAL, **74**, 4470 (1952)) a paper by H. Heusser, R. Anliker and O. Jeger appeared (*Helv. Chim. Acta*, **35**, 1537 (1952)) which reported the reduction of $\Delta^{22,23}$-ergosten-3β-ol-11-one acetate to the corresponding 3β,11α-diol with sodium and propanol-1. In that paper the hypothesis is suggested that the reduction of an 11-ketone to an 11α-ol may proceed through the 11β-ol which then epimerizes. The reduction of etiocholan-3α,11β-diol-17-one (X) to etiocholan-3α,11β,17β-triol (V), described by us, makes this explanation unsatisfactory for the etiocholane series.

(7) Katz, *Helv. Chim. Acta*, **31**, 993 (1948).

(8) T. F. Gallagher and W. P. Long, *J. Biol. Chem.*, **162**, 521 (1946).

(9) T. F. Gallagher and V. P. Hollander, *ibid.*, **162**, 533 (1946).

(10) W. P. Long and T. F. Gallagher, *ibid.*, **162**, 511 (1946).

(11) T. F. Gallagher, *ibid.*, **162**, 539 (1946).

(12) O. Wintersteiner, M. Moore and K. Reinhardt, *ibid.*, **162**, 707 (1946).

(13) C. Djerassi, O. Mancera, G. Stork and G. Rosenkranz, THIS JOURNAL, **73**, 4496 (1951); C. Djerassi, E. Batres, J. Romo and G. Rosenkranz, *ibid.*, **74**, 3634 (1952).

(13a) NOTE ADDED IN PROOF.—Recently microbiological methods for the direct introduction of the 11α-hydroxyl group have been described: see D. H. Peterson and H. C. Murray, *ibid.*, **74**, 1872 (1952); J. Fried, R. W. Thoma, J. R. Gerke, J. E. Herz, M. N. Donin and D. Perlman, *ibid.*, **74**, 3962 (1952).