

A New Product of Cholesterol by Metal-free Autoxidation in Aqueous Dispersion¹⁾

MEIJI KAWATA,^{2a)} MASAHIKO TOHMA, TAKUJI SAWAYA,
and MICHIIYA KIMURA^{2b)}

*The National Institute for Environmental Studies^{2a)} and Faculty of
Pharmaceutical Sciences, Hokkaido University^{2b)}*

(Received April 19, 1976)

Chemical structure was studied on the compound A which was one of the autoxidation products of cholesterol in an aqueous dispersion employing sodium cholesteryl sulfate as solubilizer. 5 α -Cholestane-3 β ,5,6 β ,7 α -tetrol and its 7 β -epimer were prepared as the authentic specimens. Contrary to the 7 α -tetrol and the compound A, the epimer gave an acetone and was susceptible to the oxidation with periodic acid. Identity of the compound A with the 7 α -tetrol was concluded to be unequivocal by comparing the analytical data of these compounds and of their derivatives.

During the course of study of this series,¹⁾ metal-free autoxidation of cholesterol (I) was examined in aqueous dispersions employing different kinds of detergent such as sodium stearate, sodium taurocholate, sodium cholesteryl hemisuccinate, and sodium cholesteryl sulfate, at 70° for 20 hr. Numbers of product were detected in thin-layer chromatography (TLC) and those identified were cholest-5-ene-3 β ,7 α -diol, cholest-5-ene-3 β ,7 β -diol, 5 α -cholestane-3 β ,5,6 β -triol, cholest-5-en-3 β -ol-7-one, and cholesta-3,5-dien-7-one. A polar product was also formed when I was autoxidized in an aqueous dispersion employing sodium cholesteryl sulfate as solubilizer. The present paper deals with the elucidation of chemical structure of this polar product, the compound A.

Results and Discussion

Since the compound A (II), C₂₇H₄₈O₄, colorless needles, mp 248–250°, gave a triacetate retaining a free hydroxyl group, II seemed to be a tetrol compound. Considerable amounts of cholest-5-ene-3 β ,7 α -diol (IIIa), cholest-5-ene-3 β ,7 β -diol (IVa), and 5 α -cholestane-3 β ,5,6 β -triol (V) were obtained at the same time when II was produced in the autoxidation of cholesterol (I).¹⁾ It was, therefore, assumed that chemical structure of the tetrol (II) was closely related to those of such products as IIIa, IVa, and V and had an additional tertiary hydroxyl group probably at C₅. The nuclear magnetic resonance (NMR) as well as mass (MS) spectral data, which are described in the experimental part, indicated that II was likely to be of 5 α -cholestane-3 β ,5,6 β ,7 ξ -tetrol and hence the authentic epimers at C₇ were prepared as described below.

A mixture of epimeric cholest-5-ene-3 β ,7 ξ -diols (IIIa and IVa) was obtained when 3 β -acetoxycholest-5-en-7-one (VI) was reduced with NaBH₄ in 80% dioxane at 100° for 3 hr, though their 3 β -acetates (IIIb and IVb) were formed with the same reagent at 20° for 22 hr as reported.³⁾ When IIIa and IVa were refluxed in benzene with *tert*-butyl hydroperoxide in

1) This paper constitutes Part VI of the series entitled "Metal Ion Catalyzed Oxidation of Steroids" by M. Kimura and co-workers; Part V: M. Kimura, M. Kawata, and T. Sawaya, *Chem. Pharm. Bull.* (Tokyo), **24**, 2258 (1976).

2) Location: a) *P.O. Yatabe, Ibaraki-ken, 300-21, Japan*; b) *Nishi-6-chome, Kita-12-jo, Kita-ku, Sapporo, 060, Japan*.

3) C.W. Shoppe and B.C. Newman, *J. Chem. Soc. (C)*, **1968**, 981.

the presence of vanadyl acetylacetonate, $\text{VO}(\text{acac})_2$,⁴ their epoxides (VIIa and VIIIa) were readily produced, respectively. With the same reagents the epimeric 3β -acetoxyepoxides (VIIb and VIIIb) were also obtainable from the corresponding acetates (IIIb and IVb) in an almost quantitative yield. NMR spectra of a series of stereoisomeric 4,5-epoxycholesten-3-ols showed that C_4 -proton in *cis* 4,5-epoxy-3-alcohols appeared at 2.97—3.05 ppm as a doublet ($J=4.0$ —4.5 Hz) while in the *trans* isomers the proton appeared at 2.70—2.75 ppm as a singlet.⁵ Since the epoxides (VIIb and VIIIb) exhibited the signal attributable to C_6 -proton at 3.21 (doublet, $J=4.5$ Hz) and 3.13 (singlet) ppm, respectively, they were both presumed to be *cis* 5,6-epoxy-7-alcohol. An examination of Dreiding model indicated the dihedral angle of about 80° between $\text{C}_6\alpha\text{-H}$ and $\text{C}_7\alpha\text{-H}$ in the β -epoxide. Consequently, VIIb was assumed as 3β -acetoxy- $5\alpha,6\alpha$ -epoxycholestan-7 α -ol and VIIIb as 3β -acetoxy- $5\beta,6\beta$ -epoxycholestan-7 β -ol. Compared with the usual way employing the peracid such as *m*-chloroperbenzoic acid, this epoxidation seemed to be stereo-selective, since the mixture of IIIb and IVb gave that of the epoxides (VIIb and VIIIb) without formation of any other epimers such as the $5\alpha,6\alpha$ -epoxy-7 β -ol and $5\beta,6\beta$ -epoxy-7 α -ol. It was also found to be highly advantageous for the preparation or identification of such epimers at C_7 , as described above and below, that they were best separated in the chromatography on silica gel when they were in the form of epoxide.

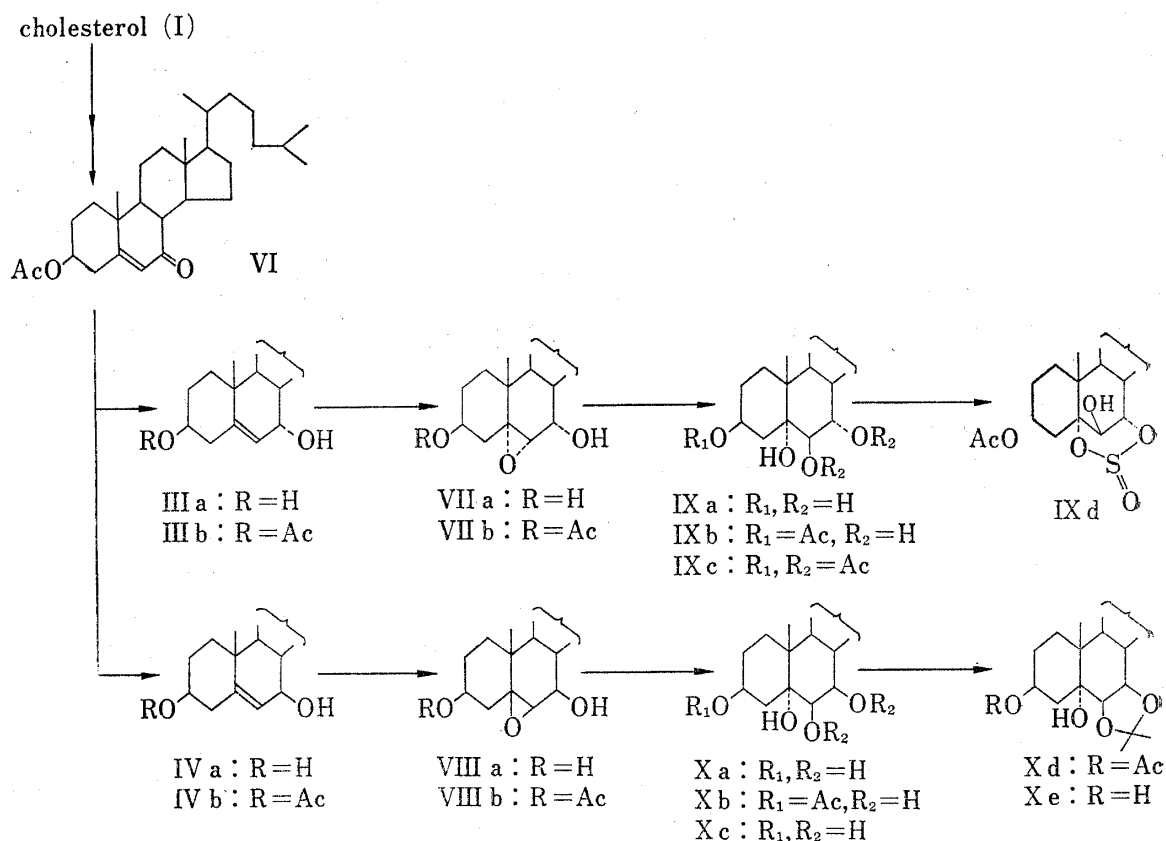


Chart 1

Hydrolysis of the epoxide VIIb with 70% HClO_4 in acetone gave 3β -acetoxy- $5\alpha,6\beta,7\alpha$ -triol (IXb) which was derived to the triacetate (IXc) and the 5,7-sulfite (IXd) by acetic anhydride and thionyl chloride, respectively. When the epimeric epoxide (VIIIb) was hydrolyzed in the same conditions, an acetone (Xd) was derived, which gave readily the

4) M.N. Sheng and J.G. Zajacek, *J. Org. Chem.*, **35**, 1839 (1970); K.B. Sharpless and R.C. Michaelson, *J. Am. Chem. Soc.*, **95**, 6136 (1973).

5) D.J. Collins and J.J. Hobbs, *Tetrahedron Letters*, **1963**, 632.

3 β -acetoxy-5 α ,6 β ,7 β -triol (Xb) by treating with 80% acetic acid. NMR spectrum of Xd showed sharp signals at 1.28 and 1.46 ppm, characteristic to the acetonide-methyl group.⁶⁾ MS spectrum of Xd revealed the base peak 503 ($M^+ - CH_3$), which is also characteristic to

TABLE I. Some Properties of the Compound A and the Specimens Concerned

	Compound A(II)	7 α -Tetrol (IXa)	7 β -Tetrol (Xa)
Structure			
mp	248–250°	250–251°	219–222°
NMR C ₁₃ -CH ₃	0.79	0.80	0.77
C ₁₀ -CH ₃	1.59	1.63	1.58
MS M ⁺	436	436	436
M ⁺ -H ₂ O	418	418	418
M ⁺ -2H ₂ O	400	400	400
M ⁺ -3H ₂ O	382	382	382
HIO ₄ oxidation	—	—	+
Acetonidation	—	—	+
Triacetate NMR -OAc	1.97 2.05 2.09	2.00 2.09 2.11	1.89 2.00 2.08

the acetonide derivative.^{6b)} The tetrols (IXa and Xa) were obtainable by the hydrolysis of the epoxides (VIIa and VIIIa) with 70% HClO₄ in methyl ethyl ketone, respectively. When they came into contact with HIO₄, the 7 α -tetrol (IXa) having the vicinal hydroxyl groups in a *trans*-diaxial orientation both at C_{5,6} and C_{6,7} remained intact. The epimeric tetrol (Xa) having axial hydroxyl group at C₆ and equatorial one at C₇, on the contrary, was susceptible to the oxidative cleavage.

Experimental data of the compound A (II), the 7 α - (IXa), and 7 β -tetrol (Xa) are summarized comparatively in Table I and their infra red (IR) spectra are shown in Fig. 1. On the basis of these results, it seems reasonable to draw a conclusion that the chemical structure of the compound A is 5 α -cholestane-3 β ,5,6 β ,7 α -tetrol.

Experimental

Melting points were taken on a micro hot-stage apparatus and are uncorrected. IR and NMR spectral measurements were run on JASCO Model DS-301 Spectrometer and Hitachi Model H-6013 Spectrometer at 60 Mc using tetramethylsilane as an internal standard, respectively. MS spectra were measured by Hitachi Model RMU-6E Spectrometer. TLC was carried out on silica gel (Wakogel B-5) plate by the solvent system of AcOEt-cyclohexane (1:1) unless otherwise stated and spots were stained by spraying H₂SO₄ and heating on a hot-plate. Abbreviation used s=singlet, d=doublet, m=multiplet, and br=broad.

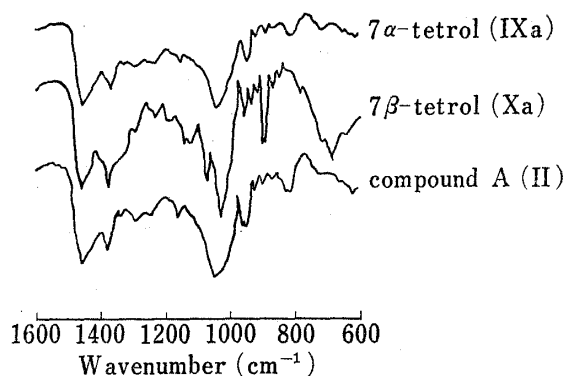


Fig. 1. IR Spectra of the Compound A and the Specimens Concerned

6) a) H.H. Sauer, E.K. Weiss, and T. Reichstein, *Helv. Chim. Acta.*, **49**, 1632 (1966); b) T. Abe and A. Kambegawa, *Chem. Pharm. Bull.* (Tokyo), **21**, 1295 (1973).

Materials and Reagents— 3β -Acetoxycholest-5-en-7-one (VI), mp 160–161°, was prepared by the method of Heusler, *et al.*⁷⁾ 3β -Acetoxycholest-5-en-7 α -ol (IIIb), mp 137°, and 3β -acetoxycholest-5-en-7 β -ol (IVb), mp 110–111°, were obtained as reported by Shoppe, *et al.*⁹⁾ Cholest-5-ene- $3\beta,7\alpha$ -diol (IIIa), mp 165–168°, and cholest-5-ene- $3\beta,7\beta$ -diol (IVa), mp 172–175°, were prepared by the modification of the Shoppe-Newman's method at 100° for 3 hr and purified by column chromatography.

HClO₄ Reagent: To methyl ethyl ketone (18 ml) was added 70% HClO₄ (0.1 ml). Other reagents were of commercial sources.

5 $\beta,6\beta$ -Epoxycholestane-3 $\beta,7\beta$ -diol (VIIIa)—A solution of *tert*-BuOOH (0.6 ml) in benzene (6 ml) was added dropwise for 20 min to a refluxing mixture of the diol (IVa, 1.927 g), VO (acac)₂ (26.5 mg), and benzene (40 ml). After the reaction mixture was refluxed for further 4 hr, the organic solvent was evaporated into dryness *in vacuo* to give a residue which was then dissolved in ether. The ether solution was washed with saturated aq. Na₂SO₃, sat. aq. NaCl, dried over anhydrous Na₂SO₄, and evaporated to dryness. The residue (2.405 g) obtained was purified by column chromatography on silica gel using the solvent system of AcOEt–benzene (15–25: 85–75) and then recrystallized from MeOH to colorless crystals, mp 170–171°, 1.31 g. *Anal.* Calcd. for C₂₇H₄₆O₃: C, 77.46; H, 11.08. Found: C, 77.52; H, 10.97. NMR(CDCl₃) δ : 3.48 (m, C₃ α -H, C₇ α -H), 3.12 (s, C₆ α -H), 0.99 (s, C₁₀-CH₃), 0.64 (s, C₁₃-CH₃).

5 $\alpha,6\alpha$ -Epoxycholestane-3 $\beta,7\alpha$ -diol (VIIa)—was similarly derived from the epimeric diol (IIIa), mp 183–185° (from MeOH). *Anal.* Calcd. for C₂₇H₄₆O₃: C, 77.46; H, 11.08. Found: C, 77.47; H, 11.16. NMR (CDCl₃) δ : 3.85 (m, C₃ α -H, C₇ β -H), 3.22 (d, $J=4.5$ Hz, C₆ β -H), 1.06 (s, C₁₀-CH₃), 0.60 (s, C₁₃-CH₃).

3 β -Acetoxy-5 $\alpha,6\alpha$ -epoxycholestan-7 α -ol (VIIb)—A solution of *tert*-BuOOH (0.64 ml) in benzene (16 ml) was added as described above to a benzene solution (34 ml) of VO (acac)₂ (26.6 mg) and the mixture (2.349 g) of 3β -acetoxycholest-5-en-7-ols (IIIb and IVb), which was obtained by reducing VI. The reaction mixture was also worked up as mentioned above and finally gave a residue (2.456 g). A benzene solution of the residue was then submitted to column chromatography on silica gel (170 g) with subsequent elution by AcOEt–benzene (5: 95). Fractions of 25 ml were collected and the eluates were examined by TLC. Fract. Nos. 144–212 were combined and evaporated to dryness *in vacuo* to give a residue (420 mg) which was recrystallized from MeOH to colorless needles, mp 144–145°. *Anal.* Calcd. for C₂₉H₄₈O₄: C, 75.60; H, 10.50. Found: C, 75.37; H, 10.50. NMR (CDCl₃) δ : 4.90 (m, C₃ α -H), 3.85 (s, C₇ β -H), 3.21 (d, $J=4.5$ Hz, C₆ β -H), 2.01 (s, C₃ β -OAc), 1.00 (s, C₁₀-CH₃), 0.62 (s, C₁₃-CH₃). Mass Spectrum m/e : 460 (M⁺).

3 β -Acetoxy-5 $\beta,6\beta$ -epoxycholestan-7 β -ol (VIIIb)—Fraction Nos. 263–395 in the above-mentioned chromatography were combined and evaporated to dryness *in vacuo* to give a residue (1.438 g) which was recrystallized from MeOH to colorless crystals, mp 130–133°. *Anal.* Calcd. for C₂₉H₄₈O₄: C, 75.60; H, 10.50. Found: C, 75.89; H, 10.59. NMR (CDCl₃) δ : 4.80 (m, C₃ α -H), 3.51 (m, C₇ α -H), 3.13 (s, C₆ α -H), 2.00 (s, C₃ β -OAc), 0.92 (s, C₁₀-CH₃), 0.64 (s, C₁₃-CH₃). Mass Spectrum m/e : 460 (M⁺).

3 β -Acetoxy-5 α -cholestane-5,6 $\beta,7\alpha$ -triol (IXb)—A mixture of VIIb (100 mg) and HClO₄ reagent (7 ml) was allowed to stand for 3 hr at room temperature. After the reaction mixture was worked up as usual, the residue obtained was purified by preparative TLC and finally recrystallized from aq. MeOH to give colorless needles, mp 225–226°. *Anal.* Calcd. for C₂₉H₅₀O₅: C, 72.76; H, 10.53. Found: C, 72.69; H, 10.36. NMR (CDCl₃) δ : 5.15 (m, C₃ α -H), 3.79, 3.63 (2H, C₆ α -, C₇ β -H), 2.05 (s, C₃ β -OAc), 1.17 (s, C₁₀-CH₃), 0.70 (s, C₁₃-CH₃). Mass Spectrum m/e : 460 (M⁺–H₂O), 442 (M⁺–2H₂O), 424 (M⁺–3H₂O).

Triacetate (IXc): mp 90–92° (from aq. MeOH). NMR (CDCl₃) δ : 5.16 (m, C₃ α -H), 4.8–4.9 (2H, C₆ α -, C₇ β -H), 2.11, 2.09 (2CH₃, C₆ β -, C₇ α -OAc), 2.00 (s, C₃ β -OAc), 1.15 (s, C₁₀-CH₃), 0.69 (s, C₁₃-CH₃).

Sulfite (IXd): To a pyridine solution (1 ml) of IXb (78.3 mg) was added a mixture of SOCl₂ (1 ml) and pyridine (1 ml) under ice-cooling. After 5 min the reaction mixture was worked up as usual and the residue (83.6 mg) obtained was purified by preparative TLC (cyclohexane–AcOEt=2: 1), and finally recrystallized from MeOH–CHCl₃ to give colorless crystals, mp 220–224°. IR ν_{\max}^{NaCl} cm⁻¹: 3480 (OH), 1730 (CO), 1195 (SO). NMR (CDCl₃) δ : 5.1–5.5 (2H, C₃ α -, C₇ β -H), 4.40 (br. s, C₆ α -H), 0.89 (s, C₁₀-CH₃), 0.70 (s, C₁₃-CH₃). Mass Spectrum m/e : 442 (M⁺–H₂SO₃), 382 (442–AcOH), 364 (382–H₂O).

3 β -Acetoxy-5 α -cholestane-5,6 $\beta,7\beta$ -triol (Xb)—A mixture of VIIIb (157 mg) and HClO₄ reagent (10 ml) was allowed to stand for 30 min at room temperature. The reaction mixture was worked up similarly to the case of IXb and gave finally colorless crystals, mp 179–180° (from MeOH). *Anal.* Calcd. for C₂₉H₅₀O₅: C, 72.76; H, 10.53. Found: C, 72.52; H, 10.45. NMR (CDCl₃) δ : 5.10 (m, C₃ α -H), 3.78, 3.46 (C₆ α -, C₇ α -H), 2.02 (s, C₃ β -OAc), 1.16 (s, C₁₀-CH₃), 0.70 (s, C₁₃-CH₃). Mass Spectrum m/e : 460 (M⁺–H₂O), 442 (M⁺–2H₂O), 424 (M⁺–3H₂O).

Triacetate (Xc): mp 100–103° (from MeOH). IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3400 (OH), 1735 (CO). NMR (CDCl₃) δ : 5.25–4.98 (3H, C₃ α -, C₆ α -, C₇ α -H), 2.08, 2.00, 1.89 (s, C₃ β -, C₆ β -, C₇ β -OAc).

Acetonide (Xd): A mixture of VIIIb (228 mg), 70% HClO₄ (0.1 ml), and acetone (18 ml) was allowed to stand at room temperature for 24 hr. After the reaction mixture was worked up as usual, the residue (265.3 mg) obtained was purified by column chromatography (cyclohexane–AcOEt=1: 1) on silica gel and finally recrystallized from MeOH–CHCl₃ to give colorless crystals, mp 81–82°. *Anal.* Calcd. for C₃₂H₅₄O₅:

7) K. Heusler and A. Wettstein, *Helv. Chim. Acta*, **35**, 284 (1952).

C, 74.09; H, 10.49. Found: C, 73.95; H, 10.37. NMR (CDCl_3) δ : 5.12 (m, $\text{C}_3\alpha\text{-H}$), 3.94, 3.74 ($\text{C}_6\alpha\text{-}$, $\text{C}_7\alpha\text{-H}$), 2.00 (s, $\text{C}_3\beta\text{-OAc}$), 1.46 (s, acetonide- CH_3), 1.28 (s, acetonide- CH_3), 1.16 (s, $\text{C}_{10}\text{-CH}_3$), 0.66 (s, $\text{C}_{13}\text{-CH}_3$). Mass Spectrum m/e : 503 ($\text{M}^+\text{-CH}_3$), 443 (503-AcOH), 425 (443- H_2O). Hydrolysis of the acetonide by refluxing with 80% AcOH for 1.5 hr gave also Xb.

5 α -Cholestane-3 β ,5,6 β ,7 α -tetrol (IXa)—A mixture of VIIa (219 mg) and HClO_4 reagent (18 ml) was allowed to stand at room temperature for 3 hr. After ether was added, the reaction mixture was washed with 5% NaHCO_3 , sat. NaCl, dried over Na_2SO_4 , and evaporated to dryness *in vacuo*. The oily residue was purified by preparative TLC (acetone-cyclohexane=1:1) and then crystallized from MeOH to colorless crystals, mp 250–251°. *Anal.* Calcd. for $\text{C}_{27}\text{H}_{48}\text{O}_4$: C, 74.26; H, 11.08. Found: C, 74.16; H, 11.03. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3360 (OH). NMR (pyridine- d_5) δ : 1.63 (s, $\text{C}_{10}\text{-CH}_3$), 0.80 (s, $\text{C}_{13}\text{-CH}_3$). Mass Spectrum m/e : 436 (M^+), 418 ($\text{M}^+\text{-H}_2\text{O}$), 400 ($\text{M}^+\text{-2H}_2\text{O}$), 382 ($\text{M}^+\text{-3H}_2\text{O}$).

5 α -Cholestane-3 β ,5,6 β ,7 β -tetrol (Xa)—A mixture of Xb (124 mg), K_2CO_3 (100 mg) dissolved in a few drops of water, and MeOH (10 ml) was allowed to stand at 50–60° over night. After CHCl_3 was added, the reaction mixture was washed with sat. NaCl, dried over Na_2SO_4 , and evaporated to dryness *in vacuo*. The residue (122 mg) obtained was recrystallized from MeOH to give colorless crystals, mp 219–222°. *Anal.* Calcd. for $\text{C}_{27}\text{H}_{48}\text{O}_4$: C, 74.26; H, 11.08. Found: C, 74.07; H, 11.09. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3360 (OH). NMR (pyridine- d_5) δ : 1.58 (s, $\text{C}_{10}\text{-CH}_3$), 0.77 (s, $\text{C}_{13}\text{-CH}_3$). Mass Spectrum m/e : 436 (M^+), 418 ($\text{M}^+\text{-H}_2\text{O}$), 400 ($\text{M}^+\text{-2H}_2\text{O}$), 382 ($\text{M}^+\text{-3H}_2\text{O}$). The tetrol (181.4 mg) was also obtained by hydrolyzing the epoxide (VIIIa, 334 mg) with HClO_4 reagent (18 ml).

Acetonide (Xe): A mixture of VIIIa (525 mg), 70% HClO_4 (0.1 mg), and acetone (15 ml) was allowed to stand at room temperature for 24 hr. After ether was added, the reaction mixture was washed with 5% NaHCO_3 , sat. NaCl, dried over Na_2SO_4 , and evaporated to dryness *in vacuo*. An oily residue (600 mg) was submitted to column chromatography on silica gel (30 g) which was eluted successively with *n*-hexane, benzene-AcOEt (95:5), and benzene-AcOEt (70:30). Fractions of 25 ml were collected and each eluate was examined by TLC. Fract. Nos. 15–22 were combined and evaporated to dryness *in vacuo*. The residue (177 mg) was recrystallized from aq. MeOH to give colorless crystals, mp 180–182° (99 mg). *Anal.* Calcd. for $\text{C}_{30}\text{H}_{52}\text{O}_4$: C, 75.58; H, 11.00. Found: C, 75.70; H, 11.00. NMR (CDCl_3) δ : 4.1–3.7 (3H, $\text{C}_3\alpha\text{-}$, $\text{C}_6\alpha\text{-}$, $\text{C}_7\alpha\text{-H}$), 1.46 (s, acetonide), 1.30 (s, acetonide), 1.16 (s, $\text{C}_{10}\text{-CH}_3$), 0.67 (s, $\text{C}_{13}\text{-CH}_3$).

Oxidation with HIO_4 : A mixture of Xa, $\text{HIO}_4 \cdot 2\text{H}_2\text{O}$ (12 mg), dioxane (0.5 ml), and water (0.05 ml) was allowed to stand at room temperature for 24 hr. The reaction mixture was worked up as usual and gave finally a residue. UV $\lambda_{\text{max}}^{\text{EtOH}}$: 223 nm. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1720 (CO). TLC of the residue, contrary to the highly polar substrate (Xa, $R_f=0.17$), gave only one spot which was less polar ($R_f=0.53$) than that given by cholesterol ($R_f=0.51$).

Compound A (II)—The isolation from the autoxidation mixture of cholesterol was reported previously.⁴⁾ mp 248–250° (from aq. EtOH). Yield: 3%. *Anal.* Calcd. for $\text{C}_{27}\text{H}_{48}\text{O}_4$: C, 74.26; H, 11.08. Found: C, 74.11; H, 10.99. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3360 (OH). NMR (pyridine- d_5) δ : 1.59 (s, $\text{C}_{10}\text{-CH}_3$), 0.79 (s, $\text{C}_{13}\text{-CH}_3$). Mass Spectrum m/e : 418 ($\text{M}^+\text{-H}_2\text{O}$), 400 ($\text{M}^+\text{-2H}_2\text{O}$), 382 ($\text{M}^+\text{-3H}_2\text{O}$).

Triacetate: amorphous powder. NMR (CDCl_3) δ : 5.13, 4.82, 4.74 (3H), 2.09, 2.05, 1.97 (s, 30Ac), 1.12 (s, $\text{C}_{10}\text{-CH}_3$), 0.67 (s, $\text{C}_{13}\text{-CH}_3$). Mass Spectrum m/e : 502 ($\text{M}^+\text{-AcOH}$), 484 ($\text{M}^+\text{-AcOH-H}_2\text{O}$), 442 ($\text{M}^+\text{-2AcOH}$), 424 ($\text{M}^+\text{-2AcOH-H}_2\text{O}$), 382 ($\text{M}^+\text{-3AcOH}$).

Acknowledgement The authors are indebted to H. Harada, T. Kawano, H. Tamura, T. Karihara, and M. Saito for technical assistance and to the staffs of the central analytical laboratory of this Institute for the measurements of NMR and MS spectra. A part of this work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, and Culture, to which the authors' thanks are due.