methyl ether (m.p. 99–104°, preparation described below) in 1 l. of dry ether was added 1300 cc. of liquid ammonia followed by 8 g. of lithium wire. After stirring for 30 minutes, 175 cc. of ethanol was added during 30 minutes, the solvents were evaporated, and the residue was carefully treated with water. The solid product was collected, washed well with water, dissolved in 800 cc. of methanol and refluxed with 480 cc. of 3 *N* hydrochloric acid for 15 minutes. Addition of water, isolation with ether, and crystallization from ether–hexane yielded 7.4 g. of 19-nor-17α-methyltestosterone (X), with m.p. 151–154°. A further purified specimen showed m.p. 155–157°, $[\alpha]_D$ +33°; λ_{max}^{EtOH} 240 mμ, log ε 4.24. Identity with the material prepared by method a was established through mixture m.p. and infrared comparison.

In one experiment, conducted as above, the Birch reduction product was purified prior to hydrolysis. After crystallization of the crude solid from ether, the enol ether was obtained in 62% yield, m.p. 129–131°, $[\alpha]_D$ +91°, no appreciable absorption in the ultraviolet.

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.82; H, 10.34.

On acid hydrolysis, as described for the unpurified material, it yielded X in *ca.* 70% yield.

17-Methylestradiol Methyl Ether (XII).[20]—To a solution of 34 g. of estrone methyl ether in 850 cc. of dry benzene was added slowly 175 cc. of an ethereal solution of *ca.* 70 g. of methylmagnesium bromide. After being refluxed for 2 hours, the reaction mixture was poured onto ice and acidified with hydrochloric acid. The aqueous layer was extracted with ether, and the combined organic solutions were washed with water, dried and evaporated. Crystallization from ether–pentane furnished 31.1 g. (87%) of product with m.p. 99–104°. A further purified sample exhibited constant m.p. 104–105°, $\nu_{max}^{CHCl_3}$ free hydroxyl band only; this material was chromatographically pure (reported: m.p. 95–100° (for a crude specimen)[19a]; m.p. 126.5–128°[19b]). The m.p. discrepancy may be due to polymorphism.

(20) *Cf.* (a) A. Cohen, J. W. Cook and C. L. Hewett, *J. Chem. Soc.*, 445 (1935); (b) B. C. Bocklage, H. J. Nicholas, E. A. Doisy, W. H. Elliott, S. A. Thayer and E. A. Doisy, *J. Biol. Chem.*, **202**, 27 (1953).

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MEXICO CITY 17, D. F.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, CHEMICAL DIVISION, MERCK & CO., INC.]

Interconversion of Adrenal Cortical Side Chains. The Transformation of Cortisone and Hydrocortisone to Corticosterone

BY D. TAUB, R. H. PETTEBONE, N. L. WENDLER AND M. TISHLER

RECEIVED MARCH 15, 1954

Cortisone and hydrocortisone acetates on treatment with methanolic hydrogen chloride followed by reduction with lithium aluminum hydride and oxidation with manganese dioxide gave Δ⁴-pregnene-11β,20β-diol-3-one-21-al dimethylacetal (IV). Hydrolysis of the latter produced the corresponding aldehyde V, which could be isomerized to corticosterone (VII) by refluxing pyridine, or preferably, by methanolic sodium methoxide treatment of its sodium bisulfite addition product VI.

Corticosterone, one of the original active hormones isolated from adrenal cortical extracts,[1] has remained relatively unavailable despite its biological importance. Cortical extracts, moreover, have constituted the chief source of the very limited supply of this substance. The published chemical procedures for its preparation include only the classical synthesis from desoxycholic acid of von Euw, Lardon and Reichstein[2] and the partial synthesis from 11-dehydrocorticosterone in low yield *via* the 3,20-disemicarbazone derivative.[3] Biological formation from desoxycorticosterone by various microörganisms[4] and by the isolated adrenal gland[5] also have been described.

The present paper outlines a brief partial synthesis of corticosterone in 20–25% over-all yield from the currently readily available hormones, cortisone and hydrocortisone, by a reaction sequence capable of extension to the general conversion of the dihydroxy cortical side chain to the ketol part structure. The reverse sequence has been carried out in effect by Sarett[6] through the conversion of 20-keto-21-acetoxypregnane derivatives to their corresponding 17α-hydroxy analogs by osmylation of the Δ¹⁷⁽²⁰⁾-cyanopregnenes.

Recently Mattox[7] observed that both 17α,21-dihydroxypregnan-20-one as well as Δ¹⁶-21-hydroxypregnen-20-one derivatives[8] are transformed by methanolic hydrogen chloride to systems bearing a glyoxal 21,21-dimethyl acetal side chain; thus, cortisone acetate (I) was found to give Δ⁴-pregnene-3,11,20-trione-21-al dimethylacetal (II) in 75% yield, an observation which we have duplicated. Application of the Mattox conditions to hydrocortisone acetate (IX) was found similarly to produce the corresponding 11β-hydroxy compound X in 51% yield.[8a]

The Δ⁹⁽¹¹⁾-anhydro compound XII, prepared independently by rearrangement of Δ⁹⁽¹¹⁾-anhydro-17-hydroxycorticosterone acetate (XI), did not appear to be present to any appreciable extent, if at all. Retention of the 11β-hydroxyl group under these conditions contrasts with predominant dehydration occurring in acetic acid, chloroform or acetonitrile containing catalytic amounts of hydrogen bromide,[9] and with the acetic acid–hydrochloric

(1) (a) T. Reichstein, *Helv. Chim. Acta*, **19**, 1107 (1936); (b) T. Reichstein, *ibid.*, **20**, 953 (1937); (c) H. L. Mason, C. S. Myers and E. C. Kendall, *J. Biol. Chem.*, **114**, 613 (1936); (d) H. L. Mason, W. M. Hoehn, B. F. McKenzie and E. C. Kendall, *ibid.*, **120**, 719 (1937).

(2) J. von Euw, A. Lardon and T. Reichstein, *Helv. Chim. Acta*, **27**, 1287 (1944), and earlier references cited therein.

(3) N. L. Wendler, Huang-Minlon and M. Tishler, THIS JOURNAL, **73**, 3818 (1951).

(4) (a) H. C. Murray and D. H. Peterson, U. S. Patent 2,602,769 (1952); (b) G. M. Shull, D. A. Kita and J. W. Davisson, U. S. Patent 2,658,023 (1953).

(5) O. Hechter, R. P. Jacobsen, R. Jeanloz, H. Levy, C. W. Marshall, G. Pincus and V. Schenker, THIS JOURNAL, **71**, 3261 (1949).

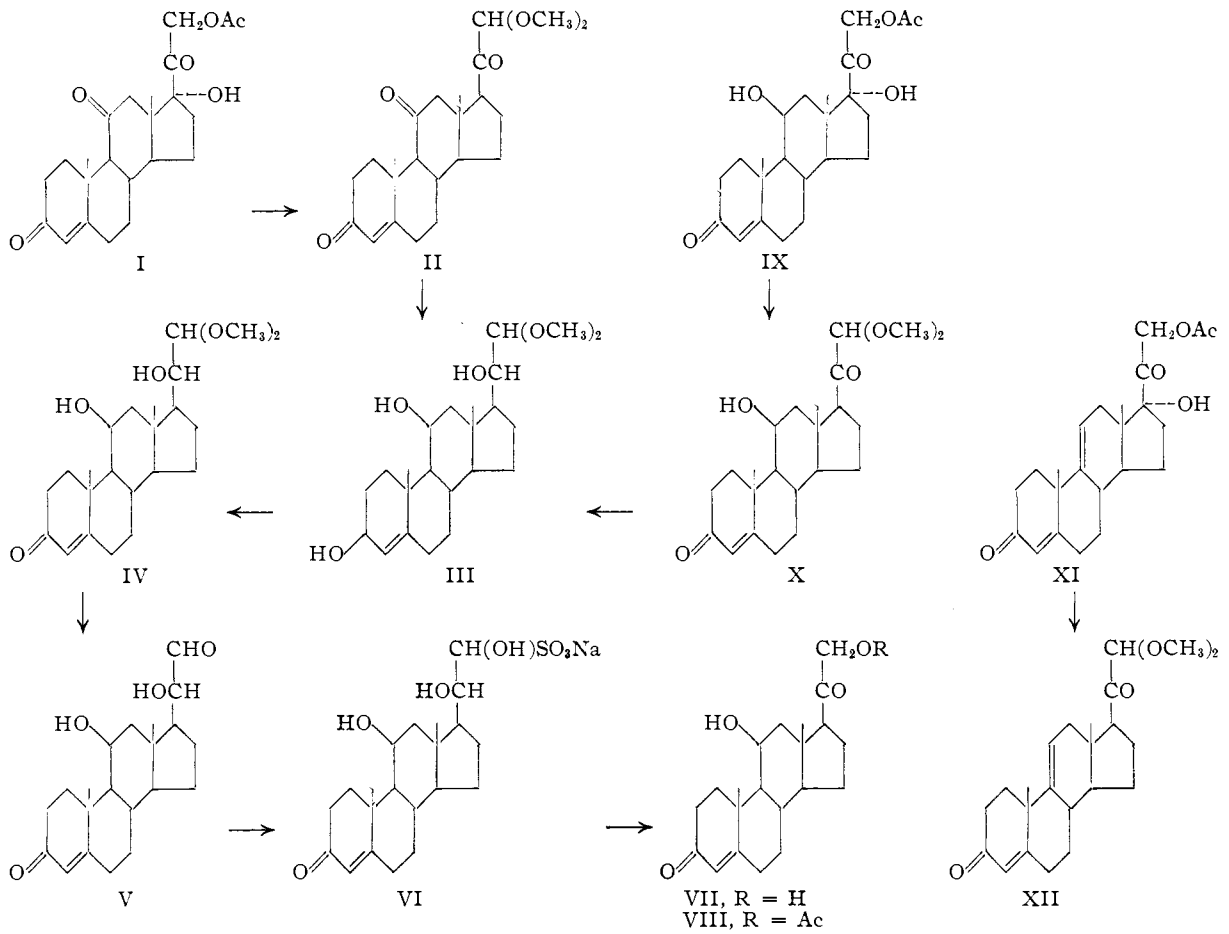
(6) L. H. Sarett, *ibid.*, **70**, 1454 (1948).

(7) V. R. Mattox, *ibid.*, **74**, 4340 (1952).

(8) E. Vischer, J. Schmidlin and A. Wettstein [*Helv. Chim. Acta*, **37**, 321 (1954)] have extended the rearrangement to 16α,21-dihydroxypregnan-20-ones.

(8a) NOTE ADDED IN PROOF.—After this manuscript was submitted the conversion of hydrocortisone acetate (IX) to the acetal X was reported by S. A. Simpson, J. F. Tait, A. Wettstein, R. Neher, J. von Euw, O. Schindler and T. Reichstein, *Helv. Chim. Acta*, **37**, 1163 (1954).

(9) R. P. Graber, A. C. Haven, Jr., and N. L. Wendler, THIS JOURNAL, **75**, 4722 (1953).



acid dehydration of corticosterone acetate (VIII).[10] The structure proof for the ol-dione acetal X was based on its analysis, infrared spectrum and its non-identity with the anhydro derivative XII; additional support was gained through the conversion of X to the 20β-hydroxy analog IV by reduction and partial oxidation as described below.

The reduction of the acetal II with lithium aluminum hydride gave a quantitative yield of mixed triols III in which the predominant configurations of the pertinent hydroxyl groups are probably 3β, 11β and 20β.[11] The triol mixture III was treated with manganese dioxide[12] in benzene to give the unsaturated ketone IV in 75% yield (based on II). The ultraviolet absorption of the total reaction product indicated the formation of 91% of the ring A chromophore, and the unaccounted 16% of the reaction mixture may have contained minor amounts of C-11 or C-20 epimers of IV. The infrared spectrum indicated the absence of saturated carbonyl functions thereby demonstrating that oxidation at C-11 or C-20 had not occurred.

A similar reduction–oxidation sequence performed on the ol-dione acetal X resulted in the same product IV, thus confirming the structure assigned to X.

The preparation of the 11-desoxy analog of IV from Δ^5-pregnene-3β-ol-20-one-21-al dimethylacetal and its conversion *via* the 21-aldehyde to desoxycorticosterone have been described by Schindler, Frey and Reichstein.[13] The most feasible procedure for hydrolysis of the acetal grouping in IV proved to be treatment with 50% aqueous acetic acid at 90° for 3 hours.[14] Under these conditions

(10) C. W. Shoppee and T. Reichstein, *Helv. Chim. Acta*, **26**, 1316 (1943).

(11) *Inter alia*, (a) L. H. Sarett, M. Feurer and K. Folkers, THIS JOURNAL, **73**, 1777 (1951); (b) P. L. Julian, E. W. Meyer, W. J. Karpel and W. Cole, *ibid.*, **73**, 1982 (1951); (c) W. G. Dauben, R. A. Micheli and J. F. Eastham, *ibid.*, **74**, 3852 (1952); (d) C. Djerassi, G. Rosenkranz, J. Pataki and St. Kaufmann, *J. Biol. Chem.*, **194**, 115 (1952); (e) W. W. Zorbach, THIS JOURNAL, **75**, 6344 (1953).

(12) (a) S. Ball, T. W. Goodwin and R. A. Morton, *Biochem. J.*, **42**, 516 (1948); (b) F. Sondheimer, C. Amendola and G. Rosenkranz [THIS JOURNAL, **75**, 5930, 5932 (1953), and earlier references cited therein] have applied the manganese dioxide procedure elegantly to the oxidation of steroid allylic alcohol and homoallylic alcohol systems. These authors, moreover, have found that, contrary to the general inertness of isolated hydroxyl groups, the 17β-hydroxyl group can be oxidized in refluxing benzene to some extent but not at room temperature. However, we have observed the oxidation of the 17β-hydroxyl function to occur during the room temperature oxidation of the triol mixture obtained from lithium aluminum hydride reduction of Δ^4-androstene-3,11,17-trione [O. Mancera, G. Rosenkranz and F. Sondheimer, *J. Chem. Soc.*, 2189 (1953)]. From this oxidation there was isolated at least 15% of Δ^4-androstene-11β-ol-3,17-dione together with the major product, Δ^4-androstene-11β,17β-diol-3-one. This observation indicates that the 17β-hydroxyl group can be oxidized differentially in the presence of the 11β-hydroxyl group by manganese dioxide. The same relative order of reactivity was found to apply in the Oppenauer oxidation of etiocholane-3α,11β,17β-triol-3-acetate [L. H. Sarett, *J. Biol. Chem.*, **173**, 185 (1948)] and probably reflects the operation of similar steric factors in both cases.

(13) W. Schindler, H. Frey and T. Reichstein, *Helv. Chim. Acta*, **24**, 360 (1941).

(14) *Cf.* (a) L. H. Sarett, M. Feurer and K. Folkers, (footnote 11a); (b) R. Antonucci, S. Bernstein, R. Littell, K. J. Sax and J. H. Williams, *J. Org. Chem.*, **17**, 1341 (1952).

the hydrolysis product V was found to be methoxyl free and negative in the tetranitromethane test for unsaturation. Stronger acidic conditions (acetone–mineral acid or aqueous acetic acid–mineral acid[13]) produced significant dehydration as evidenced by positive tetranitromethane tests, and incomplete recovery of corticosterone when the latter was subjected to the same conditions. The aldehyde group in the non-crystalline hydrolysis product V was largely masked since the infrared spectrum showed *ca.* 5% of saturated carbonyl absorption. On trituration of the product with ethyl acetate a micro-crystalline material, m.p. 165–175°, was obtained which was devoid of saturated carbonyl absorption. By analogy with the results of Reichstein and his associates[13] this material is probably a mixture of dimeric and trimeric forms of V.

On treatment of the hydrolysis product V with refluxing pyridine[13,15] the isomeric corticosterone (VII) was produced in 20% yield by direct crystallization from the reaction mixture. The yields reported by the Swiss authors for the analogous isomerizations of the corresponding 20-hydroxy-21-aldehydes to desoxycorticosterone[13] and 17-hydroxydesoxycorticosterone[15b] were, respectively, 25 and 50%. Attempted isomerization in methanolic sodium methoxide at 25° gave a mixture from which corticosterone (VII) could not be obtained, although the infrared spectrum of the product showed some intensification of saturated carbonyl absorption over that of the starting material V. It is possible that the failure of methoxide ion to catalyze the isomerization reflects the preponderance of methoxide-stable polymeric forms.

The micro-crystalline, water-soluble sodium bisulfite addition product VI was prepared in 63% yield by treatment of the hydrolysis product V in methanol with aqueous sodium bisulfite. A water solution of the derivative VI when made acidic or basic precipitated the free aldehyde V. Finally, on solution in methanolic sodium methoxide at 25° the derivative VI was transformed to corticosterone (VII) isolated by direct crystallization in 60% yield.

Acknowledgment.—We are indebted to Messrs. R. W. Walker, N. R. Trenner and F. A. Bacher and colleagues for the spectra and Mr. R. N. Boos and associates for the microanalyses reported herein.

Experimental[16]

Δ^4-Pregnene-3,11,20-trione-21-al Dimethylacetal (II).—The procedure followed was similar to that of Mattox[7] except that chloroform was omitted from the reaction mixture. Cortisone acetate (I) (10.0 g.) was suspended in dry methanolic hydrogen chloride (400 ml., 0.52 *N*). After ten minutes of agitation the material had dissolved completely to give a yellow solution which was kept at 25° 48 hours. Sodium acetate (22 g.) in water (60 ml.) was added and the solvent removed under vacuum to a volume of 75 ml. Water (100 ml.) was added, and the mixture was extracted several times with chloroform (300 ml. total). The chloroform extract was washed with 5% aqueous sodium bicarbonate and salt water and dried over sodium sulfate. The solid residue was crystallized from ether to give characteristic large dense prisms; 7.65 g. (79%), m.p. 156–158.5°, and 0.40 g. (4%), m.p. 152–156°. Recrystallization from acetone–ether raised the melting point to 160–162°, $[\alpha]_D$ +218° (acetone).[7,17]

Δ^4-Pregnene-11β-ol-3,20-dione-21-al Dimethylacetal (X).—Hydrocortisone acetate (IX) (1.00 g.), when treated with methanolic hydrogen chloride (40 ml., 0.5 *N*) as above, gave an amorphous product which solidified on trituration with ether (0.55 g., m.p. 124–128°). The deep yellow mother liquor showed no tendency to crystallize further, even on being seeded with the anhydro acetal XII. The crude solid product was freed from a minor amount of polar impurity by chromatography on neutral alumina (15 g.). Almost all the material was eluted by petroleum ether–benzene and benzene in 10 crystalline fractions all of which melted between 125–130°. Trace amounts of colored amorphous material were eluted by benzene–chloroform and chloroform and were discarded. The combined crystalline fractions were crystallized from acetone–ether to give long rectangular prisms; 472 mg. (51%), m.p. 131–133°, unchanged by further recrystallization; $[\alpha]_D$ +204° (acetone); $\lambda_{max}^{CH_3OH}$ 242 mμ, log ϵ 4.21; $\lambda\lambda_{max}^{CHCl_3}$ 2.80 μ (O–H), 5.83 μ (C=O), 5.99 μ (conj. C=O), 9.4 μ (C–O–C).

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.75; H, 8.78; CH_3O, 15.90. Found: C, 70.32; H, 8.61; CH_3O, 16.00.

$\Delta^{4,9(11)}$-Pregnadiene-3,20-dione-21-al Dimethylacetal (XII).—A suspension of $\Delta^{4,9(11)}$-pregnadiene-17α,21-diol-3,-20-dione 21-acetate (XI) (1.00 g.) in methanolic hydrogen chloride (40 ml., 0.5 *N*), stirred at 25°, still contained considerable undissolved material after 18 hours. Chloroform (15 ml.) and methanolic hydrogen chloride (10 ml., 1.25 *N*) were added, resulting in complete solution within 30 minutes. After an additional 24 hours at room temperature, the mixture was worked up as above. Chromatography on neutral alumina gave crystalline material essentially only in the petroleum ether–benzene (4:1) eluates (527 mg., 55%, m.p. 67–71°). Two recrystallizations from ether–petroleum ether gave sheaves of needles m.p. 77.5–79°, $[\alpha]_D$ +146° (acetone); $\lambda_{max}^{CH_3OH}$ 238 mμ, log ϵ 4.23; $\lambda\lambda_{max}^{nujol}$ 5.78 μ (C=O), 5.95 μ (conj. C=O), 9.3 μ (C–O–C).

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 74.17; H, 8.66; CH_3O, 16.66. Found: C, 74.19; H, 8.70; CH_3O, 16.64.

Δ^4-Pregnene-11β-diol-3-one-21-al Dimethylacetal (IV). (a) **From Δ^4-Pregnene-3,11,20-trione-21-al Dimethylacetal (II).**—A dry tetrahydrofuran (250 ml.) solution of the trione acetal II (5.00 g.) was added slowly to a stirred suspension of lithium aluminum hydride (5.0 g.) in tetrahydrofuran (250 ml.). When addition was complete, the mixture was refluxed for 75 minutes. It was then cooled to 15°, excess reagent was destroyed by cautious addition of ethyl acetate and the mixture was worked up by addition of saturated aqueous sodium sulfate until the solids had coagulated followed by anhydrous magnesium sulfate.[18] The inorganic solids were filtered, thoroughly washed with ethyl acetate and the filtrate and washings taken to dryness under vacuum. The non-crystalline product (III) (5.05 g.) was transparent in the carbonyl region of the infrared; $\lambda\lambda_{max}^{CHCl_3}$ 2.95 μ (O–H), 6.02 μ (weak) (C=C), 9.3 μ (strong) (C–O–C). When the reaction time was 30–45 minutes about 10% carbonyl absorption remained.

The total reduction product III was dissolved in dry benzene (250 ml.), precipitated manganese dioxide (50 g.)[19] was added and the mixture stirred vigorously at 25° overnight. The manganese dioxide was removed by filtration and washed repeatedly with acetone. The partly crystalline residue (4.86 g., 97%), remaining after removal of the solvents, had $\lambda_{max}^{CH_3OH}$ 242.5 mμ, log ϵ 4.14. Crystallization from acetone–ether gave 3.00 g., m.p. 156–158°, and 0.77 g., m.p. 147–151° (75% based on II). The analytical sample (needles from acetone–ether) had m.p. 157.5–158.5°; $[\alpha]_D$ +81.6° (acetone); $\lambda_{max}^{CH_3OH}$ 242.5 mμ, log ϵ 4.18; $\lambda\lambda_{max}^{CHCl_3}$ 2.86 μ (O–H), 6.00 (conj. C=O), 9.3 μ (C–O–C). The substance slowly reduced the dianisole bisdiphenyltetrazolium chloride (BT) reagent.[20]

(13) (a) H. O. L. Fischer, C. Taube and E. Baer, *Ber.*, **60**, 479 (1927); (b) T. Reichstein and J. von Euw, *Helv. Chim. Acta*, **23**, 1258 (1940).

(16) Capillary melting points are corrected.

(17) V. R. Mattox and E. C. Kendall [*J. Biol. Chem.*, **188**, 287 (1951)] give m.p. 163–164° for material recrystallized several times from 95% ethanol, $[\alpha]_D$ +214° (acetone).

(18) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, THIS JOURNAL, **74**, 4223 (1952).

(19) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen and T. Walker, *J. Chem. Soc.*, 1094 (1952).

(20) W. J. Mader and R. R. Buck, *Anal. Chem.*, **24**, 666 (1952).

Anal. Calcd. for $C_{23}H_{36}O_5$: C, 70.38; H, 9.25; CH_3O, 15.82. Found: C, 70.09; H, 8.95; CH_3O, 15.84.

(b) From Δ^4-Pregnene-11β-ol-3,20-dione-21-al Dimethylacetal (IX).—The ol-dione acetal X (100 mg.) was reduced with lithium aluminum hydride and treated with manganese dioxide as above. Two recrystallizations of the crude product (70 mg., m.p. 150–153°) from acetone–petroleum ether gave needles, m.p. 157.5–158.5°, undepressed on admixture with IV prepared from the trione acetal II. The respective infrared spectra were likewise identical.

Anal. Calcd. for $C_{23}H_{36}O_5$: C, 70.38; H, 9.25. Found: C, 70.70; H, 9.00.

Δ^4-Pregnene-11β,20β-diol-3-one-21-al (V).—The diol-one acetal IV (1.00 g.) in 50% aqueous acetic acid (20 ml.) was kept at 90–95° for three hours. The mixture was cooled to 20°, water was added and the mixture extracted with chloroform. The chloroform extract was washed with aqueous sodium bicarbonate, water and dried over sodium sulfate. The amorphous residue (990 mg.), after removal of the solvent, gave a negative tetranitromethane test for unsaturation. The BT assay[20] run *vs.* corticosterone (VII) showed the slow generation of a reducing system—28% after one hour; 43% after two hours. Normally (corticosterone) the full dye color was produced within 20 to 40 minutes, $\lambda\lambda_{max}^{nujol}$ 2.9 μ (O–H); 5.8 μ (very weak) (C=O); 6.00, 6.15 μ (conj. C=O).

Anal. Found: CH_3O, 0.1.

The product partially crystallized from ethyl acetate to give micro-crystalline material m.p. 165–175° with infrared spectrum similar to that of the total material.

Δ^4-Pregnene-11β,20β-diol-3-one-21-al Sodium Bisulfite Addition Product (VI).—To the crude hydrolysis product V (600 mg.) in methanol (40 ml.) was added sodium bisulfite (250 mg.) in water (15 ml.). The slightly turbid mixture was kept at 25° one hour and concentrated under vacuum at 20–30° until a granular precipitate appeared. Water (50 ml.) was added, and the concentration continued until the methanol had been removed completely. The precipitate was filtered, washed with water and dried (170 mg., m.p. 165–170°, of recovered polymeric forms of V). The colorless filtrate and washings were concentrated under vacuum to dryness. The water-soluble amorphous precipitate was triturated with absolute ethanol and unreacted sodium bisulfite (80 mg.) was removed by filtration. Concentration of the filtrate gave the sodium bisulfite addition product VI in three crops of hygroscopic micro-crystalline material (350 mg., 63% corrected for recovered reusable V), m.p. 165° dec. Recrystallization from absolute ethanol did not change the decomposition point. On addition of dilute hydrochloric acid or dilute sodium carbonate solution to a water solution of the derivative VI, the water-insoluble aldehyde V precipitated.

Anal. Calcd. for $C_{21}H_{31}O_7NaS$: C, 55.98; H, 6.94; S, 7.05. Found: C, 55.44; H, 7.16; S, 7.50.

Corticosterone (VII). (a) From the Hydrolysis Product (V).—The crude hydrolysis product V (160 mg.) was dissolved in dry pyridine (5.00 ml.) and the solution refluxed gently (115°) under nitrogen 5.5 hours.[13] The solvent was removed under vacuum, and the residue crystallized from ethyl acetate–ether. Corticosterone (VII) (35 mg., 20%), micro m.p. 165–175°, was obtained. Recrystallization from ethyl acetate–petroleum ether gave material with micro m.p. 176–180° (capillary m.p. 180–183°). Authentic corticosterone (VII) had micro m.p. 176–181° and the mixture, 176–180°. The respective infrared spectra were identical.

Treatment of the hydrolysis product V (70 mg.) with sodium methoxide (30 mg.) in methanol (7 ml.) under nitrogen at 25° for 30 minutes gave a residue (67 mg.) the infrared spectrum of which was very similar to that of the starting material except for a slight intensification of the weak saturated carbonyl band, indicating that no significant change had occurred.

(b) From the Sodium Bisulfite Addition Product (VI).—To the sodium bisulfite addition product VI (80 mg.) in methanol (5.00 ml.) was added freshly prepared methanolic sodium methoxide (10 ml., 0.5 *N*) under nitrogen. The pale yellow solution was stirred at 22° for one-half hour. Addition of acetic acid (0.5 ml.) neutralized the alkali and discharged the color. Most of the solvent was removed under vacuum, water was added, and the mixture was extracted with chloroform. The chloroform extract was washed with dilute aqueous sodium bicarbonate and water and dried over sodium sulfate. The residue (61 mg.) was crystallized from acetone–ether and gave the characteristic stout prisms[11] of corticosterone; 37 mg. (60%) in several crops, m.p. 174–178° and higher, raised to 179–182° in one recrystallization. The mixed melting point with an authentic sample (m.p. 180–183°) was 179–182° and the respective infrared spectra in chloroform were identical.

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.71; H, 8.95.

RAHWAY, NEW JERSEY

[CONTRIBUTION FROM THE DEPARTMENT OF PLANT BIOCHEMISTRY AND THE FOREST PRODUCTS LABORATORY, UNIVERSITY OF CALIFORNIA]

The Structure of an Arabogalactan from Jeffrey Pine (*Pinus Jeffreyi*)

BY W. H. WADMAN, ARTHUR B. ANDERSON AND W. Z. HASSID

RECEIVED MARCH 20, 1954

A water-soluble polysaccharide consisting of L-arabinose and D-galactose has been isolated from Jeffrey pine heartwood. Methylation and subsequent hydrolysis of this arabogalactan yielded 2,3,5-tri-*O*-methyl-L-arabinose, a di-*O*-methyl-L-arabinose (undetermined), 2,3,4-tri-*O*-methyl-D-galactose, and 2,4-di-*O*-methyl-D-galactose. A relatively small amount of 2,3,4,6-tetra-*O*-methyl-D-galactose, and a trace of partially methylated uronic acid also were present. On the basis of these results, the polysaccharide appears to be a highly branched molecule in which only L-arabinose residues occupy terminal positions. Ultracentrifuge measurements indicate that the polysaccharide is polydisperse, having an average molecular weight of approximately 100,000.

Arabogalactans have been found in a number of coniferous woods, particularly in larch woods. These polysaccharides are of interest in connection with wood formation and have been studied by a number of investigators.[1–5] Hydrolysis of specimens of arabogalactan from different species of larch wood yields L-arabinose and D-galactose in an approximate ratio of 1:6 moles.[2,6,7]

In studying the fractions obtained by fractional precipitation of solutions of arabogalactan and of derivatives from *Larix occidentalis*, Peterson, *et al.*,[6] demonstrated that the fractions exhibited appreciable difference in their properties, indicating that the polysaccharide is non-homogeneous. Simi-

(1) A. W. Schorger and D. F. Smith, *Ind. Eng. Chem.*, **8**, 494 (1916).

(2) L. E. Wise and F. C. Peterson, *ibid.*, **22**, 362 (1930).

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(4) N. I. Nikitin and I. A. Soloviev, *J. Applied Chem. (U.S.S.R.)*, **8**, 1016 (1935).

(5) For review see: L. E. Wise and E. C. Jahn, "Wood Chemistry," Vol. I, Reinhold Publ. Corp., New York, N. Y., 2nd Ed., 1952, pp. 644–646.

(6) F. C. Peterson, A. J. Barry, H. Unkauf and L. E. Wise, THIS JOURNAL, **62**, 2361 (1940).

(7) E. V. White, *ibid.*, **64**, 2838 (1942).