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Boron Trifluoride-catalyzed D-Homo Rearrangements of 20β-Acetoxy-5α-pregnanes[1]

SADAO AOYAMA, KAZUO KAMATA and TAICHIRO KOMENO

Shionogi Research Laboratory, Shionogi & Co., Ltd.[2]

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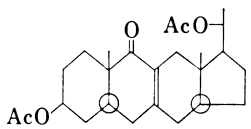
Boron trifluoride in its complex with ether or acetic acid was found to effect ready D-homo rearrangements of the 20β-acetoxy-5α-pregnanes leading to D-homo-17α-methyl-17aβ-ol acetate. The corresponding 20α-compounds, however, under the same conditions gave complex mixtures.

In our continuing work on linear steroid analogues,[3–5] it was found that the enone (**1**)[4] possessing the same side chain as 20β-acetoxypregnane, underwent ready D-homo rearrangements by the catalytic action of $BF_3 \cdot O(C_2H_5)_2$ in almost quantitative yield. Application of this reaction to 20β-acetoxy-5α-pregnanes resulted in expansion of ring D yielding D-homo-steroids in excellent yields. This reaction is thought to be of general applicability, and in the present paper we describe the formation and structure confirmation of these D-homosteroids. When the enone (**1**) was treated with ethanedithiol in the presence of $BF_3 \cdot O(C_2H_5)_2$ with the intention of reducing its carbonyl function, a substantial amount of an unknown



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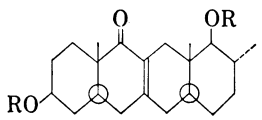
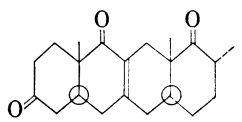


2a : R=Ac
2b : R=H



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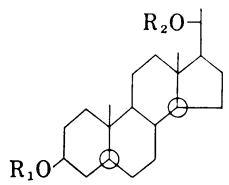
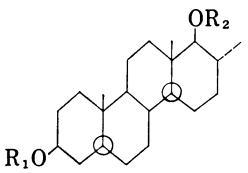


	R_1	R_2
4a	Ac	Ac
4b	Ac	H
4c	Ac	Ts



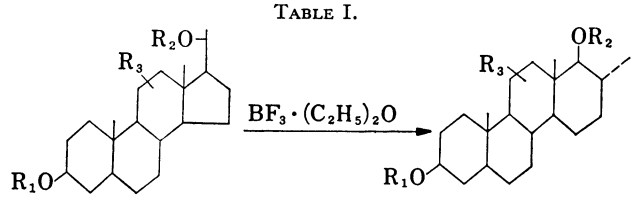
	R_1	R_2
5a	Ac	Ac
5b	H	H
5c	Ac	Ts
5d	Ac	CHO

Chart 1

1) Presented at the 90th Annual Meeting of Pharmaceutical Society of Japan, Sapporo, July 1970.
2) Location: *Fukushimaku, Osaka.*
3) Part I: S. Aoyama and K. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **18**, 481 (1970).
4) Part II: S. Aoyama and K. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **18**, 1310 (1970).
5) Part III: S. Aoyama, *Chem. Pharm. Bull.* (Tokyo), **19**, 896 (1971).

enone (**2a**) was obtained instead of the expected thioketal. To test the influence of the catalyst upon the substrate, the enone (**1**) was dissolved in $BF_3 \cdot O(C_2H_5)_2$ and left at room temperature for a few days. Unexpectedly, work-up gave a high yield of the new enone (**2a**) as a sole product. Though the enone (**2a**) failed to crystallize, upon hydrolysis it gave a crystalline enone-diol (**2b**), mp 259—261°. The ultraviolet (UV) spectra of these enones, (**1**), (**2a**), and (**2b**), exhibited absorption maxima at 245—246 mμ ($\varepsilon \approx 11000$), indicating that no big changes had occured in the environment of the conjugated ketone system. In the nuclear magnetic resonance (NMR) spectrum of **2a**, one proton attached to the carbon bearing acetoxy group appeared at τ 5.51 as a doublet (J=10.5 Hz) and a secondary methyl protons in a doublet resonated at τ 9.17 (J=6 Hz), a considerably up-field shift compared with that of the parent enone (**1**) ($\Delta\tau$ 0.35 ppm). Oxidation of the enone-diol (**2b**) with Jones reagent gave the enetrione (**3a**), the secondary methyl protons of which appeared still in a doublet (J=6.5 Hz) at τ 8.97; on treatment of **2b** with NaOD in MeOD however, the doublet collapsed to a singlet. This fact indicated that the secondary methyl group at C-20, originally located on the same carbon as an oxygen function, had changed its position to one α to a carbonyl group. These observations led us to propose a D-homo structure for the new enone (**2**). Furthermore, a large coupling constant observed for the proton attached to the carbon bearing acetoxy group (J=10.5 Hz) could be interpreted as 17α-methyl-17aβ-acetoxy for the ring D partial structure. Further confirmation of the D-homo structure was demonstrated by using usual steroids for which the structures of the corresponding D-homosteroids were already established.[6,7] BF_3-etherate treatment of 3β,20β-diacetoxy-5α-pregnane (**4a**) for 10 days at room temperature effected complete D-homo annulation reaction yielding uranediol diacetate (**5a**), which was also obtained according to the procedure described by Hirschmann[7] starting with 3β-acetoxy-20β-tosyloxy-5α-pregnane.

TABLE I.



Starting steroids No.	Substituents R_1	R_2	R_3	Products, D-homosteroids No.	mp	Yield (%)	Reaction time at 35°
4a	Ac	Ac	H_2	**5a**	161.5—163°	88	100 hr
						92	1 hr at 27°[a]
6	Ac	Ac	$\Delta^{9(11)}$	**7**	163 —164.5°	90	50 hr
8	Ac	Ac	11-keto	**9**	183 —186°	81	15 days
					195 —200°	83	24 hr at 27°[a]
10	Ac	Ac	12-keto	**11**	226.5—228°	83	18 days
12	H	Ac	H_2	**13**	168 —170°	80	21 days[b]
14	Ac	EtCO-	H_2	**15**	108.5—109.5°	91	46 hr

a) BF_3 AcOH *b*) reaction temperature 23°

A series of mainly C ring substituted 20β-acetoxy-5α-pregnanes were treated with $BF_3 \cdot O(C_2H_5)_2$ at 35° and the relative rates compared qualitatively in Table I. In general, a

6) *a*) W. Klyne, *Nature*, **166**, 559 (1950); *b*) R.S. Rosenfeld, *J. Am. Chem. Soc.*, **79**, 5540 (1957); *c*) D. K. Fukushim, S. Dobriner, and R.S. Rosenfeld, *J. Org. Chem.*, **26**, 5025 (1961).
7) H. Hirschmann, F.B. Hirschmann, and A.P. Zala, *J. Org. Chem.*, **31**, 375 (1966).

Table II. NMR Spectral Data of D-Homosteroids

Compds. No.	18-H	Δ18-H[a]	19-H	Δ19-H[a]	17aα-H J (d)
5a	9.17	−0.22	9.22	+0.03	5.67 (10.5)
7	9.21	−0.22	9.07	+0.02	5.64 (10.5)
9	9.20	−0.22	8.98	+0.01	5.22 (10.0)
11	8.77	−0.22	9.12	+0.04	5.13 (10.0)
13	9.16	−0.22	9.23	+0.03	5.67 (10.5)
15	9.16	−0.22	9.22	+0.02	5.67 (10.5)

a) Differences from those of parent steroids and positive values denote upfield shift.

factor which induces electron deficiency at C-20 would delay the reaction, and we found that introduction of a ketone function at either C-11 or C-12 caused rate retardation as expected, probably owing to the inductive effect. The reaction proceeded reasonably well with the compound (**12**) having a free hydroxyl at C-3, indicating that such a hydroxyl group, located distant from the reaction site, does not interfere with the reaction. Further, the reaction mode was the same with **14**, a substrate carrying a 20β-propionyloxy group instead of an acetoxy group at C-20. Surprisingly, when BF_3·AcOH was used in place of BF_3·$O(C_2H_5)_2$ the reaction was found to proceed very rapidly (see Table I).

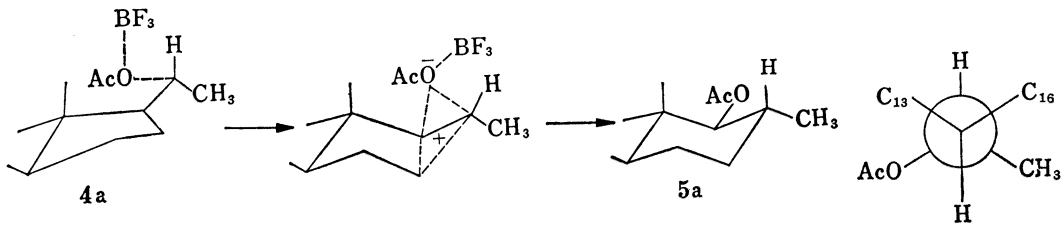


Chart 2

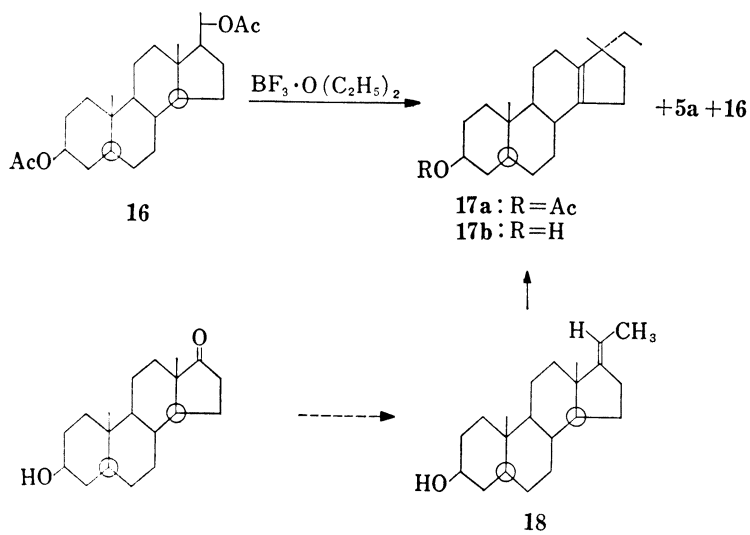


Chart 3

In Table II are listed the 18- and 19-methyl protons chemical shifts of the D-homosteroids and their differences from those of the original steroids. While there are no substan-

tial differences in the 19-methyl proton chemical shifts, distinct and constant differences of the 18-methyl proton chemical shifts between the original and their corresponding D-homosteroids are observed.[8]

This D-homo rearrangement is thought to proceed "either through a non-classical 17, 20-bridged transition state, or by internal return of boron trifluoride–coordinated acetate anion from an intimate ion–pair," in a manner similar to the rearrangement in the solvolysis of 20β-tosyloxy-pregnane described[9] by Kirk. We thought it of interest to see the behavior of 20α-substituted-5α-pregnane derivatives toward $BF_3 \cdot O(C_2H_5)_2$ (or AcOH). Thus, two examples were studies, *i.e.* 3β,20α-diacetoxy-5α-pregnane (**16**) and 3β, 20α-diacetoxy-5α-pregnan-12-one (**23**). In these cases, however, the results were complicated. Treatment of **16** with $BF_3 \cdot O(C_2H_5)_2$ for 4 days at room temperature afforded, as separable components,

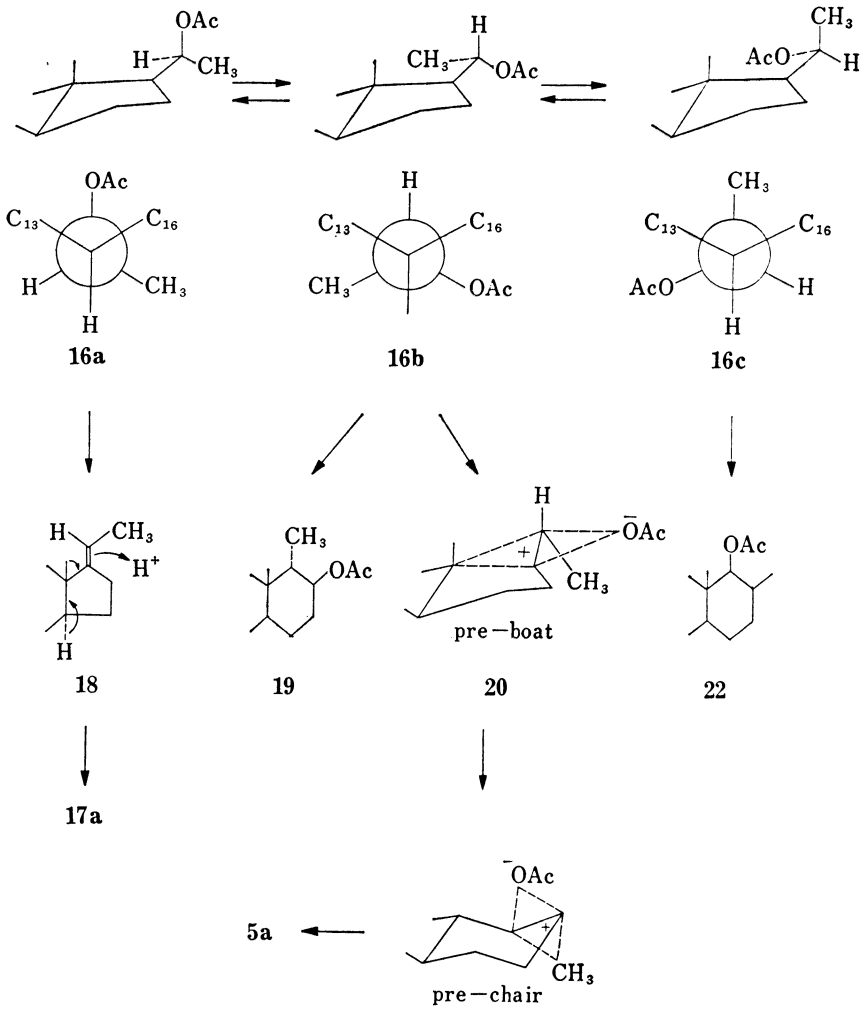


Chart 4

8) N.R. Trenner, B.H. Arison, D. Taub, and N.L. Wendler, *Proceedings*, **1961**, 214.
9) D.N. Kirk and M.P. Hartshorn "Steroid Reaction Mechanisms," Elsevier Publishing Company, Amsterdam/London/New York, 1968, p. 294.

18-nor-17α-ethyl-17β-methyl-5α-androst-13(14)-en-3β-ol acetate (**17a**) (40%), uranediol diacetate (**5a**) (8%) and the starting material (**16**) (40%). Compound (**17a**) failed to give crystals but upon hydrolysis the crystalline compound (**17b**), mp 131° was obtained. The structures for **17a** and **17b** were deduced from their spectral data and the elemental composition of **17b** and final proof was afforded by the independent synthesis of **17** according to the procedure[10] reported for an analogous compound by Goutarel *et al.* The formation of uranediol diacetate (**5a**) from the reaction with 20α-acetoxy-5α-pregnane is noteworthy. While a number of papers have dealt with the formation of D-homosteroids from 20β-substituted 5α-pregnane derivatives, there seem to be none describing its formation from 20α-counterparts. Careful examination of the starting material (**16**) by NMR and vapor phase chromatography (VPC) revealed that **5a** did not stem from a contaminant in the starting material. The yield of **5a** was raised to 13% when BF_3·AcOH was used for the reaction. Treatment of 3β,20α-diacetoxy-5α-pregnan-12-one (**23**) with $BF_3 \cdot O(C_2H_5)_2$ afforded a fairly complex mixture, which could not be resolved.

For the reaction with 3β,20α-diacetoxy-5α-pregnane (**16**), Chart 4 shows some of the possible reaction pathways. As the 17-side chain conformation of **16**, three representative conformers (**16a**, **b** and **c**) are considered. The conformer (**16a**) may lead to the major product (**17a**) through the intermediate (**18**) followed by the double bond movement including 1,2-methyl migration because of the favorable geometry for elimination of the leaving acetoxy group and the 17-hydrogen. The mechanistic pathway for the formation of uranediol diacetate (**5a**) is not straightforward. One would at the first glance expect the formation of an intermediate (or product) (**19**) by an acetoxy group migration from C-20 to C-17 with concomitant C_{13}—C_{17} bond movement to C-20 in a concerted manner. However, there was no evidence of product of **19** at least in the final work-up. A possible pathway which seems to be consistent with the actural products formed is through initial formation of the transition state (**20**) which, in turn, *via* methyl participation gives a second transition state (**21**); opening up then gives the product, uranediol diacetate (**5a**). The conformer (**16c**) is unfavored because of the 1,3-diaxial interaction between the 18 angular methyl and the 21-methyl and therefore its existence is probably negligible. Furthermore, **16c** would lead to a product such as **22** or an elimination product of **22**, neither of which could be detected.

Experimental

Melting points were determined on Yanagimoto Micromelting apparatus and are uncorrected. Optical rotations were measured in 1% EtOH–$CHCl_3$ with a Perkin Elmer Polarimeter type 141 ($c=1.0$—0.3, $l=1$ cm). Unless otherwise stated, UV spectra were recorded in 95% EtOH with a Hitachi EPE-2 spectrophotometer and IR spectra in CCl_4 by a Koken DS-201B spectrophotometer and partly by a Hitachi grating infrared spectrophotometer Model EPI-G3. NMR spectra were taken in $CDCl_3$ solution with a Varian A-60 spectrometer, TMS as internal standard. Chemical shifts are reported in τ value and apparent coupling constants and bandwidths at half heights were obtained from the 1st order analysis in Hz. For preparative and analytical TLC Silica gel G or GF (E. Merck Co.) was used as adsorbent.

Treatment of 3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α-pregn-7(11)-en-9-one (1) with $BF_3 \cdot O(C_2H_5)_2$—To a solution of **1** (100 mg) in ethanedithiol (0.4 ml) was added $BF_3 \cdot O(C_2H_5)_2$ (0.4 ml) under stirring. The solution was kept at room temperature for 1 hr, then poured into ice-cooled 10% NaOH. The mixture was extracted with ether and the ethereal layer was washed with 10% NaOH (×2) and water, dried and evaporated. The residue was found to be identical with the starting material (TLC and IR spectra). The recovered starting materal (96 mg) was again submitted to the same condition as above but left at room temperature for 2 days. Work-up as above gave a product which showed two major spots on TLC. Preparative TLC (CH_2Cl_2–AcOEt 25:1) of the product (83 mg) gave, as a less polar fraction, **1** (38 mg), crystallized from ether–petr. ether to give crystals, mp 152—155° identical with authentic (**1**) (mixed melting point and IR spectra). The polar fraction gave an oil (**2a**) (30 mg). Attempted crystalization from a variety of solvents failed. UV λ_{max} mμ (ε): 246 (10800). IR ν_{max} cm^{-1}: 1739, 1677, 1641, 1236. NMR τ: 9.25 (3H, s,

10) M. Leboeuf, A. Cavé, and R. Goutarel, *Bull. Soc. Chim. France*, **1964**, 1624.

(18-H), 9.17 (3H, d, J=6.0, 17α-Me), 9.01 (3H, s, 19-H), 7.97 (OAc), 7.90 (OAc), 5.51 (1H, d, J=10.5, 17aα-H), 5.33 (1H, m, 3-H).

Treatment of 1 with $BF_3 \cdot O(C_2H_5)_2$——The enone (**1**) (202 mg) was dissolved in $BF_3 \cdot O(C_2H_5)_2$ (3 ml) under stirring and the solution was stored for 2 days at room temperature then poured into cold 10% K_2CO_3. The mixture was extracted with ether and the ethereal layer was washed with water, dried and evaporated. The residue (200 mg) was submitted to preparative TLC (CH_2Cl_2–AcOEt 20:1). The major product extracted was an oil (**2a**) (130 mg), identical with that obtained above (TLC and IR spectra). The minor component was the starting enone (**1**) (50 mg).

Hydrolysis of 3β,17aβ-Diacetoxy-17α-methyl-9(8→7),8(9→11)-diabeo-D-homo-5α,14α-androst-7(11)-ene (2a)——Oil **2a** (130 mg) was treated with KOH (600 mg) in 80% MeOH (9 ml) at reflux for 1 hr under N_2 and poured into water. The mixture was extracted with $CHCl_3$, and the $CHCl_3$ solution was washed with water, dried and evaporated. The residue was crystallized from CH_2Cl_2–ether to give **2b** (83 mg) mp 259.5—261.5°. $[\alpha]_D^{28}$+10.8°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580, 3430, 1667, 1660, 1638. UV λ_{max} mμ (ε): 246.5 (11578). NMR (pyridine-d_5) τ: 9.05 (3H, s, 18-H), 8.97 (3H, s, 19-H), 8.82 (3H, d, J=6.0, 17α-Me), 6.98 (1H, q, $J_{17ah,17-H}$=9.0, $J_{17a,17-OH}$=6.0, 17β-OH), 3.95 (1H, br.s, 3-OH). *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.71; H, 9.83.

Jones Oxidation of 3β,17aβ-Dihydroxy-17α-methyl-9(8→7),8(9→11)-diabeo-D-homo-5α,14α-androst-7(11)-ene (2b)——Jones reagent (0.2 ml) was added dropwise into a solution of **2b** (70 mg) in acetone (7 ml) under stirring and the mixture was stirred for 15 min at room temperature, then poured into water containing a small amount of $NaHSO_3$. The mixture was extracted with $CHCl_3$ and the $CHCl_3$ solution washed with 5% K_2CO_3 and water. The dried $CHCl_3$ solution was evaporated to give a crystalline solid, which was crystallized from CH_2Cl_2–ether giving 3 mp 256—257°. $[\alpha]_D^{28}$−22.9°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1706, 1665, 1634 (infl.). NMR τ: 9.02 (3H, s, 18-H), 8.98 (3H, d, J=6.5, 17α-Me), 8.82 (3H, s, 19-H). *Anal.* Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.80; H, 8.36. The compound treated with Na in MeOD and D_2O exhibited the 17α-methyl proton signal as a singlet at τ 8.98 in its NMR spectrum.

Treatment of 3β,20β-Diacetoxy-5α-pregnane (4a) with $BF_3 \cdot O(C_2H_5)_2$——Compound **4a** (500 mg) was dissolved in $BF_3 \cdot O(C_2H_5)_2$ (7.5 ml) under stirring and the solution was kept at room temperature for 10 days. Work-up in a manner similar to that described above afforded a crystaline product (490 mg). As it was not possible to distinguish the product from the starting material by TLC, the homogeneity of the product was checked by NMR spectrum which supported its purity. Recrystallization from MeOH gave uranediol diacetate (**5a**) mp 161.5—163°. $[\alpha]_D^{25}$−31.1° (lit.[7] mp 160.5—161.5°, $[\alpha]_D^{22}$−29.0°). IR ν_{max} cm^{-1}: 1734, 1240. NMR τ: 9.22 (3H, s, 19-H), 9.21 (3H, d, J=6.5, 17α-Me), 9.17 (3H, s, 18-H), 5.67 (1H, d, J=10.5, 17aα-H). *Anal.* Calcd. for $C_{25}H_{40}O_4$: C, 74.21; H, 9.97. Found: C, 74.49; H, 9.99.

A portion (200 mg) of uranediol diacetate (**5a**) was treated with KOH (1 g) in 95% EtOH (15 ml) for 3.5 hr at reflux. Work-up gave a crystalline solid (157 mg) which was crystallized from MeOH to afford uranediol (**5b**), mp 220.5—221°. $[\alpha]_D^{25}$+6.3° (95% EtOH) [lit.[7] mp 215—216°, $[\alpha]_D^{28}$+5° (95% EtOH)].

Preparation of Uranediol[7] (5b) from 5α-Pregnane-3β,20β-diol 3-Acetate 20-Tosylate (4c)[11]——A solution of **4c** (206 mg), benzene (8 ml), acetone (12 ml) and formic acid (180 ml) was kept for 24 hr at 23°. $NaHCO_3$ (400 mg) and toluene (300 ml) were added to the reaction mixture, which was then concentrated *in vacuo* at room temperature. The residual mixture was extracted with benzene and the benzene layer was washed with aq. $NaHCO_3$ and water, dried and evaporated. The residue was crystallized from acetone to give crystals (120 mg, 17aβ-ol formate) mp 216—219°, which on treatment with KOH (1 g) in EtOH (20 ml) at reflux for 3 hr gave uranediol (92 mg), crystallized from MeOH giving prisms, mp 219—221°. This was shown to be identical with that obtained above (mixed melting point and IR spectra).

General Conditions for Reactions at 35° (see Table I)——Steroids (200 mg) were dissolved in $BF_3 \cdot O(C_2H_5)_2$ (2 ml) under stirring. The solutions obtained were kept in a thermostated oil bath (35°). Completion of the reaction was checked by TLC and/or NMR spectra measurement of samples occasionally pipetted from the reaction mixture. Disappearance of starting steroid from the reaction mixture being detected by monitoring the 18-proton signal in the NMR spectrum. For compound (**8**) the desired concentration could not be attained and so the maximum concentration attained was employed. Example **12** was run under different condifon but is listed in the same Table for convenience.

Formation of Uranediol Diacetate (5a)——After 100 hr at 35°, the solution was worked up and the residue crystallized from MeOH to give **5a**, mp 161—163° (175 mg, 88% yield).

When **4a** (200 mg) was treated with BF_3–AcOH[12] (6 ml) at 27° the reaction was found to be completed in 1 hr. Work-up gave a product (194 mg) which was subjected to preparative TLC (benzene–AcOEt 6:1) and afforded **5a** (184 mg, 92% yield) as the major product.

Formation of 3β,17aβ-Diacetoxy-17α-methyl-D-homo-5α-androst-9(11)-ene (7)——After 50 hr at 35°, the solution was worked up and the residue crystallized from MeOH to give **7**, mp 163—164° (180 mg, 90%

11) D.M. Glick and H. Hirschmann, *J. Org. Chem.*, **27**, 3212 (1962).

12) $BF_3 \cdot AcOH$ (mp 23—24°) is a slightly viscous liquid at 27° and soon after dissolving the steroid in it, the solution turned orange and became sludgy.

yield), $[\alpha]_D^{25}-62.7°$. IR ν_{max} cm^{-1}: 3030w, 1730, 1240. NMR τ: 9.21 (3H, s, 18-H), 9.20 (3H, d, J=6.0, 17α-Me), 9.07 (3H, s, 19-H), 5.64 (1H, d, J=10.5, 17aα-H), 4.73 (1H, t, J=4.0, 11-H). *Anal.* Calcd. for $C_{25}H_{38}O_4$: C, 74.60; H, 9.51. Found: C, 74.73; H, 9.60.

Formation of 3β,17aβ-Diacetoxy-17α-methyl-D-homo-5α-androstan-11-one (9)——After 15 days at 35°, the solution was worked up and the residue, showing one major spot with a different *Rf* value from that of the starting steroid was separated by preparative TLC (benzene–AcOEt 10:1, duplicate development). The major fraction was crystallized from MeOH to give **9** (162 mg, 81% yield) double mp 183—186°, 195—200°. $[\alpha]_D^{22}-29.1°$. IR ν_{max} cm^{-1}: 1737, 1717, 1238, 1026, 980. NMR τ: 9.20 (3H, s, 18-H), 9.18 (3H, d, J=6.0, 17α-Me), 8.98 (3H, s, 19-H), 5.52 (1H, d, J=10.0, 17aα-H). *Anal.* Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.65; H, 9.36.

Treatment of **8** (200 mg) with BF_3–AcOH (8 ml) for 24 hr at 27° afforded, after usual work-up, a product **9** (166 mg, 83% yield) double mp 184—186°, 196—200°, identical with that obtained above (TLC, IR spectra).

Formation of 3β,17aβ-Diacetoxy-17α-methyl-D-homo-5α-androstan-12-one (11)——After 18 days at 35° the solution was worked up and the residue was crystallized from MeOH to afford **11** (165 mg, 83% yield) mp 226.5—228°, $[\alpha]_D^{22}+46.4°$. IR ν_{max} cm^{-1}: 1755 (infl.), 1742, 1715, 1240, 1030. NMR τ: 9.15 (3H, d, J=6.0, 17α-Me), 9.12 (3H, s, 19-H), 8.77 (3H, s, 18-H), 5.13 (1H, d, J=10.0, 17aα-H). *Anal.* Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.66; H, 9.27.

Formation of 3β,17aβ-Dihydroxy-17α-methyl-D-homo-5α-androstane 17a-Monoacetate (13)——A solution of **12** (130 mg) in $CHCl_3$ (1 ml, as a co-solvent, purified over Al_2O_3 column) was treated with $BF_3 \cdot O(C_2H_5)_2$ 2 ml) at room temperature (23°) for 21 days. Work-up gave a product, crystallized from MeOH to give **13** (94 mg, 80% yield) mp 168—170°. IR ν_{max} cm^{-1}: 3600, 1750sh, 1734, 1240, 1038. NMR τ: 9.23 (3H, s, 19-H), 9.23 (3H, d, J=6.0, 17α-Me), 9.16 (3H, s, 18-H), 8.36 (1H, s, 3-OH), 6.67—6.16 (1H, centered at 6.42, 3-H), 5.67 (1H, d, J=10.5, 17aα-H). A portion of **13** was treated with Ac_2O–pyridine to give **5a** mp 161—163° identical with authentic **5a** (mixed melting point, IR spectra).

Formation of 3β,17aβ-Diacetoxy-17α-methyl-D-homo-5α-androstane 3-Acetate-17a-propionate (15)——Preparation of **14**; 3β,20β-Dihydroxy-5α-pregnane 3-acetate (500 mg) was treated with $(EtCO)_2O$–pyridine over night at room temperature. After work-up, the product was crystallized from 90% MeOH to give **14** (442 mg) mp 108.5—109.5°. $[\alpha]_D^{22}+24.9°$. IR ν_{max} cm^{-1}: 1736, 1242, 1193, 1025. NMR τ: 9.38 (3H, s, 18-H), 9.20 (3H, s, 19-H), 8.83 (3H, t, J=7.5 (1:2:1), O-CO-CH_2-$\underline{CH_3}$), 8.87 (3H, d, J=6.0, 21-H), 7.73 (2H, q, J=7.5 (1:3:3:1), O-CO-$\underline{CH_2}$-CH_3). *Anal.* Calcd. for $C_{26}H_{42}O_4$: C, 74.60; H, 10.11. Found: C, 74.42; H, 10.23.

Treatment of **14** with $BF_3 \cdot O(C_2H_5)_2$ according to the general method afforded a product, crystallized from MeOH to give **15** (182 mg, 91% yield) mp 160—161°, $[\alpha]_D^{22}-28.5°$. IR ν_{max} cm^{-1}: 1736, 1243, 1184, 1026. NMR τ: 9.22 (3H, s, 19-H), 9.22 (3H, d, J=6.0, 17α-Me), 9.16 (3H, s, 18-H), 8.87 (3H, t, J=7.5 (1:2:1), O-CO-CH_2-$\underline{CH_3}$), 7.67 (2H, q, J=7.5 (1:3:3:1), -O-CO-$\underline{CH_2}$-CH_3), 5.67 (1H, d, J=10.5, 17aα-H).

Treatment of 3β,20α-Diacetoxy-5α-pregnane (16) with $BF_3 \cdot O(C_2H_5)_2$——3β,20α-Diacetoxy-5α-pregnane was prepared from 3β-hydroxy-5α-pregnan-20-one by Na-iso-PrOH reduction following the procedure described by Kirk.[13] Special care was taken for the purification of the product. A sample with mp 167—169°, which would ordinarily be expected to be pure, was recrystallized 10 times from MeOH to give a special sample mp 169—171° (corrected) $[\alpha]_D^{22}-1.2\pm0.2°$ [lit. mp 163—165°, $[\alpha]_D-0.3°$[14]; mp 165—167°, $[\alpha]_D\pm0°$[15]; mp 164—167°, $[\alpha]_D-0.9°$ ($CHCl_3$)[16]]. The purity was also supported by the NMR and VPC.

A finely divided powder of **16** (200 mg) was dissolved in a mixture of $CHCl_3$ (1 ml) and $BF_3 \cdot O(C_2H_5)_2$ (3 ml) (or in 26 ml of BF_3·ether alone) under stirring and the solution was kept for 4 days at room temperature. Work-up gave a colored product (180 mg) which showed several spots with long tailings on TLC. Among three separable spots, two of them in the polar zone corresponded to those of the starting material (**16**) and uranediol diacetate (**5a**). Preparative TLC (benzene–AcOEt 50:1) afforded, as a less polar, major fraction, an oil (**17a**, 80—120 mg) which gave a positive tetranitromethane test and failed to crystallize. IR ν_{max} cm^{-1}: 1738, 1244, 1028. NMR τ: 9.20 (3H, s, 19-H), 9.07 (3H, s, 17β-Me), 8.00 (OAc). The upper fraction in the polar zone (100—50 mg) gave the starftng material **16** mp 167—170°, identical with an authentic sample (mixed melting point and IR spectra). The lower fraction in the polar zone (8—16 mg) was crystallized from MeOH to give **5a** mp 161—163° identical with an authentic sample (mixed melting point and IR spectra). The yield of **5a** was raised up to 13% when BF_3–AcOH was used in place of $BF_3 \cdot O(C_2H_5)_2$.

Hydrolysis of 18-Nor-17α-ethyl-17β-methyl-5α-androst-13(14)-en-3β-ol Acetate (17a)——A solution of the oil (**17a**) (160 mg) and K_2CO_3 (200 mg) in 90% MeOH (8 ml) was kept at room temperature over night. Work-up gave a crude product (138 mg), minor contaminants in which were removed by preparative TLC (CH_2Cl_2-AcOEt 20:1). Crystallization of the product (110 mg) from *n*-hexane gave crystals (**17b**) (62 mg)

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mp 129.5—131°, $[\alpha]_D$ −54.1°. IR ν_{max} cm^{-1}: 3560, 3340, 1065, 1039. NMR τ: 9.20 (3H, s, 19-H), 9.20 (3H, t, not clear, 17α-CH_2-$\underline{CH_3}$), 9.07 (3H, s, 17β-Me), 8.45 (1H, s, 3-OH), 6.38 (1H, m, 3-H). *Anal.* Calcd. for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.24; H, 11.29.

Preparation of 18-Nor-17α-ethyl-17β-methyl-5α-androst-13(14)-en-3β-ol (17b)——A solution of 3β-hydroxy-5α-pregn-17(20)-ene (18)[17] (200 mg, mp 154—158°), CH_2Cl_2 (2 ml) and H·COOH (6 ml) was kept at room temperature over night then poured into water. The mixture was extracted with CH_2Cl_2 and the CH_2Cl_2 layer washed with 5% K_2CO_3 and water, dried and evaporated. The residual oil (220 mg, formate) was treated with KOH (120 mg) in 95% MeOH at reflux for 30 min. After usual work-up the product was crystallized from ether–petr. ether to give **17b**, mp 129—131°, identical with that obtained above (mixed melting point and IR spectra).

Acetylation of pure crystalline **17b** obtained here with Ac_2O–pyridine afforded upon work-up an oil (**17a**) identical with that obtained above (IR and NMR spectra). Attempted crystallization failed.

Treatment of 3β,20α-Diacetoxy-5α-pregnan-12-one[18] (23) with $BF_3 \cdot O(C_2H_5)_2$——A solution of **23** (200 mg) in $BF_3 \cdot O(C_2H_5)_2$ (4 ml) was kept at room temperature for 4—15 days. Products from several runs showed each time complicated mixture on TLC. None of separate components could be characterized.

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