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58. Hiromu Mori, Kiyoshi Tsuneda, Kenyu Shibata, and Masanobu Sawai: Synthesis of Ecdysone. II.*2 Synthesis of and Stereochemistry of 2β,3β-Dihydroxycholestan-6-ones and Their Derivatives.

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2β,3β-Dihydroxycholestan-6-ones and their derivatives were prepared and their stereochemistry was studied. In 2β,3β-dihydroxy- or 2β,3β-diacetoxycholestan-6-ones, equilibrium mixture consisted of 5α- and 5β-compound at the ratio of 3:2. On the other hand, 5α-compound was found to be exclusively stable in 2β,3β-dihydroxycholestan-6-one acetonides.

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In prior to synthesis of ecdysone, it is desirable to prepare 2β,3β-dihydroxy-6-oxo compounds which have a partial structure of ecdysone and to investigate their stereochemistry. Generally, 5α-compound is exclusively more stable than 5β-compound in 6-oxo steroids.[1] In the case of 2β,3β-dihydroxy-6-oxo series, however, this relationship is not immediately accepted, because 1,3-diaxial non-bonded interaction between 2β-hydroxy and 19-methyl group must be considered and this interaction is surely an unstabilizing factor of 5α-compound. In fact, it is reported as a similar case that

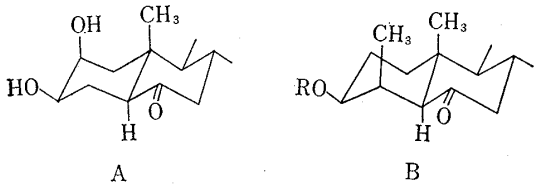

Fig. 1.

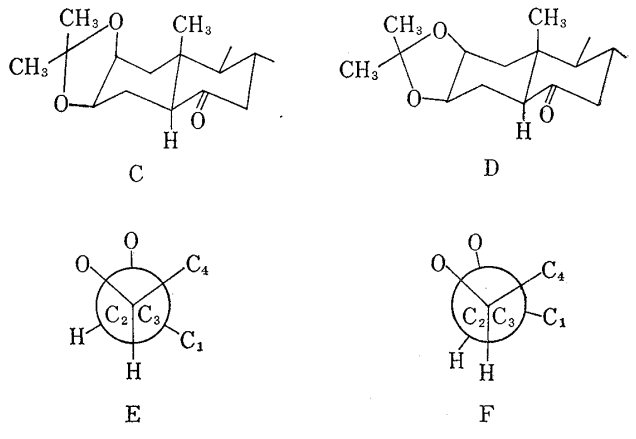

Fig. 2.

3β-hydroxy- or 3β-acetoxy-4β-methyl-5α-cholestan-6-one is isomerized to the corresponding 5β-compound by acid or alkali.[2] If 5α-compound can be isomerized to 5β-compound in 2β,3β-dihydroxy-6-oxo steroids at least partly, ecdysone would be prepared from A/B *trans*-2β,3β-dihydroxy-6-oxo compound. The object of this paper is to elucidate the stereochemical relationship in 2β,3β-dihydroxy-6-oxo and related compounds.

As a starting material to prepare 2β,3β-dihydroxy-6-oxo steroids was selected 6β-hydroxy-5α-cholestan-3-one (IV),[3] a novel preparative method of which was

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*2 Part I: This Bulletin, **15**, 460 (1967).

1) R. B. Turner: J. Am. Chem. Soc., **74**, 5362 (1952); H. B. Henbest, T. I. Wrigley: J. Chem. Soc., **1957**, 4569.

2) H. Mori: This Bulletin, **12**, 1224 (1964).

3) C. W. Shoppee, G. H. R. Summers: J. Chem. Soc., **1952**, 3361.

developed. Marker and Rohrmann[4] have reported that 5α-cholestane-3,6-dione (I) is reacted with *o*-phenylenediamine to give 3-azine (II). 3-Azine (II) prepared by their description was reduced with sodium borohydride to 6β-hydroxy-3-azine (III), which on hydrolysis with hydrochloric acid yielded 6β-hydroxy-3-one (IV) with satisfactory yield.

The preparation of 2β,3β-dihydroxy compound was made by the method reported in the preceeding paper.[5] 6β-Hydroxy-3-one (IV) was autoxidized in the presence of potassium *t*-butoxide in *t*-butanol[6] to an enol mixture of 6β-hydroxy-2,3-dione (V), and without isolation of this enol mixture in pure state, V was reduced with sodium borohydride to afford a mixture of 2,3,6β-triols (VI). In order to isolate the desired 2β,3β,6β-triol, the mixture was treated with acetone containing hydrogen chloride, and chromatographed on Florisil. The elution with ether gave 2β,3β,6β-triol 2,3-acetonide (VII) in 32~37% yield (based on IV), the evidence of the structure being described below.

Jones oxidation of triol acetonide (VII) afforded 2β,3β-dihydroxy-6-one acetonide (VIII). That the isomerization at C-5 in this reaction did not occur was readily shown from the fact that the reduction of VIII with sodium borohydride recovered VII. 2β,3β-Dihydroxy-6-one acetonide (VIII) was hydrolyzed with 10% phosphoric acid to afford 2β,3β-dihydroxy-6-one (IXa), 5α-configuraton of which could be shown by the following observation. The hydrolysis of 2β,3β,6β-triol 2,3-acetonide (VII) gave 2β,3β,6β-triol (X), which was identical with the compound derived by the reduction of 2β,3β-dihydroxy-6-one (IXa) with sodium borohydride.

2β,3β-Dihydroxy-6-one acetonide (VIII) was also obtained by another route from 3β-hydroxy-5α-cholestan-6-one (XI).[7] The protection of 6-oxo group was carried out by transformation into ethylene ketal (XII) by usual manner and XII was introduced to 3,6-dione 6-ethylene ketal (XIII)[8] by Oppenauer oxidation or Jones oxidation under mild condition. The autoxidation of 3,6-dione 6-ethylene ketal (XIII) followed by sodium borohydride reduction as the manner described above gave a mixture of 2,3-dihydroxy-6-one ethylene ketal (XV). The mixture was treated with acetone containing phosphomolybdic acid to give 2β,3β-dihydroxy-6-one acetonide (VIII), which is identical with the compound derived by the other route. The yield of VIII was 40~47% based on 3,6-dione 6-ethylene ketal (XIII). It is of interest to point out that this reaction consists of acetonide formation and hydrolysis of ethylene ketal. The specific character of acetonide formation catalyzed by phosphomolybdic acid will be described below.

The evidence that a series of compounds described above have 2β,3β-dihydroxy structures or its derivatives will be shown. Acetylation of 2β,3β-dihydroxy-6-one (IXa) with acetic anhydride at reflux temperature*3 yielded 2β,3β-diacetoxy-6-one (IXb), which on thioketalization with ethanedithiol catalyzed by boron trifluoride etherate gave the thioethylene ketal (XVI). Reductive desulfurization of XVI with W-2 Raney nickel led to the known 5α-cholestane-2β,3β-diol diacetate (XVII),[9] which was identical with an authentic sample in all respects. Thus, unambiguous proof of the structures of a series of compounds described above was given.

*3 When treated with acetic anhydride and pyridine at room temperature, acetylation was not complete.

4) R. E. Marker, E. Rohrmann : J. Am. Chem. Soc., **61**, 946 (1939).
5) H. Mori, K. Shibata, K. Tsuneda, M. Sawai : This Bulletin, **15**, 460 (1967).
6) D. H. R. Barton, S. K. Pradhan, S. Sternhell, J. F. Templeton : J. Chem. Soc., **1961**, 255; D. Arigoni, D. H. R. Barton, E. J. Corey, O. Jeger : Experientia, **16**, 41 (1960).
7) D. H. R. Barton, J. D. Cox : J. Chem. Soc., **1948**, 783.
8) This compound (XIII) was recently prepared by C. Djerassi and others (J. Am. Chem. Soc., **87**, 4892 (1965)).
9) H. B. Henbest, M. Smith : J. Chem. Soc., **1957**, 926; C. W. Shoppee, D. N. Jones, G. H. R. Summers: *Ibid.*, **1957**, 3100.

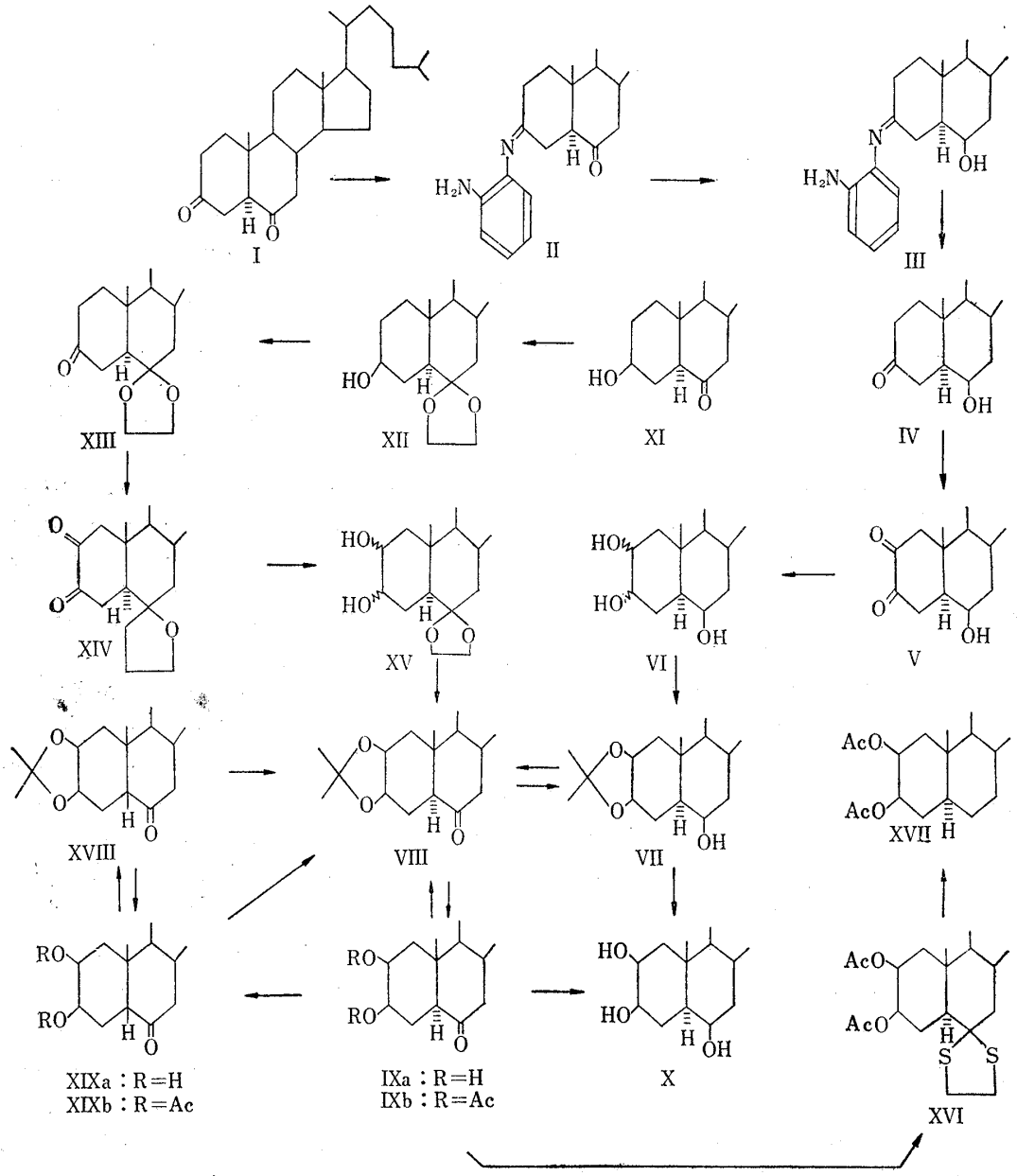

Chart 1.

Treatment of 2β,3β-dihydroxy-5α-cholestan-6-one (Ⅸa) with acid or alkali gave an equilibrium mixture. Although it is evident from infrared spectrum that Ⅸa was isomerized partly, the isolation of 5β-compound was very difficult in our hands. Accordingly, the equilibrium mixture was treated with acetone and phosphomolybdic acid at room temperature to afford an acetonide mixture. The separation of isomers was easily accomplished by combination of recrystallization and chromatography, Ⅷ and XVⅢ being isolated in about the same amount. The acetonide of 5β-compound, XVⅢ thus obtained was hydrolyzed by 10% phosphoric acid in ethanol yielded pure 2β,3β-dihydroxy-5β-cholestan-6-one (XIXa) in good yield, and diacetate (XIXb) was obtained by acetylation. When XIXa and Ⅸa were treated with acetone containing phosphomolybdic acid at room temperature, acetonide formation was rapidly occurred (only 20~30 minutes standing was fully enough for completion of acetonide formation) and the corresponding acetonides, XVⅢ and Ⅷ were obtained almost quantitatively without any epimerization at C-5. On the other hand, treatment of XIXa or Ⅸa with

acetone containing hydrogen chloride led to the same acetonide (Ⅷ). It should be noted that in spite of very weak acidity phosphomolybdic acid is very effective catalyst for acetonide formation and no epimerization at asymmetric carbon center adjacent to carbonyl group occurs.

As it was found that acetonide formation reaction catalyzed by phosphomolybdic acid is not accompanied by epimerization at C-5, the stability of 5α- and 5β-compound was assumed to be nearly equal from the observation described above. In order to elucidate this problem more exactly, optical rotation changes of Ⅸa and XIXa were measured in chloroform containing 0.2% of hydrogen chloride. Optical rotations were changed and after 30 minutes the constant rotations were obtained at $-23.5°$ in both cases (Table I). The calculation from this value shows that the equilibrium mixture consists of 5α- and 5β-compound at the radio of 3:2.*4 The similar experiment was made on the acetates, Ⅸb and XIXb. The ratio of 5α- and 5β-compound was found to be 3:2 also in this case (Table I). In acetonide series, however, the acetonide (Ⅷ) is expected to be exclusively stable isomer from the observations in acetonide formation reaction catalyzed by hydrogen chloride. In fact, the acetonide (XVⅢ) was isomerized almost quantitatively to the acetonide (Ⅷ) by hydrogen chloride.

A possible explanation for difference of stability between 2β,3β-dihydroxy or diacetoxy series and acetonide series is as follows.

Table I. Optical Rotation Changes of 2β,3β-Dihydroxy- and 2β,3β-Diacetoxycholestan-6-ones by Hydrogen Chloride in Chloroform

	5α (°C)	Equilibrium mixture (°C)	5β (°C)
2β,3β-Dihydroxycholestan-6-one	−0.5	−23.5	−58.6
2β,3β-Diacetoxycholestan-6-one	+6.5	−15.5	−50.3

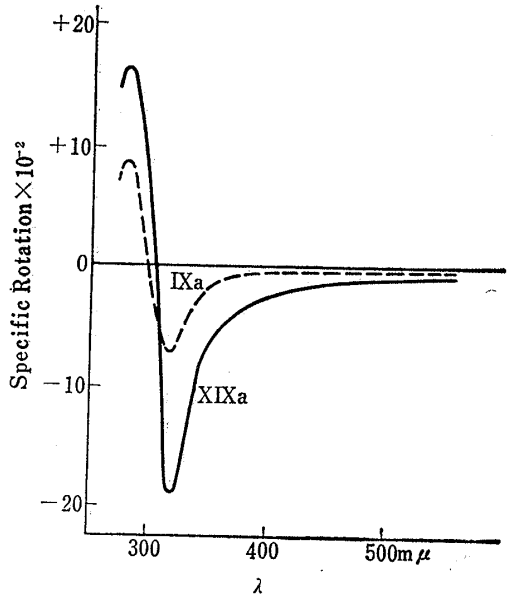

Fig. 3. Optical Rotatory Dispersion Curves of Ⅸa and XIXa

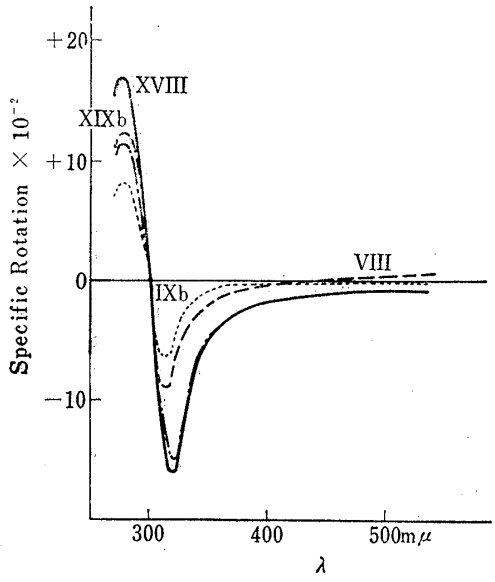

Fig. 4. Optical Rotatory Dispersion Curves of Ⅷ, XVⅢ, Ⅸb and XIXb

*4 If any compound other than 5α- or 5β-compound (Ⅸa or XIXa) is produced, the calculated value is accompanied by some error. However, the infrared spectrum of the equilibrium mixture in chloroform solution was exactly the same as that of the mixture of pure XIXa and Ⅸa at the ratio of 2:3, showing that such a by-product was not contained in the equilibrium mixture.

In Fig. 2, C shows a conformation of A and B ring in acetoide (Ⅷ), in which 2β- and 3β-oxygen bond have exactly axial and equatorial nature, respectively. Such a conformation, however, would have very strong strain in acetonide ring. A reasonable conformation, in which such a ring strain is reduced, is D where 2β-oxygen bond deformed towards the direction in which the dihedral angle between 2β- and 3β-oxygen bond is smaller than 60° as shown in F. In such a confomation, non-bonded 1,3-diaxial interaction between 2β-oxygen and 19-methyl group would be negligible. As a result, 5α-compound is exclusively stable isomer as already shown in ordinary 6-oxo terosids.

Optical rotatory dispersion curves of 2β,3β-dihydroxy-6-oxo compounds and their derivatives, Ⅸa, XIXa, Ⅸb, XIXb, Ⅷ and XVⅢ are shown in Fig. 3 and 4. All compounds hsowed negative Cotton effect curves and larger amplitudes were observed in 5β-compounds, These data are consistent with both the observations described by Djerassi and Closson[10] and the prediction from Octant rule.[11]

Experimental*5

6β-Hydroxy-5α-cholestane-3-one (IV)——To a suspension of 5α-cholestane-3,6-dione 3-mono-*o*-aminoanyl (Ⅱ) (92.6 g.) prepared by the procedure reported by Marker and Rohrmann[4] from 5α-cholestane-3,6-dione (I, 86.0 g.) in EtOH (4.00 L.) was added $NaBH_4$ (56 g.). After stirring for 7 hr. at room temperature and standing overnight, excess $NaBH_4$ was decomposed by addition of AcOH (54 ml.), and 6*N* HCl (920 ml.) was added. The solutoin was refluxed for 1 hr., and condensed under reduced pressure to a half volume. H_2O was added, and precipitates were collected by filtration. Recrystallization from acetone and acetone-*n*-hexane yielded 6β-hydroxy-5α-cholestan-3-one (Ⅳ, 44 g.), m.p. 181~183°, which did not show melting point depression on admixture with an authentic sample, and showed the same infrared spectrum.

5α-Cholestane-2β,3β,6β-triol 2,3-Acetonide (VII)——a) From Ⅳ : 6β-Hydroxy-5α-cholestan-3-one (Ⅳ, 8.8 g.) was added to *t*-BuOH (700 ml.) in which K (21 g.) was beforehand dissolved, and the solution was stirred in oxygen atmosphere for 15 min. during which 550 ml. of oxygen was absorbed. The yellow solution was poured into H_2O and acidified with 10% HCl. The product was extracted with ether and the ether layer was shaken with 20% KOH (500 ml.). The resulting suspension was centifuged and the precipitated K salt was isolated by decantation. After addition of 10% HCl, the diosphenol was extracted with ether, and the organic layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The ether was removed by distillation to give a yellow solid.

The crude diosphenol obtained above was suspended in MeOH (190 ml.) and $NaBH_4$ (4.4 g.) was added in small portions to the suspension. After stirring at room temperature for 30 min., the solution was refluxed for 30 min. Excess $NaBH_4$ was decomposed by AcOH and the solution was poured into H_2O. The product was extracted with *n*-BuOH and the organic layer was washed with 5% Na_2CO_3 and 10% NaCl. The organic solvent was distilled to dryness *in vacuo* to give a yellow solid.

Acetone (900 ml.) and 5% phosphomolybdic acid in acetone (150 ml.) was added to the product obtained above and the suspension was stirred for 4 hr. at room temperature. 30% NH_4OH being added, the suspension was poured into H_2O, and the product was extracted with ether. The ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation to afford a yellow solid, which was chromatographed on Florisil (200 g.). The product eluted by ether was recrystallized from acetone to give the acetonide (Ⅶ), m.p. 214~222° (3.25 g.). An analytical sample was obtained by further recrystallization from acetone as colorless needles. m.p. 217~222°, $[\alpha]_D^{26}$ +37° (c=1.09). *Anal.* Calcd. for $C_{30}H_{52}O_3$: C, 78.20; H, 11.38. Found : C, 77.75; H, 11.27.

b) From Ⅷ : $NaBH_4$ (100 mg.) was added to a solution of 2β,3β-dihydroxy-5α-cholestan-6-one 2,3-acetonide (Ⅷ, 35 mg.) in MeOH (40 ml.). Being stirred for 10 min. at 40°, MeOH (20 ml.) was removed by distillation. The solution was poured into H_2O and the product wes extracted with ether and the ether solution was washed with 10% HCl, 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by evaporation to afford colorless solid, the infrared spectrum of which was identical with the triol acetonide. m.p. 218~222°.

3β-Hydroxy-5α-cholestan-6-one Ethylene Ketal (XII)——A solution of 3β-hydroxy-5α-cholestan-6-one (Ⅺ, 5.9 g.) in benzene (150 ml.) and $(CH_2OH)_2$ (47 ml.) was distilled slowly to remove a trace of H_2O. *p*-TsOH (0.5 g.) was added and the solution was distilled for 5 hr., during which benzene was added to maintain a constant volume. After cooling, powdered $NaHCO_3$ was added, and then the suspension was shaken with

*5 All melting points were uncorrected, and optical rotations were measured in chloroform unless otherwise stated. Optical rotatory dispersion curves were measured in dioxane.

10) C. Djerassi, W. Closson : J. Am. Chem. Soc., **78**, 3761 (1956).

11) C. Djerassi : "Optical Rotatory Dispersion," p. 178 (1960). McGraw-Hill Book Co., N. Y.

H_2O. The benzene layer was washed with 5% $NaHCO_3$ and H_2O, and dried (Na_2SO_4). The solvent was removed *in vacuo* to give a crystalline material, which on recrystallization from EtOH containing a trace of pyridine afforded the ketal (XII, 4.9 g.), m.p. 92~100°. An analytical sample was obtained by further recrystallization from the same solvent as colorless needles, m.p. 107~109°(softened at 91°). $[\alpha]_D^{18}$ +27° (c=0.91). *Anal.* Calcd. for $C_{29}H_{50}O_3$: C, 77.97; H, 11.28. C, 77.85; H, 11.29.

5α-Cholestane-3,6-dione 6-Ethylene Ketal (XIII)——a) By Oppenauer oxidation : A solution of aluminum isopropoxide (2.0 g.) in toluene (80 ml.) was dropwise added to a solution of 3β-hydroxy-5α-cholestan-6-one 6-ethylene ketal (XII, 2.0 g.) in toluene (200 ml.) and cyclohexane (20 ml.) at reflux temperature during 1 hr., and the solution was refluxed for 4 hr. After cooling, saturated Rochelle salt was added and the organic solvent was removed by steam distillation. The product was extracted with ether, and the ether fraction was washed with Rochelle salt solution, 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation. The residue was recrystallized from acetone-MeOH containing a trace of pyridine gave the ketal (XIII, 1.02 g.), m.p. 114~116°. An analytical sample was obtained by further recrystallization from the same solvent as colorless prisms. m.p. 114~115.5°, $[\alpha]_D^{18}$ +26°(c=1.03). *Anal.* Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found : C, 78.64; H, 11.14.

b) By Jones oxidation : To a solution of 3β-hydroxy-5α-cholestan-6-one 6-ethylene ketal (20 g.) in acetone (2.0 L.) was added 8*N* CrO_3 solution (20 ml.)*6 at 0~5° with stirring. After stirring for 3 min., the suspension was poured into ice-cold H_2O, and the product was extracted with ether as soon as possible. The ether layer was washed with H_2O, 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation, and the residue was recrystallized from MeOH-acetone containing a trace of pyridine to give the ketal (XIII, 12.2 g.), m.p. 115~117°, which was identical with the sample obtained above.

2β,3β-Dihydroxy-5α-cholestan-6-one 2,3-Acetonide (VIII)——a) From VII : To a solution of 5α-cholestane-2β,3β,6β-triol 2,3-acetonide (VII, 2.65 g.) in acetone (1060 ml.) was added 8*N* CrO_3 solution*6 at 7° with stirring. After 3 min., H_2O was added and the product was extracted with ether. After being washed with 5% Na_2CO_3, and H_2O, and dried (Na_2SO_4), the solvent was removed by distillation. Recrystallization from acetone afforded the 6-oxo compound (VIII), m.p. 168.5~170°(2.3 g.). An analytical sample was obtained by further recrystallization from acetone as colorless needles. m.p. 168~170°, $[\alpha]_D^{26}$ +14°(c=0.97). ORD: $[\alpha]_{700}$ +21°, $[\alpha]_{589}$ +25°, $[\alpha]_{316}$ −871°(trough), $[\alpha]_{276}$ +1248°(peak), $[\alpha]_{265}$ +600°(c=0.338, t=27°). *Anal.* Calcd. for $C_{30}H_{50}O_3$: C, 78.55; H, 10.99. Found : C, 78.77; H, 10.93.

b) From IXa : i) With phosphomolybdic acid; A solution of 2β,3β-dihydroxy-5α-cholestan-6-one (IXa, 10 mg.) in acetone (2.0 ml.) and 5% phosphomolybdic acid in acetone (0.15 ml.) was allowed to stand at room temperature for 30 min., and 30% NH_4OH was added to the solution. H_2O was added and the product was extracted with ether. The ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4.) The solvent was removed by distillation to give colorless solid, the infrared spectrum of which was identical with that of the acetonide obtained above. Recrystallization from acetonide afforded colorless needles, m.p. 167~169°.

ii) With hydrogen chloride; A solution of 2β,3β-dihydroxy-5α-cholestan-6-one (IXa, 10 mg.) in acetone (2.0 ml.) and acetone (0.5 ml.) saturated with HCl was allowed to stand at room temperature for 30 min., and poured into 5% Na_2CO_3. The product was isolated as the same manner described above and the infrared spectrum was identical with the sample obtained above.

c) From XIXa : A solution of 2β,3β-dihydroxy-5β-cholestan-6-one (XIXa, 10 mg.) was treated with acetone containing HCl and the product was isolated as the same manner described above, and the infrared spectrum was identical with that of the sample obtained above. Recrystallization from acetone afforded colorless needles, m.p. 163~166°.

d) From XVIII : A solution of 2β,3β-dihydroxy-5β-cholestan-6-one 2,3-acetonide (XVIII, 10 mg.) was treated with acetone containing HCl and the product was isolated as the same manner described above, the infrared spectrum of which was identical with that of the sample obtained above. Recrystallization from acetone gave colorless needles, m.p. 162~165°.

e) From XIII : 5α-Cholestane-3,6-dione 6-ethylene ketal (XIII, 10.0 g.) was added to *t*-BuOH (700 ml.) in which K (21 g.) was beforehand dissolved and the resulting yellow solution was stirred in oxygen atmosphere for 15 min., during which ca. 600 ml. of oxygen was absorbed. The solution was poured into ice-H_2O and acidified with AcOH. The product was extraceted with ether, and the ether layer was washed with H_2O, 5% Na_2CO_3 and H_2O, and after addition of two drops of pyridine, the solvent was removed by distillation to give oily substance.

To a solution of the oily substance obtained above in EtOH (200 ml.) was added $NaBH_4$ (5.0 g.) and after standing at room temperature for 10 min., the solution was refluxed for 45 min. Excess $NaBH_4$ was destroyed by addition of AcOH, and the solution was poured into H_2O. The product was extracted with ether, and the ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation to yield an oily substance.

*6 A solution of CrO_3 (26.72 g.) in H_2SO_4 (23 ml.) diluted with H_2O at a volume of 100 ml. was used.

To a mixture of the oily material obtained above in acetone (800 ml.) wad added 5% phosphomolybdic acid in acetone (150 ml.). After standing at room temperature for 15 min., 30% NH_4OH and then H_2O were added, and the product was extracted with ether. The ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation to give a crystalline material, which was chromatographed on Florisil (200 mg.). 2β,3β-Dihydroxy-5α-cholestan-6-one acetonide, m.p. 168~169° (Ⅷ, 4.45 g.) was obtained by elution with *n*-hexane–EtOAc (9:1) and recrystallization.

2β,3β-Dihydroxy-5α-cholestan-6-one (IXa)——A solution of 2β,3β-dihydroxy-5α-cholestan-6-one acetonide (Ⅷ, 2.1 g.) in EtOH (500 ml.) and 10% H_3PO_4 (90 ml.) was refluxed for 1 hr. and poured into H_2O. The product was extracted with ether and the ether solution was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). Removal of the solvent afforded a white solid, which on recrystallization from acetone gave dihydroxy ketone (Ⅸa, 1.75 g.), m.p. 204~207.5°. An analytical sample was obtained by further recrystallization from acetone as colorless needles. m.p. 204~207°, $[\alpha]_D^{26}$ −1° (c=0.92). ORD: $[\alpha]_{700}$ −7°, $[\alpha]_{589}$ 0°, $[\alpha]_{314}$ −765° (trough), $[\alpha]_{278}$ +893° (peak), $[\alpha]_{272}$ +779° (c=0.211, t=20°). *Anal.* Calcd. for $C_{27}H_{46}O_3$: C, 77.46; H, 11.08. Found: C, 77.49; H, 11.12.

5α-Cholestane-2β,3β,6β-triol (X)——a) From Ⅶ: A solution of 5α-cholestane-2β,3β,6β-triol 2,3-acetonide (Ⅶ, 152 mg.) in EtOH (30 ml.) and 10% H_3PO_4 (6.0 ml.) was refluxed for 1 hr., and poured into H_2O. The product was extracted with *n*-BuOH, and the organic layer was washed with 4% NaOH and NaCl solution. The solvent was removed by distillation *in vacuo*, and solid residue was washed well with H_2O to remove NaCl. Recrystallization from MeOH gave the triol (X, 108 mg.), m.p. 213~219°. An analytical sample was obtained by further recrystallization from the same solvent as colorless leaflets. m.p. 213~219°, $[\alpha]_D^{26}$ +23° (c=0.98, dioxane). *Anal.* Calcd. from $C_{27}H_{48}O_3$: C, 77.09; H, 11.50. Found: C, 77.03; H, 11.61.

b) From Ⅸ: To a solution of 2β,3β-dihydroxy-5α-cholestan-6-one (Ⅸa, 20 mg.) in MeOH (5.0 ml.) was added $NaBH_4$ (20 mg.) under cooling with ice-cold H_2O. The solution was stirred for 20 min. and refluxed for another 20 min. AcOH (2 drops) was added and then the solution was poured into H_2O. The product was extracted with ether, and the ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). Upon removal of the solvent, solid material was obtained. Recrystallization from MeOH gave colorless leaflets, m.p. 210~216°, the infrared spectrum of which was identical with the product obtained above.

2β,3β-Diacetoxy-5α-cholestan-6-one (IXb)——2β,3β-Dihydroxy-5α-cholestan-6-one (Ⅸa, 186 mg.) was refluxed with Ac_2O (5.0 ml.) for 2 hr., and H_2O was added. The product was extracted with ether and the ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). Ether was removed by distillation and the residue was recrystallized from acetone–MeOH to give the diacetate (Ⅸb, 178 mg.) as colorless needles. m.p. 186~188°, $[\alpha]_D^{27}$ +7° (c=0.77). ORD: $[\alpha]_{700}$ +2°, $[\alpha]_{589}$ −9°, $[\alpha]_{314}$ −663° (trough), $[\alpha]_{278}$ +830° (peak), $[\alpha]_{272}$ +715° (c=0.263, t=20°). *Anal.* Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03. Found: C, 74.19; H, 9.90.

5α-Cholestane-2β,3β-diol Diacetate (VXII)——2β,3β-Diacetoxy-5α-cholestan-6-one (Ⅸb, 321 mg.) was dissolved in AcOH (18 ml.), $(CH_2SH)_2$ (0.6 ml.) and BF_3–ether (0.6 ml.) and the solution was allowed to stand at room temperature for 24 hr. Ether was added, and the ether solution was washed with 4% NaOH and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation to give an oily material.

A mixture of the material obtained above, W-2 Raney Ni (ca. 10 g.) and EtOH (50 ml.) was refluxed for 12 hr. After addition of *n*-hexane, Raney Ni was removed by filtration and the filtrate was evaporated to dryness. The residue was recrystallized from acetone–MeOH to give 5α-cholestane-2β,3β-diol diacetate (XVII, 192 mg.), m.p. 121~123° as colorless needles, which was identical with an authentic sample in all respects.

2β,3β-Dihydroxy-5β-cholestan-6-one Acetonide (XVIII)——a) From Ⅸa: A solution of 2β,3β-dihydroxy-5α-cholestan-6-one (Ⅸa, 1.5 g.) in EtOH (360 ml.) and 10% HCl (36 ml.) was refluxed for 1 hr., and poured into H_2O. The product was extracted with ether and the ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation to give an equilibrium mixture as a crystalline material.

To a suspension of the material obtained above in acetone (300 ml.) was added 5% phosphomolybdic acid in acetone (24 ml.). The material was dissolved shortly after the addition and the solution was stored at room temperature for 15 min. 30% NH_4OH and then H_2O were added and the product was extracted with ether and the ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation and the residue was recrystallized from acetone to give 2β,3β-dihydroxy-5α-cholestan-6-one acetonide (Ⅷ, 0.48 g.), m.p. 162~165°. The mother liquor was chromatographed on Florisil (40 g.) and 2β,3β-dihydroxy-5β-cholestan-6-one acetonide (XVIII, 0.61 g.), m.p. 145~147° was eluted with benzene–EtOAc (19:1). Further elution with the same solvent gave 5α-acetonide (Ⅷ, 0.15 g.). An analytical sample of 5β-acetonide was obtained by recrystallization from acetone as colorless needles. m.p. 145~147°, $[\alpha]_D^{27}$ −36° (c=1.11). ORD: $[\alpha]_{700}$ −23°, $[\alpha]_{589}$ −31°, $[\alpha]_{322}$ −1616° (trough), $[\alpha]_{278}$ +1680° (peak), $[\alpha]_{265}$ +704° (c=0.291, t=27°). *Anal.* Calcd. for $C_{30}H_{50}O_3$: C, 78.55; H, 10.99. Found: C, 78.81; H, 10.70.

b) From XIXa: A solution of 2β,3β-dihydroxy-5β-cholestan-6-one (XIXa, 10 mg.) in acetone (2.0 ml.) and 5% phosphomolybdic acid in acetone (0.15 ml.) was allowed to stand at room temperature for 30 min. 30% NH_4OH and then H_2O were added and the product was extracted with ether. The ether solution was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The removal of the solvent gave solid material, the

infrared spectrum of which was identical with the product obtained above. Recrystallization from MeOH afforded colorless needles, m.p. 144~146°.

2β,3β-Dihydroxy-5β-cholestan-6-one (XIXa)——A solution of 2β,3β-dihydroxy-5β-cholestan-6-one acetonide (XVIII, 614 mg.) in EtOH (150 ml.) and 10% H_3PO_4 (30 ml.) was refluxed for 1 hr., and poured into H_2O. The product was extracted with ether, and ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). The solvent was removed by distillation and the residue was recrystallized from acetone to give 2β,3β-dihydroxy-5β-cholestan-6-one (XIXa, 440 mg.), m.p. 177~179°. An analytical sample was obtained by further recrystallization from acetone as colorless needles. m.p. 177~179°, $[\alpha]_D^{27}$ −59°(c=0.83). ORD: $[\alpha]_{700}$ −68°, $[\alpha]_{589}$ −64°, $[\alpha]_{320}$ −1940°(trough), $[\alpha]_{278}$ +1630°(peak), $[\alpha]_{272}$ +1390°(c=0.264, t=20°). *Anal.* Calcd. for $C_{27}H_{46}O_3$: C, 77.46; H, 11.08. Found: C, 77.25; H, 11.14.

2β,3β-Diacetoxy-5β-cholestan-6-one (XIXb)——A solution of 2β,3β-dihydroxy-5β-cholestan-6-one (XIXa, 82 mg.) in Ac_2O (2.5 ml.) was refluxed for 2 hr., and poured into H_2O. The product was extracted with ether and the ether layer was washed with 5% Na_2CO_3 and H_2O, and dried (Na_2SO_4). Ether was removed by distillation and the residue was recrystallized from acetone-MeOH to afford the diacetate (XIXb, 72 mg.) as colorless needles. m.p. 142~144°, $[\alpha]_D^{19}$ −50°(c=0.74). ORD: $[\alpha]_{700}$ −19°, $[\alpha]_{589}$ −19°, $[\alpha]_{324}$ −1530° (trough), $[\alpha]_{278}$ +1170°(peak), $[\alpha]_{222}$ +1020°(c=0.260, t=20°). *Anal.* Calcd. for $C_{31}H_{50}O_5$: C, 74.06; H, 10.03. Found: C, 74.03; H, 9.74.

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