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

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

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

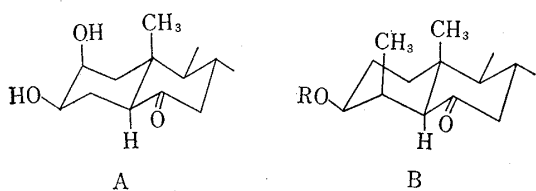


Fig. 1.

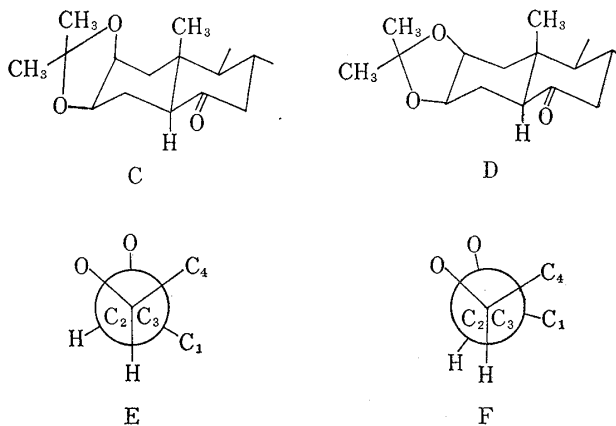


Fig. 2.

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

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

*¹ 1604 Shimosakunobe, Kawasaki-shi (森 弘, 常田 清, 柴田健雄, 沢井政信).*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 Rohrmann⁴⁾ have reported that 5 α -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 6 β -hydroxy-3-azine (III), which on hydrolysis with hydrochloric acid yielded 6 β -hydroxy-3-one (IV) with satisfactory yield.

The preparation of 2 β ,3 β -dihydroxy compound was made by the method reported in the preceding paper.⁵⁾ 6 β -Hydroxy-3-one (IV) was autoxidized in the presence of potassium *t*-butoxide in *t*-butanol⁶⁾ to an enol mixture of 6 β -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 2,3,6 β -triols (VI). In order to isolate the desired 2 β ,3 β ,6 β -triol, the mixture was treated with acetone containing hydrogen chloride, and chromatographed on Florisil. The elution with ether gave 2 β ,3 β ,6 β -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 2 β ,3 β -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. 2 β ,3 β -Dihydroxy-6-one acetonide (VIII) was hydrolyzed with 10% phosphoric acid to afford 2 β ,3 β -dihydroxy-6-one (IXa), 5 α -configuration of which could be shown by the following observation. The hydrolysis of 2 β ,3 β ,6 β -triol 2,3-acetonide (VII) gave 2 β ,3 β ,6 β -triol (X), which was identical with the compound derived by the reduction of 2 β ,3 β -dihydroxy-6-one (IXa) with sodium borohydride.

2 β ,3 β -Dihydroxy-6-one acetonide (VIII) was also obtained by another route from 3 β -hydroxy-5 α -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 2 β ,3 β -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 2 β ,3 β -dihydroxy structures or its derivatives will be shown. Acetylation of 2 β ,3 β -dihydroxy-6-one (IXa) with acetic anhydride at reflux temperature^{*3} yielded 2 β ,3 β -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 5 α -cholestane-2 β ,3 β -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.

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 5 α - and 5 β -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 5 α - and 5 β -compound at the ratio of 3:2.*⁴ The similar experiment was made on the acetates, IXb and XIXb. The ratio of 5 α - and 5 β -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 2 β ,3 β -dihydroxy or diacetoxo series and acetonide series is as follows.

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

	5 α ($^\circ$ C)	Equilibrium mixture ($^\circ$ C)	5 β ($^\circ$ C)
2 β ,3 β -Dihydroxycholestan-6-one	-0.5	-23.5	-58.6
2 β ,3 β -Diacetoxocholestan-6-one	+6.5	-15.5	-50.3

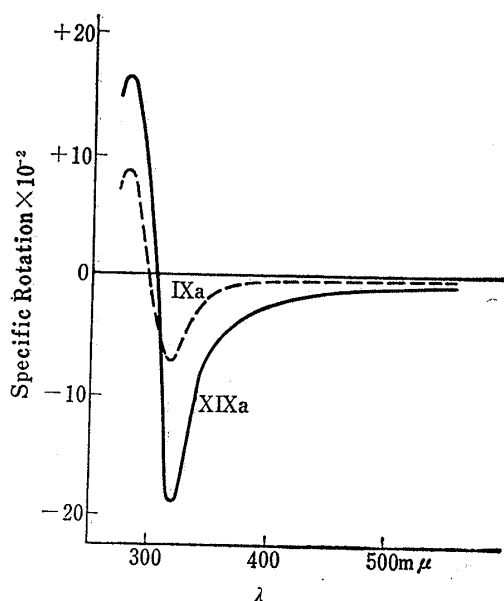


Fig. 3. Optical Rotatory Dispersion Curves of IXa and XIXa

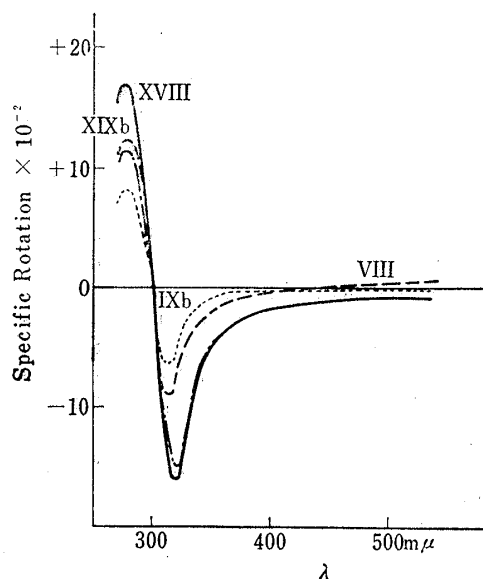


Fig. 4. Optical Rotatory Dispersion Curves of VIII, XVIII, IXb and XIXb

*⁴ If any compound other than 5 α - or 5 β -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 acetone (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 acetone 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 conformation, 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 $2\beta,3\beta$ -dihydroxy-6-oxo compounds and their derivatives, IXa, XIXa, Xb, XIXb, VIII and XVIII are shown in Fig. 3 and 4. All compounds showed negative Cotton effect curves and larger amplitudes were observed in 5β -compounds. These data are consistent with both the observations described by Djerassi and Closson¹⁰ 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*-aminoanil (II) (92.6 g.) prepared by the procedure reported by Marker and Rohrmann⁴) 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 solution 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. $181\sim 183^\circ$, which did not show melting point depression on admixture with an authentic sample, and showed the same infrared spectrum.

5α -Cholestane- $2\beta,3\beta,6\beta$ -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 centrifuged 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 acetone (VII), m.p. $214\sim 222^\circ$ (3.25 g.). An analytical sample was obtained by further recrystallization from acetone as colorless needles. m.p. $217\sim 222^\circ$, $[\alpha]_D^{25} + 37^\circ$ ($c=1.09$). Anal. Calcd. for $\text{C}_{30}\text{H}_{52}\text{O}_3$: 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 $2\beta,3\beta$ -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 was 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 acetone. m.p. $218\sim 222^\circ$.

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 $(\text{CH}_2\text{OH})_2$ (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.

H₂O. The benzene layer was washed with 5% NaHCO₃ and H₂O, and dried (Na₂SO₄). 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°). $[\alpha]_D^{18} + 27^\circ$ (c=0.91). *Anal.* Calcd. for C₂₉H₅₀O₃: C, 77.97; H, 11.28. Found: C, 77.85; H, 11.29.

5 α -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 3 β -hydroxy-5 α -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% Na₂CO₃ and H₂O, and dried (Na₂SO₄). 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°, $[\alpha]_D^{18} + 26^\circ$ (c=1.03). *Anal.* Calcd. for C₂₉H₄₈O₃: C, 78.32; H, 10.88. Found: C, 78.64; H, 11.14.

b) By Jones oxidation: To a solution of 3 β -hydroxy-5 α -cholestan-6-one 6-ethylene ketal (20 g.) in acetone (2.0 L.) was added 8N CrO₃ solution (20 ml.)*⁶ at 0~5° with stirring. After stirring for 3 min., the suspension was poured into ice-cold H₂O, and the product was extracted with ether as soon as possible. The ether layer was washed with H₂O, 5% Na₂CO₃ and H₂O, and dried (Na₂SO₄). 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.

2 β ,3 β -Dihydroxy-5 α -cholestan-6-one 2,3-Acetonide (VIII)—a) From VII: To a solution of 5 α -cholestan-2 β ,3 β ,6 β -triol 2,3-acetonide (VII, 2.65 g.) in acetone (1060 ml.) was added 8N CrO₃ solution*⁶ at 7° with stirring. After 3 min., H₂O was added and the product was extracted with ether. After being washed with 5% Na₂CO₃ and H₂O, and dried (Na₂SO₄), 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°, $[\alpha]_D^{25} + 14^\circ$ (c=0.97). ORD: $[\alpha]_{700} + 21^\circ$, $[\alpha]_{589} + 25^\circ$, $[\alpha]_{316} - 871^\circ$ (trough), $[\alpha]_{276} + 1248^\circ$ (peak), $[\alpha]_{265} + 600^\circ$ (c=0.338, t=27°). *Anal.* Calcd. for C₃₀H₅₀O₃: C, 78.55; H, 10.99. Found: C, 78.77; H, 10.93.

b) From IXa: i) With phosphomolybdic acid; A solution of 2 β ,3 β -dihydroxy-5 α -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% NH₄OH was added to the solution. H₂O was added and the product was extracted with ether. The ether layer was washed with 5% Na₂CO₃ and H₂O, and dried (Na₂SO₄). 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 2 β ,3 β -dihydroxy-5 α -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% Na₂CO₃. 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 2 β ,3 β -dihydroxy-5 β -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 2 β ,3 β -dihydroxy-5 β -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: 5 α -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-H₂O and acidified with AcOH. The product was extracted with ether, and the ether layer was washed with H₂O, 5% Na₂CO₃ and H₂O, 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 NaBH₄ (5.0 g.) and after standing at room temperature for 10 min., the solution was refluxed for 45 min. Excess NaBH₄ was destroyed by addition of AcOH, and the solution was poured into H₂O. The product was extracted with ether, and the ether layer was washed with 5% Na₂CO₃ and H₂O, and dried (Na₂SO₄). The solvent was removed by distillation to yield an oily substance.

*⁶ A solution of CrO₃ (26.72 g.) in H₂SO₄ (23 ml.) diluted with H₂O at a volume of 100 ml. was used.

To a mixture of the oily material obtained above in acetone (800 ml.) was 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.). $2\beta,3\beta$ -Dihydroxy- 5α -cholestan-6-one acetone, m.p. $168\sim 169^\circ$ (VIII, 4.45 g.) was obtained by elution with *n*-hexane-EtOAc (9:1) and recrystallization.

$2\beta,3\beta$ -Dihydroxy- 5α -cholestan-6-one (IXa)—A solution of $2\beta,3\beta$ -dihydroxy- 5α -cholestan-6-one acetone (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. $204\sim 207.5^\circ$. An analytical sample was obtained by further recrystallization from acetone as colorless needles. m.p. $204\sim 207^\circ$, $[\alpha]_D^{25} -1^\circ$ ($c=0.92$). ORD: $[\alpha]_{700} -7^\circ$, $[\alpha]_{589} 0^\circ$, $[\alpha]_{314} -765^\circ$ (trough), $[\alpha]_{278} +893^\circ$ (peak), $[\alpha]_{272} +779^\circ$ ($c=0.211$, $t=20^\circ$). Anal. Calcd. for $\text{C}_{27}\text{H}_{46}\text{O}_3$: C, 77.46; H, 11.08. Found: C, 77.49; H, 11.12.

5α -Cholestane- $2\beta,3\beta,6\beta$ -triol (X)—a) From VII: A solution of 5α -cholestane- $2\beta,3\beta,6\beta$ -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. $213\sim 219^\circ$. An analytical sample was obtained by further recrystallization from the same solvent as colorless leaflets. m.p. $213\sim 219^\circ$, $[\alpha]_D^{25} +23^\circ$ ($c=0.98$, dioxane). Anal. Calcd. from $\text{C}_{27}\text{H}_{48}\text{O}_3$: C, 77.09; H, 11.50. Found: C, 77.03; H, 11.61.

b) From IX: To a solution of $2\beta,3\beta$ -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. $210\sim 216^\circ$, the infrared spectrum of which was identical with the product obtained above.

$2\beta,3\beta$ -Diacetoxy- 5α -cholestan-6-one (IXb)— $2\beta,3\beta$ -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. $186\sim 188^\circ$, $[\alpha]_D^{25} +7^\circ$ ($c=0.77$). ORD: $[\alpha]_{700} +2^\circ$, $[\alpha]_{589} -9^\circ$, $[\alpha]_{314} -663^\circ$ (trough), $[\alpha]_{278} +830^\circ$ (peak), $[\alpha]_{272} +715^\circ$ ($c=0.263$, $t=20^\circ$). Anal. Calcd. for $\text{C}_{31}\text{H}_{50}\text{O}_5$: C, 74.06; H, 10.03. Found: C, 74.19; H, 9.90.

5α -Cholestane- $2\beta,3\beta$ -diol Diacetate (VXII)— $2\beta,3\beta$ -Diacetoxy- 5α -cholestan-6-one (IXb, 321 mg.) was dissolved in AcOH (18 ml.), $(\text{CH}_3\text{SH})_2$ (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- $2\beta,3\beta$ -diol diacetate (XVII, 192 mg.), m.p. $121\sim 123^\circ$ as colorless needles, which was identical with an authentic sample in all respects.

$2\beta,3\beta$ -Dihydroxy- 5β -cholestan-6-one Acetonide (XVIII)—a) From IXa: A solution of $2\beta,3\beta$ -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 $2\beta,3\beta$ -dihydroxy- 5α -cholestan-6-one acetone (VIII, 0.48 g.), m.p. $162\sim 165^\circ$. The mother liquor was chromatographed on Florisil (40 g.) and $2\beta,3\beta$ -dihydroxy- 5β -cholestan-6-one acetone (XVIII, 0.61 g.), m.p. $145\sim 147^\circ$ was eluted with benzene-EtOAc (19:1). Further elution with the same solvent gave 5α -acetone (VIII, 0.15 g.). An analytical sample of 5β -acetone was obtained by recrystallization from acetone as colorless needles. m.p. $145\sim 147^\circ$, $[\alpha]_D^{25} -36^\circ$ ($c=1.11$). ORD: $[\alpha]_{700} -23^\circ$, $[\alpha]_{589} -31^\circ$, $[\alpha]_{322} -1616^\circ$ (trough), $[\alpha]_{278} +1680^\circ$ (peak), $[\alpha]_{265} +704^\circ$ ($c=0.291$, $t=27^\circ$). Anal. Calcd. for $\text{C}_{30}\text{H}_{50}\text{O}_3$: C, 78.55; H, 10.99. Found: C, 78.81; H, 10.70.

b) From XIXa: A solution of $2\beta,3\beta$ -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°.

2 β ,3 β -Dihydroxy-5 β -cholestan-6-one (XIXa)—A solution of 2 β ,3 β -dihydroxy-5 β -cholestan-6-one acetone (XVIII, 614 mg.) in EtOH (150 ml.) and 10% H₃PO₄ (30 ml.) was refluxed for 1 hr., and poured into H₂O. The product was extracted with ether, and ether layer was washed with 5% Na₂CO₃ and H₂O, and dried (Na₂SO₄). The solvent was removed by distillation and the residue was recrystallized from acetone to give 2 β ,3 β -dihydroxy-5 β -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°, $[\alpha]_D^{25}$ -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 C₂₇H₄₆O₃: C, 77.46; H, 11.08. Found: C, 77.25; H, 11.14.

2 β ,3 β -Diacetoxy-5 β -cholestan-6-one (XIXb)—A solution of 2 β ,3 β -dihydroxy-5 β -cholestan-6-one (XIXa, 82 mg.) in Ac₂O (2.5 ml.) was refluxed for 2 hr., and poured into H₂O. The product was extracted with ether and the ether layer was washed with 5% Na₂CO₃ and H₂O, and dried (Na₂SO₄). 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 C₃₁H₅₀O₅: C, 74.06; H, 10.03. Found: C, 74.03; H, 9.74.

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