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REDUCTION OF CERTAIN STEROIDAL 19-SULFONIC ESTERS WITH METAL HYDRIDES

ENZO SANTANIELLO† and ELIAHU CASPI*

Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts 01545, U.S.A.

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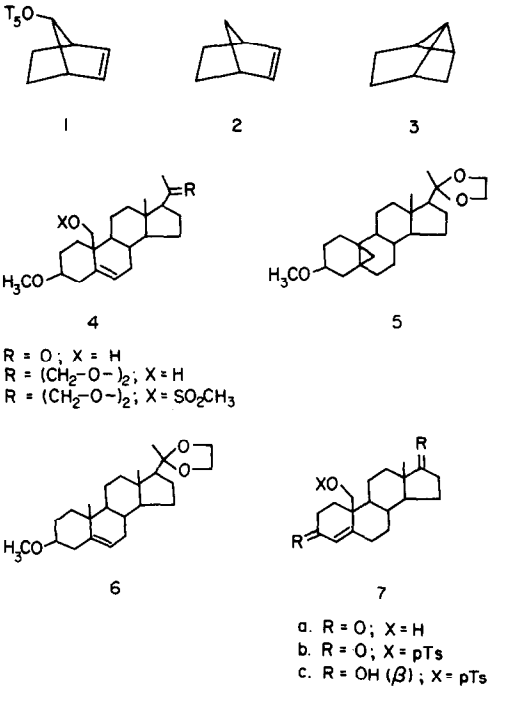
SUMMARY

For biosynthetic studies we required steroids labeled with ^2H and ^3H at C-19. The isotopic hydrogens could be introduced sequentially by stepwise reduction of appropriate 19-oxygenated substrates. The key step of the projected sequence was the conversion of the C-10-hydroxymethyl to a methyl. The approaches *via* the hydrogenolysis of steroidal 19-sulfonic esters with metal hydrides was explored and is described. Under the conditions tested only 1–2% of the needed C-10 methyl steroids were formed.

For biosynthetic studies we required specimens of pregnenolone labeled with tritium and/or deuterium at C-19. The projected introduction of isotopic hydrogens under sterically controlled conditions did not pose major conceptual problems. The plan was to reduce stepwise appropriate C-10 formyl or C-10 carbomethoxy substrates with labeled [^3H or ^2H] metal hydrides. The major task was to convert the resulting C-10 hydroxymethyl moiety to the C-10 methyl group under stereochemically controlled conditions. The shortest route seemed to be *via* the hydrogenolysis with metal hydrides of the corresponding 19-sulfonic esters. Usually this reaction proceeds with inversion of configuration [1]. The previous reports on attempted hydrogenolysis of a 19-mesylate were not encouraging [2]. In contrast, the observations on hydrogenolysis of anti-7-dehydronorbornyl tosylate (**1**) were somewhat more hopeful [3]. In the latter case treatment of (**1**) with $NaBH_4$, under controlled conditions, resulted in norbornene (**2**) and in the tetracyclic hydrocarbon (**3**) in a (4:1) ratio. It was obvious that the approach *via* hydrogenolysis of 19-hydroxysulfonate esters would at best be rather difficult. However, since we planned to introduce a large amount of tritium at C-19, a short synthetic route had distinct operational advantages. In practice, a yield as low as 10–20% in the hydrogenolysis step, to give pregnenolone analogs labeled with isotopic hydrogen(s) at C-19, was acceptable to us. Consequently, in spite of the anticipated complications, we considered the approach worthwhile evaluating.

As indicated the crucial step of the sequence was the hydrogenolysis of the 19-sulfonate esters. We concentrated, therefore, on this problem and our unsuccessful attempts to develop acceptable reaction conditions are described in this paper.



For the preparation of the 19-sulfonate esters of 19-hydroxy pregnenolone analogs it was necessary to protecting group and, therefore, used the previously thought that a 3-methyl ether might be a convenient protecting group and, therefore, used the previously prepared [4] 19-hydroxy pregnenolone 3-methyl ether (**4a**) as the starting material. Ketalization of (**4a**) (benzene–ethylene glycol, p-Ts.) proceeded in good yield and the resulting (**4b**) was converted to the 19-mesylester (**4c**). The crude, rather unstable (**4c**) was treated with $LiAlH_4$ (LAH) in tetrahydrofuran (THF) for 30 min at an ice bath temperature. The product

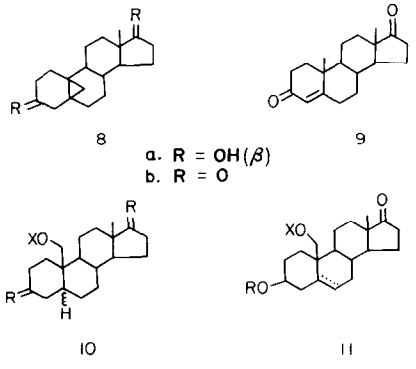
* Correspondence should be addressed to this author.

† Post-doctoral Fellow, 1973–1975; on leave of absence from the Department of Chemistry, School of Medicine, University of Milano, Milano, Italy.

obtained was the 5β,19-cyclo-(**5**). Only trace amounts of the required (**6**) were detected by g.l.c. Analogous results were obtained on treatment of a tetrahydrofuran solution of (**4c**) with LiB Et_3 H (SuperHydride; Aldrich Co.).

For practical reasons it was more convenient to continue modeling the reactions on the commercially available 19-hydroxy-C_{19} compounds, and we continued the investigation, using C_{19}-substrates.

It has been reported [5] that reduction of 3β, 17β, 19-trihydroxy-4-androstene 19-pTs ester (**7c**) with LAH yields (**8a**) and 4-androstene-3β, 17β, diol. We repeated the reaction starting with (**7a**) which was converted to (**7b**) and reduced with $NaBH_4$ in ethanol. The resulting (**7c**) was treated with LAH in tetrahydrofuran at reflux for 6 h. The recovered (**8a**) was oxidized with Jones reagent and identified as (**8b**). G.l.c. of the crude oxidation residue indicated the presence of approx. 2% of 4-androstene-3, 17-dione (**9**).



8 9

a. R = OH(β)
b. R = O

10 11

a. 5β; R = O; X = H
b. 5β; R = O; X = pTs
c. 5β; R = OH(β), X = H
d. 5β; R = $(CH_2\text{-}O\text{-})_2$; X = pTs
e. 5β; R = $(CH_2\text{-}O\text{-})_2$; X = H
f. 5α; R = $(CH_2\text{-}O\text{-})_2$; X = pTs
g. 5α; R = O; X = Ac
h. 5α; R = $(CH_2\text{-}O\text{-})_2$; X = Ac
i. 5α; R = $(CH_2\text{-}O\text{-})_2$; X = H

a. R = H; X = H; Δ^5
b. R = Ac; X = Ac; Δ^5
c. R = H, X = Ac; Δ^5
d. R = H; X = Ac; 5α-H

Our results on the hydrogenolysis of 19-sulfonate esters in the C_{21} and C_{19} series demonstrate the nearly exclusive formation of the C-5 (19) cyclic products. It is apparent that the C-5 homoallylic double bond participates in the stabilization of the developing C-19 cation and most likely a hydride ion is added at C-6. The transoid arrangement of the C-5 double bond and C-19 mesyloxy group provides for a maximal orbital overlap which favors the observed course of reaction.

Under the circumstances we explored the hydrogenolysis of the saturated (5α and 5β) 19-tosyloxy esters. The saturated derivatives represent neopentyl systems, which are known to be prone to rearrangements [6]. However, we thought that in this system the addition of a hydride ion at C-19 might satisfactorily compete with bond migration. Obviously, should a hydride ion be added at C-19, the reaction will proceed with inversion of configuration.

Hydrogenation of (**7a**) (ethanol-5% Pd-charcoal; H_2-3·5 atm) [7] gave (**10a**) which was converted to (**10b**). Treatment of (**10b**) with LAH in refluxing THF for 24 h resulted in the triol (**10c**). Some starting material (**10b**) was also recovered. When the reaction was carried on the tosyloxy-ketal (**10d**) using either LAH in THF or $LiBEt_3H$ in THF in both instances the 19-hydroxy-ketal (**10e**) was isolated as the major product. The required 5β-androstane-3, 17-bis ethylendioxide was present in approx. 0·5–1% yield as evidenced by g.l.c.

Similar results were obtained in the 5α-series. The required 19-hydroxy-5α-androstane-3, 17-bisethylenedioxide (**10f**) was prepared from 3β,19-dihydroxy-5-androsten-17-one (**11a**). The diol (**11a**) was converted to the diacetate (**11b**) and selectively saponified to the 19-mono-acetate (**11c**) [8]. The monoacetate (**11c**) was hydrogenated (methanol; 5% Pd on charcoal; H_2-18 psi) to yield (**11d**) which on oxidation with Jones reagent gave (**10g**). Ketalization of (**10g**) resulted in (**10h**) which was saponified (LAH) and the obtained (**10i**) converted to (**10f**).

The tosyl ester (**10f**), on treatment with LAH in tetrahydrofuran at ambient temperature for 24 h, gave the 19-hydroxy compound (**10i**). No more than approx. 1% of the required 5α-androstane-3,17-bis ethylene dioxide could be detected by g.l.c. Analogous results were obtained on treatment of (**10f**) with $LiBEt_3H$ in boiling THF (**2h**).

It is apparent that in the 5α and 5β-saturated series, the S—O, rather than the C—O bond, was cleaved. To the extent that the C–O bond was cleaved, a hydride addition at C-19, rather than a rearrangement, occurred. At best, minute amounts, insufficient for preparative consideration of the required 10-methyl products, were obtained. Presumably better yields of the required product would be obtained if conditions for the C–O cleavage could be developed.

EXPERIMENTAL

Physical measurements. Melting points were taken on a hot stage apparatus and are corrected. Infrared (I.R.) spectra were recorded on a Perkin–Elmer Model 237 spectrophotometer as KBr wafers. Absorption frequencies are quoted in $cm.^{-1}$

Nuclear magnetic resonance (n.m.r.) spectra were recorded in $CDCl_3$ on a Varian DA-60 spectrometer at 60 MHz. Chemical shifts are quoted in ppm downfield from tetramethylsilane as internal standard (s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet). Mass spectra were recorded on a Dupont 21-491 instrument by the direct insertion method. The temperature of the source was 210° and the ionization voltage was 70 eV. The masses of eliminated fragments are given in brackets after the molecular ion.

Chromatography. Analytical thin-layer chromatography (t.l.c.) was carried out on Baker Flex, IB-F silica gel plates (purchased from J. T. Baker Chem.

Co.) in the indicated solvent systems. The products were detected under U.V. light and were visualized by spraying with an ethanolic solution of phosphomolybdic acid (10%), and heating to 105°.

Preparative layer chromatography was carried out on plates coated with silica gel (Merck HF 254–366). Dry column and column chromatography were carried out on silica gel (Merck, 70–230 mesh). The homogeneity of products was tested by gas–liquid chromatography (g.l.c.) on a Hewlett–Packard 7620-A instrument using a 6-ft glass column (o.d. 6 mm, i.e. 2 mm) packed with SE-30, 1% on gaschrom (80–100 mesh) support. The instrument was set isothermally at the required temperature (210–250°). The column was eluted with helium (30 ml/min).

3β-Methoxy-19-hydroxy 5-pregnen-20, 20-ethylenedioxide (**4b**). A solution of (**4a**) [4] (546 mg), dry benzene (100 ml), ethylene glycol (10 ml) and p-toluensulfonic acid (30 mg) was refluxed (18 h) under a Dean–Stark water separator. After cooling, solid sodium hydrogen carbonate was added, and this was followed by the addition of a saturated solution of sodium hydrogen carbonate. The phases were separated and the benzene layer was washed with a saturated sodium hydrogen carbonate solution, water, dried and concentrated, to a residue (510 mg). Fractionation on t.l.c. [benzene–ethyl acetate (1:1 v/v)] gave homogenous (**4b**) (475 mg). A sample was crystallized from ethanol, m.p., 162–163°; I.R., ν_{max}, 3420, 3000 cm^{-1}; n.m.r. δ, 0·85(*s*, 3H, 13–CH_3), 1·30(*s*, 3H, 20–CH_3), 3·36(*s*, 3H, –OCH_3), 3·68 [*d*, 1H, 19-(CH–), J = 4 Hz], 3·87 [*d*, 1H, 19-(CH–), J = 4Hz], 3·95 [*m*, 3H, (–O–CH_2–CH_2–O–)], 5·76 [*m*, 1H, C–6(H) vinylic]; mass spectrum *m/e* 390(M^+) (−15, −30, −62), 87($C_4H_7O_2^+$).

3β-Methoxy-5β,19-cyclo-pregnan-20,20-ethylene-dioxide (**5**). A mixture of (**4b**) (133 mg), dry methylene chloride (3 ml), triethylamine (0·1 ml), and methane sulfonyl chloride (0·05 ml), [9] was stirred at 0–5° (ice bath) for 0·5 h. Sodium hydrogen carbonate was then added, the solution decanted, and the residue was washed with methylene chloride (5 ml). The combined extract was washed with a saturated sodium hydrogen carbonate solution (10 ml) water, dried and evaporated.

(a) The crude mesyl ester (**4c**) (168 mg) was dissolved in dry tetrahydrofuran (3 ml). The THF solution of (**4c**) was added with a syringe through a rubber septum to a cooled (0–5°) and stirred mixture of lithium aluminum hybride (200 mg) in dry tetrahydrofuran (2 ml) in an atmosphere of N_2. The mixture was allowed to warm up gradually to ambient temperature (0·5 h), then the reaction was terminated with ethyl acetate (20 ml). A saturated sodium sulfate solution was added (20 ml), and the resulting solid was removed by filtration. The filtrate was diluted with ethyl acetate washed with water (2 × 25 ml), dried (sodium sulfate), and evaporated to a residue (120 mg). The g.l.c. analysis of the above residue indicated the presence of approx. 65% of (**5**) and approx. 2% of (**6**). The residue was fractionated by t.l.c. [benzene–ethyl acetate (4:1 v/v)] and homogenous (**5**) was isolated (89 mg). A sample was crystallized from methanol and showed m.p., 102–103°; I.R., 3000, 1450 $cm.^{-1}$; n.m.r., δ, 0·40(*s*, 2H, 5β,19-cyclo propane), 0·75(*s*, 3H, 13–CH_3), 1·30(*s*, 3H, 20–CH_3), 3·32(*s*, 3H, –OCH_3), 3·94(*m*, 4H, (–O–CH_2–CH_2–O–)); mass spectrum, *m/e* 374(M^+) (–15, –32, –57, –73), 87($C_4H_7O^+$).

(b) A solution of (**4c**) (150 mg) in dry tetrahydrofuran (3 ml) was cooled (0–5°) and kept under N_2. Then a 1 M solution of $LiBEt_3H$ in tetrahydrofuran (1 ml) was added with a syringe through a rubber septum and the mixture was allowed to warm up gradually to the ambient temperature. The reaction was stopped by the addittion of water (10 ml) and the product was recovered with methylene chloride (10 ml). After a conventional work-up a residue (190 mg) was obtained. The g.l.c. analysis showed the presence of approx. 70% of (**5**) and < 2% of (**6**). The residue was purified by t.l.c. [benzene–ethyl acetate (4:1 v/v)] to give pure (**5**) (94 mg).

5β,19-Cycloandrostane-3, 17-dione (**8b**). The procedure of Rakhit and Gut [7] was followed with minor modifications. Freshly prepared tosylate [7] (**7b**) (130 mg) was dissolved in absolute ethanol (5 ml), then sodiun borohydride (150 mg) was added and the mixture was stored for 18 h at room temperature; ethyl acetate (20 ml) was added and the insoluble residue was removed by filtration. The filtrate was evaporated. The resulting (**7c**) (130 mg) was dissolved in dry tetrahydrofuran (10 ml), $LiAlH_4$ (250 mg) was added and the mixture was refluxed (4 h). The reaction was worked-up in a conventional manner. The recovered residue was dissolved in acetone and oxidized [7] with Jones reagent. The product of the oxidation was isolated and analyzed by g.l.c. The g.l.c. revealed the presence of approx. 75% of (**8b**) and approx. 2% of (**9**) in the residue. The mixture was fractionated by t.l.c. [benzene–ethyl acetate (4:1 v/v)] and the recovered (**8b**) was crystallized (acetone–ether) and showed a m.p., 138–140°. The physical constants of (**8b**) were in agreement with those reported [7].

19-Hydroxy-5β-androstane-3,17-dione (**10a**). A mixture of (**7a**) (1·0 g), absolute ethanol (50 ml), and 5% palladium on charcoal (350 mg) was shaken (5 min) in an atmosphere of hydrogen under 50 psi pressure. The catalyst was removed by filtration (Celite) and the filtrate was concentrated to a residue. G.l.c. analysis indicated that the residue contained approx. 65% of the 5β isomer. Crystallization from ethyl acetate gave homogenous (**10a**) (660 mg) m.p., 208–209°; I.R., 3380, 1735, 1705 $cm.^{-1}$: n.m.r., δ 0·88(*s*, 3H, 13–CH_3), 3·64 [*d*, 1H, 19-(CH–), J = 5 Hz], 4·00 [*d*, 1H, 19-(CH–), J = 5 Hz]; mass spectrum, *m/e* 302(M^+) (−18, −30, −46, −87).

19-Tosyloxy-5β-androstane-3,17-dione (**10b**). A solution of (**10a**) (200 mg) and p-toluenesulfonyl chloride (220 mg) in dry pyridine (5 ml) was stored at room temperature for (16 h). The mixture was poured on crushed ice, and after 4 h the solid was collected by

filtration, washed with water and dried (50°) to yield (**10b**) (220 mg). A sample was crystallized from acetone–hexane, m.p., 187–188° (decomposition); I.R., 2920, 1730, 1705, 1600, 1350, 1180 cm.$^{-1}$; n.m.r., δ 0·87(*s*, 3H, 13–CH_3), 2·47(*s*, 3H, aromatic), 4·04 [*d* 1H, 19-(CH–), J = 4 Hz], 4·32 [*d*, 1H, 19-(CH–), J = 5 Hz], 7·32(*d*, 2H, aromatic, J = 4 Hz) 7·78(*d*, 2H, aromatic, J = 4 Hz); MS, *m/e* 458(M^+) (−155, −172, −185).

5β-Androstane-3β, 17β, 19-triol (**10c**). (a) A solution of (**10b**) (100 mg) in dry tetrahydrofuran (3 ml) was added to a mixture of lithium aluminum hydride (200 mg) in dry tetrahydrofuran (5 ml). The mixture was refluxed (24 h) and worked up in the conventional manner. The products (80 mg) were resolved on t.l.c. [benzene–ethyl acetate (1:1 v/v)] into two bands. From the less polar zone 3β,17β,19-trihydroxy-5β-androstane-19-tosyl ester (15 mg) was obtained. The more polar fraction gave 5β-androstane-3β,17β,19-triol (**10c**) (50 mg) which was crystallized (ethyl acetate) m.p., 230–232°; I.R., ν_{max}, 3350 cm.$^{-1}$; n.m.r. δ(pyridine-*d*5), 1·03(*s*, 3H, 13–CH_3), 3·70 [*d*, 1H, 19-(CH–), J = 5 Hz]; 3·98 [*d*, 1H, 19-(CH–), J = 5 Hz]; MS, *m/e* 308(M^+) (−18, −36, −96, −114).

(b) To a solution of (**10b**) (100 mg) in dry THF (3 ml) a 1M solution of $LiBEt_3H$ in THF (0·5 ml) was added. The mixture was refluxed (24 h) and worked up in the conventional manner. The residue (120 mg) was purified by preparative t.l.c. [benzene–ethyl acetate (1:1 v/v)] to yield 3β,17β,19-trihydroxy-5β-androstane-19-tosylate (16 mg) and (**10c**) (70 mg).

19-Hydroxy-5β-androstane-3,3,17,17,bis-ethylene dioxide (**10e**). (a) A mixture of 19-hydroxy-5β-androstane-3,17-dione (**10a**) (200 mg), dry benzene (100 ml), p-toluensulfonic acid (20 mg) and ethylene glycol (4 ml) was refluxed (18 h) under a Dean–Stark water separator. The solution was cooled, solid sodium hydrogen carbonate was added and the mixture was stirred (1 h). The benzene solution was decanted, washed with aq. sodium hydrogen carbonate (100 ml), water, dried and evaporated (220 mg). By g.l.c. the residue contained approx. 90% of (**10e**). A sample was crystallized (methylenechloride–hexane) m.p., 116–117°; I.R., 3500, 2950 cm.$^{-1}$; n.m.r. δ 0·84(*s*, 3H, 13–CH_3), 3·70 [*d*, 1H, 19-(CH–), J = 5 Hz] 3·86 [*m*, 4H, 17(–O–CH_2–CH_2–O)], 3·93 [4H, 3(–O–CH_2–CH_2–O–)], [these two signals are superimposed on the doublet of 19-(CH_2–)]; MS, *m/e* 392(M^+) (−16, −31, −62, −106, −143).

(b) A solution of (**10d**) (100 mg) in dry THF (5 ml) was added to lithium aluminum hydride (150 mg) in dry tetrahydrofuran (5 ml). The mixture was refluxed (18 h) in an atmosphere of dry N_2. The mixture was processed in the conventional manner and following t.l.c. [benzene–ethyl acetate (1:1 v/v)] gave (**10e**) (65 mg). The product was identical to an authentic sample of (**10e**).

(c) To a solution of (**10d**) (100 mg) in dry tetrahydrofuran (5 ml) a 1M $LiBEt_3H$ solution in THF (0·5 ml) was added and the mixture was refluxed (6 h) under nitrogen. After the usual work-up and purification by preparative t.l.c. [benzene–ethyl acetate (1:1 v/v)] (**10e**) (70 mg) was obtained.

19-Tosyloxy-5β-androstan-3,3,17,17-bis ethylene-dioxide (**10d**). A solution of (**10e**) (180 mg) and p-toluenesulfonyl chloride (250 mg) in dry pyridine (5 ml) was stored (16 h) at room temperature. After a conventional work-up the tosylate (**10d**) was obtained (200 mg).

A sample was crystallized from acetone-hexane, m.p., 133–135°; I.R. 1600, 1440, 1365, 1160, 950 cm.$^{-1}$; n.m.r. δ 0·77(*s*, 3H, 13–CH_3), 2·46(*s*, 3H, aromatic), 3·87 [*m*, 4H, 17(–O–CH_2–CH_2–O–)], 3·92 [*m*, 4H, 3(–O CH_2–CH_2–O–)], 4·08(*d*, 2H, 19–CH_2–, J = Hz), 7·23(*d*, 2H, aromatic, J = 8 Hz), 7·84(*d*, 2H, aromatic, J = 8 Hz); MS *m/e* 546(M^+) (−154, −169, −266).

3β,19-Dihydroxy-5-androsten-17-one-3,19-diacetate (**11b**). A solution of (**11a**) (4 g) in pyridine (20 ml) and acetic anhydride (10 ml) was stored (16 h) at room temperature. The mixture was then poured on ice. After 2 h the solid (**11b**) was collected by filtration and dried. A sample was recrystallized (methanol–water), m.p., 102–104°; I.R., 2950, 1740, 1440, 1370, 1250, 1225 cm.$^{-1}$; n.m.r. δ0·93(*s*, 3H, 13-CH_3), 2·02(*s*, 3H, 3-OAc), 2·04(*s*, 3H, 19-OAc) 3·98 [*d*, 1H, 19-(CH–), J = 6 Hz], 4·60 [*d*, H, 19-(CH–) J = 6 Hz] (superimposed to the multiplet of the 3α–H), 5·7 [*m*, 1H C–6(H)]; MS *m/e* 388(M^+) (−60, −120, −135, −152, −174).

3β,19-Dihydroxy-5-androsten-17-one-19-acetate(**11c**). A mixture of (**11b**) (2 g), methanol (50 ml), water (1 ml), and potassium carbonate (1 g) was stirred for 1·5 h. Water was added (100 ml), and the product was recovered with ethyl acetate (3 × 100 ml). The ethyl acetate solution was washed, dried and evaporated to dryness. The residue (1·9 g) was chromatographed on a silica gel column [Merck (70–230 mesh)], (150 g). The fractions eluted with benzene–ethyl acetate (1:1 v/v) contained 1·42 g of (**11c**). A sample was crystallized from ethyl acetate–hexane, m.p., 121–123°; I.R. 3520, 1740, 1720, 1250 cm.$^{-1}$; n.m.r., δ 0·91(*s*, 3H, 13-CH_3), 2·05(*s*, 3H, 19-OAc) 3·96 [*d*, 1H, 19-(CH–), J = 2 Hz], 4·50 [*d*, 1H, 19-(CH–), J = 2 Hz], 5·60 [*m*, 1H, C–6(H)]; MS *m/e* 346(M^+) (−18, −60, −78, −91).

3β,19-Dihydroxy-5α-androstan-17-on-19-acetate (**11d**). A mixture of (**11c**) (1 g), absolute methanol (50 ml) and 5% Pd on charcoal (750 mg) was stirred in an atmosphere of hydrogen (16 h).

The solid was filtered (Celite) and the filtrate evaporated to a residue (0·95 g). A sample was crystallized from acetone, m.p., 130–131°; I.R. 3450, 1730 cm.$^{-1}$; n.m.r., δ 0·85(*s*, 3H, 13-CH_3), 2·05(*s*, 3H, 19-OAc), 3·60(*m*, 1H, 3αH), 4·15 [*d*, 1H, 19-(CH–), J = 6 Hz], 4·42 [*d*, 1H, 19-(CH–), J = 6 Hz]; MS *m/e* 348(M^+) (−18, −60, −78, −91, −109, −134).

19-Acetoxy-5α-androstane-3,17-dione (**10g**). To a cooled (0·5°), and stirred solution of (**11d**) (600 mg) in acetone (10 ml) Jones reagent was added dropwise

until a light brown color persisted for 5 min. Then methanol and water was added and the product was extracted with ethyl ether (3 × 30 ml). The ethyl acetate solution was washed, dried, and evaporated to a residue. Crystallization (methanol–water) afforded (**10g**) (560 mg), m.p., 69–71°; I.R., 2950, 2870, 1740 (broad.), 1725, 1245, 1040 cm.$^{-1}$; n.m.r. δ, 0·90(*s*, 3H, 13-CH_3), 2·10(*s*, 3H, 19-OAc), 4·46(*s*, 2H, 19-CH_2-); MS, *m/e* 346(−42, −60, −71, −89, −98, −112).

19-*Acetoxy*-5α-*androstane*-3,3,17,17-*bis*-*ethylene*-*dioxide* (**10h**). The ketalization of (**10g**) (0·5 g) in benzene (200 ml), p-toluenesulfonic acid (50 mg) and ethylene glycol (10 ml) was carried out as described for (**10e**). The obtained (**10h**) was crystallized (ethyl acetate) and showed m.p., 151–153°; I.R. 2950, 2870, 1740, 1245 cm.$^{-1}$; n.m.r. δ 0·80(*s*, 3H, 13-CH_3), 2·07(*s*, 3H, 19-OAc) 3·88 [*m*, 4H, (–O–CH_2–CH_2–O)], 4·14 [*d*, H, 19-(CH–), J = 6 Hz], 4·40 [*d*, 1H, 19-(CH–), J = 6 Hz]; MS, *m/e* 434(M^+) (−42, −69, −104).

19-*Hydroxy*-5α-*androstan*-3,3,17,17-*bis*-*ethylene*-*dioxide* (**10i**). (a) A mixture of (**10h**) (500 mg), lithium aluminum hydride (500 mg) and dry ethyl ether (20 ml) was refluxed for (2 h). The mixture was processed in the conventional manner and the residue (400 mg) was fractionated by preparative t.l.c. [benzene–ethyl acetate (1:1 v/v)]. The obtained (**10i**) (380 mg) was crystallized (ethyl acetate–methanol), m.p., 190–192°; I.R., 3480, 2920 cm.$^{-1}$; n.m.r. δ, 0·90(*s*, 3H, 13-CH_3), 3·88 [4H, 17(–O–CH_2–CH_2–O–)], 3·97 [*m*, 4H, 3(–O–CH_2–CH_2–O–)], MS, *m/e* 392(M^+) (−15, −18, −31, −45, −63).

(b) A mixture of (**10f**) (50 mg), lithium aluminum hydride (50 mg) and dry THF (5 ml), was stirred (24 h) at room temperature in an atmosphere of N_2. Following the conventional work-up and t.l.c., [benzene-ethyl acetate, (1:1 v/v)] and (**10i**) (32 mg), identical to an authentic sample was obtained.

(c) To (**10f**) (50 mg) in dry THF (2 ml) a 1 M $LiBEt_3H$ solution in THF (0·2 ml) was added. The mixture was refluxed (2 h) under N_2. After processing and t.l.c. (**10i**) (38 mg) was obtained.

19-*Tosyloxy*-5α-*androstan*-3,3,17,17-*bis ethylene dioxide* (**10f**). A solution of (**10i**) (100 mg) and p-toluenesulfonylchloride (105 mg) in dry pyridine (4 ml) was stored (16 h) at room temperature. The solution was poured on crushed ice and the product was extracted with ethyl acetate (3 × 10 ml). The extract was washed with water, dried and evaporated (120 mg). The oily residue was homogenous by t.l.c. but resisted crystallization. The sample showed: I.R., 1600, 1440, 1345 cm.$^{-1}$; n.m.r. δ, 0·90(*s*, 3H, 13-CH_3), 2·46(*s*, 3H, aromatic), 3·88 [*m*, 4H, 17(–O–CH_2–CH_2–O–)], 3·94 [*m*, 4H, 3(–O–CH_2–CH_2–O–)], 4·06 [*d*, 1H, 19-(CH–), J = 8 Hz], 4·26 [*d*, 1H, 19-(CH–), J = 8 Hz], 7·88(*d*, 2H, aromatic, J = 8 Hz); MS, *m/e* 546(M^+) (−44, −88, −198, −216, −244).

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