[Chem. Pharm. Bull. 12 (9) 1066 ~ 1071]

UDC 547.92 : 541.63

# 148. Yasuhiro Morisawa : Steroid Series. XIII.*1 Stereochemistry of B-Nor-5α- and -5β-6-oxocholestane Derivatives.

(*Research Laboratories, Sankyo Co., Ltd.*2)*)

A shielding contribution by a distant group has been recognized to depend on its magnetic anisotropy and the spatial relationship between the groups concerned. The magnitude of the anisotropic effect of the carbonyl group[1] and that of the carbon-carbon single bond[2] have been estimated. The downward shift of angular methyl groups in steroids by introduction of a hydroxyl group into the 1,3-diaxial position[3] 1,4-position*1,4~6) with respect to the methyl group have been observed.

In a preceding paper, the configuration and the conformation of the A-ring in B-nor-6-oxo-5β,8α-steroids were discussed mainly on the basis of the nuclear magnetic resonance spectral data. This paper is concerned with the conformation of A-ring in B-nor-5α,8β- and -5β,8β-cholestane derivatives.

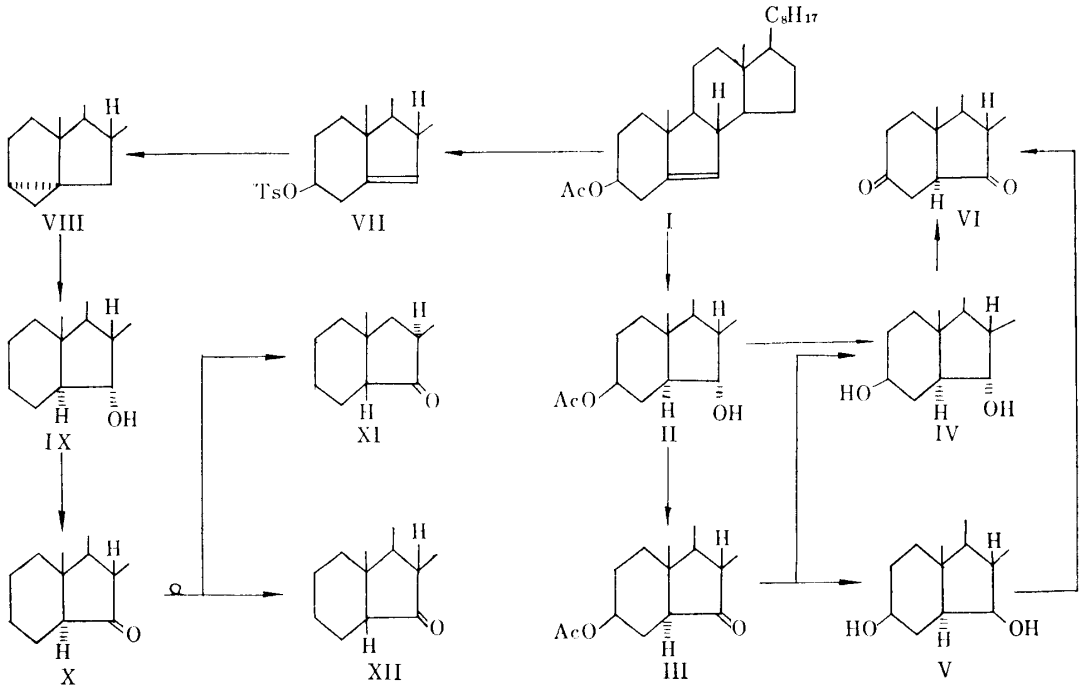


Chart 1.

3β-Acetoxy-B-norcholest-5-ene (I) was treated with sodiumborohydride in acetic acid,[7] followed by oxidation and hydrolysis of the product with hydrogen peroxide and sodium hydroxide to give B-nor-5α-cholestane-3β,6α-diol 3-acetate (II). Oxidation of II

*1 Part XII : This Bulletin, **12**, 1060 (1964).

*2 Nishishinagawa, Shinagawa-ku, Tokyo (森沢靖弘).

1) P. T. Narasimhan, M. T. Rogers : J. Phys. Chem., **63**, 1388 (1959).
2) R. F. Zürcher : Helv. Chim. Acta., **44**, 1755 (1961); J. I. Musher : J. Chem. Phys., **35**, 1159 (1961).
3) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, K. Tsuda : This Bulletin, **10**, 338 (1962).
4) R. F. Zürcher : Helv. Chim. Acta. **44**, 1380 (1961); **46**, 2054 (1963).
5) J. Jacquesy, J. Lehn, J. Levisalles : Bull. soc. chim. France, **1961**, 2444.
6) T. Okamoto, Y. Kawazoe : This Bulletin, **11**, 643 (1963).
7) J. A. Marshall, W. S. Johnson : J. Org. Chem., **28**, 595 (1963).

with chromium trioxide in pyridine or in acetic acid gave 3β-acetoxy-B-nor-5α-cholestan-6-one (Ⅲ), whose synthesis involving treatment of 3β-acetoxy-B-nor-5β-cholestan-5β,6β-epoxide with boron trifluoride-etherate was recently reported by Joska, *et al.*[8] Reduction of Ⅲ with lithium aluminum hydride afforded an epimeric pair of the diols, B-nor-5α-cholestane-3β,6α-diol (Ⅳ) and B-nor-5α-cholestane-3β,6β-diol (Ⅴ). Treatment of Ⅱ with lithium aluminum hydride furnished the same diol (Ⅳ) which was also prepared by Dauben[9] from B-norcholesterol using a hydroboration procedure. Each diol (Ⅳ and Ⅴ) was oxidized to the known B-nor-5α-cholestane-3,6-dione (Ⅵ),[9] indicating diol (Ⅴ) to be epimeric at $C_6$ with diol (Ⅳ). The 18-methyl proton resonance of the monoketone (Ⅲ) and the diketone (Ⅵ) at 9.08 τ, the same as the chemical shifts for the corresponding 5β-isomers,[10] provides further evidence for the assigned 8β-configuration of these two compounds,[8,9] since the spatial relationships between 18-methyl group and 6-carbonyl function are the same in both the 5α- and 5β-series. Furthermore the 8α-configuration was observed to shift the 18-methyl proton resonance toward higher field.*1

The tosylate (Ⅶ)[11] was treated with lithium aluminum hydride to afford 3α,5-cyclo-B-nor-5α-cholestane (Ⅷ).*3 This structure was assigned on the basis of the following observation : the nuclear magnetic resonance spectrum exhibited no vinyl proton signals but complex cyclopropyl proton signals around 9.55～9.80 τ and no end absorption (ε 240 at 220 mμ) was observable in ultraviolet spectrum. In addition the compound (Ⅷ) was found to be recovered on treatment with perphthalic acid. Hydroboration of Ⅷ with lithium aluminum hydride and boron trifluoride-etherate in tetrahydrofuran, followed by treatment with hydrogen peroxide and sodium hydroxide furnished B-nor-5α-cholestan-6α-ol (Ⅸ). The 6α-configuration was deduced from the nuclear magnetic resonance which exhibited no downward shift of 19-methyl protons as compared with 6α-hydroxyl derivatives listed in Table I. The mechanism on hydroboration of Ⅷ is now under investigation. Oxidation of Ⅸ with chromium trioxide in acetic acid or pyridine gave a monoketone (Ⅹ), whose infrared absorption band at 1733 $cm^{-1}$ indicated the presence of a five-membered ring ketone. The stereochemistry was confirmed by isomerization with alkali to the known keto-compound (Ⅻ)[12] with the stable 5β-configuration, and to another known isomeric compound (Ⅺ)[9] with 5β,8α-configuration.

In Table I are shown the 19-methyl proton resonances for 3- and/or 6-substituted B-norcholestane derivatives. All the compounds listed, except B-nor-5α-cholestane-3,6-dione (Ⅵ), B-nor-5β-cholestane-3β,6β-diol (XVI), 3β-hydroxy-B-nor-5β-cholestan-6-one (XVⅡ) and its acetate (XVⅢ), were found to exhibit peaks at 9.07～9.08 τ. These nuclear magnetic resonance data coupled with conformational analysis provided us with information concerning the A-ring conformation of some derivatives listed in Table I.

On the basis of Dreiding model analysis, the predominant chair conformation can be reasonably assigned for the A-ring of the following compounds : 3β-acetoxy-B-nor-5α-cholestan-6-one (Ⅲ), B-nor-5α-cholestane-3β,6α-diol (Ⅳ) and its 3-acetate (Ⅱ), B-nor-5α-cholestan-6α-ol (Ⅸ), B-nor-5α-cholestan-6-one (Ⅹ), and B-nor-5α-cholestan-3β-ol (XⅢ). The 19-methyl proton resonances of the 3β,6α-diol (Ⅳ) and its 3-acetate (Ⅱ) exhibited practically the same chemical shifts at 9.07～9.08 τ as those for the 6α-monool (Ⅸ) and 3β-monool (XⅢ), indicating that the introduction of 3β-hydroxyl, 3β-acetoxyl, or 6α-

*3 The formation of 3α,5-cyclo-5α-cholestane on treatment of cholesterol 3-tosylate with lithium aluminum hydride was described by H. Schmidt, *et al.* (Helv. chim. acta. **32**, 1371 (1949)).

8) J. Joska, J. Fajkoš : Collection Czechoslov. Chem. Communs., **28**, 2605 (1963).
9) W.G. Dauben, G.A. Boswell, Jr., W. Templeton, J.W. McFarland, G.H. Berezin : J. Am. Chem. Soc., **85**, 2302 (1963).
10) J. Joska, J. Fajkoš, F. Šorm : Collection Czechoslov. Chem. Communs., **28**, 82 (1963).
11) W.G. Dauben, G.J. Fonken : J. Am. Chem. Soc., **78**, 4736 (1956).
12) T. Goto : J. Am. Chem. Soc., **82**, 2005 (1960).

Table I. Chemical Shifts of 19-Methyl Protons

| | |
|---|---|
| B-Nor-5α-cholestane-3β,6α-diol 3-acetate (II) | 9.08 |
| 3β-Acetoxy-B-nor-5α-cholestan-6-one (III) | 9.08 |
| B-Nor-5α-cholestane-3β,6α-diol (IV) | 9.07 |
| B-Nor-5α-cholestane-3,6-dione (VI) | 8.93 |
| B-Nor-5α-cholestan-6α-ol (IX) | 9.07 |
| B-Nor-5α-cholestan-6-one (X) | 9.07 |
| B-Nor-5α-cholestan-3β-ol (XIII)[a] | 9.07 |
| B-Nor-5β-cholestan-3β-ol (XIV)[a] | 9.07 |
| B-Nor-5β-cholestane-3β,6α-diol (XV)[b] | 9.08 |
| B-Nor-5β-cholestane-3β,6β-diol (XVI)[b] | 9.01 |
| 3β-Hydroxy-B-nor-5β-cholestan-6-one (XVII)[b] | 8.96 |
| 3β-Acetoxy-B-nor-5β-cholestan-6-ene (XVIII)[b] | 8.95 |
| B-Nor-5β-cholestane-3α,6α-diol (XIX)[c] | 9.08 |
| B-Nor-5β-cholestane 3α,6α-oxide (XX)[d] | 9.08 |

a) The compounds (XIII) and (XIV) were synthesized according to the method of Dauben, *et al.*[9]
b) The compounds (XV) and (XVI) were synthesized according to the method of Joska, *et al.*[10]
c) The compound (XIX) was synthesized according to the method of Fajkoš, *et al.*[13]
d) The compound (XX) was synthesized according to the method of Dauben, *et al.*[14]

hydroxyl group into B-nor-5α-cholestane exert practically no influence to the 19-methyl proton shift. Replacement constants of a 3β-hydroxyl and 3β-acetoxyl groups for the 19-methyl proton resonance, described by Jacquesy[5] and Zürcher[4] in the 5α- and 5β-steroids, were not observed in the B-nor-5α-cholestane derivatives as listed in Table I. It is well established that the proton lying in conical regions extending above and below the plane of the carbonyl group shows upward shift, while that lying elsewhere exhibits downward shift.[15,16] The 19-methyl protons of 3β-acetoxy-B-nor-5α-cholestan-6-one (III) and its 3-deoxy derivative (X) showed practically the chemical shifts at 9.07~9.08 τ as those for the 6α-hydroxyl derivatives (II and IX). This can be rationalized by considering that the 19-methyl protons of 6-oxo compounds (II and X) lie on a borderline zone of the shielding, deshielding cone of the 6-carbonyl group. Measurement of Dreiding models shows that the 19-methyl groups of III and X are located approximately at the angle $\theta=57°$ and the distance $\gamma=3.6$Å as shown in Chart 2.

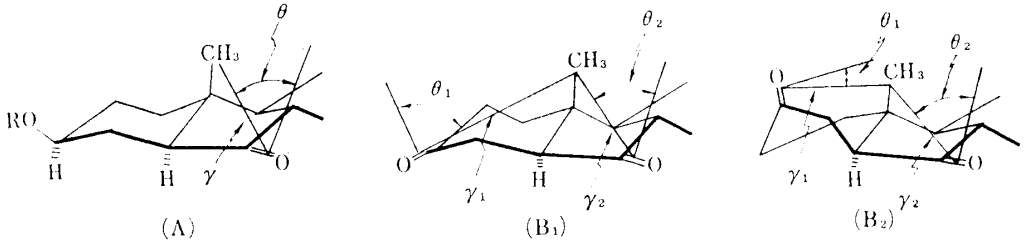


Chart 2.

The 19-methyl proton resonance of B-nor-5α-cholestane-3,6-dione (VI) appears at 8.93 τ, lowfield by 0.15 p.p.m. as compared with that of 3β-acetoxy-B-nor-5α-cholestan-6-one (III). The possible two conformations and the corresponding distances (γ) and angles (θ) between 19-methyl and 3- or 6-carbonyl group are shown in Chart 2.

13) J. Fajkoš, J. Joska, J. Pitha, F. Šorm : Collection Czechoslov. Chem. Communs., 28, 2337 (1963).
14) W. G. Dauben, G. A. Boswell, Jr., W. Templeton, J. W. McFarland, G. H. Berezin : J. Am. Chem. Soc., 85, 1672 (1963).
15) J. M. Jackmann : "Application of NMR Spectroscopy in Organic Chemistry," Pergamon Press, London 1959, p. 122.
16) D. H. Williams, N. S. Bhacca, C. Djerassi : J. Am. Chem. Soc., 85, 2810 (1963).

Dreiding model analysis shows that the sterical situation of the 19-methyl group with respect to the 6-carbonyl function of the dione (Ⅵ) is the same as in the case of 3$\beta$-acetoxy-B-nor-5$\alpha$-cholestan-6-one (Ⅲ). Accordingly the lowfield shift observed for the 19-methyl proton resonance of the dione (Ⅵ) must arise from a deshielding effect due to the 3-carbonyl function. In the A-ring boat conformation ($B_2$), the 3-carbonyl function of Ⅵ with $\theta_1=25°$ should induce a considerable upward shift of the 19-methyl proton resonance by its shielding effect. The 19-methyl protons ($\gamma_1=3.8$Å, $\theta_1=76°$) in the A-ring chair conformation ($B_1$) is situated in the deshielding field of the 3-carbonyl function, therefore the A-ring of B-nor-5$\alpha$-cholestane-3,6-dione (Ⅵ) should be in a chair conformation.

The 19-methyl proton resonances in 3$\beta$-hydroxy-B-nor-5$\beta$-cholestan-6-one (XVII) and its acetate (XVIII) appears at 8.96 and 8.95 $\tau$, respectively.

Zürcher[4] observed that the 19-methyl proton shifts of 5$\beta$-steroids appear at a lower field than those of the corresponding 5$\alpha$-steroids and he attributed these differences of the chemical shifts to the anisotropy of the carbon-carbon single bonds of the A-ring. It is interesting to note, however, that in B-norcholestane derivatives the 19-methyl proton resonances of the 5$\alpha$-series (Ⅱ, Ⅲ, Ⅳ, Ⅸ, X, and XIII) with the A-ring chair conformation showed the same chemical shifts at 9.07~9.08 $\tau$ at those for B-nor-5$\beta$-cholestan-3$\beta$-ol (XIV), B-nor-5$\beta$-cholestane-3$\beta$,6$\alpha$-diol (XV), B-nor-5$\beta$-cholestane-3$\alpha$,6$\alpha$-diol (XIX) and B-nor-5$\beta$-cholestane 3$\alpha$,6$\alpha$-oxide (XX), the latter two possess a downward boat conformation in the A-ring.[13,14]

The lower shift of the 19-methyl proton resonance by 0.11~0.12 p.p.m. in XVII and XVIII, therefore, must be caused by the anisotropic effect of the 6-carbonyl group, not by the removal of the anisotropic effect of the carbon-carbon single bonds in the A-ring by changing the configuration 5$\alpha$ into 5$\beta$. The large lowfield values observed cannot be expected merely by the steric interaction between the 19-methyl group and 3$\beta$-substituents when the negative replacement constants of 3$\beta$-substituents proposed by Zürcher were taken into consideration.

An analysis of Dreiding models of 3$\beta$-hydroxy-B-nor-5$\beta$-cholestan-6-one (XVII) and its acetate (XVIII) reveals four possible conformations for A-ring to exist as shown in Chart 3. However conformation ($C_4$) is the least probable due to the molecular ring-strain. In conformation ($C_1$) the 19-methyl group is located approximately at $\gamma=3.70$Å and $\theta=60°$ with the 6-carbonyl function and the geometrical relationships between the two groups are almost the same as in the case of 3$\beta$-acetoxy-B-nor-5$\alpha$-cholestan-6-one (Ⅲ), no anisotropic effect of the 6-carbonyl group to the 19-methyl protons being expected. In conformation ($C_2$) and ($C_3$) the distance and the angle of the 19-methyl group with respect to the 6-carbonyl function measured approximately 4.0Å and 70°.

Only conformation ($C_2$) and ($C_3$) can explain the lowfield shift of the 19-methyl protons in 3$\beta$-hydroxy-5$\beta$-cholestan-6-one (XVII) and its acetate (XVIII) as a result of the paramagnetic effect of the carbonyl function.

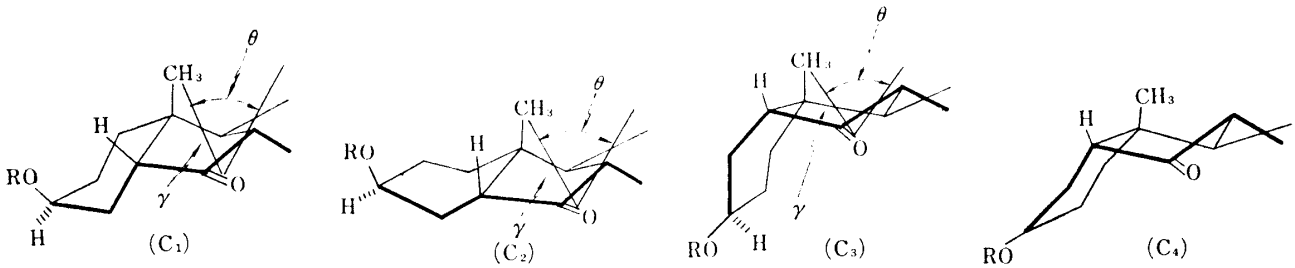


Chart 3.

The 3α-proton resonance of 3β-acetoxy-B-nor-5β-cholestan-6-one (XVIII) appeared at 4.96 τ, while the axial 3α-proton of the corresponding 5α-compound (III) exhibits a signal at 5.16 τ. The 3α-proton in conformation ($C_3$) is axially oriented and situated in the diamagnetic field due to the 6-carbonyl function and therefore it should give the same or a somewhat higher field chemical shift than 5.16 τ of the 3α-proton in III. The observed shift as 4.96 τ would be consistent with the equatorial 3α-proton of conformation ($C_2$).

## Experimental*4

The NMR spectra were obtained in about 10% $CDCl_3$ solutions of the steroids containing a trace of tetramethylsilane as an internal standard, with a Varian Associates DP-60 NMR spectrometer, operating at 60 Mc.p.s. The chemical shifts are given in τ-value.

**B-Nor-5α-cholestane-3β,6α-diol 3-Acetate (II)**——Tetrahydrofuran (15 ml.) containing AcOH (3 ml.) was added to a stirred suspension of $NaBH_4$ (1.25 g.) and B-norcholestan-3β-ol 3-acetate (I; 5 g.) in tetrahydrofuran (50 ml.) at 50° over a period of 1 hr. under $N_2$. The mixture was stirred at the same conditions for additional 4 hr. to the cooled mixture at 10° were very carefully added 10% aq. KOH solution (21 ml.) and 30% $H_2O_2$ (7 ml.) and the mixture was stirred for 1 hr. at room temperature, diluted with $H_2O$ and extracted with $Et_2O$. The extract was washed with $H_2O$ until neutral, and dried-over $Na_2SO_4$. The solvent was removed and the crystalline residue was chromatographed over neutral alumina (grade III; 120 g.). Elution with hexane gave the starting material (1.70 g.), the second eluate with hexane-benzene (8:2) afforded a crystalline product (0.21 g.), m.p. 204~206° which was not identified, and the third one with benzene gave B-nor-5α-cholestane-3β,6α-diol 3-acetate (IIa; 2.89 g.), needles of m.p. 126~127°, $[\alpha]_D^{29}$ 0° after recrystallization from MeOH. *Anal.* Calcd. for $C_{28}H_{48}O_3$: C, 77.72; H, 11.18. Found: C, 77.70; H, 10.95. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3570 (OH), 1718, 1273 (OAc).

**Oxidation of B-Nor-5α-cholestane-3β,6α-diol 3-Acetate**——i) A solution of II (500 mg.) in pyridine (10 ml.) was treated with $CrO_3$ (500 mg.)-pyridine complex solution (20 ml.) at room temperature for 10 hr. The mixture was poured into ice-water and extracted with $Et_2O$. The ethereal solution was washed consecutively with dil. AcOH, dil. $NaHCO_3$ solution and $H_2O$ until neutral. After evaporation of the solvent, the residue was crystallized from MeOH to give needles (479 mg.) of 3β-acetoxy-B-nor-5α-cholestan-6-one (IIIa), m.p. 91°, $[\alpha]_D^{25}$ +89.2° (c=2.11). *Anal.* Calcd for $C_{28}H_{46}O_3$: C, 78.09; H, 10.77. Found: C, 78.12; H, 10.64. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1740 (6-CO, OAc), 1250, 1046 (OAc).

ii) A solution of II (100 mg.) in AcOH (10 ml.) was treated with a solution of $CrO_3$ (30 mg.) in a small amount of $H_2O$ at room temperature for 1.0 hr. The reaction mixture was diluted with $H_2O$, extracted with $Et_2O$. The extract was washed with dil. $NaHCO_3$ solution, $H_2O$ and dried over $Na_2SO_4$. Evaporation of the solvent afforded a crystalline product, which was recrystallized from MeOH to give plates of m.p. 90~91°. Its IR spectrum was found to be superimposable with IIIa.

**Reduction of 3β-Acetoxy-B-nor-5α-cholestan-6-one**——A solution of III (200 mg.) in anhyd. $Et_2O$ (20 ml.) was treated with $LiAlH_4$ (50 mg.) for 1 hr. After the excess reagent was decomposed with $H_2O$, the mixture was shaken with $Et_2O$. The extract was worked up as usual and the products was chromatographed over neutral alumina (III; 15 g.). Elution with benzene-$Et_2O$ (1:1) gave B-nor-5α-cholestane-3β,6α-diol (IV; 63 mg.) of m.p. 196°, $[\alpha]_D^{25}$ +9.0° (c=1.1), after recrystallized from hexane (lit.,[8] m.p. 191~192°, $[\alpha]_D^{20}$ +7.4°). *Anal.* Calcd. for $C_{26}H_{46}O_2$: C, 79.94; H, 11.87. Found: C, 79.60; H, 11.82. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3490, 3240 (OH). Elution with $Et_2O$ gave B-nor-5α-cholestane-3β,6β-diol (V), needles of m.p. 183°, after recrystallization from hexane. *Anal.* Calcd. for $C_{26}H_{46}O_2 \cdot H_2O$: C, 76.41; H, 11.84. Found: C, 76.54; H, 12.11. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3330, 3100 (OH).

**B-Nor-5α-cholestane-3β,6α-diol (IV)**——A solution of II (240 mg.) in $Et_2O$ (30 ml.) was set aside with $LiAlH_4$ (100 mg.) at room temperature for 3 hr. The ethereal solution was washed consecutively with dil. AcOH, dil. $NaHCO_3$ solution, $H_2O$ and dried over $Na_2SO_4$. Evaporation of the solvent to give a crystalline residue (230 mg.), which was recrystallized from hexane to give B-nor-5α-cholestane-3β,6α-diol (IV) of m.p. 195° as sticks. The IR spectrum was identical with that of the sample obtained above.

**B-Nor-5α-cholestane-3,6-dione (VI)**——A solution of IV (50 mg.) in acetone (20 ml.) was treated with Jones' reagent[17,18] (0.1 ml.) at −35° for 20 min. under $N_2$. The excess reagent was decomposed with MeOH and the mixture was diluted with $H_2O$ and extracted with $Et_2O$. The product was recrystallized

*4 All melting points were uncorrected. Rotations were measured in $CHCl_3$ solution. IR spectra were determined using a Perkin-Elmer model 21 spectrophotometer.

17) K. Bowden, I. M. Heilbron, E. R. H. Jones, B. C. L. Weedon: J. Chem. Soc., **1946**, 39

18) C. Djerassi, R. R. Engle, A. Bowers: J. Org. Chem., **21**, 1547 (1956).

from MeOH to give B-nor-5$\alpha$-cholestane-3,6-dione (VI; 38 mg.), m.p. 140~141°, $[\alpha]_D^{26}$ +159° (c=2.31) (lit.[9] m.p. 138~140°, $[\alpha]_D^{0}$ +129° (c=1.09)), which was identical with the substance prepared from the diol (V) by the same procedure as for IV. *Anal.* Calcd. for $C_{26}H_{42}O_2$: C, 80.77; H, 10.95. Found: C, 80.68; H, 10.96. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1735 (6-CO), 1710 (3-CO).

**3$\alpha$,5-Cyclo-B-nor-5$\alpha$-cholestane (VIII)**——A solution of B-norcholesterol tosylate[11] (VII; 3.80 g.) in $Et_2O$ (250 ml.) was refluxed with $LiAlH_4$ (3.5 g.) for 6 hr. The excess reagent was decomposed with $H_2O$ and washed with 3% AcOH, 3% $NaHCO_3$ solution and $H_2O$ until neutral. After drying the extract over $Na_2SO_4$, the solvent was removed and the residue was recrystallized from $Et_2O$-MeOH to give 3$\alpha$,5-cyclo-B-nor-5$\alpha$-cholestane (VIII; 2.10 g., 81.7%) of m.p. 109~110° as needles, $[\alpha]_D^{25}$ −24.5° (c=3.545). *Anal.* Calcd. for $C_{26}H_{44}$: C, 87.56; H, 12.44. Found: C, 87.44; H, 12.33.

**B-Nor-5$\alpha$-cholestan-6$\alpha$-ol (IX)**——A mixed solution of 3$\alpha$,5-cyclo-B-nor-5$\alpha$-cholestane (VIII; 1.50 g.) and $BF_3$-etherate (2.20 g.) in anhyd. tetrahydrofuran (50 ml.) was added to a stirred suspension of $LiAlH_4$ (0.45 g.) in anhyd. tetrahydrofuran (30 ml.) in a period of 1 hr. under $N_2$. Stirring was continued at room temperature for an additional 1 hr. To the mixture was added 10% aq. NaOH (8 ml.) and 30% $H_2O_2$ (2.5 ml.) and the solution stirred for half an hour. The solution was poured into ice-water and extracted with $Et_2O$. The ethereal solution was worked up as usual. The residue was chromatographed over alumina (grade III; 60 g.). Elution with hexane gave the starting material of m.p. 109° (836 mg.) and the second elution with the same solvent gave B-nor-5$\alpha$-cholestan-6$\alpha$-ol (IX; 550 mg.) needles of m.p. 134°, $[\alpha]_D^{25}$ +0.8° (c=1.220), after recrystallization from MeOH. *Anal.* Calcd. for $C_{26}H_{46}O$: C, 83.35; H, 12.38. Found: C, 83.31; H, 12.22. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3540 (OH).

**B-Nor-5$\alpha$-cholestan-6-one (X)**——i) A solution of B-nor-5$\alpha$-cholestan-6$\alpha$-ol (IX; 150 mg.) in pyridine (5 ml.) was treated with $CrO_3$ (150 mg.)-pyridine (5 ml.) complex at room temperature for 16 hr. The solution was poured into ice-water and extracted with $Et_2O$, which was washed with dil. AcOH, dil. $NaHCO_3$ solution and $H_2O$. The extract, after removal of the solvent afforded a syrupy substance, which was crystallized from MeOH to give needles of B-nor-5$\alpha$-cholestan-6-one (X), m.p. 130~131°, $[\alpha]_D^{25}$ +108.5° (c=2.095). *Anal.* Calcd. for $C_{26}H_{44}O$: C, 83.80; H, 11.90. Found: C, 84.07; H, 11.99. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1730 (6-CO).

ii) A solution of IX (50 mg.) in AcOH (10 ml.) was treated with aq. $CrO_3$ solution (20 mg.) at room temperature for 16 hr. The excess reagent was decomposed with MeOH. The solution was diluted with $H_2O$ and extracted with $Et_2O$. The extract was washed with dil. $NaHCO_3$ solution, $H_2O$, and dried over $Na_2SO_4$. Evaporation of the solvent and recrystallization of the residue from MeOH gave 43 mg. of B-nor-5$\alpha$-cholestan-6-one (X) of m.p. 130°. The IR spectrum was identical with that of the product obtained above.

**Isomerization of B-Nor-5$\alpha$-cholestan-6-one**——A solution of B-nor-5$\alpha$-cholestan-6-one (X; 50 mg.) in MeOH (10 ml.) was refluxed with a solution of KOH (100 mg.) in $H_2O$ (1 ml.) for 15 min. The mixture was diluted with $H_2O$, extracted with $Et_2O$. The product from the extract was chromatographed over alumina (grade III; 15 g.). Elution with hexane-benzene (95:5) gave B-nor-5$\beta$,8$\alpha$-cholestan-6-one (XI; 23 mg.),[9] $[\alpha]_D^{24}$ −50.0° (c=1.94) as a syrupy substance which failed to crystallize. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1733 (6-CO). The second elution with hexane-benzene (9:1) gave B-nor-5$\beta$,8$\beta$-cholestan-6-one (XII; 15 mg.),[12] m.p. 98°, $[\alpha]_D^{24}$ +31.2° as needles after recrystallization from MeOH. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1735 (6-CO).

The author wishes to express his gratitude to Prof. K. Tsuda of the Institute of Applied Microbiology, University of Tokyo, and to Mr. M. Matsui, Director of this Laboratory, for their kind encouragements and to Dr. Y. Kishida for his helpful discussion. The author is also indebted to Dr. T. Onoe, Messrs. K. Ono, H. Nagashima, H. Higuchi, and T. Fujimura, and to Misses N. Sawamoto, K. Saito, M. Gonda and H. Masuda, all of this Laboratory, for elemental analysis and spectral measurements.

## Summary

A-Ring conformations in B-nor-5$\alpha$-cholestane-3$\beta$,6$\alpha$-diol (IV), the 3$\beta$-monoacetate (II), the 3,6-dione (VI), 3$\beta$-acetoxy-B-nor-5$\alpha$- and -5$\beta$-cholestan-6-one (III, XVIII) and 3$\beta$-hydroxy-B-nor-5$\beta$-cholestan-6-one (XVII) were discussed on the basis of evidence obtained from nuclear magnetic resonance spectra and conformational analysis.

(Received April 8, 1964)