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The Synthesis and Conformational Analysis of Epimeric 16-Bromo-5α,13α-androstan-17-ones[1]

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Epimeric 3β-acetoxy-16-bromo-5α,13α-androstan-17-ones were synthesized starting from 3β-acetoxy-5α,13α-androstan-17-one, and their structures were confirmed by the standard method of Fieser and Ettorre. An equilibrated mixture obtained from each one of epimers with hydrogen bromide was found to consist of 23% 16β and 77% 16α. On the basis of infrared, ultraviolet, nuclear magnetic resonance spectra and optical rotatory dispersion curves the conformation of ring D was discussed.

The steroidal ring D α-haloketones are of particular interest in that their infrared, ultraviolet and nuclear magnetic resonance spectra as well as rotatory dispersion curves provide the valuable informations on the nature of the C–halogen bond and thence on the conformation of fused cyclopentanone ring. This work has been so far limited mainly to the common C/D-*trans* ring system.[3] Of the C/D-*cis* series, 14β-steroids have previously been investigated with 16-bromo-17-ketones,[4–6] but 13α-series has not yet been examined in these respects. In this paper the authors wish to report the synthesis of two epimeric 3β-acetoxy-16-bromo-5α,13α-androstan-17-ones and their ring D conformation on the basis of the spectral properties.

The starting material, 3β-acetoxy-5α,13α-androstan-17-one (IIIb), was prepared from dehydroisoandrosterone employing the photochemical reaction followed by catalytic hydrogenation.[7–10] Treatment of IIIb with isopropenyl acetate and a catalytic amount of sulfuric acid gave 16-enol acetate (IV) in almost quantitative yield. Reaction of IV with bromine in carbon tetrachloride under non-enolizing conditions furnished α-bromoketone (V) as a sole product. Elucidation of the structure of this compound was attempted by the standard method of Fieser and Ettorre.[11] Contrary to the expectations, however, difficulties were encountered, when V was reduced with lithium aluminum hydride under the usual conditions. The reaction proceeded in abnormal manner in that the products obtained were 5α,13α-androstane-3β,17-diols with loss of bromine. This result can be attributed to the characteristic C/D-*cis* linkage, where β-side is crowded due to the cage-like structure and the rear side is also sterically hindered by the presence of 18-methyl group. The 16β-bromo-17-ketone being reduced to bromohydrin, the steric strain of these two adjacent groups is relieved by elimination of hydrogen bromide yielding 16,17-epoxide and/or 17-ketone. These in turn

1) This paper constitutes Part XV of the series entitled "Analytical Chemical Studies on Steroids": Part XIV: *J. Chromatog.*, **31**, 210 (1967).
2) Location: *Kita-4-bancho, Sendai.*
3) E.L. Eliel, N.L. Allinger, S.J. Angyal, and G.A. Morrison ,"Conformational Analysis," Interscience Publishers, New York, 1965, p. 258 and references quoted therein.
4) T. Nambara and J. Fishman, *J. Org. Chem.*, **26**, 4569 (1961).
5) C. Djerassi, J. Fishman, and T. Nambara, *Experientia*, **17**, 565 (1961).
6) T. Nambara, H. Hosoda, and S. Goya, *Chem. Pharm. Bull.* (Tokyo), **16**, 374 (1968).
7) J.P.L. Bots, *Rec. Trav. Chim.*, **77**, 1010 (1958).
8) L.J. Chinn, *J. Org. Chem.*, **30**, 4165 (1965).
9) T. Nambara, T. Kudo, H. Hosoda, and S. Goya, *J. Chromatog.*, **31**, 210 (1967).
10) J.R. Billeter and K. Miescher, *Helv. Chim. Acta*, **34**, 2053 (1951).
11) L.F. Fieser and R. Ettorre, *J. Am. Chem. Soc.*, **75**, 1700 (1953).

are further reduced with the excess reagent to give 3β,17-dihydroxy compounds as the final products. However, lithium aluminum hydride reduction at $-15°$ provided two pairs of epimeric 16β-bromo-5α,13α-androstane-3β,17-diols (VIIa, VIIIa) and their acetates (VIIb, VIIIb) as was expected. The structural correlation between free dihydroxy compound and 3-monoacetate was confirmed by leading to 3,17-diacetates (VIIc, VIIIc) on usual acetylation, respectively. The *cis*-bromohydrin structure of VIIa was justified by the formation of 17-ketone, when refluxed in methanolic potassium hydroxide. On the other

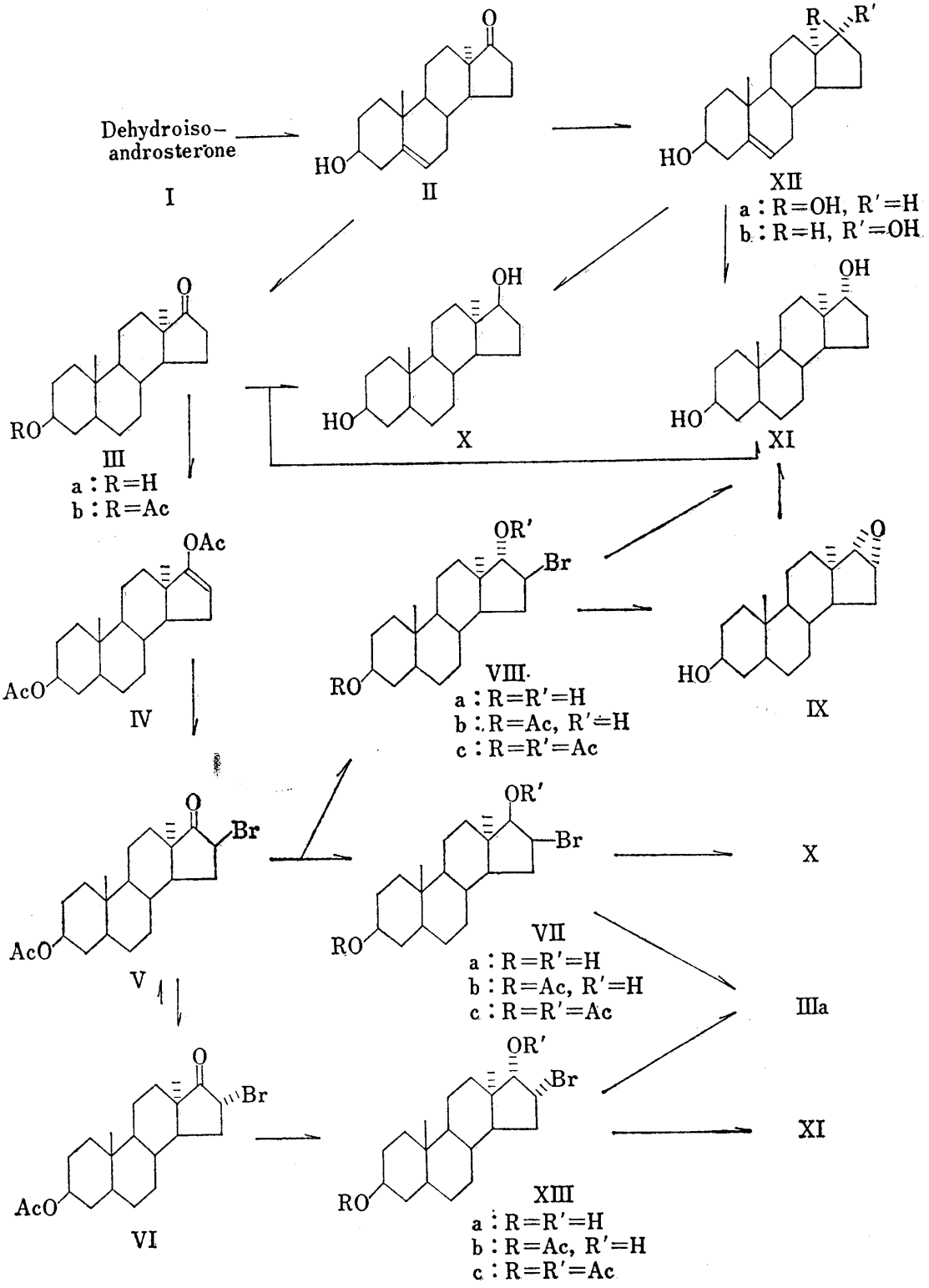


Chart 1

hand reductive dehalogenation of VIIa with hydrogen over palladium-on-barium carbonate afforded 5α,13α-androstane-3β,17β-diol (X), which proved to be identical with the authentic sample obtained from 13α-androst-5-ene-3β,17β-diol (XIIa) by catalytic hydrogenation. In addition the isomeric *trans*-bromohydrin (VIIIa) was rationalized likewise by the formation of 16α,17α-epoxide (IX) with alkali, and of 5α,13α-androstane-3β,17α-diol (XI) on hydrogenation over palladium-on-barium carbonate. Reductive cleavage of IX with lithium aluminum hydride gave solely 17α-hydroxy compound. The formation of 16β-bromo-17-ketone under non-enolizing conditions implys that in 13α-series the steric effect of 18-methyl group is more significant than that of cage-like structure due to C/D-*cis* fusion against the access of the reagent.

Treatment of 16β-bromo-17-ketone with hydrogen bromide in glacial acetic acid resulted in epimerization mixture, from which pure 3β-acetoxy-16α-bromo-5α,13α-androstan-17-one (VI) could be isolated by fractional crystallization. The optical rotation of the equilibrated mixture produced from either one of the epimers was measured and in consequence the composition was found to be 23% 16β and 77% 16α. The structure of VI was determined in the same manner as its 16-epimer. Lithium aluminum hydride reduction at −15° gave 16α,17α-bromohydrin (XIIIa) and its 3-acetate (XIIIb) accompanied with the 17-ketones (IIIa, IIIb), which would arise from the initially produced bromohydrin with facile dehydrobromination. The *cis*-bromohydrin was led to 3β,17α-dihydroxy compound (XI) on catalytic hydrogenation, and to the 17-ketone (IIIa) on treatment with alkali.

The spectral data of the two epimeric 16-bromo-17-ketones (V, VI) and their parent ketone (IIIb) are collected in Table I. The shift values of infrared and ultraviolet absorption spectra reveal that the two 16 positions in the 13α-series are equivalent and bisectional.

Table I. Rotatory Dispersion and Spectral Data

Substance	IR $\nu_{max}^{CCl_4}$ (cm^{-1})	$\Delta\nu$ (cm^{-1})	UV λ_{max}^{EtOH} (mμ)	$\Delta\lambda$ (mμ)	RD 1st extremum MeOH (mμ)	[φ]	$\Delta\lambda$ (mμ)
3β-Acetoxy-5α,13α-androstan-17-one (IIIb)	1745		295		319	−2570°	
3β-Acetoxy-16β-bromo-5α,13α-androstan-17-one (V)	1755	+10	312	+17	334	+ 590°	+15
3β-Acetoxy-16α-bromo-5α,13α-androstan-17-one (VI)	1756	+11	312	+17	338	−5225°	+19

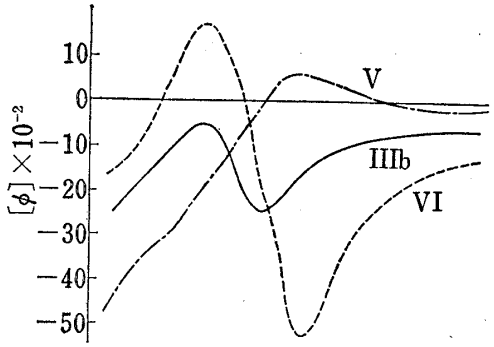


Fig. 1. Optical Rotatory Dispersion Curves of IIIb, V and VI in Methanol

Furthermore the rotatory dispersion curves support these conformational assignments of the α-bromoketones. In addition the results show that the axial haloketone rule is also applicable to cyclopentanone in fused ring system.[12-15] As illustrated in Fig. 1, 16β-bromo-17-ketone exhibits a positive Cotton effect while the epimer and the parent ketone show negative sign.

Examinations were then made on the 16-proton signals of nuclear magnetic resonance spectra of the epimeric 16-bromo-17-ketones. As can be seen in Fig. 2, 16-proton signals

12) C. Djerassi and W. Klyne, *J. Am. Chem. Soc.*, **79**, 1506 (1957).
13) C. Djerassi, J. Osiecki, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **80**, 1216 (1958).
14) A. Lardon, H.P. Sigg, and T. Reichstein, *Helv. Chim. Acta*, **42**, 1462 (1959).
15) J. Fishman and C. Djerassi, *Experientia*, **16**, 138 (1960).

appear as the X portion of an ABX system centered at 5.49 τ (J=2.2, 8.6 cps) and 5.79 τ (J=9.3, 10.2 cps), respectively. The torsional angles calculated by vector analytical technique[16] being applied to ring D, the H16, 15 dihedral angles (ϕ_{AX} and ϕ_{BX}) can be estimated for each of four possible conformations A, B, C and D. In Table II the coupling constants calculated by Abraham's equation[17] are listed and compared with the experimental results. It is evident that in the case of 16β-bromo compound the observed values are in good accordance with the calculated for conformations A and B. On the other hand in the case

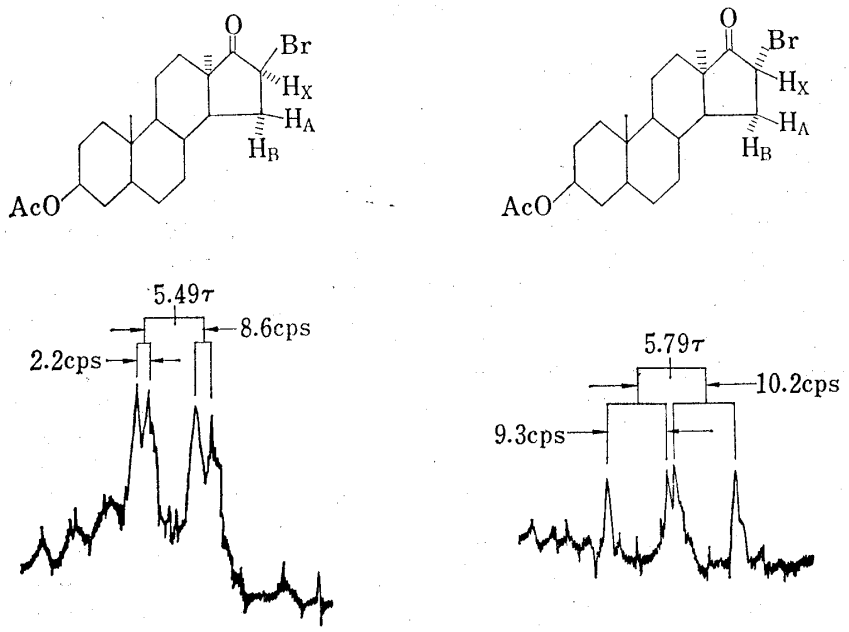
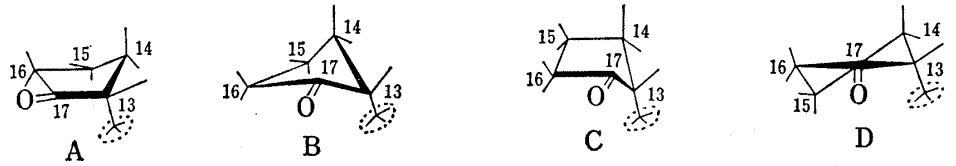


Fig. 2. Nuclear Magnetic Resonance Spectra of the Epimeric 16-Bromo-17-ketones (V and VI)

Table II. Coupling Constants derived from the Abraham's Equation

Substance	ϕ_{AX}[a]	ϕ_{BX}[a]	J_{AX}[b]	J_{BX}[b]	$J_{AX}+J_{BX}$[b]
16β-Bromo-17-ketone					
Conformation A	83.5	36.5	0.2	8.0	8.2
B	101	19	0.5	11.1	11.6
C	120	0	3.6	12.4	16.0
D	70	50	1.5	5.1	6.6
Observed					10.8
16α-Bromo-17-ketone					
Conformation A	36.5	156.5	8.0	12.0	20.0
B	19	139	11.1	8.2	19.3
C	0	120	12.4	3.6	16.0
D	50	170	5.1	13.9	19.0
Observed					19.5

a) in degrees Abraham, *et al.*[17] b) in cycles per second J=12.4 $\cos^2\phi$ ($0°\leq\phi\leq90°$) J=14.3 $\cos^2\phi$ ($90°\leq\phi\leq180°$)



16) F.V. Brutcher, Jr. and W. Bauer, Jr., *J. Am. Chem. Soc.*, **84**, 2233, 2236 (1962).
17) R.J. Abraham and J.S.E. Holker, *J. Chem. Soc.*, **1963**, 806.

of the 16α–epimer the data available exclude only conformation C. However, the above-mentioned spectroscopic results, which require bisectional bonds for 16α– and 16β–bromo substituents, are obviously inconsistent with conformation B. Thus, the data so far obtained appear to fulfill the requirement for either conformation A to both epimers or conformations B, D to 16β– and 16α–bonds, respectively.

It is hoped that further work in progress in this laboratory will provide the data necessary for a definition of the 13α–ring D conformation.

Experimental[18]

5α,13α-Androst-16-ene-3β,17-diol Diacetate (IV)——To a solution of 3β–acetoxy–5α,13α–androstan–17–one (IIIb) (530 mg) in isopropenyl acetate (20 ml) was added 30 drops of the catalyst solution (isopropenyl acetate (5 ml) and conc. H_2SO_4 (0.1 ml)) and refluxed for 1.5 hr. The reaction mixture was concentrated to one–half of its volume by slow distillation over 1 hr. An additional 10 ml of isopropenyl acetate containing 20 drops of catalyst solution was added and the solution was again concentrated to *ca.* 10 ml over another 2 hr. The resultant solution was diluted with ether and washed with cold 5% $NaHCO_3$, H_2O and dried over anhydrous Na_2SO_4. On usual work–up the residue obtained was dissolved in hexane and filtered through Al_2O_3 (7 g). Upon concentration of the filtrate a crystalline product was obtained. Recrystallization from dil. MeOH gave IV (400 mg) as colorless needles. mp 92—94°, $[\alpha]_D^{20}$ −76.5° (c=2.3). *Anal.* Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.60 ;H, 9.02.

3β-Acetoxy-16β-bromo-5α,13α-androstan-17-one (V)——To a solution of IV (200 mg) in CCl_4 (25 ml) containing anhydrous K_2CO_3 (180 mg) was added the calculated amount of Br_2 dissolved in CCl_4 dropwise with stirring at 0°. The resultant solution was washed with $NaHSO_3$ solution, H_2O and dried over anhydrous Na_2SO_4. On usual work–up a crystalline residue was obtained. Recrystallization from hexane–Me_2CO gave V (140 mg) as colorless needles. mp 174—176°, $[\alpha]_D^{23}$ −20.4° (c=4.7). *Anal.* Calcd. for $C_{21}H_{31}BrO_3$: C, 61.31; H, 7.59. Found: C, 61.56; H, 7.53.

3β-Acetoxy-16α-bromo-5α,13α-androstan-17-one (VI)——To a solution of V (100 mg) in glacial AcOH (2 ml) was added AcOH saturated with HBr (0.2 ml) and the solution was allowed to stand at room temperature for 24 hr. The resultant solution was poured into ice–water and the white precipitate was filtered and washed with H_2O. Recrystallization from MeOH gave VI (60 mg) as colorless needles. mp 196—197.5°, $[\alpha]_D^{23}$ −141.5° (c=5.2). *Anal.* Calcd. for $C_{21}H_{31}BrO_3$: C, 61.31; H, 7.59. Found: C, 61.29; H, 7.74.

Equilibration of Epimeric 16-Bromo-17-ketones (V and VI)——To a solution of each epimer (20 mg) in AcOH (2 ml) was added AcOH saturated with HBr (0.2 ml) and allowed to stand at room temperature for 24 hr. The solution was poured into ice–water and the precipitate was filtered, washed with H_2O and dried. The optical rotations were obtained on each sample. From 16β–bromo–17–ketone (V): $[\alpha]_D^{24}$ −115.0° (c=4.0); from 16α–bromo–17–ketone (VI): $[\alpha]_D^{24}$ −112.0° (c=4.0).

Lithium Aluminum Hydride Reduction of V——To a solution of V (500 mg) in anhydrous ether (60 ml) was added $LiAlH_4$ (700 mg) portionwise at −15° over 5 min. To the resultant solution was added moist ether to decompose the excess reagent and acidified with 10% H_2SO_4. The organic layer was separated, washed with H_2O and dried over anhydrous Na_2SO_4. After evaporation of solvent an oily residue obtained was dissolved in benzene and chromatographed on silica gel (25 g). Elution with benzene and recrystallization of the eluate from MeOH gave 16β–bromo–5α,13α–androstane–3β,17β–diol 3–acetate (VIIb) (100 mg) as colorless prisms. mp 170—171°, $[\alpha]_D^{27}$ −7.1° (c=3.7). *Anal.* Calcd. for $C_{21}H_{33}BrO_3$: C, 61.01; H, 8.05. Found: C, 61.09; H, 8.00.

Elution with benzene–ether (20:1) and recrystallization of the eluate from dil. MeOH gave 16β–bromo–5α,13α–androstane–3β,17α–diol 3–acetate (VIIIb) (20 mg) as colorless needles. mp 141—143°, $[\alpha]_D^{26}$ −33.8° (c=1.3). *Anal.* Calcd. for $C_{21}H_{33}BrO_3$: C, 61.01; H, 8.05. Found: C, 61.26; H, 8.06.

Elution with benzene–ether (10:1) and recrystallization of the eluate from dil. MeOH gave 16β–bromo–5α,13α–androstane–3β,17β–diol (VIIa) (120 mg) as colorless needles. mp 175—177°, $[\alpha]_D^{27}$ −33.3° (c=3.4). *Anal.* Calcd. for $C_{19}H_{31}BrO_2$: C, 61.45; H, 8.41. Found: C, 61.41; H, 8.66.

Elution with benzene–ether (10:1) and recrystallization of the eluate from dil. MeOH gave 16β–bromo–5α,13α–androstane–3β,17α–diol (VIIIa) (25 mg) as colorless needles. mp 194—196°, $[\alpha]_D^{26}$ −33.6° (c=2.5, MeOH). *Anal.* Calcd. for $C_{19}H_{31}BrO_2$: C, 61.45; H, 8.41. Found: C, 61.41; H, 8.55.

18) All melting points were taken on a micro hot–stage apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ unless otherwise stated. The infrared spectra measurements were obtained on a carefully calibrated Beckman IR–9 spectrophotometer. The ultraviolet spectra and optical rotatory dispersion measurements were obtained on Shimadzu Model MPS–50 spectrophotometer and Nihon–Bunko Model ORD/UV–5 optical rotatory dispersion recorder, respectively. The nuclear magnetic resonance spectra were measured by Hitachi H–60 spectrometer at 60 Mcps in $CDCl_3$.

16β-Bromo-5α,13α-androstane-3β,17β-diol Diacetate (VIIc)——i) VIIb (54 mg) was dissolved in pyridine (0.4 ml) and Ac_2O (0.2 ml) and the resultant solution was allowed to stand at room temperature overnight. On usual work-up a semicrystalline product was obtained. Recrystallization from MeOH gave VIIc (26 mg) as colorless needles. mp 127—128°, $[\alpha]_D^{26}$ −24.8° (c=2.9). *Anal.* Calcd. for $C_{23}H_{35}BrO_4$: C, 60.65; H, 7.75. Found: C, 60.61; H, 7.53.

ii) Prepared from VIIa in the same manner as in i). The mixed mp on admixture with the sample obtained from VIIb showed no depression.

16β-Bromo-5α,13α-androstane-3β,17α-diol Diacetate (VIIIc)——i) VIIIb (38 mg) was dissolved in pyridine (1 ml) and Ac_2O (0.5 ml) and the resultant solution was allowed to stand at room temperature overnight. On usual work-up an oily product obtained was chromatographed on silica gel (3 g). Elution with hexane–benzene (1:7) and recrystallization of the eluate from MeOH gave VIIIc (25 mg) as colorless needles. mp 177—179°, $[\alpha]_D^{28}$ −14.8° (c=1.1). *Anal.* Calcd. for $C_{23}H_{35}BrO_4$: C, 60.65; H, 7.75. Found: C, 60.89; H, 7.63.

ii) Prepared from VIIIa in the same manner as in i). The mixed mp on admixture with the sample obtained from VIIIb showed no depression.

Lithium Aluminum Hydride Reduction of VI——To a solution of VI (140 mg) in anhydrous ether (50 ml) was added $LiAlH_4$ (260 mg) at −15° during a period of 2 min. To the resultant solution was added moist ether to decompose the excess reagent and acidified with 10% H_2SO_4. The organic layer was washed with H_2O and dried over anhydrous Na_2SO_4. Upon evaporation of solvent an oily residue was obtained. The crude product was dissolved in benzene and chromatographed on silica gel (3 g). Elution with benzene and benzene–ether (20:1) gave mixtures of XIIIb and IIIb and of XIIIa and IIIa, respectively.

16α-Bromo-5α,13α-androstane-3β,17α-diol Diacetate (XIIIc)——i) XIIIa (50 mg) was dissolved in pyridine (1 ml) and Ac_2O (0.5 ml) and the resultant solution was allowed to stand at room temperature overnight. On usual work-up an oily residue obtained was chromatographed on silica gel (3.5 g). Elution with hexane–benzene (3:7) and recrystallization of the eluate from dil. MeOH gave XIIIc (20 mg) as colorless plates. mp 145—146°, $[\alpha]_D^{26}$ −141.3° (c=1.5). *Anal.* Calcd. for $C_{23}H_{35}BrO_4$: C, 60.65; H, 7.75. Found: C, 60.84; H, 7.66.

ii) Prepared from XIIIb in the same manner as in i). The mixed mp on admixture with the sample obtained from XIIIa showed no depression.

16α,17α-Epoxy-5α,13α-androstan-3β-ol (IX)——A 5% methanolic KOH solution containing VIIIa (50 mg) was refluxed for 3 hr. The resultant solution was diluted with AcOEt, washed with H_2O and dried over anhydrous Na_2SO_4. On usual work-up the residue obtained was chromatographed on silica gel (3 g). Elution with benzene–ether (15:1) and recrystallization of the eluate from hexane–Me_2CO gave IX (20 mg) as colorless leaflets. mp 114—116°, $[\alpha]_D^{29}$ −14.3° (c=3.1). *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.71; H, 10.44.

Transformation of VIIa and XIIIa into IIIa with Potassium Hydroxide——i) A 5% methanolic KOH solution containing VIIa (20 mg) was refluxed for 3 hr. The resultant solution was diluted with AcOEt, washed with H_2O and dried over anhydrous Na_2SO_4. On usual work-up a crystalline product was obtained. Recrystallization from hexane–Me_2CO gave IIIa (18 mg) as colorless plates. mp 126—128°. Mixed mp on admixture with the authentic sample showed no depression, and IR spectra of two samples were identical.

ii) XIIIa was treated with 5% methanolic KOH solution in the same manner as in i). Recrystallization of the crude product from hexane–Me_2CO gave IIIa as colorless prisms. mp 125—127°. Mixed mp on admixture with the authentic sample showed no depression.

5α,13α-Androstane-3β,17α-diol (XI)——i) By lithium aluminum hydride reduction of IIIb: To a solution of $LiAlH_4$ (500 mg) in ether (50 ml) was added a solution of IIIb (500 mg) in THF (2 ml)–ether (70 ml) dropwise with stirring during a period of 15 min and refluxed for 4 hr. To the resultant solution was added moist ether to decompose the excess reagent and acidified with 10% H_2SO_4. The organic layer was washed with H_2O and dried over anhydrous Na_2SO_4. Upon evaporation of solvent a crystalline product was obtained. Repeated recrystallization from MeOH–ether gave XI (340 mg) as colorless prisms. mp 199—200°, $[\alpha]_D^{25}$ −46.7° (c=1.2, MeOH). *Anal.* Calcd. for $C_{19}H_{32}O_2 \cdot \frac{1}{2}H_2O$: C, 75.70; H, 11.03. Found: C, 75.80; H, 11.19.

ii) By hydrogenation of 13α-androst-5-ene-3β,17α-diol——A solution of 13α-androst-5-ene-3β,17α-diol (XIIb) (40 mg) in EtOH (5 ml) was shaken with 5% Pd/C (40 mg) under a stream of H_2 overnight. After removal of catalyst by filtration, the filtrate was concentrated to give a crystalline product. Recrystallization from dil. MeOH gave XI as colorless plates. mp 194—195°. Mixed mp on admixture with the sample obtained in i) showed no depression, and IR spectra of two samples were identical.

iii) By debromination of VIIIa: A solution of VIIIa (10 mg) in MeOH (3 ml) was shaken with Pd/$BaCO_3$ (50 mg) under a stream of H_2 for 48 hr. On usual work-up the crude product obtained was chromatographed on thin-layer plate employing benzene–ether (1:1) as developer. Recrystallization of the eluate from hexane–Me_2CO gave XI (4 mg) as colorless prisms. mp 198—200°. Mixed mp on admixture with the sample obtained in i) showed no depression.

iv) By debromination of XIIIa: A solution of XIIIa (40 mg) in EtOH (15 ml) was shaken with Pd/$BaCO_3$ (200 mg) in the same manner as described in iii). On usual work-up an oily product obtained was chromatographed on silica gel (3 g). Elution with benzene–ether (9:1) and recrystallization of the eluate from

hexane–Me_2CO gave XI (30 mg) as colorless prisms. mp 196—197°. Mixed mp on admixture with the sample obtained in i) showed no depression.

v) By reductive cleavage of IX with lithium aluminum hydride: To a solution of IX (10 mg) in anhydrous ether (5 ml) was added $LiAlH_4$ (30 mg) and refluxed for 2 hr. On usual work-up a crystalline product was obtained. Recrystallization from hexane–Me_2CO gave XI (7 mg) as colorless prisms. mp 191—193°. Mixed mp on admixture with the sample obtained in i) showed no depression, and IR spectra of two samples were identical.

5α,13α-Androstane-3β,17β-diol (X)——i) By lithium aluminum hydride reduction of IIIb: After separation of XI from the $LiAlH_4$ reduction products of IIIb by fractional crystallization, the mother liquor was concentrated and chromatographed on Al_2O_3 (20 g). Elution with benzene–AcOEt (15:1) gave a mixture of 17-epimers (40 mg) and then solely X (50 mg). Recrystallization of the 2nd eluate from hexane–Me_2CO gave X as colorless plates. mp 172—173.5°. $[\alpha]_D^{26}$ −12.3° (c=1.3, MeOH). *Anal.* Calcd. for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 78.35; H, 11.03.

ii) By hydrogenation of 13α-androst-5-ene-3β,17β-diol: A solution of 13α-androst-5-ene-3β,17β-diol (XIIa) (39 mg) in EtOH (5 ml) was shaken with 5% Pd/C (25 mg) under a stream of H_2 overnight. After removal of catalyst by filtration, the filtrate was concentrated to give a crystalline product. Recrystallization from hexane–Me_2CO gave X (20 mg) as colorless prisms. mp 170—171.5°. Mixed mp on admixture with the sample obtained in i) showed no depression, and IR spectra of two samples were identical.

iii) By debromination of VIIa: A solution of VIIa (20 mg) in EtOH (10 ml) was shaken with $Pd/BaCO_3$ (100 mg) under a stream of H_2 for 40 hr. On usual work-up a crystalline product was obtained. Recrystallization from hexane–Me_2CO gave X (13 mg) as colorless prisms. mp 167—169°. Mixed mp on admixture with the sample obtained in i) showed no depression, and IR spectra of two samples were identical.

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