3 hr before work-up. Crude yield was 0.34 g (77%) from which only the L isomer was recovered, mp 118–119°, lit.[9] mp 118–119°. The infrared spectrum showed absorption at λ_{max}^{KBr} 3.04 (m) (N–H stretch), 5.74 (s) (ester C=O stretch) 5.87 (s) (C=O stretch), 6.10 (s) (amide C=O stretch), 8.18 (s) and 8.34 (s) (C–O stretch), and 13.60 (w), 14.30 μ (m) (phenyl C—H) bend).

Registry No.—A (Table V; $R_1 = CH_2C_6H_5$; $R_2 = H$), 14746-00-0; glycyl-L-phenylalanine phenylhydrazide, 14721-35-8; benzyloxycarbonyl-Gly-L-Phe-Gly-L-Phe phenylhydrazide, 14721-36-9; benzyloxycarbonyl-Gly-L-Phe-Gly ethyl ester, 2073-59-8.

Bile Acids. XXIII. A New Direct Synthesis of Allocholic Acid and Its 3β Isomer[1]

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Received August 22, 1967

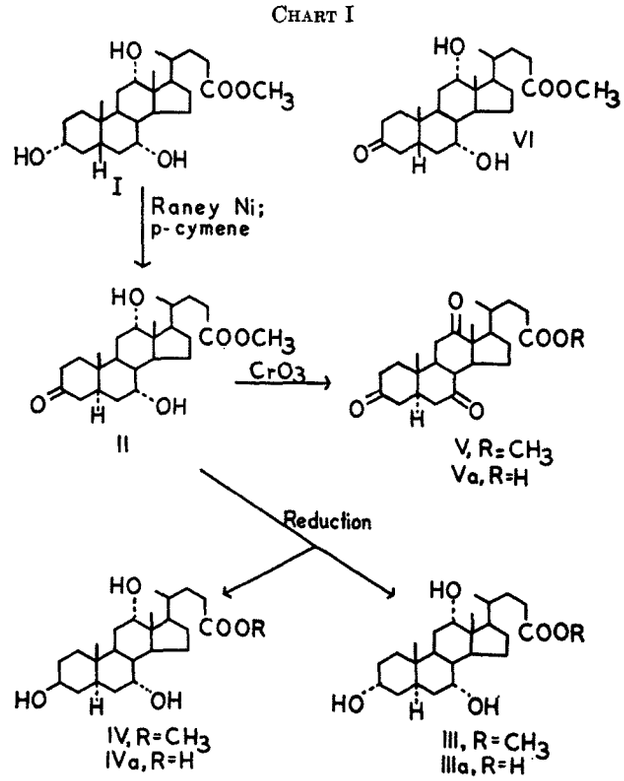
Treatment of methyl cholate with Raney nickel in boiling *p*-cymene afforded a mixture from which methyl 3-keto-7α,12α-dihydroxy-5α-cholanoate could be separated. Catalytic reduction of the latter substance provided allocholic acid as the major product; reduction with sodium borohydride afforded a better yield of the 3β epimer. Supporting evidence for the structures of these substances is provided by mass spectrometry and other physical properties and by chemical degradation. Correlation of the structures of the products of degradation with the parent substances is discussed.

Allocholic acid (3α,7α,12α-trihydroxy-5α-cholanoic acid) has recently been of great interest because of its wide-spread occurrence in a number of sources, *e.g.*, several species of fish,[2,3] snakes,[4] the salamander,[5] penguin,[6] leopard seal,[4] chicken,[7] and several mammals including man.[8,9] We have demonstrated that allocholic acid is a major biliary metabolite[10,11] in the rat after administration of cholestan-3β-ol-4-^{14}C. Continuing studies in this laboratory have shown the need for larger quantities of this material than are normally obtained from natural sources.

Synthetic allocholic acid was first reported by Anderson and Haslewood[12a] as a mixture with cholic acid from catalytic reduction of methyl 3α,12α-diacetoxy-7-keto-Δ^5-cholenoate. Subsequently[12b] they prepared allocholic acid from 3α,7β,12α-trihydroxy-6-keto-5α-cholanoic acid, a substance derived from methyl cholate. However, the latter method involves a number of steps and in our hands[10] provided a low yield of final product. The method described here consists essentially of two steps: (i) the conversion of methyl cholate (I) to methyl 3-keto-7α,12α-dihydroxy-5α-cholanoate (II) and (ii) reduction of II to methyl 3α,7α,12α-trihydroxy-5α-cholanoate (methyl allocholate) (III) followed by alkaline hydrolysis to the free acid. The melting points of the methyl and ethyl esters of allocholic acid prepared by this method agree with those of Haslewood,[4,12b] although the free acid melts at a higher temperature. In view of this difference additional studies are reported which support the assignment of structure of the intermediates and their derivatives.

The first step in this synthesis (see Chart I) was conveniently carried out utilizing the method of Chakravarti, Chakravarti, and Mitra[13] who reported that Raney nickel isomerizes *cis*-A/B to *trans*-A/B steroids

CHART I



(1) (a) This investigation was supported in part by the National Institutes of Health (Grant No. HE-07878 and AM-09992) and by an American Cancer Society Institutional Grant. (b) Presented in part at the 152nd Meeting of the American Chemical Society, New York, N. Y., Sept 1966. (c) For Paper XXII in this series, see H. J. Karavolas, W. H. Elliott, S. L. Hsia, E. A. Doisy, Jr., J. T. Matschiner, S. A. Thayer, and E. A. Doisy, *J. Biol. Chem.*, **240**, 1568 (1965). (d) The following abbreviations have been used: tlc, thin layer chromatography; plc, preparative layer chromatography; glpc, gas–liquid partition chromatography; TMSi, trimethylsilyl derivatives; R_t, retention time relative to methyl deoxycholate (methyl 3α,12α-dihydroxy-5β-cholanoate; absolute time = 29 min); R_t (TMSi), retention time relative to trimethylsilyl derivative of methyl deoxycholate (absolute time = 16.8 min).

(2) G. A. D. Haslewood, *Ann. N. Y. Acad. Sci.*, **90**, 877 (1960).

(3) T. Sasaki, *J. Biochem.* (Tokyo), **60**, 56 (1966).

(4) G. A. D. Haslewood, *Biochem. J.*, **78**, 352 (1961).

(5) K. Amimoto, *J. Biochem.* (Tokyo), **59**, 340 (1966).

(6) I. G. Anderson, G. A. D. Haslewood, and I. D. P. Wootton, *Biochem. J.*, **67**, 323 (1957).

(7) G. A. D. Haslewood in "The Biliary System," W. Taylor, Ed., F. A. Davis Co., Philadelphia, Pa., 1965, pp 106–116.

(8) A. R. Tammer, *Biochem. J.*, **98**, 25p (1966).

(9) P. Eneroth, B. Gordon, and J. Sjövall, *J. Lipid Res.*, **7**, 524 (1966).

(10) See ref given in 1c.

(11) H. J. Karavolas and W. H. Elliott in "The Biliary System," W. Taylor, Ed., F. A. Davis Co., 1965, pp 175–181.

(12) (a) I. G. Anderson and G. A. D. Haslewood, *Biochem. J.*, **74**, 37 (1960). (b) I. G. Anderson and G. A. D. Haslewood, *ibid.*, **85**, 236 (1962), reported mp 229–232°, $[\alpha]^{22}D$ +28 ± 1°, for Va; mp about 225° for III; and mp 239–41°, $[\alpha]^{22}D$ +23 ± 1°, for IIIa.

(13) D. Chakravarti, R. N. Chakravarti, and M. N. Mitra, *Nature*, **193**, 1071 (1962).

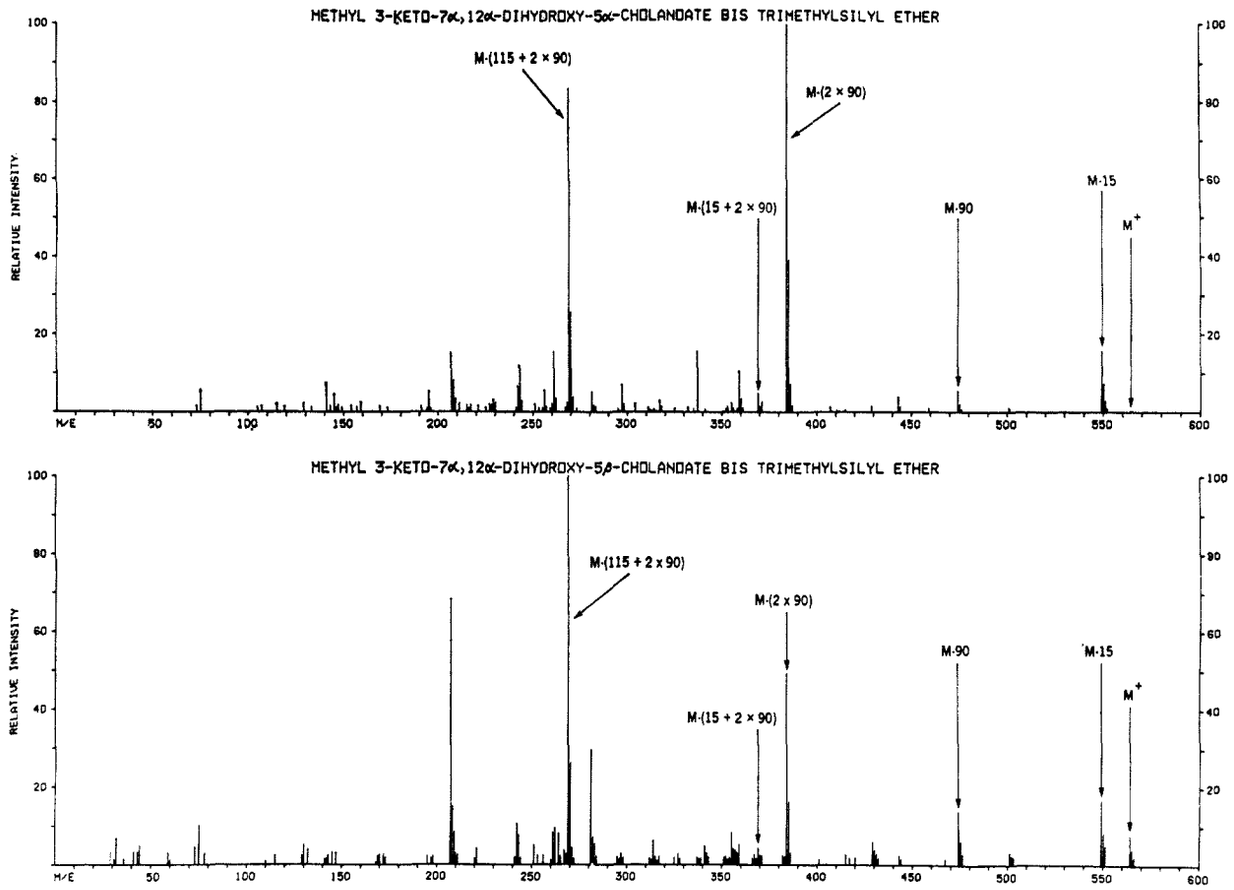


Figure 1.—The molecular ion (M^+) of methyl 3-keto-7α,12α-dihydroxy-5α-cholanoate bistrimethylsilyl ether and of its 5β epimer has m/e 564. Fragments of M − 90 and M − (2 × 90) represent loss of one and two molecules of trimethylsilanol, respectively. The fragment of m/e 269, M − (115 + 2 × 90), represents loss of the side chain at C_{17} (m/e 115) and two molecules of trimethylsilanol.

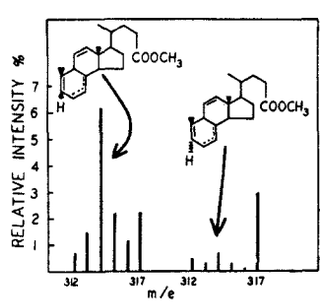


Figure 2.—The fragments of m/e 314 represents loss from M^+ of two molecules of trimethylsilanol and carbons 1, 2, 3, and 4 of ring A.

under certain conditions. For this purpose purified methyl cholate was heated in boiling *p*-cymene for 10 hr in the presence of freshly prepared Raney nickel. After the product was freed from Raney nickel and *p*-cymene, chromatography of the residue on alumina provided three major products from different fractions: A, B, and C. While the products from fractions A and B are under investigation and will be reported separately, the product from fraction C provided II in crystalline form in 12–14% yield after purification by plc on silica gel H. For the second step, II was reduced catalytically with hydrogen to provide a mixture of III and IV, which was conveniently separated by partition chromatography on Celite[14] with a yield of 68% and 15, respectively. Reduction of II with sodium borohydride provided III and IV in yields of 20 and 65%, respectively. Alkaline hydrolysis of III and IV afforded the respective acids, IIIa and IVa.

The structure of the important intermediate II was deduced from its physical and chemical properties. Compound II obviously contained a carbonyl group (ν_{max} 1704 cm^{-1}, formation of an oxime) and two hydroxyl groups (ν_{max} 1078 and 1003 cm^{-1}, formation of a diacetate, formation of a fragment, M − (2 × 90), from the TMSi derivative in mass spectrometry). See Figure 1. On oxidation with chromic acid II gave methyl 3,7,12-triketoallocholanoate (V), which afforded the known 3,7,12-triketo-5α-cholanoic acid[12b] (Va) on hydrolysis with alkali, thus locating the carbonyl and hydroxyl groups at positions 3, 7, and 12.

Confirmation of the 5α configuration of II was obtained by comparison of the mass spectra of the bistrimethylsilyl derivatives of II and its isomer, methyl 3-keto-7α,12α-dihydroxy-5β-cholanoate (VI). The relative intensities of the mass peak (m/e 314), corresponding to the ion remaining after the loss of two molecules of trimethylsilanol and carbons 1, 2, 3, and 4 of ring A from the TMSi derivative of II or VI, were 0.5 and 6.2%, respectively (see Figure 2). Budzikiewicz and Djerassi[15] have reported that cleavage of ring A is favored in 3-keto-5β steroids over the corresponding 5α analog. Additional support for the 5α configuration of II was obtained from the strongly positive Cotton effect.[16]

(14) J. T. Matschiner, T. A. Mahowald, W. H. Elliott, E. A. Doisy, Jr., S. L. Hsia, and E. A. Doisy, *J. Biol. Chem.*, **225**, 771 (1957).

(15) H. Budzikiewicz and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 1430 (1962).

(16) C. Djerassi and W. Closson, *ibid.*, **78**, 3764 (1956).

The difference in chromatographic mobility of II and VI exhibited on thin layer plates as well as in the vapor phase is in agreement with the structural difference at position 5. Table I illustrates the differences in R_f values of methyl esters of some allo (5α) and normal (5β) compounds in three different solvent systems, A, B, and C, containing 50, 20, and 5% of acetone in benzene, respectively.

TABLE I

MOBILITY OF METHYL 5α- AND 5β-CHOLANOATES

Methyl ester of substituted cholanic acid	R_f 5α-	R_f 5β-
Solvent A		
3-Keto-7α,12α-dihydroxy	0.55	0.64
3α,7α,12α-Trihydroxy	0.17	0.23
7-Keto-3α,12α-dihydroxy	0.54	0.51
Solvent B		
3-Keto-7α,12α-dihydroxy	0.065	0.093
7α,12α-Dihydroxy	0.33	0.47
3α,12α-Dihydroxy	0.20	0.15
7-Keto-12α-hydroxy	0.70	0.74
3-Keto-7α-hydroxy	0.42	0.50
3-Keto-12α-hydroxy	0.49	0.40
3,7,12-Triketo	0.57	0.61
Solvent C		
12α-Hydroxy	0.54	0.60
7α-Hydroxy	0.48	0.59

The difference in behavior of 5β and 5α compounds is also marked in glpc as shown by relative retention time (R_t) of those compounds given in Table II.

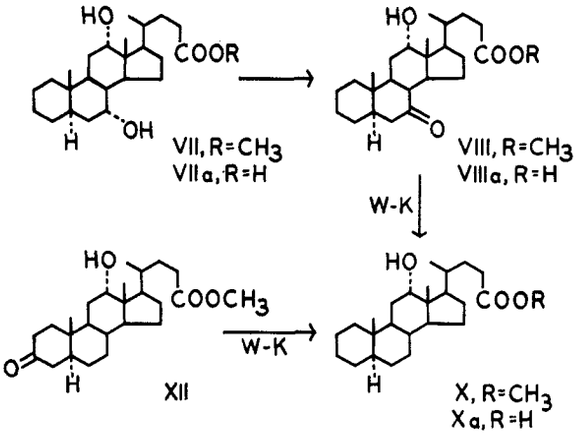
TABLE II

RETENTION TIME OF METHYL 5α- AND 5β-CHOLANOATES

Methyl ester of substituted cholanic acid	R_t 5α-	R_t 5β-
3-Keto-7α,12α-dihydroxy	6.10	4.79
7-Keto-3α,12α-dihydroxy	4.62	3.51
3α,7α,12α-Trihydroxy	2.71	2.40
7α,12α-Dihydroxy	0.91	0.83
3α,12α-Dihydroxy	1.07	1.00

Reduction of II by a modification of the Wolff–Kishner (W–K) reaction[17] followed by methylation with diazomethane afforded a dihydroxy ester (VII) which is different from the known methyl allodeoxycholate[18] and methyl allochenodeoxycholate (methyl 3α,7α-dihydroxy-5α-cholanoate).[19] Thus, the carbonyl group in II was not located at position 7 or 12. Selective oxidation of VII (Chart II) with potassium chromate in the presence of sodium acetate[20] gave methyl 7-keto-12α-hydroxy-5α-cholanoate (VIII) as the major product. Reduction of VIII by the W–K reaction followed by methylation with diazomethane afforded methyl 12α-hydroxy-5α-cholanoate (X), which was found to be identical with a sample derived from the known methyl 3-keto-12α-hydroxy-5α-cholanoate (XII) after W–K reduction and remethylation. These

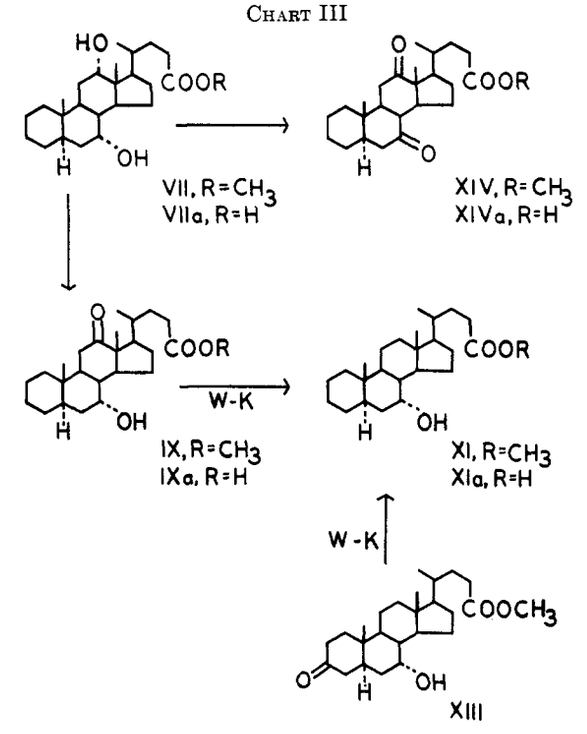
CHART II



results established the 12α orientation of one of the hydroxyl groups of II.

A minor product of selective oxidation of VII, methyl 12-keto-7α-hydroxy-5α-cholanoate (IX) was reduced by the W–K reaction (Chart III). Methylation of the residue with diazomethane afforded a monohydroxy ester (XI), methyl 7α-hydroxy-5α-cholanoate. This material was identical with a sample obtained by the W–K reaction on methyl 3-keto-7α-hydroxy-5α-cholanoate[19] followed by remethylation. Confirmatory evidence for the presence of two hydroxy groups of II at positions 7 and 12 was obtained by oxidation of the acid derived from VII with chromic acid to 7,12-diketo-5α-cholanoic acid[21] (XIVa).

CHART III



To ascertain the configuration of the 7-hydroxyl group in II, VIII was reduced with sodium and 1-propanol by the procedure of Samuelsson[22] for the preparation of 7β-hydroxycholanoic acids. After methylation and purification of the product by plc

(17) Huang-Minlon, *J. Am. Chem. Soc.*, **71**, 3301 (1949).

(18) H. Danielsson, A. Kallner, and J. Sjövall, *J. Biol. Chem.*, **238**, 3846 (1963), reported mp 134–136°, $[\alpha]^{22}D$ +56.8°, for XII; mp 174–176°, $[\alpha]^{22}D$ +35.6°, for XVIII, and mp 137–8°, $[\alpha]^{22}D$ +41.0°, for XIX.

(19) S. A. Ziller, Jr., M. N. Mitra, and W. H. Elliott, *Chem. Ind.* (London), **24**, 999 (1967).

(20) G. A. D. Haslewood, *Biochem. J.*, **37**, 109 (1943).

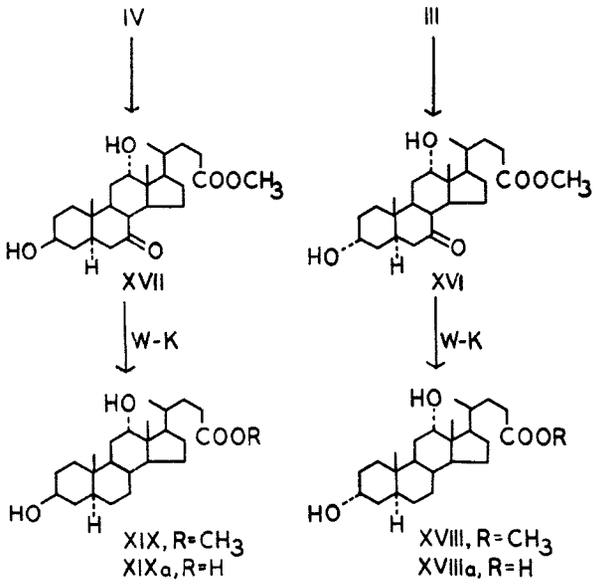
(21) K. Sasaki and T. Mochizuki, *J. Biochem.* (Tokyo), **40**, 317 (1953), reported mp 187.5–189° for XIVa and mp 122–123° for XIV.

(22) B. Samuelsson, *Acta Chem. Scand.*, **14**, 17 (1960).

the major compound (XV) was found to be different from methyl 7α,12α-dihydroxy-5α-cholanoate (VII). The R_f value of XV, molecular rotation, and gas chromatographic mobility are consistent with the equatorial conformation of the 7-hydroxyl group in XV, and thus establish the structure of II as methyl 3-keto-7α,12α-dihydroxy-5α-cholanoate.

To characterize the products of reduction of II (Chart IV) the methyl esters III and IV were selec-

CHART IV



tively oxidized with N-bromosuccinimide according to the procedure of Fieser and Rajagopalan;[23] after purification of the products by plc methyl 7-keto-3α,12α-dihydroxy-5α-cholanoate (XVI) and methyl 7-keto-3β,12α-dihydroxy-5α-cholanoate (XVII) were obtained, respectively. These two compounds differed from each other in mobility in tlc and glpc. Reduction of XVI and XVII by the Wolff–Kishner method provided 3α,12α-dihydroxy-5α-cholanoic acid (XVIIIa) and 3β,12α-dihydroxy-5α-cholanoic acid (XIXa), respectively. These acids and their methyl esters were found to be identical with the corresponding acids and methyl esters derived from methyl 3-keto-12α-hydroxy-5α-cholanoate (XII) by catalytic hydrogenation.[18] These observations support the structures proposed for allocholic acid (IIIa) and its 3β isomer, IVa.

Useful information relative to assignment of structure can frequently be obtained by comparison of the molecular rotation with a value calculated from the contribution of the various functional groups. Table III shows such a comparison of the molecular rotations of various methyl 5α-cholanoates. In general, agreement between calculated and observed values is good. The calculated values are based on a sample of methyl 5α-cholanoate ($[\alpha]^{25}D$ +22° ± 1° (*c* 0.49, in $CHCl_3$)) prepared from XIV and the values tabulated by Klyne.[24]

Table IV shows a similar comparison of the molecular rotation of II and its acetate with the calculated values

TABLE III

MOLECULAR ROTATION OF VARIOUS SUBSTITUTED METHYL 5α-CHOLANOATES

Substituents	MD, deg Calcd	MD, deg Found
None		+82
3α-Hydroxy	+87	+70[a]
3β-Hydroxy	+80	+72[a]
7α-Hydroxy	+23	+8
7β-Hydroxy	+192	+215
12α-Hydroxy	+175	+162
3α,12α-Dihydroxy	+180	+176
3β,12α-Dihydroxy	+173	+143
7α,12α-Dihydroxy	+166	+86
3α,7α,12α-Trihydroxy	+121	+111
3β,7α,12α-Trihydroxy	+114	+98
3-Keto	+153	+127
3-Keto-12α-hydroxy	+246	+209
7-Keto	−141 (+306)[b]	−161
7-Keto-12α-hydroxy	−48 (+398)[b]	−56
7-Keto-3α,12α-dihydroxy	−43 (+408)[b]	−49
7-Keto-3β,12α-dihydroxy	−50 (+401)[b]	−21

[a] Calculated from specific rotations reported by J. Jacques, H. Kagan, and G. Ourisson, "Tables of Selected Constants. 14. Optical Rotatory Power. Ia. Steroids," Pergamon Press Inc., New York, N. Y., 1965, p 377. [b] Calculated values based on W. Klyne, (see ref 24). The contribution cited therein for a 7-keto group in the 5α series is +223. The sign of this value must be in error. D. H. R. Barton and W. Klyne, *Chem. Ind.* (London), 755 (1948), originally published a value of −233 for the 7-keto group in the 5α series.

TABLE IV

MOLECULAR ROTATION OF METHYL 3-KETO-7,12-DIHYDROXY-5α-CHOLANOATES

Substituents on methyl 3-keto-5α-cholanoate	MD, deg Calcd	MD, deg Found
7α,12α-Dihydroxy (II)	+187	+155
7β,12α-Dihydroxy	+356	
7β,12β-Dihydroxy	+313	
7α,12β-Dihydroxy	+144	
7α,12α-Diacetoxy (from II)	+290	+227
7α,12α-Diacetoxy	+641	
7β,12β-Diacetoxy	+437	
7α,12β-Diacetoxy	+86	

for the isomeric substituents at positions 7 and 12. These data clearly indicate that II is methyl 3-keto-7α,12α-dihydroxy-5α-cholanoate and support the evidence previously cited.

Since the completion of these studies, Kallner[25] has published another method of preparation of II and IV based on the conversion of I to VI, desaturation and hydrolysis of VI to 7α,12α-dihydroxy-3-keto-Δ⁴-cholenoic acid, and reduction of the latter to II and IV by lithium in liquid ammonia; III was obtained from II by reduction with trimethyl phosphite and iridium chloride.

Experimental Section

Melting points were determined on a Fisher-Johns apparatus and are corrected. Infrared spectra were recorded on a Model 21 Perkin-Elmer double-beam spectrophotometer as Nujol mulls. Optical rotations were determined in methanol unless otherwise specified in a 5-cm tube using a Rudolph photoelectric polarimeter Model 200-S. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(23) L. F. Fieser and S. Rajagopalan, *J. Am. Chem. Soc.*, **71**, 3935 (1949).
(24) W. Klyne, "The Chemistry of the Steroids," Methuen and Co. Ltd., London, 1960, p 55.
(25) A. Kallner, *Acta Chem. Scand.*, **21**, 322 (1967). He reported mp 152–154°, $[\alpha]^{22}D$ +45°, for II; mp 186–187°, $[\alpha]^{22}D$ +58°, for IV; and mp 225–226°, $[\alpha]^{22}D$ +28°, for III.

Analytical tlc was carried out on 20 × 20 cm plates coated with 0.25 mm of silica gel G (Brinkmann Instruments Inc., Westbury, N. Y.); bile acids and their derivatives were located on the plate after development by spraying with 10% phosphomolybdic acid in 95% ethanol. Three different solvent systems were used for development (Table I). Unless stated otherwise plc was carried out with plates coated with 0.5 mm of silica gel H; bile acids and their derivatives were located on the plate after development by spraying with water.

Gas chromatography was carried out on an F & M Model 402 gas chromatograph with a U-shaped glass column (6 ft × 0.25 in., o.d.) packed with 3% QF-1 on Gas Chrome Q (Applied Science Laboratories, State College, Pa.) under the following conditions: flash heater, 245°; column, 230°; detector, 245°; helium, 40 psi at a flow rate of 40 cc/min. Trimethylsilyl (TMSi) derivatives were prepared according to Makita and Wells[26] and were chromatographed at 215°.

Mass spectrometry was carried out with an LKB Model 9000 single focusing gas chromatograph mass spectrometer (LKB Produkter, Stockholm, Sweden) fitted with molecule separators of the Becker-Ryhage type. A coiled glass column (8 ft × 0.25 in., o.d.) packed with 3% QF-1 on Gas Chrome Q was used for gas chromatography; the following conditions were used: flash heater, 240°; column, 215°; molecule separator, 255°; ion source, 310°; ionizing energy, 70 ev; ionizing current, 60 μA. Spectra were also obtained with the direct probe operated from ambient temperature to 110°.

Raney Nickel Catalyst.—Raney nickel catalyst, W-2, was prepared by the action of sodium hydroxide on Raney catalyst powder (no. 2813) (W. R. Grace and Co., Chattanooga, Tenn.) according to the method of Mozingo.[27]

Action of Raney Nickel on Methyl Cholate.—Dry purified methyl cholate (mp 156–157°; 10.0 g) was mixed with freshly prepared Raney nickel catalyst (*ca.* 25 g) and freshly distilled *p*-cymene (125 ml). The Raney nickel was washed with *p*-cymene just before addition and the entire mixture was quickly heated on an electric mantle in order to remove 10–15 ml of *p*-cymene by distillation The mixture was then heated for 10 hr in refluxing *p*-cymene using an air condenser. The product was filtered and the filtrate was distilled in steam to remove the *p*-cymene. The resultant semisolid was taken up in ether and the ether layer dried. After evaporation of the ether, the solid residue (8.6 g) was chromatographed on neutral Woelm alumina deactivated with 12% water; the column was eluted successively with hexane, mixtures of hexane and benzene, benzene, mixtures of benzene and ethyl acetate, and finally with ethyl acetate. Three major fractions were collected: (A) with hexane–benzene (2:1); (B) with hexane–benzene (1:1); and (C) with benzene and benzene–ethyl acetate (9:1). After evaporation of the solvents the three fractions provided residues of 2.8 g, 3.1 g, and 1.7 g, respectively.

Methyl 3-Keto-7α,12α-dihydroxy-5α-cholanoate (II).—Fraction C was purified by plc with 40% acetone in benzene on ten plates (20 × 40 cm) coated with silica gel H. The lower bands of solids on the plates were removed and extracted with acetone; evaporaton of the solvent afforded 1.2 g of crystalline residue (II). After crystallization from a mixture of acetone and hexane, prismatic needles of II were obtained: mp 156–157°; $[\alpha]^{25}D$ +37.0 ± 0.50 (*c* 1.0); ORD (*c* 0.10),$[\phi]_{435}$ +370°, $[\phi]_{307}$ +2709°, $[\phi]_{270}$ −2041°, $[\phi]_{260}$ −1487°; R_t 6.10; ν_{max} 3390, 1724, 1704, 1178, 1078, 1047, 1003, 897 cm^{-1}.

Anal. Calcd for $C_{25}H_{40}O_5$: C, 71.39; H, 9.59. Found: C, 70.91; H, 9.45.

Acetate of II.—A solution of II (250 mg) in acetic anhydride (4 ml) was cooled and added to a cooled solution of *p*-toluenesulfonic acid (250 mg) in acetic anhydride (1 ml). After an hour the mixture was treated with water and the resulting precipitate was purified by plc. The product crystallized from aqueous methanol (126 mg): mp 132–133°; $[\alpha]^{25}D$ +45.0 ± 0.5° (*c* 0.98 in $CHCl_3$); ν_{max} 1742, 1727, 1718, 1258, 1170, 1028, 855 cm^{-1}.

Anal. Calcd for $C_{29}H_{44}O_7$: C, 69.02; H, 8.79. Found: C, 69.20; H, 8.69.

Oxime of II.—To a solution of 40 mg of II in 5 ml of 95% ethanol was added a solution of 40 mg of hydroxylamine hydrochloride and 40 mg of anhydrous sodium acetate in a few drops of water. The mixture was heated at 60–70° for 0.5 hr. On cooling it gave needles of the oxime of II: mp 205–206°; $[\alpha]^{25}D$ +58.7 ± 0.5° (*c* 0.91).

Anal. Calcd for $C_{25}H_{41}O_5N$: C, 68.93; H, 9.49; N, 3.22. Found: C, 69.09; H, 9.38; N, 3.47.

Oxidation of II.—II (100 mg) was oxidized with chromic anhydride (40 mg) in 2 ml of acetic acid for 2 hr at room temperature. After purification of the oxidized product (81 mg), fine needles of methyl 3,7,12-triketo-5α-cholanoate (V) were obtained from aqueous methanol: mp 198–199°; $[\alpha]^{25}D$ +29.1 ± 1° (*c* 0.98, in $CHCl_3$); ν_{max} 1736, 1706, 1282, 1166, 1096, 811 cm^{-1}.

Anal. Calcd for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71; mol wt, 416. Found: C, 71.97; H, 8.50; mol wt (mass spectrometry), 416.

Hydrolysis of V with 5% methanolic potassium hydroxide provided the corresponding acid,[12b] Va: mp 232–233°; $[\alpha]^{25}D$ +19.8 ± 1° (*c* 0.36).

Catalytic Hydrogenation of II.—Hydrogenation of 400 mg of II was carried out in the presence of Adams catalyst in glacial acetic acid containing a few drops of concentrated hydrochloric acid. The product (398 mg) was purified by acetic acid partition chromatography.[14] Methyl allocholate (III) (285 mg) was eluted with 40% benzene in hexane. After crystallization from a mixture of acetone and hexane, crystalline plates were obtained:[12b,25] mp 225–226°; $[\alpha]^{25}D$ +26.7 ± 1° (*c* 0.84); R_t (see Table II); R_t (TMSi) 1.00; ν_{max} 3401, 3289, 1730, 1206, 1166, 1085, 1031, 1009, 957, 888, 834, 768 cm^{-1}.

Anal. Calcd for $C_{25}H_{42}O_5$: C, 71.05; H, 10.02. Found: C, 71.27; H, 10.26.

Alkaline hydrolysis of III with 5% methanolic potassium hydroxide followed by crystallization of the residue from aqueous acetone afforded long stout needles of allocholic acid[12b] (IIIa): mp 250–251°; $[\alpha]^{25}D$ +27.8 ± 0.1° (*c* 0.75); ν_{max} 3390, 3268, 1704, 1314, 1285, 1255, 1245, 1202, 1124, 1103, 1085, 1033, 1010, 958, 928, 850, 837, 768 cm^{-1}.

Anal. Calcd for $C_{24}H_{40}O_5$: C, 70.55; H, 9.87. Found: C, 70.70, 70.30; H, 9.90, 9.62.

The ethyl ester[4] of allocholic acid was prepared in the usual manner and crystallized from aqueous ethanol: mp 224–225°.

Methyl 3β,7α,12α-trihydroxy-5α-cholanoate (IV) (72 mg) was eluted with 60% benzene in hexane and was crystallized from a mixture of acetone and hexane:[25] mp 198–199°; $[\alpha]^{25}D$ +23.2° (*c* 1.0); R_f 0.23 (solvent system A); R_t 2.78; R_t (TMSi) 1.17; ν_{max} 3509, 3425, 1698, 1295, 1235, 1200, 1188, 1157, 1117, 1087, 1072, 1043, 990, 970, 960, 906, 889, 857, 817, 773, 742 cm^{-1}.

Anal. Calcd for $C_{25}H_{42}O_5$: C, 71.05; H, 10.02. Found: C, 70.71; H, 10.01.

Alkaline hydrolysis of IV afforded 3β,7α,12α-trihydroxy-5α-cholanoic acid (IVa) which provided short fine needles from a mixture of acetone and hexane: mp 241–242°; $[\alpha]^{25}D$ +25.2 ± 1° (*c* 0.68); ν_{max} 3322, 1704, 1307, 1279, 1259, 1233, 1199, 1153, 1105, 1086, 1068, 1033, 989, 956, 942, 920, 892, 858, 816 cm^{-1}.

Anal. Calcd for $C_{24}H_{40}O_5 \cdot CH_3COCH_3$: C, 69.49; H, 9.94. Found: C, 69.54; H, 9.79.

Reduction of II with Sodium Borohydride.—To a solution of 500 mg of II in 35 ml of methanol, powdered sodium borohydride (150 mg) was added and the mixture stood at room temperature for 0.5 hr. After dilution with water and acidification the product was extracted with ether; evaporation of the ether left a residue (470 mg) from which the respective isomers were separated by acetic acid partition chromatography. Crystallization of the respective fractions from acetone–hexane afforded 100 mg of III (mp 225–226°) and 340 mg of IV (mp 198–199°).

Wolff–Kishner Reduction of II.—A mixture of 800 mg of II, 1.5 g of potassium hydroxide in a few drops of water, 15 ml of triethylene glycol, and 3 ml of 85% hydrazine hydrate was heated at 110° for 1.5 hr in a reflux condenser.[17] The condenser was removed and the temperature was raised gradually during 0.5 hr to 195°. The reaction mixture was refluxed for 5 hr at 200–205°, and the solution cooled and poured into an excess of water. After acidification the precipitate was filtered and washed repeatedly with water, and the residue (747 mg) crystallized from aqueous acetone to provide needles of 7α,12α-dihydroxy-5α-cholanoic acid (VIIa): mp 236–237°; $[\alpha]^{25}D$ +22.0 ± 0.50° (*c* 1.0); ν_{max} 3390, 3257, 1718, 1704, 1081, 1031, 886 cm^{-1}.

Anal. Calcd for $C_{24}H_{40}O_4$: C, 73.43; H, 10.27. Found: C, 73.21; H, 10.16.

After methylation with diazomethane and crystallization of the product from a mixture of acetone and hexane, VIIa gave plates of methyl 7α,12α-dihydroxy-5α-cholanoate (VII): mp 170–172°; $[\alpha]^{25}D$ +21.2 ± 0.5° (*c* 0.98); R_t (TMSi) 1.24; ν_{max} 3401, 1736, 1083, 1030, 887 cm^{-1}.

(26) M. Makita and W. W. Wells, *Anal. Biochem.*, **5**, 523 (1963).

(27) R. Mozingo, "Organic Syntheses," Coll. Vol. III, Johh Wiley and Sons, Inc., New York, N. Y., 1955, p 181.

Anal. Calcd for $C_{25}H_{42}O_4$: C, 73.85; H, 10.41; mol wt, 406. Found: C, 73.66; H, 10.46; mol wt (mass spectrometry), 406.

Oxidation of VIIa.—Oxidation of VIIa (50 mg) was carried out with 20 mg of chromic anhydride in 1 ml of acetic acid in the usual manner. Crystallization of the product from aqueous acetone provided fine needles of 7,12-diketo-5α-cholanoic acid[21] (XIVa): mp 194°; $[\alpha]^{25}D$ +11.0 ± 1° (*c* 0.94); R_f 0.67 (isooctane, isopropanol, acetic acid, 60:20:2); ν_{max} 3226, 1736, 1706, 1698, 897, 789 cm^{-1}.

Anal. Calcd for $C_{24}H_{36}O_4$: C, 74.19; H, 9.34. Found: C, 73.98; H, 9.27.

After methylation of XIVa with diazomethane fine needles of methyl 7,12-diketo-5α-cholanoate (XIV) were obtained from a mixture of acetone and hexane:[21] mp 143–144°; $[\alpha]^{25}D$ +9.4 ± 0.5° (*c* 0.99); R_t 1.97 (R_t of methyl 7,12-diketo-5β-cholanoate 1.45); ν_{max} 1742, 1709, 1282, 1166, 997, 951, 872, 770 cm^{-1}.

Anal. Calcd for $C_{25}H_{38}O_4$: C, 74.59; H, 9.52; mol wt, 402. Found: C, 74.45; H, 9.40; mol wt (mass spectrometry), 402.

Selective Oxidation of VII.—To a solution of 264 mg of VII and 528 mg of sodium acetate trihydrate in 2.7 ml of acetic acid was added a solution of 106 mg of potassium chromate in a few drops of water.[20] After 6 hr the solution was diluted with water and the flocculent precipitate was filtered and dried, and the residue (262 mg) separated into three major fractions by plc with 16% acetone in benzene. The most polar fraction (35 mg) was identified as fine needles of unreacted VII: mp 171–172°; $[\alpha]^{25}D$ +21.1°. The least polar fraction (70 mg) yielded needles of XIV from acetone–hexane: mp 144°; $[\alpha]^{25}D$ +9.4°.

The middle fraction was purified by repeated plc with 12% acetone in benzene and provided two fractions. The major fraction with a faster mobility afforded a residue of 120 mg which yielded needles of methyl 7-keto-12α-hydroxy-5α-cholanoate (VIII) after crystallization from a mixture of acetone and hexane: mp 164–165°; $[\alpha]^{25}D$ −13.8 ± 0.5° (*c* 1.01); R_t 1.58 (R_t of methyl 7-keto-12α-hydroxy-5β-cholanoate 1.12); ν_{max} 3640, 3356, 1736, 1692, 1171, 1025, 895 cm^{-1}.

Anal. Calcd for $C_{25}H_{40}O_4$: C, 74.22; H, 9.97; mol wt, 404. Found: C, 74.31; H, 10.20; mol wt (mass spectrometry), 404.

Hydrolysis of VIII with 5% methanolic potassium hydroxide provided the corresponding acid, VIIIa: mp 192–193° (acetone–hexane); $[\alpha]^{25}D$ −19.1 ± 1° (*c* 0.83); ν_{max} 3484, 3322, 1706, 1304, 1280, 1078, 1043, 1025, 959, 940, 917, 853 cm^{-1}.

Anal. Calcd for $C_{24}H_{38}O_4 \cdot {}^1/_2H_2O$: C, 72.14; H, 9.83. Found: C, 72.12; H, 9.78.

The minor fraction with the slower mobility yielded a residue of 22 mg which afforded plates of methyl 12-keto-7α-hydroxy-5α-cholanoate (IX) on crystallization from a mixture of acetone and hexane: mp 127–128°; $[\alpha]^{25}D$ +41.2 ± 1° (*c* 0.29). The infrared spectrum was comparable to that of a sample of this substance prepared from VII by a different procedure as described below. Alkaline hydrolysis of IX provided the acid, IXa: mp 187–188° (acetone–water); $[\alpha]^{25}D$ +53.8° (*c* 0.71); ν_{max} 3322, 1704, 1686, 1250, 1214, 1099, 1089, 1074, 1028, 937, 852, 775, 747 cm^{-1}.

Wolff–Kishner Reduction of VIII.—VIII (60 mg) was reduced in the manner described above with a mixture of 400 mg of potassium hydroxide, 4 ml of triethylene glycol, and 0.6 ml of 85% hydrazine hydrate. The product of reduction (58 mg) provided plates of 12α-hydroxy-5α-cholanoic acid (Xa): mp 199° (acetone–hexane); $[\alpha]^{25}D$ +42.2 ± 0.5° (*c* 1.01); ν_{max} 3378, 1712, 1093, 1030, 935, 884 cm^{-1}.

Anal. Calcd for $C_{24}H_{40}O_3$: C, 76.55; H, 10.71. Found: C, 76.28; H, 10.74.

Methylation of Xa with diazomethane provided needles of methyl 12α-hydroxy-5α-cholanoate (X) from acetone–hexane: mp 118–119°; $[\alpha]^{25}D$ +41.6 ± 1° (*c* 0.97); R_t 0.37; ν_{max} 3436, 1733, 1160, 1094, 1028, 936, 886 cm^{-1}.

Anal. Calcd for $C_{25}H_{42}O_3$: C, 76.87; H, 10.84; mol wt, 390. Found: C, 76.82; H, 10.85; mol wt (mass spectrometry), 390.

Wolff–Kishner Reduction of Methyl 3-Keto-12α-hydroxy-5α-cholanoate (XII).—A reduction of 120 mg of XII[18] (mp 143–144°; $[\alpha]^{25}D$ +51.7° ± 0.50 (*c* 1.01); R_t 2.23) was carried out as described above. The reduction product (112 mg) afforded plates of Xa from a mixture of acetone and hexane: mp 198–199°; $[\alpha]^{25}D$ +42.2°. The infrared spectrum was comparable with that obtained from a sample derived from VIII.

Methyl 12-Keto-7α-hydroxy-5α-cholanoate (IX).—A sample of VII (115 mg) was partially acetylated[28] with a mixture of 5 ml of acetic anhydride and 5 ml of pyridine. After standing for 20 hr the product was poured into water, and the residue (108 mg) was purified by plc with 14% acetone in benzene. Methyl 12α-hydroxy-7α-acetoxy-5α-cholanoate was obtained as a semisolid (73 mg, R_t 1.08) and was oxidized with 25 mg of chromic anhydride. The oxidized product (68 mg) was hydrolyzed with 5% methanolic potassium hydroxide. The acid was crystallized from aqueous acetone as plates of 12-keto-7α-cholanoic acid (IXa): mp 187–188°; $[\alpha]^{25}D$ +53.8 ± 1° (*c* 0.29).

After methylation of IXa with diazomethane, purification by plc, and crystallization from acetone–hexane and aqueous methanol plates of methyl 12-keto-7α-hydroxy-5α-cholanoate (IX) were obtained: mp 128–129° (sintering at 116–117°); $[\alpha]^{25}D$ +41.2 ± 1° (*c* 0.71); R_f 0.67 (solvent system B); R_t 1.4; ν_{max} 3390, 1733, 1698, 1686, 1245, 1209, 1085, 1028, 937, 852, 775, 747 cm^{-1}.

Anal. Calcd for $C_{25}H_{40}O_4$: C, 74.22; H, 9.97; mol wt, 404. Found: C, 73.66; H, 10.07; mol wt (mass spectrometry), 404.

Wolff–Kishner Reduction of IX.—A sample of IX (50 mg) was reduced in the manner described in a mixture of 400 mg of potassium hydroxide, 4 ml of triethylene glycol, and 0.6 ml of 85% hydrazine hydrate. Crystallization of the reduction product from aqueous acetone afforded needles of 7α-hydroxy-5α-cholanoic acid (XIa): mp 155–156°; $[\alpha]^{25}D$ −1.0 ± 0.5° (*c* 1.0); ν_{max} 3279, 1701, 1255, 1236, 1212, 1096, 1029, 1014, 993, 959, 888, 778 cm^{-1}.

Anal. Calcd for $C_{24}H_{40}O_3 \cdot {}^1/_2H_2O$: C, 74.76; H, 10.72. Found: C, 74.83; H, 10.56.

Methylation of XIa with diazomethane followed by crystallization from aqueous methanol afforded plates of methyl 7α-hydroxy-5α-cholanoate (XI): mp 105–106° (the solvated crystals melted at 86–88°); $[\alpha]^{25}D$ +2.0 ± 1° (*c* 0.95); R_t 0.40; ν_{max} 3484, 1718, 1182, 1171, 1072, 1034, 1022, 897 cm^{-1}.

Anal. Calcd for $C_{25}H_{42}O_3$: C, 76.87; H, 10.84; mol wt, 390. Found: C, 76.70; H, 10.72; mol wt (mass spectrometry), 390.

Reduction of VIII with Sodium and *n*-Propanol.—A sample of VIII (20 mg) was refluxed for 3 hr in 1 ml of dry 1-propanol in the presence of 0.1 g of sodium. The solution was cooled and acidified with dilute hydrochloric acid and the precipitate filtered. It was treated with diazomethane and the product was separated into its constituents by plc. The compound (XV, 5.2 mg) with a mobility lower than VII was crystallized from a mixture of acetone and hexane: mp 175–176°; $[\alpha]^{25}D$ +76.7 ± 1° (*c* 0.45); R_f 0.17 (solvent system B); R_t 0.81.

Anal. Calcd for $C_{25}H_{42}O_4$: C, 73.85; H, 10.41. Found: C, 73.99; H, 10.27.

Methyl 7-Keto-3α,12α-dihydroxy-5α-cholanoate (XVI).—A sample of 200 mg of III was oxidized with N-bromosuccinimide (175 mg) in a mixture of 25 ml of dioxane and 4 ml of water at room temperature for 1 hr. The product was diluted with water and extracted with ether; the ethereal extract was washed with sodium bicarbonate solution and water. After evaporation of the ether the residue (199 mg) was shown to contain a number of compounds by tlc. After purification by plc the major product (71 mg) afforded plates of XVI from acetone–hexane: mp 179–180°; $[\alpha]^{25}D$ −11.6 ± 1.5° (*c* 0.76); R_f 0.54 (solvent system A); R_t 4.62; ν_{max} 3425, 3322, 1715, 1689, 1168, 1024, 1010, 899 cm^{-1}.

Anal. Calcd for $C_{25}H_{40}O_5 \cdot CH_3COCH_3$: C, 70.26; H, 9.68. Found: C, 70.62, 70.45; H, 9.70, 9.30.

Wolff–Kishner Reduction of XVI.—Methyl 7-keto-3α,12α-dihydroxy-5α-cholanoate (50 mg) was treated with a mixture of 400 mg of potassium hydroxide, 4 ml of triethylene glycol, and 0.6 ml of 85% hydrazine hydrate for 4 hr at 200°. The crude product (37 mg) was methylated with diazomethane and purified by plc. After crystallization from aqueous methanol 31 mg of methyl 3α,12α-dihydroxy-5α-cholanoate[18,28] were obtained: mp 178–179°; $[\alpha]^{25}D$ +43.3° ± 1° (c 0.48). The infrared spectrum was comparable with that reported by Hofmann and Mosbach.[28]

Methyl 7-Keto-3β,12α-dihydroxy-5α-cholanoate (XVII).—To a solution of 200 mg of sodium acetate trihydrate and 100 mg of methyl 3β,7α,12α-trihydroxy-5α-cholanoate (IV) in 1.5 ml of glacial acetic acid was added 40 mg of potassium chromate in a few drops of water. After 5 hr at room temperature water was added and the solution was extracted with ether. A residue of 98 mg was separated into different fractions by plc with 35% acetone in benzene. The fraction with R_f corresponding to a monoketodihydroxy cholanoate provided a residue of 48 mg which afforded 23 mg of XVII from acetone–hexane as needles: mp 188–189°; $[\alpha]^{25}D$ −5.1 ± 2° (*c* 0.3); R_f 0.49 (solvent system A);

(28) A. F. Hofmann and E. H. Mosbach, *J. Biol. Chem.*, **239**, 2813 (1964), reported mp 178–179°, $[\alpha]D$ +35 ± 1°, for XVIII.

R_t 4.5; ν_{max} 3425, 3344, 1718, 1709, 1300, 1271, 1244, 1195, 1174, 1081, 1031, 1003, 961, 948, 904, 857, 775 cm^{-1}.

Anal. Calcd for $C_{25}H_{40}O_5$: C, 71.39; H, 9.59. Found: C, 71.51; H, 9.68.

Wolff-Kishner Reduction of XVII.—By reduction of 50 mg of methyl 7-keto-3β,12α-dihydroxy-5α-cholanoate in a manner analogous to that described above a residue of 40 mg of 3β,12α-dihydroxy-5α-cholanoic acid was obtained. After methylation and crystallization of the ester from aqueous methanol, needles of methyl 3β,12α-dihydroxy-5α-cholanoate (XIX) were obtained:[18] mp 140–141°; $[\alpha]^{25}D$ +35.2 ± 1° (*c* 0.33); R_f 0.22 (solvent system B); R_t 1.16; ν_{max} 3413, 3344, 1718, 1214, 1043, 1027, 1010, 902 cm^{-1}.

Registry No.—II, 14772-92-0; II acetate, 15111-23-6; II oxime, 15073-84-4; III, 861-83-6; IIIa, 2464-18-8; IV, 14772-93-1; IVa, 15073-87-7; V, 15074-09-6; Va, 15073-88-8; VII, 15206-37-8; VIIa, 15073-89-9; VIII, 15073-90-2; VIIIa, 15073-91-3; IX, 15111-25-8; IXa, 15073-92-4; X, 15073-93-5; Xa, 15152-40-6; XI, 15073-94-6; XIa, 2464-18-8; XIV, 15073-95-7; XIVa, 15073-96-8; XV, 15074-10-9; XVI, 15073-97-9; XVII, 15180-34-4; XIX, 1912-56-7; ethyl ester of allocholic acid, 15073-99-1; methyl 3α,12α-dihydroxy-5α-cholanoate, 1912-65-8; methyl 3α-hydroxy-5α-cholanoate, 15074-01-8; methyl 3β-hydroxy-5α-cholanoate, 15074-02-9; methyl 3-keto-5α-cholanoate, 15074-03-0; methyl 3-keto-12α-hydroxy-5α-cholanoate, 14772-89-5; methyl 7-keto-5α-cholanoate, 15074-05-2; methyl 7β-hydroxy-5α-cholanoate, 15074-06-3; methyl 3-keto-7β,12α-dihydroxy-5α-cholanoate, 15074-07-4; methyl 3-keto-7β,12β-dihydroxy-5α-cholanoate, 15074-08-5; methyl 3-keto-7α,12β-dihydroxy-5α-cholanoate, 15093-95-5; methyl 3-keto-7β,12α-diacetoxy-5α-cholanoate, 15093-96-6; methyl 3-keto-7β,12β-diacetoxy-5α-cholanoate, 15206-38-9; methyl 3-keto-7α,12β-diacetoxy-5α-cholanoate, 15093-97-7; methyl 3-keto-7α,12α-dihydroxy-5α-cholanoate bistrimethylsilyl ether, 15093-98-8; methyl 3-keto-7α,12α-dihydroxy-5α-cholanoate bistrimethylsilyl ether, 15093-99-9.

Acknowledgment.—The expert technical assistance of Miss Mei Mei Mui and Mr. William Sweet is gratefully acknowledged. Cholic acid was generously provided by Dr. Conrad de Fiebre, The Wilson Laboratories, Chicago, Ill.

Synthesis of 1,4,5-Tri-*O*-benzoyl-2,3-dideoxy-D-*erythro*-hex-2-enulopyranose, Derivative of a Ketose-Related Glycal Having an Endocyclic Double Bond

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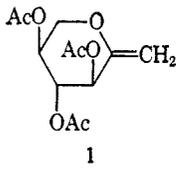
Received June 6, 1967

The benzoylation of 3-*O*-methylsulfonyl-D-fructose affords 1,2,4,5-tetra-*O*-benzoyl-3-*O*-methylsulfonyl-β-D-fructopyranose (**6**) together with an isomer of **6** which is probably one of the anomeric 1,2,4,6-tetra-*O*-benzoyl-3-*O*-methylsulfonyl-D-fructofuranoses (**7**). With hydrogen bromide, the pyranose ester (**6**) gives crystalline 1,4,5-tri-*O*-benzoyl-3-*O*-methylsulfonyl-β-D-fructopyranosyl bromide (**8**) and, with hydrogen chloride, the corresponding chloride (**9**). Treatment of **8** with silver benzoate gives **6**. The basis for the assignment of anomeric configurations to **6**, **8**, and **9** is discussed. Sodium iodide in acetone solution eliminates the bromine atom and the methylsulfonyloxy group from **8**, giving a crystalline unsaturated derivative which, upon hydrogenation over palladium, yields a mixture; from this mixture was isolated 1,5-anhydro-2,3,6-tri-*O*-benzoyl-4-deoxy-D-*lyxo*-hexitol (**11**). The isolation of **11** demonstrates that the unsaturated substance is 1,4,5-tri-*O*-benzoyl-2,3-dideoxy-D-*erythro*-hex-2-enulopyranose (**10**), a derivative of a ketose-related glycal with an endocyclic double bond.

In view of the wealth of synthetic uses which have been found for the ordinary aldopyranose-related glycals, it is somewhat surprising that more attention has not been paid to the ketose-related glycals. Of the latter, apparently only one has been synthesized, 3,4,5-tri-*O*-acetyl-1,2-dideoxy-L-*xylo*-hex-1-enulopyranose (**1**).



1

This substance, recently described by Tokuyama, Tsujino, and Kiyokawa,[1] was prepared through the action of sodium iodide in acetone solution on 3,4,6-tri-*O*-acetyl-1-*O*-*p*-tolylsulfonyl-α-L-sorbopyranosyl bromide, a procedure analogous to that which we have used earlier for the synthesis of furanose-related glycals.[2,3] Two types of ketose-related glycals may be envisaged: those with an exocyclic double bond (exemplified by **1**) and those with an endocyclic double bond (as in **10**, Chart I). We have now turned our attention to the problem of the synthesis of an example of the latter type of glycal. In view of the possibility that the glycal might prove to be a highly reactive substance, the very mild conditions involved in eliminating a bromine atom and a sulfonyloxy group from adjacent carbon atoms recommended the synthetic method used earlier.[1-3] D-Fructose was therefore converted into its 1,2:5,6-di-*O*-isopropylidene derivative (**2**)[4] through the action of acetone in the presence of a strongly acidic ion-exchange resin[5] and the remaining free hydroxyl group (at C-3) esterified with methanesulfonyl chloride to give the known[6] 1,2:4,5-di-*O*-isopropylidene-3-*O*-methylsulfonyl-D-fructopyranose (**3**). The isopropylidene groups were removed from **3** by acidic hydrolysis to give 3-*O*-methylsulfonyl-D-fructose[6] which was not iso-

(1) K. Tokuyama, E. Tsujino, and M. Kiyokawa, *Bull. Chem. Soc. Japan*, **38**, 1344 (1965).

(2) R. K. Ness and H. G. Fletcher, Jr., *J. Org. Chem.*, **28**, 435 (1963).

(3) M. Haga and R. K. Ness, *ibid.*, **30**, 158 (1965).

(4) E. Fischer, *Ber.*, **28**, 1145 (1895).

(5) Ion-exchange resins have been used by J. E. Cadotte, F. Smith, and D. Spriestersbach [*J. Am. Chem. Soc.*, **74**, 1501 (1952)] and by K. Erne [*Acta Chem. Scand.*, **9**, 893 (1955)] for the preparation of **2**; a detailed description of an improved procedure is included in the Experimental Section.

(6) B. Helferich and H. Jochinke, *Ber.*, **73**, 1049 (1940).