The method used was patterned after the procedure of Henze and Kahlenberg.[10]

(B) By Diazotization of IV.—A mixture of 100 ml. of water, 50 ml. of concentrated sulfuric acid and 5.0 g. (33.0 mmoles) of IV was chilled to 5–10°. To the cold solution was added dropwise with stirring a solution of 18.0 g. (0.26 mole) of sodium nitrite in 50 ml. of water. The solution was allowed to stand at room temperature for 48 hours during which time 2.80 g. (56%) of product, m.p. >300°, precipitated. It was identical with the product from the hydrolysis of XX as evidenced by paper chromatography and infrared spectrum.

2,4-Dichloro-5,6-trimethylenepyrimidine (XXVI).—A mixture of 15 g. (0.10 mole) of XXV and 75 ml. of phosphoryl chloride was refluxed for 30 minutes. The phosphoryl chloride was evaporated *in vacuo* and the sirupy residue was added to 400 ml. of cold, saturated aqueous sodium carbonate solution, causing the precipitation of solid. The solid was washed with 60 ml. of water and dried to give 13.6 g. (76%) of product, m.p. 69–70°; λ_{max}^{KBr} 6.37, 6.54, 7.52, 8.13, 11.45 μ (pyrimidine ring). Attempts to purify the product further by recrystallization were unsuccessful.

Anal. Calcd. for $C_7H_6Cl_2N_2$: C, 44.4; H, 3.16; Cl, 37.5. Found: C, 44.2; H, 3.31; Cl, 36.8.

2,4-Dimercapto-5,6-trimethylenepyrimidine (XXVII).—A mixture of 1.0 g. (5.3 mmoles) of XXVI, 1.20 g. (15.8 mmoles) of thiourea and 15 ml. of diglyme was refluxed for 1 hour. The solution was evaporated *in vacuo* and, to the solid residue, was added 30 ml. of 5% sodium hydroxide solution. The alkaline solution was treated with Norit and filtered and the filtrate was adjusted to *p*H 5 with glacial acetic acid, which precipitated 0.90 g. (93%) of solid, m.p. >300°. The product was dissolved in 30 ml. of 5% sodium hydroxide solution and neutralized with acetic acid to yield 0.70 g. (72%) of hygroscopic product, m.p. >300°; λ_{max}^{KBr} 3.25 (NH), 6.22, 6.43 (pyrimidine ring), 8.60 μ (C=S).

Anal. Calcd. for $C_7H_8N_2S_2$: C, 45.5; H, 4.37; S, 34.8. Found: C, 45.7; H, 4.65; S, 34.5.

4-Hydroxy-2-(methylthio)-5,6-trimethylenepyrimidine (XXIX).—To a stirred solution of 24.0 g. (0.43 mole) of potassium hydroxide, 60.0 g. (0.32 mole) of 2-methyl-2-thiopseudourea sulfate and 300 ml. of water was added dropwise 33.3 g. (0.21 mole) of 2-carbethoxycyclopentanone (III) over a period of 5 minutes. The resulting mixture was stirred 8 hours, a solution of 10 g. (0.14 mole) of potassium hydroxide in 200 ml. of water was added and the suspension was heated on the steam-bath for 30 minutes. The insoluble solid XXX (13.0 g., 30%) was collected and the filtrate was adjusted to *p*H 5 with glacial acetic acid, which precipitated 11.0 g. (29%) of XXIX, m.p. 274–276° dec. (lit.[7] m.p. 270–272°). In the infrared it had λ_{max}^{KBr} 2.93 (OH), 3.45–3.70 (acidic NH or OH), 6.10, 6.49, 6.79 μ (pyrimidine ring).

The literature[7] yield of XXIX was 8.5%. When the heating period in the above procedure was omitted, the yield of XXIX was much lower.

[2-(Methylthio)-1-cyclopentene-1-carbonyl]-urea (XXX).—The base-insoluble material isolated as a by-product in the preceding preparation of XXIX had m.p. 220–222° dec. It was recrystallized from methyl Cellosolve (1 g./30 ml.) to yield the analytical sample, m.p. 232–237° dec.; λ_{max}^{KBr} 2.93, 3.04, 3.13, 6.55 (NH), 5.93 (C=O), 6.12 μ (C=C). In the ultraviolet it had λ_{max} 308 mμ (ϵ 12,900) in 95% ethanol, and on paper chromatography in solvent system A[8] it showed a single spot with R_{Ad} 1.30.

Anal. Calcd. for $C_8H_{12}N_2O_2S$: C, 48.0; H, 6.04; N, 14.0; S, 16.0. Found: C, 48.1; H, 6.23; N, 14.4; S, 16.0.

4-Chloro-2-(methylthio)-5,6-trimethylenepyrimidine (XXXI).—A mixture of 0.90 g. (5.0 mmoles) of XXIX and 2 ml. of phosphoryl chloride was heated at 90° for 10 minutes, when complete solution resulted. The solution was poured onto 15 g. of ice and water, whereupon 1.0 g. (91%) of solid, m.p. 95–96°, precipitated. In a previous run a product was obtained which, after recrystallization from 75% aqueous ethanol, melted at 95–97°. In the infrared it had λ_{max}^{KBr} 6.36, 6.57, 7.46 μ (pyrimidine ring).

Anal. Calcd. for $C_8H_9ClN_2S$: C, 47.8; H, 4.52; Cl, 17.6. Found: C, 48.1; H, 4.79; Cl, 18.0.

4-Mercapto-2-(methylthio)-5,6-trimethylenepyrimidine (XXXII).—By use of the same procedure employed in the preparation of XXIV and XXVII, 2.5 g. (12 mmoles) of XXXI was converted to 2.0 g. (81%) of XXXII, m.p. 230–232° dec. The product was recrystallized from 50 ml. of methyl Cellosolve to yield 1.60 g. (65%) of product, m.p. 241–243° dec.; λ_{max}^{KBr} 3.23 (NH), 6.39, 6.48 (pyrimidine ring), 7.94 μ (C=S).

Anal. Calcd. for $C_8H_{10}N_2S_2$: C, 48.8; H, 5.08; S, 32.3. Found: C, 48.6; H, 5.14; S, 32.0.

MENLO PARK, CALIF.

(10) H. R. Henze and E. N. Kahlenberg, THIS JOURNAL, **80**, 1664 (1958).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TENNESSEE]

Characterization of the Products from Oxidation of Cholestenone with Osmium Tetroxide

BY JEROME F. EASTHAM, GEORGE B. MILES AND CHARLES A. KRAUTH[1]

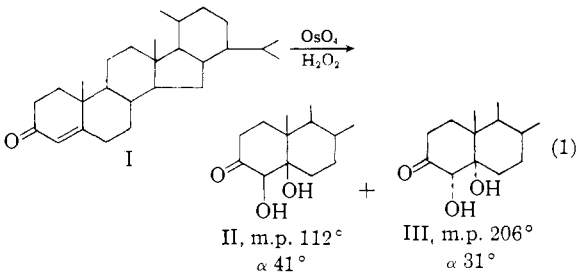
RECEIVED OCTOBER 16, 1958

Repetition of Butenandt's[1] earlier osmium tetroxide oxidation of cholestenone has yielded two 4,5-dihydroxy-3-keto steroids (diolones), only the higher melting of which was found earlier. Each diolone has been monoacetylated, diacetylated, reduced to a triol, and dehydrated. From a comparison of the rates of the latter reaction, which yields the same diosphenol from each diolone, the configurations shown in II and III have been assigned to the lower and higher melting diolones, respectively. Confirmation of this assignment has been obtained through hydrogenolysis of the carbonyl groups from the two diolones to produce the two possible *cis*-4,5-dihydroxycholestanes. These diols have been distinguished by the epimerization of the 4-hydroxy group of one to give the previously known 4β,5-dihydroxycholestane, and by the hydrogenolysis of the 4-hydroxyl group of the other to give the previously unknown 5-hydroxycoprostane.

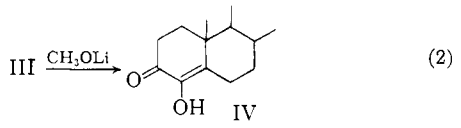
In 1938, Butenandt and Wolz found that cholestenone (I) reacts with one-tenth of an equivalent of osmium tetroxide in the presence of excess hydrogen peroxide to yield a compound $C_{27}H_{46}O_3$, m.p. 208°, which was shown as 4β,5-dihydroxycoprostan-3-one (II).[1] Repetition of the peroxide–tetroxide oxidation (equation 1) has now yielded two products, that of Butenandt and an isomeric compound, m.p. 112°. This paper reports some chemical characterization of these products and defines the stereochemistry of the pair. Our findings reveal that the higher melting compound obtained by Butenandt is in fact 4α,5-dihydroxycholestan-3-one (III, "α-diolone") and that the new isomer is 4β,5-dihydroxycoprostan-3-one (II, "β-diolone").[2]

(1) A. Butenandt and H. Wolz, *Ber.*, **71**, 1483 (1938).

(2) First presentation of these findings: Abstr. 131st Meeting, Am. Chem. Soc., Miami, Fla., 1957, p. 34-O.



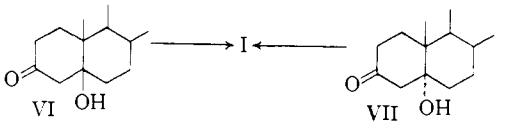
That the compounds are 4,5-dihydroxy-3-ketones has been shown by the base-catalyzed dehydration of each (equation 2) to the same known 4-hydroxycholestenone (IV), a diosphenol.[3] Although this dehydration went well in very dilute solution, where the course of the reaction was followed spectrophotometrically, when more concentrated solutions were employed for preparative purposes, a highly insoluble salt crystallized as soon as either sodium or potassium hydroxide and the diolone were mixed. The diolone could be regenerated by acidifying the salt. For preparative purposes then, it was found convenient to use as the dehydration catalyst lithium methoxide, which did not form an insoluble salt.



The dehydration could also be effected by acid, and in fact occurred so easily under a variety of conditions that in our initial attempts to determine configuration, considerable difficulty was experienced in effecting any reactions of the diolones other than dehydration. Attempted reactions which formed diosphenol instead of desired products included carbonate ester and acetonide formation (attempted to show the *cis*-glycol unit), bismuth triacetate oxidation (attempted to show the α-hydroxy-ketone unit),[4] Wolff-Kishner and Clemmensen reductions, and many carbonyl reactions. We therefore turned to a study of the rates of that very reaction to detect the configurations of the diolones.

If the two diolones differ in their A/B ring fusion, that with A/B-*cis* should dehydrate more rapidly than that with A/B-*trans*. With other 3-keto pairs differing in A/B ring juncture, it has always been observed that for reactions involving α-hydrogen activity, in the A/B-*cis* isomer the 4-position is more reactive but in the A/B-*trans* isomer the 2-position is more reactive.[5] For dehydration of the diolones loss of hydrogen must occur at the 4-position.

The rate of dehydration of each diolone to the diosphenol (IV) has been determined spectrophotometrically at 25° in 0.3 *M* hydrochloric acid in acetic acid. The β-diolone is dehydrated about two and one-half times as rapidly as the α-diolone (Table I). A similar difference (Table I) was observed with the model pair 5-hydroxycoprostan-3-one (VI) and 5-hydroxycholestan-3-one (VII), whose dehydration to cholestenone (I) was determined at 25° in 0.3 *M* hydrochloric acid in ethanol. (Dehydration of the olones (VI and VII) at 25° was too fast for convenience in the solvent employed for the diolones.) Since the reaction



rates for which data are reported in Table I all followed simple first-order kinetics, those data indicate that the β-diolone is a coprostane derivative and the α-diolone is a cholestane derivative. With the assumption that each is a *cis*-glycol,[6] the β-diolone was assigned the configuration shown in II and the α-diolone that in III. These assignments were then confirmed by chemical degradation of II and III.

TABLE I

DEHYDRATION RATE CONSTANTS AT 25°

Compound	Solvent	$k \times 10^3$ min.	k ratio
II	HOAc·HCl	8.7	2.5
III	HOAc·HCl	3.5	
VI	C_2H_5OH·HCl	3.7	2.5
VII	C_2H_5OH·HCl	1.5	

Reduction of the 3-keto group in each diolone was accomplished through its thioketal derivative, obtained in good yield from the diolone with ethanedithiol and boron trifluoride in acetic acid.[7] Hydrogenolysis of the thioketals to 4,5-dihydroxycholestanes (diols VIII and IX) was effected by refluxing each derivative with Raney nickel in dioxane. Each diol was oxidized to a 4-keto-5-hydroxy derivative (ketol) by chromium trioxide in pyridine, X and XI from VIII and IX, respectively. Since two different ketols were obtained, the original diolones II and III cannot be simple C-4 epimers.[6]

Of the four possible 4,5-dihydroxycholestanes only one, not identical with VIII or IX, has been reported.[8,9] It has not previously been assigned a configuration, but its method of synthesis by Heilbron, Shaw and Spring,[9] opening of a 4,5α-epoxide ring[10] (sequence XIV–XIII–XII, Chart I), makes it apparent that it is 4β,5-dihydroxycholes-

(3) L. F. Fieser and R. Stevenson, THIS JOURNAL, **76**, 1728 (1954); A. Butenandt, G. Schramm, A. Wolff and H. Kudszus, *Ber.*, **69**, 2779 (1936).

(4) W. Rigby, *J. Chem. Soc.*, 793 (1951).

(5) *Cf.* W. G. Dauben, R. Micheli and J. F. Eastham, THIS JOURNAL, **79**, 3852 (1952); V. H. Inhoffen, G. Stoeck, G. Killing and U. Stoeck, *Ann.*, **568**, 52 (1950); C. Djerassi and C. R. Scholz, *Experientia*, **3**, 107 (1947); A. Butenandt and A. Wolff, *Ber.*, **68**, 2091 (1935); A. Windaus and E. Kuhr, *Ann.*, **532**, 52 (1937), and **536**, 116 (1938).

(6) As umption that II and III are *cis*-glycols was made because of the known character of osmium tetroxide oxidations; *cf.* W. A. Waters in H. Gilman, "Organic Chemistry," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1953, p. 1180. It was necessary, however, to obviate the alternative possibility that they are epimers at C-4, one having been formed from the other by isomerization at that activated position.

(7) L. F. Fieser, THIS JOURNAL, **76**, 1945 (1954).

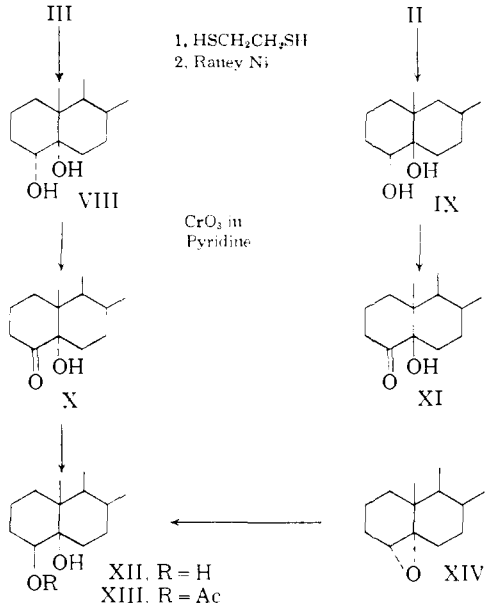
(8) W. Bergmann and E. L. Skau, *J. Org. Chem.*, **5**, 439 (1940).

(9) I. M. Heilbron, W. Shaw and F. S. Spring, *Rec. trav. chim.*, **57**, (1938).

(10) E. Josephy and F. Radt, "Elsevier's Encyclopedia of Organic Chemistry," Vol. 14-Supplement, Series III, Elsevier Publishing Co., Inc., Houston, Tex., 1956, p. 2075S.

tane (XII).[11] Proof of the configuration of diol VIII was obtained by epimerization of its 4-hydroxyl group through ketol X, which with

CHART I



sodium borohydride gave the known 4β,5-dihydroxycholestane (XII),[13] further identified by conversione to 4β-acetoxy-5-hydroxycholestane (XIII).[8,9] The shifts in molecular rotation which accompany the epimerization of the 4-hydroxyl in diol VIII corroborate the assigned configurations of the compounds involved. These shifts (Δ[M]D values, Table II) are in accord with predicted values despite vicinal action by the 5-hydroxyl group. Establishment of the configuration of diol VIII confirms the α-diolone as 4α,5-hydroxycholestan-3-one (III).[15]

With the configuration of diol VIII fixed, and the knowledge that diol IX cannot be an epimer of VIII at C-4, one can assume that the configuration shown for IX is correct. Confirmation of this was obtained by removal of the 4-hydroxyl group from IX. Treatment of diol IX with *p*-toluenesulfonyl chloride yielded the 4-tosylate ester XVII, which

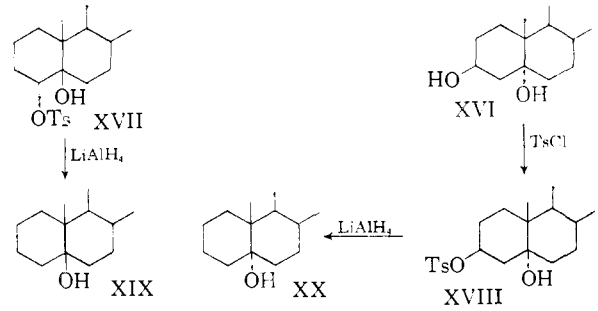
TABLE II

Compound	[M]D	Δ[M]D Found	Δ[M]D Predicted[a]
VIII	+ 55°	+96°	+100°
X	+151°	−12°	− 3°
XII	+139°		

[a] W. Klyne in E. A. Braude and F. C. Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N.Y., 1955, p. 111.

upon reduction with lithium aluminum hydride gave 5-hydroxycoprostane (XIX).[16] Since XIX is a new compound it was compared directly with its known[17] epimer, 5-hydroxycholestane (XX), which was prepared by lithium aluminum hydride reduction of 4β-tosyloxy-5-hydroxycholestane (XVIII) as shown in Chart II.[18] Although too few model compounds have been characterized to establish a Δ[M]D value for epimerization of a 5-hydroxyl group, the optical activities found for XIX and XX are in accord with the generalization that coprostane derivatives are more dextrorotatory than are the same cholestane derivatives (Table III). Establishment of the configuration of diol IX confirms the β-diolone as 4β,5-dihydroxycoprostan-3-one (II).

CHART II



Certain other new steroids were prepared in unsuccessful degradations of the diolones attempted before those of Charts I and II succeeded. Each diolone has been reduced by lithium aluminum hydride to a different triol. These triols are tentatively assigned as cholestan-3β,4α,5-triol (from the α-diolone) and coprostan-3α,4β-5-triol (from

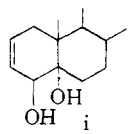
(11) Barton[12] and Furst and Plattner (Abstract of Papers, 12th International Congress of Pure and Applied Chemistry, New York, N. Y., 1951, p. 409) have pointed out that opening of a cyclohexane epoxide group occurs by the addend entering an axial position with displacement of oxygen to produce an adjacent axial hydroxyl group. The only axial approach to a 4,5α-epoxide is beta to the 4-position.

(12) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).

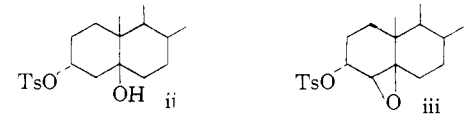
(13) The 4β-hydroxyl group is axial when the A/B ring fusion is *trans*, and hydride reduction of sterically hindered keto groups, as the 4-keto group is, yields predominately the axial alcohol.[12] Thus, reduction of cholestan-2-one, whose keto group is sterically hindered similarly to that in XII, yields largely 2β-hydroxycholestane, the axial isomer.[14]

(14) W. G. Dauben, E. J. Blanz, J. Jiu and R. A. Micheli, THIS JOURNAL, **78**, 3752 (1956).

(15) Also established is the configuration shown (i) for the dihydroxycholestene which Bergmann and Skau[8] hydrogenated to diol XII.



(16) An independent synthesis of XIX would have been desirable. Some attempts were made to do this through reduction of compounds ii and iii. However, compound XIX could not be isolated from reduction of ii or iii with lithium aluminum hydride.[28]



(17) P. A. Plattner, T. Petrzilka, and W. Lane, *Helv. Chim. Acta*, **27**, 513 (1944).

(18) Lithium aluminum hydride reduction of the 4-*p*-toluenesulfonate esters iv and v of diols VIII and XII, respectively, were carried out in attempts to prepare XX. However, iv gave no crystalline product[28] and v gave back the diol XII.

TABLE III

Compound	[M]D
5-Hydroxycholestane	+ 36°[a]
5-Hydroxycoprostane	+ 60[a]
Cholestane	+ 91[b]
Coprostane	+ 97[b]
5-Hydroxycholestan-3-one	+166[a]
5-Hydroxycoprostan-3-one	+254[a]

[a] This work. [b] W. Klyne in E. A. Braude and F. C. Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N. Y., 1955, p. 111.

the β-diolone).[19] Each diolone has been converted to two acetate esters. Acetic anhydride in pyridine with the diolones gave 4-acetoxy derivatives (*e.g.*, 4α-acetoxy-5-hydroxycholestan-3-one from III) while isopropenyl acetate with the diolones gave 4,5-diacetoxy derivatives (*e.g.*, 4β,5-diacetoxycoprostan-3-one from II). Sodium borohydride reduction of the 3-keto group only was successful with both acetate esters from the α-diolone (*e.g.*, 4α,5-diacetoxycholestan-3β-ol was prepared) and with the diacetate ester of the β-diolone (*i.e.*, 4β,5-diacetoxycoprostan-3α-ol was prepared), but attempts to degrade these substances to known compounds by reduction of their tosylates failed. No crystalline tosylates could be obtained from any of the 3-hydroxy derivatives.

Experimental[20]

Oxidation of Cholestenone (I).—To a solution of 4.0 g. of cholestenone in 150 ml. of ether there was added a solution of 0.2 g. of osmium tetroxide in 10 ml. of ether. The ethereal solution turned black. Five milliliters of 30% hydrogen peroxide was added, and on shaking, the dark color gradually faded. The mixture was allowed to stand, with occasional shaking, for 24 hours at room temperature. The ethereal solution was evaporated to leave a gummy residue distributed about the inner surface of the flask, which was then evacuated by water aspirator for approximately 24 hours, at room temperature initially and at 60–70° during the last hour. (If the residue darkened during the period of aspiration, the osmium could be removed by treatment of the mixture with 30% hydrogen peroxide and repeated aspiration.) The residue was dissolved in 50 ml. of hot ethanol, and the resultant solution was cooled. The first crop of crystals formed were removed by filtration and recrystallized from absolute ethanol to yield 1.0 g. (23%) of 4α,5-dihydroxycholestan-3-one (III), m.p. 206–208°, $[\alpha]^{25}D$ +30.9° (*c* 4.10).[1]

Dilution of the filtrate with water produced a second crop of crystals which was collected by filtration. Additional water was added dropwise to the filtrate and a third crop of crystals was collected. The second and third crops were combined and recrystallized from methanol to give 1.2 g. (28%) of 4β,5-dihydroxycoprostan-3-one (II), m.p. 112–112.5°; a polymorphic modification sinters at 112° and melts at 125–126°, $[\alpha]^{25}D$ +40.5° (*c* 2.07).

Anal. Calcd. for $C_{27}H_{46}O_3$: C, 77.46; H, 11.08. Found: C, 77.24; H, 10.85.

Base-Catalyzed Dehydration of Diolones II and III.—To a solution of 0.50 g. of 4β,5-dihydroxycoprostan-3-one (II) in 25 ml. of methanol there was added 5 ml. of a 4 *M* solution of lithium methoxide in methanol. The basic solution was refluxed for one hour and then diluted with 1 ml. of acetic acid. The solution was concentrated to a total volume of 20 ml., cooled and seeded. The crystals which formed amounted to 0.36 g. (74%) of 4-hydroxycholestenone (IV), m.p. 146–148°, $[\alpha]^{25}D$ +79.8° (*c* 2.01), λ_{max} 278 mμ, ϵ_{max} 15,000.[3]

A similar procedure with 4α,5-dihydroxycholestan-3-one produced the same diosphenol (IV). When, however, potassium methoxide (or other potassium or sodium alkalies) was substituted for the lithium methoxide, as soon as the diolone III and alkali were mixed a highly crystalline precipitate formed. Spectrophotometric analysis showed the crystalline material to contain little diosphenol. The crystalline material was virtually insoluble in organic solvents but after it had been shaken with aqueous acid and ether, the starting diolone (III) was found in the ether layer. The crystalline material, which did not have a distinct melting point (dec. >150°), is formulated as the potassium salt. The poor analytical values are attributed to contamination by diosphenol IV.

Anal. Calcd. for $C_{27}H_{45}O_3K$: C, 71.03; H, 9.87; K, 8.77. Found: C, 72.63; H, 10.07; K, 7.02.

Acid-catalyzed Dehydration of Diolones II and III.—Preliminary studies of the dehydration rates were performed using various combinations of ethanol or acetic acid as solvent and oxalic acid or hydrochloric acid at various concentrations as catalyst. Of the combinations tested, acetic acid about 0.3 *M* in hydrochloric acid was the most convenient for rate studies about room temperature. At this temperature each diolone was stable in pure acetic acid. Stock solutions of each diolone (0.023 g. per 100 ml.) and of hydrochloric acid (1 *M*) were made up in acetic acid. At time zero for a kinetic run a 2-ml. aliquot of a diolone solution and 3 ml. of the hydrochloric acid solution were diluted to 10 ml. in a volumetric flask at room temperature. A portion of the reaction solution was transferred to a quartz cell and placed in the spectrophotometer[21] sample housing, which was thermostated at 25°. Ultraviolet light absorption of the reaction solution was measured by comparison with an acetic acid blank prepared with the hydrochloric acid but without any diolone. Optical density (d_t) was measured at time intervals of 1 to 5 minutes for 90 minutes at the position of maximum absorption of the diosphenol IV, where the starting material is essentially transparent. After several hours the optical density (d_∞) of the reaction solution was that calculated for pure diosphenol. First-order rate constants for each run were taken as the slope of the straight line obtained by a plot of 2.3 log $(d_\infty/d_\infty - d_t)$ against *t* (time in minutes). Results are given in Table I.

5-Hydroxycholestan-3-one (VII).—A solution of 4 g. of the α-epoxide[22] of cholesterol and 1 g. of lithium aluminum hydride in ether was refluxed for one hour. The excess hydride was decomposed with ethyl acetate and the reaction mixture treated with dilute hydrochloric acid. The ethereal solution was washed with aqueous sodium bicarbonate, dried, and evaporated to leave a crystalline residue. Without further purification the crystalline residue was dissolved in 40 ml. of pyridine and added to a slurry of 2.8 g. of chromium trioxide in 28 ml. of pyridine. The mixture was stirred overnight at room temperature and then poured into water. The aqueous mixture was extracted with ether which was in turn washed with hydrochloric acid, dried and evaporated. The residue was recrystallized from benzene to give 2.9 g. of 5-hydroxycholestan-3-one (VII), m.p. 222–223°, $[\alpha]^{25}D$ +41.3° (*c* 2.51).

A sample of VII was acetylated with isopropenyl acetate in the usual manner (see below under diacetylation of the α-diolone). The crude product was purified by chromatography on Florisil to give **5-acetoxycholestan-3-one**, m.p. 145–147°, $[\alpha]^{25}D$ +46.9° (*c* 2.48).

Anal. Calcd. for $C_{29}H_{48}O$: C, 78.32; H, 10.88. Found: C, 78.55; H, 10.69.

5-Hydroxycoprostan-3-one (VI).—A 2.9-g. portion of the β-epoxide[23] of cholestenone was reduced with lithium aluminum hydride in the usual manner (*cf.* preparation of VII). The crude product was suspended in 100 ml. of acetic acid

(19) The tentative assignments of configuration at the 3-position are based on the well known fact (*cf.* W. G. Dauben, R. Micheli and J. F. Eastham, THIS JOURNAL, **74**, 3852 (1952)) that reduction of a 3-keto group by a complex hydride gives predominantly the epimer with equatorial hydroxyl.

(20) Melting points are reported uncorrected. Optical activities were determined with chloroform solutions and ultraviolet absorption measurements were made with ethanol solutions. Elemental analyses were performed by Weiler and Strauss, Oxford, England. All chromatography was done on Florisil absorbent using the following eluting solvents in order: petroleum ether, benzene, ether, chloroform, acetone and methanol.

(21) A Beckman model DU quartz spectrophotometer was employed.

(22) L. Ruzicka and L. Bosshard, *Helv. Chim. Acta*, **20**, 244 (1937).

(23) P. A. Plattner, H. Heusser and A. B. Kilkarni, *ibid.*, **31**, 1822 (1948).

and mixed with a solution of 1.0 g. of chromium trioxide and 0.5 ml. of water in 25 ml. of acetic acid. After one day the reaction mixture was diluted with 5.0 ml. of methanol and with sufficient water to precipitate the crude product. The crude product was recrystallized from ethanol to give colorless 5-hydroxycoprostan-3-one (VI), m.p. 248–250°, $[\alpha]^{25}D$ +63.1° (*c* 1.93).

Attempts to convert VI to the 5-acetoxy derivative by acetylation with either acetic anhydride or isopropenyl acetate were unsuccessful. Chromatography of the reaction product yielded cholestenone. Apparently the successful acetylation of VII was a consequence of its lesser susceptibility to dehydration.

Acid-catalyzed Dehydration of Olones VI and VII.—The procedure for determining the rates of dehydration of VI and VII was like that employed with II and III with the exception that ethanol was used as solvent. Acetic acid caused dehydration while the sample was being dissolved. The reaction was followed at the position of maximum absorption by cholestenone, 243 mμ, where the starting samples are essentially transparent. Results of the kinetic measurements are given in Table I.

Ethylene Thioketal Derivative of 4α,5-Dihydroxycholestan-3-one (III).—This derivative was prepared by the method of Fieser.[7] A suspension of 3.0 g. of the α-diolone in 50 ml. of acetic acid was treated with 1.5 ml. of ethanedithiol and 1.5 ml. of boron trifluoride etherate at room temperature. The mixture was stirred for several minutes and allowed to stand for approximately two hours. The thioketal derivative separated from the mixture as fine crystals. The product was recrystallized from a mixture of chloroform and ethanol to yield 3.1 g. of 4α,5-dihydroxycholestan-3-one ethylene thioketal, m.p. 242–243°.

Anal. Calcd. for $C_{29}H_{50}O_2S_2$: C, 70.41; H, 10.19; S, 12.94. Found: C, 70.14; H, 9.96; S, 12.60.

Ethylene Thioketal Derivative of 4β,5-Dihydroxycoprostan-3-one (II).—A solution of 2.0 g. of the β-diolone in 10 ml. of acetic acid was treated with 1 ml. of ethanedithiol and 1 ml. of boron trifluoride etherate at room temperature. The solution was stirred for a few minutes and allowed to stand for about 30 minutes. A thick oil which separated from the acetic acid crystallized on scratching. The crude crystalline material was recrystallized from methanol to yield 2.2 g. of 4β,5-dihydroxycoprostan-3-one ethylene thioketal, m.p. 169–170°.

Anal. Calcd. for $C_{29}H_{50}O_2S_2$: C, 70.41; H, 10.19; S, 12.94. Found: C, 70.58; H, 9.96; S, 13.12.

4α,5-Dihydroxycholestane (VIII).—Hydrogenolysis of the thioketal from III was effected in the manner described by Hauptmann.[24] To a solution of 1.5 g. of 4α,5-dihydroxycholestan-3-one ethylene thioketal in 50 ml. of 1,4-dioxane there was added 30 g. of wet Raney nickel.[25] The mixture was refluxed for 12 hours, cooled, filtered and evaporated. The residue isolated after the removal of the dioxane was recrystallized from methanol to yield 0.91 g. of 4α,5-dihydroxycholestane, m.p. 139–140°, $[\alpha]^{28}D$ +13.1° (*c* 3.50).

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96. Found: C, 79.75, 79.85; H, 11.84, 11.69.

4β,5-Dihydroxycoprostane (IX).—One gram of 4β,5-dihydroxycoprostan-3-one ethylene thioketal was dissolved in 50 ml. of 1,4-dioxane and 20 g. of wet Raney nickel was added. The mixture was refluxed for 12 hours, cooled and evaporated. The residue was dissolved in methanol and crystallization was induced by scratching. This crop of crystals, m.p. 135–136°, weighed 0.30 g. Since no additional crystals could be isolated from the filtrate, the solvent was evaporated and the residual oil was chromatographed. From the fraction eluted by benzene, 0.15 g. of product was secured. The total yield of 4β,5-dihydroxycoprostane was 0.45 g., m.p. 135–136°, $[\alpha]^{28}D$ +24.8° (*c* 2.87).

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96. Found: C, 80.31, 79.89; H, 11.98, 11.72.

5-Hydroxycholestan-4-one (X).—Diol VIII was oxidized by the method described by Poos, *et al.*[26] A solution of 0.90 g. of diol VIII in 10 ml. of pyridine was added to a mixture of 1 g. of chromium trioxide in 10 ml. of pyridine and allowed to stand at room temperature for 48 hours. At the end of this period, the pyridine mixture was diluted with 200 ml. of water and extracted with three 100-ml. portions of ether. The combined ethereal extract was washed with water, with dilute hydrochloric acid and with aqueous sodium bicarbonate and was dried. The solvent was evaporated and the residue was recrystallized three times from methanol to give material which melted 152–155°. This crystalline material was further purified by chromatography. The fraction eluted with benzene was recrystallized from methanol to yield 0.25 g. of 5-hydroxycholestan-4-one, m.p. 157–158°, $[\alpha]^{27}D$ +37.4° (*c* 0.415).

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.63; H, 11.40.

The oxidation of diol VIII was attempted under other conditions in an effort to increase the yield of ketol X. One attempted oxidation with chromium trioxide and pyridine was carried out using exactly a two-thirds to one molar ratio of chromium trioxide to diol. This reaction mixture was stirred at 10° for 48 hours but was otherwise treated as described above. The only crystalline material isolated from the reaction mixture was the starting diol.

An attempt to oxidize this same diol with N-bromosuccinimide was also carried out using a method described by Fieser and Rajagopalon.[27] A mixture of 0.87 g. of VIII, 20 ml. of ether, 3 ml. of methanol, 3 ml. of water and 0.48 g. of N-bromosuccinimide was shaken for five minutes, during which time the mixture changed from colorless to yellow-orange, was allowed to stand an additional ten minutes, and was diluted with water. The ether layer was separated, washed with aqueous base and water, dried, and evaporated. After attempts to purify the semi-crystalline residue by recrystallization from methanol were unsuccessful, the material was chromatographed and 0.40 g. of the starting diol was isolated from the fraction eluted in benzene–ether. No other crystalline material was isolated.

5-Hydroxycoprostan-4-one (XI).—The oxidation of the α-diol IX was carried out with excess chromium trioxide in pyridine in the manner used with the β-diol VIII. A 1.0-g. sample of IX, oxidized and purified as described, yielded 0.50 g. of 5β-hydroxycoprostan-4-one, m.p. 173–175°, $[\alpha]^{28}D$ +18.3° (*c* 0.835).

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.63; H, 11.72.

4β,5-Dihydroxycholestane (XII).—A solution of 0.20 g. of 5-hydroxycholestan-4-one in 10 ml. of the diethyl ether of diethylene glycol was added to a stirred suspension of 0.25 g. of sodium borohydride in 15 ml. of the same solvent. After four hours, the reaction mixture was diluted with 200 ml. of water and the crystalline precipitate was removed by filtration. Recrystallization from methanol yielded 0.17 g. of 4β,5-dihydroxycholestane, m.p. 172–173°, $[\alpha]^{27}D$ +34.2° (*c* 1.110). This compound has been previously reported, m.p. 169–170°[8] and 171–172°,[9] $[\alpha]^{25}D$ +35.5°.[9]

A solution of 0.10 g. of diol XII and 0.10 g. of *p*-toluenesulfonyl chloride in 5 ml. of pyridine was allowed to stand at 10° for a period of 48 hours. The pyridine mixture was diluted with 25 ml. of water, and the crystalline precipitate removed by filtration. This solid material was washed with water and then recrystallized from methanol. The yield of white crystalline **4β-*p*-toluenesulfonoxy-5-hydroxycholestane (v)** was 0.08 g., m.p. 138–140° with decomposition.

Anal. Calcd. for $C_{34}H_{54}O_4S$: C, 73.08; H, 9.74; S, 5.73. Found: C, 72.97; H, 9.47; S, 5.96.

A solution of 0.10 g. of diol XII and 0.5 ml. of acetic anhydride in 3 ml. of pyridine was allowed to stand at room temperature for 12 hours. The stirred reaction mixture was cooled in an ice-bath and diluted dropwise with ice-water. The precipitated product was washed with water and recrystallized from ethanol to give 0.09 g. of 4β-acetoxy-5-hydroxycholestane (XIII), m.p. 174–175°, as previously reported.[8,9]

4β-*p*-Toluenesulfonoxy-5-hydroxycoprostane (XVII).—A solution of 0.55 g. of 4β,5-dihydroxycoprostane (IX) and 0.50 g. of *p*-toluenesulfonyl chloride in 5 ml. of pyridine was allowed to stand 48 hours at 10°. The pyridine solution was diluted with 25 ml. of water and the crystalline precipitate which formed was collected, washed with water and

(24) H. Hauptmann, THIS JOURNAL, **69**, 562 (1947).

(25) R. Mozingo, *Org. Syntheses*, **21**, 15 (1941).

(26) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953).

(27) L. F. Fieser and S. Rajagopalan, *ibid.*, **71**, 3938 (1949).

recrystallized from methanol to yield 0.53 g. of 4β-*p*-toluenesulfonoxy-5-hydroxycoprostane, m.p. 125–126° dec., $[\alpha]^{28}D$ +7.3° (*c* 1.610).

Anal. Calcd. for $C_{34}H_{54}O_4S$: C, 73.08; H, 9.74; S, 5.73. Found: C, 73.05; H, 9.72; S, 5.69.

4α-*p*-Toluenesulfonoxy-5-hydroxycholestane (iv).—4α-*p*-Toluenesulfonoxy-5α-hydroxycholestane was prepared, isolated and purified from the α-diol VIII by the method described above for the β-diol IX. The initial reaction mixture consisted of 1.0 g. of diol VIII and 1.0 g. of tosyl chloride. The final product was recrystallized from methanol to yield 0.90 of 4α-*p*-toluenesulfonoxy-5α-hydroxycholestane, m.p. 137–138° dec.

Anal. Calcd. for $C_{34}H_{54}O_4S$: C, 73.08; H, 9.74; S, 5.73. Found: C, 73.04; H, 9.74; S, 5.92.

5-Hydroxycoprostane (XIX).—A solution of 0.53 g. of 4β-*p*-toluenesulfonoxy-5-hydroxycoprostane and 1.0 g. of lithium aluminum hydride in 50 ml. of anhydrous ether was stirred for three hours, and the excess lithium aluminum hydride was decomposed by the addition of 10 ml. of ethyl acetate. The complex was decomposed by the addition of dilute hydrochloric acid. The ether layer was separated, and the water layer was extracted three times with ether. The combined ether layers were washed with water and with aqueous sodium bicarbonate, and evaporated. The resultant oil was induced to crystallize by scratching and was recrystallized from methanol to yield 0.15 g. of 5-hydroxycoprostane, m.p. 96–97°, $[\alpha]^{28}D$ +15.4° (*c* 1.720).[28]

Anal. Calcd. for $C_{27}H_{48}O$: C, 83.43; H, 12.45. Found: C, 83.38; H, 12.18.

5-Hydroxycholestane (XX).—A solution of 0.80 g. of 3β,5-dihydroxycholestane (XVI)[29] and 0.80 g. of *p*-toluenesulfonyl chloride in 5 ml. of pyridine was allowed to stand at 10° for 48 hours and was then diluted with 25 ml. of water. The crystalline precipitate was recrystallized from methanol–chloroform to give 0.87 g. of **3β-*p*-toluenesulfonoxy-5-hydroxycholestane (XVIII)**, m.p. 130–135° dec.[30]

Anal. Calcd. for $C_{34}H_{54}O_4S$: C, 73.08; H, 9.74; S, 5.73. Found: C, 72.75; H, 9.54; S, 5.85.

A solution of 0.30 g. of XVIII and 0.2 g. of lithium aluminum hydride in 40 ml. of ether was stirred for two hours. After the dropwise addition of 5 ml. of ethyl acetate to decompose the excess hydride, the reduction complex was decomposed with an aqueous solution of sodium tartrate. The ether layer was separated, and the water layer was extracted three times with ether. After the combined organic extracts were dried and evaporated, the residue was induced to crystallize by scratching. The crystalline material was recrystallized from methanol to yield 0.15 g. of cholestan-5α-ol, $[\alpha]^{25}D$ +9.3°, m.p. 106–107°,[13] depressed >15° by XIX.

3-α-*p*-Toluenesulfonoxy-5-hydroxycoprostane (ii).—Eight-tenths of a gram of 3α,5-dihydroxycoprostane[31] was esterified with tosyl chloride in pyridine in the usual manner. Recrystallization of the crude product from methanol–chloroform yielded 0.93 g. of 3α-*p*-toluenesulfonoxy-5-hydroxycoprostane, m.p. 109° dec.[30]

Anal. Calcd. for $C_{34}H_{54}O_4S$: C, 73.08; H, 9.74. Found: C, 73.27; H, 9.92.

4,5β-Oxido-3α-*p*-toluenesulfonoxycoprostane (iii).—Four-tenths of a gram of 4,5β-oxido-3α-hydroxycoprostane[32] was esterified with tosyl chloride in pyridine in the usual manner. The crude product was recrystallized from methanol to yield 0.41 g. of 4,5β-oxido-3-*p*-toluenesulfonoxycoprostane, m.p. 126–127°.

Anal. Calcd. for $C_{34}H_{52}O_4S$: C, 73.34; H, 9.41; S, 5.75. Found: C, 73.45; H, 9.26; S, 5.91.

Reduction of α-Diolone III with Lithium Aluminum Hydride.—A solution of 0.50 g. of III and 0.5 g. of lithium aluminum hydride in 50 ml. of ether was refluxed for two hours. The reaction mixture was treated dropwise in turn with 2 ml. of ethyl acetate and with hydrochloric acid. The ethereal solution was washed with aqueous sodium bicarbonate, dried, and evaporated. The crystalline residue was recrystallized from benzene–petroleum ether to give 0.35 g. of **cholestan-3β,4α,5-triol** (tentative assignment[19] at 3), m.p. 213–215°.

Anal. Calcd. for $C_{27}H_{48}O_3$: C, 77.09; H, 11.50. Found: C, 77.50; H, 11.81.

Reduction of β-Diolone II with Lithium Aluminum Hydride.—In the manner described above 0.50 g. of II was reduced with lithium aluminum hydride and worked up to give **coprostan-3α,4β,5-triol** (tentative assignment[19] at 3), m.p. 80–82°.

Anal. Calcd. for $C_{27}H_{48}O_3$: C, 77.09; H, 11.50. Found: C, 77.22; H, 11.67.

Monoacetylation of the α-Diolone III.—A solution of 1.80 g. of III and 5 ml. of acetic anhydride in 30 ml. of pyridine was allowed to stand at room temperature for 12 hours. The reaction mixture was cooled in an ice-bath and diluted dropwise with ice-water. The precipitated product was washed with water and recrystallized from ethanol to give 1.80 g. of **4α-acetoxy-5-hydroxycholestan-3-one**, m.p. 223–225°, $[\alpha]^{25}D$ −22.4° (*c* 2.36).

Anal. Calcd. for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50. Found: C, 75.83; H, 10.73.

Monoacetylation of the β-Diolone II.—In the manner described above 0.90 g. of II was treated with acetic anhydride to give 0.91 g. of **4β-acetoxy-5-hydroxycoprostan-3-one**, m.p. 185–186°, $[\alpha]^{25}D$ +52.5° (*c* 3.99).

Anal. Calcd. for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50. Found: C, 76.03; H, 10.89.

Diacetylation of the α-Diolone III.—A solution of 0.20 g. of III and 0.005 g. of *p*-toluenesulfonic acid in 8 ml. of isopropenyl acetate was refluxed for two hours. Two drops of pyridine were added to the reaction solution, which was then concentrated to about 2.5-ml. volume. This volume was diluted with ether, washed with aqueous sodium bicarbonate and with water, dried and evaporated. The residue was recrystallized from methanol to give 0.12 g. of **4α,5-diacetoxycholestan-3-one**, m.p. 160–161.5°, $[\alpha]^{25}D$ +30.9° (*c* 4.12).

Anal. Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03. Found: C, 73.58; H, 9.81.

Diacetylation of the β-Diolone II.—In the manner described above 0.20 g. of II was treated with isopropenyl acetate to yield **4β,5-diacetoxycoprostan-3-one**, m.p. 156–157°, $[\alpha]^{25}D$ +65.6° (*c* 4.07).

Anal. Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03. Found: C, 73.85; H, 9.77.

Reduction of 4α,5-Diacetoxycholestan-3-one with Sodium Borohydride.—A suspension of 1.70 g. of this diacetoxy ketone in a solution of 0.5 g. of sodium borohydride and 5 ml. of water in 45 ml. of methanol was stirred until the reaction mixture became clear and homogeneous. The methanolic solution was then immediately diluted with dilute hydrochloric acid and, when hydrogen evolution ceased, extracted with ether. The ethereal solution was washed with dilute hydrochloric acid and with aqueous sodium bicarbonate, dried and evaporated. The residue was recrystallized from ethanol to give 0.87 g. of **4α,5-diacetoxycholestan-3β-ol** (tentative assignment[19] at 3), m.p. 162–164°.

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(28) After the completion of this work and its original announcement,[2] A. S. Hallsworth and H. B. Henbest (*J. Chem. Soc.*, 4604 (1957)) also reported 5-hydroxycoprostane, but with m.p. 82°, $[\alpha]D$ +37°. Their discrepancy in physical properties (decrease in m.p. and increase in $[\alpha]$) and high carbon and hydrogen analysis could be because of contamination of their material with Δ⁴-cholestene. The 5-hydroxy steroids are very susceptible to dehydration. In several attempts to isolate either 5-hydroxycoprostane (XIX) or 5-hydroxycholestane (XX) from a reaction, when the crude products resisted direct crystallization, these products were chromatographed on Florisil in the usual manner. Only hydrocarbon material came off the column! Pure samples of both XIX and XX, when chromatographed, were also converted to hydrocarbons which melted indefinitely in the range 60 to 72°, decolorized bromine solutions and resisted purification.

(29) This compound, m.p. 224–225°, was prepared by reduction of 5,6α-oxidocholestan-3β-ol with lithium aluminum hydride.

(30) This compound has been previously reported (R. B. Clayton and H. B. Henbest, *Chemistry & Industry*, 1315 (1953)) without analysis or physical constants.

(31) This compound, m.p. 191–192°, was isolated by fractional crystallization of the product from lithium aluminum hydride reduction of 4,5β-oxidocoprostan-3-one.[32]

(32) P. A. Plattner, H. Heusser and A. B. Kilkarni, *Helv. Chim. Acta*, **31**, 1822 (1948).

Anal. Calcd. for $C_{31}H_{52}O_5$: C, 73.76; H, 10.38. Found: C, 74.32; H, 10.57.

Reduction of 4α,5-diacetoxycholestan-3β-ol with lithium aluminum hydride in the usual manner gave cholestan-3β,-4α,5-triol, m.p. 212–214°, undepressed by triol prepared by direct reduction of the α-diolone III.

Reduction of 4β,5-Diacetoxycoprostan-3-one with Sodium Borohydride.—In the manner described above 0.85 g. of this diacetoxy ketone was reduced with sodium borohydride to give **4β,5-diacetoxycoprostan-3α-ol** (tentative assignment[19] at 3), m.p. 163–166°.

Anal. Calcd. for $C_{31}H_{52}O_5$: C, 73.76; H, 10.38. Found: C, 73.56; H, 10.47.

Reduction of 4β,5-diacetoxycoprostan-3α-ol with lithium aluminum hydride in the usual manner gave coprostan-3α,-4β,5-triol, m.p. 81–82°, undepressed by triol prepared by direct reduction of the β-diolone II.

Reduction of 4β-Acetoxy-5-hydroxycholestan-3-one with Sodium Borohydride.—A suspension of 1.80 g. of this ketone in a solution of 0.5 g. of sodium borohydride in 45 ml. of methanol and 5 ml. of water was stirred for seven minutes and then diluted with dilute hydrochloric acid. After the evolution of hydrogen ceased the acidic mixture was extracted with ether, which was in turn washed with aqueous sodium bicarbonate, dried and evaporated. The residue was recrystallized from ethanol to give **4α-acetoxycholestan-3β,5-diol** (tentative assignment[19] at 3), m.p. 207–208°.

Anal. Calcd. for $C_{29}H_{50}O_4$: C, 75.28; H, 10.89. Found: C, 75.29; H, 10.82.

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KNOXVILLE, TENN.

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

Steroids. CXII.[1] Cycloethylene Ketal Formation of 19-Nor-Δ^4-3-keto Steroids

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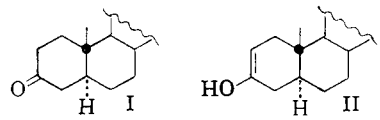
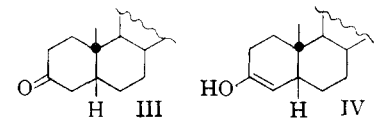
Cycloethylene ketal formation in the 19-nor-Δ^4-3-keto steroid series has been shown to produce a mixture of isomeric Δ^5 and $\Delta^{5(10)}$-3-cycloethylene ketals. The structure proofs for these double bond isomers were accomplished *via* epoxidation followed by fission of the epoxides with boron trifluoride. The resulting ketal fluorohydrins were then degraded to known or readily identified products. The results not only permit the unamibiguous location of the double bonds but also provide a complete description for the stereochemistry of the intermediate epoxides.

In connection with another problem, we have had occasion to investigate the formation of 3-cycloethylene ketals in the 19-nor steroid series and now report some of our findings.

The fact that the formation of 3-cycloethylene ketal derivatives in the 10-methyl-Δ^4-3-ketone system results in rearrangement of the double bond to the Δ^5-position has been known[2] for some time. More recently the mechanism of the reaction has received attention[3] and the conclusion reached was that the isomerization resulted from the intermediate formation of a $\Delta^{3,5}$-enol ether type compound.

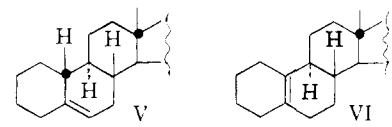
While the isomerization of the double bond was expected to occur in the 19-nor steroid series it was evident that such an isomerization could now lead to Δ^5- and/or $\Delta^{5(10)}$-cycloethylene ketal isomers. Several considerations must be taken into account in predicting the preferred position for the double bond in such cases. For example, it is known[4] that bromination of 3-keto allo steroids I leads to 2-bromo compounds, thus indicating that in the A/B *trans* series the enolic double bond is more stable in the Δ^2-position II. On the other hand, bromination and sulfonation evidence shows that in A/B *cis* steroids (III) the 3-4 position of the enolic double bond (IV) is favored.





It follows that the nature of the ring junction has an important bearing on the position for the double bond.

If these observations are now applied to the 19-nor steroid series and the B/C *trans* ring junction is equated to the A/B *trans* decalone type junction I, it might be expected that a double bond would be more stable in the Δ^5-position V rather than in the $\Delta^{5(10)}$-position VI.



Mediating against this conclusion are two factors, the first of which is that the nor steroid V does not accurately approximate the model I, since it is reasonable to expect that ring A will conformationally modify the double bond stability at Δ^5. Secondly, it is known that octalin-type double bonds are more stable when in the tetrasubstituted Δ^9-position, as may be witnessed by an interesting report[5] quantitatively describing the equilibria involved. As will be seen in the sequel, both of the possible positional isomers were obtained during the ketalization reaction.

(1) Paper CXI, A. Bowers and H. J. Ringold, THIS JOURNAL, **81**, 1264 (1959).

(2) (a) F. Fernholz and H. E. Stavely, abstracts of the 102nd Meeting of the American Chemical Society, Atlantic City, N. J., 1941, p. 39 M; see also E. Fernholz, U. S. Patents 2,356,154 and 2,378,918; (b) R. Antonucci, S. Bernstein, R. Littell, K. Sax and J. H. Williams, *J. Org. Chem.*, **17**, 1341 (1952); (c) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953).

(3) C. Djerassi and M. Gorman, *ibid.*, **75**, 3704 (1953).

(4) A. Butenandt and A. Wolff, *Ber.*, **68B**, 2091 (1935).

(5) W. G. Dauben, E. C. Martin and G. J. Fonken, *J. Org. Chem.*, **23**, 1205 (1958).