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Synthesis of Epimeric 2- and 4-Deuterio-5β-androstane-3,17-diones[1]

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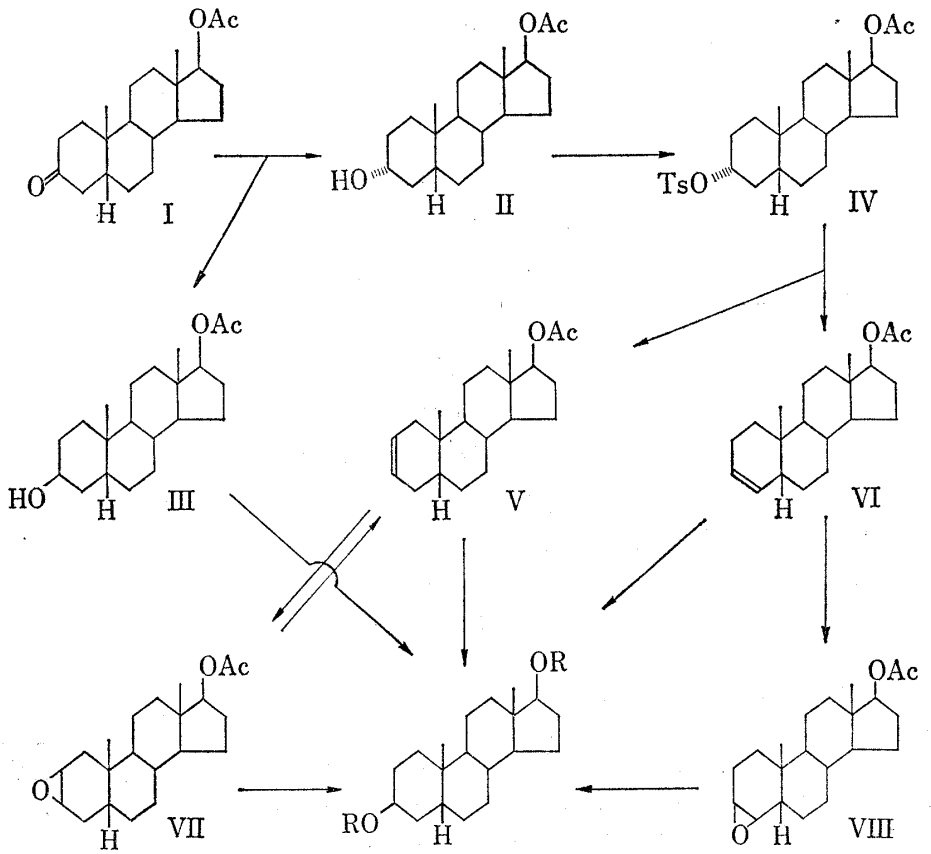
In order to clarify the stereochemistry of hydrogen loss from C-2 and C-4 during the microbial Δ^1- and Δ^4-dehydrogenation the titled compounds have been synthesized as the suitable substrates. The key intermediates leading to the desired compounds, Δ^2- and Δ^3-olefins (V, VI), were prepared from 5β-androstane-3α,17β-diol 3-tosylate 17-acetate (IV). Epoxidation with per-acid followed by *trans*-diaxial opening of the resulting β-epoxides (VII, VIII) with lithium aluminum deuteride gave 2α- and 4α-deuterio-5β-androstane-3β,17β-diols (X, XIV). On the other hand V and VI were transformed into the 2β- and 4β-deuterio-3β,17β-diols (XII, XVI) by treatment with deuterated diborane and then with hydrogen peroxide. Upon oxidation with chromium trioxide-pyridine complex these labeled diols were led to the 2- and 4-deuterated 3,17-diketones (XI, XIII, XV, XVII), respectively.

A variety of microorganisms has been shown to be capable of catalyzing the introduction of a double bond into the 1,2- and 4,5-positions of 5α- and 5β-3-ketosteroids.[3–6] The stereochemistry of Δ^1- and Δ^4-dehydrogenation, however, has not yet fully been clarified with the 5β-steroid. As a series of our studies on the biotransformation mechanism of steroids,[7] we have attempted to investigate the stereochemistry of hydrogen loss from C-2 and C-4 during the microbial dehydrogenation. The design of the experiment required the 5β-3-ketosteroid labeled with the isotope stereospecifically at α-position as the substrate for the enzymatic transformation. The present paper deals with the synthesis of two pairs of epimeric 2- and 4-deuterio-5β-androstane-3,17-diones starting from readily available testosterone.

As a preliminary experiment toward the final goal we started to establish the synthetic route to 5β-androstane-3,17-dione by which the label could be unambiguously introduced at the desired position. An initial effort was focused on the preparation of Δ^2- and Δ^3-androstene derivatives, which would serve as the key intermediate leading to the desired compounds. Reduction of 17β-acetoxy-5β-androstan-3-one (I), derivable from testosterone in two steps, with sodium borohydride under the mild conditions afforded the 3α,17β-diol 17-monoacetate (II) together with a small amount of C-3 epimer (III). On treatment with *p*-tosyl chloride and pyridine II was converted into the 3-tosylate (IV). Elimination of the oxygen function at C-3 with γ-collidine proceeded in two different directions yielding a mixture of isomeric unsaturated products in a ratio of *ca.* 2 to 1. Difficulties were encountered with the separation of these positional isomers, though they could be differentiated by thin-layer chromato-

1) This paper constitutes Part LXII of the series entitled "Analytical Chemical Studies on Steroids"; Part LXI: T. Nambara, Y.H. Bae, and M. Nokubo, *Yakugaku Zasshi*, **92**, 1157 (1972).
2) Location: *Aobayama, Sendai.*
3) R. Bentley, "Molecular Asymmetry in Biology," Vol. II, 1970, Academic Press, New York, pp. 334—340.
4) S.J. Davidson and P. Talalay, *J. Biol. Chem.*, **241**, 906 (1966).
5) V.C. Aries, P. Goddard, and M.J. Hill, *Biochim. Biophys. Acta*, **248**, 482 (1971).
6) Y.J. Abul-Hajj, *Biochem. Biophys. Res. Commun.*, **43**, 766 (1971); *idem, J. Biol. Chem.*, **247**, 686 (1972).
7) *a*) T. Nambara, H. Hosoda, T. Anjyo, M. Yamauchi, and J. Mohri, *Chem. Pharm. Bull.* (Tokyo), **20**, 287 (1972); *b*) T. Nambara, T. Anjyo, and H. Hosoda, *ibid.*, **20**, 853 (1972); *c*) T. Anjyo, M. Ito, H. Hosoda, and T. Nambara, *Chem. Ind.* (London), **1972**, 384.

graphy (TLC) on silica gel plate impregnated with silver nitrate.[8] Repeated fractional crystallization from methanol gave 5β-androst-3-en-17β-ol acetate (VI) in poor yield. Therefore the crude product was submitted to further elaboration without purification. Oxidation with *m*-chloroperbenzoic acid gave a mixture of two isomeric epoxides (VII, VIII), whose separation could be efficiently achieved by the preparative TLC. Configuration of both epoxides should be β, because the attack of the reagent would be initiated from the less-hindered β-side of the molecule having A/B-*cis* fusion. One of these proved to be identical with the 3β,4β-epoxide derived from the pure Δ^3-olefin. On treatment with sodium iodide and zinc dust the 2β,3β-epoxide was easily transformed into the Δ^2-unsaturated compound (V), which was evidently distinguished from the Δ^3-isomer by inspection of the nuclear magnetic resonance (NMR) spectra.



IXa : R=H
IXb : R=Ac

Ac=CH_3CO–, Ts=*p*-$CH_3C_6H_4SO_2$–

Chart 1

The 2β,3β-epoxide was then reduced with lithium aluminum hydride. As was expected the *trans*-diaxial opening of the oxido ring took place to give 5β-androstane-3β,17β-diol (IXa) in a reasonable yield. Similarly the 3β,4β-epoxide was submitted to the reductive cleavage with metal hydride. Judged from the result of TLC, separation of the expected 3β,17β-diol from the by-products appeared to be difficult and hence the desired compound was isolated as the 3,17-diacetate (IXb) on usual acetylation. The preliminary studies for the labeling

8) A.S. Gupta and S. Dev, *J. Chromatog.*, **12**, 189 (1963); R. Ikan, *ibid.*, **17**, 591 (1965); R. Ikan and M. Cudzinovaski, *ibid.*, **18**, 422 (1965).

of the isotope at 2β- and 4β-positions were then carried out employing the Δ^2- and Δ^3-unsaturated compounds. In both cases the reaction with diborane did take place at the β-side of the double bond to give the 3β-hydroxylic compound (IXa). Hereupon these synthetic routes proved to be promising to introduce the isotope specifically into C-2 and C-4 positions of 5β-androstane-3,17-dione.

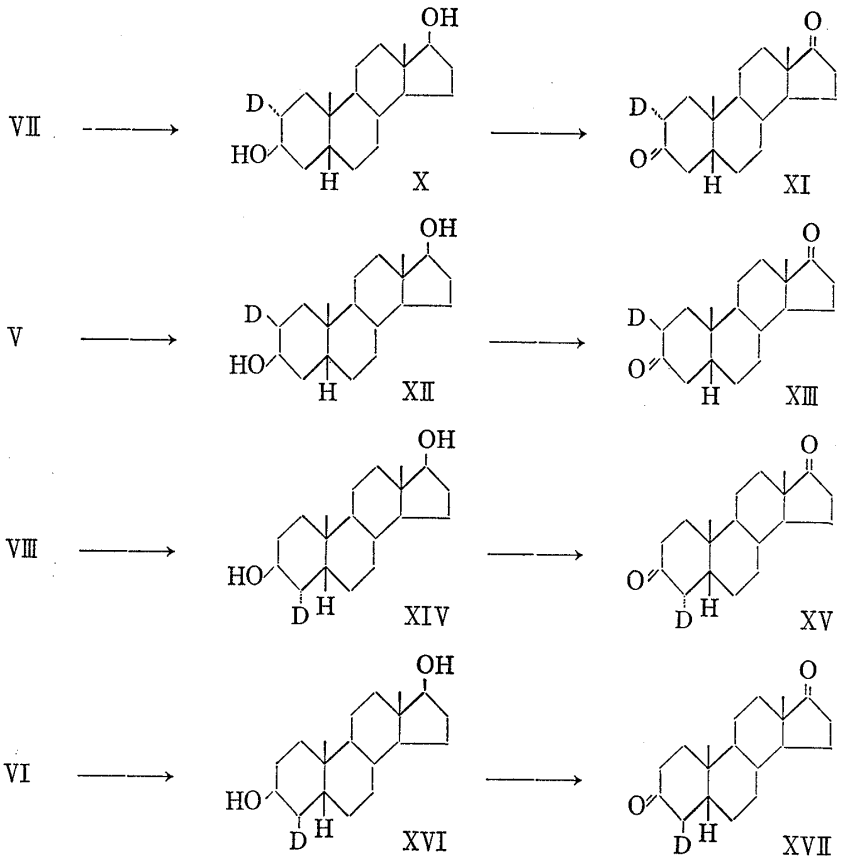


Chart 2

The synthesis of the 2α-deuterated substrate was undertaken utilizing the *trans*-diaxial opening reaction of the 2β,3β-oxido ring. Treatment of VII with lithium aluminum deuteride provided the 2α-deuterio-3β,17β-diol (X) and subsequent oxidation with chromium trioxide-pyridine complex gave the desired 2α-deuterio-5β-androstane-3,17-dione (XI). The epimeric 2β-deuterio compound was then prepared from V. Hydroboration with deuterated diborane freshly prepared from lithium aluminum deuteride and boron trifluoride[7a] gave the *cis*-addition product, 2β-deuterio-3β,17β-diol (XII), which in turn was oxidized to the desired 2β-deuterio-5β-androstane-3,17-dione (XIII). The epimeric 4-deuterated substrates were prepared in the manner as mentioned above. Reductive cleavage of VIII with lithium aluminum deuteride gave the 4α-deuterio-3β,17β-diol (XIV), which on chromium trioxide oxidation was led to the desired 4α-deuterio-5β-androstane-3,17-dione (XV). The remaining 4β-deuterio-3,17-diketone (XVII) was synthesized from VI through the 4β-deuterio-3β,17β-diol (XVI) by hydroboration with deuterated diborane and then with hydrogen peroxide followed by oxidation with chromium trioxide-pyridine complex.

The infrared (IR) spectra of non-labeled 5β-androstane-3,17-dione and two pairs of epimeric 2- and 4-deuterated steroids (XI, XIII, XV, XVII) were different each another in the finger print region. The locality and quantity of the isotope in these labeled steroids were determined by mass spectral technique. Inspection of the molecular ion peak, which appeared at *m/e* 289 with an increment of one mass unit, revealed that the deuterium contents of the labeled compounds were all *ca.* 98%.

It is hoped that the facile availability of the specifically labeled substrates may serve to clarify the microbial dehydrogenation mechanism of 5β-3-ketosteroid.

Experimental[9]

Reduction of 17β-Acetoxy-5β-androstan-3-one (I) with Sodium Borohydride——To a solution of I (335 mg) in THF (4 ml) was added a solution of $NaBH_4$ (350 mg) in H_2O (1 ml) under ice-cooling and allowed to stand for 20 min. After addition of a few drops of AcOH the reaction mixture was diluted with ether, washed with 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was recrystallized from acetone–hexane to give 5β-androstane-3α,17β-diol 17-acetate (II) (250 mg) as colorless needles. mp 172—173°. $[\alpha]_D^{23}$ +14.8° (c=0.51). *Anal.* Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.12; H, 10.23. NMR (5% solution in $CDCl_3$) δ: 0.76 (3H, s, 18-CH_3), 0.93 (3H, s, 19-CH_3), 2.01 (3H, s, -OCOCH_3), 3.30—3.80 (1H, m, $W_{1/2}$=20 Hz, 3β-H), 4.57 (1H, t, J=8 Hz, 17α-H). The mother liquor was submitted to the preparative TLC using benzene–ether (3:1) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.34) and recrystallization of the eluate from acetone–hexane gave 5β-androstane-3β,17β-diol 17-acetate (III) (27 mg) as colorless needles. mp 137—138°. $[\alpha]_D^{20}$ +9.2° (c=0.49). *Anal.* Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.56; H, 10.23. NMR (5% solution in $CDCl_3$) δ: 0.76 (3H, s, 18-CH_3), 0.97 (3H, s, 19-CH_3), 2.01 (3H, s, -OCOCH_3), 4.10 (1H, m, $W_{1/2}$=7 Hz, 3α-H), 4.57 (1H, t, J=8 Hz, 17α-H). Elution of the adsorbent corresponding to the spot (*Rf* 0.28) gave an additional 43 mg of II.

5β-Androstane-3α,17β-diol 17-Acetate 3-*p*-Toluenesulfonate (IV)——To a solution of II (250 mg) in pyridine (3 ml) was added *p*-TsCl (400 mg) portionwise and stirred at room temperature for 3 days. The resulting solution was diluted with ether, washed with 5% HCl and H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was recrystallized from hexane to give IV (300 mg) as colorless leaflets. mp 134—136°. $[\alpha]_D^{21}$ +29.8° (c=1.34). *Anal.* Calcd. for $C_{28}H_{40}O_5S$: C, 68.83; H, 8.25. Found: C, 69.20; H, 8.19. NMR (5% solution in $CDCl_3$) δ: 0.75 (3H, s, 18-CH_3), 0.90 (3H, s, 19-CH_3), 2.02 (3H, s, -OCOCH_3), 2.43 (3H, s, Ar-CH_3), 4.50 (1H, m, 3β-H), 4.57 (1H, t, J=8 Hz, 17α-H), 7.30, 7.78 (4H, d, J=8 Hz, Ar-H).

Reaction of IV with γ-Collidine——A solution of IV (2.5 g) in γ-collidine (18 ml) was refluxed for 1.5 hr. The resulting solution was diluted with ether, washed with 5% HCl, 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. On usual work-up the crystalline product was obtained. Fractional crystallization from MeOH several times gave 5β-androst-3-en-17β-ol acetate (VI) (310 mg) as colorless plates. mp 141—142°. NMR (5% solution in $CDCl_3$) δ: 0.79 (3H, s, 18-CH_3), 0.95 (3H, s, 19-CH_3), 2.03 (3H, s, -OCOCH_3), 4.57 (1H, t, J=8 Hz, 17α-H), 5.18—5.84 (2H, m, 3- and 4-H). de Pault, *et al.* prepared this compound by the different method (reported: mp 138—140°).[10] The mother liquor was submitted to further step without purification.

3β,4β-Epoxy-5β-androstan-17β-ol Acetate (VIII)——To a solution of VI (10 mg) in $CHCl_3$ (5 ml) was added *m*-chloroperbenzoic acid (15 mg) and allowed to stand at room temperature overnight. The resulting solution was diluted with ether, washed with 5% Na_2SO_3, 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was recrystallized from MeOH to give VIII (10 mg) as colorless needles. mp 198—201°. NMR (5% solution in $CDCl_3$) δ: 0.78 (3H, s, 18-CH_3), 0.87 (3H, s, 19-CH_3), 2.03 (3H, s, -OCOCH_3), 2.84 (1H, d, J=4.5 Hz, 4α-H), 3.20 (1H, m, 3α-H), 4.57 (1H, t, J=8 Hz, 17α-H). Bascoul, *et al.* prepared this compound by the different method (reported: mp 195—196°).[11]

5β-Androst-2-en-17β-ol Acetate (V)——To a solution of VII (9 mg) in AcOH (3 ml) were added a solution of NaI (10 mg) and AcONa (4 mg) in H_2O (0.2 ml) and Zn dust (8 mg), and stirred at room temperature for 2 hr. After removal of the precipitate by filtration the filtrate was diluted with ether, washed with H_2O, 5% $NaHCO_3$ and H_2O successively, and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was recrystallized from MeOH to give V (5 mg) as colorless needles. mp 98—99°. $[\alpha]_D^{21}$ −5.8° (c=0.60). *Anal.* Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.36; H, 10.07. NMR(5% solution in $CDCl_3$) δ: 0.78 (3H, s, 18-CH_3), 0.97 (3H, s, 19-CH_3), 2.02 (3H, s, -OCOCH_3), 4.57 (1H, t, J=8 Hz, 17α-H), 5.56 (2H, broad s, 2- and 3-H).

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9) All melting points were taken on a micro hot-stage apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$. NMR spectra were obtained on Hitachi Model R-20 spectrometer at 60 MHz employing tetramethylsilane as an internal standard. Abbreviation used s=singlet, d=doublet, t=triplet, and m=multiplet. IR spectra were run on JASCO Model IR-S spectrometer. Mass spectra were measured by Hitachi Model RMU-7 spectrometer. For the preparative TLC silica gel H (E. Merck AG) was used as an adsorbent.

10) A.C. de Pault and J. Bascoul, *Bull. Soc. Chim. France*, **1966**, 939.

11) J. Bascoul and A.C. de Pault, *Bull. Soc. Chim. France*, **1966**, 945.

Epoxidation of V and VI——To a solution of the mixture of V and VI (70 mg) in $CHCl_3$ (5 ml) was added *m*-chloroperbenzoic acid (70 mg) and allowed to stand at room temperature overnight. The resulting solution was diluted with ether, washed with 5% Na_2SO_3, 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was submitted to the preparative TLC using benzene–ether (3:1) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.76) and recrystallization of the eluate from MeOH gave 2β,3β-epoxy-5β-androstan-17β-ol acetate (VII) (24 mg) as colorless needles. mp 129—131°. $[\alpha]_D^{21}$ +3.3° (c=0.60). *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.75; H, 9.79. NMR (5% solution in $CDCl_3$) δ: 0.77 (3H, s, 18-CH_3), 0.89 (3H, s, 19-CH_3), 2.03 (3H, s, -OCOCH_3), 2.90—3.30 (2H, m, 2α-, and 3α-H), 4.57 (1H, t, J=8 Hz, 17α-H). Elution of the adsorbent corresponding to the spot (*Rf* 0.83) gave VIII (45 mg). mp 198—201°.

Reduction of VII with Lithium Aluminum Hydride——To a solution of VII (8 mg) in THF (4 ml) was added $LiAlH_4$ (20 mg) and refluxed for 5 hr. After decomposition of the excess reagent with moist ether, 25% Rochelle salt solution was added and extracted with AcOEt. The organic layer was separated, washed with H_2O and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was submitted to the preparative TLC using benzene–ether (1: 2) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.51) and recrystallization of the eluate from acetone–hexane gave IXa (5 mg) as colorless plates. mp 165—167°. Mixed melting point on admixture with the authentic sample[12] showed no depression and IR spectra of two samples were entirely identical.

Hydroboration of V——To a stirred solution of $LiAlH_4$ (50 mg) in ether (6 ml) were added the solutions of V (13.8 mg) in ether (6 ml) and of BF_3-etherate (260 mg) in ether (6 ml) at 0° over a period of 30 min under a stream of N_2 gas. After stirring at room temperature for 1 hr the excess reagent was decomposed by careful addition of moist ether. The organic layer was washed with 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. Evaporation of solvent gave an oily residue. To a stirred solution of this product dissolved in THF (6 ml) were added 10% NaOH (4 ml) and 30% H_2O_2 (4 ml), and stirred at 0° for 1 hr. The resulting solution was diluted with H_2O and extracted with AcOEt. The organic layer was separated, washed with 5% $NaHSO_3$ and H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was submitted to the preparative TLC using benzene–ether (1: 2) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.51) and recrystallization of the eluate from acetone–hexane gave IXa (5 mg) as colorless plates. mp 164—165°. Mixed melting point on admixture with the authentic sample showed no depression and IR spectra of two samples were entirely identical.

5β-Androstane-3β,17β-diol Diacetate (IXb)——Treatment of IXa (5 mg) with Ac_2O (0.5 ml) and pyridine (1 ml) gave the acetylated product, which was sumbitted to the preparative TLC using benzene–ether (6:1) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.46) and recrystallization of the eluate from MeOH gave IXb (3 mg) as colorless needles. mp 108—110° (reported mp 106—107°).[12]

Reduction of VIII with Lithium Aluminum Hydride——To a solution of VIII (30 mg) in THF (15 ml) was added $LiAlH_4$ (100 mg) and refluxed for 20 hr. The reaction mixture was processed in the manner as described in VII. The crude product thus obtained was submitted to the preparative TLC using benzene–ether (1: 2) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.51) gave the crystalline product (20 mg). Treatment with Ac_2O (1 ml) and pyridine (2 ml) in the usual manner gave the acetylated product, which was sumbitted to the preparative TLC using benzene–ether (6:1) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.46) and recrystallization of the eluate from MeOH gave IXb (8 mg) as colorless needles. mp 108—110°. Mixed melting point on admixture with the authentic sample showed no depression and IR spectra of two samples were entirely identical.

Hydroboration of VI——To a stirred solution of $LiAlH_4$ (20 mg) in ether (2 ml) were added the solutions of VI (10 mg) in ether (2 ml) and of BF_3-etherate (170 mg) in ether (2 ml) at 0° over a period of 30 min under a stream of N_2 gas. The reaction mixture was processed in the manner as described in V. The crude product thus obtained was submitted to the preparative TLC using benzene–ether (1: 2) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.51) and recrystallization of the eluate from acetone–hexane gave IXa (6 mg) as colorless plates. mp 163—165°. Mixed melting point on admixture with the authentic sample showed no depression and IR spectra of two samples were entirely identical.

2α-Deuterio-5β-androstane-3β,17β-diol (X)——To a solution of VII (60 mg) in THF (2 ml) was added $LiAlD_4$ (100 mg) and refluxed for 5 hr. After decomposition of the excess reagent with moist ether, 25% Rochelle salt solution was added and extracted with AcOEt. The organic layer was separated, washed with H_2O and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was submitted to the preparative TLC using benzene–ether (1: 2) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.51) and recrystallization of the eluate from acetone–hexane gave X (56 mg) as colorless plates. mp 164—165°. Mixed melting point on admixture with the authentic sample showed no depression.

12) J. Fajkoš and V. Sanda, *Collection Czech. Chem. Commun.*, **27**, 355 (1962).

2α-Deuterio-5β-androstane-3,17-dione (XI)——To a solution of X (56 mg) in pyridine (1 ml) was added CrO_3–pyridine complex (2 ml) and allowed to stand at room temperature overnight. The reaction mixture was diluted with ether, washed with 10% AcOH, 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was submitted to the preparative TLC using benzene–ether (2:1) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.42) and recrystallization of the eluate from acetone–hexane gave XI (30 mg) as colorless needles. mp 130—132°. Mixed melting point on admixture with the authentic sample[13] showed no depression. Mass Spectrum *m/e*: 289 (M^+).

2β-Deuterio-5β-androstane-3β,17β-diol (XII)——To a stirred solution of $LiAlD_4$ (170 mg) in ether (5 ml) were added the solutions of V (77 mg) in ether (5 ml) and of BF_3-etherate (1 g) in ether (5 ml) at 0° over a period of 30 min under a stream of N_2 gas. After stirring at room temperature for 1 hr the excess reagent was decomposed by careful addition of moist ether. The organic layer was washed with 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. Evaporation of solvent gave an oily residue. To a stirred solution of this product dissolved in THF (10 ml) were added 10% NaOH (7 ml) and 30% H_2O_2 (7 ml) and allowed to stand at 0° for 1hr. The resulting solution was diluted with AcOEt, washed with H_2O, 5% $NaHSO_3$ and H_2O successively, and dried over anhydrous Na_2SO_4. After evaporation of solvent the crude product was submitted to the preparative TLC using benzene–ether (1: 2) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.51) and recrystallization of the eluate from acetone–hexane gave XII (30 mg) as colorless plates. mp 164—165°.

2β-Deuterio-5β-androstane-3,17-dione (XIII)——XII (30 mg) was treated with CrO_3–pyridine complex (2 ml) in the manner as described in XI. The preparative TLC followed by recrystallization from acetone–hexane gave XIII (20 mg) as colorless plates. mp 130—132°. Mixed melting point on admixture with the authentic sample[13] showed no depression. Mass Spectrum *m/e*: 289 (M^+).

4α-Deuterio-5β-androstane-3,17-dione (XV)——A solution of VIII (204 mg) in THF (8 ml) was refluxed with $LiAlD_4$ (300 mg) for 18 hr. After usual work-up the crude product was submitted to the preparative TLC using benzene–ether (1: 2) as developing solvent. Elution of the adsorbent corresponding to the spot (*Rf* 0.51) gave crude 4α-deuterio-5β-androstane-3β,17β-diol (XIV) as crystalline product. XIV was treated with CrO_3–pyridine complex (2 ml) in the manner as described in XI. The preparative TLC followed by recrystallization from acetone–hexane gave XV (50 mg) as colorless plates. mp 131—132°. Mixed melting point on admixture with the authentic sample[13] showed no depression. Mass Spectrum *m/e*: 289 (M^+).

4β-Deuterio-5β-androstane-3β,17β-diol (XVI)——VI (151 mg) was treated with $LiAlD_4$ (309 mg) and BF_3-etherate (2.6 g) in the manner as described in XII. Recrystallization from acetone–hexane gave XVI (65 mg) as colorless plates. mp 161—163°. Mixed melting point on admixture with the authentic sample showed no depression.

4β-Deuterio-5β-androstane-3,17-dione (XVII)——XVI (65 mg) was treated with CrO_3–pyridine complex in the manner as described in XI. The preparative TLC followed by recrystallization from acetone–hexane gave XVII (50 mg) as colorless plates. mp 132—133.5°. Mixed melting point on admixture with the authentic sample[13] showed no depression. Mass Spectrum *m/e*: 289 (M^+).

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13) O. Halpern, P. Crabbé, A.D. Cross, I. Delfin, L. Cervantes, and A. Bowers, *Steroids*, 4, 1 (1964).