gave 2.46 g. of the N-acetate (Xb) as colorless needles, m.p. 282~284°(decomp.). $[\alpha]_D^{23.5}$ +113.2±2° (c=1.023, pyridine). *Anal.* Calcd. for $C_{22}H_{28}O_2N_2S$: C, 68.72; H, 7.34; N, 7.29; S, 8.34. Found: C, 68.71; H, 7.46; N, 7.38; S, 8.55. UV $\lambda_{max}^{95\%\ EtOH}$ mμ (ε): 241 (18,800), 287 (11,430). IR ν_{max}^{Nujol} cm^{-1}: 3230, 3068, 1694, 1665, 1616, 1552.

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Summary

2′-Methylthiazolo[5′,4′-16.17]androsta-15,16-dien-3β-ol (Ⅷ) was prepared by an established method from 3β-acetoxy-16β-bromoandrost-5-en-17-one (Ⅵ) and thioacetamide. Consequently the aromatic compound (Ⅳ) which was obtained by dehydration of the by-product (Ⅲ) of the Beckmann rearrangement of the oxime-mixture (Ia) and (Ib) of 3β-acetoxy-17α-hydroxy-16β-thiocyanatopregn-5-en-20-one and which was assigned an uncorrect thiazol structure (Ⅷ) in the previous paper, should be 3′-methylisothiazolo[5′,4′-16,17]androsta-5,16-dien-3β-ol acetate. 2′-Amino-16,17-disubstituted thiazolo-compound was also prepared from (Ⅵ) and thiourea.

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194. Katsumi Tanabe and Ryozo Hayashi: Steroid Series. IX.[1] A New Route to 6-Nitrosteroid Derivatives.

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Although many examples of the addition of nitrosyl chloride to the carbon-carbon double bond of a large variety of compounds are reported in the literature, there has been no report of such a reaction in the steroid field. In this paper the authors wish to describe the addition of nitrosyl chloride to the steroidal double bond at the 5,6-position and the conversion of the adducts to 6-nitrosteroid derivatives.

Cholesterol acetate (Ia) was treated in carbon tetrachloride solution with excess of nitrosyl chloride to give a crystalline product (Ⅱa) of m.p. 140~141° in a high yield, which showed a positive Beilstein test and exhibited a characteristic absorption band for a nitro alkane group at 1553 cm^{-1} in the infrared region.[2] Its analytical values correctly corresponded with the composition of $C_{29}H_{48}O_4NCl$. On treatment with either pyridine or alumina, (Ⅱa) was smoothly converted into the known 6-nitrocholesterol acetate (Ⅲa) of m.p. 102~104°, $[\alpha]_D$ −78.4°. When treated with zinc dust in acetic acid-ether, the compound (Ⅱa) was found to eliminate readily the chloro-nitro group to regenerate cholesterol acetate (Ia) in an almost quantitative yield. From these observations the structure 5-chloro-6β-nitro-5α-cholestan-3β-ol acetate was assigned to the product, the stereochemical assignment being based on the following considerations.

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1) Part Ⅷ: This Bulletin, **10**, 445 (1962).

2) L. J. Bellamy: "The Infrared Spectra of Complex Molecules," 298 (1958). John Wiley & Sons, Inc., New York.

The formation of nitro derivative from nitrosyl chloride involves oxidation of the initially formed nitroso compound in the presence of excess reagent.

The infrared absorption band due to the 3β-hydroxyl stretching vibration of (Va), the acidic hydrolytic product of (IIa), was found to occur at 3629 cm^{-1} in dilute carbon tetrachloride solution, which had exactly the same location as that of 5α-cholestan-3β-ol.*2 This suggested that the 5-chloro substituent in (Va) must possess the α-configuration, since the epimeric 5β-chloro compound would be expected, as pointed out by Nickon,[3] to lower the frequency to some extent due to the intramolecular hydrogen bonding between those two groups.

It is well established that addition of bromine[4] or hypochlorous acid[5] to the steroidal C_5-double bond affords the *trans*-diaxial (i.e. 5α,6β) product and the groups introduced are readily eliminated on treatment with zinc dust in acetic acid to reproduce the parent ethylenic linkage. The analogous elimination behavior of (IIa) under similar conditions would indicate the C_6-nitro substituent to be β-orientated as shown.

That both chloro and nitro groups in (Va) retained the same configurations as those of the acetate (IIa) was indicated by the same order of a large negative rotation contribution resulting from the two groups as compared with the corresponding 5α-H compound (cf. Table I).

Table I.

Compound	$[M_D]$ (5α-Cl, 6β-NO_2)	$[M_D]$ (5α-H)	$\Delta[M_D]$
5α-Cholestan-3β-ol acetate	−421[a]	+ 56[b]	−478
5α-Cholestan-3β-ol	−351[a]	+ 89[b]	−440
3β-Hydroxy-5α-androstan-17-one acetate	−270[a]	+219[b]	−489
3β-Hydroxy-5α-androstan-17-one	−222[a]	+261[b]	−483

a) This paper
b) J.P. Mathieu and A. Petit: "Pouvoir Rotatoire Naturel. 1. Steroides," (1956). Masson & Co., Paris.

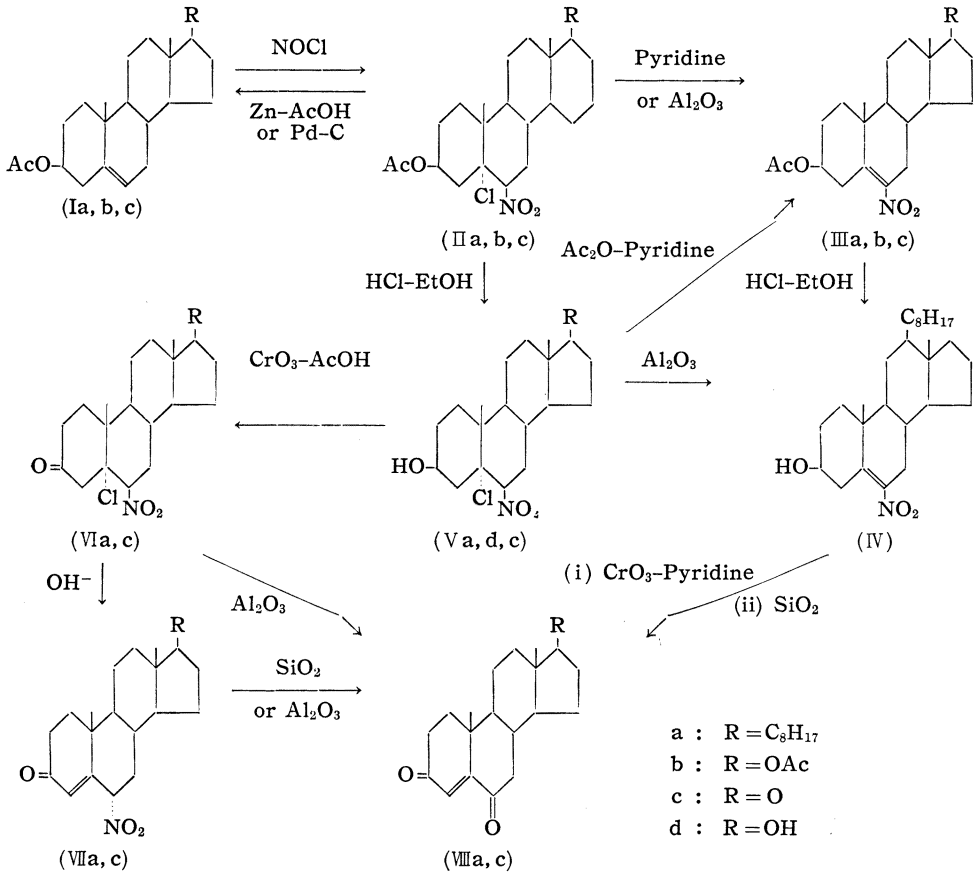
The acetate (IIa) was subjected to catalytic hydrogenation in the presence of palladium carbon in ethanol containing a small amount of benzene. The absorption of hydrogen occurred smoothly until three equivalent moles had been consumed. The product isolated, however, was not the expected 6-amino derivative but the mixture of cholesterol acetate (Ia) and ammonium chloride. The result suggested that hydrogenation over palladium-carbon catalytically eliminated the chloro-nitro group from (IIa) and the liberated group was then further reduced to ammonium chloride. This reaction is reminiscent of the formation of cholest-5-ene accompanied by 5α-chlorocholestane on treatment of 5-chloro-6β-iodo-5α-cholestane under a similar condition.[6] It is noteworthy that, when this reaction was carried out in a non-polar solvent such as hexane or in ethanol containing a few drops of hydrochloric acid, no absorption of hydrogen took place and only the starting material was recovered.

5-Chloro-6β-nitro-5α-cholestan-3β-ol (Va) prepared by hydrolysis of (IIa) with hydrochloric acid in ethanol was converted to 6-nitrocholesterol acetate (IIIa) with concomitant elimination of hydrogen chloride on acetylation with acetic anhydride in

*2 Spectra were taken on a Perkin-Elmer double beam recording spectrophotometer, Model 21, equipped with a sodium chloride prism in highly diluted carbon tetrachloride solution (2×10^{-3} molar) in order to eliminate intermolecular effects. Chart-scale of 10 cm. μ was used, with very slow scanning.

3) A. Nickon: J. Am. Chem. Soc., **79**, 243 (1957).
4) L.F. Fieser, M. Fieser: "Steroids," 38 (1959). Reinhold Publ. Corp., New York.
5) S. Mori: Nippon Kagaku Zasshi, **71**, 600 (1950).
6) C.W. Shoppee, R. Lack: J. Chem. Soc., **1960**, 4864.

pyridine. On passing through a column of alumina the compound (Va) yielded 6-nitrocholestrol (IV) which was identical with the substance obtained by hydrolysis of (IIIa) with hydrochloric acid in ethanol.



Oxidation of (Va) with chromium trioxide in acetic acid gave 5-chloro-6β-nitro-5α-cholestan-3-one (VIa), which furnished an amorphous product when treated in a basic medium, e.g. potassium hydroxide in methanol, potassium acetate in ethanol, and pyridine. The crude substance thus obtained exhibited infrared absorption band at 1690, 1625, and 1555 cm^{-1} attributable to a 6-nitro-Δ^4-3-ketone system, in addition to a weak band at 1520 cm^{-1} indicating the presence of a small quantity of material having a nitro-olefin structure (cf. IV). An absorption maximum at 247~250 mμ (ε<7,000) in the ultraviolet region suggested the presence of a third substance with a Δ^4-3,6-diketone system. Chromatographic separation of this mixture on silica gel afforded 6α-nitrocholest-4-en-3-one (VIIa) and cholest-4-ene-3,6-dione (VIIIa). The above mentioned nitro-olefin could not be isolated. It was apparently changed into (VIIIa) during chromatography. This was supported when 6-nitrocholesterol (IV) was oxidized with chromium trioxide-pyridine complex followed by chromatography of the product on silica gel to afford the compound (VIIIa). The latter compound was also formed from both (VIa) and (VIIa) on passing through a column of alumina or silica gel. Thus, the 3-oxo-Δ^{4or5}-6-nitro structure appears to suffer catalytic hydrolysis during chromatography.

The structure of 6α-nitrocholest-4-en-3-one (VIIa) was based on a strong band in the infrared at 1558 cm^{-1} characteristic of a nitro-alkane group, the doublet at 1692

and 1626 cm^{-1} due to the Δ^4-3-ketone chromophore, and a maximum at 233 mμ (ε 13,900) in the ultraviolet spectrum. The 6α-stereochemistry was tentatively assigned by analogy with the corresponding derivative (VIIc) of the androstane series with the established 6α-nitro substituent obtained by similar procedures as described below.

A similar series of reactions starting from androst-5-ene-3β,17β-diol diacetate (Ib) and 3β-hydroxyandrost-5-en-17-one acetate (Ic) proceeded through intermediates (IIb) and (Vd), (IIc) and (Vc), respectively, to the same 5-chloro-6β-nitro-5α-androstane-3,17-dione (VIc). Contrary to the cholestane series, the chloro-nitro compound (VIc), on alkaline treatment, afforded the known 6α-nitroandrost-4-en-3-one (VIIc)[7] as a homogenous product, which after purification had m.p. 197~198° and displayed bands in the infrared region at 1736 (17-CO), 1675, 1617 (Δ^4-3-ketone), 1558 cm^{-1} (nitro-alkane group) and in the ultraviolet region at 230 mμ (ε 16,800).

The stability under mild alkaline conditions as well as the characteristic positive specific rotation of (VIIc) as compared with the epimeric 6β-nitro derivative[7] indicates that it has the stable 6α(equatorial)-configuration, whose formation from (VIc) with the 6β-substituent can well be explained by the inversion of the group upon mild alkaline treatment.

An attempt to prepare the 6-amino derivative from 5α-nitro compound (VIIc) by catalytic hydrogenation using palladium-carbon ended in failure, no hydrogen being absorbed and the starting material being recovered unchanged.

On passing through an alumina column, (VIIc) was converted into androst-4-ene-3,6,17-trione (VIIIc) as yellow crystals of m.p. 224.° Treatment of (IIb) with alumina and (IIc) with pyridine yielded 6-nitroandrost-5-ene-3β,17β-diol diacetate (IIIb) and 3β-hydroxy-6-nitroandrost-5-en-17-one acetate (IIIc), respectively.

Experimental*3

5-Chloro-6β-nitro-5α-cholestan-3β-ol Acetate (IIa)——To a solution of 2.2 g. of cholestreol acetate (Ia) in 50 cc. of dehyd. CCl_4, 14 g. of 25% NOCl-CCl_4 solution (10 mol. equiv. of NOCl) was added at −20° and the mixture was allowed to stand at 0~3° for 5 days in a dark place. The solvent and excess reagent were removed under a reduced pressure to leave a white amorphous product, which gave a crystalline mass of m.p. 134~137° by trituration with small amounts of EtOH. Yield, 2.5 g. (92%). Recrystallization from EtOH afforded 5-chloro-6β-nitro-5α-cholestan-3β-ol acetate (IIa) as leaflets, m.p. 140~141°, $[\alpha]_D^{28}$ −82.6° (c=1.53). *Anal.* Calcd. for $C_{29}H_{48}O_4NCl$: C, 68.27; H, 9.48; N, 2.74; Cl, 6.95. Found: C, 68.42; H, 9.02; N, 3.11; Cl, 6.98. IR λ_{max}^{Nujol} cm^{-1}: 1740 (AcO), 1553 (NO_2-alkane).

6-Nitrocholest-5-en-3β-ol Acetate (IIIa)——(i) A solution of 0.76 g. of 5-chloro-6β-nitro-5α-cholestan-3β-ol acetate (IIa) in 6 cc. of dehyd. pyridine after being leftr standing overnight at room temperature was poured into ice-water, neutralized with 2*N* HCl, and extracted with Et_2O. The extract was washed with H_2O, dried, and the solvent was evaporated to give crystals of m.p. 92~98°. Recrystallization from EtOH gave 6-nitrocholest-5-en-3β-ol acetate (IIIa) as needles, m.p. 102~103°, $[\alpha]_D^{26}$ −78.4° (c=1.18) (reported m.p. 104°,[8] $[\alpha]_D$ −80°). Yield, 0.67 g. (95%). *Anal.* Calcd. for $C_{29}H_{47}O_4N$: C, 73.53; H, 10.00; N, 2.96. Found: C, 73.83; H, 9.69; N, 3.21. UV λ_{max}^{EtOH}: 257 mμ (ε 2,180). IR λ_{max}^{Nujol} cm^{-1}: 1748 (AcO), 1520 (NO_2-alkene).

(ii) A solution of 0.2 g. of (IIa) in benzene was passed through a column of Al_2O_3 (12 g; woelm, grade IV). The eluate with the same solvent gave (IIIa) of m.p. 96~100° in a quantitative yield. After recrystallization from EtOH it melted at 102~104°.

(iii) A mixture of 60 mg. of 5-chloro-6β-nitro-5α-cholestan-3β-ol (Va), 3 cc. of pyridine, and 2 cc. of Ac_2O was set aside for 20 hr. at room temperature, poured into ice-water, and neutralized with 2*N* HCl. The Et_2O extract afforded 67 mg. of (IIIa), which melted at 102~104° after recrystallization from EtOH.

*3 All melting points were uncorrected. Rotations were measured in $CHCl_3$ solution except where noted.

7) A. Bowers, M.B. Sánchez, H.J. Ringold: J. Am. Chem. Soc., 81, 3702 (1959).
8) L.F. Fieser, M. Fieser: "Steroids," 44 (1959). Reinhold Publ. Corp., New York.

5-Chloro-6β-nitro-5α-cholestan-3β-ol (Va)——A solution of 0.4 g. of 5-chloro-6β-nitro-5α-cholestan-3β-ol acetate (IIa), 100 cc. of EtOH, and 10 cc. of conc. HCl was allowed to stand for 40 hr. at room temperature. Most of EtOH was removed under a reduced pressure to leave 0.37 g. of 5-chloro-6β-nitro-5α-cholestan-3β-ol (Va). After one recrystallization from EtOH it melted at 98~104°, $[\alpha]_D^{27}$ −75.9°(c=1.26). *Anal.* Calcd. for $C_{27}H_{46}O_3NCl$: C, 69.27; H, 9.91; N, 2.99; Cl, 7.58. Found: C, 69.28; H, 9.99; N, 3.19; Cl, 7.43. IR λ_{max}^{Nujol} cm^{-1}: 3480 (OH), 1556 (NO_2-alkane).

6-Nitrocholest-5-en-3β-ol (IV)——(i) A solution of 50 mg. of 5-chloro-6β-nitro-5α-cholestan-3β-ol (Va) in Et_2O was passed through a column of Al_2O_3 (7 g.; Woelm, grade III). The Et_2O eluate, after removal of the solvent, gave 40 mg. of a residue, which was recrystallized from MeOH-H_2O to afford 6-nitrocholest-5-en-3β-ol (IV) as leaflets of m.p. 122~124°. *Anal.* Calcd. for $C_{27}H_{45}O_3N$: C, 75.13; H, 10.51; N, 3.25. Found: C, 75.27; H, 10.40; N, 3.26: UV λ_{max}^{EtOH}: 262 mμ (ε 2,020). IR λ_{max}^{Nujol} cm^{-1}: 3330 (OH), 1518 (NO_2-alkene).

(ii) A mixture of 0.329 g. of 6-nitrocholest-5-en-3β-ol acetate (IIIa), 100 cc. of EtOH, and 10 cc. of conc. HCl was left to stand for 20 hr. at room temperature, condensed to a small volume, and diluted with H_2O. The Et_2O extract was washed with H_2O, dried, and the solvent was evaporated to give 6-nitrocholest-5-en-3β-ol (IV), which melted at 119~121° after one recrystallization from EtOH-H_2O. Yield, 0.128 g. Identity was confirmed by mixed melting point and comparison of IR spectra with the sample obtained as above.

5-Chloro-6β-nitro-5α-cholestan-3-one (VIa)——A solution of 75 mg. of CrO_3 in 5 cc. of 90% AcOH was added dropwise to a stirred solution of 234 mg. of 5-chloro-6β-nitro-5α-cholestan-3β-ol (Va) in 70 cc. of AcOH at 15°, and the mixture was left to stand for 5.5 hr. at room temperature. After decomposition of the excess reagent by addition of 4 cc. of EtOH, the solvent was removed under a reduced pressure. The residue was triturated with small amounts of EtOH to yield 185 mg. of 5-chloro-6β-nitro-5α-cholestan-3-one (VIa) of m.p. 142~144°(decomp.), which was raised by recrystallization from EtOH to 150~151°(decomp.), $[\alpha]_D^{29}$ −85.5°(c=1.41). *Anal.* Calcd. for $C_{27}H_{44}O_3NCl$: C, 69.57; H, 9.51; N, 3.00; Cl, 7.61. Found: C, 69.37; H, 9.24; N, 3.10; Cl, 7.33. IR λ_{max}^{Nujol} cm^{-1}: 1724 (CO), 1548 (NO_2-alkane).

6α-Nitrocholest-4-en-3-one (VIIa) and Cholest-4-ene-3,6-dione (VIIIa)——(i) After standing a solution of 1.02 g. of 5-chloro-6β-nitro-5α-cholestan-3-one (VIa) in 10 cc. of dehyd. pyridine for 20 hr. at room temperature, the solvent was removed under a reduced pressure and the residue was dissolved in Et_2O. The Et_2O solution was washed with H_2O, dried, and the solvent was evaporated to give 1.0 g. of an amorphous substance (IR λ_{max}^{Nujol} cm^{-1}: 1690, 1625, 1555, 1520. UV λ_{max}^{EtOH}: 248~250 mμ (ε 7,000)), which was chromatographed on a column of silica gel (45 g.). The benzene eluate afforded 0.565 g. of 6α-nitrocholest-4-en-3-one (VIIa) as an amorphous powder, which although failed to crystallize, exhibited UV λ_{max}^{EtOH}: 232 mμ (ε 13,900) and IR λ_{max}^{Nujol} cm^{-1}: 1692, 1626 (Δ^4-3-CO), 1558 (NO_2-alkane). The benzene and benzene-Et_2O (9:1) eluate yilded 0.274 g. of cholest-4-ene-3,6-dione (VIIIa), which recrystallized from MeOH to leaflets of m.p. 122~124°. UV λ_{max}^{EtOH}: 248 mμ (ε 11,600). IR λ_{max}^{Nujol} cm^{-1}: 1686, 1605 (Δ^4-3,6-diketone). Identity was confirmed by comparison with an authentic sample.

6α-Nitrocholest-4-en-3-one (VIIa; 0.35 g.) was rechromatographed using 20 g. of silica gel. The benzene-Et_2O (9:1) eluate afforded 0.13 g. of cholest-4-ene-3,6-dione (VIIIa) of m.p. 121~125°.

(ii) A solution of 97 mg. of 5-chloro-6β-nitro-5α-cholestan-3-one (VIa) in benzene was passed through a column of Al_2O_3 (11 g.; Woelm, grade III). The eluate with the same solvent gave 53 mg. of cholest-4-ene-3,6-dione (VIIIa) of m.p. 122~124°(from MeOH).

(iii) To a solution of 128 mg. of 6-nitrocholest-5-en-3β-ol (IV) in 4 cc. of pyridine 45 mg. of CrO_3 was added. The mixture, after being left standing for 14 hr. at room temperature, was poured into ice-water and neutralized with 2*N* HCl. The Et_2O extract was washed with H_2O, dried, and the solvent removed. An oily residue was chromatographed on 6 g. of silica gel. Benzene eluate afforded 28 mg. of cholest-4-ene-3,6-dione (VIIIa), which showed m.p. 121~122° after recrystallization from MeOH.

5-Chloro-6β-nitro-5α-androstane-3β,17β-diol Diacetate (IIb)——To a solution of 4.28 g. of androst-5-ene-3β,17β-diol diacetate (Ib) in 80 cc. of anhyd. CCl_4, 38 g. of 20% NOCl-CCl_4 solution (10 mol. equiv. of NOCl) was added at −20°, and the mixture was left to stand for 5 days at 0~3° in a dark place. The solvent and excess reagent were removed under a reduced pressure to yield a white amorphous product, which gave 4.2 g. (80.4%) of 5-chloro-6β-nitro-5α-androstane-3β,17β-diol diacetate (IIb) of m.p. 143~146° by trituration with EtOH, and the melting point was raised by recrystallization from EtOH to 144~146°, $[\alpha]_D^{28}$ −102.5°(c=1.09). *Anal.* Calcd. for $C_{23}H_{34}O_6NCl$: C, 60.58; H, 7.51; N, 3.07; Cl, 7.77. Found: C, 60.61; H, 7.41; N, 3.12; Cl, 7.88. IR λ_{max}^{Nujol} cm^{-1}: 1736 (AcO), 1548 (NO_2-alkane).

3β-Hydroxy-5-chloro-6β-nitro-5α-androstan-17-one Acetate (IIc)——To a solution of 3.3 g. of 3β-hydroxyandorst-5-en-17-one acetate (Ic) in 25 cc. of anhyd. CCl_4, 16.4 g. of 20% NOCl-CCl_4 solution (5 mol. equiv. of NOCl) was added at −20°. The mixture was allowed to stand for 13 hr. at 0~3° in a dark place. A deposited crystalline product was collected by filtration and washed with hexane. 3β-Hydroxy-5-chloro-6β-nitro-5α-androstan-17-one acetate (IIc) thus obtained had m.p. 205~207°,

weighed 2.4 g. The filtrate after evaporation of the solvent afforded an amorphous residue, which crystallized to 1.2 g. of (IIc) having m.p. 203~205° on trituration with small amounts of EtOH. The total yield amounts to 87.3%. Recrystallization from benzene afforded prisms of m.p. 209~210°, $[\alpha]_D^{27}$ −65.5°(c=2.32). *Anal.* Calcd. for $C_{21}H_{30}O_5NCl$: C, 61.23; H, 7.34; N, 3.40; Cl, 8.61. Found: C, 61.05; H, 7.76; N, 3.42; Cl, 8.56. IR λ_{max}^{Nujol} cm^{-1}: 1735 (AcO), 1543 (NO_2-alkane).

6-Nitroandrost-5-ene-3β,17β-diol Diacetate (IIIb)——A solution of 0.6 g. of 5-chloro-6β-nitro-5α-androstane-3β,17β-diol diacetate (IIb) in benzene was passed through a column of Al_2O_3 (34 g.; Woelm, grade III). 6-nitroandrost-5-ene-3β,17β-diol diacetate (IIIb) with m.p. 165~168° was obtained from the benzene eluate in a nearly quantitative yield. Recrystallization from EtOH gave prisms of m.p. 169~170°, $[\alpha]_D^{26}$ −98.0°(c=1.96). *Anal.* Calcd. for $C_{23}H_{33}O_6N$: C, 65.85; H, 7.93; N, 3.34. Found: C, 65.51; H, 8.23; N, 3.56. UV λ_{max}^{EtOH}: 257 mμ (ε 2,400). IR λ_{max}^{Nujol} cm^{-1}: 1748, 1736 (AcO), 1524 (NO_2-alkene).

3β-Hydroxy-6-nitroandrost-5-en-17-one Acetate (IIIc)——A solution of 0.3 g. of 3β-hydroxy-5-chloro-6β-nitro-5α-androstan-17-one acetate (IIc) in 6 cc. of pyridine was set aside for 18 hr. at room temperature. The solvent was removed under a reduced pressure and the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried, and the solvent evaporated. Trituration of the amorphous residue with EtOH gave 3β-hydroxy-6-nitroandrost-5-en-17-one acetate (IIIc) of m.p. 213~215° in a nearly quantitative yield, which afforded scaly needles of m.p. 215~216°, $[\alpha]_D^{28}$ −58.3° (c=1.62) on recrystallization from EtOH. *Anal.* Calcd. for $C_{21}H_{29}O_5N$: C, 67.18; H, 7.79; N, 3.73. 3.73. Found: C, 67.06; H, 7.60; N, 3.69. UV λ_{max}^{EtOH}: 256 mμ (ε 2,370). IR λ_{max}^{Nujol} cm^{-1}: 1745 (AcO, 17-CO), 1520 (NO_2-alkene).

5-Chloro-6β-nitro-5α-androstane-3β,17β-diol Diacetate (Vd)——A solution of 1 g. of 5-chlor-6β-nitro-5α-androstane-3β,17β-diol diacetate (1g.) (IIb) was dissolved in 40 cc. of EtOH and 6 cc. of conc. HCl was allowed to stand for 20 hr. at room temperature. The solvent was condensed under a reduced pressure to deposit crystals, which were collected by filtration, washed with H_2O and EtOH, and dried to furnish 0.8 g. of 5-chloro-6β-nitro-5α-androstane-3β,17β-diol (Vd) of m.p. 162~165°, which was raised by recrystallization from hexane-EtOH to 188~189°(decomp.), $[\alpha]_D^{28}$ −112°(c=1.16). *Anal.* Calcd. for $C_{19}H_{30}O_4NCl$: C, 61.35; H, 8.13; N, 3.76; Cl, 9.54. Found: C, 61.30; H, 8.01; N, 3.45; Cl, 9.64. IR λ_{max}^{Nujol} cm^{-1}: 3450 (OH), 1550 (NO_2-alkane).

3β-Hydroxy-5-chloro-6β-nitro-5α-androstan-17-one (Vc)——A suspension of 2 g. of 3β-hydroxy-5-chloro-6β-nitro-5α-androstan-17-one acetate (IIc) in 200 cc. of EtOH, 50 cc. of $CHCl_3$, and 20 cc. of conc. HCl was stirred for 20 hr. at room temperature. As the reaction proceeded all the crystals dissolved into the solution. The solvent was condensed under a reduced pressure to deposit crystals, which were collected by filtration, washed with H_2O, and dried. The crude 3β-hydroxy-5-chloro-6β-nitro-5α-androstan-17-one (Vc) of m.p. 198~202° weighed 1.74 g. On recrystallization from hexane-EtOH it showed m.p. 201~203°, $[\alpha]_D^{28}$ −59.8°(c=2.02). *Anal.* Calcd. for $C_{19}H_{28}O_4NCl$: C, 61.93; H, 7.63; N, 3.79; Cl, 9.58. Found: C, 61.89; H, 7.75; N, 3.93; Cl, 9.77. IR λ_{max}^{Nujol} cm^{-1}: 3580 (OH), 1727 (17-CO), 1543 (NO_2-alkane).

5-Chloro-6β-nitro-5α-androstane-3,17-dione (VIc)——(i) A solution of 0.76 g. of CrO_3 in 45 cc. of 90% AcOH was added dropwise to a solution of 1.31 g. of 5-chloro-6β-nitro-5α-androstane-3β,17β-diol (Vd) in 250 cc. of AcOH at 15~20°, and the mixture was left to stand for 20 hr. at room temperature. The excess reagent was decomposed by addition of EtOH, and the solvent was evaporated under a reduced pressure. The residue was dissolved in $CHCl_3$, the solution washed with H_2O, and dried, and the solvent was removed to leave an amorphous residue, which gave 5-chloro-6β-nitro-5α-androstane-3,17-dione (VIc) as needles of m.p. 158~159°, $[\alpha]_D^{27}$ −55.7°(c=0.67) after recrystallization from hexane-Me_2CO. *Anal.* Calcd. for $C_{19}H_{26}O_4NCl$: C, 62.03; H, 7.13; N, 3.80; Cl, 9.91. Found: C, 61.79; H, 6.92; N, 3.92; Cl, 9.83. IR λ_{max}^{Nujol} cm^{-1}: 1724 (CO), 1555 (NO_2-alkane).

(ii) To a solution of 0.322 g. of 3β-hydroxy-5-chloro-6β-nitro-5α-androstan-17-one (Vc) in 18 cc. of AcOH a solution of 0.128 g. of CrO_3 in 4 cc. of 90% AcOH was added dropwise at 15~20°. The mixture was worked up as described above. 5-Chloro-6β-nitro-5α-androstane-3,17-dione (VIc) obtained was dimorphous, showing m.p. 128~129°(decomp.) on recrystallization from EtOH, and m.p. 154~155° from hexane-Me_2CO. The IR spectra of both forms and that obtained in a preceding section were all identical.

6α-Nitroandrost-4-ene-3,17-dione (VIIc)——(i) After standing a mixture of 0.5 g. of 5-chloro-6β-nitro-5α-androstane-3,17-dione (VIc) and 0.2 g. of anhyd. AcOK in 70 cc. of abs. EtOH for 14 hr. at room temperature, the solvent was removed under a reduced pressure. The residue was extracted with Et_2O, the extract washed with H_2O, and dried. Removal of the solvent left 0.45 g. of a yellow crystalline substance, which was purified by recrystallization from hexane-Me_2CO to give 6α-nitroandrost-4-ene-3,17-dione (VIIc) as needles of m.p. 197~198°, $[\alpha]_D^{27}$ +149°(c=2.21). *Anal.* Calcd. for $C_{19}H_{25}O_4N$: C, 68.86; H, 7.60; N, 4.23. Found: C, 68.83; H, 7.39; N, 4.35. UV λ_{max}^{EtOH}: 227~230 mμ (ε 16,800). IR λ_{max}^{Nujol} cm^{-1}: 1736 (17-CO), 1675, 1617 (Δ^4-3-CO), 1558 (NO_2-alkane).

(ii) A mixture of 0.2 g. of (VIc) and 12 cc. of 3% KOH-MeOH was set aside for 20 hr. at room

temperature, then neutralized with AcOH, and diluted with H_2O. The precipitates were collected and recrystallized from hexane-Me_2CO to give (VIIc) of m.p. 197~198°, $[\alpha]_D^{26}$ +153°(c=1.14). The IR spectrum was identical with that of the sample prepared as above.

(iii) A solution of 0.3 g. of (VIc) under 4 cc. of pyridine was allowed to stand for 20 hr. at room temperature. The solvent was removed in a reduced pressure to give a crystalline residue, which was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried, and the solvent was evaporated. The residue was recrystallized from hexane-Me_2CO to give (VIIIc) of m.p. 194~195°, $[\alpha]_D^{27}$ 156°(c=1.10), whose IR spectrum was identical with that of the sample obtained as above.

Androst-4-ene-3,6,17-trione (VIIIc)——A benzene solution of 28 mg. of 6α-nitroandrost-4-ene-3,17-dione (VIIc) was passed through a column of Al_2O_3 (15 g.; Woelm, grade III). The eluate of the same solvent and AcOEt afforded 153 mg. (84.5%) of androst-4-ene-3,6,17-trione (VIIIc) of m.p. 222~224°(from EtOH), $[\alpha]_D^{25}$+33.6°(c=1.1, Me_2CO) as yellow prisms. The identity was confirmed by mixed melting point and comparison of the IR spectra with an authentic sample. *Anal.* Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.86; H, 7.82. UV λ_{max}^{EtOH}: 249 mμ (ε 10,500). IR λ_{max}^{Nujol} cm^{-1}: 1739 (17-CO), 1678, 1608 (Δ^4-3,6-dione).

Treatment of (II) with Zinc-dust in Ether-Acetic Acid——(i) To a mixture of 0.2 g. of 5-chloro-6β-nitro-5α-cholestan-3β-ol acetate (IIa) in 10 cc. of Et_2O and 1 cc. of AcOH 0.5 g. of Zn-dust was added with stirring at room temperature. After stirring for 45 min. Zn-dust was removed by filtration. The filtrate was washed with H_2O and dried. Removal of the solvent gave a crystalline residue, which was recrystallized from EtOH to 0.13 g. of cholesterol acetate (Ia) of m.p. 111.5~114°. Identity was proved by mixed melting point and comparison of IR spectra with an authentic sample.

(ii) 5-Chloro-6β-nitro-5α-androstane-3β,17β-diol diacetate (IIb; 0.2 g.) was treated with Zn-dust in Et_2O-AcOH in the same manner as described above, and 0.13 g. of androst-5-ene-3β,17β-diol diacetate (Ib) was obtained, m.p. 157~159°(from EtOH).

(iii) 3β-Hydroxy-5-chloro-6β-nitro-5α-androstan-17-one acetate (IIc; 0.2 g.) was treated with 0.5 g. of Zn-dust in 40 cc. of Et_2O and 4 cc. of AcOH as described above. An oily residue obtained was chromatographed on a column of Al_2O_3 to give 0.11 g. of 3β-hydroxyandrost-5-en-17-one acetate (Ic) of m.p. 167~169°.

Treatment of 5-Chloro-6β-nitro-5α-cholestan-3β-ol Acetate (IIa) with Pd-C——A solution of 0.53 g. of (IIa) in 80 cc. of abs. EtOH containing 2 cc. of anhyd. benzene was shaken in an atmosphere of H_2 over 0.1 g. of 10% Pd-C. In 95 min. 115 cc. of H_2 was absorbed. After filtration of the catalyst the solvent was removed under a reduced pressure to yield a crystalline substance, which gave cholesterol acetate (Ia) of m.p. 111~113° as needles after recrystallization from EtOH. The mother liquor was condensed to dryness and the residue was washed with Et_2O to leave 0.05 g. of NH_4Cl ($AgNO_3$ and Nessler reagent).

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Summary

Treatment of cholesterol acetate (Ia), androst-5-ene-3β,17β-diol diacetate (Ib), and 3β-hydroxyandrost-5-en-17-one acetate (Ic) with nitrosyl chloride afforded the corresponding 5α-chloro-6β-nitro compound in high yield. The adduct could be converted readily to a Δ^5-6-nitro compound on treatment under basic conditions and also into a Δ^4-3-oxo-6α-nitrosteroid derivative.

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