ON STEROIDS. CXLI.*

REACTION OF SILVER FLUORIDE WITH SOME 6α-BROMO-B-NORSTEROIDS

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The main products of solvolysis of 6α-bromo derivatives *II* and *X* are unsaturated compounds *III* and *IV*, and *XI*, respectively. The solvolysis of the $C_{(6)}$–Br bond in compounds *XIII*, *XX*, *XXII*, and *XXX* takes place with the participation of the substituents in the position 5β under formation mainly of epoxides and hydroxy derivatives *XIV*, *XXI*, *XXIII*, and *XXXI*.

In an effort to prepare analogues of the antiandrogenous B-nor-17-methyl testosterone[1–3] (*I*) for biological tests we investigated reactions of various 6α-bromo derivatives of B-norsteroids with silver fluoride.

This reagent has been used from the time of Moissan[4–6] for the transformation of inorganic and organic halogenides to fluorides[7]. In steroid chemistry it was used, for exanple, for the introduction of fluorine into the positions 3β (ref.[8]), 16β (ref.[9]), and 21 (refs[10,11]). It was further applied in dehydrohalogenations leading to vinyl ethers[12–17].

In view of low nucleophilicity of the fluoride ion it seemed suitable to carry out the reactions in aprotic medium[18,19]. However, when carrying out the reaction of 6α-bromo-B-nor-4-cholesten-3-one[20] (*II*) with silver fluoride we observed that the composition of the mixture of products is approximately the same irrespective of whether it was carried out in dimethylformamide or aqueous tetrahydrofuran: in both cases halogen-free compounds were formed. Preparative chromatography on silica gel gave as the main products the isomers *III* and *IV*. Less polar isomer *III* which was isolated in a 29% yield is sensitive to oxidation, but fresh preparations give in their PMR and UV spectra maxima which prove that the newly introduced double bond is not conjugated with the Δ^4-3-keto system, and that it is of a ditertiary character. Air oxidation or reaction with peroxides transforms this compound to a mixture of compounds of peroxidic character (positive reaction with ferrous ammonium sulfate and potassium thiocyanate[21]) among which a hydroperoxy derivative prevails in which both double bonds are conjugated with the 3-keto group.

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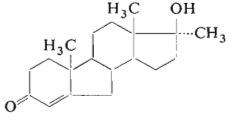
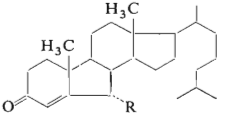
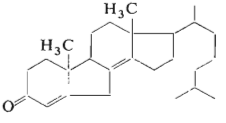
We formulate this compound as 14-hydroperoxy-B-nor-4,6-cholestadien-3-one (*V*); its formation suggests that in the original dienone *III* the double bond was in the position 8(9) or 8(14). Molecular optical rotation of dienone *III* is more positive than the corresponding value of B-norcholestenone[22] (*VI*), which is an evidence for the B-nor-4,8(14)-cholestadien-3-one structure. According to its UV spectrum substance *IV* contains both double bonds in direct conjugation with the keto group. The structure of B-nor-4,6-cholestadien-3-one is also proved unambiguously by IR and PMR spectra. When the reaction was carried out in aqueous medium we were also able to isolate hydroxy ketones *VII*–*IX* as admixtures. Ketones *VII* and *VIII* were identified as 6α- and 6β-hydroxy-B-nor-4-cholesten-3-ones by comparison with authentic samples[23]. Colour reaction of isomer *IX* with blue tetrazolium chloride[24] proves that the hydroxy group is situated in α-position to the carbonyl group; however, we did not attempt the proof of the configuration because of the low yield of the reaction.



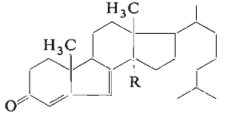
I



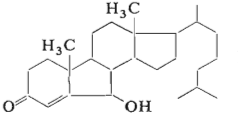
II, R = Br
VI, R = H
VIII, R = OH



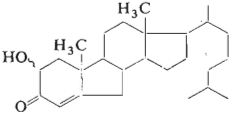
III



IV, R = H
V, R = OOH



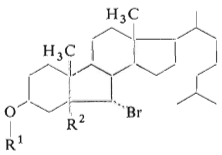
VII



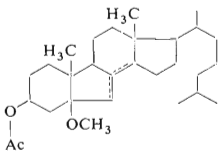
IX

The detection of *III*, *IV*, *VII*–*IX* after the reaction of bromo derivative *II* shows that the substituted B-norcholestane is very prone to elimination (*III* and *IV* represent 72% of the products) and unwilling to be substituted. This tendency is also apparent in another reaction taking place *via* a carbonium ion: both epimeric 6-hydroxy-B-nor-4-cholesten-3-ones (*VII* and *VIII*) react with 2-chloro-1,1,2-trifluorotriethylamine[25] under formation of an identical mixture of elimination products (*III* and *IV*) in addition to traces of an unidentified fluoro derivative. The formation of compounds *III*, *IV*, *VII*–*IX* in solvolysis of bromo derivative *II* may be explained by the formation of an intermediary carbonium ion which undergoes elimination directly (*IV*) or after rearrangement (*III*). The by-products are the products of unspecific hydration

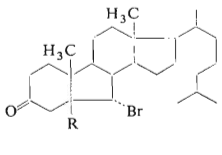
of this carbonium ion directly (*VII* and *VIII*) or after its rearrangement[26] to an ion with the charge at $C_{(2)}$. We expected a lower tendency to elimination under formation of a double bond in the case of solvolysis of these 6α-bromo derivatives which do not contain a Δ^4 double bond. As a suitable model we took 5β-methoxy derivative[20] *X* in which the methoxy group could aid the stabilisation of the carbonium ion formed and also the stereospecific course of the possible substitution reaction[9]. Under the effect of silver fluoride on methoxy derivative *X* in aqueous and non-aqueous medium we again obtained a similar mixture in which isomers of molecular weight 444 and probable structure *XI* prevailed. Elemental analyses, PMR, and IR spectra show that in this reaction elimination of hydrogen bromide took place under preservation of oxygen-containing substituents.



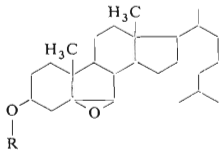
X, R^1 = Ac, R^2 = CH_3O
XIII, R^1 = Ac, R^2 = Br
XIX, R^1 = Ac, R^2 = OH
XX, R^1 = Ac, R^2 = OAc
XXII, R^1 = H, R^2 = OH



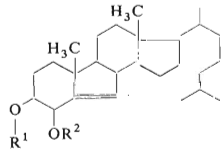
XI



XII, R = F
XXXIV, R = OH



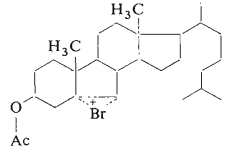
XIV, R = Ac
XXIII, R = H
XXVI, R = CH_2SCH_3



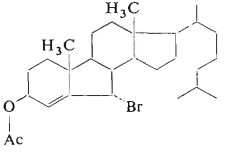
XV, R^1 = Ac, R^2 = H
XVI, R^1 = H, R^2 = Ac

5β-Fluoro-6α-bromo-B-nor-5β-cholestan-3-one[20] (*XII*) is quite resistent to the effect of an aqueous silver fluoride solution, in agreement with the known fact that the reactivity of halogenides is appreciably decreased by substitution with an additional halogen on the neighbouring carbon[7]. 5β,6α-Dibromo derivative[20] *XIII* reacts under the same conditions smoothly and gives epoxide[27] *XIV* and both monoacetates of B-nor-5-cholesten-3β,4β-diol (*XV* and *XVI*) the structures of which were corroborated by comparison with authentic samples[28]. As tertiary halogenides are more

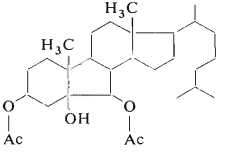
reactive than secondary ones[29] in reactions of S_N1 type it should be supposed that the solvolysis of $C_{(5)}$-Br bond took place first under formation of a carbonium ion with the charge at $C_{(5)}$ or of bromonium ion[20] *XVII*. The elimination of a proton in the first and the hydration in the second case lead to 3β-acetoxy-6α-bromo-B-nor-4-cholestene (*XVIII*) and 3β-acetoxy-6α-bromo-B-nor-5β-cholestan-5-ol (*XIX*), respectively. The first of these supposed intermediates would afford with an additional equivalent of silver fluoride in water both products of solvolysis with allylic rearrangement (*XV*, *XVI*) and the second would be transformed to epoxide *XIV*. We supported this interpretation by the following experiments: Under the given conditions bromohydrin *XIX* gives smoothly epoxide *XIV*, and 3β,5-diacetoxy-6α-bromo-B-nor-5β-cholestane[20] (*XX*) gives hydroxy derivative *XXI* identical with an authentic specimen[23]; this demonstrates the ability of the acetoxy group to react under these conditions with the carbonium ion[30,31] formed. From bromo derivative *XX* only a single hydroxy derivative *XXI* is formed and from the supposed bromo derivative *XVIII* two isomers (*XV* and *XVI*) are formed in consequence of an easy O,O-acyl migration; in the equilibrium mixture of monoacetates of 3β,4β-dihydroxy derivatives both isomers are present in similar proportion[28], while in the case of acetate of 5β,6β-dihydroxy derivative a general tendency is apparent in the acyl group to migrate in such a way as would lead to the ester of the less branched alcohol[32].



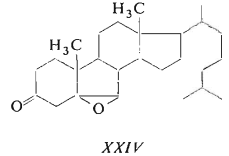
XVII



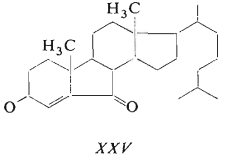
XVIII



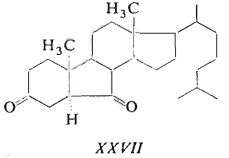
XXI



XXIV



XXV

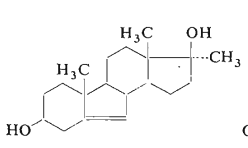


XXVII

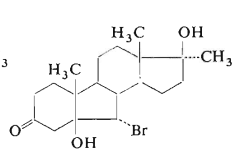
The formation of epoxide and bromohydrin or dibromide by means of aqueous silver fluoride solution was not described so far, but cases are known when such a reaction was achieved under the effect of moist silver oxide[33–35]. Although in this reaction hydrogen fluoride is liberated the medium remains more or less neutral[36] in consequence of excess silver fluoride, which enables this method to be used for

the preparation of 5,6β-epoxy-B-nor-5β-cholestan-3-one (*XXIV*). We were unable to prepare the latter compound either by oxidation of hydroxy derivative *XXIII* with chromium trioxide in pyridine or with Jones reagent, when only B-nor-4-cholestene-3,6-dione[37] (*XXV*) is formed, or by oxidation with dimethyl sulfoxide leading only to anomalous thioether[38] *XXVI*.

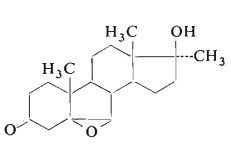
β,γ-Epoxy ketones rearrange in alkaline and acid medium to unsaturated γ-hydroxy ketones[39–41] or even to γ-diketones[42]. We found that epoxy ketone *XXIV* rearranges under a short effect of silica gel to hydroxy ketone *VII*, while after a prolonged effect of silica gel B-nor-5α-cholestane-3,6-dione[43] (*XXVII*) is formed. We made use of this experience for a four-step synthesis of the pharmacologically interesting 6β-17β-dihydroxy-17α-methyl-B-nor-4-androsten-3-one[23] (*XXVIII*) from 17α-methyl-B-nor-5-androsten-3β,17β-diol[44] (*XXIX*). The addition of hypobromous acid[20] followed by oxidation of the hydroxy group and the subsequent effect of silver fluoride gave rise to epoxide *XXXI*. The isomerisation of epoxide *XXXI* was carried out with silica gel and the required derivative *XXVIII* was obtained in an overall yield of 46%. As a by-product substance *XXXII* was isolated, containing oxo groups in the five- and six-membered ring. We proposed the 5α-configuration for this substance on the basis of the molecular rotation difference method and confirmed it on the basis of its easy isomerisation to diketone *XXXIII* which has a much more negative molecular rotation value, typical of the isomerisation of 6-keto-B-nor-steroids of the 5α-series to the 5β-isomer[45]. Hence, substances *XXXII* and *XXXIII* must have the structures of 17β-hydroxy-17α-methyl-B-nor-5α-androstane-3,6-dione and 17β-hydroxy-17α-methyl-B-nor-5β-androstane-3,6-dione. The results of biological tests of some prepared substances will be published later.



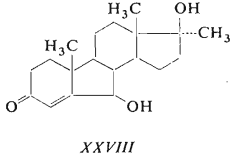
XXIX



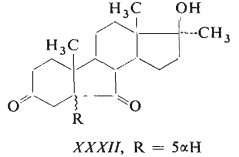
XXX



XXXI



XXVIII



XXXII, R = 5αH
XXXIII, R = 5βH

EXPERIMENTAL

The melting points were determined on a Kofler block and they are uncorrected. The IR spectra, specific rotation, and circular dichroism were measured in chloroform, the PMR spectra in deuteriochloroform, taking tetramethylsilane as internal standard and using a Varian 100 apparatus. The UV spectra were measured in alcohol.

Reaction of 6α-Bromo-B-nor-4-cholesten-3-one (*II*) with Silver Fluoride

A solution of 120 mg of bromo derivative[20] *II* in 2 ml of tetrahydrofuran was stirred with a solution of silver fluoride in water (50%, 2 ml) under nitrogen for 18 h. The reaction mixture was diluted with water, the product extracted with light petroleum, and chromatographed on a thin layer of silica gel (10% of ether in benzene, double development). Single zones absorbing in the UV light were eluted with ether. The following compounds were obtained: B-*Nor*-4,8(14)-*cholestadien*-3-*one* (III), 29 mg, m.p. 102—104°C (methanol); $[\alpha]_D^{20}$ +47° (*c* 0·5); mass spectrum: M^+/e 368; IR spectrum: 1674 cm^{-1}; UV spectrum: 234 nm (log ε 4·19); PMR spectrum: 0·855 (d, J = 6 Hz, 6 protons), 0·885 (s, 3 protons), 0·918 (d, J = 6·5 Hz, 3 protons), 0·97 (s, 3 protons), 3·03 (mt), 5·80 (mt, 1 proton), p.p.m.. For $C_{26}H_{40}O$ (368·6) calculated: 84·72% C, 10·94% H; found: 84·46% C, 11·12% H. B-*Nor*-4,6-*cholestadien*-3-*one* (IV), 42 mg, m.p. 149—151°C (acetone); $[\alpha]_D^{20}$ +222° (*c* 1·1); IR spectrum: 1642 and 1605 cm^{-1}; UV spectrum: 301 nm (log ε 4·51); PMR spectrum: 0·608 (s, 3 protons), 0·862 (d, J = 6 Hz, 6 protons), 0·95 (d, J = 6 Hz, 3 protons), 1·17 (s, 3 protons), 5·70 (s, 1 proton), 5·91 (br. s, 1 proton) p.p.m. For $C_{26}H_{40}O$ (368·6) calculated: 84·72% C, 10·94% H; found: 85·02% C, 11·00% H. 6β-*Hydroxy*-B-*nor*-4-*cholesten*-3-*one* (VII), 8 mg, m.p. 174—175°C (heptane), mixture melting point with an authentic specimen[23] was undepressed. 6α-*Hydroxy*-B-*nor*-4-*cholesten*-3-*one* (VIII), 7 mg, IR spectrum identical with that of an authentic sample[23]. 2-*Hydroxy*-B-*nor*-4-*cholesten*-3-*one* (IX), 5 mg, resists attempts at crystallisation. IR spectrum: 3600, 1665, 910 cm^{-1}; PMR spectrum: 0·72 (s, 3 protons), 0·93 (d, J = 6 Hz), 0·870 (d, J a 6 Hz), 1·175 (s), 3·50 (mt), 5·98 (mt) p.p.m. Reaction with blue tetrazolium is positive[24].

14α-Hydroperoxy-B-nor-4,6-cholestadien-3-one (*V*)

Ketone *III* (40 mg) was allowed to stand at 0°C for 14 days and the reaction mixture was chromatographed on a thin layer of silica gel (20% ether in benzene), Components of R_F 0·00, 0·20 and 0·26 quench the fluorescence in the UV light and give a coloured reaction with ammonium ferrous sulfate and potassium thiocyanate[21]. The prevailing component of this mixture (R_F 0·26) was eluted with ether (18 mg), m.p. 144—146°C (decomposition begins at 120°C); IR spectrum: 1612, 1642, 3300, and 3500 cm^{-1}; UV spectrum: 297 nm (log ε 4·10); mass spectrum[46]: M^+/e 400, 398, 384, 382; $[\alpha]_D^{20}$ +113° (*c* 0·6). The substance does not give reproducible elemental analyses.

Reaction of 2-Chloro-1,1,2-trifluorotriethylamine

a) *With* 6α-*hydroxy*-B-*nor*-4-*cholesten*-3-*one* (VIII): To a solution of 30 mg of hydroxy derivative *VIII* in 1 ml of dichloromethane 7 drops of 2-chloro-1,1,2-trifluorotriethylamine[25] were added and the mixture allowed to stand at room temperature for 18 h. The reaction mixture was diluted with light petroleum, washed with a solution of potassium hydrogen carbonate, dried over sodium sulfate, and chromatographed on a thin layer of silica gel. The main product was eluted with ether and the residue (19 mg) crystallised from acetone. B.p. 149—151°C, mixture melting point with compound *IV* was undepressed. b) *With* 6β-*hydroxy*-B-*nor*-4-*cholesten*-3-*one* (VII): To a solution of 110 mg of hydroxy derivative *VII* in 1·5 ml of dichloromethane 15 drops of the reagent[25] were added and the mixture allowed to stand at +5°C for 3 h. The mixture was worked

up as in a) and then chromatographed on a silica gel column (6 g, with 2·5% acetone in light petroleum). The main product (77 mg) was identical with the compound prepared as above. The by-products represent a mixture of less polar substances which were not easily separable. One of them contained traces of fluorine.

Reaction of 3β-Acetoxy-5-methoxy-6α-bromo-B-nor-5β-cholestane (*X*) with Silver Fluoride

a) *In aqueous tetrahydrofuran*: 38 mg of bromo derivative[20] *X* in 2 ml of tetrahydrofuran were stirred with 0·4 ml of silver fluoride solution (50%). After 48 h the mixture was diluted with light petroleum, washed with water, dried over sodium sulfate, and evaporated to dryness under reduced pressure. The residue did not contain either bromine or fluorine. The prevailing component (28 mg) was isolated by means of silica gel thin-layer chromatography (10% acetone in light petroleum); mass spectrum: $M^+/e = 444$; IR spectrum: 1 725, 1 256, 1 632, 1 023, 1 095, 1 106 cm^{-1}. For $C_{29}H_{49}O_3$ (444·7) calculated: 78·33% C, 10·88% H; found: 78·16% C, 11·03% H. b) *In acetonitrile*: 50 mg of compound *X* were shaken with a suspension of 400 mg of silver fluoride in 1 ml of acetonitrile. After 48 h shaking inorganic material was filtered off under suction and the mixture was diluted with water and extracted with light petroleum. According to thin-layer chromatography the main reaction product was identical with the prevailing component obtained under *a*. According to elemental analysis the product does not contain halogen.

Reaction of 5-Fluoro-6α-bromo-B-nor-5β-cholestan-3-one (*XII*) with Silver Fluoride

A solution of fluoro ketone[20] *XII* (136 mg) in 2 ml of tetrahydrofuran was mixed with 1 ml of silver fluoride solution in water (50%). After 48 h standing the mixture was diluted with benzene, the aqueous layer was separated, the organic layer was washed with water, filtered through a small column of sodium sulfate, and evaporated to dryness *in vacuo*. M.p. 156—157°C (acetone), undepressed after addition of the starting compound *XII*. According to thin-layer chromatography the mother liquors contain substance *XII* exclusively.

3β-Acetoxy-5,6β-epoxy-B-nor-5β-cholestane (*XIV*)

A solution of 350 mg of bromohydrin[20] *XIX* in 3 ml of tetrahydrofuran was mixed with 1 ml of 50% aqueous silver fluoride solution and stirred for 20 h when the mixture was diluted with water and the product extracted with light petroleum. The extract was washed, dried, and evaporated to dryness. Crystallisation from ethanol gave 245 mg of epoxide *XIV*, m.p. 79—81°C. The mixture melting point with an authentic sample was undepressed. For $C_{28}H_{46}O_3$ (430·6) calculated: 78·09% C, 10·77% H; found: 78·11% C, 10·80% H.

Reaction of 3β-Acetoxy-5,6-dibromo-B-nor-5β-cholestane (*XIII*) with Silver Fluoride

Dibromo derivative[20] *XIII* (300 mg) was reacted with silver fluoride solution as in the preceding case. An analogous working up of the reaction mixture gave a product free of bromine (195 mg) which on chromatography on silica gel (10 g, benzene) gave gradually: *epoxide* XIV (110 mg), m.p. 79—81°C, mixed melting point with an authentic sample undepressed; IR spectrum identical with that of epoxide *XIV*; 3β-*acetoxy*-B-*nor*-5-*cholesten*-4β-*ol* (XV, 28 mg), m.p. 116—118°C (methanol), mixture melting point with an authentic sample[27] undepressed; 4β-*acetoxy*-B-*nor*-5-*cholesten*-3β-*ol* (XVI) (65 mg), m.p. 125—127°C (methanol); IR spectrum: 3 590, 1 730, 1 248, 1 053 cm^{-1}, identical with the spectrum of an authentic specimen[27]; $[\alpha]_D^{20}$ —117° (*c* 1·1); PMR spectrum: 0·655 (s, 3 protons), 0·850 (d, $J = 6$ Hz, 6 protons), 0·910 (d, $J = 6$ Hz, 3 protons), 0·960 (s, 3 protons), 2·04 (s, 3 protons), 5·53 (mt, 1 proton), 5·90 (mt, 1 proton) p.p.m. For $C_{28}H_{46}O_3$ (430·6) calculated: 78·09% C, 10·77% H; found: 78·11% C, 10·81% H.

3β,6β-Diacetoxy-B-nor-5β-cholestan-5-ol (*XXI*)

A solution of 3β,5-diacetoxy-6α-bromo-B-nor-5β-cholestane (*XX*, 130 mg) in 2 ml of tetrahydrofuran was stirred with 1 ml of 50% silver fluoride in water for 18 h. The mixture was diluted with water and extracted with light petroleum, washed and dried over sodium sulfate. After crystallisation from methanol the product (88 mg, m.p. 104—107°C) melted at 106—108°C, mixed melting point with an authentic sample[23] undepressed; IR spectrum (CCl_4): 3 590, 1 739, 1 246 cm^{-1}; PMR spectrum: 0·68 (s, 3 protons), 0·865 (d, J = 6·3 Hz, 6 protons), 0·915 (d, J = 6 Hz, 3 protons), 0·935 (s, 3 protons), 2·03 (s, 3 protons), 2·075 (s, 3 protons), 4·46 (d, J = 7·6 Hz, 1 proton), 5·05 (mt, 1 proton) p.p.m. For $C_{30}H_{50}O_5$ (490·7) calculated: 73·43% C, 10·27% H; found: 73·50% C, 10·39% H.

5,6β-Epoxy-B-nor-5β-cholestan-3β-ol (*XXIII*)

A solution of diol *XXII* (65 mg) in 2 ml of tetrahydrofuran was stirred with a solution of silver fluoride in water (0·5 ml, 50%). After 18 h stirring the mixture was partitioned between water and light petroleum and after drying evaporated to dryness. The residue (50 mg, 164—168°C) was crystallised from light petroleum, m.p. 168—169°C, undepressed on admixture of an authentic sample[27]. For $C_{18}H_{26}O_3$ (290·4) calculated: 74·44% C, 9·03% H; found: 74·26% C, 9·14% H.

5,6β-Epoxy-B-nor-5β-cholestan-3-one (*XXIV*)

A solution (200 mg) of bromohydrin[20] *XXXIV* in 2 ml of tetrahydrofuran was stirred with 1 ml of a 50% silver fluoride solution for 20 h. The clear supernatant was decanted and the precipitate washed with benzene. The combined benzene solutions were dried over sodium sulfate and evaporated to dryness. The residue (165 mg, m.p. 120—130°C) represents a mixture of two main products of R_F 0·80 and 0·15 (according to thin-layer chromatography in 20% ether in benzene). The residue was dissolved rapidly in 1·5 ml of acetone at elevated temperature and then cooled immediately. The product (106 mg) had m.p. 144—146°C, $[\alpha]_D^{20}$ +75° (*c* 1·2); ORD: a +81; IR spectrum (CCl_4): 1 725 cm^{-1}; PMR spectrum: 0·65 (s, 3 protons), 0·94 (s, 3 protons), 0·87 (d, J = 6·2 Hz, 6 protons), 0·91 (d, J = 6 Hz, 3 protons), 2·21 and 2·89 (AB system, J = = 18 Hz), 3·13 (s, 1 proton) p.p.m. For $C_{26}H_{42}O_2$ (386·6) calculated: 80·77% C, 10·95% H; found: 80·52% C, 10·76% H.

B-Nor-5α-cholestane-3,6-dione (*XXVII*)

a) *From epoxy ketone* XXIV: 20 mg of compound *XXIV* were dissolved in dichloromethane and applied onto a silica gel plate, 20 × 20 × 0·1 cm, and allowed to stand at room temperature for 18 h. Standard samples of epoxide *XXIV*, hydroxy derivative *VII*, and diketone *XXVII* were then applied at the edges of the plate, and it was developed immediately in 20% ether in benzene. The zone corresponding to ketone *XXIV* was eluted with methanol, the extract eveporated to dryness *in vacuo*, and the residue dissolved in dichloromethane and filtered through a layer of sodium sulfate. The product (16 mg) was crystallised from methanol, m.p. 136—138°C, mixed melting point with an authentic sample[43] undepressed. b) *From* 6β-*hydroxy*-B-*nor*-4-*cholesten*-3-*one* (VII): Applying the same procedure as under *a*) diketone *XXVII* (16 mg) was prepared from 20 mg of compound *VII*; it was identical with an authentic sample[43].

6β-Hydroxy-B-nor-4-cholesten-3-one (*VII*)

Substance *XXIV* (40 mg) was dissolved in dichloromethane and applied onto a silica gel plate and allowed to stand at room temperature for one hour. The plate was developed in a mixture

of ether and benzene as in the preceding paragraph; the only zone absorbing under UV light was eluted with ether (38 mg). M.p. 173—175°C (acetone–heptane), undepressed on admixture of an authentic specimen[23].

B-Nor-4-cholestene-3,6-dione (*XXV*)

a) To a stirred solution of epoxide *XXIII* in acetone 1·1 equivalent of Jones reagent was added dropwise at —15°C and after 5 min stirring the solution was poured into a solution of sodium hydrogen sulfite and extracted with ether. According to thin-layer chromatography on silica gel the product was a mixture of the starting substance and diketone *XXV*. *b*) To a stirred suspension of chromium trioxide (0·8 g) in 10 ml of pyridine a solution of hydroxy derivative *XXIII* (0·3 g) in 3 ml of pyridine was added dropwise at 0°C. After 20 h standing the mixture was worked up in the conventional manner and the product was crystallised from methanol. M.p. 116—117°C (190 mg), undepressed on admixture of an authentic sample. The IR spectrum was also identical with that of authentic sample.

5,6β-Epoxy-B-nor-5β-cholestan-3β-yl Methylthiomethyl Ether (*XXVI*)

Epoxide *XXIII* (700 mg) was dissolved in a mixture of 3 ml of dimethyl sulfoxide and 3 ml of acetic anhydride and allowed to stand for 4 days. The separated product (600 mg) was filtered with suction and crystallised from methanol; m.p. 105—106°C; $[\alpha]_D^{20}$ +16° (*c* 1·8); IR spectrum: 1070 cm^{-1}; mass spectrum: $M^+/e = 448$; PMR spectrum: 0·625 (s, 3 protons), 0·865 (d, J = 6·1 Hz, 6 protons), 0·895 (d, J = 6 Hz, 3 protons), 0·865 (s, 3 protons), 2·035 (s, 3 protons), 3·16 (s, 1 proton), 3·92 (mt, 1 proton), 4·64 (s, 2 protons) p.p.m. For $C_{28}H_{48}O_2S$ (448·7) calculated: 74·93% C, 10·75% H; found: 74·86% C, 10·54% H.

5,6β-Epoxy-17β-hydroxy-17α-methyl-B-nor-5β-androstan-3-one (*XXXI*)

A solution of 5,17β-dihydroxy-6α-bromo-17α-methyl-B-nor-5β-androstan-3-one (*XXX*), 460 mg) in 5 ml of tetrahydrofuran was stirred with 2 ml of a 50% aqueous silver fluoride solution for 20 h. The mixture was diluted with 50 ml of benzene and filtered through a small column of sodium sulfate. The filtrate was evaporated to dryness under reduced pressure and the residue crystallised twice from acetone; yield 100 mg, m.p. 145—175°C (decomp.), $[\alpha]_D^{20}$ +75° (*c* 1·2); IR spectrum: 3605, 1718 cm^{-1}. For $C_{19}H_{28}O_3$ (304·4) calculated: 74·96% C, 9·27% H; found: 74·86% C, 9·31% H.

6β,17β-Dihydroxy-17α-methyl-B-nor-4-androsten-3-one (*XXVIII*)

a) Epoxide *XXXI* (18 mg) was dissolved in chloroform and applied onto a thin layer of silica gel and allowed to stand there at room temperature for 2 h. The plate was then developed with a mixture of acetone (30%) in light petroleum. The single absorbing zone (under UV light) was eluted with methanol and the residue was dissolved in ethyl acetate, filtered through a small column of sodium sulfate and crystallised from a mixture of ethyl acetate and heptane; m.p. 115—117° and 174—175°C, undepressed on admixture of an authentic sample[23]; $[\alpha]_D^{20}$ —50° (*c* 0·4); IR spectrum: 3600, 1660 cm^{-1}, identical with a spectrum of an authentic sample; PMR spectrum: 0·918 (*c*, 3 protons), 1·204 (s, 3 protons), 1·230 (s, 3 protons), 4·25 (d, J = 4·5 Hz, 1 proton), 5·98 (d, J = 1·4 Hz, 1 proton) p.p.m.; CD: $\Delta\varepsilon$ +2·68 (340 nm); For $C_{19}H_{28}O_3$ (304·4) calculated: 74·86% C, 9·27% H; found: 74·80% C, 9·12% H. *b*) Diol *XXIX* was reacted (300 mg) with B-bromoacetamide in moist tetrahydrofuran and the crude bromohydrin formed[20] was then oxidised without further purification with Jones reagent. The product (*XXX*) was then submitted to reaction

with silver fluoride in a mixture of water and tetrahydrofuran, and after working up of the reaction mixture the obtained material was applied onto 6 silica gel plates (20 × 20 × 0·1 cm). After 2 h standing the plates were developed in a mixture of acetone (20%) and light petroleum, and the zone absorbing under the UV light was eluted with methanol. The residue was dissolved in ethyl acetate and filtered through a small column of sodium sulfate. Crystallisation from a mixture of ethyl acetate and heptane afforded 145 mg of compound *XXVIII*, identical with the sample prepared under *a*.

17β-Hydroxy-17α-methyl-B-nor-5α-androstane-3,6-dione (*XXXII*)

The non-polar component from the previous chromatography was obtained by elution with methanol, filtration of its ethyl acetate solution through a layer of sodium sulfate and crystallisation of the residue (45 mg) from a mixture of ether and heptane; m.p. 153—155°C; $[\alpha]_D^{20}$ +67° (*c* 0·5); IR spectrum: 1738, 1714, 3605 cm^{-1}. For $C_{19}H_{28}O_3$ (304·4) calculated: 74·96% C, 9·27% H; found: 75·09% C, 9·38% H.

17β-Hydroxy-17α-methyl-B-nor-5β-androstene-3,6-dione (*XXXIII*)

A solution of diketone *XXXII* (70 mg) in 1 ml of chloroform and 10 ml of methanol was allowed to stand in the presence of 0·3 ml of conc. hydrochloric acid at 37°C for 20 h. The reaction mixture was concentrated under reduced pressure to one third of its original volume, then additioned with approx. 50 ml of benzene and evaporated again to 1/3 of its volume. The solution was washed with water, dried over sodium sulfate, filtered, evaporated, and crystallised form acetone and heptane; m.p. 169—171°C; $[\alpha]_D^{20}$ −77° (*c* 1·0); IR spectrum: 3600, 1735, 1715 cm^{-1}. For $C_{19}H_{28}O_3$ (304·4) calculated: 74·96% C, 9·27% H; found: 75·15% C, 9·41% H.

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