SYNTHESIS OF 5,6-CYCLOPROPANOCHOLESTANE DERIVATIVES WITH AN OXYGEN FUNCTION IN POSITION 7*

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Synthesis of the all four possible isomeric 7-hydroxy-5,6-cyclopropanocholestane derivatives is described starting from 5-cholesten-7-one and using Simmons–Smith methylenation.

In connection with our studies of solvolytic reactions of cyclosteroids we became interested in steroids carrying the cyclopropane ring in position 5,6 and an oxygen function in position 7, *i.e.* in compounds represented by formulae *XI*, *XIV*, *XVII* and *XX*.

To synthesise the olefines *IX* and *X* required for the subsequent Simmons–Smith methylenation we set out from 3β-hydroxy-5-cholesten-7-one (*I*) which was transformed to the mesylate *II*. To remove the oxygen function at $C_{(3)}$ we made use of the reaction described by Fujimoto and Tatsuno[1] in which the mesyloxy derivative is treated with zinc dust and sodium iodide. However, this reaction did not proceed as smothly as described by Kočovský and Černý[2] giving rise in our case to a mixture of three compounds – the ketones *III*, *IV* and *V*. The mutual proportion of these products may be influenced by using different solvents and the best yields of the desired product *IV* obtained in 1,2-dimethoxyethane were only about 30%. Somewhat better yields were obtained by an alternative route in which the ketone *VI* was brominated with bromine to the bromo ketones *VII* and *VIII* known from the literature[3]. On dehydrobromination with lithium salts in dimethylformamide both bromo ketones afforded the desired unsaturated ketone *IV* (the described procedures[4,5] gave unsatisfactory yields of ketone *IV*).

Metal hydride reduction of this ketone gave a mixture of the epimeric allylic alcohols *IX* and *X* from which the 7β-compound *IX* was isolated by crystallisation. The mother liquors contained according to the spectral evidence also the 7α isomer *X*. Attempts to isolate this alcohol by chromatography or crystallization from the mixture were unsuccessful. However, the epimers were easily separated after the methylene addition.

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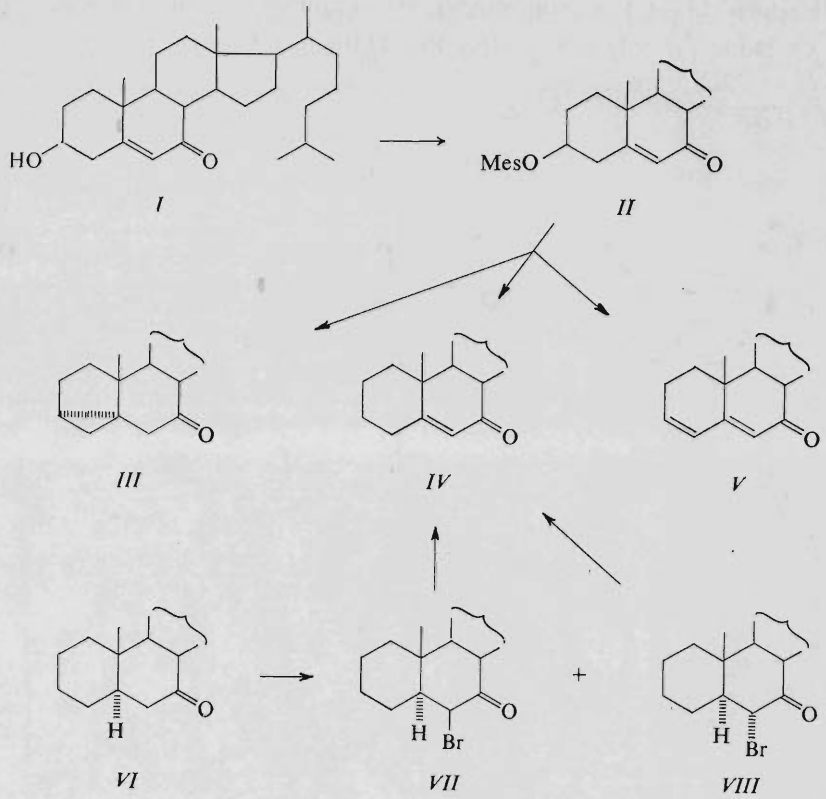
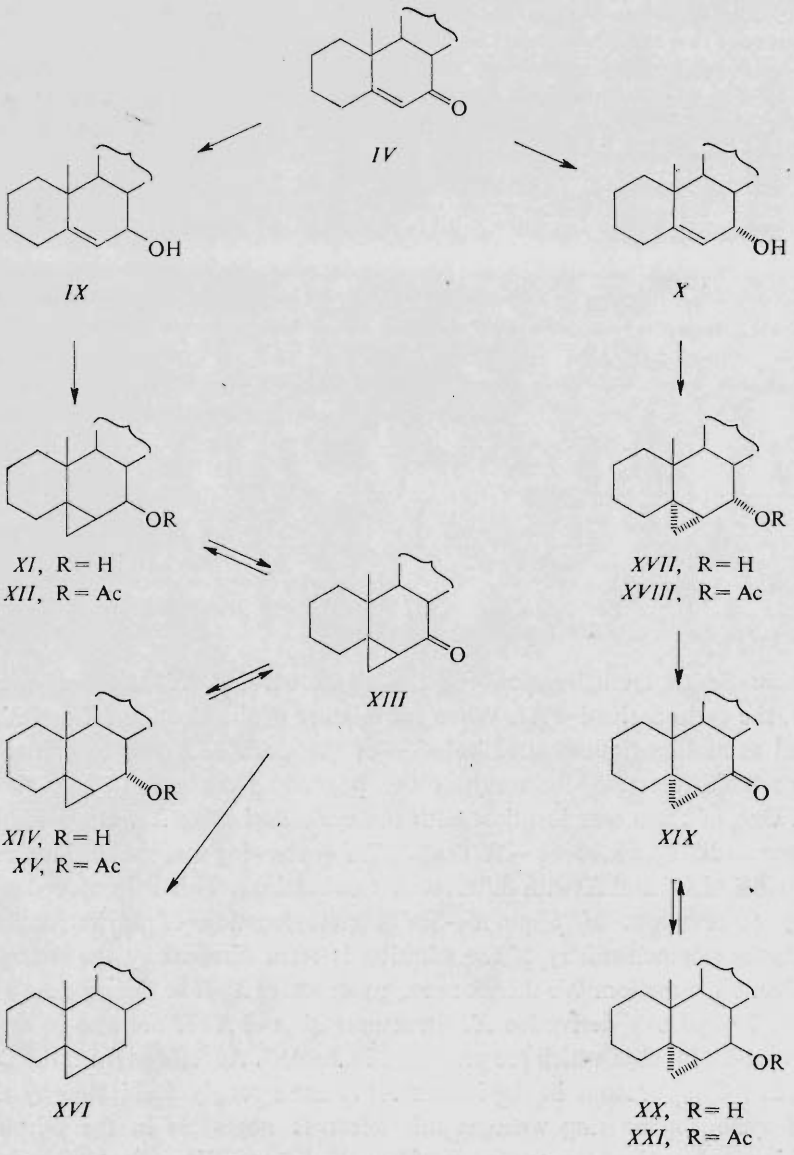


I *II* *III* *IV* *V* *VI* *VII* *VIII*

Simmons–Smith methylenation[6] of the allylic alcohol *IX* afforded one single product, the cyclo derivative *XI*. When the mixture of the alcohols *IX* and *X*, which remained as mother liquors after isolation of the alcohol *IX* was submitted to the Simmons–Smith reaction, the resulting two products were separated by chromatography. One of them was identical with the cyclo derivative *XI*. On oxidation the alcohols gave different ketones – *XIII* and *XIX* – showing that the addition proceeds in each alcohol *IX* and *X* with different stereochemistry. This is in accordance with frequent observations of Simmons–Smith methylenation of allylic alcohols[7–11] in which the stereochemistry of the addition is often directed by the configuration of the alcoholic function. We therefore assign structure *XVII* to the product obtained from the 7α-hydroxy derivative *X*. Structures *XI* and *XVII* are also in agreement with the ^{1}H-NMR data which are presented in Table I. As follows from the Dreiding models, the $C_{(19)}$ protons in the isomer *XVII* are strongly deshielded by the 5,6α situated cyclopropane ring whereas this effect is negligible in the β-isomer *XI*. In addition, removal of the oxo group from the ketone *XIII* afforded the known[12] hydrocarbon *XVI*. Hydride reduction of the ketone *XIII* gave the 7α-hydroxy deriva-

tive *XIV* as the main product along with the 7β-epimer *XI*. The isomeric ketone *XIX* afforded on reduction only one product, the 7β-alcohol *XX*. All four isomers *XI*, *XIV*, *XVII* and *XX* were also characterised as the corresponding acetates *XII*, *XV*, *XVIII* and *XXI*.



EXPERIMENTAL

Melting points were determined on a Kofler block. Optical measurements were carried out in chloroform with an error of ±3°. The infrared spectra were recorded on the Zeiss UR 20 spectrometer in tetrachloromethane. The ^{1}H-NMR spectra were recorded on the Tesla 60 MHz instrument in deuteriochloroform and corrected to tetramethylsilane. The chemical shift is given in ppm. The mass spectrum was recorded on the mass spectrometer AEI MS 902. 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. Plates with 200 × 200 × 0·7 mm silica gel were used for preparative TLC. Usual working up of a solution implies washing the solution with 5% aqueous hydrochloric acid, water, 5% aqueous potassium hydrogen carbonate solution, water, drying with sodium sulphate, and evaporation of the solvent *in vacuo*. Ligroin refers to the fraction of b.p. 40—62°C.

3β-Methanesulphonyloxy-5-cholesten-7-one (*II*)

The alcohol *I* (48 g) in pyridine (750 ml) was treated under cooling with methanesulphonyl chloride (100 ml) and allowed to stand at 5°C for 18 h. The mixture was decomposed with ice and water and the product was isolated with ether. The ethereal solution was worked up and the residue after evaporation of the solvent was crystallised from acetone–methanol to yield 40 g of the mesylate *II*, m.p. 170—180°C (decomposition), $[\alpha]_D^{20}$ −83° (*c* 6·57). IR spectrum (in chloroform): 1 673, 1 635 (C=C—C=O), 1 364, 1 337, 1 176 cm^{-1} (mesylate). ^{1}H-NMR spectrum: 0·68 (s, 18-H), 0·86 (d, J = 5·5 Hz, 26-H and 27-H), 0·91 (d, J = 5 Hz, 21-H), 1·22 (s, 19-H), 3·00 (s, 3β-mesylate), 4·55 (mt, $W_{1/2}$ = 25 Hz, 3α-H), 5·54 (s, 6-H). For $C_{28}H_{46}O_4S$ (476·7) calculated: 70·55% C, 9·30% H, 6·73% S; found: 70·19% C, 9·30% H, 6·98% S.

3α,5-Cyclo-5α-cholestan-7-one (*III*)

a) *In* 1,2-*dimethoxyethane*: 3β-Methanesulphonyloxy-5-cholesten-7-one (*II*) (1 g) in 1,2-dimethoxyethane (25 ml) was treated with sodium iodide (1 g) and zinc dust (1 g) and refluxed under stirring for 2 h. The mixture was then treated with additional sodium iodide and zinc dust (1 g each) and refluxed for 3 h. After cooling off the solids were removed by filtration and the filtrate was diluted with water. The product was extracted into ether and the ethereal solution was washed with water, dried, and the solvent was distilled off. The residue

TABLE I
Chemical shifts values (ppm) of 19-H signals

Compound	19-H	Δ
5α-Cholestan-7α-ol[a]	0·78	+0·29
5α,6α-Cyclopropano-cholestan-7α-ol (*XI*)	1·07	
5α-Cholestan-7β-ol[a]	0·81	+0·06
5β,6β-Cyclopropano-cholestan-7β-ol (*XVII*)	0·87	

[a] Calculated according to cit.[13].

was chromatographed on a silica gel column (200 g) in ligroin–ether (33 : 1). Fractions with the most lipophilic product afforded after working up 355 mg of a solid which on crystallisation from methanol gave 237 mg of the ketone *III*, m.p. 88—89°C, $[\alpha]_D^{20}$ —6° (*c* 1·00) in accordance with the literature[14]. IR spectrum: 3 060 (cyclopropane), 1 717 cm^{-1} (carbonyl), ^{1}H-NMR spectrum: 0·46 (t, $J = 3$ Hz, $J' = 5$ Hz) and 0·085 (dd, $J = 5$ Hz, $J' = 8$ Hz, cyclopropane protons), 0·67 (s, 18-H), 1·14 (s, 19-H), 0·90 (d, $J = 5$ Hz, 21-H), 0·855 (d, $J = 5·5$ Hz, 26-H and 27-H), 2·91 (d, $J = 13$ Hz, 6-H). Mass spectrum: $M^{+\cdot}$ 384. For $C_{27}H_{44}O$ (384·6) calculated: 84·31% C, 11·53% H; found: 83·59% C, 11·59% H.

b) *In diethylene glycol dimethyl ether*: The mesylate *II* (10 g) in diethylene glycol dimethyl ether (200 ml) was treated with sodium iodide (20 g) and zinc dust (20 g) and refluxed under stirring for 2 h. Working up as described ad *a*) yielded 4·4 g of *III*, m.p. 88—89°C, $[\alpha]_D^{20}$ —5° (*c* 1·13).

c) *In acetone*: The mesylate *II* (1 g) in acetone (20 ml) was refluxed under stirring with sodium iodide (2 g) and zinc dust (2 g) for 8 h. The mixture was worked up as described under *a*); yield 194 mg of *III*, m.p. 88—89, $[\alpha]_D^{20}$ —5° (*c* 1·19).

5-Cholesten-7-one (*IV*)

a) Elution of the chromatography from the foregoing experiment under *a*) with ligroin–ether (33 : 1) and working up of the corresponding fractions afforded 213 mg of a solid residue. Crystallisation from methanol yielded 146 mg of the unsaturated ketone *IV*, m.p. 130—131°C, $[\alpha]_D^{20}$ —136° (*c* 1·12) in accordance with the literature[4]. IR spectrum: 1 677, 1 631 cm^{-1} (C=C—C=O). ^{1}H-NMR spectrum: 0·86 (d, $J = 5·5$ Hz, 26-H and 27-H), 0·93 (d, $J = 5·5$ Hz, 21-H), 1·18 (s, 19-H), 0·68 (s, 18-H), 5·63 (s, $W_{1/2} = 3$ Hz, 6-H). For $C_{27}H_{44}O$ (384·7) calculated: 84·31% C, 11·53% H; found: 84·65% C, 11·80% H.

b) Elution of the chromatography from the foregoing experiment under *b*) with the same solvent mixture, working up of the corresponding fractions and crystallisation from methanol gave 3·1 g of *IV*, m.p. 130—131°C, $[\alpha]_D^{20}$ —135° (*c* 1·19).

c) Elution of the chromatography from the foregoing experiment under *c*) with the same solvent mixture afforded after working up of the corresponding fractions and crystallisation from methanol 113 mg of *IV*, m.p. 130—131°C, $[\alpha]_D^{20}$ —136° (*c* 1·11).

d) 6β-Bromo-5α-cholestan-7-one (*VII*) (1 g) in dimethylformamide (20 ml) was heated with lithium bromide (1 g) and lithium carbonate (1 g) at 140°C under nitrogen for 6 h. After cooling off the mixture was diluted with water and the product taken into ether. The ethereal solution was worked up and the residue after evaporation of the solvents was chromatographed on a silica gel column (100 g) in ligroin–ether (19 : 1). Working up of the corresponding fractions gave 710 mg of a product which was crystallised from methanol to yield 590 mg of *IV*, m.p. 130 to 131°C, $[\alpha]_D^{20}$ —138° (*c* 0·82).

e) 6α-Bromo-5α-cholestan-7-one[12] (*VIII*) (100 mg) in dimethylformamide (5 ml) was treated with lithium bromide (200 mg) and lithium carbonate (200 g) similarly as under *d*). Working up and chromatography over silica gel (20 g) gave 115 mg of a crude product. Crystallisation from methanol yielded 72 mg of *IV*, m.p. 130—131°C, $[\alpha]_D^{20}$ —132° (*c* 1·18).

3,5-Cholestadien-7-one (*V*)

a) Elution of the chromatography after isolation of the ketone *IV* under *a*) with the same solvent mixture yielded after working up of the fractions 139 mg of a crude product which was

crystallised from methanol to yield 65 mg of the dienone *V*, m.p. 110–114°C, $[\alpha]_D^{20}$ −30° (*c* 1·04) in accordance with the literature[15]. IR spectrum: 1 666, 1 628, 1 598 cm^{-1} (C=C—C=C—C=O). ^{1}H-NMR spectrum: 0·68 (s, 18-H), 0·83 (d, J = 5·5 Hz, 26-H and 27-H), 0·905 (d, J = 5·5 Hz, 21-H), 1·08 (s, 19-H), 5·59 (s, 6-H), 6·12 (s, 3-H and 4-H). For $C_{27}H_{42}O$ (382·6) calculated: 84·75% C, 11·17% H; found: 85·03% C, 11·06% H.

b) Elution of the chromatography after isolation of the ketone *IV* under *b*), working up and crystallisation gave 200 mg of *V*, m.p. 110–114°C, $[\alpha]_D^{20}$ −30° (*c* 1·14).

c) Elution of the polar component after isolation of the ketone *IV* under *c*) and crystallisation yielded 240 mg of *V*, m.p. 109–114°C, $[\alpha]_D^{20}$ −28° (*c* 1·18).

6β-Bromo-5α-cholestan-7-one (*VII*)

The ketone *VI* (1 g) in chloroform (5 ml) was treated with a solution of bromine (400 mg) in chloroform (4 ml) and allowed to stand at room temperature for 30 min. The solvent was removed *in vacuo* and the residue was chromatographed over silica gel (100 g) in ligroin–ether (49 : 1). Fractions with the lipophilic bromo ketone were combined, solvents removed and the residue (540 mg) was crystallised from methanol to yield 385 mg of the bromo ketone *VII*, m.p. 106 to 107°C, $[\alpha]_D^{20}$ +67° (*c* 1·16) in accordance with the literature[3]. IR spectrum: 1 712 cm^{-1} (carbonyl). Mass spectrum: $M^{+\cdot}$ 464. ^{1}H-NMR spectrum: 0·67 (s, 18-H), 0·845 (d, J = 5·5 Hz, 26-H and 27-H), 0·90 (d, J = 5 Hz, 21-H), 1·23 (s, 19-H), 4·06 (d, J = 2·5 Hz, 6α-H). For $C_{27}H_{45}BrO$ (465·6) calculated: 69·65% C, 9·74% H, 17·17% Br; found: 69·40% C, 9·72% H, 17·10% Br.

6α-Bromo-5α-cholestan-7-one (*VIII*)

Elution of the chromatography from the foregoing experiment with ligroin–ether (33 : 1) afforded fractions with the polar bromo ketone. Combination and evaporation of the solvents yielded a residue (627 mg) which was crystallised from chloroform–methanol to yield 350 mg of the bromo ketone *VIII*, m.p. 153–154°C, $[\alpha]_D^{20}$ −7° (*c* 1·17) in accordance with the literature[3]. IR spectrum: 1 729 cm^{-1} (carbonyl). Mass spectrum: $M^{+\cdot}$ 464. ^{1}H-NMR spectrum: 0·64 (s, 18-H), 0·84 (d, J = 5·5 Hz, 26-H and 27-H), 0·89 (d, J = 5 Hz, 21-H), 1·085 (s, 19-H), 4·57 (d, J = 12 Hz, 6β-H). For $C_{27}H_{45}BrO$ (465·6) calculated: 69·65% C, 9·74% H, 17·17% Br; found: 69·35% C, 9·68% H, 16·80% Br.

5-Cholesten-7β-ol (*IX*)

a) A solution of the ketone *IV* (800 mg) in ethyl acetate (50 ml) was treated with lithium tri-tert-butoxyaluminium hydride (1·6 g). After 1 h at room temperature the mixture was treated with 800 mg of the hydride, set aside for 4 h and poured into water, the excess hydride was decomposed with acetic acid, and the product was taken into ether. The ethereal solution was worked up, dried, and solvents removed. The residue was chromatographed on a silica gel column in ligroin–ether (19 : 1). Fractions with the alcohol *IX* were worked up to yield 635 mg of a product which crystallised from methanol only with difficulties. Yield 210 mg of the alcohol *IX*, m.p. 90–93°C, $[\alpha]_D^{20}$ −14° (*c* 1·1). Literature[5,16,17] records melting points ranging from 91 to 94°C and optical rotations between 0° to −9°. IR spectrum: 3 610, 1 674, 1 682 (inflex), 1 021, 951 cm^{-1} (C=C—C—OH). ^{1}H-NMR spectrum: 0·685 (s, 18-H), 0·86 (d, J = 5·5 Hz, 26-H and 27-H), 0·92 (d, J = 5 Hz, 21-H), 0·97 ((s, 19-H), 3·80 (mt, $W_{1/2}$ = 11 Hz, 7α-H), 5·17 (s, 6-H). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·40% C, 12·03% H.

b) A solution of the ketone *IV* (2 g) in ether (100 ml) was treated with lithium aluminium hydride (1 g) and set aside for 10 min. The excess hydride was decomposed with ethyl acetate and methanol, the mixture was then poured into 2% hydrochloric acid and the product was extracted with ether. Working up afforded 1·92 g of a product which on crystallisation from methanol gave 965 mg of the alcohol *IX*, m.p. 91—93·5°C, $[\alpha]_D^{20}$ −8° (*c* 1·15). The mother liquors (950 mg) resisted all attempts at further crystallisation or isolation of the alcohol *X*.

5·6β-Cyclopropano-5β-cholestan-7β-ol (*XI*)

a) From 5-cholesten-7β-ol (IX) *by Simmons–Smith methylenation*: Zn–Cu couple was prepared by adding zinc dust (1·3 g) into a solution of cupric acetate monohydrate (300 mg) in acetic acid (12·5 ml) at 50—60°C and shaking until the solution decolorised. Fresh acetic acid was added (12·5 ml) and the sedimented zinc was decanted with eight portions (about 15 ml each) of absolute ether. A solution of the olefin *IX* (300 mg) in ether (20 ml) was then added to the couple and refluxed under nitrogen for 1 h. The mixture was then poured into 5% sodium hydrogen carbonate, the ethereal solution was washed with 5% sodium hydrogen carbonate, water, 5% hydrochloric acid, with water, sodium hydrogen carbonate, water, 10% sodium thiosulphate, water, dried over magnesium sulphate and ether was distilled off *in vacuo*. The residue was dissolved in ether (50 ml), treated with a solution of perphthalic acid (300 mg) in ether (3 ml) and allowed to stand for 18 h. The mixture was diluted with ether, the excess peracid was extracted into 5% sodium carbonate, the ethereal solution was dried, and ether removed. The residue was chromatographed over silica gel (50 g) in ligroin–ether (9 : 1). Fractions with the lipophilic component were worked up to yield 300 mg of a product which on crystallisation from methanol afforded 190 mg of the cyclo derivative *XI*, m.p. 126—128°C, $[\alpha]_D^{20}$ +18° (*c* 4·0). IR spectrum: 3 605, 1 033, 1 018, 991 (hydroxyl), 3 070 cm^{-1} (cyclopropane). ^{1}H-NMR spectrum: −0·08 to +0·18 (q) and 0·33—0·53 (t) (cyclopropane protons), 0·63 (s, 18-H), 0·86 (d, J = 5·5 Hz, 26-H and 27-H), 0·87 (s, 19-H), 0·90 (d, J = 5 Hz, 21-H), 3·60 (mt, $W_{1/2}$ = 24 Hz, 7α-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 84·17% C, 12·16% H.

b) *From 5,6β-cyclopropano-5β-cholestan-7-one* (XIII): Elution of the chromatography after preparation of the alcohol *XIV* under *a*) with the same solvent mixture gave fractions with the polar component. Working up gave 24 mg of a product which on crystallisation from methanol yielded 6 mg of the alcohol *XI*, m.p. 123—126°C, $[\alpha]_D^{20}$ +17° (*c* 2·0).

c) *From 5,6β-cyclopropano-5β-cholestan-7β-ol 7-acetate* (XII): A solution of the acetate *XII* (100 mg) in methanol (5 ml) was treated with a solution of potassium hydroxide (400 mg) in methanol (6 ml) and refluxed for 1 h. Methanol was removed under reduced pressure, the residue was treated with water, and the product was extracted with ether. The ethereal solution was washed with water, dried, and ether removed. The residue was crystallised from methanol to yield 60 mg of the alcohol *XI*, m.p. 125—127°C, $[\alpha]_D^{20}$ +19° (*c* 1·16).

d) *From the mother liquors after crystallisation of* IX: Elution of the chromatography after isolation of the α-adduct *XVII* with the same solvent mixture afforded after working up of the fractions with the polar component 3·2 g of a product. Crystallisation from methanol gave 2·4 g of the alcohol *XI*, m.p. 124—127°C, $[\alpha]_D^{20}$ +16° (*c* 1·2).

5,6β-Cyclopropano-5β-cholestan-7β-ol 7-Acetate (*XII*)

The alcohol *XI* (200 mg) was acetylated with acetic anhydride (3 ml) in pyridine (5 ml) at room temperature for 18 h. The mixture was decomposed with ice, diluted with water, and the product was isolated with ether. Working up gave 220 mg of a crude product which on crystallisation

from methanol yielded 150 mg of the acetate *XII*, m.p. 83–84°C, $[\alpha]_D^{20}$ −38° (*c* 1·32). IR spectrum: 3 075, 3 005 (cyclopropane), 1 728, 1 259, 1 020 cm^{-1} (acetate). ^{1}H-NMR spectrum: −0·12 to +0·22 and from 0·52 (two mt, cyclopropane protons), 0·625 (s, 18-H), 0·85 (d, J = 5·5 Hz, 26-H and 28-H), 0·87 (s, 19-H), 0·885 (d, J = 5 Hz, 21-H), 2·01 (s, acetate), 4·88 (mt, $W_{1/2}$ = 23 Hz, 7α-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·53% C, 11·39% H.

5,6β-Cyclopropano-5β-cholestan-7-one (*XIII*)

a) A solution of the alcohol *XI* (300 mg) in acetone (20 ml) was treated with excess Jones' reagent and set aside for 5 min. The excess reagent was removed with methanol and after 10 min the mixture was diluted with water and the product was isolated with ether. The ethereal solution was worked up to yield 300 mg of a solid product. Crystallisation from methanol afforded 88 mg of an analytical sample of the ketone *XIII*, m.p. 109–111°C, $[\alpha]_D^{20}$ −77° (*c* 1·3). IR spectrum: 3 095, 3 012 (cyclopropane), 1 691 cm^{-1} (carbonyl), ^{1}H-NMR spectrum: 0·63 (s, 18-H), 0·86 (d, J = 5·5 Hz, 26-H and 27-H), 0·89 (d, J = 4·5 Hz, 21-H), 1·06 (s, 19-H). For $C_{28}H_{46}O$ (398·6) calculated: 84·35% C, 11·63% H; found: 84·49% C, 11·93% H.

b) The alcohol *XIV* (200 mg) in acetone (15 ml) was oxidised with excess Jones' reagent as described under *a*). Working up gave 61 mg of the analytical sample of *XIII*. The mother liquors afforded on crystallisation from methanol–water additional 102 mg of *XIII*, m.p. 108–110°C, $[\alpha]_D^{20}$ −72° (*c* 1·1).

5,6β-Cyclopropano-5β-cholestan-7α-ol (*XIV*)

a) A solution of the ketone *XIII* (150 mg) in ether (10 ml) was treated with lithium aluminium hydride (300 mg) and allowed to stand at room temperature for 15 min. The excess hydride was removed with wet ether and ethyl acetate, the ethereal solution was washed with 5% hydrochloric acid and worked up. The residue after evaporation of the solvent (150 mg) consisted of two components. Chromatography on a silica gel column (50 g) in ligroin–ether (19 : 1) gave fractions with the lipophilic component. Working up afforded 110 mg of a product which on crystallisation from methanol yielded 45 mg of the alcohol *XIV*, m.p. 74–77°C, $[\alpha]_D^{20}$ −53° (*c* 1·50). IR spectrum: 3 625 (hydroxyl), 3 075 cm^{-1} (cyclopropane). ^{1}H-NMR spectrum: −0·07 to 0·55 (mt, cyclopropane protons), 0·63 (s, 18-H), 0·86 (d, J = 5·5 Hz, 26-H and 27-H), 0·92 (s, 19-H), 0·92 (d, J = 5·5 Hz, 21-H), 3·97 (mt, $W_{1/2}$ = 6 Hz, 7β-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·55% C, 12·08% H.

b) A solution of the acetate *XV* (740 mg) in methanol (50 ml) was refluxed with a solution of potassium hydroxide (2·5 g) in methanol (5 ml) for 2 h. Methanol was removed under reduced pressure, the residue was treated with water, and the product was extracted into ether. The ethereal solution was washed with water, dried, and ether removed. The residue (580 mg) was crystallised from methanol to yield 315 mg of *XIV*, m.p. 74–77°C, $[\alpha]_D^{20}$ −52° (*c* 1·16).

5,6β-Cyclopropano-5β-cholestan-7α-ol 7-Acetate (*XV*)

The alcohol *XIV* (1 g) in pyridine (5 ml) was acetylated with acetic anhydride (3 ml) at room temperature for 18 h. The mixture was decomposed with ice and water and the product was isolated with ether. Working up afforded an oily product which was purified by filtration over silica gel in ligroin–ether (9 : 1). Crystallisation from methanol gave 720 mg of the acetate *XV*, m.p. 76–78°C, $[\alpha]_D^{20}$ −71° (*c* 2·02). IR spectrum: 3 075, 3 010 (cyclopropane), 1 731, 1 248, 1 020 cm^{-1} (acetate). ^{1}H-NMR spectrum: 0·03–0·46 (mt, cyclopropane proton), 0·62 (s, 18-H),

0·86 (d, $J = 6$ Hz, 26-J and 27-H), 0·89 (d, $J = 5·5$ Hz, 21-H), 0·90 (s, 19-H), 2·07 (s, 7α-acetate), 5·42 (mt, $W_{1/2} = 5$ Hz, 7β-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·34% C, 11·38% H; found: 81·00% C, 11·27% H.

5,6β-Cyclopropano-5β-cholestane (*XVI*)

A solution of the ketone *XIII* (100 mg) in ethylene glycol (10 ml) was refluxed with hydrazin hydrate (80%; 5 ml) for 2 h. After cooling off to room temperature the mixture was treated with a solution of potassium hydroxide (400 mg) in water (0·5 ml) and heated to 195°C for 2 h. After cooling off the mixture was poured into saturated sodium chloride solution (10 ml) and the product was taken into ether. Working up afforded a mixture of the starting material and the required hydrocarbon. Chromatography on a silica gel column (20 g) in ligroin–ether (24 : 1) afforded next to the starting *XIII* (55 mg) the lipophilic component (28 mg) which on crystallisation from methanol yielded 14 mg of the hydrocarbon *XVI*, m.p. 68—66°C, $[\alpha]_D^{20}$ −27° (*c* 1·12) in accordance with the literature[9].

5,6α-Cyclopropano-5α-cholestan-7α-ol (*XVII*)

The mother liquors after crystallisation of the alcohol *IX* (3·5 g) were submitted to the Simmons–Smith methylenation as described for the preparation of the cyclopropano derivative *XI* under *a*). Similar working up and epoxidation afforded a product which next to epoxides contained two components. It was chromatographed over silica gel (250 g) in ligroin–ether (19 : 1). Fractions with the lipophilic component gave 75 mg of a residue which after crystallisation from methanol yielded 32 mg of *XVII*, m.p. 116—117°C, $[\alpha]_D^{20}$ −105° (*c* 2·16). IR spectrum: 3 645, 3 625, 1 128, 1 054, 1 025 (hydroxyl), 3 070 cm^{-1} (cyclopropane). ^{1}H-NMR spectrum: 0·03 (dd, $J = 4$ Hz, $J' = 9·5$ Hz) and 0·28 to 0·72 (mt, cyclopropane protons), 0·62 (s, 18-H), 0·865 (d, $J = 5·5$ Hz, 26-H and 27-H), 0·92 (d, $J = 4·5$ Hz, 21-H), 1·07 (s, 19-H), 4·14 (mt, $W_{1/2} = 16$ Hz, 7β-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 84·38% C, 12·32% H.

5,6α-Cyclopropano-5α-cholestan-7α-ol 7-Acetate (*XVIII*)

The alcohol *XVII* (200 mg) was acetylated with acetic anhydride (2 ml) in pyridine (5 ml) at room temperature for 18 h. Working up and crystallisation from methanol yielded 108 mg of *XVIII*, m.p. 102—105°C, $[\alpha]_D^{20}$ −82° (*c* 2·20). IR spectrum: 3 080 (cyclopropane), 1 747, 1 250 cm^{-1} (acetate). ^{1}H-NMR spectrum (100 MHz Varian instrument): −0·06 to 0·12 and 0·30—0·52 (two mt, cyclopropane protons), 0·61 (s, 18-H), 0·87 (d, $J = 6·5$ Hz, 26-H and 27-H), 0·91 (d, $J =$ = 6 Hz, 21-H), 1·07 (s, 19-H), 2·03 (s, acetate), 4·98 (dd, $J = 6$ Hz, $J' = 7·5$ Hz, 7β-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·06% C, 11·22% H.

5,6α-Cyclopropano-5α-cholestan-7-one (*XIX*)

a) A solution of the alcohol *XVII* (800 mg) in acetone (70 ml) was treated with excess Jones' reagent and set aside for 10 min. The excess oxidising agent was removed with methanol, the mixture was diluted with water and the product was isolated with ether. The ethereal solution was worked up to yield 790 mg of a product which on crystallisation from methanol afforded 562 mg of the ketone *XIX*, m.p. 111—113°C, $[\alpha]_D^{20}$ +40° (*c* 0·78). IR spectrum: 3 085, 3 015 (cyclopropane), 1 680 cm^{-1} (carbonyl). ^{1}H-NMR spectrum: 0·67 (s, 18-H), 0·86 (d, $J = 5·5$ Hz, 26-H and 27-H), 0·90 (d, $J = 5$ Hz, 21-H), 1·02 (s, 19-H). For $C_{28}H_{46}O$ (398·6) calculated: 84·35% C, 11·63% H; found: 84·45% C, 11·45% H.

b) The alcohol *XX* (180 mg) in acetone (15 ml) was oxidised with Jones' reagent as described under *a*). Working up afforded a product (175 mg) which was crystallised from methanol to yield 115 mg of *XIX*, m.p. 110–113°C, $[\alpha]_D^{20}$ +42° (*c* 1·19).

5,6α-Cyclopropano-5α-cholestan-7β-ol (*XX*)

A solution of the ketone *XIX* (240 mg) in ether (25 ml) was treated with lithium aluminium hydride (240 mg) and set aside for 20 min. The excess hydride was decomposed with wet ether and with ethyl acetate, the solution was washed with 5% hydrochloric acid and worked up. The residue (230 mg) was filtered through a column of silica gel in ligroin–ether (9 : 1). The purified product (170 mg) was crystallised from methanol to yield 45 mg of the alcohol *XX*; the mother liquors afforded additional 61 mg of *XX*, m.p. 107–110°C, $[\alpha]_D^{20}$ −16° (*c* 2·89). IR spectrum: 3 625, 1 024 (hydroxyl), 3 070 cm^{-1} (cyclopropane). ^{1}H-NMR spectrum: −0·06 to 0·60 (mt, cyclopropane protons), 0·65 (s, 18-H), 0·86 (d, J = 6 Hz, 26-H and 28-H), 0·92 (d, J = 5 Hz, 21-H), 1·12 (s, 19-H), 3·70 (mt, $W_{1/2}$ = 8 Hz, 7α-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·52% C, 11·88% H.

5,6α-Cyclopropano-5α-cholestan-7β-ol 7-Acetate (*XXI*)

The alcohol *XX* (112 mg) in pyridine (1 ml) was acetylated with acetic anhydride (0·6 ml) at room temperature for 18 h. The mixture was decomposed with ice and water and the product was taken into ether. Working up afforded an oily residue which was purified by filtration through a silica gel column (15 g) in ligroin–ether (33 : 1). Working up of the corresponding fractions yielded 95 mg of the acetate *XXI*, which resisted all attempts at crystallisation; $[\alpha]_D^{20}$ 0° (*c* 1·54). IR spectrum: 3 070 (cyclopropane), 1 734, 1 245 cm^{-1} (acetate). ^{1}H-NMR spectrum (100 MHz-Varian instrument): 0·34 to 0·59 (mt, cyclopropane protons), 0·64 (s, 18-H), 0·86 (d, J = 6·5 Hz, 26-H and 27-H), 0·89 (d, J = 6 Hz, 21-H), 1·13 (s, 19-H), 2·04 (s, 7β-acetate), 4·74 (d, J = 6·5 Hz, 6α-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·34% C, 11·38% H; found: 81·00% C, 11·26% H.

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REFERENCES

1. Fujimoto Y., Tatsuno T.: Tetrahedron Lett. *1976*, 3325.
2. Kočovský P., Černý V.: This Journal *44*, 246 (1979).
3. Nickon A., Castle M. A., Harada R., Berkoff Ch. E., Williams R. O.: J. Amer. Chem. Soc. *85*, 2185 (1963).
4. Barton D. H. R., Robinson C. H.: J. Chem. Soc. *1954*, 3045.
5. Nickon A., Bagli J. F.: J. Amer. Chem. Soc. *83*, 1498 (1961).
6. Simmon H. E., Smith R. D.: J. Amer. Chem. Soc. *80*, 5323 (1958).
7. Dauben W. G., Berezin G. H.: J. Amer. Chem. Soc. *85*, 468 (1963).
8. Schmidt O., Prezewowsky K., Schulz G., Weichert R.: Chem. Ber. *101*, 939 (1968).
9. Gloor J., Schaffner K., Jeger O.: Helv. Chim. Acta *54*, 1864 (1971).

10. Dauben W. G., Fullerton D. S.: J. Org. Chem. *36*, 3277 (1971).
11. Amice P., Conia J. M.: C. R. Acad. Sci. Ser. C *271*, 948 (1970).
12. Kohout L., Fajkoš J.: This Journal *37*, 3490 (1972).
13. Bridgeman J. E., Cherry P. C., Clegg A. S., Evans J. M., Jones Sir Ewart R. H., Kasal A., Kumar V., Meakins G. D., Morisawa Y., Richards E. E., Woodgate P. D.: J. Chem. Soc. (C) *1970*, 250.
14. Černý V.: This Journal *38*, 1563 (1973).
15. McKenna J., Norymberski J. K., Stubbs R. D.: J. Chem. Soc. *1959*, 2502.
16. Guenard D., Beugelmans R.: Tetrahedron *32*, 781 (1976).
17. Dimroth K., Trautmann G.: Chem. Ber. *69*, 669 (1936).

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