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Thiosteroids. XXVI.[1] Steroidal Transannular 2,5-Epoxide and Related Compounds

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A number of 3α-substituted (H, OH, OAc or SCN)-2β,5α-dihydroxycholestanes upon treatment with mesyl chloride and pyridine gave the corresponding 2α,5α-epoxides. These structures were established by the nuclear magnetic resonance spectra and by chemical conversions. In addition, the reaction of a series of 5α-hydroxy-2α,3α-epoxysteroids with hydrobromic acid leading to the 3α-hydroxy-2α,5α-epoxysteroids was studied. The reaction mechanism was also discussed.

In 1953, photosensitized oxidation of cholest-2,4-diene to cholest-3-ene-2α,5α-peroxide was reported by Conca and Bergmann.[3] Some studies which implied the formation of a 2α,5α-epoxide, oxabicyclo [2,2,1] heptane system, have also appeared,[4] but the results have not fully been established. In the previous paper,[1] we reported that the treatment of cholestane-2β,3α,5α-triol (IIb) with pyridine and mesyl chloride gave the transannular 2α,5α-epoxide (IIIa) containing 3α-mesyloxy group in high yield. Its structure was assumed from the evidence based on the nuclear magnetic resonance (NMR) spectrum. We wish to describe here the elucidation of the structure of the compound by chemical means as well as the syntheses of the related compounds.

At first the skeleton of the compound was established in the following way. The alcohol (IIIb), which was derived from the mesylate (IIIa) or the acetate (IIIc) by ester–fission with lithium aluminum hydride,[1] was oxidized to the ketone (V) with Jones reagent in 82.5% yield. This ketone exhibits an absorption band due to the five–membered ring ketone at 1763 cm^{-1} in the infrared (IR) spectrum. Its NMR spectrum shows a doublet ($J \approx 7.0$ Hz) corresponding to the proton attached to the carbon bearing an ether oxygen at 5.62 τ and an AB pattern due to the 4-methylene moiety at 7.55 and 7.95 τ as a pair of doublets ($J_{AB} \approx -18$ Hz). Heating the ketone with boron trifluoride etherate in a mixture of acetic acid and acetic anhydride resulted in the cleavage of the ether–linkage yielding 2α-acetoxycholest-4-en-3-one (XI) in 53% yield. Huang–Minlon reduction of the epoxyketone (V) afforded the compound (VIa), $C_{27}H_{46}O$, which contains an ether–oxygen ($\nu_{C-O}^{CS_2}$ 974 cm^{-1} and no OH).

This compound was found to be different from cholestan-3α,5α-epoxide[5] by comparison with the authentic sample. Furthermore, the NMR spectrum of VIa shows a peak due to one proton attached to the carbon carrying the ether oxygen at 5.62 τ as a triplet ($J \approx 5.0$ Hz)

1) Part XXV: T. Komeno and H. Itani, *Chem. Pharm. Bull.* (Tokyo), **18**, 608 (1970).
2) Location: *Fukushima–ku, Osaka.*
3) R.J. Conca and W. Bergmann, *J. Org. Chem.*, **18**, 1104 (1953).
4) W.J. Wechster reported that the photolysis product of 5α,11α-dihydroxypregnane-3,6,20-trione 3,20-bisethyleneketal 11-acetate was preliminarily assigned to 11α-acetoxy-3,6,20-trioxopregnan-2α,5α-epoxide 3,20-bisethyleneketal based on elemental analysis, the infrared spectrum (no OH), and the NMR spectrum, *J. Org. Chem.*, **31**, 2136 (1966). However, his assignment of a triplet ($J=5.0$ Hz) at 5.72 τ for the assigned bridge head proton seems to be improbable, since only one exo-proton neighbouring to the bridge head proton is to be present in the proposed structure. J.A. Waters and B. Witkop (*J. Am. Chem. Soc.*, **89**, 1022 (1967)) reported that photoreduction of estradiol yields a product tentatively assigned as 3α,10α-epoxide without complete establishment of the structure.
5) R.B. Clayton, H.B. Henbest and M. Smith, *J. Chem. Soc.*, **1957**, 1982.

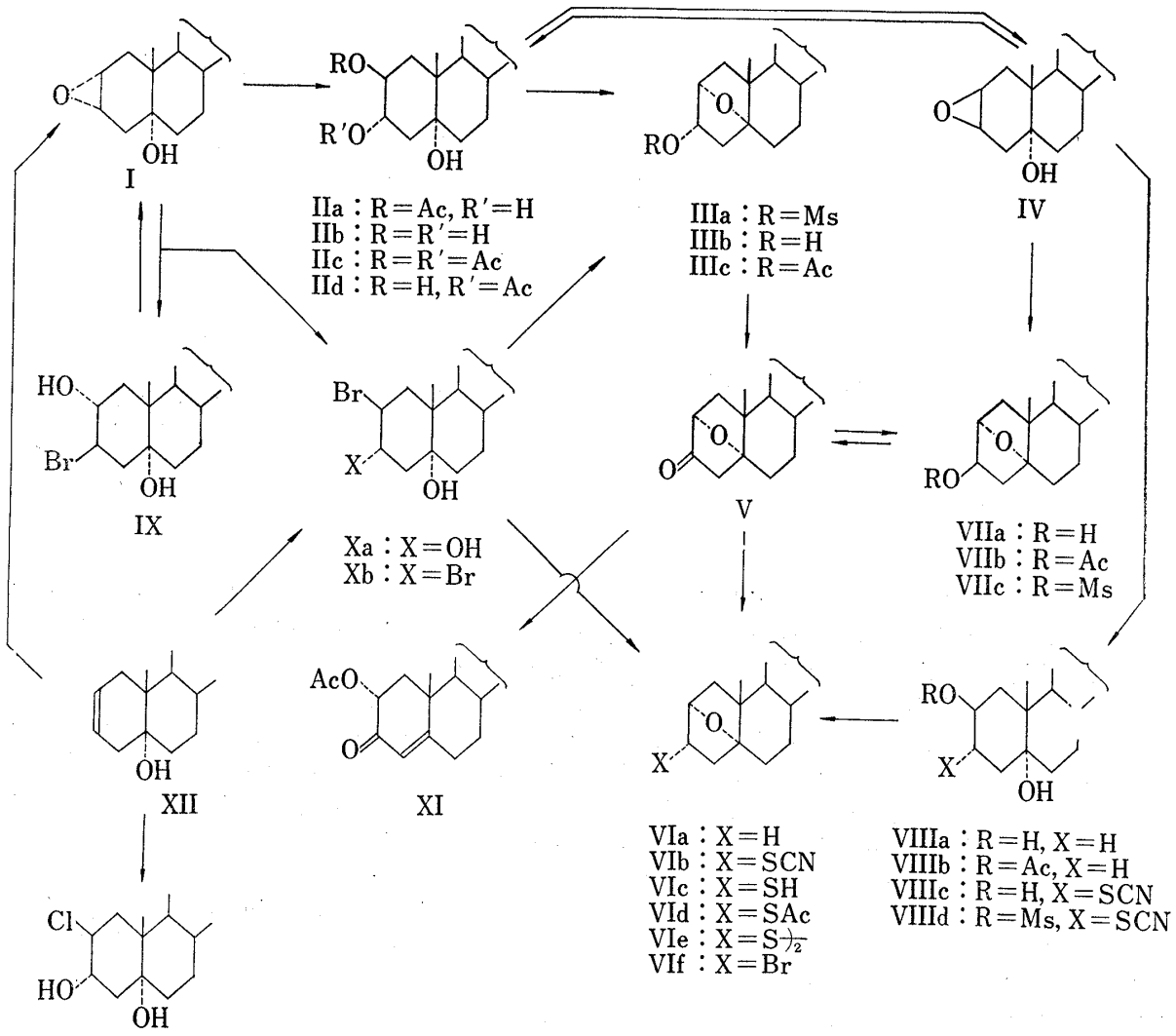


Chart 1

characteristic of the bridge–head proton of 7-oxabicyclo [2,2,1] heptane.[6] On the other hand, 5α-hydroxycholestan-2β,3β-epoxide (IV)[1] was reduced with lithium aluminum hydride to the 2β,5α-diol (VIIIa), the configuration of which was supported by the NMR spectrum. Mesylation of the diol (VIIIa) in the usual way furnished the foregoing ether (VIa) in 85% yield. Moreover, brief treatment of 2β-mesyloxy-5α-hydroxycholestane-3α-thiocyanate (VIIId)[1] with pyridine gave the thiocyanate (VIb) having an ether linkage, which was further converted to the ether (VIa) by reduction with lithium aluminum hydride.[7] Bromination of 5α-hydroxycholest-2-ene (XII) afforded the dibromide (Xb) which was treated briefly with pyridine to give the monobromide (VIf) carrying an ether linkage.[8] This bromide on hydrogenation over Raney nickel gave the above mentioned ether (VIa) in a quantitative yield. From these facts the ether (VIa) was confirmed to be cholestan-2α,5α-epoxide. In the NMR spectrum of the thiocyanate (VIb) and the monobromide (VIf), each bridge–head

6) D. Gagnaire and E.P. Subiza, *Bull. Soc. Chim. France*, **1963**, 2627; F.A.L. Anet, *Can. J. Chem.*, **39**, 789 (1961); T.J. Flautt and W.F. Erman, *J. Am. Chem. Soc.*, **85**, 3212 (1963).

7) It will be noted that the formation of the thiol (VIc) could not be observed judging from TLC, in contrast to the formation of IIIb in the reduction of the mesylate (IIIa).

8) A. Shani and F. Sondheimer reported a similar cyclization in a decalin system. *J. Am. Chem. Soc.*, **89**, 6310 (1967). However, their assignment for each proton in the NMR spectrum of the transannular epoxide seems to be confused.

proton appears as a doublet ($J \approx 6.0$ Hz) and, hence, these compounds should have 3α-*exo* substituents.[6] Reduction of the thiocyanate (VIb) with diisobutyl aluminum hydride at low temperature proceeded smoothly yielding the thiol (VIc), which was acetylated to the thiol acetate (VId) and was oxidized to the disulfide (VIe) by treatment with lead tetraacetate in quantitative yield.

Reduction of the epoxyketone (V) with lithium aluminum hydride gave the epoxyalcohol (VIIa), which is different from the 3α-alcohol (IIIb) and was reconcverted to the parent ketone by Jones oxidation. From the mechanistic considerations involving the preferential *exo* attack of the aluminum hydride ion,[9] the configuration of the hydroxyl group at C-3 in the alcohol (VIIa) should be *endo*, β. Acetolysis of 5α-hydroxycholestan-2β,3β-epoxide (IV) also afforded as minor products the alcohol (VIIa) (5%) and its acetate (VIIb) (5%) directly,[10] but the major product was cholestane-2β,3α,5α-triol 3-monoacetate (IId), the structure of which was confirmed by its conversion to the 2,3-diacetate (IIc) and 3α-acetoxy-2α,5α-epoxide (IIIc).

As an alternative preparation of the 2α,5α-epoxy derivatives, the reaction of 5α-hydroxycholestan-2α,3α-epoxide (I) with aqueous hydrobromic acid in methylene chloride (or ether) was carried out in a two-phase system. There found two products right after the disappearance of the starting material. Upon the work-up in this stage one of them, predominating over the other, could be isolated by direct recrystallization and characterized as 2β-bromo-3α,5α-diol (Xa) by its conversion to the parent epoxide (I) with alkali and further by the examination of the NMR spectrum (19-H: 8.71 τ). As the reaction time was prolonged this compound (Xa) gradually changed to 3α-hydroxy-2α,5α-epoxide (IIIb) and the final work-up after 5—7 hours afforded 66.5% of IIIb and 18.5% of the minor substance which had been formed from the early stage of the reaction and remained unchanged. The structure of the minor substance was found to be 3β-bromo-2α,5α-diol (IX) by its reconversion to the parent epoxide (I) on treatment with alkali and further evidence for the structure was gained by its NMR spectrum (19-H: 9.09 τ).[11] A similar treatment of the epoxide (I) with aqueous hydrochloric acid did not afford the transannular epoxide (IIIb) but only 2β-chloro-3α,5α-diol (XIII). It is of interest to notice that the reaction of 2β-bromo-3α,5α-diol with aqueous hydrobromic acid gave rise to the transannular epoxidation under the condition without base such a pyridine. The reaction probably involves the participation of the 5α-oxygen to the developing carbonium ion formed at C_2 after the extrusion of the bromine in a solvolytic manner.[12] Fur-

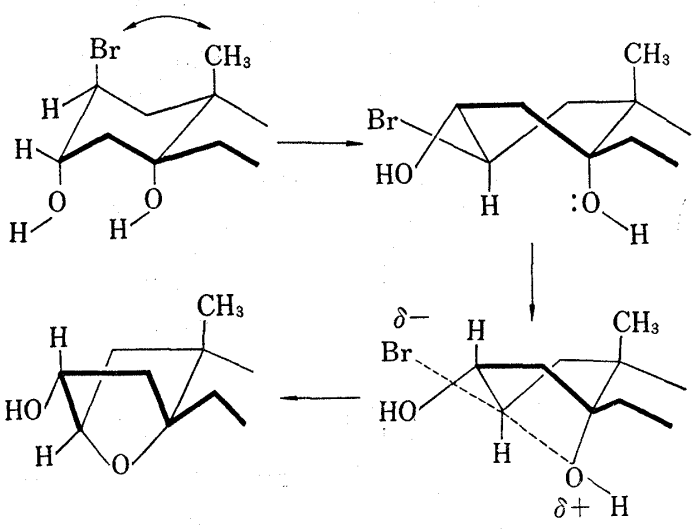


Fig. 1

9) S. Beckmann and R. Mezger, *Chem. Ber.*, **89**, 2738 (1956).

10) Similar and more facile formation of a transannular epoxide in the acidolysis of a seven-membered ring system, *i.e.* widdrol β-oxide, was observed by C. Enzell. *Acta. Chem. Scand.*, **16**, 1553 (1962).

11) A similar but exclusively diequatorial cleavage of 4β-hydroxycholestan-5β,6β-epoxide was observed by S. Greenfield, E. Glotter, L. Lavie and Y. Kashman, *Tetrahedron*, **22**, 1103 (1966); *J. Chem. Soc.*, (*C*), **1967**, 1460.

12) In the reaction of 2α,3α-epoxyandrostane-5α,17β-diol 17-monoacetate (XXVIIIc) with hydrobromic acid, the transannular epoxide (XXXIIId) was accompanied by a small amount of a solvolytic compound, which was preliminarily assigned to be androst-5-ene-2α,3α,17β-triol 17-monoacetate based on the acetonide formation (see experimental).

thermore driving force of this reaction would be the relief of steric compression between the angular methyl group and the bromine atom which are disposed in 1,3-diaxial relation. Thus, the distorsion of the A-ring would allow the close arrangement of $C_5\alpha$-oxgen and the C_2-carbon and then permit the transannular epoxide formation.

This consideration prompted us to study the reaction of 5β-hydroxycholestan-2β,3β-epoxide (XX) as well as 5α,17β-dihydroxy-19-norandrostan-2α,3α-epoxide (XXVIIId) with hydrobromic acid. In the former case, the expected product, 2α-bromocholestane-3β,5β-diol would have no such interaction but instead would have an interaction between the 9α-hydrogen and the bromine.

The epoxide (XX) was synthesized in low yield in the following way. Dehydration of cholestane-3β,5α,6β-triol 3-monotosylate (XIVb) with collidine gave cholest-2-ene-5α,6β-diol (XVa), which was converted to the diacetate (XVb) by forced acetylation in the presence of acid catalyst. Heating the diacetate with potassium hydroxide in absolute ethanol[13] (or more desirably in iso-propanol) resulted in the formation of cholest-2-en-5β,6β-epoxide (XVI) in good yield. Reduction of the epoxide with lithium aluminum hydride afforded 76.7% of 5α-androst-2-en-6β-ol (XVII) as well as 17% of cholest-2-en-5β-ol (XVIII).[14] Epoxidation of both olefins with *m*-chloroperbenzoic acid yielded the corresponding epoxides, XIX and XX. The latter compound was characterized as the expected 5β-hydroxycholestan-2β,3β-epoxide (XX) by the IR spectrum exhibiting an absorption band due to the intramolecularly hydrogen-bonded hydroxyl group at 3519 cm^{-1} and by the NMR spectrum showing the same

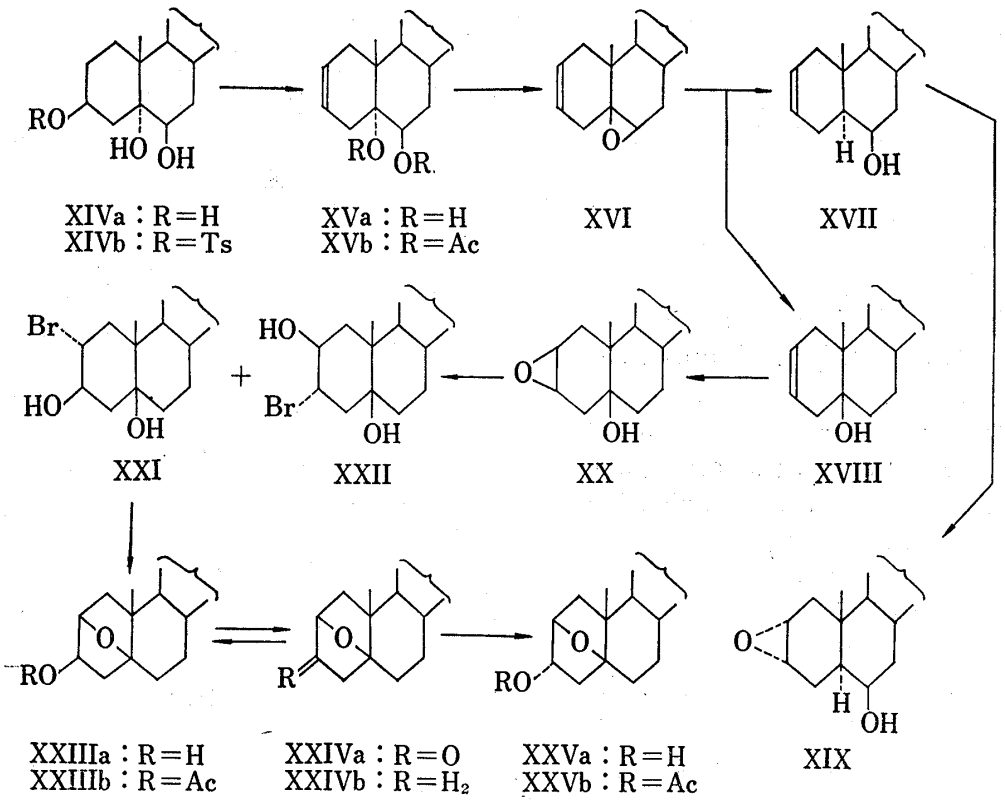
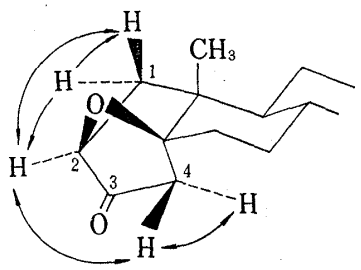


Chart 2

13) 5β,6β-Epoxycholestan-3β-ol could be prepared in this manner. L.F. Fieser and M. Fieser, "Steroids," Reinhold Co., New York, 1959, p. 198 and cited ref.

14) H.B. Henbest and J.A. Wilson reported that reduction of 3β-hydroxycholestan-5β,6β-epoxide with lithium aluminum hydride gave 3β,5β-diol in 43% yield, *J. Chem. Soc.*, **1957**, 1958. On the other hand no reaction of 3α-chlorocholestan-5β,6β-epoxide with the reagent was observed by M. Shiota, T. Ogihara and Y. Watanabe, *Bull. Chem. Soc. Japan*, **34**, 40 (1961).

signal pattern as that of 25D,5β-spirostan-2β,3β-epoxide[15] due to the protons attached to the epoxy moiety. Under the condition similar to that employed for I the epoxide (XX) gave a mixture of bromodiols, 88.5% of XXI and 5.8% of XXII, but no transannular epoxide. However, brief treatment of the diaxial bromohydrin (XXI) with pyridine gave 3β-hydroxy-2β,5β-epoxide (XXIIIa) in quantitative yield. This epoxide was characterized by the IR spectrum which exhibits an absorption band due to the bonded hydroxyl group at 3584 cm^{-1} and also by the NMR spectrum showing the bridge-head proton at 5.77 τ as a doublet ($J \approx 6.5$ Hz). Jones oxidation of the compound (XXIIIa) afforded 3-oxo-2β,5β-epoxide (XXIVa), whose structure was confirmed by the 100 MHz NMR spectrum using a spin-decoupling method.[16] (Fig. 2) This ketone upon Huang-Minlon reduction gave cholestan-2β,5β-epoxide (XXIVb) in low yield, which was confirmed on the basis of the NMR spectrum showing the bridge-head proton at 5.58 τ as a triplet ($J \approx$ 5.0 Hz). Reduction of the ketone with lithium aluminum hydride afforded 8.0% of 3β-hydroxy-2β,5β-epoxide (XXIIIa) and 74.3% of 3α-hydroxy-2β,5β-epoxide (XXVa). The structure of XXVa was established by the NMR spectrum of its acetate (XXVb) which exhibits the bridge-head proton at 5.50 τ as a triplet ($J \approx 5.0$ Hz).



$J_{2\alpha:1\beta}$ 6.8Hz
$J_{2\alpha:1\alpha}$ 0.5Hz
$J_{2\alpha:4\beta}$ 1.5Hz
$J_{1\alpha:1\beta}$ −13.0Hz
$J_{4\alpha:4\beta}$ −18.5Hz

1α−H 8.592 τ
1β−H 8.266 τ
2α−H 5.715 τ
4α−H 7.277 τ
4β−H 7.967 τ

Fig. 2

Finally the reaction of 5α-hydroxy-2α,3α-epoxide with hydrobromic acid was applied to the androstane and pregnane series. The starting materials which contain the partial structure of 3β,5α-diol, (XXVIa), (XXVIb) and (XXVIc), were prepared from 20-ethylenedioxypregn-5-en-3β-ol, 17-ethylenedioxyandrost-5-en-3β-ol, and 19-norandrost-5-ene-3β,17β-diol, respectively, by conversions involving epoxidation with peracid, reduction with lithium aluminum hydride, and then hydrolysis of the ketal moiety. The 19-nor compound, 3β,5α,17β-triol, was converted to the 3,17-dibenzoate which was partially hydrolyzed to the 17-monobenzoate (XXVIc). Dehydration of these 3β,5α-diols through the tosylates gave the 2-en-5α-ols, (XXVIIa), (XXVIIb), (XXVIId), accompanied by a small amount of the 3,5-dienes. Reduction of the 17-ketone (XXVIIb), followed by acetylation afforded 17β-acetoxyandrost-2-en-5α-ol (XXVIIc). Epoxidation of these 2-en-5α-ols with *m*-chloroperbenzoic acid gave the corresponding 2α,3α-epoxides (XXVIIIa), (XXVIIIb), (XXVIIIc), (XXVIIId). The 19-nor compound (XXVIId) afforded a significant amount of the 2β,3β-epoxide (XXIX). The structures of XXVIIId and XXIX were confirmed by the fact that both compounds were transformed to the identical 2β,3α,5α,17β-tetraol 17-monobenzoate (XXXa) by treatment with perchloric acid and that the IR spectrum of XXVIIId shows the absorption band due to the bonded hydroxyl group at 3504 cm^{-1}.

These 5α-hydroxy-2α,3α-epoxides, (XXVIIIa), (XXVIIIb), (XXVIIIc), (XXVIIId), were treated with hydrobromic acid in a manner similar to that described above, affording the corresponding 3α-hydroxy-2α,5α-epoxides, (XXXIIIa), (XXXIIIb), (XXXIIId), accompanied

15) T. Komeno, S. Ishihara, H. Itani, H. Iwakura and K. Takeda, *Chem. Pharm. Bull.* (Tokyo), **17**, 2110 (1969).

16) The experiment was achieved by Dr. S. Sato and Dr. K. Tori in this laboratory, using a Varian HA-100 spectrometer. The authors express their indebtedness to them.

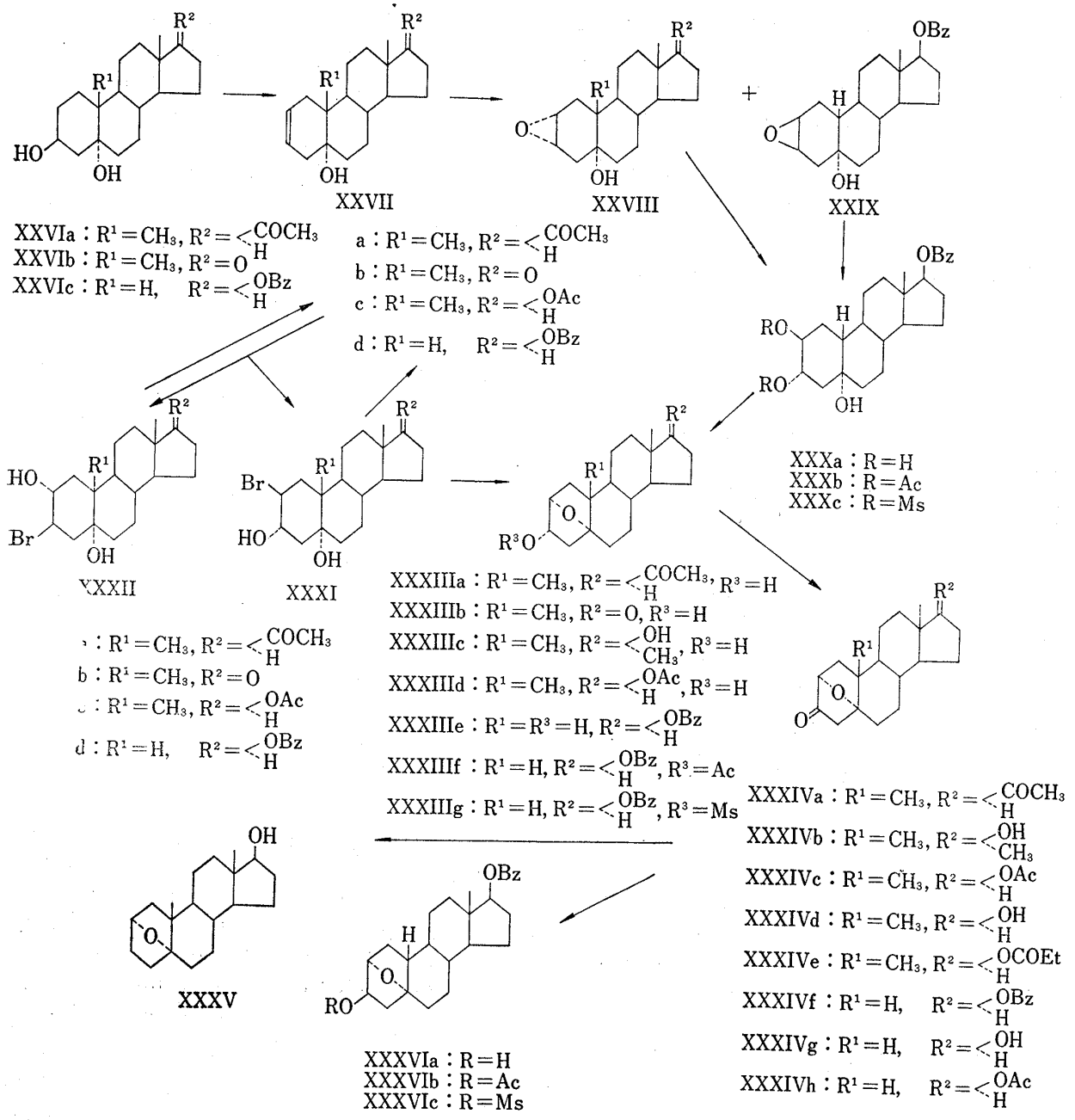


Chart 3

by a small amount of the trans diequatorial bromohydrins, (XXXIIa), (XXXIIc), except the case of the 19-nor compound (XXVIIId). As expected from the foregoing argument the reaction of XXVIIId with hydrobromic acid gave only a mixture of the bromohydrins, (XXXId), (XXXIId), and did not proceed further. Heating this mixture in pyridine resulted in the formation of the 3α-hydroxy-2α,5α-epoxide (XXXIIIe) as well as the unchanged diequatorial bromohydrin (XXXIId). Similarly, treatment of 19-nor-2β,3α,5α,17β-tetraol (XXXa) with mesyl chloride and pyridine at room temperature afforded the 2,3-dimesylate (XXXc) and not 3α-mesyloxy-2α,5α-epoxide (XXXIIIg), which was obtained by heating the mesylate in pyridine.

Treatment of 3α-hydroxy-17-oxoandrostan-2α,5α-epoxide (XXXIIIb) with methyl lithium gave 17-methyl carbinol (XXXIIIc). Oxidation of these 3α-hydroxy-2α,5α-epoxides afforded the corresponding 3-ketones, (XXXIVa), (XXXIVb), (XXXIVc), (XXXIVf). The 19-nor compounds (XXXIVf) was reduced with sodium borohydride to the 3β (*endo*)-hydroxy-2α,5α-epoxide (XXXVIa) in a quite similar manner as found above.

Experimental[17]

3-Oxocholestan-2α,5α-epoxide (V)——a) From 3α-Hydroxycholestan-2α,5α-epoxide (IIIb): To a solution of 384 mg of IIIb in 10 ml of acetone was added 0.3 ml of 8N Jones reagent.[18] The resulting mixture was stirred at room temperature for 10 min, poured into ice-water, and extracted with ether. The usual work up gave the product, which was recrystallized from acetone yielding 317 mg (82.5%) of V, mp 163.5—164°, $[\alpha]_D^{21}$ +52.9±0.8° (c=1.023). IR ν_{max} cm^{-1}: 1763, 997, 936, 810, $\nu_{max}^{CS_2}$ cm^{-1}: 1768, 994, 984, 809. NMR τ: (18-H) 9.32, (19-H) 9.01, (4α-H) 7.95d, (4β-H) 7.55d ($J_{4\alpha:4\beta}\approx-18.0$), (2β-H) 5.74d ($J_{2\beta:1\alpha}\approx7.0$ Hz). *Anal.* Calcd. for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.76; H, 11.03.

b) From 3β-Hydroxycholestan-2α,5α-epoxide (VIIa): The hydroxyepoxide (VIIa) (20 mg) was oxidized with 0.02 ml of 8N Jones reagent in 2 ml of acetone to give 15 mg of the ketone (V), mp 162—164°, which was identified with the above compound by mixed mp and comparison of the IR spectrum.

2α-Acetoxycholest-4-en-3-one (XI)——To a solution of 179 mg of the ketone (V) in a mixture of 6 ml of AcOH and 3 ml of Ac_2O, was added 15 drops of $BF_3\cdot OEt_2$. The mixture was stirred at room temperature for 5 hr, then warmed on a steam bath for an additional 30 min, poured into ice-water, and extracted with ether. The ethereal solution was washed with 10% Na_2CO_3 and water, dried over Na_2SO_4, and evaporated to dryness under reduced pressure. The residue was submitted to preparative TLC using cyclohexane–AcOEt (3:1) as developing solvent. The fraction corresponded to the main spot was recrystallized from MeOH to afford 105 mg (53.1%) of XI, mp 141—142°, $[\alpha]_D^{22}$ +65.3±0.8 (c=1.068) (reported mp 141—142°). IR $\nu_{max}^{CS_2}$ cm^{-1}: 1750, 1697, 1621, 1235, 1215, 882. UV λ_{max} mμ (ε): 245.5 (14900), 306 (100). NMR τ: (18-H) 9.30, (19-H) 8.68, (AcO) 7.85, (2β-H) 4.56d-d ($J_{2\beta:1\alpha}\approx13.8$, $J_{2\beta:1\beta}\approx6.0$ Hz); (4-H) 4.27. This compound was identified with the authentic sample prepared by oxidation of cholestenone with $Pb(OAc)_4$.[19]

Cholestan-2α,5α-epoxide (VIa)——a) From 3-Oxocholestan-2α,5α-epoxide (V): A mixture of 60 mg of V, 220 mg of KOH, 1.1 ml of 80% $NH_2\cdot NH_2\cdot H_2O$, and 6.7 ml of triethylene glycol was refluxed at 130° for 70 min then distilled until the inner temperature reached to 210°. The remained mixture was heated at the same temperature for 2 hr. After cooling the mixture was poured into ice-water and extracted with ether. The usual work-up gave the product, which was submitted to preparative TLC using cyclohexane–AcOEt (4:1) as developing solvent. The fraction corresponded to the main spot was recrystallized from MeOH to yield 36 mg (62.2%) of VIa, mp 104—105°, $[\alpha]_D^{20}$ +27.5±1.0 (c=1.153). IR ν_{max} cm^{-1}: 975, $\nu_{max}^{CS_2}$ cm^{-1}: 974. NMR τ: (18-H) 9.33, (19-H) 9.04, (2β-H) 5.62t ($J_{2\beta:1\alpha}=J_{2\beta:3\alpha}\approx5.0$ Hz). *Anal.* Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.80; H, 11.98.

b) From Cholestane-2β,5α-diol (VIIIa): A mixture of 138 mg of VIIIa, 0.2 ml of MsCl, and 2 ml of pyridine was allowed to stand at 0° in a refrigerator overnight. After dilution with ice-water the mixture was extracted with ether. The ethereal solution was washed successively with 10% HCl, 10% Na_2CO_3, and water, dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the product was effected by preparative TLC using cyclohexane–AcOEt (4:1) as developing solvent. The fraction (107 mg) corresponded to the main spot was recrystallized from MeOH to yield 95 mg (72.1%) of VIa, mp 104—105°.

c) From 3α-Thiocyanatocholestan-2α,5α-epoxide (VIb): To a suspension of 250 mg of $LiAlH_4$ in 1 ml of dry ether a solution of 100 mg of VIb in 1 ml of dry ether was added dropwise with stirring for 5 min. The reaction mixture was stirred at room temperature for 2 hr. The usual work-up afforded 83 mg of the solid, which was recrystallized from MeOH to yield 75 mg of VIa, mp 104—105°.

d) From 3α-Bromocholestan-2α,5α-epoxide (VIf): The bromide (VIf) (50 mg) was hydrogenated over 0.4 ml of freshly prepared W-2 Raney Ni in 2 ml of tetrahydrofuran. After removal of the catalyst by filtration the solvent was evaporated under reduced pressure. The residue was submitted to preparative TLC. Recrystallization from MeOH gave 40 mg (96%) of VIa, mp 103—104.5°.

Identification of the compounds described in a), b), c) and d) was done by a mixed mp, comparison of the IR spectrum and TLC.

Cholestane-2β,5α-diol (VIIIa)——To a suspension of 100 mg of $LiAlH_4$ in 10 ml of dry ether a solution of 419 mg of 5α-hydroxy-2β,3β-oxide (IV) in 20 ml of dry ether was added dropwise with stirring. The reaction mixture was agitated for 5 hr and worked up in the usual way. Recrystallization of the product from aqueous MeOH afforded 347 mg (82.1%) of VIIIa, mp 168—170°, $[\alpha]_D^{20}$ +19.7±0.5° (c=0.956). IR ν_{max} cm^{-1}: 3368. NMR τ: (18-H) 9.34, (19-H) 8.80, (2α-H) 5.81 (W h/2=8.0 Hz). *Anal.* Calcd. for

17) All melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were determined in 1% EtOH–$CHCl_3$ with a Perkin Elmer Polarimeter, type 141. UV spectra were recorded with a Hitachi EPS-2 spectrophotometer. Unless otherwise stated IR spectra were determined in Nujol mulls with a Koken DS-201B spectrophotometer. Intramolecular hydrogen bonding was measured in about 1.5×10^{-3}M CCl_4 solution using 20 mm cell. All NMR spectra were run in $CDCl_3$ solutions with a Varian A-60 spectrometer, TMS serving as internal standard. Apparent coupling constants were obtained from the 1st order analysis. For preparative TLC Silica gel G (E. Merck Co.) was used as an adsorbent.

18) C. Djerassi, R.R. Engle and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1957).

$C_{27}H_{48}O_2$: C, 80.14; H, 11.96. Found: C, 80.17; H, 11.85. Acetylation of 119 mg of VIIIa with 2 ml of pyridine and 1 ml of Ac_2O gave 139 mg of the monoacetate (VIIIb), as an amorphous substance. NMR τ: (18-H) 9.35, (19-H) 8.91, (OAc) 7.99, (2α-H) 4.88 (W h/2=9.0 Hz).

3α-Thiocyanatocholestan-2α,5α-epoxide (VIb)——A mixture of 150 mg of 2β,5α-dihydroxycholestane-3α-thiocyanate (VIIIc),[1] 1.5 ml of pyridine and 0.35 ml of MsCl was allowed to stand at 0° in a refrigerator overnight. The usual work-up afforded 185 mg of the product, which was recrystallized from ether–CH_2Cl_2 to yield the pure sample (VIIId), mp 117—119°, $[\alpha]_D^{23}$ −2.4±0.4° (c=1.008). IR ν_{max} cm^{-1}: 3501, 2147, 1172, 900. *Anal.* Calcd. for $C_{29}H_{49}O_4NS_2$: C, 64.52; H, 9.15; N, 2.59; S, 11.85. Found: C, 64.37; H, 9.04; N, 2.59; S, 12.01. In another run, 1.285 g of VIIIc was treated with 2.6 ml of MsCl in 14 ml of pyridine. After work-up in the same way as described above, the crude mesylate (*ca.* 4.0 g) was dissolved in 30 ml of pyridine. The reaction mixture was warmed to 80° on a steam bath for 2 hr. After cooling, this was poured into ice-water and extracted with ether. The usual work-up afforded 1.206 g of the solid, which was recrystallized from ether–MeOH to yield 961 mg (78.0%) of VIb, mp 108—110°, $[\alpha]_D^{23}$ −43.4±0.8° (c=0.997). IR ν_{max} cm^{-1}: 2156, 981. NMR τ: (18-H) 9.35, (19-H) 9.07, (4β-H) 7.42d-d ($J_{4\beta:4\alpha}\approx-14.0$, $J_{4\beta:3\beta}\approx8.0$), (3$\beta$-H) 6.52d-d ($J_{3\beta:4\alpha}\approx8.0$, $J_{3\beta:4\alpha}\approx4.0$), (2$\beta$-H) 5.57d ($J_{2\beta:1\alpha}$=6.0 Hz). *Anal.* Calcd. for $C_{28}H_{45}ONS$: C, 75.79; H, 10.22; N, 3.16; S, 7.23. Found: C, 75.62; H, 9.93; N, 2.91; S, 7.33.

3α-Mercaptocholestan-2α,5α-epoxide (VIc)——To a cold solution of 815 mg of the thiocyanate (VIb) in 30 ml of tetrahydrofuran 5.3 ml of 18.4 mM solution of (i-Bu)$_2$AlH in tetrahydrofuran was added at 3° with stirring in a stream of N_2. After agitation for 1.5 hr, the mixtuer was poured into iced 5% HCl, and extracted with a mixture of ether and CH_2Cl_2 (2:1). The organic layer was worked up in the usual way to yield 795 mg of the product, which was submitted to preparative TLC using benzene–cyclohexane (7:3) as developing solvent. The fraction corresponded to the main spot was recrystallized from acetone to give 505 mg (65.7%) of VIc, mp 114—115°, $[\alpha]_D^{23}$ +19.6±0.7° (c=0.911). IR ν_{max} cm^{-1}=2548 w, 929. NMR τ: (18-H) 9.34, (19-H) 9.09, (3β-H,4-H) unresolved multiplet 7.11—7.59, (2β-H) 5.83d ($J_{1\alpha:2\beta}\approx5.9$ Hz). *Anal.* Calcd. for $C_{27}H_{46}OS$: C, 77.45; H, 11.07; S, 7.66. Found: C, 77.68; H, 11.08; S, 7.75. Acetylation of this compound with pyridine and Ac_2O afforded the acetate (VId), which was recrystallized from ether–MeOH to yield the pure sample, mp 112—113°, $[\alpha]_D^{23}$ −35.8±0.8 (c=0.977). IR ν_{max} cm^{-1}: 1692, 1114, 979. UV λ_{max}^{MeOH} mμ (ε): 232 (4470). NMR τ: (18-H) 9.35, (19-H) 9.04, (AcS) 7.72, (4β-H) 7.49d-d ($J_{4\beta:4\alpha}\approx-14.0$, $J_{4\beta:3\beta}\approx8.5$), (3$\beta$-H) 6.49d-d ($J_{3\beta:4\beta}\approx8.5$, $J_{3\beta:4\alpha}\approx4.5$), (2$\beta$-H) 5.81d ($J_{2\beta:1\alpha}\approx6.0$ Hz). *Anal.* Calcd. for $C_{29}H_{48}O_2S$: C, 75.60; H, 10.50; S, 6.96. Found: C, 75.78; H, 10.60; S, 7.03. A mixture of 262 mg of Pb(OAc)$_4$, 78 mg of $CaCO_3$, and 6.1 ml of cyclohexane was refluxed with stirring for 30 min. To the mixture 48 mg of the thiol (VIc) was added and the reaction mixture was refluxed with stirring for 1 hr. After cooling the solid was removed by filtration and washed with CH_2Cl_2. The combined filtrates were washed successively with 10% HCl, 10% Na_2CO_3 and water, dried, and evaporated to dryness. The product was recrystallized from CH_2Cl_2 acetone to yield 43 mg of the disulfide (VIe), mp 280.5—282.5°, $[\alpha]_D^{23}$ −17.8±4.3° (c=0.489). IR ν_{max} cm^{-1}: 976. UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (620). NMR τ: (18-H) 9.34, (19-H) 9.07, (4β-H) 7.62d-d ($J_{4\alpha:4\beta}\approx-14.0$, $J_{3\beta:4\beta}\approx8.0$), (3$\beta$-H) 6.96d-d ($J_{3\beta:4\beta}\approx8.0$, $J_{3\beta:4\alpha}\approx4.0$), (2$\beta$-H) 5.60d ($J_{2\beta:1\alpha}\approx5.6$ Hz). Mol. wt. Calcd., 835.4; Found, 847. *Anal.* Calcd. for $C_{54}H_{90}O_2S_2$: C, 77.63; H, 10.86; S, 7.68. Found: C, 77.71; H, 10.88; S, 7.55.

3α-Bromocholestan-2α,5α-epoxide (VIf)——To a solution of 509 mg of the olefin (XII) in 6 ml of CCl_4, 0.5 ml of 0.49 mM Br_2–CCl_4 was added dropwise with stirring. After agitation for an additional 10 min, the solution was concentrated at 20° under reduced pressure. The residue was recrystallized from acetone to afford the pure sample of Xb, mp 125—126°, $[\alpha]_D^{22}$ +84.6±1.6° (c=0.777). IR ν_{max} cm^{-1}: 3584, 1173. NMR τ: (18-H) 9.34, (19-H) 8.82, (2α-H, 3β-H) *ca.* 5.15 m. *Anal.* Calcd. for $C_{27}H_{46}OBr_2$: C, 59.34; H, 8.48; Br, 29.25. Found: C, 59.48; H, 8.48; Br, 29.09. The mother liquor (500 mg) was dissolved in 15 ml of pyridine and the mixture was allowed to stand at room temperature overnight. The usual work-up afforded the solid, which was recrystallized from acetone to give 298 mg (70.2%) of VIf, mp 121—124°, $[\alpha]_D^{22}$ +23.6±0.8° (c=0.837). IR ν_{max} cm^{-1}: 995, 983. NMR τ: (18-H) 9.34, (19-H) 9.09, (4β-H) 7.26d-d ($J_{4\alpha:4\beta}\approx-14.5$, $J_{4\beta:3\beta}\approx7.5$), (3$\beta$-H) 6.00d-d ($J_{3\beta:4\beta}\approx7.5$, $J_{3\beta:4\alpha}\approx3.5$), (2$\beta$-H) 5.55d ($J_{2\beta:1\alpha}\approx6.0$ Hz). *Anal.* Calcd. for $C_{27}H_{45}OBr$: C, 69.66; H, 9.74; Br, 17.17. Found: C, 69.66; H, 9.69; Br, 17.35.

3β-Hydroxycholestan-2α,5α-epoxide (VIIa)——The ketone (V) (100 mg) was reduced with 34 mg of $LiAlH_4$ in 6 ml of dry ether at room temperature for 1 hr. The usual work-up afforded 101 mg of the solid, which upon recrystallization from *n*-hexane yielded 82 mg (81.6%) of VIIa, mp 164—165.5°, $[\alpha]_D^{20}$ +25.3±0.7° (c=0.965). IR ν_{max} cm^{-1}: 3443, 977, 807. NMR τ: (18-H) 9.33, (19-H) 8.97, (2β-H, 3α-H) *ca.* 5.74 m. *Anal.* Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.34; H, 11.48. Acetylation in the usual way gave the acetate (VIIb), which was recrystallized from MeOH to give the pure sample, mp 108—110°, $[\alpha]_D^{23}$ +34.9±2° (c=1.003). IR ν_{max} cm^{-1}: 1732, 1245, 1058, 990, 981. NMR τ: (18-H) 9.33, (19-H) 9.00, (AcO) 7.97, (2β-H) 5.50 m, (3α-H) 5.13 m. *Anal.* Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.06; H, 10.64. Mesylation of VIIa in the usual way afforded the mesylate (VIIc), which upon recrystallization from hexane gave the pure sample, mp 128.0—129.5°, $[\alpha]_D^{23}$ +28.7±0.6° (c=0.943). IR ν_{max} cm^{-1}: 1179, 1164, 1009, 910, 893, 850. NMR τ: (18-H) 9.33, (19-H) 8.98, (MsO) 7.00, (2β-H) 5.50 m, (3α-H) 5.10 m. *Anal.* Calcd. for $C_{28}H_{48}O_4S$: C, 69.95; H, 10.06; S, 6.70. Found: C, 69.97; H, 10.13; S, 6.80.

Cleavage of 5α-Hydroxycholestan-2β,3β-epoxide (IV)——A solution of 304 mg of IV in 6 ml of AcOH was heated on a steam bath for 4.5 hr, then poured into ice-water, and extracted with ether. The ether layer was worked up in the usual way. Separation of the products was effected by preparative TLC using cyclohexane–AcOEt (2:1) as developing solvent. The most mobile fraction afforded 18 mg (5.4%) of the solid, identical with 3β-acetoxy-2α,5α-epoxide (VIIb). The second mobile fraction gave 38 mg of an unidentified substance and the third mobile fraction yielded 129 mg (37.0%) of 2β,3α,5α-triol 3-monoacetate (IId), which was recrystallized from acetone–hexane. mp 149—151°, $[\alpha]_D^{23}$ +27.9±2° (c=0.971). IR ν_{max} cm^{-1}: 3509, 3405, 1714, 1703, 1260, 1246, 1045, 1026. NMR τ: (18-H) 9.34, (19-H) 8.86, (AcO) 7.93, (2α-H) 5.92 (W h/2≈10.0), (3β-H) 5.00 (W h/2≈10.0 Hz). *Anal.* Calcd. for $C_{29}H_{50}O_4$: C, 75.28; H, 10.89. Found: C, 75.10; H, 10.87. The forth mobile fraction afforded 20 mg (5.0%) of the solid identical with 3β-hydroxy-2α,5α-epoxide (VIIa). The most polar fraction gave 60 mg of a mixture, which was not studied further.

Identification of the triol monoacetate was carried out in the following way. Acetylation of this compound with pyridine and Ac_2O yielded the diacetate (IIc), mp 122—123°, identified with the authentic sample.[1] The monoacetate (39 mg) was treated with 0.1 ml of MsCl in 0.5 ml of pyridine overight. Work-up gave 28 mg (74.9%) of 3α-acetoxy-2α,5α-epoxide (IIIc), mp 82—84°, which was identified by mixed mp, comparison of the IR spectrum and TLC.

The Reaction of 5α-Hydroxycholestan-2α,3α-epoxide (I) with Hydrobromic Acid——a) To a solution of 200 mg of I in 10 ml of ether 0.2 ml of 48% HBr was added. The reaction mixture was stirred for 30 min, then poured into ice-water, and extracted with ether. After the usual work-up, two recrystallization from ether–pet. ether afforded 120 mg of the bromodiol (Xa), mp 124—126°, $[\alpha]_D^{21}$ +29.2±0.6° (c=1.004). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3468, 3328, 1053, 869. NMR τ: (18-H) 9.34, (19-H) 8.71. *Anal.* Calcd. for $C_{27}H_{47}O_2Br$: C, 67.06; H, 9.80; Br, 16.53. Found: C, 67.11; H, 9.73; Br, 16.82. The bromide (25 mg) was treated with 30 mg of KOH in a mixture of 3 ml of tetrahydrofuran and 3 ml of MeOH for 10 min and 17 mg of the epoxide (I) was regenerated.

b) A mixture of 200 mg of I, 10 ml of CH_2Cl_2, and 0.3 ml of 48% HBr was stirred at room temperature for 5.5 hr. After work-up the product (223 mg) was submitted to preparative TLC using cyclohexane–AcOEt (7:3) as developing solvent. The more mobile fraction afforded 38 mg of IX, which was recrystallized from ether–pet. ether. mp 182—183°, $[\alpha]_D^{22}$ +11.2±0.4° (c=0.875). IR $\nu_{max}^{CS_2}$ cm^{-1}: 3560, 1051, 698. NMR τ: (18-H) 9.35, (19-H) 9.09, (2β-H) 6.08t-d ($J_{2\beta:1\alpha}=J_{2\beta:3\alpha}\approx10.0$, $J_{2\beta:1\alpha}\approx5.0$), (3α-H) 5.58t-d ($J_{2\beta:3\alpha}=J_{3\alpha:4\beta}\approx10.0$, $J_{3\alpha:4\alpha}\approx6.0$ Hz). *Anal.* Calcd. for $C_{27}H_{47}O_2Br$: C, 67.06; H, 9.80; Br, 16.53. Found: C, 67.07; H, 9.77; Br, 16.91. Treatment of 14 mg of the bromide with 25 mg of KOH in a mixture of 3 ml of tetrahydrofuran and 2 ml of MeOH for 30 min gave 10 mg of the parent oxide (I). The less mobile fraction was recrystallized from aqueous acetone to give 133 mg (66.5%) of IIIb, mp 151—152°, which was identified by mixed mp, comparison of the IR spectrum and TLC. The most polar fraction yielded 7 mg of the solid whose IR spectrum shows only an absorption due to hydroxyl group.

2β-Chlorocholestane-3α,5α-diol (XIII)——A mixture of 100 mg of the epoxide (I), 0.15 ml of 36% HCl, and 5 ml of ether was stirred for 30 min. Work-up in a manner similar to that described above afforded the product, which upon recrystallization from ether–pet. ether gave 70 mg of XIII, mp 135—136°, $[\alpha]_D^{22}$ +23.7±0.5° (c=1.032). IR $\nu_{max}^{CS_2}$: 3590, 3481, 3321, 1054, 873, 698. *Anal.* Calcd. for $C_{27}H_{47}O_2Cl$: C, 73.85; H, 10.79; Cl, 8.07. Found: C, 73.45; H, 10.56; Cl, 8.46. On treatment of XIII with either HCl or pyridine only the starting material was recovered.

5α,6β-Diacetoxycholest-2-ene (XVb)——To a cold solution of 41 g of cholestane-3β,5α,6β-triol (XIVa)[20] in 500 ml of pyridine 25 g of TsCl was added portionwise with stirring. The resulting mixture was allowed to stand at room temperature for 2 days, then poured into ice-water, acidified with 2N HCl, and extracted with ether. The usual work-up afforded 54 g of the solid (XIVb), which was used for the next step without purification. A solution of this material in 260 ml of 2,4,6-collidine was heated to 140° for 1 hr. After cooled to room temperature, the mixture was poured into iced 2N HCl and extracted with ether. The usual work-up gave 40 g of the oily residue, which upon crystallization from ether–pet. ether afforded 11.68 g of XVa. The mother liquor was chromatographed over 600 g of Al_2O_3. The fractions eluted with pet. ether–benzene (3:1) gave 2.9 g of an oily mixture. The fractions eluted with pet. ether–benzene (1:1) and benzene were crystallized from ether–pet. ether to yield 7.52 g of XVa. The combined crystals (19.2 g) was dissolved in a mixture of 150 ml of AcOH and 100 ml of Ac_2O and to this 770 mg of p-TsOH–H_2O was added. The resulting mixture was allowed to stand at room temperature overnight, then poured into ice water, and extracted with ether. After the usual work-up, recrystallization from MeOH gave 15.7 g (33% overall yield) of the pure ene-diol diacetate (XVb), mp 130—132°, $[\alpha]_D^{22}$ −33.1±0.7° (c=1.024). IR ν_{max} cm^{-1}:

19) E. Seebeck and T. Reichstein, *Helv. Chim. Acta*, **27**, 948 (1944); F. Sondheimer, S. Kaufmann, J. Romo, H. Martinez and G. Rosenkranz, *J. Am. Chem. Soc.*, **75**, 4712 (1953); L.F. Fieser and M.A. Romero, *ibid.*, **75**, 4716 (1953).

20) R.H. Pickard and J. Yates, *J. Chem. Soc.*, **1908**, 1678; L.F. Fieser and S. Rajagopalan, *J. Am. Chem. Soc.*, **71**, 3938 (1949).

3026, 1746, 1733, 1658, 1250, 1235, 1210, 1036, 1018. NMR τ: (18-H) 9.30, (19-H) 8.94, (AcO) 8.05, 7.94, (2-H, 3-H) 4.45 m (2H), (6α-H) 4.12 (W h/2≈5.5 Hz). *Anal.* Calcd. for $C_{31}H_{50}O_4$: C, 76.50; H, 10.36. Found: C, 76.57; H, 10.35.

Cholest-2-en-5β,6β-epoxide (XVI)——a) A solution of 1.0 g of the above diacetate (XVb) and 2.0 g of KOH in 20 ml of absolute EtOH was refluxed for 3 hr. Extraction with ether and crystallization from pet. ether gave 260 mg of the diol (XVa). The mother liquor (475 mg) was chromatographed over 15 g of Al_2O_3. The fractions eluted with pet. ether were recrystallized from MeOH to afford 247 mg (30.5%) of the epoxide (XVI), mp 79—80°, $[\alpha]_D^{23}$ +16.3±0.5° (c=1.005). IR ν_{max} cm^{-1}: 3040, 1645, 859, 815. NMR τ: (18-H) 9.36, (19-H) 9.02, (6α-H) 7.00d ($J_{6\alpha:7\beta}$≈2.5 Hz),[21] (2-H, 3-H) 4.22 m (2H). *Anal.* Calcd. for $C_{27}H_{44}O$: C, 84.31; H, 11.53. Found: C, 84.45; H, 11.51. The fractions eluted with pet. ether–benzene (4:1) gave 24 mg of a mixture. The fractions eluted with pet. ether–benzene (1:1) yielded 211 mg of XVa. The combined yield of XVa was 59%.

b) A solution of 57.3 g of the diacetate (XVb), 60 g of KOH in 1.2 liter of *i*-PrOH was refluxed for 2.5 hr. The work-up gave 48 g of the residue, which was chromatographed over 1 kg of Al_2O_3. The fractions eluted with pet. ether and pet. ether–benzene (9:1) were recrystallized from ether–MeOH to give 27.0 g (59.5%) of the epoxide (XVI). From the fractions eluted with benzene–ether (9:1, 4:1), 11.2 g (22.4%) of the diol (XVa) was recovered.

Reduction of Cholest-2-en-5β,6β-epoxide (XVI)——A mixture of 4.5 g of XVI, 700 mg of $LiAlH_4$, and 200 ml of dry ether was stirred at room temperature for 8 hr. After the usual work-up, the product was submitted to column chromatography over 500 g of silica gel G, using cyclohexane–AcOEt (5:1) as eluting solvent. The first fraction eluted with 220 ml of the solvent gave 3.210 g of 5α-cholest-2-en-6β-ol (XVIII), which was recrystallized from aqueous acetone, mp 93—94°, $[\alpha]_D^{23}$ +47.8±0.9° (c=0.941). IR ν_{max} cm^{-1}: 3406, 3016, 1658, 1048, 1020, 724. NMR τ: (18-H) 9.29, (19-H) 9.03, (6α-H) 6.15 m (W h/2≈5.5 Hz), (2-H, 3-H) 4.37 m (2H). *Anal.* Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.83; H, 11.92. The second fractions eluted with 80 ml of the solvent gave a mixture of XVII and XVIII, which was separated by preparative TLC affording 255 mg of XVII and 320 mg of XVIII. The combined yield of XVII was 3.465 g (76.7%). The third fraction eluted with 150 ml of the solvent yielded 450 mg of cholest-2-en-5β-ol (XVIII), which was recrystallized from aqueous acetone. The combined yield of XVIII was 770 mg (17%), mp 78—79°, $[\alpha]_D^{23}$ +43.6±0.9° (c=0.892). IR ν_{max} cm^{-1}: 3490, 3014, 1664. NMR τ: (18-H) 9 35, (19-H) 9.05, (2-H, 3-H) 4.43 m (2H). *Anal.* Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.66; H, 11.98.

6β-Hydroxy-5α-cholestan-2α,3α-epoxide (XIX)——The olefin (XVII) (1.227 g) was oxidized with 777 mg of *m*-chloroperbenzoic acid in 20 ml of CH_2Cl_2. After the usual work-up recrystallization from MeOH yielded 1.170 g of XIX, mp 168—169°, $[\alpha]_D^{20}$ +20.9±0.9° (c=0.683). IR ν_{max} cm^{-1}: 3465, 1048, 804. NMR τ: (18-H)9.32, (19-H) 9.02, (2-H, 3-H) 6.83 m (2H), (6α-H) 6.25 m (W h/2≈6.5 Hz). *Anal.* Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.41; H, 11.49.

5β-Hydroxycholestan-2β,3β-epoxide (XX)——The olefin (XVIII) (1.247 g) was oxidized with 790 mg of *m*-chloroperbenzoic acid in 25 ml of CH_2Cl_2. After the usual work-up recrystallization from MeOH afforded 1.166 g (92.0%) of XX, mp 163—165°, $[\alpha]_D^{23}$ +41.3±0.9° (c=0.959). IR ν_{max} cm^{-1}: 3461, 1061, 812. NMR τ: (18-H) 9.34, (19-H) 9.08, (2-H, 3-H) 6.79 m (2H). *Anal.* Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.58; H, 11.49.

The Reaction of 5β-Hydroxycholestan-2β,3β-epoxide (XX) with Hydrobromic Acid——A mixture of 1.166 g of XX, 30 ml of CH_2Cl_2, and 1.2 ml of 48% HBr was stirred at room temperature for 1 hr. The organic layer was washed with 10% Na_2CO_3 and water, dried, and evaporated under reduced pressure. Two recrystallization from acetone afforded 955 mg (68.3%) of the bromodiol (XXI), mp 112—114° (decomp.), $[\alpha]_D^{24}$ +23.6±0.6° (c=0.967). IR ν_{max} cm^{-1}: 3400, 3220, 1088, 1080, 1058, 873. NMR τ: (18-H) 9.33, (19-H) 9.08, (2-H, 3-H) 5.77 m (2H). *Anal.* Calcd. for $C_{27}H_{47}O_2Br$: C, 67.06; H, 9.80; Br, 16.53. Found: C, 67.18; H, 9.77; Br, 16.64. The mother liquor (458 mg), which was a mixture of XXI and XXII judging from TLC, was dissolved in 10 ml of pyridine and the solution was warmed on a steam bath for 3 hr. After the usual work-up the product was separated by preparative TLC using cyclohexane–AcOEt (2:1) as developing solvent. The more mobile fraction afforded 81 mg (5.8%) of the bromodiol (XXII), which was recrystallized from acetone, mp 195—196°, $[\alpha]_D^{23}$ +41.6±0.8° (c=0.975). IR ν_{max} cm^{-1}: 3265, 1090, 1060, 1044, 1017, 1004, 846. NMR τ: (18-H) 9.35, (19-H) 9.08. *Anal.* Calcd. for $C_{27}H_{47}O_2Br$: C, 67.06; H, 9.80. Found: C, 67.09; H, 9.68. The less mobile fraction was recrystallized from acetone to yield 236 mg (20.2%) of 3β-hydroxy-2β,5β-epoxide (XXIIIa), mp 163—165°, $[\alpha]_D^{24}$ +78.9±1.2° (c=0.958). IR ν_{max} cm^{-1}: 3460, 1079, 983, 944, 905. NMR τ: (18-H) 9.33, (19-H) 9.07, (4α-H) 7.38d-d ($J_{4\alpha:4\beta}$≈−14.0, $J_{4\alpha:3\alpha}$≈6.5), (2α-H) 5.77d ($J_{2\alpha:1\beta}$≈6.5), (3α-H) 6.45d ($J_{3\alpha:4\alpha}$≈6.5 Hz). *Anal.* Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 80.77; H, 11.46. Treatment of 850 mg of pure (XXI) with 20 ml of pyridine in a similar manner as above afforded 702 mg (a quantitative yield) of XXIIIa. Acetylation of this compound in the usual way gave the acetate (XXIIIb), mp 81.5—83°, $[\alpha]_D^{23}$ +65.9±1.0° (c=1.109). IR ν_{max} cm^{-1}: 1733, 1259, 1241, 1066, 1035, 975, 945, 908. NMR τ: (18-H) 9.32, (19-H) 9.05, (AcO) 7.94, (4α-H) 7.30d-d ($J_{4\alpha:4\beta}$≈−14.0, $J_{4\alpha:3\alpha}$

21) A.D. Cross, *J. Am. Chem. Soc.*, **84**, 3206 (1962).

≈7.0), (2α-H) 5.59d ($J_{2\alpha:1\beta}$≈6.5), (3α-H) 5.40d-d ($J_{3\alpha:4\alpha}$≈7.0, $J_{3\alpha:4\beta}$≈1.5 Hz). *Anal.* Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.61; H, 11.09.

Treatment of both bromodiols, XXI and XXII, with KOH–MeOH in ether led to the recovery of the parent epoxide (XX).

In the reaction of XX with HBr prolongation of the reaction time (5—7 hr) also gave a mixture of XXI and XXII, and not the transannular epoxide (XXIIIa).

3-Oxocholestan-2β,5β-epoxide (XXIVa)——A solution of 651 mg of XXIIIa in a mixture of 6 ml of acetone and 1 ml of CH_2Cl_2 was treated with 0.12 ml of Jones reagent for 10 min. Purification of the product was effected by preparative TLC using cyclohexane–AcOEt (4:1) as developing solvent. The more mobile fraction was recrystallized from MeOH to give 140 mg (89.6%) of XXIVa, mp 98—99°, $[\alpha]_D^{23}$ +54.3±1.0° (c=0.931). IR ν_{max} cm^{-1}: 1766, 979, 929. NMR τ: (18-H) 9.31, (19-H) 8.98, (2α-H) 5.70d ($J_{2\alpha:1\beta}$≈6.5 Hz). *Anal.* Calcd. for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.93; H, 11.07. From the less mobile fraction 8 mg (5.1%) of the starting material was recovered.

Cholestan-2β,5β-epoxide (XXIVb)——A mixture of 258 mg of the ketone (XXIVa), 2 ml of 80% $NH_2\cdot NH_2\cdot H_2O$, 500 mg of KOH, and 15 ml of triethylene glycol was treated similarly as was employed for VIa. The product was submitted to preprarative TLC using cyclohexane–AcOEt (9:1) as developing solvent. The more mobile fraction gave 110 mg of a noncrystalline material, which was not studied further. The less mobile fraction was recrystallized from MeOH to yield 74 mg (29.7%) of XXIVb, mp 77—78°, $[\alpha]_D^{22}$+72.9±1.2° (c=0.913). IR ν_{max} cm^{-1}: 980, 947, 935. NMR τ: (18-H) 9.31, (19-H) 9.08, (2α-H) 5.58t ($J_{2\alpha:1\beta}$≈$J_{2\alpha:3\beta}$≈5.0 Hz). *Anal.* Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.90; H, 12.00.

3α-Hydroxycholestan-2β,5β-epoxide (XXVa)—— A cold solution of 320 mg of the ketone (XXIVa) in 5 ml of dry ether was reduced with 31 mg of $LiAlH_4$ for 1 hr. After the usual work-up, the product was submitted to preparative TLC using cyclohexane–AcOEt (2:1) as developing solvent. The less mobile fraction yielded 26 mg (7.9%) of the exo alcohol (XXIIIa), which was identified by mixed mp, comparison of the IR spectrum and TLC. The more mobile fraction was recrystallized from MeOH to give 243 mg (74.3%) of XXVa, mp 136—137°, $[\alpha]_D^{22}$ +70.6±1.4° (c=0.780). IR ν_{max} cm^{-1}: 3415, 1105, 968, 940. NMR τ: (18-H) 9.32, (19-H) 9.04, (2α-H) 5.74 m, (3β-H) 5.74 m. *Anal.* Calcd. for $C_{27}H_{46}O_2\cdot\frac{1}{3}H_2O$: C, 79.51; H, 11.51. Found: C, 79.22; H, 11.61. Acetylation with pyridine–Ac_2O afforded the acetate (XXVb), which was recrystallized from ether–MeOH. mp 100.5—101.5°, $[\alpha]_D^{23}$ +58.9±0.7° (c=0.923). IR ν_{max} cm^{-1}: 1747, 1240, 1075, 1049, 975, 941, 922. NMR τ: (18-H) 9.31, (19-H) 9.03, (AcO) 7.95, (2α-H) 5.50t ($J_{2\alpha:1\beta}$=$J_{2\alpha:3\beta}$ ≈5.0 Hz), (3β-H) 5.18 m. *Anal.* Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.37; H, 10.74.

5α-Hydroxypregn-2-en-20-one (XXVIIa)——A mixture of 25 g of pregnenolone, 20 ml of ethylene glycol, 1.5 g of p-TsOH·H_2O, 800 ml of dry benzene was refluxed with constant removal of water for 23 hr. After cooled to the room temperature the mixture was poured into iced 10% Na_2CO_3 and extracted with $CHCl_3$. The solvent was removed and the crude ketal was dissolved in 250 ml of $CHCl_3$ and treated with 23.3 g of m-chloroperbenzoic acid at room temperature for 1 hr. After the usual work-up the product was reduced with 5.6 g of $LiAlH_4$ in a mixture of 250 ml of dry tetrahydrofuran and 200 ml of dry ether under reflux for 2 hr. The work-up afforded 26.3 g of the solid, which was warmed to 80° in 300 ml of 70% AcOH for 1 hr. After dilution with water, the precipitate was collected by filtration, washed with water, and dried leaving 21 g of the crude material of XXVIa. Recrystallization from CH_2Cl_2–MeOH afforded 12.5 g of the pure (XXVIa) in 50% overall yield from pregnenolone. The diol (XXVIa) was treated with 9.28 g of p-TsCl and 150 ml of pyridine giving the tosylate which on heating at 140° in 31 ml of collidine afforded 11.7 g of the olefin products, which were chromatographed over 200 g of Al_2O_3. The fractions eluted with pet. ether–benzene (9:1) were recrystallized from MeOH to afford 1.336 g (11%) of pregna-3,5-dien-20-one, mp 122—124°, $[\alpha]_D^{22}$ −39.0±0.6° (c=1.036). IR ν_{max} cm^{-1}: 3027, 1702, 1651, 840. *Anal.* Calcd. for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.45; H, 10.27. The fractions eluted with pet. ether–benzene (4:1—1:1) and benzene were recrestallized from CH_2Cl_2–acetone to give 7.682 g (65%) of XXVIIa, mp 174—175°, $[\alpha]_D^{22}$ +124.5±1.5° (c=1.021). IR ν_{max} cm^{-1}: 3460, 3018, 1693, 1660. *Anal.* Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.67; H, 10.22.

17β-Acetoxyandrost-2-en-5α-ol (XXVIIc)——Dehydroepiandrosterone (25 g) was converted to 3β,5α-dihydroxyandrostan-17-one (XXVIb) in a manner similar to that described for XXVIa. Tosylation of this compound, followed by heating in 2,4,6-collidine gave the crude product, which was recrystallized from acetone to afford 11.1 g (66.7%) of XXVIIb. This ketone (11.1 g) was reduced with 1.5 g of $NaBH_4$ in 110 ml of MeOH to yield the 17β-ol, whose acetylation in the usual way gave the acetate. Recrystallization from hexane and further from MeOH yielded 8.476 g of XXVIIc, mp 152—153.5°, $[\alpha]_D^{23}$ +31.1±0.6° (c=1.046). IR ν_{max} cm^{-1}: 3530, 3012, 1730, 1658, 1263, 1252, 1037, 1022, 664. *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.69; H, 9.64.

17β-Benzoyloxy-19-norandrost-2-en-5α-ol (XXVIId)——19-Norandrost-5-ene-3β,17β-diol 17-monoacetate[22] (11.0 g) was treated with 10.5 g of m-chloroperbenzoic acid in 120 ml of CH_2Cl_2 at room temperature for 1 hr. Extraction with CH_2Cl_2 gave 12 g of a mixture of epoxides, which was reduced with 2.9 g of $LiAlH_4$

22) J. Iriarte, C. Djerassi and H.J. Ringold, *J. Am. Chem. Soc.*, **81**, 436 (1959).

in a mixture of 160 ml of dry tetrahydrofuran and 100 ml of dry ether under reflux for 2.5 hr. The mixture was concentrated to the half of the volume under reduced pressure, then cooled, and poured into iced 2N HCl. The precipitate was filtered off, washed with water, and dried. The mixture of triols (8.4 g) was benzoylated with 11 ml of PhCOCl and 250 ml of pyridine at room temperature for 1.5 hr. Extraction with CH_2Cl_2 afforded 14.1 g of the residue, which was crystallized from ether to give 11.7 g of 19-norandrostane-3β,5α,17β-triol 3,17-dibenzoate in 67.3% overall yield. Recrystallization from acetone yielded the pure sample, mp 217—218.5°, $[\alpha]_D^{23}$ +29.2±0.7° (c=1.014). IR ν_{max} cm^{-1}: 3535, 3065, 1713, 1708, 1603, 1585, 1287, 1272, 1117, 715, 705. NMR τ: (18-H) 9.04, (17α-H) 5.13, (3α-H) 4.66 m (W h/2=24 Hz), (Ph–H) 2.52 m (6H), 1.96 m (4H). *Anal.* Calcd. for $C_{32}H_{38}O_5$: C, 76.46; H, 7.62. Found: C, 76.41; H, 7.59. To a solution of 11.35 g of this dibenzoate in a mixture of 200 ml of tetrahydrofuran and 480 ml of MeOH a solution of 16 g of K_2CO_3 in 40 ml of water was added. The resulting mixture was refluxed for 1.5 hr, then concentrated to half the original volume under reduced pressure, and diluted with water. The precipitate was filtered off, washed with water, and dried. Crystallization from $CHCl_3$ afforded 1.4 g of the triol. The filtrate was evaporated to dryness and the residue was cystallized from ether to give the solid, which upon recrystallization from CH_2Cl_2–acetone yielded 4.36 g (47.7%) of the triol 17-monobenzoate (XXVIc), mp 222.5—223°, $[\alpha]_D^{23}$ +47.0±0.9° (c=1.019). IR ν_{max} cm^{-1}: 3456, 3350, 3008, 1728, 1605, 1581, 1275, 1110, 715. NMR τ: (18-H) 9.05, (3α-H) 6.05 (W h/2≈27 Hz), (17α-H) 5.14, (Ph–H) 2.53 m (3H), 1.97 m (2H). *Anal.* Calcd. for $C_{25}H_{34}O_4$: C, 75.34; H, 8.60. Found: C, 75.45; H, 8.55. The combined mother liquors contain the 3,17-di- and the 3-mono-benzoate, judging from TLC. This mixture and the recovered triol were combined and benzoylated with 5.4 ml of PhCOCl and 130 ml of pyridine for 2 hr. After work–up, crystallization from ether gave 4.7 g (40.7%) of the triol 3.17-dibenzoate.

To a cold solution of 23.5 g of XXVIc in 180 ml of pyridine 19.0 g of *p*-TsCl was added. The reulting mixture was allowed to stand at room temperature overnight, poured into ice water, and extracted with CH_2Cl_2. After the usual work–up, the tosylate (31.4 g) was heated to 165° in 156 ml of 2,4,6-collidine for 1 hr. Extraction with CH_2Cl_2 gave 22.27 g of the semi-solid, which was chromatographed over 565 g of Al_2O_3. The fractions eluted with pet. ether–benzene (9:1) were recrystallized from acetone to afford 4.37 g (20.1%) of 17-benzoyloxy-19-norandrosta-3,5-diene, mp 125—127°, $[\alpha]_D^{21}$ −62.2±1.0° (c=0.987). IR ν_{max} cm^{-1}: 3056, 3018, 1713, 1604, 1587, 1275, 1119, 708. UV λ_{max}^{MeOH} mμ (ε): 229.5 (30910). NMR τ: (18-H) 9.04, (17α-H) 5.11, (3-H, 4-H, 6-H) 4.58—3.92 m (3H), (Ph–H) 2.52 m (3H), 1.96 m (2H). *Anal.* Calcd. for $C_{25}H_{30}O_3$: C, 82.83; H, 8.34. Found: C, 82.67; H, 8.31. The fractions eluted with pet. ether–beznene (4:1—1:1) gave *ca.* 1.0 g of a mixture. The fractions eluted with benzene and benzene–ether (9:1, 4:1) were recrystallized from acetone to yield 13.55 g (56.0%) of XXVIId, mp 165.5—166°, $[\alpha]_D^{23}$ +89.0±1.3° (c=0.976). IR ν_{max} cm^{-1}: 3507, 3015, 1697, 1656, 1602, 1583, 1290, 1281, 1124, 714. NMR τ: (18-H) 9.04, (2-H, 3-H) 4.32 m (2H), (17α-H) 5.11, (Ph–H) 2.52 m (3H), 1.94 m (2H). *Anal.* Calcd. for $C_{25}H_{32}O_3$: C, 78.91; H, 8.48. Found: C, 78.74; H, 8.48.

5α-Hydroxy-20-oxopregnan-2α,3α-epoxide (XXVIIIa)——Treatment of 7.682 g of XXVIIa with 6.02 g of *m*-chloroperbenzoic acid in 200 ml of CH_2Cl_2 for 1 hr gave the solid, which upon recrystallization from aqueous acetone afforded 7.177 g (89.2%) of XXVIIIa, mp 176—178°, $[\alpha]_D^{22}$ +89.8±1° (c=1.105). IR ν_{max} cm^{-1}: 3490, 1698, 805. *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.95; H, 9.69.

5α-Hydroxy-17-oxoandrostan-2α,3α-epoxide (XXVIIIb)——Treatment of 3.0 g of XXVIIb with 3.1 g of *m*-chloroperbenzoic acid in 70 ml of CH_2Cl_2 for 1.5 hr gave the solid, which upon recrystallization from acetone–hexane afforded 2.787 g of XXVIIIb, mp 173—175°, $[\alpha]_D^{22}$ +82.8±1.2° (c=1.001). IR ν_{max} cm^{-1}: 3478, 1740, 1005, 807, 800. *Anal.* Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.93; H, 9.28.

2α,3α-Epoxyandrostane-5α,17β-diol 17-Monoacetate (XXVIIIc)——Treatment of 8.356 g of XXVIIc with 6.12 g of *m*-chloroperbenzoic acid in 125 ml of $CHCl_3$ for 1 hr gave the solid, which upon recrystallization from aqueous acetone yielded 8.2 g (93.6%) of XXVIIIc, mp 151—152°, $[\alpha]_D^{22}$ +1.5±0.3° (c=1.014). IR ν_{max} cm^{-1}: 3515, 3497, 1735, 1266, 1046, 811, 802. *Anal.* Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.47; H, 9.19.

2α,3α-Epoxy-19-norandrostane-5α,17β-diol 17-Monobenzoate (XXVIIId)——Treatment of 2.927 g of XXVIId with 1.9 g of *m*-chloroperbenzoic acid in 40 ml of CH_2Cl_2 for 1.5 hr gave the solid, which was submitted to preparative TLC, using CH_2Cl_2–ether (9:1) as developing solvent. The more mobile fraction was recrystallized from acetone to afford 2.40 g (78.6%) of XXVIIId, mp 204—206°, $[\alpha]_D^{23}$ +76.8±1.2° (c=0.993). IR $\nu_{OH}^{CCl_4}$ cm^{-1}: 3504, ν_{max} cm^{-1}: 3457, 3022, 1717, 1601, 1584, 1271, 1116, 802, 707. NMR τ: (18-H) 9.06, (2β-H, 3β-H) 6.71 m (2H), (17α-H) 5.14, (Ph–H) 2.54 m (3H), 1.98 m (2H). *Anal.* Calcd. for $C_{25}H_{32}O_4$: C, 75.73; H, 8.13. Found: C, 75.58; H, 8.18. Treatment of XXVIIId with pyridine–Ac_2O at room temperature afforded the unchanged (XXVIIId). The less mobile fraction was recrystallized from acetone gave 532 mg (17.4%) of the 2β,3β-epoxide (XXIX), mp 243—245°, $[\alpha]_D^{25}$ +63.5±1.9° (c=0.535). IR $\nu_{OH}^{CCl_4}$ cm^{-1}: 3613, ν_{max} cm^{-1}: 3416, 3060, 1712, 1600, 1582, 1274, 1116, 707. NMR τ: (18-H) 9.07, (2α-H, 3α-H) 6.81 m (2H), (17α-H) 5.14, (Ph–H) 2.52 m (3H), 1.98 m (2H).

19-Norandrostane-2β,3α,5α,17β-tetraol 17-Monobenzoate (XXXa)——a) From the α-Epoxide (XXVIIId): A mixture of 70 mg of XXVIIId, 19 ml of acetone, and 3.2 ml of 6% $HClO_4$ was stirred at room temperature for 2 hr, poured into iced water, and extracted with $CHCl_3$. After the usual work–up recrystallization

from acetone gave 53 mg of XXXa, mp 221—222°, $[\alpha]_D^{23}$ +48.2±0.9° (c=1.027). IR ν_{max} cm^{-1}: 3345, 1715, 1603, 1587, 1280, 1119, 1034, 707. NMR τ: (18-H) 9.04, (2α-H, 3β-H) 6.13 m (W h/2≈8.5), 5.98 m (W h/2 ≈8.5 Hz), (17α-H) 5.10, (Ph–H) 2.46 m (3H), 1.90 m (2H). *Anal.* Calcd. for $C_{25}H_{34}O_5$: C, 72.43; H, 8.27. Found: C, 72.13; H, 8.27. Acetylation of 112 mg of XXXa with pyridine–Ac_2O in the usual way afforded the diacetate, which upon recrystallization from acetone–hexane gave 112 mg of XXXb, mp 202—204°, $[\alpha]_D^{24}$ +58.1±1.0° (c=0.967). IR ν_{max} cm^{-1}: 3541, 1748, 1736, 1704, 1604, 1588, 1288, 1251, 1245, 1112, 717. NMR τ: (18-H) 9.05, (AcO) 7.93, (17α-H) 5.13, (2α-H, 3β-H) 4.99 m (2H, W h/2≈5.0 Hz), (Ph–H) 2.52 m (3H), 1.95 m (2H). *Anal.* Calcd. for $C_{29}H_{38}O_7$: C, 69.85; H, 7.68. Found: C, 69.77; H, 7.63.

b) From the β-Epoxide (XXIX): Treatment of 201 mg of the β-epoxide (XXIX) in the same way as described above afforded 172 mg of the compound identical with XXXa, which was established by mixed mp and comparison of the IR spectrum.

The Reaction of 5α-Hydroxy-20-oxopregnan-2α,3α-epoxide (XXVIIIa) with Hydrobromic Acid——A mixture of 2.118 g of XXVIIIa, 20 ml of CH_2Cl_2, and 21 ml of 48% HBr was stirred at room temperature for 7 hr. The separation of the products was effected by column chromatography over 200 g of silica gel G using cyclohexane–AcOEt (1:1) containing 5% EtOH as eluting solvent. The first fraction eluted with 300 ml of the solvent gave 123 mg of a mixture. The second fraction eluted with 80 ml of the solvent was recrystallized from CH_2Cl_2–acetone to yield 365 mg (14%) of the bromooxodiol (XXXIIa), mp 166—168°, $[\alpha]_D^{22}$ +66.1±0.9° (c=1.020). IR ν_{max} cm^{-1}: 3390, 1689, 695. NMR τ: (18-H) 9.37, (19-H) 8.95, (21-H) 7.88, (2β-H) 5.98t–d ($J_{2\beta:1\alpha}=J_{2\beta:3\alpha}$≈10.0, $J_{2\beta:1\beta}$≈4.0), (3α-H) 5.47t–d ($J_{3\alpha:2\beta}=J_{3\alpha:4\beta}$≈10.0, $J_{3\alpha:4\alpha}$≈4.0 Hz). *Anal.* Calcd. for $C_{21}H_{33}O_3Br$: C, 61.00; H, 8.05; Br, 19.33. Found: C, 60.79; H, 8.12; Br, 20.19. Treatment of this bromooxodiol with KOH–MeOH regenerated the parent epoxide (XXVIIIa) in 94.5% yield. The third fraction eluted with 90 ml of the solvent gave no material. The forth fraction eluted with 310 ml of the solvent was recrystallized from acetone–hexane to afford 1.530 g (72.0%) of XXXIIIa, mp 190—192°, $[\alpha]_D^{22}$ +94.1±1.2° (c=1.045). IR ν_{max} cm^{-1}: 3460, 1693, 953, 945, 865. *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.70; H, 9.73.

2α,5α-Epoxypregnane-3,20-dione (XXXIVa)——A solution of 1.430 g of XXXIIIa in a mixture of 20 ml of CH_2Cl_2 and 90 ml of acetone was oxidized with 2.13 ml of Jones reagent for 30 min. After work-up recrystallization from acetone afforded 1.109 g (77.5%) of XXXIVa, mp 210—211°, $[\alpha]_D^{22}$ +132.5±2.0° (c=1.002). IR ν_{max} cm^{-1}: 1762, 1695, 992, 977. NMR τ: (18-H) 9.35, (19-H) 8.98, (21-H) 7.88, (2β-H) 5.71d ($J_{2\beta:1\alpha}$≈7.0 Hz). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.40; H, 9.21.

3-Oxo-17α-methyl-17β-hydroxyandrostan-2α,5α-epoxide (XXXIVb)——A mixture of 2.78 g of XXVIIIb, 28 ml of CH_2Cl_2 and 2.8 ml of 48% HBr was stirred overnight, and worked up. The product was treated with 30 ml of 5% KOH–MeOH for 2.5 hr. Extraction with ether–CH_2Cl_2 (3:1) gave 2.7 g of an amorphous material, which was chromatographed over 70 g of Al_2O_3. The fractions eluted with pet ether–benzene (1:1) gave 722 mg of a mixture. The fractions eluted with pet. ether–benzene (1:1, 1:2) afforded 125 mg of the parent epoxide (XXVIIIb). The fractions eluted with benzene were recrystallized from acetone to yield 1.026 g (36.9%) of XXXIIIb. A solution of 1.026 g of XXXIIIb in 25 ml of dry tetrahydrofuran was added dropwise to a stirred solution of MeLi prepared from 240 mg of Li, 1.8 ml of CH_3I and 10 ml of dry ether. The resulting mixture was stirred at room temperature overnight, then poured into an iced solution saturated with NH_4Cl, and extracted with ether. The usual work-up afforded 1.05 g of an oily meterial, which upon recrystallization from acetone–hexane gave 687 mg of XXXIIIc, which was oxidized with 1.72 ml of Jones reagent in 15 ml of $CHCl_3$–acetone (4:1) for 25 min. Recrystallization from acetone–hexane gave 410 mg of XXXIVb, mp 162.5—164°, $[\alpha]_D^{24}$ +31.6±1.4° (c=0.522). IR ν_{max} cm^{-1}: 3490, 1749, 1253, 1079, 994. UV $\lambda_{max}^{isooctane}$ mμ (ε): 300 (20). *Anal.* Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.28; H, 9.51.

The Reaction of 2α,3α-Epoxyandrostane-5α,17β-diol 17-Monoacetate (XXVIIIc) with Hydrobromic Acid——A mixture of 5.0 g of XXVIIIc, 50 ml of CH_2Cl_2 and 5 ml of 48% HBr was stirred for 3.5 hr. After work-up, recrystallization from CH_2Cl_2–acetone yielded 2.138 g of XXXIIId, mp 217—218.5°, $[\alpha]_D^{22}$ +7.1±0.3° (c=0.972). IR ν_{max} cm^{-1}: 3446, 1733, 1252, 1050, 1031, 966, 960. *Anal.* Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.34; H, 9.14. The mother liquor (*ca.* 3.1 g) was submitted to column chromatography over 300 g of silica gel G, using $CHCl_3$–acetone (4:1) as eluting solvent. The first frcation eluted with 250 ml of the solvent afforded 728 mg of a mixture of materials, which shows at least four spots on TLC and was not studied further. The second fraction eluted with 160 ml of the solvent was recrystallized from acetone–hexane to yield 1.036 g of the bromotriol monoacetate (XXXIIc), mp 153—155°, $[\alpha]_D^{22}$ −6.6±0.3° (c=0.981). IR ν_{max} cm^{-1}: 3434, 1736, 1701, 1270, 1255, 1044, 700. NMR τ: (18-H) 9.22, (19-H) 8.95, (AcO) 7.97, (2β-H) 6.10t–d ($J_{2\beta:1\alpha}=J_{2\beta:3\alpha}$≈10.0, $J_{2\beta:1\beta}$≈5.5), (3α-H) 5.59t–d ($J_{3\alpha:2\beta}=J_{3\alpha:4\beta}$≈10.0, $J_{3\alpha:4\alpha}$ ≈6.0 Hz), (17α-H) 5.38. *Anal.* Calcd. for $C_{21}H_{33}O_4Br$: C, 58.74; H, 7.55; Br, 18.61. Found: C, 58.62; H, 7.73; Br, 18.85. The third fraction eluted with 320 ml of the solvent was recrystallizaed from ether–pet. ether to give 921 mg of XXXIIId. The combined yield of XXXIIId was 3.059 g (61.1%). The forth fraction eluted with 440 ml of the solvent was recrystallized from acetone to afford 227 mg (4.3%) of the compound, mp 207—209°, $[\alpha]_D^{22}$ −59.0±0.8° (c=1.042). IR ν_{max} cm^{-1}: 3364, 1740, 1261, 1240, 1059, 1038. NMR τ: (18-H) 9.20, (19-H) 8.98, (AcO) 7.98, (2β-H) 6.22 m, (3β-H) 6.09 m, (17α-H) 5.41, (6-H) 4.57. *Anal.*

Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.51; H, 9.15. This compound was tentatively assumed to be androst-5-ene-2α,3α,17β-triol 17-monoacetate based on the NMR spectrum and from the evidence that the compound afforded the acetonide as follows. A solution of 97 mg of this triol and 14 mg of *p*-TsOH·H_2O, in 5 ml of acetone was refluxed for 4 hr, then poured into iced 10% Na_2CO_3, and extracted with CH_2Cl_2. After the usual work-up recrystallization from aqueous MeOH gave 74 mg of the acetonide, mp 124—126°, $[\alpha]_D^{22}$ −29.9±0.6 (c=1.040). IR ν_{max} cm^{-1}: 1738, 1373, 1251, 1063, 1028. NMR τ: (18-H) 9.20, (19-H) 9.05, (AcO) 7.98, (gem-dimethyl) 8.70, 8.58, (2β-H, 3β-H) 5.73, (17α-H) 5.38, (6-H) 4.58. *Anal.* Calcd. for $C_{24}H_{36}O_4$: C, 74.19, H, 9.34. Found: C, 73.90, H, 9.34.

3-Oxo-17β-hydroxyandrostan-2α,5α-epoxide (XXXIVd)——A solution of 517 mg of XXXIIId in a mixture of 5 ml of CH_2Cl_2 and 20 ml of acetone was oxidized with 0.8 ml of Jones reagent for 10 min. After the usual work-up recrystallization from acetone–hexane gave 399 mg (77.8%) of XXXIVc, mp 165—167°, $[\alpha]_D^{22}$ +39.5±0.6° (c=1.072). IR ν_{max} cm^{-1}: 1762, 1733, 1245, 1026, 985. NMR τ: (18-H) 9.19, (19-H) 8.99, (AcO) 7.97, (2β-H) 5.72d ($J_{2\beta:1\alpha}$≈7.0 Hz), (17α-H) 5.38. *Anal.* Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 73.03; H, 8.66. A solution of 1.520 g of XXXIVc in 30 ml of 5% KOH–MeOH was allowed to stand at room temperature overnight. Extraction with CH_2Cl_2 gave the solid, which upon recrystallization from acetone–hexane afforded 980 mg (73.4%) of XXXIVd, mp 132—134°, $[\alpha]_D^{22}$ +55.5±0.8° (c=1.009). IR ν_{max} cm^{-1}: 3524, 1755, 1078, 1065, 990, 804. *Anal.* Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.09; H, 9.18. This compound (886 mg) was acylated by treatment with 6 ml of pyridine and 4 ml of $(EtCO)_2O$ for 5 hr. After the usual work-up recrystallization from acetone–hexane yielded 842 mg (85.8%) of the propionate (XXXIVe), mp 144—145.5°, $[\alpha]_D^{24}$ +39.6±0.8° (c=1.022). IR ν_{max} cm^{-1}: 1767, 1734, 1189, 1078, 982, 812. *Anal.* Calcd. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.14; H, 9.08.

17β-Hydroxyandrostan-2α,5α-epoxide (XXXV)——A mixture of 1.077 g of XXXIVc, 9.3 ml of 80% $NH_2\cdot NH_2\cdot H_2O$, 3.5 g of KOH, and 70 ml of triethyleneglycol was treated in a manner similar to that described in the case of VIa—a. The usual work-up afforded 810 mg of the solid, which was purified by preparative TLC using cyclohexane–AcOEt (1:1) as developing solvent. The fraction corresponded to the major spot was recrystallized from aqueous MeOH to give 301 mg of XXXV, mp 104.5—105°, $[\alpha]_D^{24}$ +17.2±0.6° (c=0.975). IR ν_{max} cm^{-1}: 3502, 3370, 3346, 1063, 1050, 1021, 963, 956. *Anal.* Calcd. for $C_{19}H_{30}O_2\cdot\frac{1}{4}H_2O$: C, 77.37; H, 10.42. Found: C, 77.63; H, 10.45.

The Reaction of 5α,17β-Dihydroxy-19-norandrostan-2α,3α-epoxide 17-Monobenzoate (XXVIIId) with Hydrobromic Acid——a) A mixture of 2.40 g of XXVIIId, 24 ml of CH_2Cl_2, and 3.5 ml of 48% HBr was stirred at room temperature for 2 hr. Work-up gave 2.94 g of the solid, which was twice recrystallized from acetone–hexane to afford 150 mg (5.2%) of the bromide (XXXId), mp 126—127°, $[\alpha]_D^{23}$ +40.6±0.9° (c=0.968). IR ν_{max} cm^{-1}: 3338, 3160, 1715, 1603, 1589, 1276, 1116, 1025, 708. NMR τ: (18-H) 9.05, (4α-H) 7.87d-d ($J_{4\alpha:4\beta}$≈−14.9, $J_{4\alpha:3\beta}$≈3.0), (3β-H) 5.96t-d ($J_{3\beta:2\alpha}=J_{3\beta:4\alpha}=J_{3\beta:4\beta}$≈3.0 Hz), (2α-H) 5.54 m (W h/2 ≈12.0 Hz). *Anal.* Calcd. for $C_{25}H_{33}O_4Br$: C, 62.89; H, 6.97; Br, 16.74. Found: C, 63.04; H, 7.01; Br, 16.67. To a solution of 15 mg of this compound in a mixture of 2 ml of tetrahydrofuran and 6 ml of MeOH a solution of 20 mg of K_2CO_3 in 2 ml of H_2O was added. The resulting mixture was stirred at room temperature for 1 hr. The usual work-up gave 11 mg of the parent epoxide (XXVIIId), mp 204—205°.

The mother liquor (2.79 g), which shows two spots corresponded to the bromide, XXXId and XXXIId, on TLC, was dissolved in 28 ml of pyridine. The solution was heated to 100° for 6.5 hr and extraction with CH_2Cl_2 gave 2.28 g of the solid, which was recrystallized from acetone to yield 1.309 g of the 2,5-epoxide (XXXIIIe), mp 200—201.5°, $[\alpha]_D^{23}$ +79.2±1.2° (c=0.978). IR $\nu_{OH}^{CCl_4}$ cm^{-1}: 3585, ν_{max} cm^{-1}: 3426, 3056, 1714, 1601, 1584, 1288, 1117, 725. NMR τ: (18-H) 9.07, (4β-H) 8.08d-d ($J_{4\beta:4\alpha}$≈−13.5, $J_{4\beta:3\beta}$≈6.8), (3β-H) 6.15d-d ($J_{3\beta:4\alpha}$≈1.7, $J_{3\beta:4\beta}$≈6.8), (2β-H) 5.73d ($J_{2\beta:1\alpha}$≈4.0 Hz), (17α-H) 5.14, (Ph-H) 2.52 m (3H), 1.97 m (2H). *Anal.* Calcd. for $C_{25}H_{32}O_4$: C, 75.73; H, 8.13. Found: C, 75.76; H, 8.06. The mother liquor of XXXIIIe was evaporated to dryness leaving 970 mg of materials, which were separated by preparative TLC, using CH_2Cl_2–AcOEt (1:1) as developing solvent. The less mobile fraction was recrystallized from acetone to give 669 mg of XXXIIIe. The combined yield of XXXIIIe was 1.978 g (82.5%). The more mobile fraction was recrystallized from acetone–hexane to afford 157 mg (5.4%) of the bromide (XXXIId), mp 182—183°, $[\alpha]_D^{23}$ +33.5±0.8° (c=1.009). IR ν_{max} cm^{-1}: 3548, 3480, 1712, 1603, 1586, 1273, 1115, 710. NMR τ: (18-H) 9.05, (4β-H) 8.11d-d ($J_{4\alpha:4\beta}$≈−13.3, $J_{4\beta:3\alpha}$≈12.0), (4α-H) 7.76d-d ($J_{4\alpha:4\beta}$≈−13.3, $J_{4\alpha:3\alpha}$≈5.0), (2β-H) 6.43b-t ($J_{2\beta:1\alpha}$≈10.0), (3α-H) 5.67octet ($J_{2\beta:3\alpha}$≈10.0, $J_{3\alpha:4\beta}$≈12.0, $J_{3\alpha:4\alpha}$≈5.0 Hz), (17α-H) 5.14, (Ph-H) 2.53 m (3H), 1.97 m (2H). *Anal.* Calcd. for $C_{25}H_{33}O_4Br$: C, 62.89; H, 6.97; Br, 16.74. Found: C, 62.84; H, 6.93; Br, 17.04.

b) In another run treatment of 110 mg of the epoxide (XXVIIId) with 0.16 ml of 48% HBr and 1.1 ml of CH_2Cl_2 for 5 hr gave 136 mg of a mixture of bromides, XXXId and XXXIId, which was treated with 1.3 ml of pyridine at room temperature overnight. However, no reaction was observed from the check of TLC, and heating to 100° for 7 hr, followed by preparative TLC afforded 76 mg of the 2,5-epoxide (XXXIIIe), mp 200—201.5°.

3α-Acetoxy-17β-benzoyloxy-19-norandrostan-2α,5α-epoxide (XXXIIIf)——The above mentioned 2α,5α-epoxide (XXXIIIe) (130 mg) was acetylated with 1 ml of pyridine and 0.5 ml of Ac_2O in the usual way. Recrystallization from acetone–hexane afforded 107 mg of the acetate (XXXIIIf), mp 144—144.5°, $[\alpha]_D^{24}$

$+65.8\pm1.1°$ ($c=1.013$). IR ν_{max} cm^{-1}: 1747, 1717, 1603, 1587, 1250, 1240, 1286, 1116, 718. NMR τ: (18-H) 9.05, (AcO) 7.97, (2β-H) 5.74d ($J_{2\beta:1\alpha}\approx5.0$), (3$\beta$-H) 5.26d–d ($J_{3\beta:4\alpha}\approx3.0$, $J_{3\beta:4\beta}\approx7.0$ Hz), (17α-H) 5.14, (Ph–H) 2.52 m (3H), 1.96 m (2H). *Anal.* Calcd. for $C_{27}H_{34}O_5$: C, 73.94; H, 7.82. Found: C, 74.09; H, 7.79.

3α-Mesyloxy-17β-benzoyloxy-19-norandrostan-2α,5α-epoxide (XXXIIIg)——a) From XXXIIIe: Mesylation of XXXIIIe with pyridine–MsCl in the usual way and recrystallization from acetone–hexane gave the mesylate, (XXXIIIg), mp 157.5—159°, $[\alpha]_D^{24}$ $+64.2\pm1.1°$ ($c=0.987$). IR ν_{max} cm^{-1}: 1716, 1603, 1585, 1346, 1275, 1175, 1111, 964, 937, 900, 716. NMR τ: (18-H) 9.05, (MsO) 6.99, (4β-H) 7.96d–d ($J_{4\alpha:4\beta}=-14.0$, $J_{4\beta:3\beta}\approx6.5$), (2$\beta$-H) 5.38d ($J_{2\beta:1\alpha}\approx4.5$), (3$\beta$-H) 5.19d–d ($J_{3\beta:4\alpha}\approx2.5$, $J_{3\beta:4\beta}\approx6.5$ Hz), (17α-H) 5.14, (Ph–H) 2.52 m (3H), 1.96 m (2H). *Anal.* Calcd. for $C_{26}H_{34}O_6S$: C, 65.80; H, 7.22; S, 6.76. Found: C, 65.94; H, 7.17; S, 6.64.

b) From XXXc: The tetraol monobenzoate (XXXa) (30 mg) was treated with 0.15 ml of MsCl in 0.75 ml of pyridine. After agitation for 2 hr, the mixture was worked up to give 46 mg of the product, which exhibits absorption bands due to a hydroxyl and a mesyloxy groups in the IR spectrum. A solution of this material in 0.5 ml of pyridine was heated on a steam bath for 2 hr. After the usual work–up, the purification was effected by preparative TLC using cyclohexane–AcOEt (8:7) as developing solvent. The less mobile fraction afforded 2 mg (5.6%) of the 3α-hydroxy-2α,5α-epoxide (XXXIIIe). The more mobile fraction gave 29 mg of the 3α-mesyloxy-2α,5α-epoxide (XXXIIIg). These compounds were identified by mixed mp, comparison of the IR spectrum and TLC.

3-Oxo-17β-benzoyloxy-19-norandrostan-2α,5α-epoxide (XXXIVf)——a) By Jones Oxidation: To a stirred solution of 1.878 g of XXXIIIe in a mixture of 12 ml of CH_2Cl_2 and 54 ml of acetone, 1.5 ml of Jones reagent was added dropwise. After stirred for 10 min, the mixture was worked up as usual and the product (1.512 g) was purified by preparative TLC using cyclohexane–AcOEt (2:1) as developing solvent. The less mobile fraction afforded 224 mg (11.9%) of the starting material. The more mobile fraction was recrystallized from acetone–hexane to give 1.144 g (61.3%) of the ketone (XXXIVf), mp 187—189°, $[\alpha]_D^{22}$ $+121.8\pm1.7°$ ($c=1.000$). IR ν_{max} cm^{-1}: 3059, 1768, 1706, 1602, 1587, 1280, 1110, 715. NMR τ: (18-H) 9.03, (4α-H) 7.98d, (4β-H) 7.82d ($J_{4\alpha:4\beta}\approx-17.5$), (2$\beta$-H) 5.63d ($J_{2\beta:1\alpha}\approx5.5$ Hz), (17α-H) 5.13, (Ph–H) 2.50 m (3H), 1.97 m (2H). *Anal.* Calcd. for $C_{25}H_{30}O_4$: C, 76.11; H, 7.62. Found: C, 76.20; H, 7.66.

b) By Moffatt Oxidation[23]: To a stirred suspension of 792 mg of XXXIIIe in 3 ml of dimethylsulfoxide successively a solution of 193 mg of pyridinium trifluoroacetate in 3.8 ml of dry benzene and 133 mg of dicyclohexylcarbodiimide was added under a stream of N_2. The resulting mixture was allowed to stand at room temperature with stirring for 23 hr. After cooled with ice, the mixture was treated with a solution of 5.4 g of oxalic acid in 70 ml of absolute MeOH for 1.5 hr and then 70 ml of water was added. The urea derivative formed was filtered off, and washed with benzene. Extraction with benzene afforded 866 mg of the solid, which was purified by preparative TLC using benzene–ether (4:1) as developing solvent. The fraction corresponded to the main spot was recrystallized from acetone–hexane to give 710 mg (90%) of the ketone (XXXIVf) mp 187—189°.

3-Oxo-17β-hydroxy-19-norandrostan-2α,5α-epoxide (XXXIVg)——A mixture of 698 mg of XXXIVf, 70 ml of tetrahydrofuran, and 140 ml of 5% KOH–MeOH was stirred at room temperature for 20 hr, then poured into water, and extracted with CH_2Cl_2. The usual work–up gave 530 mg of the residue which was three times recrystallized from acetone–hexane to afford 296 mg (57.7%) of XXXIVg, mp 123—124.5° $[\alpha]_D^{23}$ $+108.8\pm1.6°$ ($c=0.902$). IR ν_{max} cm^{-1}: 3283, 1767, 1063, 1022, 1008, 988, 982, 965, 798. NMR τ: (18-H) 9.23, (17α-H) 6.33, (2β-H) 5.69d ($J_{2\beta:1\alpha}\approx5.9$ Hz). *Anal.* Calcd. for $C_{18}H_{26}O_3$: C, 74.45; H, 9.03. Found: C, 74.30; H, 9.08. The mother liquor (228 mg) was acetylated with 0.6 ml of pyridine and 0.3 ml of Ac_2O. The usual work–up afforded the product, which was purified by preparative TLC. Recrystallization from acetone–hexane gave 191 mg of the acetate (XXXIVh), mp 151—152°, $[\alpha]_D^{23}$ $+88.5\pm1.2°$ ($c=1.051$), IR ν_{max} cm^{-1}: 1768, 1733, 1255, 1242, 1045, 992, 804. NMR τ: (18-H) 9.18, (AcO) 7.97, (2β-H) 5.67d ($J_{2\beta:1\alpha}\approx5.9$ Hz), (17α-H) 5.37. *Anal.* Calcd. for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.52; H, 8.48.

2α,5α-Epoxy-19-norandrostane-3β,17β-diol 17-Monobenzoate (XXXVIa)——A mixture of 856 mg of the ketone (XXXIVf), 13 ml of MeOH, and 99 mg of $NaBH_4$ was stirred at room temperature for 2 hr. Extraction with CH_2Cl_2 afforded 863 mg of the solid which was submitted to preparative TLC using cyclohexane–AcOEt (1:1) as developing solvent. The less mobile fraction gave 58 mg (6.2%) of the 3α-alcohol (XXXIIIe), mp 200—201.5°, which was identified by mixed mp, comparison of the IR spectrum and TLC. The more mobile fraction was recrystallized from ether–pet. ether to yield 797 mg (92.7%) of the 3β-alcohol (XXXVIa), mp 164—166°, $[\alpha]_D^{24}$ $+77.2\pm1.2°$ ($c=0.992$). IR ν_{max} cm^{-1}: 3378, 1719, 1606, 1588, 1277, 1116, 974, 712. NMR τ: (18-H) 9.04, (2β-H, 3α-H) 5.49 m (2H, W h/2$\approx$12.5 Hz), (17-H) 5.14, (Ph-H) 2.53 m (3H), 1.97 (2H). *Anal.* Calcd. for $C_{25}H_{32}O_4$: C, 75.73; H, 8.13. Found: C, 75.57; H, 8.07. Acetylation of 130 mg of XXXVIa with 1 ml of pyridine and 0.5 ml of Ac_2O in the usual way and recrystallization from acetone–hexane gave 121 mg of the acetate (XXXVIb), mp 146—147°, $[\alpha]_D^{24}$ $+81.1\pm1.3°$ ($c=0.946$). IR ν_{max} cm^{-1}: 3058, 1731,

23) K.E. Pfitzner and J.G. Moffatt, *J. Am. Chem. Soc.*, **87**, 5670 (1965).

1716, 1602, 1586, 1273, 1233, 1117, 708. NMR τ: (18-H) 9.05, (AcO) 7.97, (2β-H) 5.45t ($J_{2\beta:1\alpha}=J_{2\beta:3\alpha}\approx5.0$ Hz), (3α-H, 17α-H) *ca.* 5.13 m (2H), (Ph–H) 2.53 m (3H), 1.97 m (2H). *Anal.* Calcd. for $C_{27}H_{34}O_5$: C, 73.94; H, 7.82. Found: C, 74.17; H, 7.91. Mesylation of 328 mg of XXXVIa with 3.3 ml of pyridine and 0.4 ml of MsCl in the usual way and recrystallization from acetone–hexane afforded 330 mg of the mesylate (XXXVIc), mp 176—178°, $[\alpha]_D^{24}$ +78.8±1.2° (c=0.977). IR ν_{max} cm^{-1}: 1715, 1603, 1587, 1348, 1281, 1175, 1122, 978, 891, 711. NMR τ: (18-H) 9.05, (MsO) 7.00, (2β-H) 5.43t ($J_{2\beta,1\alpha}=J_{2\beta:3\alpha}\approx4.0$ Hz), (3α-H, 17α-H) *ca.* 5.12 m (2H), (Ph–H) 2.50 m (3H), 1.95 m (2H). *Anal.* Calcd. for $C_{26}H_{34}O_6S$: C, 65.80; H, 7.22; S, 6.76. Found: C, 66.06; H, 7.23; S, 6.88.

The oppenauer oxidation of 600 mg of the 3β-alcohol (XXXVIa), using 2 ml of cyclohexanone, 58 mg of Al(Oi-Pr)$_3$, and 6.2 ml of toluene, gave the product which was purified by preparative TLC using cyclohexane–AcOEt (4:1) as developing solvent. The fraction corresponded to the main product afforded 72 mg (72.4%) of the ketone identical with XXXIVf by mixed mp, comparison of the IR spectrum and TLC.

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