BROMINATION OF 19-ACETOXY-4β,5-CYCLOPROPANO-5β--CHOLESTAN-3-ONE*

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Bromination of the ketone *II* with Jacques' reagent afforded the dibromo ketone *IV* and the monobromo ketone *V*. On metal hydride reduction both bromo ketones gave the isomeric bromohydrins *VIII*, *X*, and *XII* the structures of which were established by standard reactions and by spectral evidence. Dehydrohalogenation of the bromo ketone *V* yielded the unsaturated ketone *VII*.

In connection with our work on 19-hydroxylated steroids with modified skeleton we became interested in such derivatives carrying a cyclopropane ring and a double bond in the A ring of the steroid nucleus. In this paper we describe a study on bromination of 19-acetoxy-4β,5-cyclopropano-5β-cholestan-3-one (*II*) and synthesis of the unsaturated ketone *VII*.

Bromination of the ketone[1] *II* with Jacques' reagent afforded a mixture of the dibromo ketone *IV* and the monobromo ketone *V*. The latter compound was conveniently obtained also on bromination of the enol acetate *III* which was prepared from the ketone *II* on reaction with isopropenyl acetate. The structures of the bromo ketones follow from chemical as well as from spectral evidence. In the dibromo ketone *IV* the ^{1}H NMR spectrum proved the location of the bromine atoms at $C_{(2)}$. Metal hydride reduction of both bromo ketones afforded a mixture of the three bromohydrins *VIII*, *X*, and *XII*. Reduction of the dibromo ketone *IV* is therefore accompanied by reductive removal of one bromine atom, and evidently, by partial inversion at $C_{(2)}$. This follows from further reactions: The bromohydrins *X* and *XII* afforded, on Jones' oxidation, back the bromo ketone *V*, whereas the bromohydrin *VIII* was oxidized to a new bromo ketone, the 2α-isomer *XV*. This new bromo ketone when reduced with lithium tri-tert-butoxyaluminium hydride yielded again the mixture of the three bromohydrins *VIII*, *X*, and *XII*. Configurations of the hydroxy groups and the bromine atoms in these bromohydrins and in the bromo ketones was proved by standard reactions. On reductive dehalogenation with tri-n-butyltin hydride the bromohydrins *VIII* and *X* yielded the known[1] 3α-hydroxy derivative *XIV* whereas

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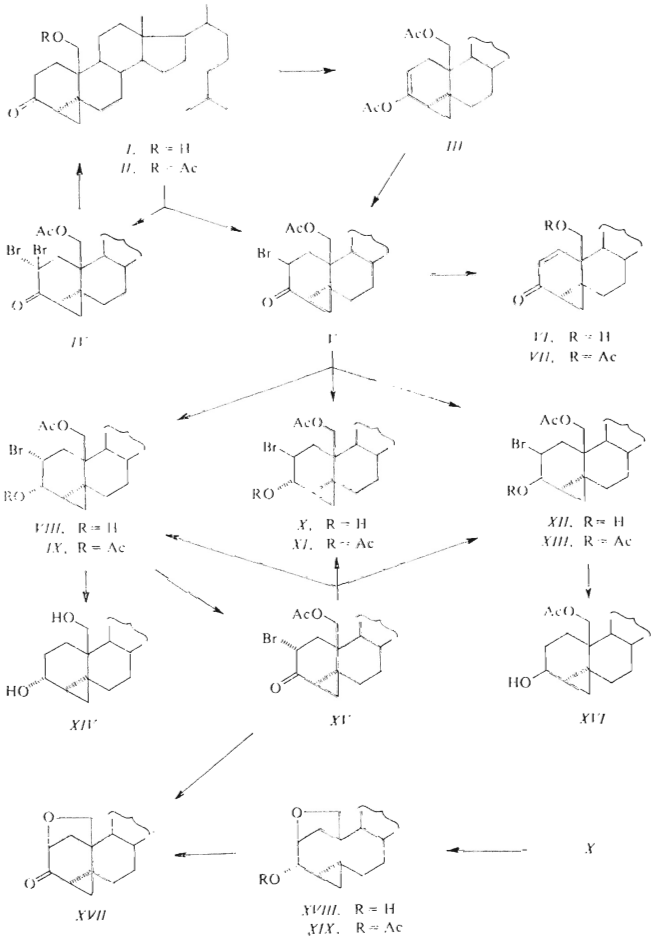
the bromohydrin *XII* afforded under similar conditions the 3β-isomer[1] *XVI*. On alkali treatment the *cis* isomers *VIII* and *XII* gave the ketone[1] *I*, the *trans* isomer *X*



however, afforded smoothly the 2β,19-epoxide *XVIII* which evidently was formed by subsequent participation of the expected 2α,3α-epoxide with the substituent at $C_{(19)}$. This is, probably, a consequence of a considerable strain in the A ring induced by annelation with the two three-membered rings. No trace of the 2α,3α-epoxide was detected. Oxidation of the alcohol *XVIII* gave the ketone *XVII* which in turn was obtained from the both bromo ketones, *V* and *XV*, with methanolic potassium hydroxide. Similar type of reactions has been observed previously[2,3]. These bromo ketones when exposed to equilibrating conditions (acetic acid–hydrobromic acid) afforded an equilibrium mixture in which the 2β-isomer *V* predominated (about 85%). This bromo ketone afforded on dehydrohalogenation with collidine the desired unsaturated ketone *VII*. ^{1}H NMR data of the bromohydrins and bromo ketones (see Experimental) suggest again that the conformation of the A ring is strongly influenced by configuration of the substituent at $C_{(2)}$ as was observed[4] in the 19-unsubstituted series.

EXPERIMENTAL

Melting points were determined on a Kofler block. Optical rotations were carried out in chloroform with an error of ±3°. The infrared spectra were recorded on a Zeiss UR 20 spectrometer in tetrachloromethane. The CD spectra were recorded on a Roussel-Jouan CD-185 spectrometer in methanol. The ^{1}H NMR spectra were recorded at 200 MHz on a Varian XL-200 instrument in deuteriochloroform. Tetramethylsilane was used as internal standard. The chemical shifts are given on δ-scale. The identity of samples was checked by mixture melting point determination, by thin-layer chromatography (TLC) and by spectral evidence. Usual working-up of a solution implies washing the solution with 5% aqueous hydrochloric acid, water, 5% aqueous sodium hydrogen carbonate, water, drying over magnesium sulphate, and evaporation of the solvent under reduced pressure. Ligroin refers to the fraction of b.p. 40–60 °C.

19-Hydroxy-4β,5-cyclopropano-5β-cholestan-3-one (*I*)

a) A solution of the bromohydrin *VIII* (80 mg) in methanol (15 ml) was heated with a solution of potassium hydroxide (80 mg) in methanol (3 ml) for 1 h at 45°C. The reaction mixture was diluted with water and the product was washed with water, dried, and the solvent was distilled off. Crystallisation from ethyl acetate gave 35 mg of the ketone *I*, m.p. 190–191°C, $[\alpha]_D^{20}$ + 75° (*c* 1·4), identical with the authentic sample[1].

b) The bromohydrin *XII* (60 mg) was treated with potassium hydroxide (50 mg) similarly as described above. Working up and crystallisation from ethyl acetate yielded 25 mg of the ketone *I*, m.p. 191–192°C, $[\alpha]_D^{20}$ + 75° (*c* 1·0).

19-Acetoxy-4β,5-cyclopropano-5β-cholestan-3-one (*II*)

The dibromo ketone *IV* (100 mg) in benzene (2 ml) was treated with a molar benzene solution of tri-n-butyltin hydride (0·5 ml) and refluxed under the presence of azobisisobutyronitrile (5 mg) for 45 min. The mixture was adsorbed on a silica gel column (6 g) and the product was eluted with benzene. Working up of the corresponding fractions and crystallisation from methanol

afforded 32 mg of the ketone *II*, m.p. 83–85°C, $[\alpha]_D^{20}$ +87° (*c* 1·1), identical with the authentic sample[1].

3,19-Diacetoxy-4β,5-cyclopropano-5β-cholest-2-ene (*III*)

The ketone *II* (3·5 g) was dissolved in isopropenyl acetate (70 ml), conc. sulphuric acid was added (3 drops), and about 35 ml of the distillate were collected in the course of 2 h. Fresh isopropenyl acetate and suluhuric acid were added and about 60 ml were distilled off within 2 h. The residual reagent was removed under reduced pressure and the product was taken into ligroin. The solution was washed with a sodium hydrogen carbonate solution, dried, and the crude enol acetate was chromatographed over silica gel (150 g) in ligroin–ether (4 : 1). Working up of the corresponding fractions afforded 3·4 g of the oily diacetate *III*, $[\alpha]_D^{20}$ +34° (*c* 1·4). For $C_{32}H_{50}O_4$ (498·7) calculated: 77·06% C, 10·11% H; found: 76·82% C, 10·05% H.

19-Acetoxy-2,2-dibromo-4β,5-cyclopropano-5β-cholestan-3-one (*IV*)

The ketone *II* (1 g) in tetrahydrofuran (15 ml) was treated with Jacques' reagent (1·2 g) and allowed to stand for 25 min. The mixture was poured in 5% sodium hydrogen carbonate and the product was extracted with ether. The ethereal solution was washed with 5% sodium thiosulphate, water, dried, and ether was removed. The residue consisted according to the TLC of the bromo ketones *IV* and *V*. It was chromatographed on a silica gel column (100 g) in ligroin–ether (9 : 1). Fractions with the polar component were combined, solvents removed, and the residue was crystallised from methanol to yield 420 mg of the dibromo ketone *IV*, m.p. 112–113°C, $[\alpha]_D^{20}$ +105° (*c* 1·2). IR spectrum: 3 020 (cyclopropane), 1 747, 1 237, 1 223, 1 039 (acetate), 1 707 cm^{-1} (carbonyl). ^1H NMR spectrum: 0·68 (s, 18-H), 2·11 (s, acetate), 3·44 and 3·25 (two d, J_{gem} = −17·2 Hz, 1-H), 3·92 and 4·56 (two d, J_{gem} = −11·7 Hz, 19-H). For $C_{30}H_{46}Br_2O_3$ (614·5) calculated: 58·63% C, 7·54% H, 26·01% Br; 59·22% C, 7·76% H, 26·22% Br.

19-Acetoxy-2β-bromo-4β,5-cyclopropano-5β-cholestan-3-one (*V*)

a) Fractions with the lipophilic component from the foregoing experiment afforded after working up and crystallisation from methanol 135 mg of the bromo ketone *V*, m.p. 88–89°C, $[\alpha]_D^{20}$ +64° (*c* 1·3). IR spectrum: 3 095, 3 025 (cyclopropane), 1 748, 1 239, 1 041 (acetate), 1 703 cm^{-1} (carbonyl). CD spectrum: $\Delta\varepsilon_{308}$ +2·07. ^1H NMR spectrum: 0·67 (s, 18-H), 2·11 (s, acetate), 2·23 (dd, J_{gem} = −14·9 Hz, 1β-H), 2·38 (dd, 1α-H), 4·03 and 4·64 (two d, J_{gem} = = −11·5 Hz, 19-H), 4·18 (ddd, $J_{2\alpha,1\beta}$ = 12 Hz, $J_{2\alpha,1\alpha}$ = 8·0 Hz, $J_{2\alpha,4\alpha}$ = 1·2 Hz, 2α-H). For $C_{30}H_{47}BrO_3$ (535·6) calculated: 67·28% C, 8·84% H, 14·92% Br; found: 67·56% C, 9·12% H, 14·90% Br.

b) The enol acetate *III* (4·6 g) in tetrachloromethane (80 ml) was treated dropwise under stirring with a solution of bromine (0·51 ml) in tetrachloromethane (30 ml) at 0°C. The reaction mixture was washed with 5% sodium thiosulphate, 5% sodium hydrogen carbonate, water, and dried. The residue after evaporation of the solvent was chromatographed over silica gel (300 g) in ligroin–ether (9 : 1). Working up of the corresponding fractions and crystallisation from ether–methanol gave 3·2 g of the bromo ketone *V*, m.p. 90–92°C, $[\alpha]_D^{20}$ +64° (*c* 1·4).

c) The bromohydrin *X* (100 mg) in acetone (10 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 10 min. The excess oxidizing agent was removed with methanol, the mixture was diluted with water, and the product was taken into ethyl acetate. Usual working up and crystallisation from ether–methanol gave 45 mg of the bromo ketone *V*, m.p. 88–90°C, $[\alpha]_D^{20}$ +63° (*c* 1·1).

d) The bromohydrin *XII* (95 mg) was oxidized with Jones' reagent as described in the foregoing experiment. Similar working up and crystallisation from ether–methanol gave 50 mg of the bromo ketone *V*, m.p. 90–92°C, $[\alpha]_D^{20}$ +63° (*c* 1·2).

e) A solution of the bromo ketone *XV* (200 mg) in acetic acid (10 ml) was treated with 45% hydrobromic acid (0·2 ml) and allowed to stand at room temperature for 2 h. The mixture was diluted with water and the product was isolated with ether. The ethereal solution was washed with 5% sodium thiosulphate, 5% sodium hydrogen carbonate, water, dried, and ether was removed. The residue contained about 85% of the ketone *V* and 15% of the starting ketone *XV*. The mixture was separated on a silica gel column (25 g) in ligroin–ether (9 : 1). Fractions with the lipophilic component were combined, solvents removed, and the residue was crystallised from ether–methanol to yield 145 mg of the bromo ketone *V*, m.p. 89–90°C, $[\alpha]_D^{20}$ +61° (*c* 1·5).

f) The bromo ketone *V* (200 mg) was treated with hydrobromic acid as described above to yield similar mixture of the isomeric bromo ketones *V* and *XV*. Separation afforded 150 mg of the starting bromo ketone *V*.

19-Hydroxy-4β,5-cyclopropano-5β-cholest-1-en-3-one (*VI*)

The acetate *VII* (100 mg) in methanol (20 ml) was hydrolysed with potassium hydroxide (100 mg) in methanol (5 ml) at room temperature for 2 h. The excess alkali was removed with acetic acid and solvents were distilled off *in vacuo*. The residue was taken into ethyl acetate, the extract was washed with 5% sodium hydrogen carbonate, water, dried, and solvent removed. The residue was crystallised from methanol to yield 45 mg of the alcohol *VI*, m.p. 186–188°C, $[\alpha]_D^{20}$ +248°. (*c* 1·5). IR spectrum: 3 630 (hydroxyl), 1 668, 1 610 cm^{-1} (carbonyl). For $C_{28}H_{44}O_2$ (412·6) calculated: 81·50% C, 10·75% H; found: 81·31% C, 10·61% H.

19-Acetoxy-4β,5-cyclopropano-5β-cholest-1-en-3-one (*VII*)

A solution of the bromo ketone *V* (1·6 g) in *sym*-collidine (40 ml) was refluxed for 8 h. Collidine was distilled off under reduced pressure, the residue was diluted with water, and the product was taken into ether. Usual working up afforded about 1 g of a mixture of the starting bromo ketone and the desired olefin. It was chromatographed on a silica gel column (200 g) in ligroin–ether (9 : 1). Fractions with the lipophilic component gave 450 mg of the starting material. Further elution yielded after working up 370 mg of a crude product which after crystallisation from methanol gave 270 mg of the olefin *VII*, m.p. 98–100°C, $[\alpha]_D^{20}$ +226° (*c* 1·4). IR spectrum: 3 090, 3 010 (cyclopropane), 3 035 (C=C), 1 745, 1 239, 1 230, 1 045 (acetate), 1 676, 1 620 cm^{-1} (carbonyl). ^1H NMR spectrum: 0·68 (s, 18-H), 2·06 (s, acetate), 4·35 and 4·74 (two d, $J_{gem} = -11·5$ Hz. 19-H), 5·80 (dd, $J_{2,4\alpha} = 1·5$ Hz, 2-H), 6·59 (d, $J_{1,2} = 10·6$ Hz, 1-H). For $C_{30}H_{46}O_3$ (454·7) calculated: 79·24% C, 10·20% H; found: 79·27% C, 10·24% H.

2α-Bromo-4β,5-cyclopropano-5β-cholestane-3α,19-diol 19-Acetate (*VIII*)

a) The bromo ketone *V* (2 g) in tetrahydrofuran (30 ml) was treated with lithium tri-tert-butoxyaluminium hydride (4 g) and allowed to stand at room temperature for 2 h. The excess hydride was decomposed with acetic acid, the mixture was diluted with water, and the product was taken into ether. Usual working up afforded a mixture of the bromohydrins *VIII*, *X*, and *XII*, in which the compound *X* predominated. The mixture was separated on a silica gel column (200 g) in ligroin–ether (13 : 1). Fractions with the most lipophilic component were worked up and the product was crystallised from methanol to afford 220 mg of the bromohydrin *VIII*, m.p. 140–142°C.

$[\alpha]_D^{20}$ +42° (*c* 1·3). IR spectrum: 3 580 (hydroxyl), 3 095, 3 075, 3 010 (cyclopropane), 1 745, 1 236 cm^{-1} (acetate). For $C_{30}H_{49}BrO_3$ (537·6) calculated: 67·01% C, 9·18% H, 14·86% Br; found: 66·90% C, 9·01% H, 14·59% Br.

b) The bromo ketone *XV* (1 g) afforded on reduction with lithium tri-tert-butoxyaluminium hydride (2 g) in tetrahydrofuran (20 ml) similar mixture of the three bromohydrins like the epimeric bromohydrin *V* in the foregoing experiment. Working up, chromatography, and crystallisation from methanol gave 100 mg of the bromohydrin *VIII*, m.p. 140–141°C, $[\alpha]_D^{20}$ +43° (*c* 1·1).

c) Reduction of the dibromo ketone *IV* (750 mg) under analogous conditions as described above gave again the mixture of the three bromohydrins, however, with the isomer *VIII* predominating. Chromatography and crystallisation from methanol gave 400 mg of the bromo ketone *VIII*, m.p. 141–143°C, $[\alpha]_D^{20}$ +40° (*c* 1·2).

3α,19-Diacetoxy-2α-bromo-4β,5-cyclopropano-5β-cholestane (*IX*)

The bromohydrin *VIII* (80 mg) in pyridine (1 ml) was acetylated with acetic anhydride (0·4 ml) at room temperature for 20 h. The acetylation mixture was decomposed with ice, diluted with water, and the product was extracted with ether. Usual working up and crystallisation from methanol yielded 55 mg of the acetate *IX*, m.p. 130–131°C, $[\alpha]_D^{20}$ +78° (*c* 1·3). ^{1}H NMR spectrum: 0·32 (dd, $J_{cycl.,4\alpha}$ = 9·2 Hz, J_{gem} = −6 Hz, cyclopropane), 0·69 (s, 18-H), 2·09 and 2·18 (two s, acetates), 3·99 and 4·36 (two d, J_{gem} = −11·2 Hz, 19-H), 4·21 (mt, $J_{2\beta,1\alpha}$ = 11·4 Hz, $J_{2\beta,1\beta}$ = = 7·4 Hz, $J_{2\beta,3\beta}$ = 2·6 Hz, 2β-H), 5·43 (t, $J_{3\beta,4\alpha}$ = 3·3 Hz, 3β-H).

2β-Bromo-4β,5-cyclopropano-5β-cholestane-3α,19-diol 19-Acetate (*X*)

Elution of the chromatography after isolation of the bromohydrin *VIII* under *a*) afforded fractions with the product of medium polarity. Working up gave 1·1 g of the oily, TLC pure bromohydrin *X*. Similarly, from the experiment under *b*) 420 mg and under *c*) 110 mg of the bromohydrin *X* were obtained; $[\alpha]_D^{20}$ 0° (*c* 1·6). IR spectrum: 3·585 (hydroxyl), 3 060 (cyclopropane), 1 743, 1 239 cm^{-1} (acetate). For $C_{30}H_{49}BrO_3$ (537·6) calculated: 67·01% C, 9·18% H, 14·86% Br; found: 67·12% C, 8·93% H, 14·66% Br.

3α-19-Diacetoxy-2β-bromo-4β,5-cyclopropano-5β-cholestane (*XI*)

The bromohydrin *X* (100 mg) was acetylated with acetic anhydride (0·5 ml) in pyridine (1 ml) 20 h at room temperature. Usual working up afforded 95 mg of the oily acetate *XI*, $[\alpha]_D^{20}$ +32° (*c* 1·2). ^{1}H NMR spectrum: 0·49 and 0·72 (two dd, $J_{cycl.,4\alpha}$ = 12·0 Hz, $J_{cycl.,4\alpha}$ = 5·4 Hz, J_{gem} = = −7·5 Hz (cyclopropane protons), 0·67 (s, 18-H), 2·08 and 2·15 (two s, acetates), 4·02 and 4·49 (two d, J_{gem} = −11·5 Hz, 19-H), 4·14 (mt, $J_{2\alpha,1\beta}$ = 14·0 Hz, $J_{2\alpha,1\alpha}$ = 4·2 Hz, $J_{2\alpha,3\beta}$ = 8·5 Hz, 2α-H), 5·13 (d, 3β-H). For $C_{32}H_{51}BrO_4$ (578·6) calculated: 66·41% C, 8·71% H, 13·81% Br; found: 66·29% C, 8·50% H, 13·53% Br.

2β-Bromo-4β,5-cyclopropano-5β-cholestane-3β,19-diol 19-Acetate (*XII*)

Elution of the chromatographic columns from the three experiments after isolation of the bromohydrin *VIII* yielded fractions with the most polar component. Working up and crystallisation from methanol gave 210 mg of the bromo ketone *XII* from the first experiment (under *a*), 105 mg from the second experiment (under *b*) and 93 mg from the third one (under *c*); m.p. 95–96°C,

$[\alpha]_D^{20} -32°$ (*c* 1·3). IR spectrum: 3 562 (hydroxyl), 3 075 (cyclopropane), 1 743, 1 239, 1 038 cm^{-1} (acetate). For $C_{30}H_{49}BrO_3$ (537·6) calculated: 67·01% C, 9·18% H, 14·86% Br; found: 67·08% C, 8·96% H, 14·98% Br.

3β,19-diacetoxy-2β-bromo-4β,5-cyclopropano-5β-cholestane (*XIII*)

The bromohydrin *XII* (50 mg) was acetylated with acetic anhydride (0·3 ml) in pyridine (0·7 ml) for 20 h at room temperature. Usual working up and crystallisation from methanol afforded 35 mg of the diacetate *XIII*, m.p. 124—126°C, $[\alpha]_D^{20} -60°$ (*c* 1·1). ^1H NMR spectrum: 0·31 (dd, $J_{cycl.,4\alpha} = 9·4$ Hz, $J_{gem} = -5·6$ Hz, one cyclopropane proton), 0·68 (s, 18-H), 2·09 and 2·12 (two s, acetates), 4·05 and 4·38 (two d, $J_{gem} = -11·4$ Hz, 19-H), 4·43 (mt, $J_{2\alpha,1\beta} = 13·0$ Hz, $J_{2\alpha,1\alpha} = 3·5$ Hz, 2α-H), 5·33 (dd, $J_{3\alpha,2\alpha} = 5·1$ Hz, $J_{3\alpha,4\alpha} = 7·9$ Hz, 3α-H). For $C_{32}H_{51}BrO_4$ (578·6) calculated: 66·41% C, 8·71% H, 13·81% Br; found: 66·25% C, 8·59% H, 13·40% Br.

4β,5-Cyclopropano-5β-cholestane-3α,19-diol (*XIV*)

The bromohydrin *VIII* (200 mg) in benzene (4 ml) was treated with a molar solution of tri-n-butyltin hydride (1 ml) and refluxed under the presence of azobisisobutyronitrile for 45 min. The mixture was filtered through a silica gel column and the product was eluted with benzene. Evaporation of the solvent afforded about 130 mg of an oily product which was dissolved in methanol (5 ml) and refluxed for 30 min with a solution of potassium hydroxide (50 mg) in methanol (2 ml). The excess alkali was removed with acetic acid and solvents were distilled off under reduced pressure. The residue was diluted with water and the product was isolated with ether. Usual working up and crystallisation from methanol gave 96 mg of the diol *XIV*, m.p. 199—201°C, $[\alpha]_D^{20} +32°$ (*c* 1·4) in accordance with the literature[1] and identical with the authentic sample.

19-Acetoxy-2α-bromo-4β,5-cyclopropano-5β-cholestan-3-one (*XV*)

The bromohydrin *VIII* (100 mg) in acetone (10 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 10 min. Methanol was added to remove the excess reagent, the mixture was diluted with water, and the product was isolated with ether. Usual working up and crystallisation from methanol afforded 65 mg of the bromo ketone *XV*, m.p. 124—125°C, $[\alpha]_D^{20} +76°$ (*c* 1·5). IR spectrum: 3 095, 3 025 (cyclopropane), 1 746 (acetate), 1 702 cm^{-1} (carbonyl). CD spectrum: $\Delta\varepsilon_{283} +3·43$. ^1H NMR spectrum: 0·68 (s, 18-H), 2·09 (s, acetate), 2·47 (dd, $J_{gem} = -17·4$ Hz, 1α-H), 2·63 (dd, 1β-H), 3·99 and 4·59 (two d, $J_{gem} = -11·5$ Hz, 19-H), 4·55 (dd, $J_{2\beta,1\beta} = 8·5$ Hz, $J_{2\beta,1\alpha} = 1·6$ Hz, 2β-H). For $C_{30}H_{47}BrO_3$ (535·6) calculated: 67·28% C, 8·84% H, 14·92% Br; found: 66·98% C, 8·85% H, 15·30% Br.

4β,5-Cyclopropano-5β-cholestane-3β,19-diol 19-Acetate (*XVI*)

The bromohydrin *XII* (50 mg) in benzene (2 ml) was treated with a molar solution of tri-n-butyltin hydride (0·3 ml) in benzene ad refluxed with azobisisobutyronitrile (5 mg) for 1 h. The mixture was worked up as described for the preparation of the 3α-isomer *XIV* and the product was crystallised from methanol to yield 20 mg of the diol monoacetate *XVI*, m.p. 91—93°C, $[\alpha]_D^{20} +10°$ (*c* 1·2), identical with the authentic sample[1].

2β,19-Epoxy-4β,5-cyclopropano-5β-cholestan-3-one (*XVII*)

a) The bromo ketone *V* (200 mg) in methanol (50 ml) was treated with a solution of potassium hydroxide (200 mg) in methanol (20 ml) and allowed to stand at 25°C for 4 h. The alkali was

removed with acetic acid and the solvent was distilled off under reduced pressure. The product was isolated with ether in the usual way and the residue after evaporation of ether was chromatographed on a silica gel column (15 g) in ligroin–ether (9 : 1). Working up of the corresponding fractions yielded 110 mg of a crude product which after crystallisation from methanol afforded 70 mg of the epoxide *XVII*, m.p. 101—102°C, $[\alpha]_D^{20}$ −4° (*c* 1·2). IR spectrum: 3 090 (cyclopropane), 1 708 (carbonyl), 1 240, 1 121, 1 028, 909 cm^{-1} (epoxide). ^1H NMR spectrum: 0·65 (s, 18-H), 1·80 (d, J_{gem} = −12·1 Hz, 1β-H), 2·39 (dd, 1α-H), 3·65 and 3·84 (two d, J_{gem} = −7·7 Hz, 19-H), 4·12 (dd, $J_{2\alpha,1\beta}$ = 6·6 Hz, $J_{2\alpha,4\alpha}$ = 0·8 Hz, 2α-H). For $C_{28}H_{44}O_2$ (412·6) calculated: 81·50% C, 10·75% H; found: 81·40% C, 10·70% H.

b) The bromo ketone *XV* (200 mg) was treated with potassium hydroxide as described in the previous experiment. Similar working up and crystallisation from methanol afforded 90 mg of the epoxide *XVII*, m.p. 101—103°C, $[\alpha]_D^{20}$ −5° (*c* 1·6).

c) A solution of the alcohol *XVIII* (50 mg) in acetone (5 ml) was oxidized with excess Jones' reagent for 10 min at room temperature. Methanol was added the mixture was diluted with water and the product was isolated with ether as usual. Crystallisation from methanol yielded 30 mg of the ketone *XVII*, m.p. 101—102°C, $[\alpha]_D^{20}$ −4° (*c* 1·1).

2β,19-Epoxy-4β,5-cyclopropano-5β-cholestan-3α-ol (*XVIII*)

A solution of the bromohydrin *X* (200 mg) in methanol (20 ml) was heated for 1 h at 45°C with a solution of potassium hydroxide (200 mg) in methanol (5 ml). The mixture was diluted with water and the product was taken into ethyl acetate. Usual working up, chromatography over silica gel (15 g) in ligroin–ether (4 : 1) and crystallisation from ethyl acetate yielded 80 mg of the alcohol *XVIII*, m.p. 188—189°C, $[\alpha]_D^{20}$ −72° (*c* 1·1). IR spectrum: 3 065, 3 010 (cyclopropane), 3 630, 3 370, 3 320 (hydroxyl), 1 101 cm^{-1} (epoxide). Mass spectrum: M^+ 414. For $C_{28}H_{46}O_2$ (414·6) calculated: 81·10% C, 11·18% H; found: 80·95% C, 10·90% H.

2β,19-Epoxy-4β,5cyclopropano-5β-cholestan-3α-ol 3-Acetate (*XIX*)

The alcohol *XVIII* (60 mg) was acetylated with acetic anhydride (0·3 ml) in pyridine (1 ml) at room temperature for 20 h. Usual working up yielded a product which was chromatographed on silica gel column (10 g) in ligroin–ether (19 : 1). Working up of the corresponding fractions and crystallisation from methanol gave 35 mg of the acetate *XIX*, m.p. 165—166°C, $[\alpha]_D^{20}$ −37° (*c* 1·1). For $C_{30}H_{48}O_3$ (456·7) calculated: 78·90% C, 10·59% H; found: 78·79% C, 10·48% H.

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