by crystallization from ether–hexane. Admixture with chloride X depressed the melting point. Methanol and methanol containing 1% acetic acid eluted 89 mg. of impure acid V, m.p. 206–221°. A sample of acetate XI was recrystallized three times from ether–hexane for analysis; colorless needles, m.p. 191.5–192.5°, $[\alpha]^{24}D$ 45.9° (*c* 1.051, in $CHCl_3$).

Anal. Calcd. for $C_{24}H_{34}O_5$: C, 71.61; H, 8.51. Found: C, 71.67; H, 8.44.

In another series of experiments 3.1 g. of acetate XI was obtained from 4.8 g. of chloride X.

4β-Bromo-3,11,20-trioxo-21-acetoxy-17α-methylpregnane (XIV).—To a solution of 2.5 g. of the triketo acetate XI, m.p. 186–191°, in 50 cc. of acetic acid were added, at room temperature, two drops of a 25% hydrogen bromide solution in acetic acid and subsequently, dropwise and with stirring, within 25 minutes, 993 mg. of bromine in 12.6 cc. of acetic acid. Part of the reaction product crystallized during the end of the bromine addition. The rest of the product was precipitated with water. The bromide was filtered off, washed repeatedly with water and dried. The almost colorless crystals (2.569 g.) melted with decomposition between 173 and 179°. Extraction of the mother liquors afforded another crop of 180 mg. By crystallizations from methylene chloride–methanol, 1.95 g. of bromide XIV, m.p. 179–186° dec., was obtained. A sample was recrystallized for analysis, m.p. 184° dec., $[\alpha]^{26}D$ 46.2° (*c* 1.043, in $CHCl_3$).

Anal. Calcd. for $C_{24}H_{33}O_5Br$: Br, 16.6. Found: Br, 16.15.

Debromination.—The crystalline mother liquors of the above described crystallizations of bromide XIV (836 mg.) were dissolved in 15 cc. of acetic acid and 1.5 cc. of water and debrominated in the usual manner with 1.5 g. of zinc dust at 80–90°. There was obtained 770 mg. of crystalline, partly yellowish acetoxy triketone XI, m.p. 168–177°, giving no depression of melting point upon admixture with authentic XI. Considering this recovery of starting material, the yield of purified bromide XII was 94.2%.

11-Dehydro-17α-methylcorticosterone Acetate (XIIa).—The purified bromide XIV (1.95 g., m.p. 179–186°) was dissolved in 61 cc. of absolute, alcohol-free chloroform and 102 cc. of dry *t*-butyl alcohol and the air was displaced with carbon dioxide. To the mixture was added 620 mg. of recrystallized semicarbazide base and the flask was again flushed with carbon dioxide, sealed and shaken repeatedly. The usual typical color changes were observed.[20] After 130 minutes, unreacted semicarbazide was filtered off and the filtrate was taken to dryness *in vacuo*. To the powdery residue 85 cc. of ethanol and 5 cc. of water were added and the solution was reduced *in vacuo*, at 50°, to 45 cc. After dilution with a further 400 cc. of water the mixture was cooled to −10°. The crystalline precipitate was filtered, washed repeatedly with water and dried *in vacuo*. Thus, 1.735 g. of **semicarbazone XIII**, m.p. 223–225°, λ_{max}^{EtOH} 270 mμ (log ε 4.5), was obtained. Extraction of the mother liquors afforded another 25 mg. of less pure material.

The semicarbazone (1.735 g.) was dissolved in 53 cc. of acetic acid and 19 cc. of water and the air was displaced with carbon dioxide. To the mixture was added 4.6 cc. of an aqueous 1.66 *N* pyruvic acid solution and the flask was flushed with carbon dioxide and sealed. After 17.5 hours the mixture was poured into water and extracted with ether. The organic solution was washed with iced sodium bicarbonate and sodium carbonate solutions, cold dilute hydrochloric acid, iced bicarbonate solution and water and was dried. Removal of the solvent afforded 1.504 g. (92.8%) of crude acetoxy triketone XIIa, which crystallized after trituration with ether–hexane (m.p. 141.5–144.5°). One crystallization gave 837 mg. of crystals, melting at 153.5–154.5°. Chromatography and recrystallizations of the mother liquors afforded 405 mg. of a slightly less pure crop of the same material (total yield of purified acetate XIIa, 76.7%). A sample was recrystallized twice for analysis; colorless, hygroscopic needles, m.p. 157–158°, $[\alpha]^{24}D$ 170° (*c* 0.79, in $CHCl_3$); λ_{max}^{EtOH} 237 mμ (log ε 4.4); $\gamma_{max}^{CHCl_3}$ 1750 and 1720 cm.$^{-1}$ (21-acetoxy-20-ketone doublet); 1710 cm.$^{-1}$ (11-ketone); 1670 and 1620 cm.$^{-1}$ (Δ^4-3-ketone doublet); γ_{max}^{KBr} 1740 and 1708 cm.$^{-1}$ (21-acetoxy-20-ketone doublet), 1698 cm.$^{-1}$ (11-ketone), 1671 and 1621 cm.$^{-1}$ (Δ^4-3-ketone doublet), 1230 cm.$^{-1}$ (acetate).

Anal. Calcd. for $C_{24}H_{32}O_5$: C, 71.97; H, 8.05. Found: C, 72.23; H, 7.96.

11-Dehydro-17α-methylcorticosterone (XII).—A solution of 440 mg. of the acetate XIIa, m.p. 152–155°, in 44 cc. of methanol was flushed with nitrogen and subsequently there was added 455 mg. of potassium bicarbonate in 7.8 cc. of water at room temperature. The air was displaced with nitrogen and the flask was sealed. Crystals formed but disappeared again after 12 hours. The solution was kept in a nitrogen atmosphere for 90 hours and was subsequently diluted with 450 cc. of ice-water. No precipitate formed. The solution was extracted with 12 l. of ether and the ethereal solution was washed to neutral and worked up in the usual manner. There was obtained 397 mg. of almost colorless ketol XII, m.p. 154.5–155°, giving a marked depression of m.p. with acetate XIIa and a positive blue tetrazolium test. The product could best be recrystallized from acetone–water or from ether. A sample was recrystallized twice from ether for analysis; cubes, m.p. 154–155.5°; $[\alpha]^{22}D$ 174.2° (*c* 0.97, in $CHCl_3$); λ_{max}^{EtOH} 238 mμ (log ε 4.2); γ_{max}^{KBr} 3425 cm.$^{-1}$ (assoc. hydroxyl) 1700 and 1695 cm.$^{-1}$ (11,20-diketone), 1666 and 1616 cm.$^{-1}$ (Δ^4-3-ketone doublet).

Anal. Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.90; H, 8.28.

Acetylation.—A solution of 60 mg. of ketol XII, m.p. 155°, in 1.5 cc. of pyridine was flushed with nitrogen and mixed with 0.8 cc. of acetic anhydride. The solution was again flushed with nitrogen, the flask was sealed and kept at room temperature for 17 hours. Subsequently 40 cc. of ice-water was added and after 40 minutes the reaction product was worked up in the usual fashion. There was obtained 74 mg. of crystalline acetate XIIa, m.p. 154–156.5°, not depressed upon admixture with authentic acetate XIIa. The product was recrystallized from ether–hexane for analysis; m.p. 156–156.5°.

Anal. Calcd. for $C_{24}H_{32}O_5$: C, 71.97; H, 8.05. Found: C, 72.12; H, 8.26.

LONDON, ONTARIO, CANADA

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

5-Cholestene-3β,26-diol

BY IRVING SCHEER, MALCOLM J. THOMPSON AND ERICH MOSETTIG

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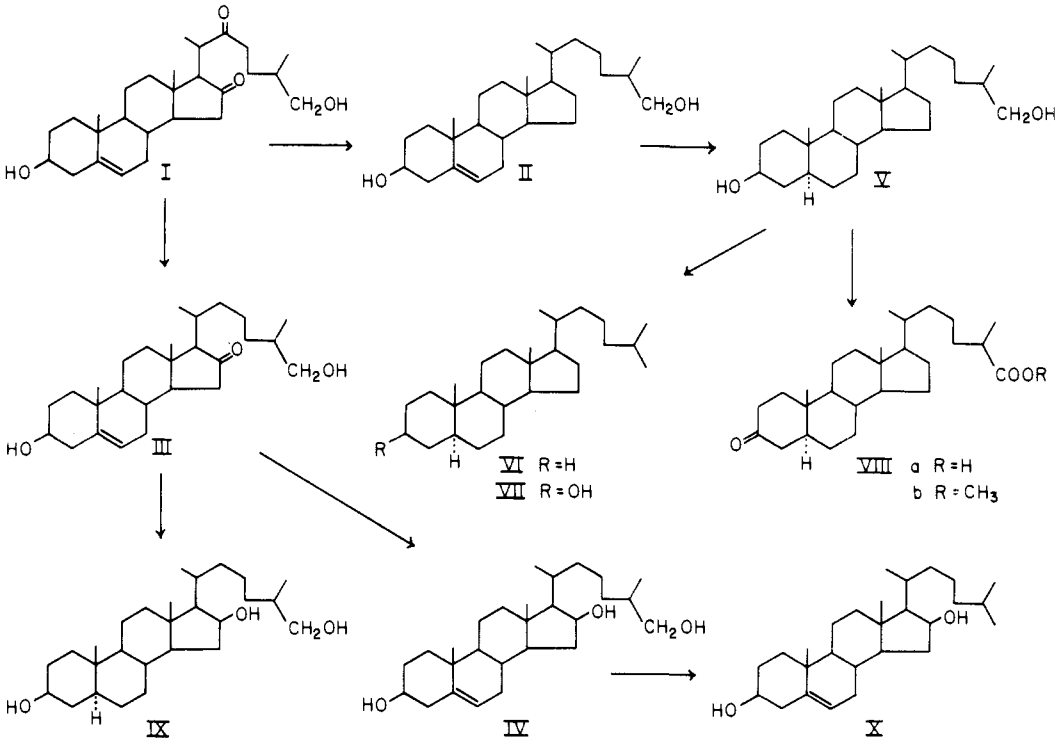
The preparation of 5-cholestene-3β,26-diol (II) from kryptogenin (I) is described.

5-Cholestene-3β,26-diol (II) is of interest since it may be an intermediate in the catabolism of cholesterol to bile acids and therefore it appeared desirable to prepare this compound for reference purposes. This paper describes the preparation of II from kryptogenin (I).

Clemmensen reduction of I yielded a crystalline mixture of II and 5-cholestene-3β,26-diol-16-one (III) in approximately a 1:1 ratio. After chromatography on alumina, the residue from the mother liquor yielded crystalline III. The initial mixture of II and III was quite inseparable even after ex-

tensive chromatography or recrystallization. However, when this mixture was treated with sodium borohydride in aqueous methanol a mixture of tetrahydrodiosgenin (IV) and II was obtained which could be separated readily by chromatography on alumina. For routine preparation of II, the crystalline mixture obtained from the Clemmensen reaction was not separated. Instead, it was subjected to Wolff–Kishner reduction (Huang-Minlon modification) to yield II as the sole product. The over-all yield of II from I, in this procedure, was 41%. Attempts to reduce kryptogenin directly by the Wolff–Kishner method yielded intractable resins.



Compound II could be hydrogenated (PtO_2, acetic acid, 25°) readily to cholestane-3β,26-diol (V). Deoxylation of V by tosylation and subsequent reduction with lithium aluminum hydride[1] gave cholestane (VI) in 67% yield. By selective tosylation of the hydroxyl group at C-26 and subsequent reduction of the tosylate with lithium aluminum hydride, V yielded cholestan-3β-ol (VII). Similar treatment of II gave anomalous results since under the conditions necessary for selective tosylation (*p*-toluenesulfonyl chloride, pyridine, −5 to −10°) only unchanged starting material, in quantitative amounts, was recovered. It seems that the presence of the 5,6-double bond in II does not account for this behavior since IV, under similar conditions readily yields a crystalline C-26 deoxy compound, 5-cholestene-3β,16β-diol (X). Furthermore, it should be noted that II is far less soluble ($^1/_5$) in cold pyridine than either IV or V and a variety of other compounds of similar structure.[2] The selective mesylation of II proceeds poorly, giving a mixture of oily reaction products from which about 13% of cholesterol was obtained by reduction with lithium aluminum hydride.

Oxidation of V (chromic acid, acetone, 20°) gave 26-carboxycholestan-3-one (VIIIa) which exhibited strong, broad absorption at 1709 cm.$^{-1}$ and the typical broad absorption of carboxylic acids in the 2500–2700 cm.$^{-1}$ region of the infrared spectrum (CS_2). The spectrum of the methyl ester (VIIIb) had two sharp bands in the carbonyl region at 1715 cm.$^{-1}$ (ketone) and 1739 cm.$^{-1}$ (ester carbonyl). The above sequence of reactions clearly established the structure of II.

Evidence for the structure of III was obtained in the following manner. The infrared spectrum of III exhibited strong absorption at 1736 cm.$^{-1}$ characteristic of a carbonyl group on a five-membered ring. The compound readily yielded a crystalline diacetate and an oxime. Catalytic hydrogenation (PtO_2) of III yielded tetrahydrotigogenin (IX), reduction with sodium borohydride gave tetrahydrodiosgenin (see above), and removal of the carbonyl group (Wolff–Kishner, Huang-Minlon) afforded II in an 85% yield.

Acknowledgment.—We wish to express our appreciation to Dr. G. Rosenkranz of Syntex, S.A., for a generous supply of kryptogenin. The infrared spectra were determined by Mr. Harold K. Miller. Microanalyses are by the Analytical Service Laboratory of this Institute under the direction of Dr. William C. Alford.

Experimental[3]

5-Cholestene-3β,26-diol (II).—To a refluxing mixture of 7.0 g. of kryptogenin (I), 150.0 g. of zinc amalgam (freshly

(1) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949).

(2) I. Scheer and E. Mosettig, THIS JOURNAL, **77**, 1820 (1955).

(3) Melting points were determined on the Kofler block. Unless otherwise noted, rotations were determined in approximately 1% solutions in chloroform. Infrared spectra were obtained with a Perkin–Elmer Model 21 double beam spectrophotometer with sodium chloride prism and cells.

prepared), 500 ml. of 95% ethanol and 10 ml. of concd. hydrochloric acid was added 115 ml. of concd. hydrochloric acid in 2 hours. Refluxing was continued for 30 min. after this addition. The mixture was cooled, decanted from the zinc, and poured into 1.5 l. of cold water and allowed to stand at 3° for 18 hours. The semi-crystalline residue was collected and dissolved in ether. The ethereal solution was washed with water, 2% sodium bicarbonate solution, water and dried over sodium sulfate. The solution was concentrated to dryness *in vacuo* and the residue crystallized from ethyl acetate to yield 3.7 g. of a 1:1 mixture of 5-cholestene-3β,26-diol (II) and 5-cholestene-3β,26-diol-16-one (III), m.p. 155–160°, $[\alpha]^{20}D$ −92°. This mixture could not be purified either by chromatography on alumina or recrystallization from various solvents. A solution of 3.0 g. of the mixture of II and III, 60 ml. of triethylene glycol, 6 ml. of hydrazine (95%) and 4.0 g. of potassium hydroxide was refluxed gently at 150° for 30 min. Solvent was distilled until the temperature was raised to 195° and the reaction maintained at this temperature for 2 hours. The cooled mixture was poured into 500 ml. of 0.5 *N* hydrochloric acid. The resultant precipitate was collected, washed thoroughly with water and dried. Recrystallization from ethyl acetate afforded 2.69 g. (41.2% from kryptogenin) of II as fine white needles, m.p. 177–178°, $[\alpha]^{20}D$ −30°, ν_{max}^{Kbr} 3279 cm.$^{-1}$ (hydroxyl).

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.51. Found: C, 80.31; H, 11.54.

II was separated from the crystalline Clemmensen reaction mixture in the following manner. To a solution of 0.5 g. of the mixture of II and III in 35 ml. of methanol was added a solution of 1.0 g. of sodium borohydride in 2 ml. of water and the mixture allowed to stand overnight at room temperature. The solution was diluted with water and the crystalline precipitate was collected, washed with water and dried. The product was chromatographed on Woelm neutral alumina and the fraction eluted with benzene–chloroform (6:1) was crystallized from ethyl acetate to yield 0.2 g. of **II** as white needles identical in every respect (melting point, rotation, infrared spectra, derivatives) with the material obtained from the Wolff–Kishner reaction. The fractions eluted with benzene–chloroform (3:1 and 1:1) were crystallized from ethyl acetate and yielded 0.24 g. of **tetrahydrodiosgenin (IV)**, m.p. 177–179°, identical with an authentic sample prepared from the Clemmensen reduction of diosgenin.[4]

The **diacetate** of II (acetic anhydride–pyridine, 18 hours, 25°) was obtained as white plates from methanol, m.p. 128–129°, $[\alpha]^{20}D$ −35°.

Anal. Calcd. for $C_{31}H_{50}O_4$: C, 76.50; H, 10.36. Found: C, 76.46; H, 10.13.

The **di-3,5-dinitrobenzoate** of II (3,5-dinitrobenzoyl chloride–pyridine, 4 hours, steam-bath) was crystallized from acetone–methanol as thin needles, m.p. 187–188°, $[\alpha]^{20}D$ −7.5°.

Anal. Calcd. for $C_{41}H_{50}O_{12}N_4$: C, 62.27; H, 6.31; N, 7.09. Found: C, 62.05; H, 6.38; N, 7.05.

Cholesterol from II.—To a solution of 0.3 g. of II in 8 ml. of dry pyridine at 0° was added 0.093 g. of methanesulfonyl chloride in 4 ml. of pyridine by dropwise addition over a 1-hour period. The solution was allowed to stand overnight at 0°. The pale pink solution was poured on ice and water and the precipitate was extracted with ether. The ethereal solution was washed with cold 5% hydrochloric acid, water, 2% sodium bicarbonate solution, water and dried over sodium sulfate. On evaporation *in vacuo* a pink semi-solid residue was obtained which was reduced without further purification. The residue was dissolved in 32 ml. of benzene and the solution was concentrated to a volume of 22 ml. After the addition of 22 ml. of dry ether and 3 ml. of a 1.6 *M* solution of lithium aluminum hydride in ether, the reaction mixture was refluxed overnight. The mixture was cooled, treated with a few drops of ethyl acetate and 10 ml. of 6 *N* hydrochloric acid. The aqueous layer was separated, extracted with ether and the extracts combined with the benzene–ether layer. The combined extracts were washed with 10% sodium bicarbonate solution and with water, dried over sodium sulfate and evaporated to dryness *in vacuo*. The solid residue was crystallized from benzene–pet. ether (30–60°) to yield 0.16 g. of starting material, m.p. 170–175°. The mother liquor was concentrated to dryness *in vacuo* and the residue crystallized from ethyl acetate to yield 0.01 g. of cholesterol as white needles, m.p. 147.5–148.5°, identical in every respect with an authentic sample. A second crop weighing 0.03 g. and melting at 143–145° was obtained. The combined yield of cholesterol was 13.9%.

Cholestane-3β,26-diol (V).—A mixture of 0.5 g. of 5-cholestene-3β,26-diol (II), 0.05 g. of Adams catalyst and 40 ml. of acetic acid was shaken with hydrogen at room temperature and pressure. Hydrogenation was complete in 20 min. and gave 0.45 g. (90%) of **V** as white needles, analytically pure, m.p. 179–181°, $[\alpha]^{20}D$ +28°.

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96. Found: C, 80.31; H, 11.71.

A mixture with 5-cholestene-3β,26-diol melted at 167–174°. The **diacetate** (acetic anhydride, 1-hour, steam-bath) was obtained as white needles from methanol, m.p. 120–120.5°, $[\alpha]^{20}D$ +11°.

Anal. Calcd. for $C_{31}H_{52}O_4$: C, 76.18; H, 10.72. Found: C, 76.03; H, 11.01.

26-Carboxycholestan-3-one (VIIIa).—To a stirred solution of 185 mg. of cholestane-3β,26-diol (V) in 200 ml. of acetone at 20° was added, dropwise, an 8 *N* solution of chromic acid in sulfuric acid and water until a persistent orange-brown coloration indicated that oxidation was complete.[5] The mixture was diluted with water and the precipitate was collected and dissolved in ether. The ethereal solution was extracted with 3% sodium hydroxide solution The aqueous alkaline solution was acidified with 6 *N* hydrochloric acid and the resultant white precipitate was filtered and crystallized from dilute ethanol to yield 85 mg. (44.5%) of **VIIIa** as microscopic white needles, m.p. 156–158°, $[\alpha]^{20}D$ +32°, ν^{CS_2} 2700–2500 cm.$^{-1}$ weak broad absorption, 1709 cm.$^{-1}$ strong carbonyl absorption.

Anal. Calcd. for $C_{27}H_{45}O_3$: C, 77.65; H, 10.86. Found: C, 78.00; H, 10.60.

Treatment of VIIIa with diazomethane in the usual manner gave the **methyl ester VIIIb**, m.p. 99–101°, ν^{CS_2} 1739 cm.$^{-1}$ (ester carbonyl) and 1715 cm.$^{-1}$ (ketone).

Anal. Calcd. for $C_{28}H_{47}O_3$: C, 77.90; H, 10.98. Found: C, 77.92; H, 11.01.

Cholestan-3β-ol (VII) from V.—A solution of 0.304 g. of cholestane-3β,26-diol (V) in 6 ml. of dry pyridine was cooled to 0° and to it was added a solution of 0.156 g. of *p*-toluenesulfonyl chloride in 3 ml. of dry pyridine over a 30-min. period. The temperature of the reaction mixture was maintained at 0 to 5° during this addition then allowed to come slowly to room temperature. The mixture stood overnight at room temperature. The colorless solution was poured into ice and water and the semi-crystalline precipitate was ether extracted. The ethereal solution was washed with cold 5% hydrochloric acid, water, 2% sodium bicarbonate solution, water and dried over sodium sulfate. The solution was concentrated to dryness *in vacuo*. Crystallization from benzene yielded 0.1 g. of starting material V and about 0.2 g. of non-crystalline material. The non-crystalline residue was dissolved in 30 ml. of benzene and the solution concentrated to a volume of 10 ml. (to remove water). After the addition of 10 ml. of dry ether and 3 ml. of 1.6 *M* solution of lithium aluminum hydride in ether the reaction mixture was refluxed overnight. The mixture was cooled, a few drops of ethyl acetate was added to it, and then treated with 25 ml. of 6 *N* hydrochloric acid. The aqueous layer was separated, extracted with ether and the extracts combined with the benzene–ether layer. The non-aqueous layer was washed with 2% sodium bicarbonate solution and with water, dried over sodium sulfate and concentrated to dryness *in vacuo*. The crystalline residue was chromatographed on benzene–hexane washed alumina. The fraction eluted with benzene–chloroform 6:1 and crystallized from dilute methanol yielded 0.12 g. of crude **cholestan-3β-ol (VII)**. Recrystallization from methanol gave 0.09 g. (30.8%) of white plates, m.p. 142–143° (lit.[6] m.p. 141.5–142°), no depression with an authentic sample of cholestan-3β-ol and identical infrared spectra.

Cholestane (VI) from V.—A solution of 0.25 g. of cholestane-3β,26-diol (V), 5 ml. of dry pyridine and 0.5 g. of *p*-

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(6) R. Willstätter and E. M. Mayer, *Ber.*, **41**, 2199 (1908).

toluenesulfonyl chloride was allowed to stand overnight at room temperature. The colorless solution was poured on ice and water and the oily precipitate was extracted with ether. The ethereal solution was washed with water, 5% hydrochloric acid, water, 2% sodium bicarbonate solution and dried over sodium sulfate. The solution was concentrated to dryness *in vacuo* and the oily residue dissolved in 25 ml. of benzene. The benzene solution was concentrated to 15 ml. and 15 ml. of dry ether and 6 ml. of a 1.6 *M* lithium aluminum hydride solution in ether added. The mixture was refluxed overnight, treated with a few drops of ethyl acetate and 15 ml. of 6 *N* hydrochloric acid. The aqueous layer was separated, washed twice with ether and the washings combined with the benzene–ether layer. The benzene–ether solution was washed with 10% sodium bicarbonate solution and water and dried over sodium sulfate. The solution was concentrated to dryness *in vacuo* and the residue was crystallized from ether–ethanol to yield 0.14 g. of cholestane (VI), white plates, m.p. 75–77°, negative tetranitromethane test. Chromatography on neutral alumina afforded 0.13 g. of plates, m.p. 79.5–80°, $[\alpha]^{20}D$ +25°, from the fraction eluted with hexane. This material was identical with an authentic sample of cholestane.

The mother liquor from the lithium aluminum hydride reduction was chromatographed on neutral alumina. The fraction eluted with hexane yielded a colorless semi-solid residue which gave a strong positive test with tetranitromethane. The oily crystals were dissolved in 10 ml. of dioxane and shaken under hydrogen in a stainless steel bomb for 24 hours at 150° and 1500 p.s.i. in the presence of 2 ml. of Raney nickel in ethanol. An additional 0.025 g. of VI, m.p. 80–82°, was obtained from this reaction.

5-Cholestene-3β,26-diol-16-one (III).—The mother liquor from the Clemmensen reduction of kryptogenin described above was concentrated to dryness *in vacuo* and the residue chromatographed on benzene-washed alumina to give 2.0 g. of non-crystalline material from the fractions eluted with benzene–chloroform 9:1 and 6:1. This material could not be crystallized and was discarded. From the fraction eluted with benzene–chloroform 1:1 was obtained 0.3 g. of **5-cholestene-3β,26-diol-16-one** as white plates, m.p. 170–171°, $[\alpha]^{20}D$ −156°, $\nu_{max}^{CHCl_3}$ 3623 cm.$^{-1}$ and 3448 cm.$^{-1}$ (hydroxyl), 1736 cm.$^{-1}$ (carbonyl on a five-membered ring).

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.84; H, 10.65. Found: C, 77.96; H, 10.78.

The **diacetate** was crystallized from methanol; m.p. 114–116°, $[\alpha]^{20}D$ −118°.

Anal. Calcd. for $C_{31}H_{48}O_5$: C, 74.36; H, 9.66. Found: C, 74.56; H, 9.43.

The **oxime** was crystallized from methanol; m.p. 193–196°, $[\alpha]^{20}D$ −73° (EtOH).

Anal. Calcd. for $C_{27}H_{45}O_3N$: C, 75.13; H, 10.51; N, 3.25. Found: C, 75.25; H, 10.75; N, 3.24.

When 0.1 g. of III, 0.01 g. of Adams catalyst and 25 ml. of acetic acid was shaken with hydrogen at room temperature and pressure for two hours, 0.08 g. of **tetrahydrotigogenin (IX)** was obtained (from ethyl acetate), m.p. 199–200°, identical with an authentic sample.

Treatment of III with sodium borohydride in aqueous methanol, as described above for the reduction of the mixture of II and III, yielded tetrahydrodiosgenin (IV) in 80% yield.

When III was subjected to Wolff–Kishner reduction, as described above for the preparation of II, an 85% yield of 5-cholestene-3β,26-diol (II) was obtained.

5-Cholestene-3β,16β-diol (X).—Tetrahydrodiosgenin (IV) (0.3 g.) was tosylated and reduced in exactly the same manner as described above for the preparation of VII from V. The resulting crystalline residue was chromatographed on benzene–chloroform (7:1) washed alumina. The fraction eluted with benzene–chloroform 6:1 was crystallized from dilute methanol to yield 0.08 g. (27.7%) of analytically pure, white needles of **X**, m.p. 176.5–178°, $[\alpha]^{20}D$ −33°.

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.51. Found: C, 80.38; H, 11.39.

Further elution with benzene–chloroform (3:1 and 1:1) yielded 0.17 g. of starting material after crystallization of the combined fractions from dilute methanol.

The **diacetate** of X was obtained as colorless plates from methanol; m.p. 174–176°.

Anal. Calcd. for $C_{31}H_{50}O_4$: C, 76.50; H, 10.36. Found: C, 76.23; H, 10.39.

BETHESDA, MARYLAND

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF CALIFORNIA]

Reactions of B-Norcholesterol

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The preparation of B-norcholesterol and the intermediates used in its preparation, as reported earlier by Sorm and Dykova, was investigated and the structures unequivocally established. Various transformations of this modified sterol involving oxidation, reduction and *i*-ether formation were studied. The results obtained showed that in this nucleus with a 5-membered B-ring, the *trans–anti–trans* arrangement is the stable configuration. The rate of acetolysis of the tosylate was found to be approximately half that of the cholesterol derivative. Comparison of molecular rotational differences in this series with those of the cholesterol series is given.

In recent years, it has become increasingly evident that, by modification of the natural steroid hormones, it is possible either to increase or decrease certain physiological properties of this series of compounds. Such modifications as expansion of ring D to a six-membered ring,[1] contraction of ring A to a five-membered ring,[2] removal of the angular methyl group at C_{10}[3] or C_{13},[4] introduction of different functional groups, such as double bonds,[5–8] methyl groups[9] or fluorine atoms,[9,10] into the nucleus are examples of the types of structural changes which have been studied. To date, no investigation has been reported which has studied how critical the sizes of rings B and C in the

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