SOLVOLYSIS OF WESTPHALEN-TYPE COMPOUNDS*

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Action of some nucleophilic reagents (CH_3COOAg, CH_3COOK, $LiAlH_4$) on 6β-chloro- and 6β-methanesulfonyloxy-5-methyl-19-nor-5β-cholest-9-enes *VIII*–*XII* affords predominantly A-homo-B,19-dinor-5β-cholest-9-ene derivatives, arising by rearrangement and substitution (*XIII*, *XXIV*) or rearrangement and elimination (*e.g. XX*). Hydrogenolysis of compounds of the type *VIII* with lithium aluminium hydride gives, in addition, a product of rearrangement, fragmentation and further reduction (*XXVI*), and 5-methyl-6α,10-cyclo-19-nor-5β,9β,10α-cholestan-3β-ol (*XXX*).

In our earlier paper[1] we described the propensity of Westphalen-type compounds (*I*) to rearrange to A-homo-B-nor derivatives of the type *II*. Using a specifically labelled substrate, we have proved that the rearrangement is accompanied by a 5 to 4a hydride (or deuteride) shift (see the $A \rightarrow B$ isomerization in Scheme 1). Our finding, however, was at variance with the existing reports[2,3] on solvolysis and hydrogenolysis of structurally analogous compounds: Brial and Mousseron-Canet[3] claimed that the acetolysis product of the 6β-methanesulfonate *III* contained the hydroxy derivative *IV* and the diene *V*. After hydrogenolysis with lithium aluminium hydride these authors isolated, in addition to the diene *V*, further two compounds to which they ascribed the structures *VI* and *VII*. Since working with 3β-fluoro derivatives of the type *III* did not allow an unequivocal structural assignment of the new products, we prepared more suitable oxygen-containing derivatives of Westphalen-type compounds (*VIII*–*XII*) and subjected them to reactions, already applied to the 3β-fluoride *III*. We have verified that both 6β-chloro derivatives (*e.g. XI*) and 6β-methanesulfonyloxy derivatives (*e.g. VIII*) on treatment with identical reagents yield mixtures of identical products differing only slightly in the ratio of the products. In a model experiment we have shown that these differences are caused only by different reaction temperatures (the more reactive 6β-methanesulfonate *XI* was reduced in boiling ether whereas the corresponding 6β-chloride required boiling dioxane) (Scheme 2).

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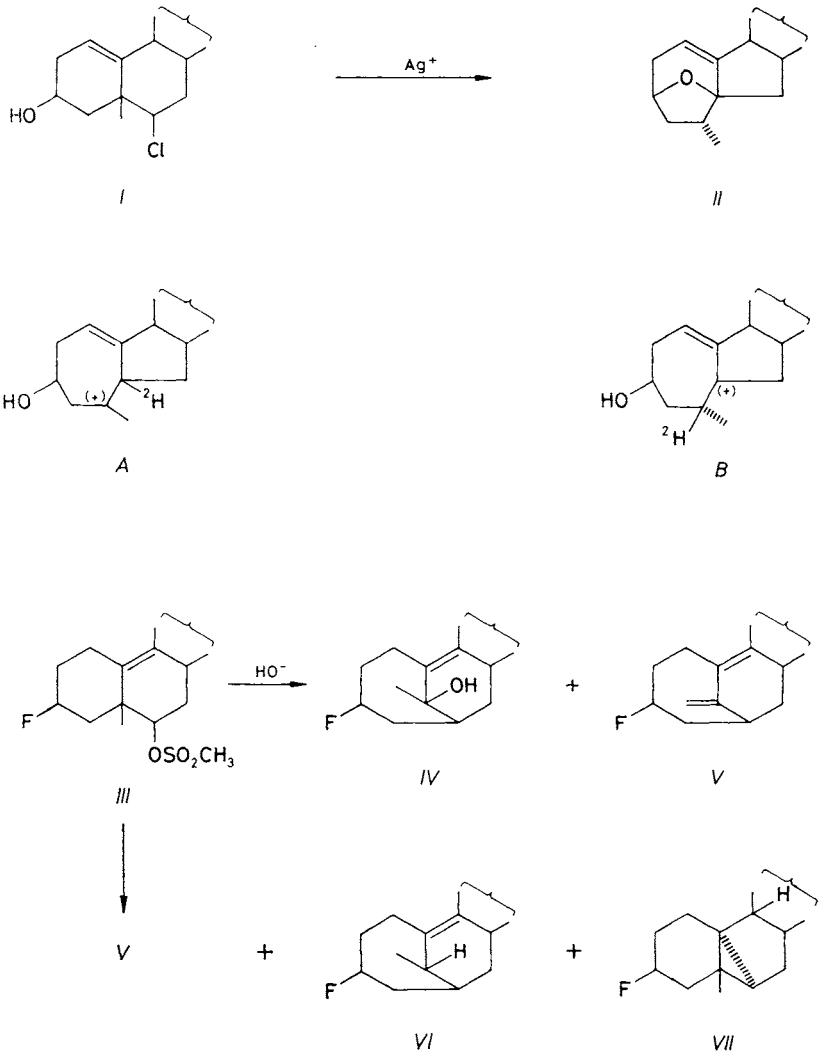
Acetolysis of compound *IX* with potassium acetate in aqueous acetone afforded the hydroxy derivative *XIII* whose spectral characteristics corresponded to those published for the analogously prepared compound, to which the French authors ascribed the structure *IV*. Short-lasting catalytic hydrogenation of compound *XIII*

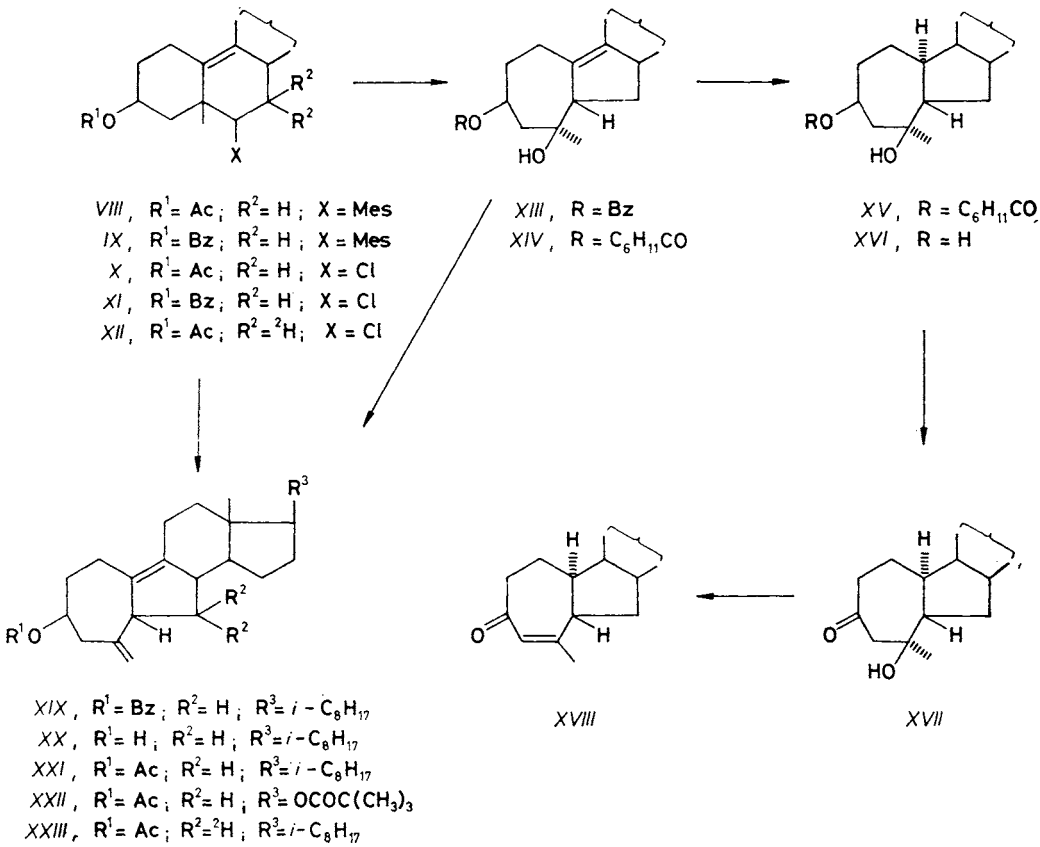


Partial formulae represent cholestene derivatives; Ac = CH_3CO, Bz = C_6H_5CO, Mes = = CH_3SO_3

SCHEME 1

afforded the hexahydrobenzoyloxy derivative *XIV* whereas prolonged hydrogenation led to the octahydro compound *XV* which on hydrolysis (*XVI*), oxidation (*XVII*) and dehydration afforded the α,β-unsaturated ketone *XVIII* (UV spectrum). This finding confirms that the tertiary hydroxyl group, arising in acetolysis, is in a β-position relative to the oxygen-bearing carbon atom $C_{(3)}$, which is compatible with the expected structure *XIII*; on the other hand, in a structure of the type *IV* the hydroxyl is in the γ-position relative to the $C_{(3)}$ atom. The new chirality center at the $C_{(4a)}$ atom was assigned (*S*)-configuration since the IR spectra of the hydroxy esters *XIII*–*XV* revealed an intramolecular hydrogen bond. We ascribe the 5β-configuration to compounds *XIII*–*XVII* on the basis of analogy with the rearrangement of this type, observed previously[1].

The spectral and chemical characteristics of the acetolysis side-product arising from *XIX* are similar to the analogously prepared compound, assigned[2] the structure



SCHEME 2

V. Moreover, the ^{1}H NMR spectrum of *XIX* and its derivatives *XX*–*XXII* exhibits a one-proton multiplet at δ 3·30–3·40 (ΣJ = 16 Hz) which we ascribe to the proton in position 5 whose signal is shifted outside the envelope of methylene signals thanks to double allylic character. This assumption was confirmed by the spectrum of the corresponding 6,6-dideuterio derivative *XXIII*: as expected, the proton signal at δ 3·33 loses its multiplet character and appears only as a broad singlet. Decoupled 200 MHz spectra of the analogous androstane derivative *XXII* revealed a coupling of the proton in position 5 (mt, δ 3·36) with the exomethylene protons (narrow multiplets with ΣJ = 3·0 and ΣJ = 2·4 Hz at δ 4·91 and 4·95, respectively). On the other hand, no relation between the multiplet at δ 3·36 and the 3α proton multiplet (δ 4·73, ΣJ = 27·8 Hz) has been found. Also these data are compatible with a structure of the type *XIX* but not *V*. Hydrogenation of compound *XIX*, followed by hydrolysis, gave the known[1,4] 4aα-methyl-A-homo-B,19-dinor-5β,10α-cholestan-3β-ol (*XXVIII*). Since the compound *XIX* can be obtained also by hydrogenation of *XIII*, this correlation confirms the structure of compounds *XIII*–*XVIII* as well.

Acetolysis of 6β-substituted compounds of the Westphalen type with silver acetate in acetic acid afforded mainly the corresponding elimination product (*XIX*) and its derivatives. Compound *XX* is also obtained as the principal product in the reaction of 6β-chloro and 6β-methanesulfonyloxy derivatives *VIII*–*XI* with lithium aluminium hydride, along with three minor products. Chromatographically most similar to *XX* was a compound, shown by mass and infrared spectroscopy to be its 4a,4b--dihydro derivative. Since it was hydrogenated to the known compound *XXVIII*, we conclude that it is a product of nucleophilic substitution with the hydride ion, *i.e.* 4aα-methyl-A-homo-B,19-dinor-5β,10α-cholest-9-en-3β-ol (*XXIV*).

The hydrogenolysis of compounds *VIII*–*XI* gave also a more lipophilic product *XXVI* of composition $C_{27}H_{46}O$, which was a primary alcohol (oxidation to an acid, ^{1}H NMR spectrum), containing an isopropenyl group. Since its perhydro derivative exhibits a molecular ion $C_{27}H_{50}O$, compound *XXVI* posseses a structure with open A ring. Hydrogenolysis with lithium aluminium deuteride gave compound *XXVII*, containing 1 deuterium atom in position 3 (^{1}H NMR spectrum).

The more polar hydrogenolysis product *XXX* showed a molecular peak corresponding to composition $C_{27}H_{46}O$, and its IR spectrum exhibited a hydroxyl band. It was therefore obvious that the compound contains another ring or double bond in the steroid molecule. Neither chemical nor spectral properties of *XXX* indicated any double bond (no reaction with peroxy acid, no signals corresponding to sp^2 hybridization in the ^{1}H or ^{13}C NMR spectra). Therefore, we assume (analogously to compound *VI*; ref.[2]) that the compound is 5-methyl-6α,10-cyclo-19--nor-5β,9β,10α-cholestan-3β-ol, described by formula *XXX*. In its ^{1}H NMR spectrum (200 MHz) we unequivocally identified signals due to the protons at $C_{(18)}$, a further tertiary methyl group, three secondary methyl groups of the cholestane side chain and the 3-proton. No signals typical of cyclopropane hydrogen atoms

were present in the ^{1}H NMR spectra; this is compatible with a cyclopropane ring fused to two other rings. The existence of the cyclopropane ring has been, however, proved by ^{13}C NMR spectroscopy: Fig. 1 shows two APT spectra measured with $\tau = 7$ msec (*a*) and $\tau = 5$ msec (*b*). From the known[5] dependences of signal amplitude on $^1J_{C-H}$ and on the number of directly bonded protons it is obvious that the first spectrum contains signals of all the carbon atoms whereas in the second one the amplitude of all the signals is reduced, except those of quaternary and tertiary carbon atoms with $^1J_{C-H} \geqq 140$ Hz. The chemical shift of the signal at δ 67·63 indicates the $C_{(3)}$ atom. In the spectrum (*a*) the signals due to the cholestane side chain carbon atoms were assigned on the basis of chemical shifts published[6] for 5β-cholestan-3β-ol; the carbon atom in the $C_{(5)}$ methyl corresponds thus to the signal at δ 19·99. The three signals at δ 25·98, 33·10, and 44·97 in the spectrum (*b*) are due to quaternary carbon atoms as confirmed by comparison with the normal ^{13}C NMR spectrum taken without proton decoupling. The signal of the highest chemical shift corresponds to the $C_{(13)}$ atom, as follows from the above-mentioned comparison with the values for 5β-cholestan-3β-ol. The remaining two signals can be thus ascribed to the cyclopropane ring atoms $C_{(5)}$ and $C_{(10)}$. The atom $C_{(6)}$ of this ring appears as the signal at δ 31·35 since its amplitude (as well as that of the signal at δ 67·63) is not substantially reduced with lower τ-value, indicating a large coupling constant. This was confirmed also by the ^{13}C NMR spectrum in which a doublet at δ 31·35 with $^1J_{C-H} \sim 165$ Hz agrees with the published[7] data for cyclopropane derivatives. These results give evidence of the fate of Westphalen derivatives with a nucleofuge in the position 6β under solvolysis conditions. Our interpretation is based on the existing knowledge[8] about conformation of the ring B in compounds of the type *VIII*: models show that in the most stable half-chair conformation[8] of the ring B the $C_{(5)}$—$C_{(10)}$ bond is antiperiplanar to the bond linking the substituent to the atom $C_{(6)}$. The positive charge, formed by departure of the leaving group from the position 6, is compensated by the rearranging $C_{(5)}$—$C_{(10)}$ bond under formation of the A-homo-B,19-dinor skeleton[1] with the positive charge in position 4a (*A*, see Scheme 3). The further fate of this species depends to a great extent on the reaction conditions. In a medium with low activity of a suitable nucleophile the elimination of proton, leading to derivatives of the diene *XX*, prevails. Another transformation of the ion *A*, preferred particularly at higher temperatures, is the fragmentation* of the ring A, affording the aldehyde *B* which is reduced further under the reaction conditions.

* Usually[8], the fragmentation proceeds well in the conformation that guarantees an antiperiplanar orientation of the leaving group and the band to be broken. Higher temperature enhances the formation of compound *XXVI* from *VIII*, probably because it increases the population either of the conformer of the ion *A*, suitable for the rearrangement[9], or directly of the conformer of *VIII* with ring A in the boat conformation in which the cleaved $C_{(3)}$—$C_{(4)}$ bond is in a synperiplanar orientation relative to the rearranging $C_{(5)}$—$C_{(10)}$ bond.

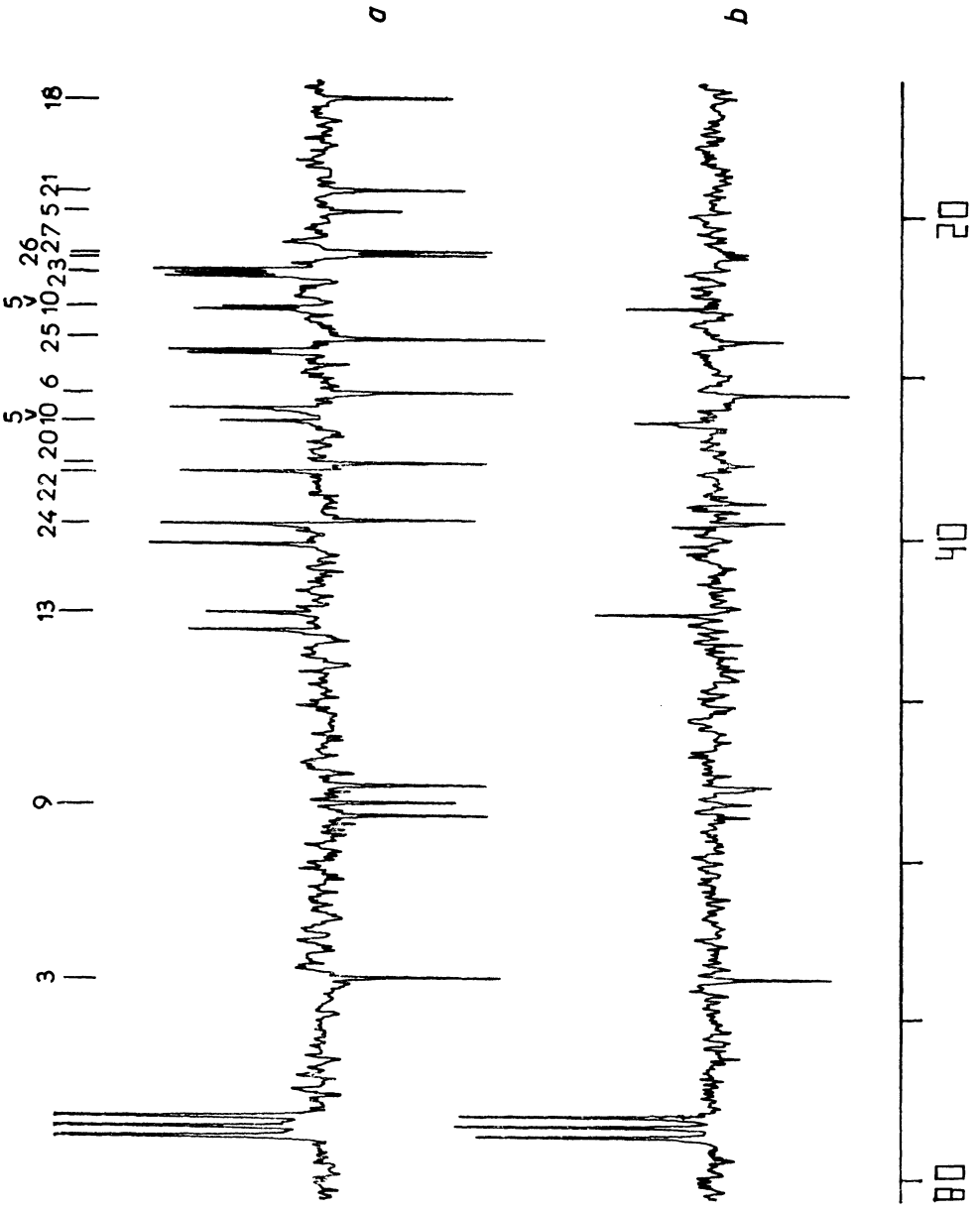
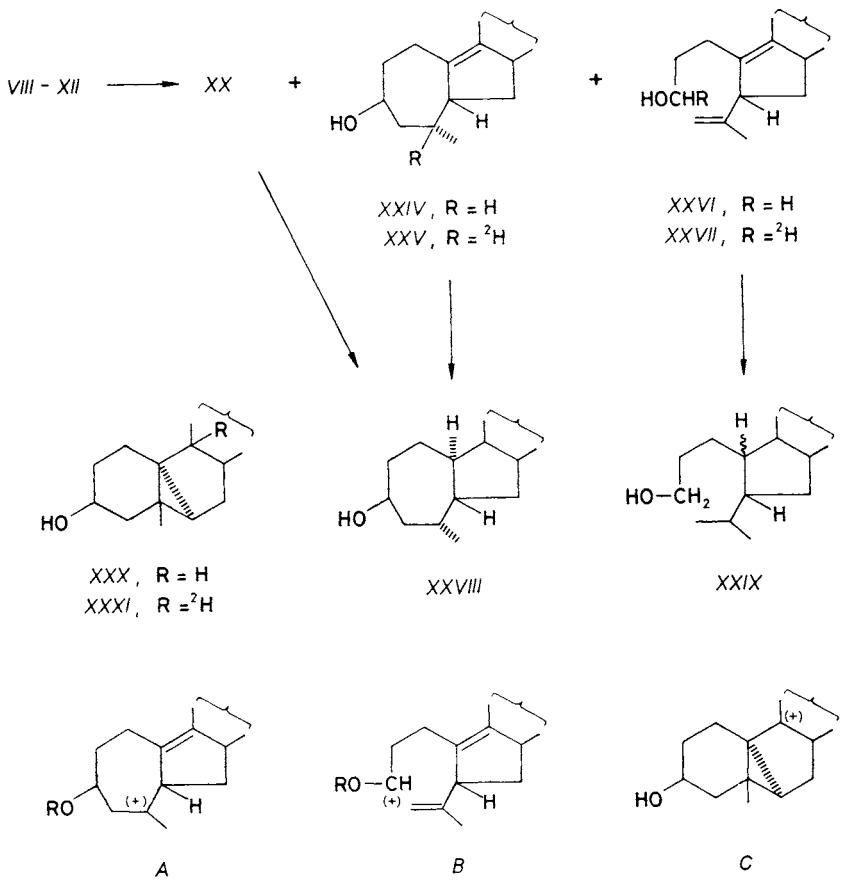


FIG. 1
Two APT ^{13}C NMR spectra of compound *XXX*, measured with relaxation times 7 msec (*a*) and 5 msec (*b*)

At higher nucleophile activity in the medium, the ion *A* undergoes mainly substitution that leads almost exclusively to products of nucleophile attack (*e.g* OH^-, H^-, D^-) from the β-side (*XIII*, *XXIV*, *XXV*). Still another reaction pathway was observed in the hydrogenolysis in which the carbonium ion, formed in position 6, participates with the 9(10)-double bond to give the carbonium ion (*C*). This reacts with the hydride or deuteride ion to the respective cyclopropane derivatives *XXX* and *XXXI*.



SCHEME 3

The mentioned results show that in the solvolysis of Westphalen-type compounds, containing a nucleofuge in position 6β, the $C_{(5)}$—$C_{(10)}$ instead of $C_{(4)}$—$C_{(5)}$[2] bond migrates and the formed carbocation affords then products of substitution, elimination, fragmentation and cyclization.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected; optical rotations were measured in chloroform, accuracy ±2°. Infrared spectra were taken on a Zeiss UR 20 spectrometer in tetrachloromethane, unless stated otherwise. ^{1}H NMR spectra were recorded on Tesla 5 476 (60 MHz; see Table I) or Varian XL 200 (200 MHz; see the individual compounds) instruments in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts are given in the δ-scale, coupling constants in Hz. Mass spectra were measured on an AEI MS 902 spectrometer; masses of some fragments together with their relative abundances (% of the base peak) are given in parentheses (for signals for which the fragments are given, also the corresponding

TABLE I

Characteristic parameters of the 60 MHz ^{1}H NMR spectra. Only the spectra measured on a Tesla 60 spectrometer are summarized, those taken on a Varian 200 instrument are described in the Experimental. Measured in deuteriochloroform with tetramethylsilane as internal standard, chemical shifts are given in the δ-scale (ppm), interaction constants in Hz

Compound	3-H	4b-H	18-H[a]	Other signals[b]
VIII	5·02[c]	—	0·78	4·75[d], 1·26[e], 2·05[f], 3·01[g]
IX	5·35[c]	—	0·81	4·60[d], 1·34[e], 3·01[g]
X	5·10[c]	—	0·80	3·98[d], 1·24[e], 2·06[f]
XI	5·37[c]	—	0·80	4·05[d], 1·34[e]
XII	5·10[c]	—	0·80	3·98[h], 2·05[f], 1·24[e]
XIII	5·48[i]	1·20[b]	0·73	—
XIV	5·17[i]	1·12[b]	0·72	—
XV	5·12[i]	1·12[b]	0·66	—
XVI	4·03[i]	1·13[b]	0·65	—
XVII	—	1·12[b]	0·70	2·51[j], 2·95[j]
XVIII	—	1·91[b]	0·70	2·60[k], 5·89[l]
XIX	4·90[i]	4·90[m]	0·74	3·35[n]
XX	3·70[i]	4·84[m]	0·74	3·25[n]
XXI	4·73[i]	4·92[m]	0·74	2·02[f], 3·33[n]
XXII	4·75[i]	4·92[m]	0·89	2·03[f], 1·20[o], 3·33[n], 4·55[p]
XXV	3·80[i]	0·90[b]	0·74	—
XXVI	3·60[q]	1·59[r]	0·73	3·22[s], 4·66[t]
XXVII	3·58[u]	1·59[r]	0·74	3·20[s], 4·64[t]
XXVIII	3·92[i]	0·90[v]	0·65	—

[a] Singlet; [b] all the spectra contain doublets at δ 0·85 (J = 6) and at δ 0·91 (J = 6) of protons at $C_{(26)}$, $C_{(27)}$ and $C_{(21)}$, in the spectra of benzoyloxy derivatives (*e.g. VIII*) aromatic protons appear as multiplets at δ 7·48 and δ 8·06; [c] mt, Σ J = 8; [d] dd, J = 4 and 10, 6-**H**; [e] s, 5β-CH_3; [f] s, $OCOCH_3$; [g] s, OSO_2CH_3; [h] mt, Σ J = 4; [i] mt, Σ J = 27; [j] d, J = 12, 4-**H**; [k] mt, Σ J = 19, 2-**H**; [l] mt, Σ J = 6, 4-**H**; [m] bs, 2 H; [n] mt, Σ J = 16, 1 H, 5β-**H**; [o] s, 9 H, $OCOC(CH_3)_3$; [p] t, 1 H, Σ J = 16, 17α-**H**; [q] t, J = 6, 2 H; [r] d, J = 1; [s] bd, J = 9, 1 H, 5β-**H**; [t] d, J = 1, 2 protons, 4-**H**; [u] t, J = 6, 1 H; [v] d, J = 7, 3 H.

metastable peak was always found). Reactions, in which compounds of the type *XIX* were formed or employed, were carried out in peroxide-free solvents and in the absence of direct light.

3β-Acetoxy-6β-methanesulfonyloxy-5-methyl-19-nor-5β-cholest-9-ene (*VIII*)

Methanesulfonyl chloride (0·8 ml) was added at 0°C to a solution of 3β-acetoxy-5-methyl-19-nor-5β-cholest-9-en-6β-ol[11] (0·5 g) in pyridine (2 ml). After standing at 0°C for 1 h, the mixture was decomposed by pouring into an ice–water mixture, the product was taken up in ether and, under ice-cooling, washed successively with dilute hydrochloric acid (5%), water, an aqueous solution of sodium hydrogen carbonate and water, and dried over sodium sulfate. The solvent was evaporated and the residue dried over phosphorus pentoxide at 20°C and hPa. According to thin-layer chromatography (TLC) on silica gel (benzene with 5% ether) and ^{1}H NMR spectra (see Table I), the product was sufficiently pure and, because of its instability, it was not purified further.

3β-Benzoyloxy-6β-methanesulfonyloxy-5-methyl-19-nor-5β-cholest-9-ene (*IX*)

Benzoate of the Westphalen diol[12] was similarly acylated with methanesulfonyl chloride: the product also resisted crystallization attempts, was sensitive to adsorbents and unstable at ambient temperature. It was sufficiently pure for further experiments (as shown by TLC and ^{1}H NMR spectra).

[7,7-$^2H_2$]-3β-Acetoxy-6β-chloro-5-methyl-19-nor-5β-cholest-9-ene (*XII*)

[7,7-$^2H_2$]-Cholest-5-en-3β-ol[13] (0·7 g) was oxidized with *m*-chloroperoxybenzoic acid (440 mg) in chloroform (8 ml) at 0°C. After standing for 24 h, the mixture was washed with solutions of potassium carbonate, sodium thiosulfate and water, dried over sodium sulfate and the solvent was evaporated. The residue was crystallized from ethyl acetate at −18°C and the obtained material (250 mg) was acetylated with acetic anhydride (2 ml) in pyridine (4 ml) at 20°C. The usual work-up afforded 240 mg of [7,7-$^2H_2$]-3β-acetoxy-5,6α-oxido-5α-cholestane without any detectable amount of the 5β,6β-oxide (^{1}H NMR spectrum). The product was dissolved in chloroform (1·8 ml) and shaken for 10 min with hydrochloric acid (1·8 ml). The organic layer was evaporated, the aqueous one washed once with chloroform and the combined extracts were washed successively with water, aqueous solution of potassium hydrogen carbonate, water, and dried over sodium sulfate. The solvent was evaporated and the remaining [7,7-$^2H_2$]-3β-acetoxy-6β-chloro-5α-cholestan-5-ol (240 mg) was dissolved in acetic anhydride (13·5 ml). The mixture was boiled and 2·3 ml of distillate was collected. After cooling a solution (0·66 ml) of sulfuric acid in acetic anhydride (1 drop in 1 ml) was added. The mixture was allowed to stand at 30°C for 30 min and at 20°C for 2 h and poured into a mixture of saturated aqueous solution of sodium chloride (50 ml) and ice. The precipitated product *XII* was collected on filter, washed with water, dried and crystallized from dichloromethane–methanol; m.p. 137–138°C (225 mg). For $C_{29}H_{45}.{}^2H_2ClO_2$ (465·1) calculated: 74·88% C, 10·62% H; found: 75·01% C, 10·49% H.

3β-Benzoyloxy-4aβ-hydroxy-4aα-methyl-A-homo-B,19-dinor-5β-cholest-9-ene (*XIII*)

A solution of methanesulfonate *IX* (1 g) in acetone (220 ml) was mixed with a solution of potassium acetate (2·5 g) in water (80 ml). The mixture was refluxed in a nitrogen atmosphere for 5 h, concentrated and extracted with chloroform. The extract was washed with water, dried by filtration through sodium sulfate, the solvent evaporated and the obtained product purified by thin-layer chromatography (TLC) on silica gel; $[\alpha]_D^{20}$ +52° (*c* 1·4); IR spectrum: 3 610 (OH), 1 719,

1 696, 1 276 cm^{-1}, intramolecular hydrogen bond: 3 539 cm^{-1}. For $C_{34}H_{50}O_3 . 2 H_2O$ (542·7) calculated: 75·23% C, 10·03% H; found: 74·94% C, 9·85% H.

3β-Hexahydrobenzoyloxy-4a-methyl-A-homo-B,19-dinor-5β,10α-cholestan-4aβ-ol (*XV*)

Compound *XIII* (2·5 g) in acetic acid (15 ml) was hydrogenated over Adams catalyst (200 mg). After 7 h the catalyst was filtered off, washed with acetic acid and the filtrate concentrated *in vacuo*. Chromatography on silica gel followed by crystallization from acetone–heptane gave 1·9 g of the product, m.p. 135—137°C; $[\alpha]_D^{20}$ +29° (*c* 0·9). Mass spectrum (*m/z*): 514 (M^+, 3), 496 (M — H_2O, 1), 403 (6), 386 (M — C_6H_5COOH, 100), 368 (386 — H_2O, 27), 328 (13), 302 (15), 287 (23), 273 (18). IR spectrum: 3 615, 3 500 (OH), 1 723, 1 708, 1 193, 1 177 (COO—) cm^{-1}; intramolecular hydrogen bond: 3 550 (30%) cm^{-1}. ^1H NMR spectrum (200 MHz): 0·66 (s, 3 H, 18-H), 1·12 (s, 3 H, 4a-H), 3·81 (mt, ΣJ = 26·8, 3α-H). For $C_{34}H_{58}O_3$ (514·8) calculated: 79·32% C, 11·36% H; found: 79·16% C, 11·52% H.

Hydrogenation for a shorter time resulted in reduction of the aromatic ring only. Mass spectrum of compound *XIV* (*m/z*): 512 (M^+, 21), 497 (M — CH_3, 2), 494 (M — H_2O, 3), 384 (M — $C_6H_{11}COOH$, 100), 366 (384 — H_2O, 18), 326 (M — C_3H_6O, 80). The hydrogenation was followed by TLC on silica gel in light petroleum with 10% acetone (starting compound R_F = 0·35, hexahydro derivative *XIV* 0·35, octahydro derivative *XV* 0·50).

3β,4aβ-Dihydroxy-4aα-methyl-B,19-dinor-5β,10α-cholestane (*XVI*)

Hexahydrobenzoate *XV* (220 mg) was refluxed with a solution of lithium aluminium hydride (about 100 mg) in dioxane (5 ml) in nitrogen atmosphere for 8 h. The excess reagent was destroyed by several drops of aqueous sodium sulfate solution and the mixture was filtered through anhydrous sodium sulfate which was then washed with warm chloroform. The product was crystallized from tetrachloromethane; m.p. 90—92°C; $[\alpha]_D^{20}$ +34° (*c* 1·1), mass spectrum (*m/z*): 404 (M^+, 71), 386 (M — H_2O, 100), 371 (386 — CH_3, 52), 368 (386 — H_2O, 46). IR spectrum: 3 605, 1 021 (OH) cm^{-1}; no intramolecular hydrogen bond, free OH group band at 3 621 cm^{-1}. For $C_{27}H_{48}O_2 . 0·5 CH_3COCH_3$ (433·7) calculated: 78·92% C, 11·85% H; found: 79·23% C, 11·79% H.

4aβ-Hydroxy-4aα-methyl-A-homo-B,19-dinor-5β,10α-cholestan-3-one (*XVII*)

Jones reagent was added dropwise at 0°C to a stirred solution of diol *XVI* (104 mg) in a minimum amount of acetone. After 5 min, the mixture was poured into a solution of potassium hydrogen carbonate, extracted with chloroform and the extract washed with water, dried over sodium sulfate and taken down. The product was purified by TLC on silica gel (ether–toluene 1 : 1) and crystallized from acetone–heptane; m.p. 119—120°C (76 mg); $[\alpha]_D^{20}$ —42° (*c* 1·8). Mass spectrum (*m/z*): 402 (M^+, 50), 384 (M — H_2O, 50), 369 (384 — CH_3, 23), 359 (M — 43, 22), 344 (M — CH_3COCH_3, 50), 326 (384 — CH_3COCH_3, 19), 301 (359 — CH_3COCH_3, 53), 43 (CH_3CO^+, 100). IR spectrum: 3 610 (OH), 1 702, 1 693 sh (C=O) cm^{-1}. For $C_{27}H_{46}O_2$ (402·6) calculated: 80·54% C, 11·52% H; found: 80·27% C, 11·19% H.

4a-Methyl-A-homo-B,19-dinor-5β,10α-cholest-4-en-3-one (*XVIII*)

A solution of 3-hydroxy ketone *XVII* (90 mg) in acetic acid (10 ml) was refluxed under nitrogen for 6 h. Concentration *in vacuo* and TLC on silica gel (toluene with 20% ether) gave the non-polar *XVIII* (53 mg) which did not crystallize; $[\alpha]_D^{20}$ —13° (*c* 0·9). Mass spectrum (*m/z*): 384 (M^+, 100),

369 (M − CH_3, 20), 366 (M − H_2O, 10), 356 (M − 28, 23), 271 (M − 113, 42), 244 (18), 216 (244 − 28, 15). IR spectrum: 1 660, 1 621 (C=C—C=O) cm^{-1}. UV spectrum (heptane): ε = 9 700 (234 nm). For $C_{27}H_{44}O$ (384·6) calculated: 84·31% C, 11·53% H; found: 84·09% Cl 11·64% H.

Reaction of *VIII* with Lithium Aluminium Hydride

a) A solution of compound *VIII* (500 mg) in ether (5 ml) was added dropwise under nitrogen to a boiling stirred solution of lithium aluminium hydride (about 200 mg) in ether (7 ml). After boiling for 4 h, the excess hydride was decomposed with a solution of sodium sulfate and the mixture was filtered through anhydrous sodium sulfate. The solvent was removed *in vacuo*, the residue dissolved in chloroform, applied on a thin layer of silica gel and developed in toluene, containing 2% of ethyl acetate. The lipophilic 3-hydroxy-4a-methyl-A-homo-B,19-dinor-3,4-seco-5β-cholestane-4,9-diene (*XXVI*; 35 mg) was eluted with chloroform; m.p. 79—80°C, $[\alpha]_D^{20}$ +95° (*c* 0·9). IR spectrum 3 637, 1 059 (OH), 3 078, 1 642, 891 (C=C) cm^{-1}. Mass spectrum (*m/z*): 386 (M^+, 100), 371 (M − CH_3, 8), 343 (M − C_3H_7, 16), 372 (M − $CH_2CH_2CH_2OH$, 36), 231 (4), 229 (4). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·61% C, 12·10% H. The main product-containing zone (just above the standard cholesterol spot) afforded 276 mg of a mixture of *XX* and *XXIV*, which were separated by chromatography on silica gel, pretreated with 5% silver nitrate (*vide infra*). The polar product zone (identical in polarity with the cholesterol standard) gave crude cyclopropane derivative *XXX* (58 mg) which was purified by chromatography on silver nitrate–impregnated silica gel to afford pure 5-methyl-6α,10-cyclo-19-nor-5β,9β,10α-cholestan-3β-ol (*XXX*; 39 mg), m.p. 104—105°C (methanol). Mass spectrum (*m/z*): 386 (M^+, 100), 371 (M − CH_3, 29), 368 (M − H_2O, 48), 353 (368 − CH_3, 25). ^{1}H NMR spectrum (200 MHz): 0·859 and 0·864 (doublets, J = 6·6 Hz, 26- and 27-H), 0·91 (d, J = 6·5, 3 H, 21-H), 0·62 (s, 3 H, 18-H), 1·24 (s, 3 H, 5β-CH_3), 3·53 (mt, ΣJ = 27·6, 1 H, 3-H). ^{13}C NMR spectrum (carbon atom): 12·97 (18), 18·71 (21), 19·99 (5β-CH_3), 22·55 and 22·81 (26 and 27), 28 (25), 35·70 (20), 23·87 (23), 36·26 (22), 39·50 (24), 44·97 (13), 67·63 (3), 25·98 and 33·10 (5 and 10), 56·70 (9), 31·35 (6).

Separation of *XX* and *XXIV*: The mixture in light petroleum was applied on a silica gel column (5% $AgNO_3$, 10 ml). Elution with toluene, containing 2% of ethyl acetate, afforded 51 mg of 4aα-methyl-A-homo-B,19-dinor-5β-cholest-9-en-3β-ol (*XXIV*), $[\alpha]_D^{20}$ +62° (*c* 1·0). Mass spectrum (*m/z*): 386 (M^+, 100), 368 (M − H_2O, 37), 353 (368 − CH_3, 12), 326 (M − C_3H_8O, 47). ^{1}H NMR spectrum (200 MHz): 0·75 (s, 3 H, 18-H), 0·92 (d, J = 7·1, 3 H, 4a-CH_3), 3·81 (mt, ΣJ = 26·8, 1 H, 3α-H). IR spectrum: 3 620, 1 041, 1 012 (OH) cm^{-1}. For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·49% C, 11·76% H. Further fractions contained 146 mg of 3β-hydroxy-4a-methyl-A-homo-B,19-dinor-5β-cholesta-4a(4b),9-diene (*XX*), $[\alpha]_D^{20}$ +59° (*c* 0·9). Mass spectrum (*m/z*): 384 (M^+, 100), 369 (M − CH_3, 9), 366 (M − H_2O, 36), 355 (M − 29, 17). IR spectrum: 3 625, 1 033 (OH), 1 640, 896, 3 075 (C=C) cm^{-1}. For $C_{27}H_{44}O$ (384·6) calculated: 84·31% C, 11·53% H; found: 83·97% C, 11·14% H.

b) Compound *VIII* (2 g) was reduced as described above but the reaction was performed in boiling dioxane instead of in ether. The reaction mixture gave 495 mg of the seco derivative *XXVI*, 701 mg of the diene *XX*, 190 mg of the olefin *XXIV* and 105 mg of the cyclopropano derivative *XXX*.

Reaction of 6β-Methanesulfonate *VIII* with Lithium Aluminium Deuteride

Compound *VIII* (500 mg) was reduced with lithium aluminium deuteride in boiling ether as described above. After 7 h, the mixture was worked up in the same manner as described. The

following deuterated (mass spectroscopy) products were obtained: [3-^{2}H]-3-Hydroxy-4a-methyl--A-homo-B,19-dinor-3,4-seco-5β-cholesta,4,9-diene (*XXVII*). IR spectrum: 3 635, 1082, 1 046 (OH), 3 075, 1 643, 982 (C=CH_2), 2 145 (C-^{2}H) cm^{-1}. ^{1}H NMR spectrum was identical with that of *XXVI* save the integrated area of the $C_{(3)}$-proton triplet. [4aβ-^{2}H]-4aα-Methyl-A-homo-B,19--dinor-5β-cholest-9-en-3β-ol (*XXV*). Mass spectrum (*m/z*): 387 (M^+, 100), 372 (M − CH_3, 7), 344 (M − C_3H_7, 13), 327 (M − C_3H_6OH, 30). IR spectrum: 3 625, 1 066, 1 056, 1 039, 1 031, 1 013 (OH), 1 659 (C=C), 2 130 (C—^{2}H) cm^{-1}. ^{1}H NMR spectrum was identical with that of *XXIV* save the multiplicity of the signal of the methyl group in position 4a. [9β-^{2}H]-5-Methyl--6,10-cyclo-5β,9β,10α-cholestan-3β-ol (*XXXI*). Mass spectrum (*m/z*): 387 (M^+, 54), 369 (M − H_2O, 100), 354 (369 − CH_3, 12), 327 (6), 274 (M − C_8H_{17}, 10), 256 (369 − C_8H_{17}, 27). ^{13}C NMR spectrum (carbon atom): 12·95 (18), 18·70 (21), 20·01 (5β-CH_3), 22·56 and 22·81 (26 and 27), 25·95 and 33·04 (6 and 10), 27·99 (25), 31·32 (6), 35·71 (20), 36·25 (22), 39·50 (24), 44·96 (13), 67·63 (3). IR spectrum: 3 620, 1 043, 1 029 (OH), 2 075, 2 045 (C^{2}H) cm^{-1}.

Reaction of *IX* with lithium aluminium hydride was performed in the same manner; the isolation of compound *XXX* was complicated by the fact that benzyl alcohol, arising in the reaction, had practically the same R_F.

Reaction of *X* with lithium aluminium hydride was carried out in boiling dioxane for 6 h, and the mixture processed as described above. The yields indicated higher proportion of the fragmentation product (*XXVI*) as compared with the elimination and substitution products (*XX*, *XXIV*, and *XXX*) (a similar result was obtained by reduction of *VIII* in boiling dioxane).

3β-Acetoxy-4a-methyl-17β-pivaloyloxy-A-homo-B,19--dinor-5β-androsta-4a(4b),9-diene (*XXII*)

3β-Acetoxy-6β-chloro-5-methyl-17β-pivaloyloxy-19-nor-5β-androst-9-ene[14] (50 mg) and silver acetate (250 mg) were suspended in acetic acid (6 ml) and the apparatus was repeatedly evacuated and filled with argon. After reflux for 20 h with exclusion of light and air, the mixture was cooled, the solvent removed *in vacuo* and the residue extracted with chloroform. The chloroform extract was concentrated, applied on a thin layer of silica gel, and the plates were developed with benzene, containing 10% of ether (freshly washed with aqueous ferrous sulfate). The non-polar product (R_F 0·70) was crystallized from methanol; m.p. 101—102°C, yield 12 mg. ^{1}H NMR spectrum (200 MHz): 0·90 (s, 3 H, 18-**H**), 1·20 (s, 9 H, $COC(CH_3)_3$), 2·02 (s, 3 H, $OCOCH_3$), 3·36 (mt, ΣJ = 16, 1 H, 5β-**H**), 4·54 (dd, J = 7·3 and 9·3, 1 H, 17α-**H**), 4·73 (mt, ΣJ = 27·8, 1 H, 3α-**H**), 4·91 (mt, ΣJ = 3·0, 1 H, 4b-**H**) and 4·95 (mt, ΣJ = 2·4, 1 H, 4b-**H**). For $C_{26}H_{38}O_4$ (414·6) calculated: 75·32% C, 9·24% H; found: 75·29% C, 9·31% H.

3β-Acetoxy-4a-methyl-A-homo-B,19-dinor-5β-cholesta-4a(4b),9-diene (*XXI*)

A mixture of compound *X* (60 mg), silver acetate (350 mg) and acetic acid (6 ml) was refluxed under argon in the dark for 20 h. After cooling, the mixture was poured into a mixture of ice and ammonium hydroxide (20 ml). The product was taken up with chloroform (under nitrogen), the extract was washed with water and dried by filtration through Celite and sodium sulfate. The solvent was evaporated and the residue purified by TLC. $[\alpha]_D^{20}$ +44° (*c* 0·9). Mass spectrum (*m/z*): 426 (M^+, 19), 411 (M − CH_3, 1), 366 (M − CH_3COOH, 100), 253 (366 − C_8H_{17}, 14), IR spectrum: 1 739, 1 243 ($COCH_3$), 3 080, 1 645, 910 (C=C) cm^{-1}. For $C_{29}H_{46}O_2$ (426·7) calculated: 81·63% C, 10·87% H; found: 81·09% C, 10·55% H.

[6,6-^{2}H]-3β-Acetoxy-4a-methyl-A-homo-B,19-dinor-5β-cholesta-4a(4b),9-diene (*XXIII*)

Compound *XII* (60 mg) was converted into the diene *XXIII* (17 mg) by the above-described procedure. Mass spectrum (*m/z*): 428 (M^+, 17), 368 (M — CH_3COOH, 100), 255 (M — CH_3COOH — C_8H_{17}, 15). ^{1}H NMR spectrum (200 MHz): 0·75 (s, 3 H, 18-H), 2·02 (s, 3 H, $OCOCH_3$), 3·33 (bs, 1 H, 5-H), 4·73 (mt, ΣJ = 28·0, 3-H), 4·90 (dd, J = 3·0, 1 H, 4b-H), 4·93 (mt, ΣJ = 2·8, 1 H, 4b-H).

3β-Benzoyloxy-4a-methyl-A-homo-B,19-dinor-5β-cholesta-4a(4b),9-diene (*XIX*)

a) A mixture of the benzoyloxy chloride *XI* (75 mg), silver acetate (300 mg) and acetic acid (6 ml) was refluxed in an argon atmosphere for 20 h and then processed as described in the preparation of compound *XXI*. Thin-layer chromatography afforded 25 mg of the oily product *XIX*; $[\alpha]_D^{20}$ +49° (*c* 1·0). Mass spectrum (*m/z*): 488 (M^+, 7), 366 (M — C_6H_5COOH, 100), 253 (366 — C_8H_{17}, 100). For $C_{34}H_{48}O_2 . H_2O$ (506·7) calculated: 80·58% C, 9·95% H; found: 80·76% C, 9·74% H.

b) Hydroxy derivative *XX* (86 mg) was benzoylated with a mixture of pyridine (0·2 ml) and benzoyl chloride (0·1 ml) at 20°C under argon in the dark. After standing for 2 h, the mixture was poured on ice and the product taken up in light petroleum. The solution was washed successively with dilute hydrochloric acid, water, an aqueous solution of potassium hydrogen carbonate and water, and dried over sodium sulfate. The product was purified by TLC and found to be identical (IR spectrum) with the compound prepared under *a*).

4aα-Methyl-A-homo-B,19-dinor-5β,10α-cholestan-3β-ol (*XXVIII*)

a) Hydrogenation of diene *XX* (40 mg) in acetic acid (3 ml) over platinum oxide (20 mg) gave a mixture of two compounds which were separated by TLC. The main (lipophilic) product crystallized from methanol; m.p. 133—135°C, undepressed by an authentic sample[1].

b) Hydrogenation of hydroxy derivative *XXIV* (36 mg) under the same conditions afforded the same product *XXVIII*.

4a-Methyl-A-homo-B,19-dinor-3,4-seco-5β,10ξ-cholestan-3-ol (*XXIX*)

Hydrogenation of compound *XXVI* (100 mg) in acetic acid (3 ml) over platinum catalyst (20 mg) gave chromatographically pure (TLC) product; $[\alpha]_D^{20}$ +30° (*c* 1·1). Mass spectrum (*m/z*): 390 (M^+, 45), 345 (M — C_2H_5O, 100). ^{1}H NMR spectrum (60 MHz): 0·75 (d, J = 6, 6 H, 4- and 4b-H), 3·58 (t, J = 6, 2 H, 3-H).

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