PREPARATION OF SOME 5-METHYL-19-NOR-5β-CHOLESTANE DERIVATIVES*

P.Kočovský and V.Černý

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6

Received February 2nd, 1976

Mono- and diesters of 5-methyl-19-nor-5β-cholest-9(10-)ene-3β,6β-diol (Westphalen diol, *X*—*XVI*) were prepared from 5α-cholestane-3β,5,6β-triol esters *III*—*IX*. Syntheses of isomeric ketones *XIX*, *XXII* and *XXVII* are reported.

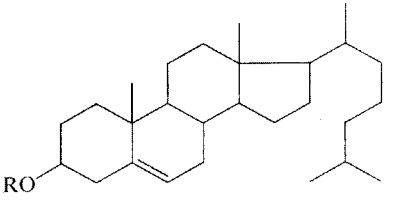
As part of a programme aimed at preparation and investigation of Westphalen-type steroids, compounds substituted with a ketonic function at positions 3, 4, or 6 (*i.e.* ketones *XIX*, *XXI* and *XXVII*) were required.

For the preparation of the ketone *XIX*, cholesteryl benzoate (*Ia*) was chosen as starting material. The presence of a benzoyloxy grouping appeared advantageous both for making possible a selective protection of the 3-hydroxyl and for good crystallization properties of the compounds involved. Peracid oxidation of the benzoate *Ia* gave a mixture of epimeric epoxides *IIa* which was converted to the single diol[1] *III* on treatment with aqueous perchloric acid. Acetylation of the diol *III* afforded the known[2,3] diester *IV* which gave the product of Westphalen rearrangement *X* after treatment with potassium hydrogen sulfate in acetic anhydride. Selective hydrolysis of the 6-acetoxy group was achieved with aqueous hydrochloric acid in methanolic solution to give the 6-hydroxy derivative *XIII* in good yield. The monobenzoate *XIII* was prepared by an alternative route from the 6-hydroxy derivative *III* *via* the nitrates *V* and *XI*. This experiment proved the possibility of protecting the 6β-hydroxyl by its conversion into the nitrate ester. It also demonstrated the ability of 6-nitrates to undergo the Westphalen rearrangement. Jones' oxidation of the hydroxy derivative *XIII* yielded the ketone *XVII* in which the ketonic function was removed by Huang-Minlon reduction; this procedure gives *XVIII* (ref.[4]) with simultaneous hydrolysis of the benzoyloxy grouping. The subsequent Jones' oxidation furnished the required ketone *XIX*.

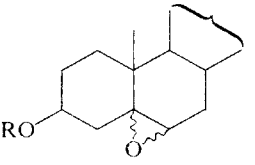
In the preparation of the isomeric ketone *XXII* cholesteryl acetate (*Ib*) was used as the starting material. After epoxidation and cleavage of the mixture of epimeric

* Part CLXXXIV in the series On Steroids; Part CLXXXIII: This Journal *41*, 2040 (1976).

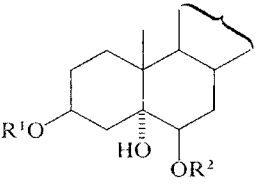
epoxides *IIb* analogously as before, the 6-hydroxyl in *VII* (ref.[5,6]) was protected by benzoylation to give the diester[7] *VIII*. This step was followed by hydrolysis with potassium hydrogen carbonate to obtain the monobenzoate *IX* which could be easily purified and was submitted to Westphalen rearrangement. The acetyl derivative[7] *XIV* thus obtained was hydrolyzed with aqueous hydrochloric acid in methanol to afford the hydroxy derivative *XV* in good yield. The final steps, *i.e.* Jones' oxidation



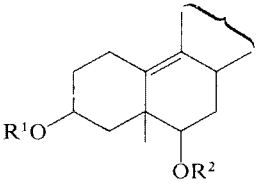
Ia, R = Bz
Ib, R = Ac



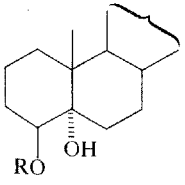
IIa, R = Bz
IIb, R = Ac



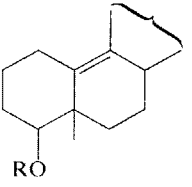
III, R^1 = Bz, R^2 = H
IV, R^1 = Bz, R^2 = Ac
V, R^1 = Bz, R^2 = NO_2
VI, R^1 = Bz, R^2 = Bz
VII, R^1 = Ac, R^2 = H
VIII, R^1 = Ac, R^2 = Bz
IX, R^1 = H, R^2 = Bz



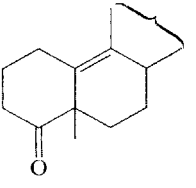
X, R^1 = Bz, R^2 = Ac
XI, R^1 = Bz, R^2 = NO_2
XII, R^1 = Bz, R^2 = Bz
XIII, R^1 = Bz, R^2 = H
XIV, R^1 = Ac, R^2 = Bz
XV, R^1 = H, R^2 = Bz
XVI, R^1 = H, R^2 = H



XXIII, R = Ac
XXIV, R = H



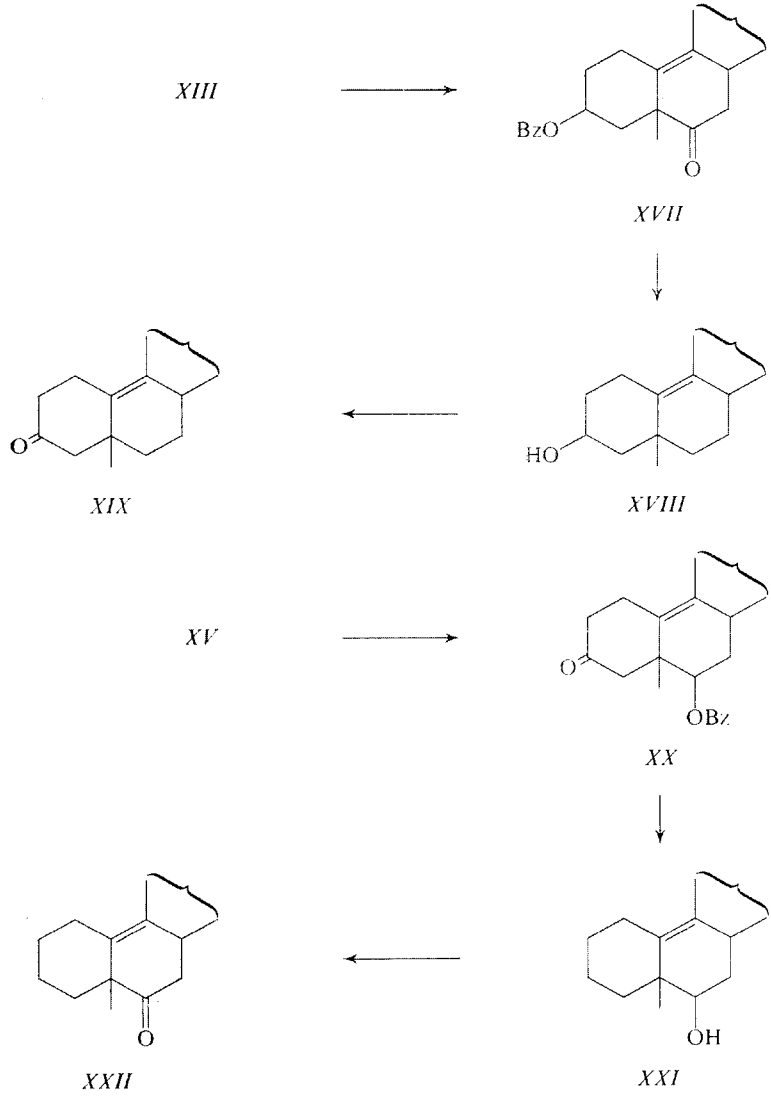
XXV, R = Ac
XXVI, R = H



XXVII

to *XX*, Huang-Minlon reduction to *XXI* and oxidation to the 6-ketone *XXII*, were conducted in the usual manner.

Both monobenzoates *XIII* and *XV* were correlated with each other, with the known[1] benzoate *III* and with Westphalen diol *XVI* in the following manner. Benzoylation of *XIII* and *XV* gave the dibenzoate *XII* which was also obtained from *III* by benzoylation to the dibenzoate *VI* followed by Westphalen rearrangement of the latter.



This dibenzoate *XII* was converted to Westphalen diol[8] *XVI* by alkaline hydrolysis.

Last of all, the ketone[9] *XXVII* was prepared from the known *XXIII* (or *XXIV*) (ref.[9]) by Westphalen rearrangement to *XXV* followed by conversion of the latter to the alcohol *XXVI* and Jones' oxidation of the latter.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 50°C/0·2 Torr. Optical rotation measurements were carried out in chloroform with an error of ±1°. The infrared spectra were recorded on the Zeiss UR 20 spectrometer in tetrachloromethane unless otherwise stated. The ^{1}H-NMR spectra were recorded on the Varian HA-100 instrument in deuteriochloroform and corrected to tetramethylsilane (7·25 p.p.m.). Chemical shifts are given in p.p.m. Apparent coupling constants were obtained from the first order analysis. The mass spectra were recorded on the mass spectrometer AEI MS 907. The CD spectra were recorded on the Dichrographe II (Jouan-Roussel) in methanol. The identity of samples prepared by different routes was checked by mixture melting point determination, by thin-layer chromatography (TLC) and by infrared and ^{1}H-NMR spectra. Usual work up of an etheral solution means washing the solution with aqueous 5% hydrochloric acid, water, 5% potassium hydrogen carbonate solution, water, drying with sodium sulphate and evaporation of the solvent *in vacuo*.

5α-Cholestane-3β,5,6β-triol 3-Monobenzoate (*III*)

Cholesteryl benzoate (*I*, 800 g) in benzene (4 l) and chloroform (1·3 l) were treated with a solution of perphthalic acid (600 g) in ether (5 l) and allowed to stand at room temperature for 18 h. The mixture was poured into water, the excess peracid was extracted with a sodium carbonate solution, the etheral solution was washed with water, dried, and the solvent evaporated *in vacuo*. The residue was dissolved in dioxane (4 l) and acetone (2 l) at 60°C, treated with 5% perchloric acid (1 l), and after 2 hours at room temperature about 2/3 of the solvents were removed under reduced pressure. The precipitated crystalline diol *III* (580 g) was filtered off under suction, washed with 50% aqueous methanol, water, and dried in air. A sample was crystallized from a mixture of acetone, methanol and water; m.p. 230–231°C, $[\alpha]_D^{20}$ −8·6° (*c* 2·3); literature reports[1] 222–223°C, $[\alpha]_D^{20}$ −5°. IR spectrum (chloroform): 1281, 1708, 3460, 3602, 3634 cm^{-1}. ^{1}H-NMR spectrum: 0·69 (3 H, s, 18-H), 1·22 (3 H, s, 19-H). For $C_{34}H_{52}O_4$ (524·8) calculated: 77·82% C, 9·99% H; found: 77·69% C, 9·96% H.

5α-Cholestane-3β,5,6β-triol 3-Benzoate 6-Acetate (*IV*)

The alcohol *III* (5 g) in pyridine (25 ml) was acetylated with acetic anhydride (5 ml) at room temperature for 8 h. The mixture was decomposed with ice, the product taken up in ether and worked up. The residue was crystallized from a mixture of acetone, methanol and water to yield the acetate *IV* (3·6 g), m.p. 164–165°C (literature reports[2,3] 162–164°C), $[\alpha]_D^{20}$ −28° (*c* 2·2) (literature reports[2,3] −24°). IR spectrum: 1242, 1278, 1700 sh, 1720, 1737, 3495, 3595 cm^{-1}. ^{1}H-NMR spectrum: 0·70 (3 H, s, 18-H), 1·20 (3 H, s, 19-H). For $C_{36}H_{54}O_5$ (566·8) calculated: 76·28% C, 9·60% H; found: 76·34% C, 9·72% H.

5α-Cholestane-3β,5,6β-triol 3-Benzoate 6-Nitrate (*V*)

A solution of the diol *III* (100 g) in chloroform (2·8 l) was treated at −30 to −20°C with a reagent prepared from acetic anhydride (600 ml) and 65% nitric acid (140 ml) at −30°C. The mixture was kept at −20 to −10°C for 30 minutes and an additional 30 minutes at −5 to 0°C. The solution was poured onto ice and neutralized with sodium hydrogen carbonate solution. The organic layer was washed with 5% potassium hydrogen carbonate solution, water, dried, and the solvent was removed under reduced pressure. The residue was crystallized from a mixture of acetone, methanol and water to yield the nitrate *V* (81·2 g), m.p. 188–190°C (dec.), $[\alpha]_D^{20}$ −37° (*c* 1·8). IR spectrum (chloroform): 857, 1284, 1634, 1714, 3460, 3595 cm^{-1}. ^{1}H-NMR spectrum: 0·69 (3 H, s, 18-H), 1·18 (3 H, s, 19-H), 4·92 (1 H, t, J = 2·8 Hz, 6α-H). For $C_{34}H_{51}NO_6$ (569·8): calculated: 71·67% C, 9·02% H; found: 71·70% C, 9·02% HN.

5α-Cholestane-3α,5,6β-triol 3,6-Dibenzoate (*VI*)

The alcohol *III* (1 g) was benzoylated with benzoyl chloride (2 ml) in pyridine (5 ml) at room temperature for 3 h. The mixture was decomposed with ice, the product taken up in ether and worked up as usual. The residue was crystallized from a mixture of methanol, acetone and water to yield the dibenzoate *VI* (650 mg), m.p. 136–139°C, $[\alpha]_D^{20}$ −67° (*c* 1·7). IR spectrum: 1275, 1698, 1720, 3500, 3590 cm^{-1}. For $C_{41}H_{56}O_5$ (628·9) calculated: 78·30% C, 8·98% H; found: 78·42% C, 8·91% H.

5α-Cholestane-3β,5,6β-triol 3-Acetate 6-Benzoate (*VIII*)

a) *From 5α-cholestane-3α,5,6β-triol 3-monoacetate*[5,6] (VII): The diol *VII* (350 g) in pyridine (1 l) was benzoylated with benzoyl chloride (150 ml) at room temperature for 3 h. The mixture was decomposed with ice, the product taken up in ether and worked up. The residue was crystallized from ether at −30°C to yield the benzoate *VIII* (260 g), m.p. 104–108°C and 162–163°C literature reports[7] 159–160°C), $[\alpha]_D^{20}$ −64° (*c* 1·8). IR spectrum: 1247, 1275, 1721, 1735 sh., 3495, 3600 cm^{-1}. For $C_{36}H_{54}O_5$ (566·8) calculated: 76·28% C, 9·60% H; found: 76·30% C, 9·48% H.

b) *From 5α-cholestane-3β,5,6β-triol 6-monobenzoate* (IX): The diol *IX* (300 mg) was acetylated with acetic anhydride (1 ml) in pyridine (5 ml) at room temperature overnight. The mixture was decomposed with ice, the product taken up in ether and worked up as usual. The residue was crystallized from ether at −30°C to yield the acetate *VIII*. Found: 76·41% C, 9·57% H.

5α-Cholestane-3β,5,6β-triol 6-Monobenzoate (*IX*)

A solution of the acetate *VIII* (20 g) in methanol (500 ml) was treated with a solution of potassium hydrogen carbonate (10 g) in water (50 ml) and refluxed for 1 h. The reaction mixture was diluted with hot water (300 ml) and set aside at room temperature for 3 h. The crystalline product (11 g) was filtered off under suction, washed with 50% aqueous methanol and water and dried in air. A sample was crystallized from aqueous methanol; m.p. 125–127°C, $[\alpha]_D^{20}$ −36° (chloroform–methanol 1 : 1, *c* 1·8). IR spectrum (chloroform): 1278, 1695 sh., 1712, 3490, 3610 cm^{-1}. ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·33 (3 H, s, 19-H). For $C_{34}H_{52}O_4$ (524·8) calculated: 77·82% C, 9·99% H; found: 77·83% C, 9·97% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol 3-Benzoate 6-Acetate (*X*)

Method A: The diol *III* (400 g) was refluxed with acetic anhydride (2 l) for 30 minutes. To the stirred mixture finely powdered potassium hydrogen sulfate (50 g) at 90°C was added and the mixture was stirred for an additional 30 minutes at the same temperature. The solution was poured onto ice and pyridine, the product was filtered off under suction after 3 h, dissolved in ether and worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to yield the product *X* (210 g), m.p. 142–143°C, $[\alpha]_D^{20}$ +122° (*c* 1·9). IR spectrum: 1243, 1273, 1720, 1736 cm^{-1}. ^{1}H-NMR spectrum: 0·82 (3 H, s, 18-H), 1·33 (3 H, s, 5β-methyl), 4·81 (1 H, dd, $J_{6\alpha,7\beta}$ = 11 Hz, $J_{6\alpha,7\beta}$ = 5 Hz). For $C_{36}H_{52}O_4$ (548·8) calculated: 78·79% C, 9·55% H; found: 78·83% C, 9·56% H.

Method B: Finely powdered potassium hydrogen sulfate (100 mg) was added to a stirred solution of the compound *IV* (1 g) in acetic anhydride (20 ml) at 90°C, the mixture was stirred for 30 minutes at the same temperature and worked up as before. Crystallization gave product *X* (480 mg). Found: 78·65% C, 9·55% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol 3-Benzoate 6-Nitrate (*XI*)

To a stirred solution of nitrate *V* (1·2 g) in acetic anhydride (40 ml) finely powdered potassium hydrogen sulfate (1 g) was added at 90°C; the mixture was stirred at the same temperature for an additional 20 minutes, poured onto ice, the product was taken up in ether and worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to yield the product *XI* (600 mg), m.p. 161–162°C, $[\alpha]_D^{20}$ +114° (*c* 2·0). IR spectrum (chloroform): 864, 1288, 1627, 1711 cm^{-1}. ^{1}H-NMR spectrum: 0·84 (3 H, s, 18-H), 1·36 (3 H, s. 5β-methyl), 4·97 (1 H, dd, $J_{6\alpha,7\beta}$ = 10·4 Hz, $J_{6\alpha,7\alpha}$ = 4·8 Hz). For $C_{34}H_{49}NO_5$ (551·8) calculated: 74·01% C, 8·95% H; found: 74·12% C, 8·96% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol 3,6-Dibenzoate (*XII*)

a) *From 5α-cholestane-3β,5,6β-triol 3,6-dibenzoate* (VI): To a stirred solution of dibenzoate *VI* (1 g) in acetic anhydride (10 ml) finely powdered potassium hydrogen sulfate (60 mg) was added at 90°C, the mixture was stirred at the same temperature for an additional 45 minutes, poured onto ice, the product was taken up in ether and worked up as usual. The residue was crystallized twice from a mixture of acetone, methanol and water to afford the dibenzoate *XII* (360 mg), m.p. 181–183°C, $[\alpha]_D^{20}$ +118° (*c* 1·7). IR spectrum: 1277, 1715 sh., 1721 cm^{-1}. ^{1}H-NMR spectrum: 0·84 (3 H, s. 18-H), 1·50 (3 H, s, 5β-methyl), 5·07 (1 H, dd, $J_{6\alpha,7\beta}$ = 10 Hz, $J_{6\alpha,7\alpha}$ = 5 Hz). For $C_{41}H_{54}O_4$ (610·9) calculated: 80·61% C, 8·91% H; found: 80·69% C, 9·00% H.

b) *From 5-methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol 3-monobenzoate* (XIII): The alcohol *XIII* (200 mg) in pyridine (3 ml) was benzoylated with benzoyl chloride (0·3 ml) at room temperature for 3 h. The mixture was decomposed with ice, the product taken up in ether and worked up as usual. The residue was crystallized from a mixture of ethanol and water to yield the dibenzoate *XII* (160 mg), m.p. 182–183°C, $[\alpha]_D^{20}$ +121 (*c* 1·9). Found: 80·68% C. 8·98% H.

c) *From 5-methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol 6-monobenzoate* (XV): Alcohol *XV* (300 mg) was benzoylated with benzoyl chloride (2 ml) in pyridine (5 ml) at room temperature overnight. The mixture was decomposed with ice, the product taken up in ether and worked up as usual. The residue was crystallized from a mixture of ethanol and water to afford the dibenzoate *XII* (180 mg), m.p. 182–183°C. Found: 80·70% C, 8·96% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol 3-Monobenzoate (*XIII*)

a) *From 5-methyl-19-nor-5β-cholest-9(10)-diol 3-benzoate 6-acetate* (X): The diester *X* (200 g) in chloroform (800 ml) and methanol (8 l) was treated with concentrated hydrochloric acid (150 ml) and allowed to stand for 2 days at 30°C. About 1/2 of the solvents was distilled off under reduced pressure, the precipitated crystalline product was filtered off under suction, washed with 50% aqueous methanol and recrystallized from ethanol to afford the alcohol *XIII* (126 g), m.p. 163–164°C and 175–176°C, $[\alpha]_D^{20}$ +120° (*c* 1·7). IR spectrum: 1276, 1718, 3520, 3626 cm^{-1}. ^{1}H-NMR spectrum: 0·81 (3 H, s, 18-H), 1·24 (3 H, s, 5β-methyl), 3·56 (1 H, dd, $J_{6\alpha,7\beta}$ = 11 Hz, $J_{6\alpha,7\alpha}$ = 5 Hz). For $C_{34}H_{50}O_3$ (506·8) calculated: 80·58% C, 9·94% H; found: 80·54% C, 9·90% H.

b) *From 5-methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol 3-benzoate 6-nitrate* (XI): Zinc powder (1 g) was added to a stirred solution of nitrate *XI* (150 mg) in acetic acid (20 ml) and ether (20 ml) and the mixture was stirred for an additional 15 minutes. The inorganic material was separated by filtration, washed with methanol, the filtrate evaporated under reduced pressure, the residue dissolved in ether, extracted with aqueous potassium hydrogen carbonate solution, water, dried and evaporated. The residue was crystallized from ethanol to yield the alcohol *XIII* (630 mg), m.p. 162–163°C and 174–175°C. Found: 80·69% C, 9·93% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-3β,6βdiol 3-Acetate 6-Benzoate (*XIV*)

The diol *IX* (10 g) was refluxed in acetic anhydride (60 ml) for 30 minutes. To the stirred mixture finely powdered potassium hydrogen sulfate (3 g) was added at 90°C and the mixture was stirred at the same temperature for an additional 45 minutes. The solution was poured onto ice and pyridine, the product taken up in ether and worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to afford the product *XIV* (5·6 g), 159–160°C (literature reports[7] 157–158°C), $[\alpha]_D^{20}$ +65° (*c* 2·4). IR spectrum: 1245, 1274, 1722, 1741 cm^{-1}. ^{1}H-NMR spectrum: 0·82 (3 H, s, 18-H), 1·37 (3 H, s, 5β-methyl). For $C_{36}H_{52}O_4$ (548·8) calculated: 78·79% C, 9·55% H; found: 78·72% C, 9·64% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol 6-Monobenzoate (*XV*)

The diester *XIV* (35 g) in chloroform (350 ml) and methanol (1·1 l) was treated with concentrated hydrochloric acid (30 ml) and allowed to stand for 2 days at 35°C. Solvents were distilled off under reduced pressure, the residue was treated with ether and water, the organic layer was washed with an aqueous potassium hydrogen carbonate solution, water dried and evaporated. The residue was crystallized from a mixture of ethyl acetate and ligroin to yield the alcohol *XV* (32 g), m.p. 106–109°C, $[\alpha]_D^{20}$ +53° (*c* 2·5). IR spectrum: 1275, 1715, 3520, 3627 cm^{-1}. For $C_{34}H_{50}O_3$ (506·8) calculated: 80·58% C, 9·94% H; found: 80·53% C, 9·91% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-3β,6β-diol (*XVI*)

A solution of the dibenzoate *XII* (200 mg) and potassium hydroxide (200 mg) in methanol (20 ml) was refluxed for 3 h. Methanol was distilled off under reduced pressure, the residue was treated with ether and water, the organic layer was washed with water, dried and evaporated. The residue was crystallized from a mixture of acetone, methanol and water to afford the diol *XVI* (25 mg), m.p. 79–80°C (literature reports[8] 80°C), $[\alpha]_D^{20}$ +119° (*c* 2·1); literature reports[8] +118°. For $C_{27}H_{46}O_2$ (402·7) calculated: 80·54% C, 11·54% H; found: 80·46% C, 11·67% H.

3β-Benzoyloxy-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (*XVII*)

The alcohol *XIII* (100 g) in acetone (3·5 l) was treated with excess Jones' reagent (80 ml) at room temperature for 10 minutes. The excess oxidizing agent was destroyed with methanol, ether was added, the mixture was washed with water, an aqueous potassium hydrogen carbonate solution, water, dried, and evaporated. The residue was crystallized from a mixture of acetone, methanol and water to yield the ketone *XVII* (76 g), m.p. 130—131°C, $[\alpha]_D^{20}$ +26° (*c* 1·7). IR spectrum: 1274, 1714 sh., 1720 cm^{-1}. ^{1}H-NMR spectrum: 0·78 (3 H, s, 18-H), 1·46 (3 H, s, 5β-methyl). CD spectrum: $\Delta\varepsilon$ −2·46, 295 nm (ketone), $\Delta\varepsilon$ +2·08, 225 nm (benzoate). For $C_{34}H_{48}O_3$ (504·8) calculated: 80·91% C, 9·95% H; found: 81·09% C, 9·54% H.

5-Methyl-19-nor-5β-cholest-9(10)-en-3β-ol (*XVIII*)

The solution of ketone *XVII* (75 g) in triethylene glycol (1 l) was treated with 98% hydrazine hydrate (80 ml) and solid potassium hydroxide (60 g) and heated at 140°C for 1 h. Then the temperature was allowed to rise to 200°C and the mixture was kept at this temperature for 3 h. After cooling off, the mixture was diluted with water, the precipitated product was collected by filtration under suction, washed with water, dissolved in ether, and worked up as usual[1]. The residue was crystallized from a mixture of methanol and water to yield the alcohol *XVIII* (36 g), m.p. 133—134°C, (literature reports[4] 130—131°C), $[\alpha]_D^{20}$ +66° (*c* 2·2) (literature reports[4] $[\alpha]_D$ +160°). IR spectrum: 3495, 3626 cm^{-1}. ^{1}H-NMR spectrum: 0·78 (3 H, s, 18-H), 1·24 (3 H, s, 5β-methyl). For $C_{27}H_{46}O$ (386·7) calculated: 83·87% C, 11·99% H; found: 83·83% C, 11·93% H.

5-Methyl-19-nor-5β-cholest-9(10)-en-3-one (*XIX*)

The alcohol *XVIII* (1·1 g) in acetone (50 ml) was treated with excess Jones' reagent (0·8 ml) at room temperature for 5 minutes. The excess of oxidizing agent was destroyed with methanol, ether was added, and the mixture was washed with water, aqueous potassium hydrogen carbonate solution, water, dried, and evaporated to afford the noncrystalline ketone *XIX* (1 g), $[\alpha]_D^{20}$ +20° (*c* 1·7). IR spectrum: 1713 cm^{-1}. ^{1}H-NMR spectrum: 0·81 (3 H, s, 18-H), 1·02 (3 H, s, 5β-methyl). CD spectrum: $\Delta\varepsilon$ −0·44, 290 nm. For $C_{27}H_{44}O$ (384·6) calculated: 84·34% C, 11·53% H; found: 84·20% C, 11·53% H.

6β-Benzoyloxy-5-methyl-19-nor-5β-cholest-9(10)-en-3-one (*XX*)

The alcohol *XV* (3 g) in acetone (60 ml) was treated with excess Jones' reagent at room temperature for 5 minutes. The excess oxidizing agent was destroyed with methanol, ether was added, and the mixture was washed with water, an aqueous potassium hydrogen carbonate solution, water, dried, and evaporated. The residue was chromatographed on a silica gel column (150 g) in a mixture of light petroleum and ether (97 : 3). Working up the corresponding fractions afforded the noncrystalline ketone *XX* (2·8 g), $[\alpha]_D^{20}$ +12° (*c* 2·6). IR spectrum: 1273, 1710 sh., 1720 cm^{-1}. ^{1}H-NMR spectrum: 0·85 (3 H, s, 18-H), 1·22 (3 H, s, 5β-methyl), 5·07 (1 H, dd, $J_{6\alpha,7\beta} = 9$ Hz, $J_{6\alpha,7\alpha} = 4$ Hz). CD spectrum: $\Delta\varepsilon$ −0·16, 352 nm; $\Delta\varepsilon$ +0·12, 313 nm; $\Delta\varepsilon$ −0·37, 281 nm; $\Delta\varepsilon$ +4·08, 225 nm. For $C_{34}H_{48}O_3$ (504·8) calculated: 80·91% C, 9·95% H; found: 80·90% C, 9·54% H.

5-Methyl-19-nor-5β-cholest-9(10)-en-6β-ol (*XXI*)

A solution of the ketone *XX* (1·3 g) in triethylene glycol (65 ml) was treated with 98% hydrazine hydrate (7 ml) and potassium hydroxide (1·6 g) and heated at 140°C for 1 h. Then the tempera-

ture was allowed to rise to 200–210°C and the mixture was kept at this temperature for 3 h. After cooling off the mixture was diluted with water, the precipitated product was collected by filtration under suction, dissolved in ether and worked up as asual. The residue was chromatographed on a silica gel column (75 g) in a mixture of light petroleum and ether (9 : 1). Working up the corresponding fractions and crystallization from a mixture of acetone, methanol and water afforded the alcohol *XXI* (560 mg), m.p. 128–129°C, $[\alpha]_D^{20}$ +126° (*c* 1·9). IR spectrum: 3490, 3630 cm^{-1}. ^{1}H-NMR spectrum: 0·80 (3 H, s, 18-H), 1·05 (3 H, s, 5β-methyl), 3·5 (1 H, dd, $J_{6\alpha,7\beta}$ = 10 Hz, $J_{6\alpha,7\alpha}$ = 4 Hz). For $C_{27}H_{46}O$ (386·7) calculated: 83·87% C, 11·99% H; found: 83·81% C, 12·06% H.

5-Methyl-19-nor-5β-cholest-9(10)-en-6-one (*XXII*)

The alcohol *XXI* (100 mg) in acetone (5 ml) was treated with excess Jones' reagent at room temperature for 5 minutes. The excess oxidizing agent was destroyed with methanol, ether was added, and the mixture was washed with water, aqueous potassium hydrogen carbonate solution, water, and dried. Evaporation of the solvent afforded the noncrystalline ketone *XXII* (89 mg), IR spectrum: 1711 cm^{-1}. ^{1}H-NMR spectrum: 0·79 (3 H, s, 18-H), 1·15 (3 H, s, 5β-methyl). CD spectrum: $\Delta\varepsilon$ −1·77, 295 nm, $\Delta\varepsilon$ +0·98, 230 nm. For $C_{27}H_{44}O$ (384·6) calculated: 84·31% C, 11·53% H; found: 84·27% C, 11·49% H.

5-Methyl-19-nor-5β-cholest-9(10)-en-4β-ol 4-Acetate (*XXV*)

a) *From 5α-cholestan-4β,5-diol* (XXIV): The diol *XXIV* (5 g) was refluxed with acetic anhydride (100 ml) for 30 minutes. Finely powdered potassium hydrogen carbonate (1·5 g) was added to the stirred mixture at 90°C and the mixture was stirred for an additional 30 minutes at the same temperature. The solution was poured onto ice and pyridine, the product was allowed to stand for three hours, filtered off under suction, dissolved in ether and worked up as usual. The residue was chromatographed on a silica gel column in a mixture of light petroleum and ether (9 : 1). Working up the corresponding fractions (3·1 g) and crystallization from a mixture of acetone, ethanol and water afforded the rearranged acetate *XXV* (1·7 g), m.p. 102–103°C (literature reports[9] 95–96°C), $[\alpha]_D^{20}$ +47° (*c* 1·7) (literature reports[9] $[\alpha]_D^{20}$ +54°). IR spectrum: 1246, 1746 cm^{-1}. ^{1}H-NMR spectrum: 0·86 (3 H, s, 18-H), 1·05 (3 H, s, 5β-methyl), 4·75 (1 H, dd, $J_{4\alpha,3\beta}$ = 10 Hz, $J_{4\alpha,3\alpha}$ = 6 Hz). For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·30% C, 11·24% H.

b) *From 5α-cholestane-4β,5-diol 4-acetate* (XXIII): Finely powdered potassium hydrogen sulfate (100 mg) was added to a stirred solution of the acetate *XXIII* (100 mg) in acetic anhydride (5 ml) at 90°C and the mixture was stirred for an additional 30 minutes at the same temperature. The solution was poured onto ice and pyridine, the product was extracted with ether and worked up. The residue was chromatographed on one preparative silica gel G plate (20 × 20 cm) with a mixture of light petroleum and benzene (1 : 1), the corresponding zone was collected, the product eluted with ether and crystallized from a mixture of acetone, methanol and water to afford the rearranged product *XXV* (23 mg). Found: 81·32% C, 11·33% H.

5-Methyl-19-nor-5β-cholest-9(10)-en-4β-ol (*XXVI*)

a) A solution of acetate *XXV* (1·5 g) and potassium hydroxide (1 g) in methanol (100 ml) was refluxed for 3 h. Methanol was distilled off under reduced pressure, the residue was treated with ether and water, the organic layer was washed with water, dried and evaporated to afford the oily alcohol *XXVI* (1·4 g), $[\alpha]_D^{20}$ +56° (*c* 5·1). IR spectrum: 3460, 3627 cm^{-1}. ^{1}H-NMR spectrum:

0·79 (3 H, s, 18-H), 1·00 (3 H, s, 5β-methyl), 2·98 (1 H, dd, $J_{4\alpha,3\beta} = 10$ Hz, $J_{4\alpha,3\alpha} = 5$ Hz). For $C_{27}H_{46}O$ (386·7) calculated: 83·87% C, 11·99% H; found: 83·92% C, 12·01% H.

b) The acetate *XXV* (100 mg) in ether (20 ml) was refluxed with lithium aluminum hydride (50 mg) for 15 minutes. The mixture was decomposed with saturated aqueous sodium sulfate solution, the product extracted with ether and the ethereal solution worked up. Evaporation of the solvent afforded the noncrystalline alcohol *XXVI* (96 mg). Found: 83·90% C, 11·97% H.

5-Methyl-19-nor-5β-cholest-9(10)-en-4-one (*XXVII*)

The alcohol *XXVI* (1·5 g) in acetone (30 ml) was treated with excess Jones' reagent (2 ml) at room temperature for 5 minutes. The excess oxidizing agent was decomposed with methanol, ether was added, and the mixture was washed with water, an aqueous potassium hydrogen carbonate solution, water and dried. Evaporation of the solvent afforded the noncrystalline ketone *XXVII* (1·3 g), $[\alpha]_D^{20} + 36°$ (*c* 4·0). IR spectrum: 1 711 cm^{-1}. ^{1}H-NMR spectrum: 0·78 (3 H, s, 18-H), 1·25 (3 H, s, 5β-methyl). CD spectrum: $\Delta\varepsilon$ +1·71, 304 nm; $\Delta\varepsilon$ −5·64, 222 nm. For $C_{27}H_{44}O$ (384·7) calculated: 84·31% C, 11·53% H; found: 84·34% C, 11·52% H.

The analyses were carried out in the Analytical Laboratory of this Institute (head Dr J. Horáček). The IR and CD spectra were recorded by Mrs K. Matoušková and Mr P. Formánek and interpreted by Dr S. Vašíčková, the mass spectra by Dr A. Trka. ^{1}H-NMR *spectra were recorded by Drs M. Buděšínský, M. Synáčková and M. Masojídková.*

REFERENCES

1. Tsuda K., Kazuno T.: J. Pharm. Soc. Jap. *58*, 522 (1938).
2. Petrow V.: J. Chem. Soc. *1937*, 1077.
3. Bourdon R., Ranisteano S.: Bull. Soc. Chim. Fr. *1960*, 1982.
4. Wicha J.: Tetrahedron Lett. *1972*, 2877.
5. Hattori J.: J. Pharm. Soc. Jap. *59*, 411 (1939).
6. Coleby B., Keller M., Weiss J.: J. Chem. Soc. *1954*, 66.
7. Kirk D. N.: Tetrahedron *31*, 1299 (1975).
8. Jones D. N., Summers G. H. R.: J. Chem. Soc. *1959*, 2594.
9. Coxon J. M., Hartshorn M. P.: Tetrahedron Lett. *1969*, 105.

Translated by the author (V. Č.).