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Steroid Series. III.[1] Ozonization of 3-Acetoxy-Δ^5-steroids in the Presence of Formaldehyde.

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Earlier report[2] seemed to indicate that the preparation of a normal ozonide of cholesterol and cholesterol acetate is a somewhat difficult subject; under usual conditions they afford overozonized products, taking up 3~7 atoms of oxygen. Lettré and Jahn[3] conducted ozonization of cholesterol acetate in alcohol-free carbon tetrachloride, chloroform, or petroleum ether at low temperature under the conditions to avoid overozonization, and in these cases also failed to obtain a normal ozonide, but rather isolated unidentifiable crystalline products corresponding to $C_{29}H_{48}O_6$ of m.p. 126° and $C_{29}H_{48}O_5$ of m.p. 197~198° in only 1.8% and 3.2% yield, respectively.

Berenstein and his collaborators[4] designed an elaborate apparatus and produced a normal ozonide of cholesterol in a good yield, but could not reduce the product. Cornforth and his associates[5] succeeded later in reducing the ozonide with zinc dust in acetic acid at 25° for 60 hours and obtained 3β-hydroxy-5-oxo-5,6-secocholestan-6-al (IVa, 3-OH) as an etherate of m.p. 55~60°.

According to Criegee[6] the action of ozone on an olefinic linkage produces an unstable intermediate addition product, which then splits into a carbonyl compound and a zwitter ion. The mode of reaction of ozonization depends chiefly upon the way with which the zwitter ion stabilizes itself.

In the case of cholesterol acetate, the intermediate zwitter ion may be formulated as (II),*2 whose carbonyl group at C-5 seems to be fairly sterically hindered.*3 In such an environment, as Criegee described, the zwitter ion would prefer to form polymerization and/or rearrangement products rather than to recombine with 5-carbonyl group to give an ozonide of Staudinger's formulation.[7] These circumstances might be considered to cause the cumbersome problem on ozonization of double bond at C-5 in cholesterol. Such being the case, the ozonization of cholesterol in the presence of high concentration of such a reac-

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*2 As shown by the work of Lettre, *et al.*[3] the formulation of the zwitter ion as (II) may be preferred rather than the other possible one (VII).

*3 The 5-carbonyl group of (IVa) or its free alcohol was reported to be inert to carbonyl reagents.[3,5]

1) Part II : This Bulletin, **7**, 811 (1959).
2) O. Diels : Ber., **41**, 2596 (1908); C. Harries : *Ibid.*, **45**, 943 (1912); O. v. Fürth, G. Felsenreich : Biochem. Z., **69**, 416 (1915).
3) H. Lettré, A. Jahn : Ann., **608**, 43 (1957).
4) M. Berenstein, A. Georg, E. Briner : Helv. Chim. Acta, **29**, 258 (1946).
5) J. W. Cornforth, G. D. Hunter, G. Popjak : Biochem. J., **54**, 590 (1953).
6) R. Criegee, A. Kerckow, H. Zinke : Ber., **88**, 1883 (1955); R. Criegee, G. Blust, G. Lohaus : Ann., **583**, 5 (1953); R. Criegee : *Ibid.*, **583**, 1 (1953).
7) H. Staudinger : Ber., **58**, 1088 (1925).

tive carbonyl compound as formaldehyde will probably afford a stabilized trioxolane compound (III; $R=C_8H_{17}$), as a result of intermolecular combination of the zwitter ion with the reactive carbonyl compound present in the reaction mixture, and the trioxolane so formed will then be converted by reduction to 3β-acetoxy-5-oxo-5,6-secocholestan-6-al (IVa).

With these expectations, cholesterol acetate (Ia) was treated in dichloromethane with an ozonized air in the presence of formaldehyde under cooling with dry ice-acetone mixture. The solution turned light blue at the end of absorption of a slight excess of equivalent moles of ozone, showing no coloration with tetranitromethane. The ozonized mixture was then reduced with zinc dust and acetic acid with stirring at room temperature until iodine was no longer liberated on addition of potassium iodide in acetic acid to a sample of the solution, requiring 3.5 hours.

A vitreous ozonolysis product thus obtained was subjected to chromatography on acid-washed alumina. The first fraction gave a small amount of crystalline material melting at 112~114° with $[\alpha]_D$ −1.3°, which proved to be identical with 5,6β-epoxy-5β-cholestan-3β-ol acetate by the comparison with an authentic sample prepared by the method of Plattner, *et al.*[8]

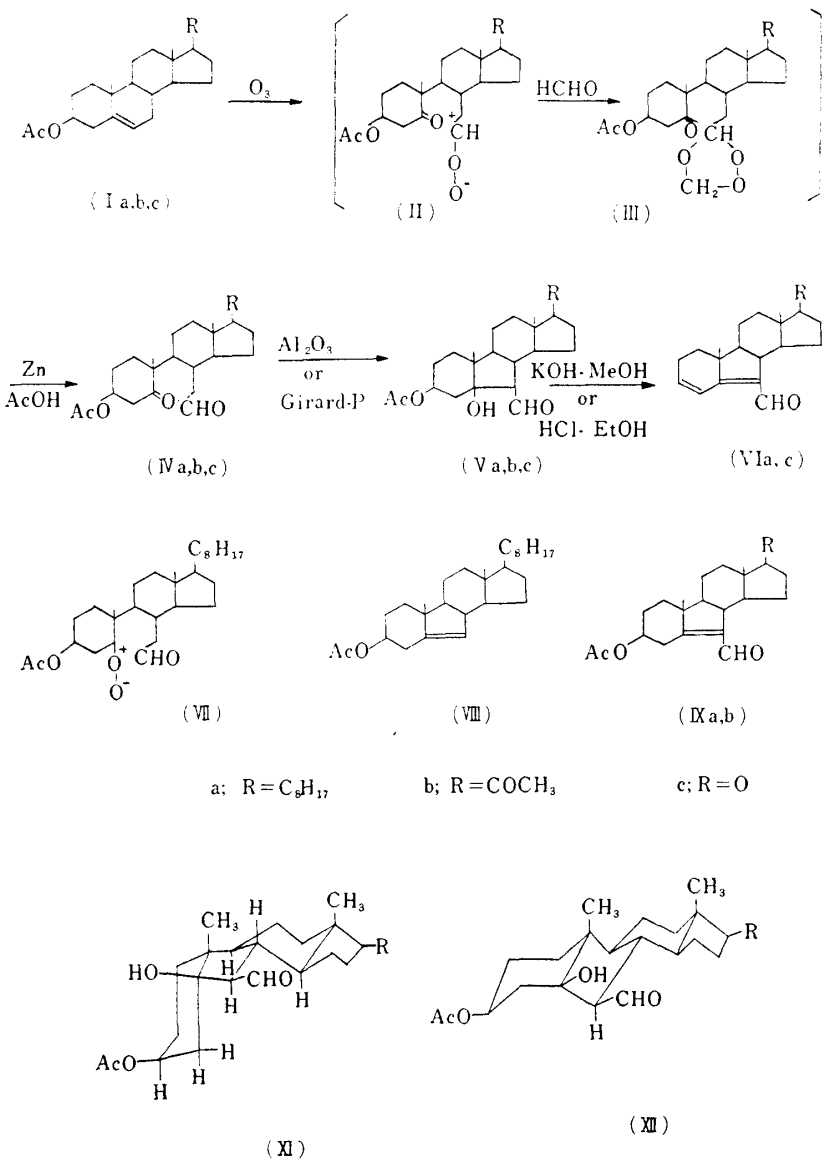
The second fraction furnished a substance of m.p. 93.5~95° in 44% yield, which analysed for $C_{29}H_{48}O_4$, and was positive to silver mirror test, exhibiting absorption bands at 3410 (OH), 2740, 1721 (CHO), and 1736 (AcO) cm^{-1}. The substance was recovered unchanged on treatment with acetic anhydride and pyridine at room temperature, indicating the presence of a tertiary hydroxyl group, and this compound, as will be described in a succeeding paper,[9] was converted to the known B-norcholesterol acetate (VIII) by procedures which might be uneffective on its basic skeleton. From these facts the structure, 6β-formyl-B-nor-5β-cholestane-3,5-diol 3-acetate (Va) was assigned to this substance, the stereochemical assignment being based on the following considerations.

When the crude ozonolysis mixture was treated with Girard-P reagent in ethanol containing acetic acid, followed by heating the resulting water-soluble hydrazone in the presence of hydrochloric acid, (Va) was found to be formed also even under these acidic conditions. The 6-formyl group therefore has probably a more stable configuration. The B/C ring juncture in (Va) should be retained in the *trans*-form since the method of its preparation is considered to leave that center intact, and 5-hydroxyl group, as will be described in a succeeding paper,[9] has the same β-configuration as the 3-acetoxyl group. In such a structure (XI or XII), as indicated by the Stuart Model, the 6α-formyl group is greatly hindered by 4α-, 9α-, and 14α-hydrogen atoms, while 6β-configuration is relatively unhindered. Thus, 6-formyl group was deduced to have β-configuration, which just corresponds to the quasi-equatorial bond with respect to both A/B and B/C ring systems.

The formation of (Va) can well be interpreted through an intramolecular aldol condensation of the intermediate ketoaldehyde, 3β-acetoxy-5-oxo-5,6-secocholestan-6-al (IVa), during chromatography. In fact, the ozonolysis mixture prior to submitting to chromatography showed, in addition to the bands at 2688 (CHO) and 1739 (AcO) cm^{-1}, a characteristic absorption band for a six-membered ring ketone at 1704 cm^{-1}, suggesting the presence of (IVa). This was further confirmed by converting it to the known phenylhydrazone of (IVa), m.p. 196~197°, whose melting point and spectral data were well in agreement with those reported by Lettré, *et al.*[10] In view of the ionic mechanism of aldol condensation, the assignment of the thermodynamically more stable configuration to 6-formyl group is now well understood.

Treatment of (Va) with Brady's reagent followed by chromatography gave, together with the corresponding 2,4-dinitrophenylhydrazone of m.p. 131~134°, with an absorption

8) P. A. Plattner, T. Petrzilka, W. Lang : Helv. Chim. Acta, **27**, 513 (1944).
9) Part V : This Bulletin, **9**, 12 (1961).
10) H. Lettré, A. Jahn, R. Pfirrmann : Ann., **615**, 222 (1958); H. Lettré, D. Hotz : *Ibid.*, **620**, 63 (1959).



maximum at 360 mμ (ε 23,800), those of 6-formyl-B-norcholesterol acetate (IXa) and 6-formyl-B-norcholesta-3,5-diene (VIa), one of m.p. 209~210° with an absorption maximum at 384 mμ (ε 27,700), and another of m.p. 261~264° with an absorption maximum at 400 mμ (ε 32,900), respectively. The ultraviolet absorption data conformed closely with the generalization of Roberts and Green.[11]

By either heating with methanolic potassium hydroxide or keeping at room temperature in ethanolic hydrogen chloride, (Va) readily eliminated elements of water and acetic acid to give 6-formyl-B-norcholesta-3,5-diene (VIa) of m.p. 105~106°, which had been prepared by Cornforth, *et al.*[5] as an oily material on treatment of 3β-hydroxy-5-oxo-5,6-secocholestan-6-al (IVa : 3-OH) with ethanolic sulfuric acid. The structure (VIa) was indicated by its composition ($C_{27}H_{42}O$) and spectroscopic characteristics (λ_{max} 293 mμ; ν_{max} cm^{-1} : 2725, 1668, 1610, and 1554).

In order to prove the presence of formaldehyde in the ozonization process, cholesterol acetate was ozonized without formaldehyde under otherwise exactly the same conditions as described above. The ozonide thus obtained was found to resist reduction; namely,

11) J.D. Roberts, C. Green : J. Am. Chem. Soc., **68**, 214 (1946).

after stirring with zinc dust and acetic acid at room temperature for more than six hours, the solution still remained positive to the potassium iodide test. The products separated by chromatography were 6-formyl-B-norcholesta-3,5-diene (VIa; 3.8%), 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (Va; 8.2%), and 5,6β-epoxy-5β-cholestan-3β-ol acetate (9%), together with a small amount of two kind of crystalline materials with compositions of $C_{29}H_{48}O_{4\sim5}$ and $C_{29}H_{48}O_4$, both exhibiting positive test for active oxygen with potassium iodide. It should be noted that 5β,6β-epoxide was isolated by the action of ozone on cholesterol acetate.

The ozonolysis in the presence of formaldehyde was then applied to 3β-acetoxypregn-5-en-20-one (Ib) and 3β-acetoxyandrost-5-en-17-one (Ic), and the reaction was found to proceed in the same way as in cholesterol acetate.

Thus, the ozonolysis reaction mixture of 3β-acetoxypregn-5-en-20-one (Ib) was chromatographed on acid-washed alumina. The first fraction eluted with benzene afforded 3β-acetoxy-6-formyl-B-norpregn-5-en-20-one (IXb), melting at 181~181.5°, in 13.7% yield, whose structure was followed from its analytical values and spectroscopic data (λ_{max} 251.5 mμ (ε 12,800); ν_{max} cm^{-1} : 1730 (AcO), 1695 (20-CO), 1669 (conjugated CHO), and 1610 (Δ^5)). The fraction eluted with a mixture of benzene and ether gave a substance of m.p. 104~106.5° in 43% yield, exhibiting absorption bands at 3505 (OH), 2717 (CHO), 1736 (AcO), 1720 (CHO), and 1702 (20-CO) cm^{-1}, to which the structure, 3β-acetoxy-5-hydroxy-6β-formyl-B-nor-5β-pregnan-20-one (Vb), was assigned.

3β-Acetoxyandrost-5-en-17-one (Ic) was ozonized in a similar manner and the resulting ozonide was reduced with zinc dust and acetic acid. The reaction mixture, on chromatography over acid-washed alumina, afforded a small amount of 6-formyl-B-norandrosta-3,5-dien-17-one (VIc) of m.p. 184~186° (λ_{max} 291 mμ (ε 20,900); ν_{max} cm^{-1} : 2740 (CHO), 1736 (17-CO), 1661 (conjugated CHO), 1610, 1562 ($\Delta^{3,5}$)), and 3β-acetoxy-5-hydroxy-6β-formyl-B-nor-5β-androstan-17-one (Vc) of m.p. 132~134° in 42% yield, which exhibited absorption bands at 3546 (OH), 2747 (CHO), 1739 (3-AcO and 17-CO), and 1724 (CHO) cm^{-1}. The stereochemical assignments of (Vb) and (Vc) were made by analogy with the cholesterol series.

Experimental*4

Ozonization of Cholesterol Acetate (Ia) in the Presence of HCHO—Through a solution of 17.15 g. (0.04 mole) of cholesterol acetate (Ia) in 800 cc. of anhyd. CH_2Cl_2 and 23 g. (0.7 mole) of HCHO, freshly regenerated on pyrolysis of paraformaldehyde, a stream of ozonized air (0.36 mmole of O_3/min.) was passed under chilling with dry ice-Me_2CO mixture for 140 min. (corresponding to 0.05 mole of O_3), the solution becoming pale blue and negative to $C(NO_2)_4$ test. To the solution was added 40 g. of Zn dust and 100 cc. of AcOH, and the suspension, after stirring for 3.5 hr. at room temperature, became negative to KI in AcOH test. After filtration, the filtrate was washed successively with H_2O, 5% $NaHCO_3$ solution, and H_2O, and dried. Removal of the solvent under a reduced pressure gave 16.7 g. of a colorless viscous substance (IVa). IR ν_{max}^{Nujol} cm^{-1} : 2688 (CHO), 1739 (AcO), 1704 (six-membered ring ketone).

The phenylhydrazone crystallized from MeOH-AcOEt to yellow fine needles of m.p. 196~197°. *Anal.* Calcd. for $C_{35}H_{54}O_3N_2$: N, 5.08. Found : N, 5.17. UV : λ_{max}^{EtOH} 268.5 mμ (ε 9,840) (reported[10] m.p. 196~197°, UV : λ_{max}^{EtOH} 270 mμ).

The crude ozonolysis product (IVa; 13.3 g.) dissolved in 30 cc. of benzene was chromatographed on a column of 370 g. of acid-washed alumina.

(i) The fraction (800 cc.) eluted with benzene gave 0.5 g. of crude crystals melting at 96~102°, which was rechromatographed on alumina. Elution with a mixture of petr. ether-benzene (3:1 to 1:1) afforded 0.377 g. of crystals of m.p. 101~103°, which was recrystallized from MeOH to give 5,6β-epoxy-5β-cholestan-3β-ol acetate as needles of m.p. 112~114°, $[\alpha]_D^{20.5}$ −1.3° (c=3.08). *Anal.* Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found : C, 78.28; H, 10.76. This proved to be identical with an authentic sample by a mixed m.p. determination and infrared spectra.

*4 All m.p.s are uncorrected. Rotations were measured in $CHCl_3$.

(ii) The fractions eluted with further 240 cc. of benzene and with 400 cc. of benzene-Et_2O (2:1) gave 0.8 g. of an oily substance.
(iii) The combined fractions eluted with further 1760 cc. of benzene-Et_2O (2:1), 560 cc. of benzene-Et_2O (1:1), and 320 cc. of Et_2O gave 6.55 g. (44%) of 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (Va), m.p. 88~93°, which was recrystallized from MeOH to needles melting at 93.5~95°. *Anal.* Calcd. for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50. Found: C, 75.68; H, 10.86. IR ν_{max}^{Nujol} cm^{-1}: 3410 (OH), 2740 (CHO), 1763 (AcO), 1721 (CHO).
(iv) The combined fractions eluted with 500 cc. of Et_2O, 800 cc. of $CHCl_3$, and 320 cc. of MeOH gave 2.96 g. of an oily substance, which was not investigated further.

Treatment of (IVa) with Girard-P Reagent—A mixture of 0.84 g. of crude (IVa) obtained in the preceding experiment, 10 cc. of 95% EtOH, 1 cc. of AcOH, and 0.41 g. of Girard-P reagent was refluxed for 1 hr. on a steam bath, then poured into 100-cc. mixture of H_2O and an equal volume of saturated NaCl solution, and extracted three times with Et_2O. The combined extract was washed with H_2O, dried, and the solvent was evaporated, leaving 0.24 g. of an oily residue.

To the aqueous layer was added an amount of conc. HCl sufficient to make 0.5*N* solution and the mixture was warmed at 60° for 20 min. on a water bath, then kept at room temperature for several hours, and extracted with Et_2O. The extract was washed with 2% $NaHCO_3$ solution and dried. Removal of the solvent afforded 0.55 g. of colorless viscous residue, which on standing crystallized. This was proved identical with 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (Va) by comparison of the infrared spectra.

Reaction of (Va) with Carbonyl Reagents—(i) Brady's reagent was added to a solution of 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (Va) in EtOH. The precipitated yellowish orange crystals, which turned to dark-red viscous oil on standing, was extracted with CH_2Cl_2. The extract, after washing, drying, and removal of the solvent, gave an oily residue, which was chromatographed on alumina. The first fraction eluted with benzene, after removal of the solvent and recrystallization from benzene, gave 2,4-dininrophenylhydrazone of 6β-formyl-B-norcholesta-3,5-diene (VIa) as deep red scales, m.p. 261~264° (decomp.). *Anal.* Calcd. for $C_{33}H_{46}O_4N_4$: C, 70.43; H, 8.29; N, N, 9.96. Found: C, 70.42; H, 8.37; N, 10.11. UV: λ_{max}^{EtOH} 400 mμ (ε 32,900).

The second fraction eluted with the same solvent gave 2,4-dinitrophenylhydrazone of 6-formyl-B-norcholesterol acetate (IXa) as orange needles (from EtOH), m.p. 209~210°. *Anal.* Calcd. for $C_{35}H_{50}O_6N_4$: C, 67.50; H, 8.09; N, 9.00. Found: C, 67.30; H, 7.76; N, 9.28. UV: λ_{max}^{EtOH} 384 mμ (ε 27,700).

The third fraction eluted with Et_2O gave 2,4-dinitrophenylhydrazone of 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (Va) as orange needles of m.p. 131~134° (from EtOH). *Anal.* Calcd. for $C_{35}H_{52}O_7N_4$: C, 65.60; H, 8.18; N, 8.74. Found: C, 65.61; H, 8.09; N, 8.55. UV: λ_{max}^{EtOH} 360 mμ (ε 23,800).
Semicarbazone of (Va): White microcrystals (from AcOEt), m.p. 213~213.5° (decomp.). *Anal.* Calcd. for $C_{30}H_{51}O_4N_3$: C, 69.19; H, 9.93; N, 8.11. Found: C, 69.37; H, 9.81; N, 8.11.

6-Formyl-B-norcholesta-3,5-diene (VIa)—(i) A solution of 0.26 g. of 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (Va) in 28 cc. of 0.7% KOH-MeOH was refluxed for 1 hr. on a steam bath. The reaction mixture was poured into H_2O, extracted with Et_2O, the extract was washed with H_2O, and dried. Removal of the solvent afforded 0.223 g. of an oily residue, which was chromatographed on alumina. Elution with petr. ether-benzene (3:1) gave 6-formyl-B-norcholesta-3,5-diene (VIa) as needles of m.p. 105~106° (from MeOH), $[\alpha]_D^{27.5}$ −171.7° (c=0.73). *Anal.* Calcd. for $C_{27}H_{42}O$: C, 84.75; H, 11.07. Found: C, 84.69; H, 10.96. UV: λ_{max}^{EtOH} 293 mμ (ε 19,300). IR ν_{max}^{Nujol} cm^{-1}: 2725 (CHO), 1668 (conjngated CHO), 1610, 1554 ($\Delta^{3,5}$).
The 2,4-dinitrophenylhydrazone crystallized from benzene to deep red scales, m.p. 262~264° (decomp.), which was identical with the sample isolated in the above-described experiment.
(ii) A solution of 100 mg. of (Va) in 5 cc. of 99% EtOH and 0.5 cc. of conc. HCl was set aside for 20 hr. at room temperature. Treatment of the mixture as in the preceding experiment gave 60 mg. (75%) of (VIa) melting at 104~106°, which showed no depression of m.p. on admixture with the sample obtained as above.

Ozonization of Cholesterol Acetate (Ia) without HCHO—Through a solution of 8.58 g. (0.02 mole) of (Ia) in 200 cc. of anhyd. CH_2Cl_2, a stream of ozonized air (0.7 mmoles of O_3/min.) was passed under chilling with dry ice-Me_2CO mixture for 34 min., absorbing equivalent to 0.024 mole of O_3. To this mixture, 10 g. of Zn dust and 30 cc. of AcOH were added and the suspension was stirred at room temperature for 6 hr., the solution still remaining positive to KI in AcOH test. Treatment of the mixture as in the preceding experiment gave 9.3 g. of a viscous residue, which was chromatographed on a column of 360 g. of acid-washed alumina.
(i) The fraction eluted with a mixture of petr. ether-benzene (1:1) gave 0.292 g. of a crystalline residue melting at 101~104°, which was rechromatographed on alumina. Eluate with petr. ether-benzene (2:1), after recrystallization from MeOH, gave needles of m.p. 103~106°, which were identified with 6-formyl-B-norcholesta-3,5-diene (VIa) by mixed m.p. determination and infrared spectra.

(ii) The fractions eluted with benzene and benzene-Et_2O (5:1) afforded 0.796 g. of a residue of m.p. 94~102°, which melted at 112~113° after recrystallization from MeOH. This proved identical with an authentic 5,6β-epoxy-5β-cholestan-3β-ol acetate.
(iii) The fraction eluted with benzene-Et_2O (2:1) gave 0.3 g. of crystalline residue, which was recrystallized from MeOH to needles, m.p. 221~223° (decomp.), with positive test to KI-AcOH. *Anal.* Calcd. for $C_{29}H_{48}O_{4.5}$: C, 74.31; H, 10.32. Found : C, 74.48; H, 10.08.
(iv) The second fraction eluted with the same mixture of solvents gave 0.76 g. of a viscous residue, whose infrared spectrum agreed with that of 6β-formyl-B-nor-5β-cholestane-3β,5-diol 3-acetate (Va).
(v) The fraction eluted with Et_2O gave 0.5 g. of a crystalline residue, which melted at 235~236° on recrystallization from MeOH and was positive to KI-AcOH test. *Anal.* Calcd. for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50. Found : C, 75.89; H, 10.38.

Ozonization of 3β-Acetoxypregn-5-en-20-one (Ib) in the Presence of HCHO—A solution of 10.75 g. (0.03 mole) of (Ib) in 800 cc. of anhyd. CH_2Cl_2 and 14 g. (0.33 mole) of freshly pyrolysed HCHO was treated with ozonized air (0.5 mmoles of O_3/min.) for 65 min. under chilling with dry ice-Me_2CO mixture. Reduction of the ozonide with 20 g. of Zn dust and 80 cc. of AcOH for 3 hr. afforded 12.0 g. of a viscous residue, which was chromatographed on 400 g. of acid-washed alumina.
(i) The fraction eluted with benzene, after removal of the solvent, gave 1.53 g. of a crystalline residue melting at 176~178°, which, on recrystallization from MeOH, gave 3β-acetoxy-6-formyl-B-norpregn-5-en-20-one (IXb) of m.p. 181~181.5°, $[\alpha]_D^{29}$ −27.5° (c=1.13). *Anal.* Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found : C, 74.34; H, 9.02. UV : λ_{max}^{EtOH} 251.5 mμ (ε 12,800). IR ν_{max}^{Nujol} cm^{-1} : 1730 (AcO), 1695 (20-CO), 1669 (conjugated CHO), 1610 (Δ^5).
2,4-Dintrophenylhydrazone : Needles (from EtOH), m.p. 248~250° (decomp.). *Anal.* Calcd. for $C_{35}H_{40}O_{10}N_8$: C, 57.38; H, 5.50; N, 15.29. Found : C, 57.08; H, 5.30; N, 15.22. UV : λ_{max}^{EtOH} 371 mμ (ε 45,400).
(ii) The fraction eluted with benzene-Et_2O (2:1 to 1:1) gave 5.18 g. (43%) of a crystalline residue melting at 97~103°, which was recrystallized from Et_2O to give 3β-acetoxy-5-hydroxy-6β-formyl-B-nor-5β-pregnan-20-one (Vb) as microcrystals, m.p. 104~106.5°, $[\alpha]_D^{29}$ +71.1° (c=1.1). *Anal.* Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found : C, 70.93; H, 8.67. IR ν_{max}^{Nujol} cm^{-1} : 3505 (OH), 2717 (CHO), 1736 (AcO), 1720 (CHO), 1702 (20-CO).
(iii) The fraction eluted with Et_2O gave 0.61 g. of a crystalline material of m.p. 202~210°, which was not further investigated.
(iv) The fraction eluted with $CHCl_3$ gave 0.273 g. of an oily substance.

Ozonization of 3β-Acetoxyandrost-5-en-17-one (Ic) in the Presence of HCHO—A solution of 7.25 g. of (Ic) dissolved in 800 cc. of anhyd. CH_2Cl_2 containing 12 g. of freshly pyrolysed HCHO was treated with ozonized air (0.3 mmoles of O_3/min.) for 90 min. Reduction of the ozonide with 20 g. of Zn dust and 80 cc. of AcOH for 4 hr. and treatment as described for (Ia) afforded 8.5 g. of a viscous substance, which was chromatographed on 300 g. of acid-washed alumina.
(i) The fraction eluted with benzene-Et_2O (3:1), after removal of the solvent, gave 0.34 g. of a crystalline residue, m.p. 160~170°, which was recrystallized from MeOH to give 6-formyl-B-norandrosta-3,5-dien-17-one (VIc) as rectangles, m.p. 184~186°, $[\alpha]_D^{29}$ −88.7° (c=1.51). *Anal.* Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found : C, 80.44; H, 8.74. UV : λ_{max}^{EtOH} 291 mμ (ε 20,900). IR ν_{max}^{Nujol} cm^{-1} : 2740 (CHO), 1736 (17-CO), 1661 (conjugated CHO), 1610, 1562 ($\Delta^{3,5}$).
(ii) The second fraction eluted with the same mixture of solvents gave 1.25 g. of an oily residue.
(iii) Elutions with benzene-Et_2O (1:1) and Et_2O gave 3.32 g. of a crystalline residue, which was recrystallized from Et_2O to give 3β-acetoxy-5-hydroxy-6β-formyl-B-nor-5β-androstan-17-one (Vc) of m.p. 132~134°, $[\alpha]_D^{29}$ +74.7° (c=2.41). *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found : C, 69.30; H, 8.18. IR ν_{max}^{Nujol} cm^{-1} : 3546 (OH), 2747 (CHO), 1739 (3-AcO and 17-CO), 1724 (CHO).

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Summary

Cholesterol acetate, 3β-acetoxypregn-5-en-20-one, and 3β-acetoxyandrost-5-en-17-one were ozonized in the presence of formaldehyde. Reductive fission of the ozonides followed by chromatography on acid-washed alumina afforded 3β-acetoxy-5β-hydroxy-6β-formyl-B-norsteroids of the cholestane, pregnane, and androstane series.

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