81. Ken'ichi Takeda, Taichiro Komeno, and Kikuo Igarashi :

Bile Acids and Steroids. VI. On the Saponification of 7-Oxo-6-bromocholanic Acids.*

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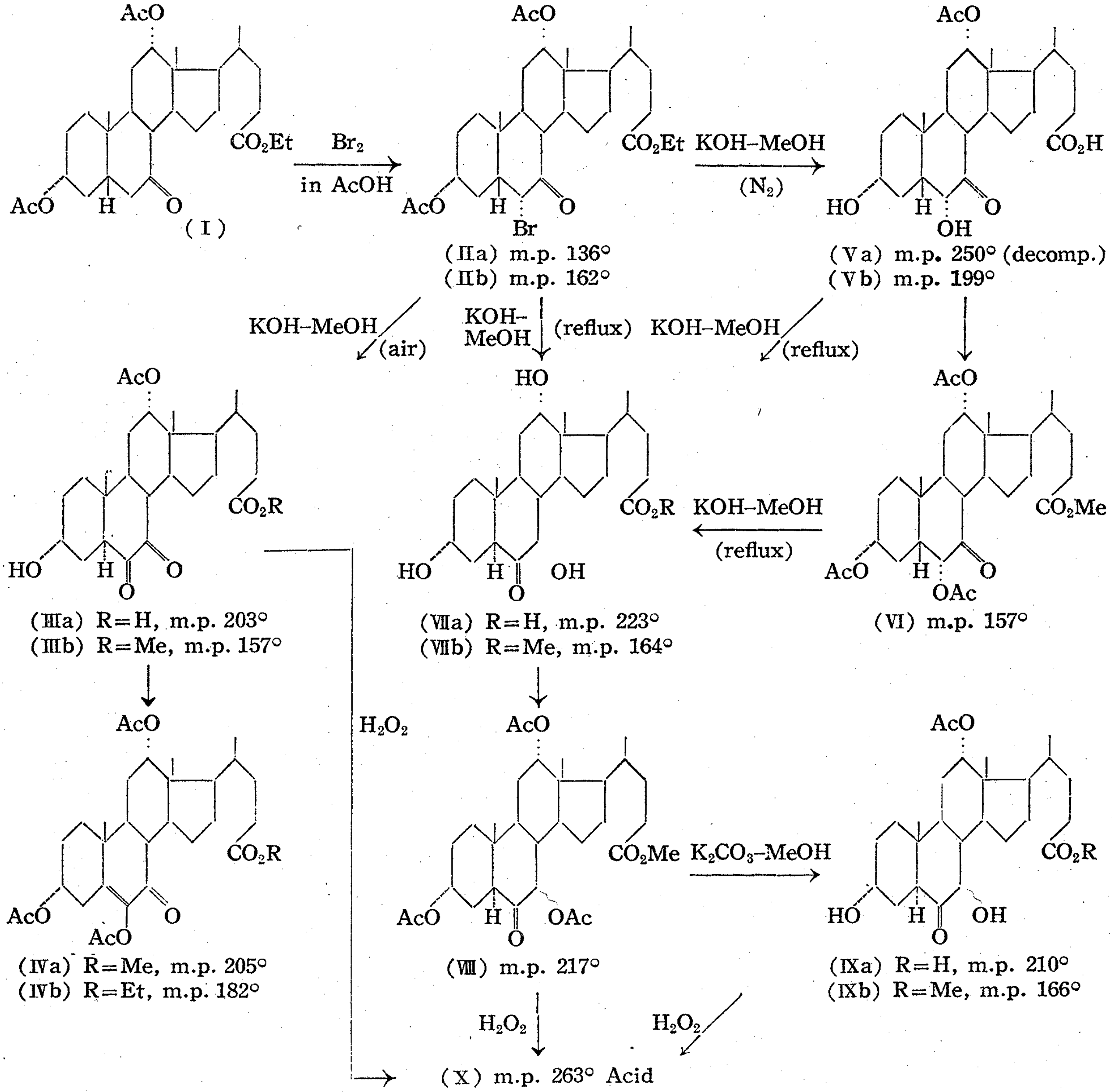
The previous paper[1] in this series indicated that the bromination of ethyl 3α,12α-diacetoxy-7-oxocholanate (I) gave two products, (IIa), m.p. 136°, and (IIb), m.p. 162°, which were both C_6-bromo compounds having 6α-bromine atoms, but not steric isomers caused by configuration of the bromine atoms.

The present paper describes the results of the saponification of these bromo compounds by potassium hydroxide in methanolic solution. Saponification of the bromo compound



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** Imafuku, Amagasaki, Hyogo-ken (武田健一, 米野太一郎, 五十嵐喜九男).

1) K. Takeda, T. Komeno : J. Biochem. (Japan), 41, 385(1954).

(IIa) at a room temperature in methanol solution with 10% potassium hydroxide solution gave the acid, m.p. 203°, showing positive color reaction with ferric chloride. This compound was identical with 6,7-dioxo compound (III) which was obtained previously by Sasaki[2] through oxidation of (I) with selenium dioxide. The ultraviolet absorption maximum of its enol acetate (IV) had shifted about 35 mμ toward shorter wave lengths as compared with the maximum of the parent substance. This result is in full agreement with the case[3] of 2,3- and 3,4-dioxo compounds of steroids. In this case, the result of the reaction reveals that saponification and oxidation had occurred simultaneously and suggests the catalytic action of oxygen in the air.

Therefore, when the bromo compound (IIa or IIb) was saponified in a nitrogen stream, the desired ketol was obtained as expected. Saponification of the bromo compound (IIa or IIb) at room temperature chiefly gave ketol monoacetate (Va), m.p. 250°(decomp.), showing negative color reaction with ferric chloride. In these experiments, the isomer (Vb), m.p. 199°, is occasionally obtained. These two isomers also gave the same triacetate methyl ester, m.p. 157°, but no further examinations were made.

Table I. Comparison of the Acid, m.p. 250°, with That of m.p. 199°

		Acid, m.p. 250°	Acid, m.p. 199°
Optical rotation		$[\alpha]_D^{16}$: +45.9°(MeOH)	$[\alpha]_D^{15.5}$: +46.4°(MeOH)
Ultraviolet absorption		λ_{max}^{EtOH} 277 mμ ($\log \varepsilon = 2.07$)	λ_{max}^{EtOH} 277 mμ ($\log \varepsilon = 2.41$)
Infrared absorption (in Nujol)	-OH	2.89, 3.12 μ	2.90, 2.97 μ
	-C=O	5.73, 5.87 μ	5.79, 5.82 μ
	-C-O-	7.80 μ	7.80 μ

Esterification, followed by acetylation, of the mother liquor of (V) produced a small amount of triacetate methyl ester (VI), m.p. 157°, of (V), monoenol acetate (IV), m.p. 205°, of 6,7-diketone (III), and the compound (VIII), m.p. 217°.

Saponification of the bromo compound (IIa) by refluxing in potassium hydroxide-methanol chiefly gave the ketol (VIIa), m.p. 223°, showing negative color reaction with ferric chloride. By esterification, followed by acetylation, of the mother liquor, triacetate methyl ester (VIII), m.p. 217°, of (VII), identical with that of m.p. 217° obtained by the saponification of (IIa) or (IIb) with cold alkali, was isolated. The ketol-acid (VIIa) was also obtained by the saponification of the previously obtained ketol (Va) or its triacetate methyl ester (VI) in a nitrogen stream with hot alkali, but the reaction in the air produced the diketone (IIIa) as a by-product. Partial saponification of the triacetate methyl ester (VIII) gave the monoacetate acid (IXa), m.p. 210°. The results of the above findings suggest that (VII) might be the 6-oxo compound of the allo-type[4] formed by the rearrangement of the ketol (V), and that the acetyl groups of (VI) and (IXa) might be in 12α-hydroxy groups from these activities. Such rearrangement is observed in the conversion of methyl 3α-acetoxy-12-oxo-11-bromocholanate to Marker-Lawson's acid[5](3α,12β-dihydroxy-11-oxocholanic acid).

When (VIII) or (IXa) was oxidized with alkaline hydrogen peroxide or pervanadinic acid-hydrogen peroxide, there was obtained a tricarboxylic acid, m.p. 263°, in either

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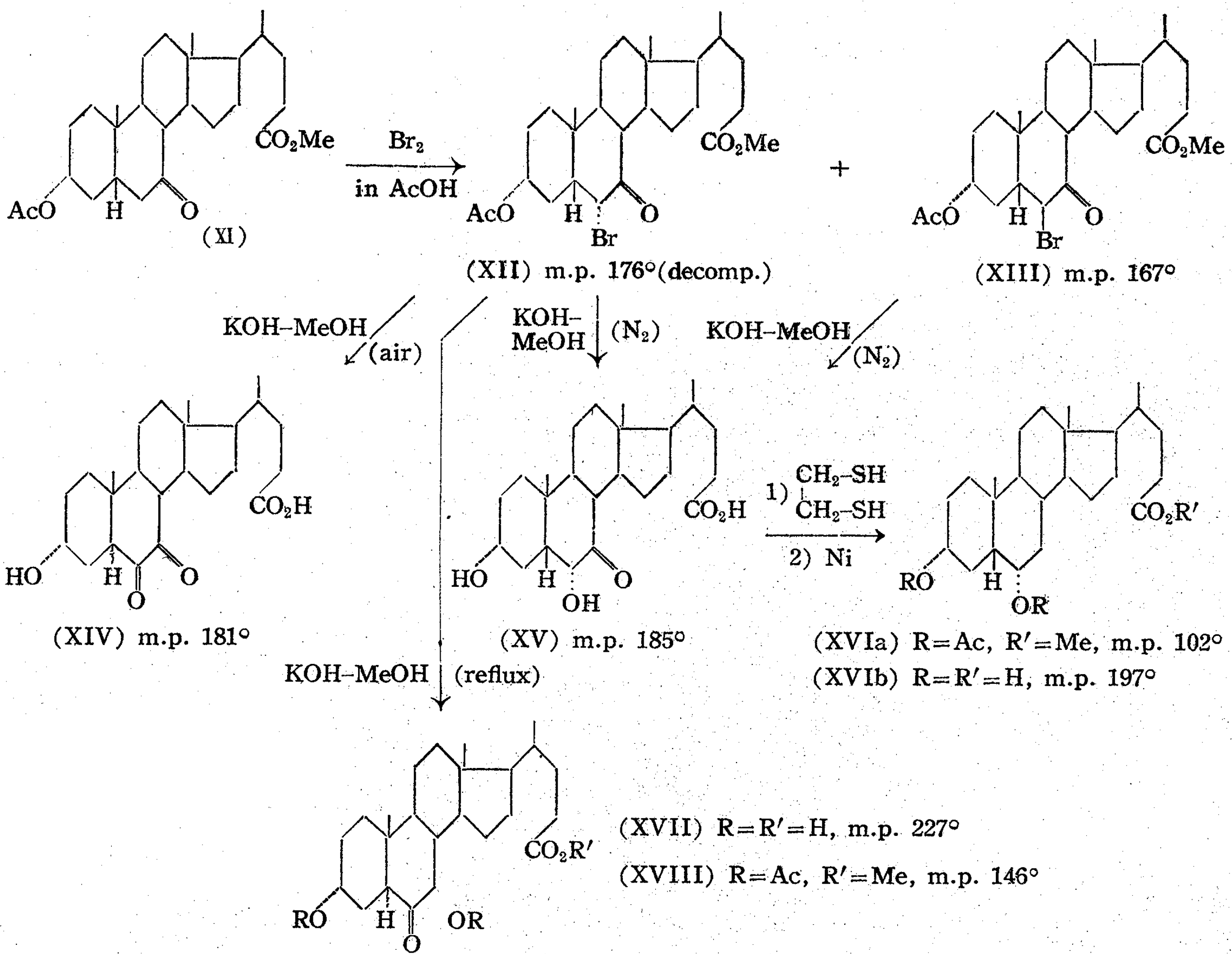
2) K. Sasaki: Presented at the 26th General Meeting of the Biochemical Society of Japan in Sendai, April 27, 1954.

3) L. F. Fieser, M. Fieser: "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Corp., U. S. A., 195(1949).

4) When 7-oxo-6-ol undergoes rearrangement to 6-oxo-7-ol with hot alkali, the ring A:B junction should readily take a *trans*-configuration because of the stabilization resulting from the keto-enolization. See also L. F. Fieser, M. Fieser "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Corp., U. S. A., 112(1949).

5) R. E. Marker, E. J. Lawson: J. Am. Chem. Soc., **60**, 1334(1938); B. B. Longwell, O. Wintersteiner: J. Am. Chem. Soc., **62**, 200(1940). On the configuration of 12β-hydroxyl group, cf. T. F. Gallagher: J. Biol. Chem., **162**, 539(1946).

case, which was identical with that obtained by Sasaki⁶⁾ by the oxidation of the diketone (Ⅲa). From this fact it is assumed that the ring A : B has a *trans*-configuration.



(XI)

(XII) m.p. 176°(decomp.)

(XIII) m.p. 167°

(XIV) m.p. 181°

(XV) m.p. 185°

(XVIa) R=Ac, R′=Me, m.p. 102°

(XVIb) R=R′=H, m.p. 197°

(XVII) R=R′=H, m.p. 227°

(XVIII) R=Ac, R′=Me, m.p. 146°

Similar results were obtained when methyl 3α-acetoxy-6α(or β)-bromo-7-oxocholanate (XII or XIII)⁷⁾ was treated with potassium hydroxide-methanol as (Ⅱ). The saponification in the usual manner gave the diketone (XIV), m.p. 181°, showing positive color reaction with ferric chloride, but its enol acetate has not yet been isolated as crystals.

The reaction with cold alkali in a nitrogen stream produced the ketol (XV), m.p. 185°, showing negative color reaction with ferric chloride, whereas the reaction with hot alkali produced the ketol (XVII), m.p. 227°, showing negative color reaction with ferric chloride. Based on the above results and the fact that the ketol (XVII) is also obtained by the saponification of (XV) with hot alkali, the ketol (XVII) is assumed to be 6-oxo-7-hydroxy compound of the allo-type. In these cases the yield of the products by saponification with hot alkali was always unsatisfactory as compared with the cases with cold alkali.

Unexpectedly, only the same ketol was always obtained by saponification of the 6-bromo compound which was inferred as the 6α- or 6β-bromo compound. As for the configurations of the hydroxyl groups in these ketols, it is assumed that they must be contrary to the original configurations of the bromine atoms as a result of the Walden inversion.

The infrared spectra of these ketols showed that absorption bands (5.87 μ or 5.96 μ)

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6) Further details will be reported by K. Sasaki in subsequent papers.

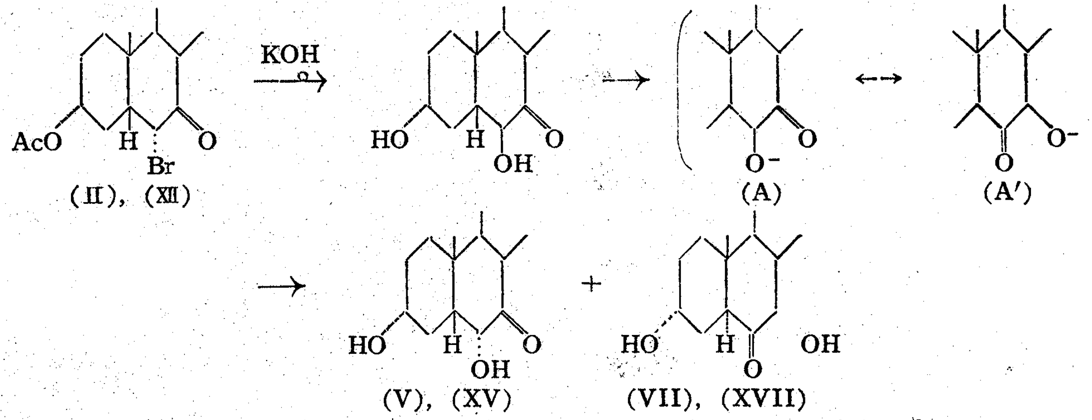
7) K. Takeda, K. Igarashi, T. Komeno : This Bulletin, **2**, 348(1954).

of the ketone in free acids had shifted toward a considerably longer wave lengths, whereas the absorption bands of these acetates had shifted toward a shorter wave lengths as compared with the usual absorption of a ketone (i.e., normal 7-ketone, 5.82 μ, allo-6-ketone, 5.84 μ).

TABLE II. Infrared Spectral Absorption of Ketols (in Nujol)

		Free ketol(μ)		Acyl ketol(μ)	
		-OH	C=O		C=O
Normal Ketol	(Va)	2.89, 3.12	5.73, 5.87	(VI)	5.77
	(XV)	2.86, 3.04 3.68, 3.88	5.88		
Allo Ketol	(VII)	2.82, 3.06 3.66, 3.73, 3.85	5.83, 5.92	(VIII)	5.76, 5.81
	(IXa)	2.82, 3.10 3.66, 3.74, 3.87	5.74, 5.81, 5.94		
	(IXb)	2.86	5.80, 5.87		
	(XVII)	2.83, 3.09 3.67, 3.78, 3.86	5.82, 5.96	(XVIII)	5.78

Accordingly, it may be supposed that the hydroxyl groups in the above ketols are stabilized in the equatorial position through the intermediate (A, A′) as shown in the following chart:



The presence of such an epimerisation may also be inferred in the rearrangement[8] of both 3α,11α-dihydroxy- and 3α,11β-dihydroxy-12-oxocholanic acid to the Marker-Lawson's acid by warm alkali, in which 12β-hydroxy group is equatorial. From the correlation of optical rotations of the above bromo compounds and normal ketols, it has also been inferred that such configurations are correct. The difference between optical rotations of 6-hydroxy-7-oxo compounds and 6α-bromo-7-oxo compounds was far smaller than the difference between optical rotations of ketols and 6β-bromo-7-oxo compound, and showed that no change was produced in the configuration when 6-bromo compound was converted to 6-hydroxy-7-oxo compound.

When 3α,6ξ-dihydroxy-7-oxocholanic acid (XV), having the simplest structure, was converted to a thioketal by its condensation with ethanedithiol and reduced with Raney nickel, α-hyodesoxycholic acid[9] (3α,6α-dihydroxycholanic acid) was obtained as expected. Identification with an authentic sample was made by admixture and infrared spectral determination.

This fact led to the conclusion that the 6-hydroxyl group has α-configuration by epimerization, irrespective of the configurations of the parent bromo compounds, in normal series at least. However, the fact[10] that 11α-bromo-12-oxo- and 11β-bromo-12-oxo-

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[8] T. F. Gallagher: J. Biol. Chem., **162**, 539(1946).

[9] Further details will be reported in the near future.

[10] Recently, 3α,12α-dihydroxy-11-oxocholanic acid was synthesized by G. Baumgartner and Ch. Tamm (Helv. Chim. Acta, **37**, 674(1954)).

cholanic acid were respectively converted to 11β-hydroxy-12-oxo- and 11α-hydroxy-12-oxo-cholanic acid by cold alkali, caused by the Walden inversion, will cause a steric hindrance of the methyl groups at C_{10}- and C_{13}-positions and difficulty in epimerization.

Similarly, it is assumed that the 7-hydroxyl group will have a β-configuration (equatorial) in allo-6-oxo compound, but further experimental studies are being made toward elucidation of the configuration and will be published in the near future.

The authors are grateful to Messrs. Ieki, Miyahara, and Hirai, and to Miss Nakai for elemental analyses and to Messrs. Inaba, Tori, and Matsui for spectral measurements.

Experimental

(1) **3α-Hydroxy-12α-acetoxy-6,7-dioxocholanic Acid (IIIa)**—To 4 g. of ethyl 3α,12α-diacetoxy-6α-bromo-7-oxocholanate (IIa), m.p. 136°, dissolved in 220 cc. EtOH, 4 g. KOH in 40 cc. H_2O was added. After the solution was allowed to stand at room temperature for 3 days, it was evaporated as much as possible *in vacuo*, below 50°, on a steam bath, cooled, added with water, and acidified with HCl. The precipitate was collected, washed well with water, dried, and added with a small amount of AcOEt. The crystals that separated out were collected and recrystallized from dil. MeOH to small cubes, m.p. 201~203° (42.7% yield); λ_{max}^{EtOH} 276 mμ (log ε=4.01). *Anal.* Calcd. for $C_{26}H_{38}O_7$: C, 67.51; H, 8.88. Found : C, 67.39; H, 8.43. This substance turned greenish black with $FeCl_3$.

Methyl Ester (IIIb)—The above acid was esterified with 1% methanolic HCl or CH_2N_2 in ether, and recrystallized from either a little amount of MeOH or dil. MeOH to give silky crystals, m.p. 155~157°. *Anal.* Calcd. for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Found : C, 68.01; H, 8.54.

(2) **Methyl 3α,12α-Diacetoxy-6,7-dioxocholanate Monoenol Acetate (IVa)**—a) The resinous substance (2.5 g.) obtained from the mother liquor of the solution of AcOEt in the above reaction was esterified with CH_2N_2 in ether, warmed for 3 hrs. on a steam bath in 6 cc. of Ac_2O and 6 cc. of pyridine then poured into water, and extracted with ether. The ethereal solution was washed with dil. mineral acid, water, alkali, and water, dried over Na_2SO_4, and evaporated. The residue was crystallized from ether and petroleum ether, and 0.6 g. of crystals, m.p. 173~200°, was obtained. Two recrystallizations from MeOH gave plates, m.p. 203~205°; λ_{max}^{EtOH} 241 mμ (log ε=4.03). *Anal.* Calcd. for $C_{31}H_{44}O_9$: C, 66.41; H, 7.91. Found : C, 66.40; H, 7.92. This substance showed negative color reaction with $FeCl_3$.

b) The crystalline methyl ester (IIIb) was acetylated with Ac_2O and pyridine in the usual manner and recrystallized from MeOH to give plates, m.p. 203~205°. A mixed melting point with the product by the method of (a) showed no depression.

Ethyl 3α,12α-Diacetoxy-6,7-dioxocholanate Monoenol Acetate (IVb)—The acid (IIIa), m.p. 203°, was esterified with EtOH-HCl, acetylated with Ac_2O and pyridine, and recrystallized from MeOH to crystals of m.p. 180~182°. *Anal.* Calcd. for $C_{32}H_{46}O_9$: C, 66.88; H, 8.07. Found : C, 66.43; H, 7.92.

(3) **3α,6α-Dihydroxy-12α-acetoxy-7-oxocholanic Acid (Va)(Vb), Methyl 3α,6α,12α-Triacetoxy-7-oxocholanate (VI), and Methyl 3α,7ξ,12α-Triacetoxy-6-oxoallocholanate (VIII)** a) (Reaction with cold alkali)—To 6 g. of ethyl 3α,12α-diacetoxy-6α-bromo-7-oxocholanate (IIa), dissolved in 360 cc. of MeOH, 12 g. of KOH in 60 cc. of water was added in N_2 stream. The solution was allowed to stand at room temperature for 4 days in a flask substituted with N_2, evaporated *in vacuo* at 35~40° on a steam bath, diluted with water, acidified with HCl, salted out with NaCl, and extracted with AcOEt. Condensation of the extract gave crystals which were recrystallized from dil. MeOH to needles (Vb), m.p. 199° (32% yield); λ_{max}^{EtOH} 277 mμ (log ε=2.41); λ_{max}^{Nujol} 2.90, 2.97, 5.79, 5.82 μ. $[\alpha]_D^{15.5}$: +46.4° (c=0.2674, l=1, MeOH). *Anal.* Calcd. for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68; CH_3CO, 9.27. Found : C, 66.84; H, 8.25; CH_3CO, 9.33.

The resin (3.1 g.) obtained from the mother liquor of AcOEt in the above reaction was esterified with MeOH-HCl, acetylated with Ac_2O-pyridine, and 3.2 g. of a resin was obtained which was crystallized from ether and petroleum ether to 0.3 g. of 6,7-dioxo monoenol acetate (IVa), m.p. 205° (5.3% yield). Further, the residue obtained from the mother liquor was chromatographed as a solution in a benzene-petroleum ether mixture and 1.3 g. of plates (VI), m.p. 155~157°, were obtained from the eluate (23% yield). This substance was also obtained by acetylation of the above acid (Vb), m.p. 199°; $\lambda_{max}^{dioxane}$ 280~284 mμ (log ε=1.55); $[\alpha]_D^{19}$: +80.2° (c=0.5562, l=1, MeOH); λ_{max}^{Nujol} 5.77, 8.08 μ. *Anal.* Calcd. for $C_{31}H_{46}O_9$: C, 66.27; H, 8.24. Found : C, 66.44; H, 8.35.

Recrystallization of the eluate of benzene from MeOH gave 200 mg. of (VIII), m.p. 217° (described later) (3.5% yield).

b) In another run, a mixture of the bromo compound (IIa)(8 g.) dissolved in 480 cc. of MeOH and KOH (16 g.) in 80 cc. of water was allowed to stand overnight at a room temperature in an atmosphere of N_2 and treated as above. There was chiefly obtained 2.9 g. of small cubes (Va), m.p.

250° (decomp.), which also gave (VI), m.p. 157°, by methyl-esterification and acetylation. λ_{max}^{EtOH} 277 mμ(log ε=2.07); λ_{max}^{Nujol} 2.89, 3.12, 5.73, 5.87 μ; $[\alpha]_D^{16}$: +45.9°(c=0.2769, l=1, MeOH). *Anal.* Calcd. for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68; CH_3CO, 9.27. Found: C, 66.86; H, 8.66; CH_3CO, 9.35.

Further the treatment of the mother liquor as described in (a) gave 500 mg. of (VI), m.p. 157°, and 200 mg. of (VIII), m.p. 217°, which were identified by admixture with the samples obtained above.

c) A mixture of ethyl 3α,12α-diacetoxy-6α-bromo-7-oxocholanate (IIb), m.p. 162°, (1.2 g.) dissolved in 72 cc. of MeOH and KOH (2.4 g.) in 12 cc. of water was allowed to stand at room temperature for 5 days in nitrogen atmosphere and treated as above. As the free acid was not obtained as crystals, it was esterified and acetylated in the usual manner. From the ethereal solution was obtained 170 mg. of 6,7-dioxo monoenol acetate (IVa), m.p. 205°, which was identified by admixture with an authentic sample. Further, by the chromatographic purification of the resin obtained from the mother liquor, 240 mg. of (VI), m.p. 157°, and 30 mg. of (VIII), m.p. 217°, were obtained, which were identified by admixture with the samples prepared by the above method.

(4) **3α,7ξ,12α-Trihydroxy-6-oxoallocholanic Acid (VIIa), Methyl 3α,6α,12α-Triacetoxy-7-oxocholanate (VI), and Methyl 3α,7ξ,12α-Triacetoxy-6-oxoallocholanate (VIII)** (Reaction with hot alkali)—a) A mixture of ethyl 3α,12α-diacetoxy-6α-bromo-7-oxocholanate (IIa)(4 g.) dissolved in 70 cc. of MeOH and KOH (8 g.) in 10 cc. of water was refluxed for 3 hours on a steam bath in N_2 stream, evaporated *in vacuo*, added with water, acidified with dilute HCl, and extracted with AcOEt. After the condensation of the extract, recrystallization from methanol gave 0.6 g. of needles (VIIa), m.p. 221~223°. λ_{max}^{Nujol} 2.82, 3.06, 3.66, 3.73, 3.85, 5.83, 5.92 μ. $[\alpha]_D^{17}$: +31.4°(c=0.3245, l=1, MeOH). *Anal.* Calcd. for $C_{24}H_{38}O_6$: C, 68.22; H, 9.06. Found: C, 68.51; H, 9.47.

Further, 2.7 g. of the resin obtained from the mother liquor was esterified with H_2SO_4-MeOH and acetylated with Ac_2O-pyridine. By the chromatographic separation, 400 mg. of (VI), m.p. 155~157°, was obtained from benzene-petroleum ether eluate and a little amount of (VIII), m.p. 215~217°, from the benzene eluate. The latter substance was also obtained by methyl-esterification, followed by acetylation, of the above acid (VIIa), m.p. 221~223°. $\lambda_{max}^{dioxane}$ 280~284 mμ(log ε=1.48); λ_{max}^{Nujol} 5.76, 5.81 μ; $[\alpha]_D^{19}$: +82.8°(c=0.2633, l=1, MeOH). *Anal.* Calcd. for $C_{31}H_{46}O_9$: C, 66.27; H, 8.24. Found: C, 66.14; H, 8.56.

The methyl ester (VIIb) was obtained by esterification of the above free acid (VIIa) and recrystallized from dilute MeOH to plates, m.p. 162~163.5°. *Anal.* Calcd. for $C_{25}H_{40}O_6$: C, 68.78; H, 9.23. Found: C, 69.15; H, 9.12.

b) A mixture of methyl 3α,6α,12α-triacetoxy-7-oxocholanate (300 mg.) and KOH (300 mg.) dissolved in 4 cc. of MeOH and a little amount of water was refluxed for 2.5 hours on a steam bath, and treated as above. From the EtOAc solution 100 mg. of free allo-acid (VIIa), m.p. 221~223°, crystallized out, which was converted to the methyl ester triacetate (VIII), m.p. 215~217°, by methyl-esterification and acetylation. These substances were identified by admixture.

When the mother liquor was methyl-esterified and acetylated, 50 mg. of 6,7-dioxo monoenol acetate (IVa) was obtained, which was identified by admixture.

(5) **3α,7ξ-Dihydroxy-12α-acetoxy-6-oxoallocholanic Acid (IXa) and its Methyl Ester (IXb)**—A mixture of 410 mg. of methyl 3α,7ξ,12α-triacetoxy-6-oxoallocholanate (VIII) and 180 mg. of K_2CO_3 dissolved in 8 cc. of MeOH and 1 cc. of water was refluxed on a steam bath for 6 hrs. and treated in the usual manner. Recrystallization from dil. MeOH gave 3α,7ξ-dihydroxy-12α-acetoxy-6-oxoallocholanic acid (IXa), m.p. 210°, and its admixture with 3α,6ξ-dihydroxy-12α-acetoxy-7-oxocholanic acid (Vb) showed depression. λ_{max}^{Nujol} 2.82, 3.10, 3.66, 3.74, 3.87, 5.74, 5.81, 5.94 μ. *Anal.* Calcd. for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68. Found: C, 67.43; H, 8.54.

The methyl ester (IXb) of the acid (IXa) was obtained by esterification with CH_2N_2 in ether and recrystallized from ether to prisms, m.p. 164~166°. λ_{max}^{Nujol} 2.86, 5.80, 5.87 μ. *Anal.* Calcd. for $C_{27}H_{42}O_7$: C, 67.76; H, 8.84; CH_3CO, 9.00. Found: C, 67.39; H, 8.99; CH_3CO, 9.39.

(6) **Acid (XI), m.p. 261~263°**—a) A mixture of methyl 3α,7ξ,12α-triacetoxy-6-oxoallocholanate (VIII)(500 mg.) and KOH (500 mg.) in 40 cc. of MeOH, added with 1 cc. of 30% H_2O_2, was allowed to stand overnight at room temperature and treated in the usual manner. As the free acid obtained was resinous, it was esterified with CH_2N_2 in ether and acetylated with Ac_2O-pyridine. After 250 mg. of unchanged triacetate methyl ester (VIII) was removed, the mother liquor was chromatographed and there was obtained 100 mg. of crystals, m.p. 130~140°, from the benzene-petroleum ether eluate. As it was difficult to purify, the substance was saponified with K_2CO_3 in MeOH, and recrystallized from EtOH to needles, m.p. 261~263°, which showed no depression on admixture with the sample prepared by Sasaki by the oxidation of 6,7-diketo compound (IIIa).

b) A mixture of 3α,7ξ-dihydroxy-12α-acetoxy-6-oxoallocholanic acid (300 mg.) dissolved in 20 cc. of MeOH, a proper amount of pervanadinic acid, and 2 cc. of 30% H_2O_2 was warmed on a steam bath for 8 hrs. After H_2O_2 was consumed, further 2 cc. of H_2O_2 was added, warmed, and the treatment as above also gave the same acid, m.p. 261~263°, as in a).

(7) **3α-Hydroxy-6,7-dioxocholanic Acid (XIV)**—A mixture of methyl 3α-acetoxy-6α-bromo-7-

oxocholanate (XII)(2 g.) dissolved in 110 cc. of dioxane and MeOH (60 cc.) and KOH (4 g.) in 30 cc. of water was allowed to stand at room temperature for 2 days, evaporated *in vacuo*, and treated in the usual manner. There was obtained 500 mg. of crystals, m.p. 179~181°, which turned green black with $FeCl_3$. λ_{max}^{EtOH} 276 mμ(log ε=3.90); λ_{max}^{Nujol} 2.89, 2.99, 5.88, 5.98, 6.07 μ. $[\alpha]_D^{15.5}$: −63.1° (c=0.28865, l=1, MeOH). *Anal.* Calcd. for $C_{24}H_{36}O_5$: C, 71.25; H, 8.97. Found: C, 70.98; H, 9.18.

The enol acetate of this substance was not obtained as crystals. λ_{max}^{EtOH} 240 mμ(log ε=3.96), 282 (3.72).

(8) **3α,6α-Dihydroxy-7-oxocholanic Acid (XV)**—A mixture of methyl 3α-acetoxy-6α-bromo-7-oxocholanate (XII)(1 g.) and KOH (2 g.) in 10 cc. of water and 60 cc. of MeOH was allowed to stand at room temperature for 2 days with occasional shaking, dissolved completely, then allowed to stand overnight. The solvent was evaporated in N_2 stream under a reduced pressure, added with water, acidified with HCl, and extracted with ether. Crystallization of ethereal residue gave crystals, m.p. 182~184°, and recrystallization from MeOH and EtOAc gave prisms, m.p. 183~185°, which showed no color reaction with $FeCl_3$. λ_{max}^{EtOH} 279 mμ(log ε=1.77); λ_{max}^{Nujol} 2.86, 3.04, 3.68, 3.88, 5.88 μ; $[\alpha]_D^{15}$: −62.5°(c=0.33297, l=1, MeOH). *Anal.* Calcd. for $C_{24}H_{38}O_5$: C, 70.90; H, 9.42. Found: C, 70.86; H, 9.40.

The methyl ester diacetate of this substance was not obtained as crystals.

b) A mixture of methyl 3α-acetoxy-6β-bromo-7-oxocholanate (XIII)(500 mg.) and KOH (1 g.) in 30 cc. of MeOH and 5 cc. of water was worked up as above. The crystals, m.p. 160~180°(yield, 400 mg.), obtained were recrystallized from MeOH and AcOEt to prisms, m.p. 181~183°, which was identified with (XV) prepared by method (a) by admixture and infrared absorption spectra. $[\alpha]_D^{15}$: −62.6°(c=0.35127, l=1, MeOH) was in good agreement with that of (XV).

(9) **3α,7ξ-Dihydroxy-6-oxoallocholanic Acid (XVII) and its Methyl Ester Diacetate (XVIII)**—a) A mixture of methyl 3α-acetoxy-6α-bromo-7-oxocholanate (XII)(3 g.) and KOH (7.5 g.) in 70 cc. of MeOH and 10 cc. of water was refluxed on a steam bath for 3 hrs. in N_2 stream, evaporated *in vacuo*, acidified with HCl, and extracted with EtOAc. By the condensation of the extract, there was obtained 500 mg. of needles, m.p. 225°(decomp.), which was recrystallized from EtOH to needles, (XVII), m.p. 227°(decomp.). This substance showed no color reaction with $FeCl_3$. λ_{max}^{EtOH} 279 mμ (log ε=1.76); λ_{max}^{Nujol} 2.83, 3.09, 3.67, 3.78, 3.86, 5.82, 5.96 μ. $[\alpha]_D^{15}$: +46.4°(c=0.24033, l=1, MeOH). *Anal.* Calcd. for $C_{24}H_{38}O_5$: C, 70.90; H, 9.42. Found: C, 70.58; H, 9.44.

The mother liquor gave further impure 3α,6α-dihydroxy-7-oxocholanic acid (XV), m.p. 160~175°. By esterification with methanolic HCl and acetylation with Ac_2O-pyridine, methyl 3α,7ξ-diacetoxy-6-oxoallocholanate (XVIII) was obtained as crystals, which were recrystallized from MeOH to needles (XVIII), m.p. 144~146°. *Anal.* Calcd. for $C_{29}H_{44}O_7$: C, 69.02; H, 8.79. Found: C, 69.23; H, 8.88.

b) A mixture of 3α,6α-dihydroxy-7-oxocholanic acid (XV)(300 mg.) and KOH (800 mg.) in 10 cc. of MeOH and 1 cc. of water was refluxed on a steam bath for 3 hrs. in N_2 stream. Treatment as above gave 100 mg. of the free acid, m.p. 227° (decomp.), which was converted to the methyl ester diacetate, m.p. 144~146°. The melting points of the products were not depressed by admixture with (XVII) and (XVIII), respectively.

Summary

While saponification of the two isomers of ethyl 3α,12α-diacetoxy-6α-bromo-7-oxocholanate with cold alkali gave the α-diketone and α-ketol, saponification with hot alkali gave another α-ketol, which was inferred as allo-6-oxo-7-ol from its degradation product. Similarly, saponification of methyl 3α-acetoxy-6α-bromo-7-oxocholanate with cold alkali gave α-diketone and α-ketol, and the 6β-bromo compound also gave the same ketol, which was identified as having 6α-hydroxyl group by conversion to α-hyodesoxycholic acid. Saponification with hot alkali also gave another α-ketol, which was inferred as allo-6-oxo-7-ol by analogy with the above-mentioned α-ketol.

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