250–260°, at still lower pressure (2 mm.), distillation of the remaining material occurred, giving 180 mg. of a viscous yellow oil which displayed but a single carbonyl band in the infrared at 1680 cm.$^{-1}$. Chromatography on a 0.8 × 10 cm. column of activated alumina furnished a major fraction of *ca.* 85 mg. with benzene–petroleum ether (4:1) which partially crystallized on standing to yield clusters from methanol, m.p. 87–89°, $[\alpha]^{CHCl_3}D$ 0°, λ_{max} 265 mμ (log ε 4.2) and 305 mμ (log ε 3.4).[5] Further characterization of this substance (VII) was deferred in order to retain sufficient material to complete the degradation scheme.

Conversion of VII to 3,9-Dimethylanthracene (IX).—To a stirred solution of 0.3 g. of lithium aluminum hydride in 20 ml. of anhydrous ether, the above crude ketone VII was added rapidly in ether solution. After stirring for an additional ten minutes the excess reagent was destroyed with ethyl acetate in ether, the mixture treated with cold dilute hydrochloric acid and the product recovered by ether extraction. This material was then transferred to a long Pyrex tube (300 × 10 mm., partially constricted at the lower end), 50 mg. of 10% palladium–charcoal was introduced and the contents heated carefully at 310–330° (bath) for 30 minutes. At the end of this period gas evolution appeared to be complete, and the product was taken up in petroleum ether (30–40°) and purified by elution from a 1.2 × 10 cm. column of strongly activated alumina. A nearly colorless fraction which exhibited a strong blue fluorescence in ultraviolet light was eluted slowly with petroleum ether and crystallized readily from ethanol as light cream colored needle clusters, weighing 23 mg. and melting at 81–84°. Recrystallized from ethyl acetate–methanol these had a melting point of 84.5–85° which was undepressed on admixture with an authentic sample of 3,9-dimethylanthracene prepared essentially by the method of Barnett and Goodway[7] but improved in yield by employing methyllithium in the addition step to 3-methyl-9-anthrone, as suggested by Phillips and Cason.[8,14] The picrate crystallized from ethanol as dark maroon needles, m.p. 127.5–128°, also undepressed with an authentic sample.

Anal. Calcd. for $C_{22}H_{17}O_7N_3$ (435.38): C, 60.69; H, 3.94. Found: C, 60.89; H, 4.02.

When it was mixed with a sample of 2,9-dimethylanthracene, m.p. 82–83°,[8,14] the melting point of the dehydrogenation product was depressed to 61–73°. The ultraviolet spectrum of 3,9-dimethylanthracene was found to be very similar to that of 2,9-dimethylanthracene, reported by Phillips and Cason,[8] and showed λ_{max} (log ε) values of 260 mμ (5.4), 334 mμ (3.5) (shoulder), 348 mμ (3.7), 368 mμ (3.8) and 387 mμ (3.75).

(14) The author gratefully acknowledges the assistance of Mr. Delhert Meyer in the preparation of this authentic sample of 3,9-dimethylanthracene and also that of 2,9-dimethylanthracene.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Formation of Five- and Six-membered Rings by the Acyloin Condensation. VI. Cyclization of the Cholesterol *a* Ring *via* a 2,3-Secodiester

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RECEIVED MARCH 27, 1957

Cyclization of 2,3-secocholestane-2,3-dioic acid dimethyl ester (I) by an acyloin condensation in homogeneous medium afforded a mixture, from which an acyloin assigned the structure 3β-hydroxycholestane-2-one (II) was isolated in 82% yield. Minor products of the reaction were an isomeric 2-hydroxycholestane-3-one, cholestane-2α,3β-diol, and 2,3-secocholestane-2,3-dioic acid. Reduction of the acetate derivative of II with sodium borohydride and with sodium led to the new epimeric cholestane-2β,3β-diol and a diol of unassigned structure, respectively. By formation of the tosylate derivative, subsequent reduction with sodium borohydride and treatment with collidine, the ketol II was converted to cholestane-2-one in excellent yield.

Previous communications in this series have reported the formation of steroid C and D rings in high yield by the acyloin reaction in homogeneous solution. In each instance only one of the four possible isomeric acyloins was isolated. These cases do not favor a Dieckmann-type of condensation, and no such side product was detected. However, it seemed worthwhile to extend the scope of the acyloin reaction to include a steroid diester in which the α-carbon atoms are unsubstituted and which could yield a five-membered ring by a Dieckmann condensation. The 2,3-secocholestane series was chosen as a representative model for the condensation, due both to structural features and to the intrinsic interest in oxygenated cholestane derivatives.

Essentially the method of Sheehan, Coderre and Cruickshank[1] for the acyloin condensation of dimethyl marrianolate methyl ether was followed for the cyclization of the diester I. A ratio of exactly 4 moles of sodium per mole of diester dissolved in a medium containing 60% liquid ammonia and 40% anhydrous ether was employed. Chromatography of the crude reaction mixture afforded 3β-hydroxycholestane-2-one(II) in 82% yield, an isomeric 2-hydroxycholestanone (III) in 5% yield and cholestane-2α,3β-diol (IV) in 2% yield. The basic extracts from the crude reaction mixture afforded 2,3-secocholestane-2,3-dioic acid (V) in 1% yield.

From physical and chemical evidence the structure 3β-hydroxycholestane-2-one was assigned for the acyloin II. The infrared spectrum of this material showed all the characteristic absorption bands associated with an acyloin: a rather weak hydroxyl band at 3515 cm.$^{-1}$ (2.82 μ) and a strong carbonyl band at 1715 cm.$^{-1}$ (5.85 μ) characteristic of a six-membered ring carbonyl.[2]

The crude acyloin mixture VI was oxidized to 2,3-secocholestane-2,3-dioic acid (IV) with chromic acid and converted by means of cupric acetate to the dione VII, which was isolated as the quinoxaline derivative VIII in 89% over-all yield. The quinoxaline VIII gave no depression of melting point upon admixture with a sample of cholestane-2,3-dione quinoxaline prepared by an unambiguous route. This method involved formation of 2-isonitrosocholestane-3-one, conversion to cholestane-2,3-dione with pyruvic acid and treat-

(1) J. C. Sheehan, R. A. Coderre and P. A. Cruickshank, THIS JOURNAL, 75, 6231 (1953).

(2) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 128.

ment of the crude material with *o*-phenylenediamine.

The dione VII was characterized further by alkaline peroxide cleavage to the known diacid V and conversion of the unpurified dione VII to a diosphenol. Cholestane-2,3-dione exists in two diosphenol forms: form A, m.p. 144–145°; form B, m.p. 162–163°.[3] The melting point of our product suggests a mixture of these two forms. The crude dione VII was converted by potassium hydroxide to the pure diosphenol IXa, demonstrated to be identical with diosphenol form A of cholestane-2,3-dione by comparison with an authentic sample prepared by the method of Stiller and Rosenheim.[3] Conversion to form B (IXb) was accomplished by reflux with acid.

The preceding evidence establishes the product as a 2,3-cholestane acyloin. That partial condensation to a Dieckmann product had not occurred was confirmed by sodium borohydride reduction of the acyloin mixture VI to an isomeric mixture of glycols X. The carbonyl band was completely absent in the infrared spectrum of this material indicating that the peak at 5.85 μ in the spectrum of the acyloin product was due to a ketone and not in part to an ester. Lithium aluminum hydride reduction of the acyloin mixture X similarly led to a quantitative formation of the isomeric glycols.

The possibility of obtaining a single ketone, depending upon the stereochemistry of the glycols, prompted us to attempt the dehydration of this isomeric mixture by pyridine hydrochloride fusion. Dehydration of the epimeric estriols formed by sodium borohydride reduction of 16-keto-17β-estradiol-3-methyl ether, for example, gave estrone as the only product,[4] while 2,5-dimethylcyclohexanone was the exclusive product from the dehydration of 1,4-dimethylcyclohexane-*trans*-1,2-diol by mineral acid.[4,5] The main product on fusion of the isomeric glycols X with pyridine hydrochloride was, surprisingly, a cholestanol dioxane-type dimer, formed by *inter*molecular dehydration.

A simple approach to the elucidation of both the configurational and positional isomerism of the acyloin II would be removal of the ketone function by means of Raney nickel desulfurization of the ethylene thioketal. In an analogous manner, removal of the 16-keto group from 16-keto-17β-estradiol-3-methyl ether by hydrogenolysis of the thioketal acetate derivative was effected smoothly in good yield.[1] Surprisingly, desulfurization of the ethylene-thioketal-acetate derivative XII of the acyloin II led to the formation of cholestane (XIII) as the only product. Similar results were obtained when the diethanethioketal acetate derivative was hydrogenolyzed with Raney nickel.

Treatment of the acyloin mixture VI with acetic anhydride gave a monoacetate derivative XI in 82% yield. Reduction of the acetoxyketone XI with zinc dust and hydrochloric acid at 70° gave principally cholestane and a 14% yield of cholestane-2-one (XIV). Except for possible equilibration of the acyloin during reaction, this would establish the α-ketol as a 3-hydroxycholestane-2-one.

The positional isomerism of the acyloin II was convincingly demonstrated. Treatment of the acyloin mixture VI with *p*-toluenesulfonyl chloride in pyridine yielded the tosylate (80%) XV. Mild reduction with sodium borohydride and subsequent detosylation in refluxing collidine gave cholestane-2-one (XIV) in 84% yield. The ketone was identified by comparison with an authentic sample of cholestane-2-one prepared according to the method of Ruzicka, Plattner and Furrer.[6]

Although eliminations of equatorial tosylates often proceed with ring contraction, the formation of cholestane-2-one can be explained by assuming a transformation of the cholestane A ring into the boat conformation, thereby permitting planar elimination. The reaction is analogous to the detosylation of *cis*-2-hydroxymenthol *p*-toluenesulfonate.[7]

Sodium borohydride reduction and subsequent hydrolysis of the acetoxyketone XI afforded an 84% yield of cholestane-2β,3β-diol (XVII), which formed a nicely crystalline acetonide XVIII. The diol XVII upon treatment with *p*-toluenesulfonyl chloride formed a monotosylate identical in every respect with the hydroxytosylate XVI.

Preferential tosylation of the 3-position of the diol XVII indicates that it was the more reactive hydroxyl group. Since *p*-toluenesulfonyl chloride does not react readily with axial hydroxyl groups under normal conditions for tosylation of alcohols, it is inferred that the hydroxyl group of the diol XVII is a 3β-equatorial hydroxyl group; consequently, the hydroxyl group of the acyloin II must be a 3β-hydroxyl group also. The structure 3β-hydroxycholestane-2-one and cholestane-2β,3β-diol are therefore assigned for the acyloin II and the diol XVII, respectively. Sodium reduction of 3β-acetoxycholestane-2-one (XI) in a liquid ammonia–ethanol medium afforded a diol of unassigned structure in 86% yield.

The properties and derivatives of the acyloin II are very similar to the α-ketol reported by Ruzicka, Plattner and Aeschbacher.[8] The acetate XI was saponified by dilute methanolic potassium hydroxide after 36 hr. to the corresponding acyloin II, identical with the 3β-hydroxycholestane-2-one obtained directly from the acyloin condensation.

The isomeric acyloin III, m.p. 125–126°, $[\alpha]_D$ 39°, was converted to a monoacetate, gave a positive test for an acyloin on treatment with bismuth oxide, and the infrared spectrum showed all the characteristic bands associated with an α-ketol: a weak hydroxyl band at 3450 cm.$^{-1}$ (2.90 μ) and a strong carbonyl band 1700 cm.$^{-1}$ (5.88 μ). The physical properties of III compare favorably with the known 2-hydroxycholestane-3-one, m.p. 125–126°, $[\alpha]_D$ 38°.[20]

The infrared spectrum of the diol IV showed a

(3) E. T. Stiller and O. Rosenheim, *J. Chem. Soc.*, 353 (1938).

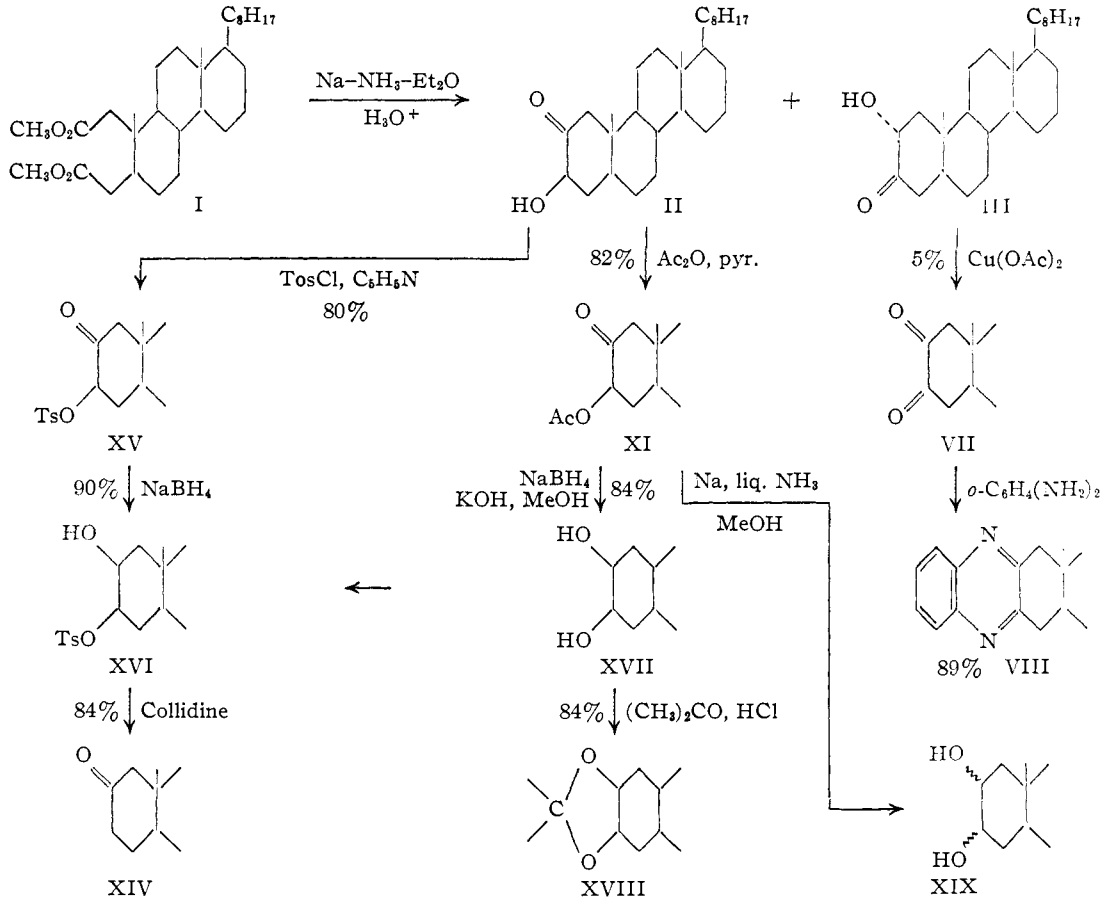
(4) J. C. Sheehan, W. F. Erman and P. A. Cruickshank, THIS JOURNAL, **79**, 147 (1953).

(5) M. Mousseron, R. Jacquier and H. Cristol, *Compt. rend.*, **236**, 927 (1953).

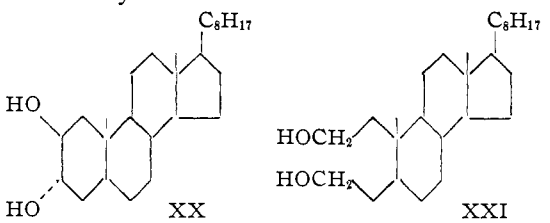
(6) L. Ruzicka, Pl. A. Plattner and M. Furrer, *Helv. Chim. Acta*, **27**, 524 (1944).

(7) P. R. Jefferies and B. Milligen, *Chemistry & Industry*, 487 (1956).

(8) L. Ruzicka, P. A. Plattner and R. Aeschbacher, *Helv. Chim. Acta*, **21**, 866 (1938).



broad hydroxyl band at 3400 cm.$^{-1}$ (2.95 μ) but gave no evidence of carbonyl or double bond. A test for unsaturation with tetranitromethane was negative. The physical properties of IV did not correspond to cholestane-2β,3β-diol (XVII), to the reported cholestane-2β,3α-diol (XX)[9,10] or to 2,3-secocholestane-2,3-diol (XXI) prepared by reduction of the corresponding diester I with lithium aluminum hydride.[10a]



The cyclization of 2,3-secocholestane-2,3-dioic acid dimethyl ester is another example of the stereospecific formation of a single isomer as the main product of an acyloin condensation in homogeneous medium. It is difficult from the evidence available to account for this phenomenon. From these and previous experiments,[1,11] one criterion seems to be the formation of an equatorial hydroxyl group.

(9) R. E. Marker and L. Plambeck, Jr., THIS JOURNAL, **61**, 1332 (1939).

(10) A. Furst and Pl. A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949).

(10a) NOTE ADDED IN PROOF.—However, the constants of IV are in good agreement with those reported recently for cholestane-2α,3β-diol: H. B. Henbest and M. Smith, *J. Chem. Soc.*, 926 (1957).

(11) J. C. Sheehan, R. C. Coderre, L. A. Cohen and R. C. O'Neill, THIS JOURNAL, **74**, 6155 (1952).

Reported methods for the synthesis of cholestane-2-one involve lengthy procedures which result in relatively poor yields from the readily available cholestanol. Ruzicka's synthesis,[6] which gives the best over-all yield, affords the ketone in 21% over-all yield in nine steps from cholestanol. A shorter six-step route to cholestane-2-one by a path derived from the present work gives the ketone in 41% over-all yield from cholestanol. The procedure involves cyclization of the 2,3-secocholestane diester, formation of the tosylate derivative of the resulting acyloin, subsequent reduction with sodium borohydride and detosylation in refluxing collidine.

We gratefully acknowledge support of this research by a Union Carbide and Carbon Co. Fellowship for W.F.E. and a U. S. Public Health Service Grant.

Experimental[12]

Acyloin Condensation of 2,3-Secocholestane-2,3-dioic Acid Dimethyl Ester (I).—Essentially the method of Sheehan, Coderre and Cruickshank[1] for the acyloin condensation of dimethyl marrianolate methyl ether was employed. To a solution of 1.84 g. (0.080 g.-atom) of sodium in 200 ml. of dry ether and 300 ml. of anhydrous liquid ammonia was added 9.2 g. (0.020 mole) of 2,3-secocholestane-2,3-dioic acid dimethyl ester (I)[13] in 200 ml. of dry ether over a period of 90 minutes. To the suspension of sodium enolate of acyloin in ether was added 2 ml. of methanol in 100 ml. of

(12) All melting points are corrected. We are indebted to Dr. S. N. Nagy and his associates for the microanalyses and to Dr. N. A. Nelson and his associates for the infrared and ultraviolet spectra.

(13) B. Heath-Brown, I. M. Heilbron and E. R. H. Jones, *J. Chem. Soc.*, 1482 (1940).

ether; vigorous stirring was continued for 30 minutes and the mixture acidified with 50 ml. of 5% hydrochloric acid. After partition and separation, the aqueous layer was extracted with ether, the ether washed with 5% sodium bicarbonate solution and water and dried over magnesium sulfate. Evaporation of ether under reduced pressure afforded 7.6 g. of colorless VI, m.p. 96–101°.

From the sodium bicarbonate extracts, after acidification and extraction with ether, there was obtained 0.052 g. (1%) of 2,3-secocholestane-2,3-dioic acid (V).

A solution of 1 g. of VI in 50 ml. of petroleum ether and 30 ml. of benzene was chromatographed over 50 g. of ethyl acetate washed Brockman Activity III alumina, using successively mixtures of petroleum ether, benzene, ether and methanol as eluents. From the benzene–2% ether eluate there was obtained 0.082 g. (82%) of 3β-hydroxycholestane-2-one (II) as colorless plates, m.p. 101–104°. Repeated recrystallization from methanol gave a constant m.p. 105–107°, $[\alpha]^{25.6}D$ +63° (*c* 1.40 in chloroform); λ^{Chf} 2.82 (3515 cm.$^{-1}$), 5.85μ (1715 cm.$^{-1}$).

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.72; H, 11.45.

Elution with 5–10% ether in benzene yielded 54 mg. (5%) of the α-ketol III as colorless plates, m.p. 121–123°. Two recrystallizations from methanol gave a constant melting point, 125–126°, $[\alpha]^{25}D$ +39°; λ^{KBr} 2.90 μ (3450 cm.$^{-1}$), 5.88 μ (1700 cm.$^{-1}$).

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.65; H, 11.53.

Elution with methanol–ether afforded 14 mg. (1.4%) of the diol IV as colorless plates, m.p. 208–210°. For analysis the diol was recrystallized from methanol, m.p. 210–211°, $[\alpha]^{26.5}D$ +22.6° (0.89 in chloroform), λ^{KBr} 2.95 μ (3400 cm.$^{-1}$).

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.14; H, 11.96. Found: C, 79.98; H, 11.71.

Cholestane-2,3-dione Quinoxaline (VIII). A. From Acyloin Mixture VI.—A solution of 1 g. of the acyloin mixture VI, m.p. 96–101°, in 225 ml. of absolute methanol was heated under reflux for 2 hr. with 12.5 g. (0.063 mole) of cupric acetate. After evaporation of the methanol to one-half volume under reduced pressure, the reaction mixture was diluted with 500 ml. of 0.8 *N* hydrochloric acid and the precipitated solid extracted with ether. The ethereal layers were washed successively with dilute hydrochloric acid, 5% sodium bicarbonate and water. Evaporation afforded 0.95 g. of the pale yellow solid VII, m.p. 130–133°.

A mixture of 500 mg. of the dione VII and 500 mg. of *o*-phenylenediamine was fused 30 minutes at 145–150° under a nitrogen atmosphere. Recrystallization of the cooled residue from ethyl acetate afforded 520 mg. (89%) of the quinoxaline VIII as pale buff-colored needles, m.p. 177–179°. Treatment with charcoal and repeated recrystallization from ethyl acetate gave colorless needles, m.p. 179–180°.

Anal. Calcd. for $C_{33}H_{48}N_2$: C, 83.82; H, 10.25; N, 5.93. Found: C, 83.77; H, 10.42; N, 6.12.

The aforementioned quinoxaline gave no depression of melting point upon admixture with the authentic quinoxaline derivative of cholestane-2,3-dione prepared from cholestan-one (*vide infra*).

B. From Cholestanone.—To a solution of 1 g. (0.003 mole) of cholestanone[14] in 20 ml. of freshly distilled *t*-butyl alcohol was added 0.102 g. (0.003 mole) of freshly cut potassium. The mixture was stirred vigorously for 30 minutes under a nitrogen atmosphere until all the potassium had dissolved. To this solution 35 ml. (0.304 g., 0.003 mole) of isoamyl nitrite was added and the solution stirred overnight at room temperature. After dilution with 150 ml. of water, the basic solution was washed with ether, then acidified with 5% hydrochloric acid and extracted with ether. Evaporation of solvent led to an oily residue which solidified on standing. Recrystallization from ethanol gave 0.8073 g. (80%), m.p. 203–205°.

A suspension of 0.8073 g. (0.002 mole) of the aforementioned 2-isonitrosocholestane-3-one, m.p. 203–205°, and 2.0 g. (0.02 mole) of pyruvic acid in 25 ml. of glacial acetic acid and 10 ml. of water was refluxed 4 hr. Upon cooling, 0.207 g. (0.002 mole) of pyruvic acid oxime, m.p. 169–174° was deposited.

(14) L. F. Fieser and X. A. Dominguez, THIS JOURNAL, **75**, 1704 (1953).

The residue obtained after evaporation of the solvents under reduced pressure was taken up in ether and the ethereal layer extracted three times with 20% potassium hydroxide solution. The solid potassium salt which formed at the interface, after collecting and washing with ether, was acidified with hydrochloric acid. The yellow suspension was taken up in ether, the ether washed with water and evaporated to dryness to yield 0.4107 g. (53%) of pale yellow crystalline solid, m.p. 139–143°.

A 350-mg. sample of the above cholestane-2,3-dione was fused with 350 mg. of *o*-phenylenediamine. Recrystallization from ethyl acetate gave 0.30 g. (74%; 31.5% over-all from cholestanone) of the quinoxaline of cholestane-2,3-dione, m.p. 174–176°. Recrystallization and charcoal decolorization gave pale yellow needles, m.p. 179–180°.

Anal. Calcd. for $C_{33}H_{48}N_2$: C, 83.82; H, 10.25; N, 5.93. Found: C, 83.40; H, 10.07; N, 5.94.

Peroxide Oxidation of Cholestane-2,3-dione (VII).—A solution of 1.25 ml. of 2 *N* potassium hydroxide was added dropwise to a refluxing solution of 100 mg. (0.0003 mole) of the dione VII, m.p. 130–133°, in 25 ml. of ethanol and 0.6 ml. of 30% hydrogen peroxide. The mixture was warmed on a steam-bath for 10 minutes and stored at 20° for 15 hr. The colorless solution, after removal of ethanol under reduced pressure at 20°, was diluted with water and washed with ether. The aqueous layer, after acidification with 50 ml. of 5% hydrochloric acid, was extracted with ether, the ethereal layer washed with water and evaporated to dryness. The residue, 0.60 g. (58%), m.p. 189–193°, after recrystallization from acetic acid melted at 196–197°. Admixture of the above material with authentic 2,3-secocholestane-2,3-dioic acid,[13] m.p. 196–197°, showed no depression of melting point.

Diosphenol Forms IXa and IXb of Cholestane-2,3-dione.—The method of Stiller and Rosenheim[3] for the isolation of the diosphenol forms of cholestane-2,3-dione was employed. A solution of 500 mg. (0.0013 mole) of the diketone VII, m.p. 130–133°, in 200 ml. of ether was extracted three times with 200-ml. portions of 20% potassium hydroxide. The crude residue obtained after acidification and purification[3] amounted to 0.46 g. (92%), m.p. 138–141°. Repeated recrystallization from acetic acid–ethyl acetate gave a constant m.p. 141–142°.

There was no depression of melting point upon admixture with an authentic sample of the diosphenol *form A* of cholestane-2,3-dione, m.p. 139–142°, prepared by the method of Stiller and Rosenheim.[3]

A suspension of 400 mg. of the above diosphenol, m.p. 138–141°, in 3 ml. of glacial acetic acid and 0.05 ml. of concentrated hydrochloric acid was refluxed 6 minutes on the steam-bath. The mixture on cooling precipitated a yellow solid which, after four recrystallizations from ethyl acetate, amounted to 0.05 g. (12.5%), m.p. 160–162° (reported for cholestane-2,3-dione diosphenol *form B*, m.p. 161–162°).[3]

Sodium Borohydride Reduction of Acyloin Product VI.—Treatment of a solution of 200 mg. of the acyloin mixture VI, m.p. 96–101°, in 200 ml. of absolute methanol with 400 mg. of sodium borohydride in 50 ml. of methanol afforded, after acidification and extraction with ether, 200 mg. (100%) of colorless solid, m.p. 155–170°. Recrystallization from methanol raised the melting point to 165–172°, but further recrystallization from the same solvent failed to give a sharp melting point.

Anal. Calcd. for $C_{27}H_{40}O_2$: C, 80.14; H, 11.96. Found: C, 79.86; H, 12.00.

Pyridine Hydrochloride Fusion of the Isomeric Cholestane-2,3-diols (X).—A mixture of 1.5 g. (0.004 mole) of the isomeric glycols, m.p. 155–170°, and 7.0 g. of anhydrous pyridine hydrochloride was fused 1 hr. at 200–220° under a nitrogen atmosphere. Upon cooling, 15 ml. of 5% hydrochloric acid was added, the solid pulverized and the mixture extracted with ether. The colorless solid which collected at the interface, after washing with ether and water, amounted to 1.10 g. (74%), m.p. 316–318°. Recrystallization from benzene–petroleum ether gave fine, matted needles, m.p. 328–330° dec., $[\alpha]^{25}D$ +26.0° (*c* 0.66 in chloroform), λ^{KBr} 8.78 μ (1140 cm.$^{-1}$), 9.05 μ (1105 cm.$^{-1}$), 9.40 μ (1065 cm.$^{-1}$).

Anal. Calcd. for $C_{54}H_{92}O_2$: C, 83.87; H, 11.99; mol. wt., 773. Found: C, 83.69; H, 12.02; mol. wt. (Rast), 844 ± 84.

The product was insoluble in acid, base and polar solvents, partially soluble in most organic solvents and very soluble in benzene. It gave a negative test for unsaturation with tetranitromethane and did not consume bromine or permanganate.

A solution of 25 mg. of the dimer, m.p. 328–330°, in 25 ml. of dioxane and 5 ml. of 20% hydrochloric acid was refluxed for 45 minutes. There was obtained after dilution with water a quantitative recovery of starting material.

3β-Acetoxycholestane-2-one (XI).—A solution of 5 g. (0.012 mole) of the acyloin mixture VI, m.p. 96–101°, in 50 ml. of dry pyridine and 30 ml. of acetic anhydride was stored at room temperature for 14 hr., then poured into 250 ml. of cold water. After 6 hr. at 0–5°, the crystalline precipitate was collected and dried under reduced pressure to yield 5.41 g. (98.5%) of crystalline acetate, m.p. 135–141°. Recrystallization from methanol gave 4.61 g. (83.5%) of 3β-acetoxycholestane-2-one as colorless needles, m.p. 143–144°. The product was recrystallized for analysis, m.p. 144–145°, $[\alpha]^{26.5}D$ +74° (*c* 1.98 in chloroform); oxime, m.p. 178–179°; λ^{KBr} 5.70 μ (1755 cm.$^{-1}$), 5.78 μ (1730 cm.$^{-1}$).

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.82. Found: C, 78.30; H, 10.59.

3β-Acetoxycholestane-2-one Ethylenethioketal (XII).—A solution of 96.2 mg. (0.0002 mole) of 3β-acetoxycholestane-2-one (XI), m.p. 144–145°, in 5 ml. of glacial acetic acid was treated with 0.2 ml. (0.178 g., 0.0019 mole) of ethanedithiol and 0.2 ml. of boron fluoride etherate at 40–50°. The solution on cooling to room temperature deposited the thioketal XII as colorless plates, 74.9 mg. (78%), m.p. 185–187°. Two recrystallizations from acetic acid gave a constant m.p. 188–189°, $[\alpha]^{26}D$ +4.6° (*c* 0.52 in chloroform).

Anal. Calcd. for $C_{31}H_{52}O_2S_2$: C, 71.50; H, 10.07; S, 12.29. Found: C, 71.66; H, 10.31; S, 12.66.

Raney Nickel Treatment of 3β-Acetoxycholestane-2-one Ethylenethioketal (XII).—A solution of 74 mg. (0.0001 mole) of the thioketal XII, m.p. 185–187°, in 100 ml. of dioxane was refluxed 7 hr. with 2.0 g. of Raney nickel. The reaction mixture was filtered to remove catalyst and the filtrate evaporated to dryness. Crystallization of the residue from methanol gave 42 mg. (80%) of cholestane as colorless plates, m.p. 77–79°. Repeated recrystallization from ethyl acetate–methanol gave a constant m.p. 80–81°, $[\alpha]^{25}D$ +29.8° (*c* 0.56 in chloroform). There was no depression of melting point upon admixture with authentic cholestane, m.p. 78–79°.

Raney Nickel Hydrogenation of 3β-Acetoxycholestane-2-one Diethylmercaptal.—To 91.9 mg. (0.0002 mole) of XI, m.p. 143–144°, dissolved in 5 ml. of anhydrous benzene was added 200 mg. of freshly fused zinc chloride and 0.2 ml. (0.16 g., 0.0026 mole) of ethanethiol. The benzene solution was saturated with anhydrous hydrogen chloride, and, after storage overnight at room temperature, the solution was decanted from zinc chloride and diluted with anhydrous ether. The organic layers were washed successively with 5% sodium hydroxide and water and evaporated to dryness. The residue was dissolved in 100 ml. of dioxane and the solution refluxed 12 hr. in the presence of 1 g. of Raney nickel, to afford 50 mg. (70%) of cholestane as colorless plates, m.p. 79–81°, undepressed on admixture with an authentic sample.

Zinc Dust Reduction of 3β-Acetoxycholestane-2-one (XI).—To a refluxing solution of 400 mg. (0.0009 mole) of XI in 20 ml. of glacial acetic acid was added 0.5 g. of zinc dust followed by 5 ml. of concentrated hydrochloric acid. Addition of zinc dust and hydrochloric acid was continued at 30-minute intervals over a period of 2 hr., while refluxing was continued for an additional hour after final treatment with zinc dust. Upon cooling, the mixture was diluted with water, extracted with ether, the ethereal solution washed with 2 *N* sodium carbonate and water and evaporated to dryness. The oily residue, which failed to crystallize from methanol, was dissolved in petroleum ether–benzene and chromatographed through 15 g. of Brockman Activity III alumina.

Elution with 33% benzene–petroleum ether afforded 90 mg. (27%) of cholestane, m.p. 76–78° after recrystallization from methanol. The combined fractions, after recrystallization from methanol as colorless plates, m.p. 78–79°, gave no depression of melting point upon admixture with authentic cholestane.

Elution with 10% petroleum ether–benzene led to 50 mg. (14%) of cholestane-2-one (XIV) as colorless needles, m.p. 125–127°.

Upon admixture of the product XIV with an authentic sample of cholestane-3-one,[14] m.p. 128–129°, there was a marked depression of m.p., 111–122°.

Admixture of the product with an authentic sample of cholestane-2-one, prepared by the method of Ruzicka,[6] m.p. 129–130°, gave no depression of m.p., 126–128°.

Further elution with benzene and benzene–ether removed 110 mg. of 3β-acetoxycholestane-2-one, m.p. 139–141°, which gave no depression of melting point upon admixture with starting material.

3β-Hydroxycholestane-2-one 3β-*p*-Toluenesulfonate (XV).—To a solution of 1 g. (0.0025 mole) of the acyloin mixture VI, m.p. 96–101°, in 50 ml. of dry pyridine cooled to 0.5° in an ice-bath, was added 2.50 g. (0.013 mole) of *p*-toluenesulfonyl chloride. The mixture was maintained at 0–5° for 1 hr. with occasional swirling, then stored 20 hr. at room temperature. The solution was poured into 800 ml. of cold water and the suspension stored 24 hr. at 0–5°. The precipitated solid, after collection and recrystallization from methanol–acetone, yielded 1.17 g. (80%) of colorless plates, m.p. 168–170°. Two recrystallizations from ether gave matted plates, m.p. 170–171°.

Anal. Calcd. for $C_{34}H_{52}O_4S$: C, 73.34; H, 9.41; S, 5.76. Found: C, 73.11; H, 9.14; S, 5.58.

2β,3β-Dihydroxycholestane 3β-*p*-Toluenesulfonate (XVI).—The α-ketotosylate XV (0.962 g., 0.0018 mole) was dissolved by heating in a mixture of 25 ml. of pyridine and 125 ml. of absolute methanol. The cooled solution, after treatment with a solution of 1 g. (0.026 mole) of sodium borohydride in 50 ml. of methanol, was swirled at room temperature for 30 minutes, then poured into a solution of 20 ml. of acetone in 250 ml. of cold water in order to decompose excess sodium borohydride. The mixture was acidified by dilution with 50 ml. of 10% hydrochloric acid and stored at 0–5° for 4 hr. The crystalline precipitate, after washing with water–methanol and drying under reduced pressure, amounted to 0.950 g. (99%), m.p. 152–155°. Recrystallization from acetone produced 0.86 g. (90%) of colorless plates, m.p. 164–165°, $[\alpha]^{25}D$ +13.0° (*c* 0.47 in chloroform).

Anal. Calcd. for $C_{34}H_{54}O_4S$: C, 73.08; H, 9.74; S, 5.72. Found: C, 73.37; H, 9.89; S, 5.61.

B. From Cholestane-2β,3β-diol (XVII).—A cold solution of 100 mg. of XVII, m.p. 174–176°, in 10 ml. of dry pyridine, treated with 250 mg. of *p*-toluenesulfonyl chloride, was maintained at 0–5° for 1 hr., then stored at room temperature for 15 hr. The derivative was precipitated by dilution with 100 ml. of ice-water and storage for 2 hr. at 0–5°. There was obtained, after recrystallization from acetone–ether, 80 mg. (55%) of cholestane-2β,3β-diol 3β-*p*-toluenesulfonate as colorless plates, m.p. 164–165°. A second recrystallization raised the melting point to 164.5–165°, $[\alpha]^{25}D$ +13.2° (*c* 1.48 in chloroform).

Admixture of the product with the tosylate XVI, m.p. 164–165°, obtained by sodium borohydride reduction of 3β-hydroxycholestane-2-one 3β-*p*-toluenesulfonate, gave no depression of melting point, 164–165°.

Cholestane-2-one (XIV).—A solution of 80 mg. (0.0001 mole) of the hydroxytosylate XVI in 50 ml. of dry collidine was refluxed under a nitrogen atmosphere for 4 hr. at 185–190°. The cooled solution was diluted with 150 ml. of 0.7 *N* sulfuric acid and extracted with ether. The ethereal layer, after washing with dilute sulfuric acid, 5% sodium bicarbonate and water, was concentrated to dryness. The residue, after recrystallization from methanol in colorless needles, m.p. 128–129°, amounted to 43 mg. (84%), $[\alpha]^{26}D$ +48.4° (*c* 1.09 in chloroform), λ^{KBr} 5.85 μ (1710 cm.$^{-1}$).

Anal. Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.54; H, 11.66.

The mixed melting point with an authentic sample of cholestane-3-one,[14] m.p. 128–129°, showed a marked depression of m.p., 109–119°. Admixture of the product with an authentic sample of cholestane-2-one,[6] m.p. 129–130°, gave no depression of melting point, 129–130°.

Cholestane-2β,3β-diol (XVII).—A solution of 0.282 g. (0.0006 mole) of the acetoxyketone XI, m.p. 144–145°, and 1 g. (0.02 mole) of sodium borohydride in 250 ml. of methanol was stored at room temperature for 90 minutes. A

solution of 5.6 g. (0.10 mole) of potassium hydroxide in 5 ml. of water and 45 ml. of methanol was added and the mixture refluxed gently for 2 hr. After removal of the bulk of methanol under reduced pressure, the cooled solution was diluted with water, acidified and extracted with ether. Evaporation of ether and crystallization from methanol afforded 215 mg. (84%) of XVII as colorless needles, m.p. 174–176°. For analysis the product was recrystallized twice from methanol, m.p. 176–176.5°, $[\alpha]^{25}D$ +34° (*c* 0.32 in chloroform), λ^{KBr} 2.94 μ (3400 cm.$^{-1}$).

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.14; H, 11.96. Found: C, 79.89; H, 12.17.

Cholestane-2β,3β-diol Acetonide (XVIII).—To 100 mg. of XVII, m.p. 174–176°, dissolved in 50 ml. of anhydrous acetone was added 5 ml. of acetone saturated with hydrogen chloride. The mixture was swirled 75 minutes, then poured into 200 ml. of 5% potassium carbonate solution. The oily precipitate was extracted with ether, washed with water, dried over magnesium sulfate and evaporated to dryness. Recrystallization from methanol yielded 91 mg. (84%) of the acetonide as colorless plates, m.p. 110–112°. Further recrystallization raised the melting point to 117–118°.

Anal. Calcd. for $C_{30}H_{52}O_2$: C, 81.02; H, 11.79. Found: C, 81.12; H, 11.55.

Diol (XIX).—A solution which was made of 94 mg. (0.0002 mole) of 3β-acetoxycholestane-2-one (XI), m.p. 144–145°, in 50 ml. of ether was added to a vigorously stirred solution of 150 ml. of liquid ammonia, 50 ml. of ether and 25 ml. of absolute methanol in a 500-ml. round-bottomed flask fitted with mechanical stirrer, dropping funnel and Dry Ice condenser. Cautiously, 3 g. of sodium was added in 0.2-g. portions over a period of 30 minutes, vigorous stirring being continued 30 minutes. After evaporation of liquid ammonia overnight, the mixture was acidified with 5% hydrochloric acid and the organic layer partitioned. The aqueous layer was extracted with ether, the combined ethereal layers washed with 5% sodium bicarbonate and water, dried over magnesium sulfate and evaporated to dryness. Recrystallization from methanol led to 74 mg. (86%) of XIX as colorless needles, m.p. 175–188°. A sample recrystallized from absolute methanol in needles, m.p. 182–183°, $[\alpha]^{25}D$ +37.2° (*c* 0.29 in chloroform), λ^{KBr} 2.94 μ (3400 cm.$^{-1}$).

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96. Found: C, 79.91; H, 12.01.

A mixture of a sample of XIX with the *cis*-diol XVII, m.p. 174–176°, showed a marked depression in melting point, 150–165°.

Conversion of 3β-Acetoxycholestane-2-one (XI) to 3β-Hydroxycholestane-2-one (II).—A solution of 200 mg. (0.0001 mole) of the acetoxyketone XI, dissolved by heating in 100 ml. of absolute methanol, was cooled to room temperature and treated with 100 ml. of *N* potassium hydroxide solution. After storage for 36 hr. at room temperature, the mixture was diluted with water and acidified to litmus; the precipitated solid was taken up in ether, the ether washed with 5% sodium bicarbonate and evaporated to dryness. The residue, after recrystallization from aqueous methanol, yielded 47 mg. (26%) of colorless plates, m.p. 100–105°. After three rerystallizations from methanol the product melted at 104–105°, $[\alpha]^{25}D$ +64° (*c* 1.31 in chloroform).

A mixture of the product with a sample of the α-hydroxyketone II, m.p. 105–107°, from chromatography of acyloin VI gave no depression of m.p. 104–105°.

2-Acetoxycholestane-3-one (XXII).—A solution of 50 mg. of the α-ketol III, m.p. 120–125°, in 1 ml. of dry pyridine and 2 ml. of acetic anhydride was stored 12 hr. at room temperature. Lyophilization of the solvents and recrystallization of the residue from methanol afforded 35 mg. (65%) of the acetate XXII as colorless needles, m.p. 139–141°. A sample recrystallized from methanol for analysis melted at 147–149°.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.17; H, 10.59.

A mixture of the acetate XXII with a sample of 3β-acetoxycholestane-2-one (XI), m.p. 144–145°, gave a marked depression in melting point, 125–137°.

2,3-Secocholestane-2,3-diol (XXI).—To a rapidly stirred slurry of 0.5 g. of lithium aluminum hydride in 200 ml. of anhydrous ether was added dropwise, over a period of 20 minutes, 500 mg. (0.001 mole) of the diester XV. Stirring was continued 30 minutes under a nitrogen atmosphere after final addition of the diester. Acidification and ether extraction led to 0.425 g. (98%) of XXI as colorless prisms, m.p. 155–156°, after recrystallization from methanol. A sample for analysis recrystallized from benzene–petroleum ether in fine needles, m.p. 155–156°, $[\alpha]^{24.9}D$ +5.2° (*c* 0.56 in chloroform), λ^{KBr} 2.99 μ (3300 cm.$^{-1}$).

Anal. Calcd. for $C_{27}H_{50}O_2$: C, 79.74; H, 12.39. Found: C, 79.89; H, 12.11.

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, PURDUE UNIVERSITY]

Galactomannan from Soy Bean Hulls[1,2]

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RECEIVED MAY 8, 1957

Water at 40° removes from acetone extracted soy bean hulls a galactomannan in 2% yield. The ratio of D-galactose units to D-mannose units is 2:3. Periodate analysis as well as examination of the products from hydrolysis of the methylated polysaccharide indicate the presence of a chain of 1 → 4 linked D-mannopyranose units with D-galactopyranosyl units joined to certain D-mannose units by 1 → 6 linkages. The structure is similar to guaran but is of lower molecular weight.

Large tonnages of crop residues are produced each year which are potential industrial raw materials. Thus a description of the amounts and of the chemical nature of polysaccharides present in crop residues would be helpful to prospective industrial users. This Laboratory has characterized some of the polysaccharides present in corn cobs and corn hulls, which are two readily available crop residues. Now attention is turned to soy bean hulls which are available at soy bean processing plants.

Acetone-extracted soy bean hulls contain 8% lignin, 64% alpha cellulose and 16% hemicelluloses extractable with alkaline solution. Of these hull hemicelluloses, one is found to be a galactomannan which is totally extractable in 2% yield by water at 40°. The galactomannans guaran and locust bean gum have attained significant industrial importance. Galactomannans from various sources exhibit quite different ratios[3] of D-galactose units to D-mannose units. Soy bean hull galactomannan has a D-galactose unit to D-mannose unit ratio of 2:3

(1) Presented before the Division of Carbohydrate Chemistry at the 131st Meeting of the American Chemical Society, Miami, Florida, in April, 1957.

(2) Journal Paper No. 1105 of the Purdue University Agricultural Experiment Station, Lafayette, Indiana.

(3) R. L. Whistler and C. L. Smart, "Polysaccharide Chemistry," Academic Press Inc., New York, N. Y., 1953, p. 291; E. Anderson, *Ind. Eng. Chem.*, **41**, 2887 (1949).