STEROID DERIVATIVES. LXXIV.*

CLEAVAGE OF STEROID (16*S*)-SPIRO-[16,2′]-OXIRANS OF 20-PREGNANONE SERIES WITH HYDROGEN BROMIDE

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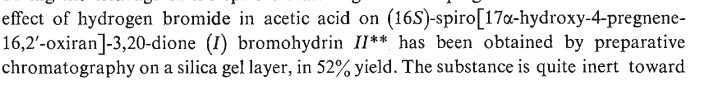
Reaction of (16*S*)-spiro[17α-hydroxy-4-pregnene-16,2′-oxiran]-3,20-dione(*I*) and (16*S*)-spiro-[3β-acetoxy-17α-hydroxy-5-pregnene-16,2′-oxiran]-20-one (*V*) with hydrogen bromide in acetic acid gave corresponding 16β-bromomethyl-16α,17α-dihydroxy-17β-methyl-17a-ones *II* and *VI* respectively. The structure of these compounds was proved by a synthesis starting with 3β-acetoxy-17α-hydroxy-16-methylene-5-pregnen-20-one (*XVIII*). The reaction of the spiro-oxiran derivative *IV* with chromium(II) chloride, giving rise to chlorohydrin *IX*, is also in agreement with the proposed structure for D-homosteroids.

In one of our preceding papers the preparation and some reactions of steroidal (16*S*)-spiro-[16,2′]oxirans were described and it was proved that spiro-oxirans of the androstane series are cleaved by hydrogen bromide under formation of 16β-bromomethyl-16α-hydroxy compounds[1]. A more complex situation has now been observed during the cleavage of the spiro-oxiran ring in the 20-pregnanone series. Under the effect of hydrogen bromide in acetic acid on (16*S*)-spiro[17α-hydroxy-4-pregnene-16,2′-oxiran]-3,20-dione (*I*) bromohydrin *II*** has been obtained by preparative chromatography on a silica gel layer, in 52% yield. The substance is quite inert toward



I, 4-en-3-one
V, 3β-acetoxy-5-ene

II, 4-en-3-one, R = Br
VI, 3β-acetoxy-5-ene, R = Br
IX, 4-en-3-one, R = Cl

IV, 4-en-3-one
VII, 3β-acetoxy-5-ene
VIII, 3β-hydroxy-5-ene

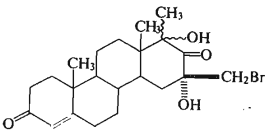
* Part LXXIII: This Journal *37*, 1577 (1972).

** As a side product a polar substance is formed, m.p. 357—359°C, which does not contain bromine. According to its PMR spectrum it is not a D-homosteroid.

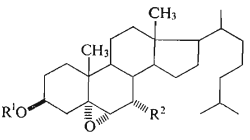
acetylation with acetic anhydride in pyridine at room temperature, which corresponds to the tertiary character of the hydroxyl groups present. With potassium acetate or potassium hydrogen carbonate bromohydrin *II* did not change to the starting spiro-oxiran *I*, but an isomeric substance (*IV*) was obtained which could be easily transformed back to bromohydrin *II* with hydrogen bromide in acetic acid. Probably during the original opening of the oxiran ring in compound *I* a skeletal rearrangement took place and bromohydrin *II* as well as the isomeric oxido compound *IV*, already possessed this more stable, rearranged, structure. In the PMR spectra of bromohydrin *II* and the oxido compound *IV* the singlet 18-H was distinctly shifted downfield by a value which agrees well the characteristic shift (22–24 c.p.s.) for the transition from the pregnane to the D-homoandrostane series[2,3]. It was necessary to choose between two possible D-homo structures *II* or *III*, differing in the position of the carbonyl group, as it is known from the literature[3] that the shift of the angular 13-methyl group is identical in both structures. This is complemented by the possibility of the isomerism on $C_{(17)}$ (or $C_{(17a)}$). The result of the IR spectroscopy (a carbonyl maximum at 1705 cm^{-1}) was irrelevant because the diagnostic difference of approximately 25 cm^{-1} (1697 and 1722 cm^{-1} of the carbonyl at $C_{(17)}$ or $C_{(17a)}$), observed on 16-unsubstituted[4] D-homosteroids, decreases in analogous 16α-hydroxy compounds[3] to 1707 and 1712 cm^{-1} and it is not significant. The negative shift of molecular rotation (−62°) for the pair *I* and *IV*, which is otherwise characteristic of other 17-keto isomers[4], must also be considered with reserve because the vicinal effect of spiro-oxiran ring may be different in five and six-membered rings.

(16*S*)-spiro[3β-acetoxy-17α-hydroxy-5-pregnene-16,2′-oxiran]-20-one (*V*) also gave on reaction with hydrogen bromide a rearranged bromohydrin *VI*. Reaction of compound *VI* with potassium acetate gave spiro-oxiran, compound *VII*, which could be transformed back to bromohydrin *VI* under the effect of hydrogen bromide in acetic acid. An analogous course of the rearrangement of starting compounds *I* and *V* was proved by hydrolysis of 3β-acetate *VII* with potassium hydrogen carbonate to 3β-hydroxy derivative *VIII*. This was transformed by Oppenauer oxidation to 3-keto derivative *IV*, identical with a substance prepared by the following reaction sequence *I* → *II* → *IV*.

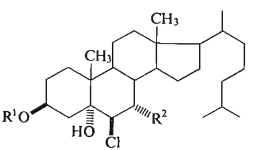
Bromohydrin *II* seemed unsuitable for chemical proof of the structure; the reaction of epoxide *IV* with chromium(II) chloride seemed more promissing. It is known[5] that α,β-oxido ketones are changed in this reaction to α,β-unsaturated ketones. In the case of epoxide derived from structure *III* the formation of a substance with a 16-exomethylene group could be expected. In contrast to this, substances with an isolated epoxide ring react with chromous chloride under formation of corresponding chlorohydrins, as for example in the case of cyclohexene oxide[5]. This finding was corroborated by the reaction of chromous chloride with 3β-hydroxy-5,6α-oxido-5α-cholestane (*X*), which gave the known[6] 6β-chloro-3β, 5-dihydroxy-5α-cholestane (*XI*). With 3β-benzoyloxy-7α-hydroxy-5,6α-oxido-5α-cholestane[7] (*XII*) it gave 3β-



III

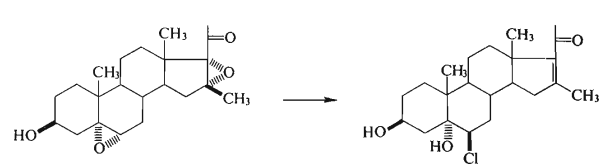


X, $R^1 = R^2 = H$
XII, $R^1 = Bz$, $R^2 = OH$

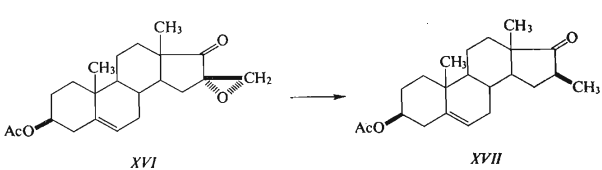


XI, $R^1 = R^2 = H$
XIII, $R^1 = Bz$, $R^2 = OH$

benzoyloxy-6β-chloro-5,7α-dihydroxy-5α-cholestane (*XIII*) (chlorohydrin *XIII* was transformed back to epoxide *XII* with potassium acetate in acetone), and eventually, with 3β-hydroxy-16β-methyl-5,6α;16α,17α-dioxido-5α-pregnan-20-one (*XIV*) it afforded 6β-chloro-3β,5-dihydroxy-16-methyl-5α,16-pregnen-20-one (*XV*). The course of the reaction of chromium(II) chloride with (16*S*)-spiro[3β-acetoxy-5-androstene-16,2′-oxiran]-17-one[1] (*XVI*) was unexpected. The expected 3β-acetoxy-16-methylene-5-androsten-17-one was not formed as the product of the almost instantaneous reaction, but a compound which was formulated on the basis of its elemental analysis and PMR spectrum as 3β-acetoxy-16-methyl-5-androsten-17-one. The physical con-



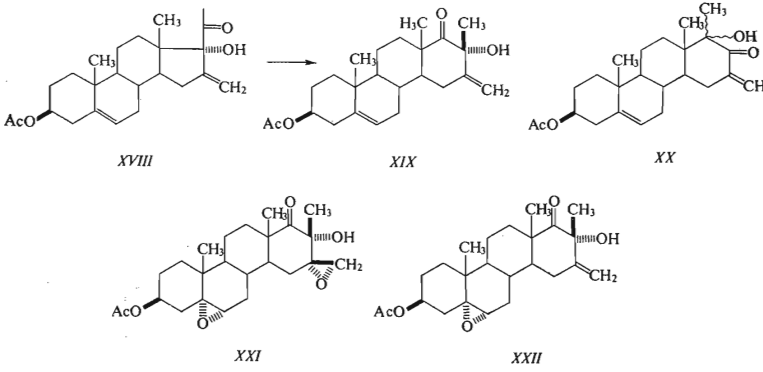
XIV *XV*



XVI *XVII*

stants of this substance were identical with those of the known[8,20] 16β-methyl isomer (*XVII*). It is evident that this reaction is not based on the cleavage of the epoxide oxygen and subsequent reduction of the 16-exomethylene group formed, because 3β-acetoxy-16-methylene-5-androsten-17-one does not react with chromous chloride even after 24 hours of contact. From the reaction of spiro-oxiran *IV* with chromous chloride chlorohydrin *IX* was isolated which was transformed back to the starting epoxide *IV* under the effect of alkalies, while the experiment aimed at acetylation was unsuccessful. The PMR spectrum of substance *IX* was identical with that of bromohydrin *II*. The formation of chlorohydrin *IX* indicated that the epoxy ring in compound *IV* is not in the α,β-position to the keto group, and hence, that it must be a derivative of 17a-ketone.

An unambigous proof of the structure of the above mentioned D-homosteroids, including the configuration of the methyl and the hydroxyl group at $C_{(17)}$ was carried out by the following sequence of reactions. 3β-Acetoxy-17α-hydroxy-16-methylene-5-pregnen-20-one[9] (*XVIII*) was submitted to D-homo rearrangement under the influence of boron trifluoride etherate in dioxan. The formation of 17a-ketone could be expected, because it is known from the literature that Lewis acids lead to D-homosteroids with 17β-methyl-17α-hydroxy-17a-ketone structure as the main products[10–17]. In this manner 3β-acetoxy-17α-hydroxy-17β-methyl-16-methylene-D-homo-5-androsten-17a-one (*XIX*) was prepared in high yield. It did not absorb in the UV region and, therefore, it could not be the isomeric 17-ketone *XX*. Epoxidation of compound *XIX* with perphthalic acid gave a mixture of three substances of different polarity, which were separated by preparative silica gel thin-layer chromatography. A small amount of the least polar starting substance was thus obtained.



XVIII *XIX* *XX*

XXI *XXII*

A more polar substance was also isolated in 23% yield which was formulated as 3β-acetoxy-17α-hydroxy-17β-methyl-16-methylene-5,6α-oxido-D-homo-5α-androstan-17a-one (*XXII*), and, eventually, the most polar substance (in 39% yield) the elemental composition and the PMR spectrum of which were in accordance with the structure of (16*S*)-spiro[3β-acetoxy-17α-hydroxy-17β-methyl-5,6α-oxido-D-homo-5α-androstane-16,2′-oxiran]-17a-one (*XXI*). The same product was isolated also as the predominant component from a mixture obtained on reaction of perphthalic acid with spiro-oxiran derivative *VII*. The identity of both substances shows that all the substances mentioned possess the structure of D-homosteroids of the 17a-keto type. In addition, it may be assumed that the configuration of the hydroxy group in the position 17 is α in these compounds, because it is known that the epoxidation of allylic double bonds with peracids takes place from the hydroxyl group side[7,18], and, simultaneously, that acid catalysed D-homorearrangements are not accompanied by a change of configuration at $C_{(16)}$[13,19].

The formation of D-homosteroids of the type *II* and *VI* on cleavage of the oxiran compounds *I* or *V*, respectively, with hydrogen bromide proves that the course of the rearrangements is based on the migration of the 16,17-bond, *i.e.* that it is similar to D-homo rearrangements caused by Lewis acids. In the reaction mixture the presence of an appreciable amount of the rearranged bromohydrin may be demonstrated by thin-layer chromatography even after a few seconds, in addition to the starting substance. However, in no case could the presence of another similarly polar substance be demonstrated, which could have the structure of the primarily formed bromohydrin with a five-membered D-ring. A rapid and smooth course of the rearrangement is probably affected by the appreciable interaction between the angular 13-methyl, by the bulky 16β-bromomethyl group formed, and by the side chain in the position 17β. This assumption is in agreement with the experience that substances with a substituent in the position 16β undergo D-homo isomerisation more easily than substances with a substituent in the position 16α, or unsubstituted substances[14,16,19].

EXPERIMENTAL

The melting points were determined on a Kofler microblock. Optical rotations were measured in chloroform unless stated otherwise, with a ±3° precision. Samples for analysis were dried over phosphorus pentoxide at 0·1 Torr for 24 h. The UV spectra were measured on a Zeiss spectrophotometer, Model VSU-1 (NaCl prisms, quartz cell 1 cm thick), in methanol, IR spectra on a double-beam Zeiss spectrophotometer, Model UR-10, in 6% chloroform solutions. The PMR spectra were taken on a Zeiss ZKR 60 apparatus, at 60 Mc, in deuteriochloroform, with tetramethylsilane as internal standard. The values of the chemical shifts are given in p.p.m. on the δ-scale. Thin-layer chromatography was carried out with silica gel CH, Lachema Brno, preparative thin-layer chromatography on Silpearl (silica gel) from Kavalier, Votice (on plates 100 × 20 cm, 1 mm layer thickness, the same systems for both types of chromatographies).

16β-Bromomethyl-16α,17α-dihydroxy-17β-methyl-D-homo-4-androstene-3,17a-dione (*II*)

a) To a suspension of (16*S*)-spiro[17α-hydroxy-4-pregnene-16,2′-oxiran]-3,20-dione (*I*) (1 g) in acetic acid (6 ml) a solution of hydrogen bromide in acetic acid (3·6 ml; 70 mg of HBr/1 ml)

was added dropwise under stirring and cooling to +10°C. After 5 min the cooling was interrupted and the mixture stirred at room temperature for another 10 min. The mixture was diluted with water (100 ml) and allowed to stand overnight. The separated product was filtered off with suction, washed with water, dried, and chromatographed on silica gel in chloroform–methanol (98 : 2). Yield 635 mg (52%) of a chromatographically pure substance which was crystallised from methanol, affording 498 mg of bromohydrin *II*, m.p. 218–220°C (decomp.); $[\alpha]_D^{25}$ +6 (*c* 0·9); UV spectrum: λ_{max} 240 nm (log ε 4·20); IR spectrum: 3 530, 3 450 (hydroxyl), 1 705 (six-membered ring carbonyl), 1 662, 1 619 cm^{-1} (conjugated carbonyl); PMR spectrum: 1·17, 1·21 (10-CH_3, 13-CH_3), 1·44 (17β-CH_3), 3·60 (CH_2Br), 4·50 (OH), 5·75 (4 H). For $C_{22}H_{31}BrO_4$ (439·4) calculated: 60·13% C, 7·11% H; found: 59·89% C, 7·25% H. *b*) To a solution of epoxide *IV* (20 mg) in acetic acid (0·2 ml) a solution of hydrogen bromide in acetic acid (0·05 ml; 210 mg of HBr/ml) was added and the mixture allowed to stand at room temperature for 10 minutes. After dilution with water the product was extracted with ether and the extract washed with water, potassium hydrogen carbonate solution, and water. After drying over sodium sulfate, filtration and evaporation of the solvent the crude residue was crystallised from methanol. Yield 16 mg (65%) of bromohydrin *II*, m.p. 215–219°C (decomp.), identical according to its IR spectrum with bromohydrin *II* prepared as under *a*).

(16*S*)-Spiro[17α-hydroxy-17β-methyl-D-homo-4-androstene-16,2′-oxiran]-3,17a-dione (*IV*)

a) A mixture of bromohydrin *II* (80 mg) and potassium acetate (240 mg) in acetone (6 ml) was refluxed for 6 h. The reaction mixture was concentrated, diluted with water (50 ml), and the separated product filtered off, washed with water, dried, and crystallised from acetone. Yield 44 mg (67%) of compound *IV*, m.p. 231–234°C; $[\alpha]_D^{24}$ +46° (*c* 1·4); UV spectrum: λ_{max} 241 nm (log ε 4·19); IR spectrum: 3 520 (hydroxyl), 1 708 (carbonyl in a six-membered ring), 1 664, 1 619, 890 cm^{-1} (conjugated carbonyl); PMR spectrum: 1·23, 1·26 (10-CH_3, 13-CH_3), 1·57 (17β-CH_3), 2·70, 3·05 (AB q, J = 6 Hz, CH_2O), 3·23 (OH), 5·75 (4-H). For $C_{22}H_{30}O_4$ (358·5) calculated: 73·71% C, 8·44% H; found: 73·57% C, 8·49% H. *b*) A mixture of chlorohydrin *IX* (20 mg) and potassium acetate (60 mg) in acetone (1 ml) was refluxed for 6 h. The working up of the reaction mixture as under *a*) and crystallisation of the crude product from acetone gave 10 mg (55%) of epoxide *IV*, m.p. 232–234°C, identical with the product *IV* prepared under *a*). *c*) Derivative *VII* (100 mg) was hydrolysed with potassium hydrogen carbonate (100 mg) in methanol (5 ml) at room temperature overnight. The reaction mixture was concentrated *in vacuo*, diluted with water, extracted with ether, and the extract worked up in the conventional manner. The dried 3β-hydroxy derivative *VIII* (79 mg) was dissolved in toluene (5 ml) and refluxed for 1 h with cyclohexanone (1 ml) and aluminum isopropoxide (100 mg, 0·45 ml of a solution in toluene) under exclusion of air humidity. Volatile components were eliminated by steam distillation and the product was filtered off, washed with water, dried, and crystallised from acetone. Yield 39 mg (44%) of derivative *IV*, m.p. 230–233°C, identical with the substance prepared under *a*).

3β-Acetoxy-16β-bromomethyl-16α,17α-dihydroxy-17β-methyl-D-homo-5-androsten-17a-one (*VI*)

a) A solution of compound *V* (200 mg) in acetic acid (2 ml) was cooled and mixed with a solution of hydrogen bromide in acetic acid (0·9 ml; 68 mg HBr/1 ml). After 10 min standing the reaction mixture was worked up by the procedure described for compound *II*. The main product was isolated by preparative thin-layer chromatography on silica gel (chloroform). Yield 112 mg (47%) of bromohydrin *VI*, which after crystallisation from methanol gave an analytically pure product, m.p. 264–266°C (decomp); $[\alpha]_D^{21}$ −98° (*c* 2·0). For $C_{24}H_{35}BrO_5$ (483·4) calculated:

59·62% C, 7·30% H; found: 59·89% C, 7·21% H. *b*) A mixture of derivative *VII* (35 mg), acetic acid (1 ml), and hydrogen bromide in acetic acid (0·1 ml; 187 mg HBr/1 ml) was allowed to stand at room temperature for 10 minutes and then worked up by the procedure used for compound *II*. Crystallisation from methanol gave 29 mg (69%) of bromohydrin *VI*, m.p. 261—264°C (decomp.), identical with compound *VI* prepared under *a*).

(16*S*)-Spiro[3β-acetoxy-17α-hydroxy-17β-methyl-D-homo-5-androstene-16,2′-oxiran]-17a-one (*VII*)

A solution of bromohydrin *VI* (70 mg) in acetone (6 ml) was refluxed with potassium acetate (200 mg) for 6 h. The reaction mixture was worked up as in the case of compound *IV*. Yield 39 mg (67%) of derivative *VII*, m.p. 210—211°C (methanol); $[\alpha]_D^{22}$ −88° (*c* 1·4). For $C_{24}H_{34}O_5$ (402·5) calculated: 71·61% C, 8·51% H; found: 71·22% C, 8·39% H.

16β-Chloromethyl-16α,17α-dihydroxy-17β-methyl-D-homo-4-androstene-3,17a-dione (*IX*)

A solution of epoxide *IV* (94 mg) in a mixture of acetic acid and methanol (1 : 1, 3 ml) was mixed under nitrogen with a methanolic solution of chromium(II) chloride which was prepared on reduction of 200 mg of chromium(III) chloride in methanol with zinc and hydrochloric acid under a layer of light petroleum. The reaction mixture was allowed to stand overnight at room temperature, concentrated to a small volume *in vacuo*, diluted with water, and extracted with ether. The ethereal extract was washed with water, a solution of $KHCO_3$, and water, then dried over sodium sulfate and evaporated to dryness under reduced pressure. The crude residue (82 mg) was recrystallised from methanol. Yield 65 mg (63%) of chlorohydrin *IX*, m.p. 208—211°C (decomp.); $[\alpha]_D^{24}$ +21° (*c* 2·5); UV spectrum λ_{max} 238 nm (log ε 4·05); IR spectrum: 3450 (hydroxyl), 1700 (carbonyl in a six-membered ring), 1660, 1618 cm^{-1} (conjugated carbonyl); PMR spectrum: 1·08, 1·10 (10-CH_3, 13-CH_3), 1·42 (17β-CH_3), 3·66 (CH_2Cl), 4·47 (OH), 5·72 (4-H). For $C_{22}H_{31}.ClO_4$ (394·9) calculated: 66·90% C, 7·91% H; found: 66·49% C, 7·96% H.

6β-Chloro-3β,5-dihydroxy-5α-cholestane (*XI*)

A solution of epoxide *X* (100 mg) in a mixture of acetic acid and methanol (1 : 1, 2 ml) was reduced by the procedure applied for compound *IX*. The crude product was crystallised from benzene. Yield 83 mg (76%) of chlorohydrin *XI*, m.p. 174—176°C (decomp.), $[\alpha]_D^{22}$ −7° (*c* 1·3). For $C_{27}H_{47}ClO_2$ (439·1) calculated: 8·07% Cl; found: 7·59% Cl. Literature[6] gives m.p. 164 to 174°C, $[\alpha]_D$ −9°.

3β-Benzoyloxy-6β-chloro-5,7α-dihydroxy-5α-cholestane (*XIII*)

Epoxide *XII* (200 mg) in a mixture of acetic acid and tetrahydrofurane (1 : 1, 6 ml) was reduced by the procedure used for substance *IX*. Crystallisation from methanol gave 125 mg (59%) of chlorohydrin *XIII*, m.p. 201—203°C; $[\alpha]_D^{22}$ −22° (*c* 1·1). For $C_{34}H_{51}ClO_4$ (559·2) calculated: 6·34% Cl; found: 6·69% Cl. Chlorohydrin *XIII* was transformed back to the starting oxido compound *XII* with potassium acetate.

6β-Chloro-3β,5-dihydroxy-16-methyl-5α-pregn-16-ene-20-one (*XV*)

A solution of epoxide *XIV* (100 mg) in a mixture of acetic acid and methanol (1 : 1, 2 ml) was reduced as above (compound *IX*). Crystallisation of the crude product from ethyl acetate gave

66 mg (63%) of chlorohydrin *XV*, m.p. 199–201°C; $[\alpha]_D^{24}$ −59° (*c* 0·8, dioxane); UV spectrum: λ_{max} 252 nm (log ε 3·88). For $C_{22}H_{33}ClO_3$ (380·9) calculated: 9·31% Cl; found: 9·19% Cl.

3β-Acetoxy-16β-methyl-5-androsten-17-one (*XVII*)

To a solution of epoxide *XVI* (100 mg) in a mixture of acetic acid and methanol (1 : 1, 4 ml) a methanolic chromium(II) chloride solution was added and the reaction mixture allowed to stand at room temperature for 1 min. After dilution with water the product was extracted with ether and the extract worked up in the conventional manner. The residue weighed 89 mg and consisted according to thin-layer chromatography of a main product, having the same R_F value as the starting material, and a series of more polar minor components. After preparative chromatography on a thin-layer of silica gel (double development in benzene–chloroform 2 : 1) 61 mg (63%) of pure 16β-methyl derivative *XVII* were obtained, m.p. 138–139°C (ethanol); $[\alpha]_D^{21}$ −2° (*c* 1·2); without maximum in the UV region; IR spectrum: hydroxyl absent, 1 720, 1 252, 1 031 (acetate), 1 638 cm^{-1} (5-double bond); PMR spectrum: 0·83 (13-CH_3), 1·20 (10-CH_3), 1·20 (d, 16-CH_3), 2·00 (acetate-H), 4·60 (3-H), 5·38 (6-H). For $C_{22}H_{32}O_3$ (344·5) calculated: 76·70% C, 9·36% H; found: 76·70% C, 9·19% H. Literature[20] gives m.p. 140–143°C, $[\alpha]_D$ −5°.

3β-Acetoxy-17α-hydroxy-17β-methyl-16-methylene-D-homo-5-androsten-17a-one (*XIX*)

A mixture of compound *XVIII* (15 g), dioxane (500 ml), and boron trifluoride etherate (15 ml) was allowed to stand at room temperature overnight; it was diluted with water (8 l, containing 50 g of $KHCO_3$) and the separated product was filtered off with suction, washed with water, dried, and chromatographed on a silica gel column (500 g). Elution with chloroform–methanol mixture (98 : 2, 95 : 5) gave 12·8 g of a residue which was crystallised from methanol. Yield 11·4 g (76%) of D-homosteroid *XIX*, m.p. 163–164°C; $[\alpha]_D^{21}$ −85° (*c* 4·4); no maximum in the UV region; IR spectrum: 3 580 (free hydroxyl), 3 480 (bound hydroxyl), 1 720, 1 260, 1 040 (acetate), 1 700 (carbonyl in a six-membered ring), 1 648 cm^{-1} (exomethylene); PMR spectrum: 1·01 (13-CH_3), 1·18 (10-CH_3), 1·48 (17-CH_3), 2·00 (acetate-H), 3·95 (OH), 4·60 (m, 3-H), 5·24, 4·90 (CH_2=C), 5·41 (d, 6-H). For $C_{24}H_{34}O_4$ (386·5) calculated: 74·57% C, 8·87% H; found: 74·59% C, 8·75% H.

(16*S*)-Spiro[3β-acetoxy-17α-hydroxy-17β-methyl-5,6α-oxido-D-homo-5α-androstane-16,2′-oxiran]-17a-one (*XXI*)

a) To a solution of compound *XIX* (1 g) in chloroform (20 ml) a perphthalic acid solution in ether (20 ml; 82 mg/1 ml) was added and the reaction mixture allowed to stand at room temperature overnight. After dilution with ether (50 ml) and washing with $KHCO_3$ solution and water it was dried over sodium sulfate and evaporated in a vacuum to dryness. The crude residue (950 mg) was separated by preparative thin-layer chromatography on silica gel (double development with chloroform). From the least polar zone 160 mg (16%) of the starting material *XIX* were isolated. The more polar zone afforded 240 mg (23%) of 3β-acetoxy-17α-hydroxy-17β-methyl-16-methylene-5,6α-oxido-D-homo-5α-androstan-17a-one (*XXII*), m.p. 188–189°C (methanol); $[\alpha]_D^{21}$ −70° (*c* 2·4); PMR spectrum: 1·06, 1·11 (10-CH_3, 13-CH_3), 1·48 (17-CH_3), 1·98 (acetate-H), 2·90 (d, J = 5 Hz, 6-H), 3·85 (OH), 4·90 (m, 3-H), 5·24, 4·88 (CH_2=C). For $C_{24}H_{34}O_5$ (402·5) calculated: 71·61% C, 8·51% H; found: 71·22% C, 8·30% H. From the most polar zone 422 mg (39%) of compound *XXI* were isolated, m.p. 223–225°C (methanol); $[\alpha]_D^{21}$ −80° (*c* 3·1); PMR spectrum: 1·14, 1·06 (10-CH_3, 13-CH_3), 1·48 (17-CH_3), 2·00 (acetate-H), 2·90 (d, J = 5 Hz, 6-H), 2·95, 2·64 (AB q, J = 5 Hz, CH_2O), 3·24 (OH), 4·84 (3-H), olefinic hydrogen absent. For $C_{24}H_{34}O_6$ (418·5) calculated: 68·87% C, 8·19% H; found: 68·57% C, 8·01% H. *b*) To a solution

of compound *VII* (100 mg) in chloroform (2 ml), perphthalic acid solution in ether (2 ml; 82 mg/l ml) was added and the mixture worked up as in the case of compound *XIX*. Using preparative thin-layer chromatography on silica gel 42 mg of the main product were isolated which after crystallisation from methanol gave compound *XXI*, m.p. 221–224°C, identical with the compound prepared under *a*).

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