THE BROMINATION OF THE EPIMERIC 4,5-CYCLOPROPANOCHOLESTAN-3-ONES*

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Bromination of the epimeric 4,5-cyclopropanocholestan-3-ones *I* and *XIII* has been studied and structures of the products were established by chemical and spectral means. Conformation of the A ring in the bromo ketones and bromohydrins is discussed on the basis of spectral evidence.

In the course of our studies of steroid cyclopropane derivatives we became interested in stereochemistry of these compounds. Models suggest that in the 4,5-cyclopropano steroids, and especially in the β-series, the A ring is sufficiently flexible to adopt different conformations when they are enforced by proper substitution. In this paper we present our studies on bromination of the epimeric 4,5-cyclopropanocholestan-3-ones *I* and *XIII* and on conformation of the A ring in the bromo derivatives obtained during these studies.

Bromination of the ketone[1] *I* was carried out with Jacques' reagent in tetrahydrofuran and with bromine in acetic acid. Both methods gave mixtures of the same compounds (bromo ketones *II*, *III*, and *IV*) but their proportions were different for each method. With Jacques' reagent the dibromoketone *II* was formed as the main product and only very little of the bromo ketone *III* was obtained. On the other hand, this bromo ketone – product of the cleavage of the cyclopropane ring – represented the main component in the mixture resulting on bromination with bromine in acetic acid. The structures of these products follow from spectral as well as from chemical evidence: On dehalogenation with tri-n-butyltin hydride the bromo ketones *II* and *IV* yielded the starting ketone *I*, whereas the dibromo derivative *III* afforded under similar conditions the known[2] 5-methyl-5α-cholestan-3-one (*XXIX*). This proves that the cyclopropanocholestane skeleton remained unchanged in the bromo ketones *II* and *IV* in contrast to the bromo ketone *III* where the cyclopropane ring underwent cleavage with the hydrobromic acid present in the bromination reaction mixture. To prove the position and the configuration of the bromine atom in the bromo ketone *IV* it was reduced to the bromohydrin *VIII* which on oxidation with Jones' reagent

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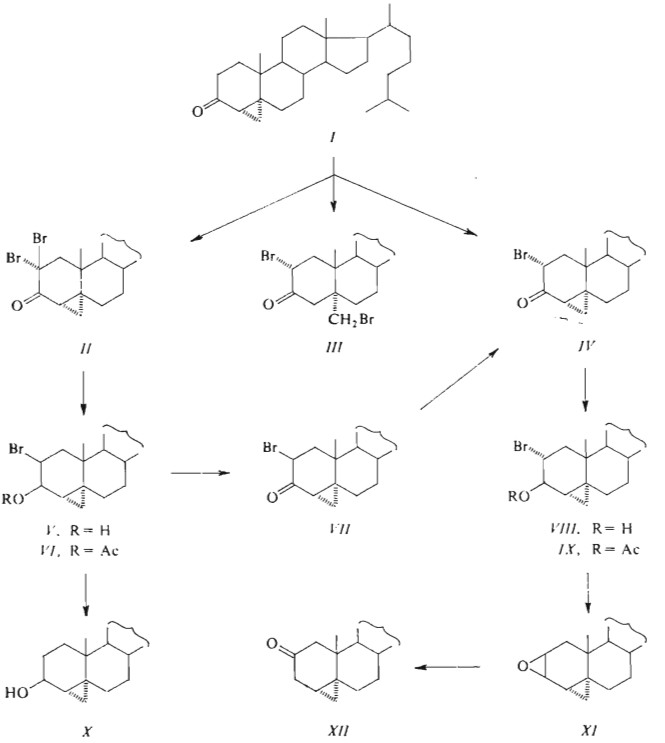
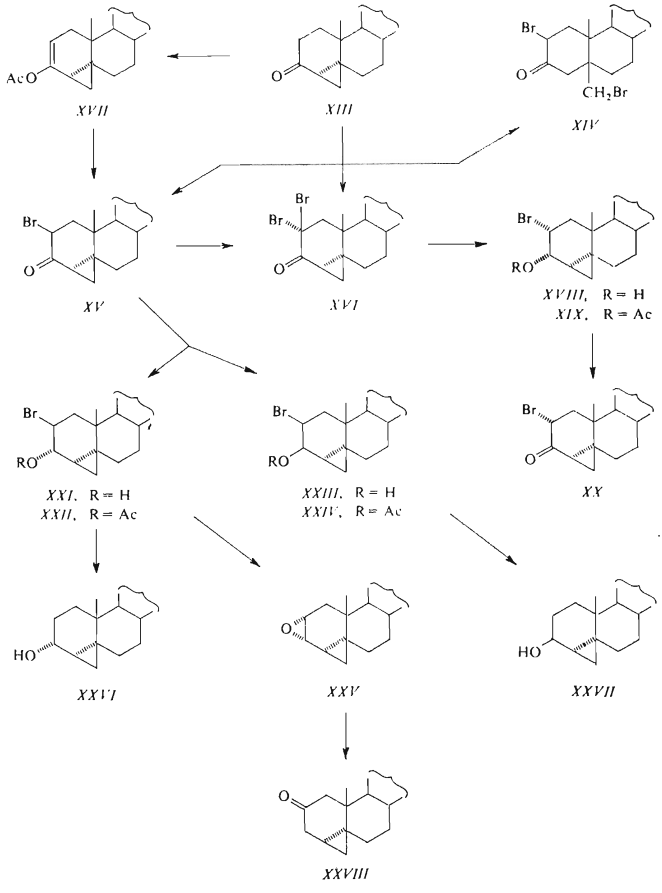
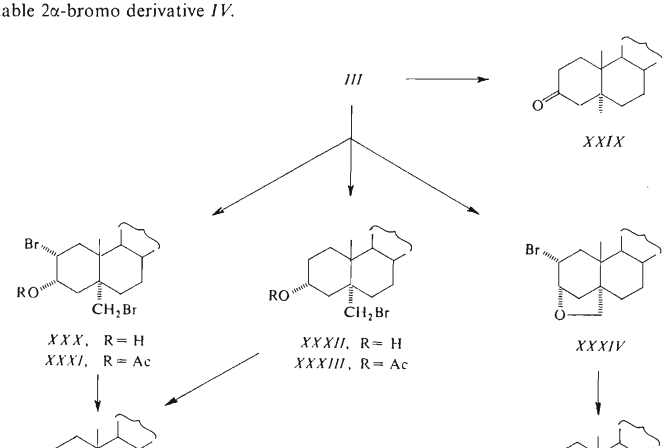
afforded back the starting bromo ketone *IV*. The configuration of the bromine atom therefore remained unchanged during the hydride reduction. Removal of the bromine atom in this bromohydrin gave the known[3] 3β-hydroxy derivative *X* and treatment with methanolic potassium hydroxide gave rise to the epoxide *XI*. We may therefore conclude that the bromine atom and the hydroxy group in the bromohydrin *VIII* have mutual *trans* orientation and the bromine atom has 2α- and the hydroxyl 3β-configuration. In the epoxide *XI* the oxygen ring must also be β-oriented. This epoxide is extremely unstable and even a short contact with silica gel causes rearrangement to the ketone *XII*.



In the dibromo derivative *II* the both bromine atoms are, according to the spectral evidence, attached to the carbon atom 2. Reduction with lithium tri-tert-butoxyaluminium hydride was accompanied by loss of one bromine atom to yield the bromo-



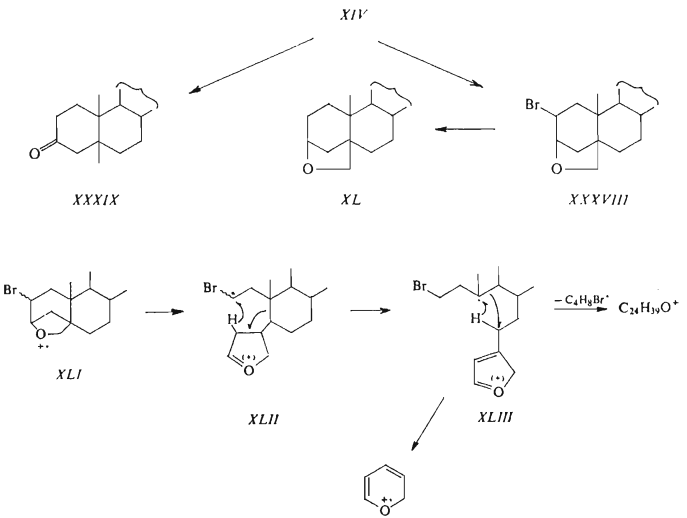
hydrin *V*. Dehalogenation afforded again the 3β-alcohol[3] *X* but alkali treatment led to the ketone *I*. This proves the structure of this bromohydrin as a 2β-bromo-3β-ol. Jones' oxidation yielded the bromo ketone *VII* which proved to be the thermodynamically unstable isomer and under enolising conditions isomerised readily to the stable 2α-bromo derivative *IV*.



When the dibromo ketone *III* was reduced under analogous conditions a mixture of three compounds resulted: One dibromo and two monobromo derivatives. On oxidation the dibromo derivative yielded the starting dibromo ketone *III* and acetylation gave an acetate with axial proton at $C_{(2)}$ and equatorial proton at $C_{(3)}$ (see experimental part). This points to structure *XXX* for the product of reduction and to structure *XXXI* for the corresponding acetate. Dehalogenation afforded the acetate *XXXVI* which after hydrolysis to the alcohol *XXXV* and oxidation gave the known[2] ketone *XXIX*. This ketone on metal hydride reduction yielded a mixture of the alcohols epimeric at $C_{(3)}$ containing about 90% of the axial 3α-isomer *XXXV*. Evidently, the steric influence of the 5α-methyl group is responsible for this anomalous course of reduction[4]. The second product obtained from the dibromo ketone *III* with lithium tri-tert-butoxyaluminium hydride contained one bromine atom and after acetylation and dehalogenation gave again the acetate *XXXVI*. Together with ^{1}H NMR evidence

this proves the structure *XXXII* for this reduction product. The third bromo derivative contained no hydroxy group and IR spectrum showed the presence of an ether grouping in the molecule. In the mass spectrum the elemental composition of the molecular ion $M^{+\cdot}$ ($C_{28}H_{47}BrO$) suggests that a new ring was closed. The presence of the ions $C_5H_6O^{+\cdot}$ and $C_{24}H_{39}O^+$ $(M - C_4H_8Br)^+$ presumably formed by a fragmentation presented by forms *XLI*–*XLIII* is consistent with an ether link between the oxygen at $C_{(3)}$ and methyl group at $C_{(5)}$. This ,together with the ^1H NMR evidence, proves the structure *XXXIV* for this product. Reduction with tri-n-butyltin hydride led to a clean dehalogenation affording the cyclic ether *XXXVII*.

Analogous results were obtained in the 4β,5β-cyclopropano series. Bromination of the ketone[1] *XIII* was again carried out with Jacques' reagent as well as with bromine in acetic acid the latter method giving rise predominantly to the bromomethylcompound *XIV* accompanied by the expected bromo ketones *XV* and *XVI*. In the reaction mixture obtained on bromination with Jacques' reagent the dibromo ketone *XVI* represented the main component in the mixture of the three bromo derivative. The bromo ketone *XV* was also obtained in a clean reaction on bromination of the enol acetate *XVII* and the dibromo ketone *XVI* was easily prepared as the sole product on bromination of the bromo ketone *XV* with Jacques' reagent; no cleavage of the cyclopropane ring was observed. Again, structures of these bromo ketones (*XIV*, *XV*, and *XVI*) follow from spectral and chemical evidence. Bromo ketones *XV* and *XVI* yielded back the starting ketone *XIII* on dehalogenation. In this case, the metal hydride reduction of the bromo ketone *XV* afforded the two at $C_{(3)}$ epimeric bromohydrins *XXI* and *XXIII* both of them giving back the bromo ketone *XV* on oxidation. Removal of the bromine atom and isolation of the known alcohols[1,2] *XXVI* and *XXVII*, respectively, proved the configurations of the hydroxy groups at $C_{(3)}$ in these compounds. On alkali treatment the bromohydrin *XXIII* yielded the ketone *XIII* in contrast to the epimer *XXI* which afforded smoothly the epoxide *XXV*. This epoxide, like its isomer in the 4α,5α-cyclopropano series, rearranged readily to the corresponding ketone *XXVIII*. Reduction of the dibromo ketone *XVI* was accompanied by loss of one bromine atom to yield the bromohydrin *XVIII* the structure of which was again proved by dehalogenation to the alcohol *XXVI* and by transformation to the ketone *XIII* by alkali. In analogy with the 4α,5α-cyclopropano series oxidation of this bromohydrin yielded the unstable bromo ketone *XX* which isomerised quantitatively to the stable bromo ketone *XV* when exposed to enolising conditions. The third product of bromination of the ketone *XIII* – the bromomethyl derivative *XIV* – afforded on dehalogenation the known[5] 5-methyl-5β-cholestan-3-one (*XXXIX*) and its structure follows from the ^1H NMR spectrum. In contrast to the isomeric compound *III* the metal hydride reduction of *XIV* gave rise smoothly to one single product, the cyclic ether *XXXVIII*, yielding the bromine-free oxide on dehalogenation. Again, the structures of these ethers were proved by spectral evidence, analogously as described above for the isomeric oxides *XXXIV* and *XXXVII*.



Having securely established the configurations of the substituents in our bromo derivatives by chemical means we turned our attention to the conformation of the A ring in these compounds. Table I shows the IR data for the four isomeric bromo ketones *IV*, *VII*, *XV*, and *XX*. It is a well known fact that the shift of the carbonyl maximum

TABLE I
Infrared Spectra of Bromo Ketones

Compound	ν(C=O) cm^{-1}	Shifts of cm^{-1}
4α,5-Cyclopropano-5α-cholestan-3-one (*I*)	1 693	—
2α-Bromo-4α,5-cyclopropano-5α-cholestan-3-one (*IV*)	1 700	+7
2β-Bromo-4α,5-cyclopropano-5α-cholestan-3-one (*VII*)	1 700	+7
4β,5-Cyclopropano-5β-cholestan-3-one (*XIII*)	1 688	—
2α-Bromo-4β,5-cyclopropano-5β-cholestan-3-one (*XX*)	1 696	+8
2β-Bromo-4β,5-cyclopropano-5β-cholestan-3-one (*XV*)	1 698	+10

in IR region caused by introduction of a halogen atom in the neighbouring position is highly dependent on the angle between the two dipols, this being about -5 to $+3\ cm^{-1}$ for an axial and $+13$ to $+30\ cm^{-1}$ for an equatorial substituent. In our case the absolute values of the corresponding shifts are almost identical and lie well between the values characteristic for axial and for equatorial halogens. From this, and from the coupling constants of the proton at $C_{(2)}$ with the protons at $C_{(1)}$ we may conclude that the A ring in the bromo ketones always adopts a conformation in which the C—O dipol at $C_{(3)}$ bisects the angle between the bonds at $C_{(2)}$.

Somewhat different situation is in the bromohydrin acetates where the bromine atom always adopts equatorial conformation as follows from ^{1}H NMR evidence. In the bromohydrin acetate *XIX* the 2β-proton shows diaxial coupling with the 1α-proton like the 2α-proton with the 1β-proton in the isomers *XXII* and *XXIV*. This, together with the model considerations based on further spectral evidence (see Experimental) is consistent with the 3β-equatorial twist-chair conformation (Fig. 1) of the A ring in the bromohydrin acetate *XIX* and with the 3β-axial conformation (Fig. 2) in the isomers *XXII* and *XXIV*. In the α-cyclopropano series models suggest the possibility of two conformations of ring A – a twist-chair (Fig. 3) and a twist-boat

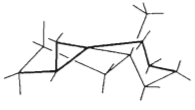


FIG. 1
Conformation of the ring A in the bromohydrin acetate *XIX*

FIG. 2
Conformation of the ring A in the bromohydrin acetates *XXII* and *XXIV*

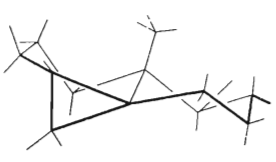


FIG. 3
Conformation of the ring A in the bromohydrin acetate *IX*

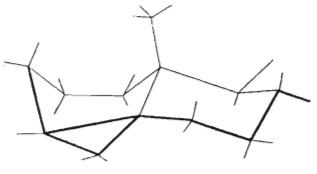


FIG. 4
Conformation of the ring A in the bromohydrin acetate *VI*

(Fig. 4). In the 2α-bromo derivative *IX* the 2β-proton shows again a diaxial coupling with the 1α-proton which points to the twist-chair conformation (Fig. 3) in which the 2α-bromine atom is equatorial. In the 2β-bromo compound *VI* the coupling constants of the 2α-proton with the protons at $C_{(1)}$ ($J_{2\alpha,1\alpha}$ = 10·1 Hz and $J_{2\alpha,1\beta}$ = 6·6 Hz) suggest a twist-boat conformation (Fig. 4) of the A ring again with equatorial conformation of the bromine atom. Dreiding models explain well this behaviour of the A ring. The 4,5-cyclopropano steroid skeleton represents a strained system in which the A ring cannot adopt the energetically favourable chair conformation. The 1,3-diaxial non-bonded interaction of the 2β-bromine atom with the $C_{(10)}$ methyl group is sufficient to cause the conformational changes between the twist forms of the A ring.

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 the Zeiss UR 20 spectrometer in tetrachloromethane. The CD spectra were recorded on the 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. Mass spectra were recorded on a JEOL JMS D-100 spectrometer at 75 eV. The samples were introduced using a direct inlet heated to 140°C. 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.

4α,5-Cyclopropano-5α-cholestan-3-one (*I*)

a) A solution of the dibromo ketone *II* (90 mg) in benzene (2 ml) was treated with a molar benzene solution of tri-n-butyltin hydride (0·7 ml) and refluxed with azobisisobutyronitrile (10 mg) for 1 h. The mixture was chromatographed on a silica gel column (6 g) in benzene. Fractions with the desired product were worked up and the residue was crystallised from methanol to yield 45 mg of the ketone *I*, m.p. 137–138°C, $[\alpha]_D^{20}$ +12° (*c* 0·8), identical with the authentic[1] compound.

b) The bromo ketone *VII* (80 mg) was treated with tri-n-butyltin hydride as described under *a*). Similar working up and crystallisation from methanol afforded 35 mg of the ketone *I*, m.p. 134 to 135°C, $[\alpha]_D^{20}$ +13° (*c* 0·7), identical with the authentic[1] sample.

c) The bromo ketone *IV* (110 mg) was debrominated with tri-n-butyltin hydride and the reaction mixture was worked up as described under *a*). Crystallisation from methanol gave 72 mg of the ketone *I*, m.p. 135–137°C, $[\alpha]_D^{20}$ +12° (*c* 1·2).

d) The bromohydrin *V* (140 mg) was refluxed with a solution of potassium hydroxide (200 mg) in ethanol (6 ml) for 5 h. The alkali was removed with acetic acid and the solvents were distilled off under reduced pressure. The residue was taken into ether and the ethereal solution was worked up. The bromine free residue was crystallised from methanol to yield 72 mg of the ketone *I*, m.p. 136–137°C, $[\alpha]_D^{20}$ +11° (*c* 1·1).

2,2-Dibromo-4α,5-cyclopropano-5α-cholestan-3-one (*II*)

The ketone *I* (3 g) in tetrahydrofuran (40 ml) was treated with Jacques' reagent (5 g) and allowed to stand at room temperature for 15 min. The reaction mixture was poured into 5% sodium hydrogen carbonate and the product was extracted with ether. The ethereal solution was washed with 5% sodium thiosulphate, 1% hydrochloric acid, 5% sodium hydrogen carbonate, water, and dried over magnesium sulphate. The residue after evaporation of ether consisted of the bromo derivatives *II*, *III*, and *IV*, the dibromo ketone *II* being the most lipophilic and main component. The mixture was chromatographed on a silica gel column (250 g) in benzene. Fractions with the dibromoketone were combined, solvent removed, and the residue was crystallised from ethanol to afford 1·7 g of the dibromo ketone *II*, m.p. 152°C, $[\alpha]_D^{20}$ −23° (*c* 1·3). ^{1}H NMR spectrum: 0·68 (s, 18-H), 1·27 (s, 19-H), 2·93 (d, J_{gem} = −16·5 Hz, 1α-H), 3·40 (d, 1β-H). For $C_{28}H_{44}Br_2O$ (556·5) calculated: 60·43% C, 7·97% H, 28·72% Br; found: 60·28% C, 7·81% H, 28·63% Br.

2α-Bromo-5-bromomethyl-5α-cholestan-3-one (*III*)

a) Elution of the chromatographic column of the foregoing experiment with benzene gave fractions with the more polar component. Working up gave 210 mg of the oily dibromo derivative *III*, $[\alpha]_D^{20}$ +20° (*c* 2·5). ^{1}H NMR spectrum: 0·68 (s, 18-H), 1·37 (s, 19-H), 2·03 (dd, J_{gem} = −13·7 Hz, 1α-H), 2·44 (dd, J = 2·9 Hz, 4β-H), 2·53 (dd, 1β-H), 2·81 (d, J_{gem} = −15·3 Hz, 4α-H), 3·15 and 4·00 (two dd, J_{gem} = −10·8 Hz, $-CH_2Br$), 4·74 (dd, $J_{2\beta,1\beta}$ = 7·6 Hz, $J_{2\beta,1\alpha}$ = 12·2 Hz, 2β-H). For $C_{28}H_{46}Br_2I$ (558·5) calculated: 60·21% C, 8·22% H, 28·55% Br; found: 60·05% C, 8·05% H, 28·30% Br.

b) A solution of the ketone *I* (1 g) in chloroform (15 ml) was treated with 48% hydrobromic acid in acetic acid (5 drops) and with a chloroform solution of bromine (500 mg in 5 ml of chloroform). The mixture was heated to 40°C and decolorisation took place within few seconds. It was diluted with ether, washed with 5% sodium thiosulphate, 5% sodium hydrogen carbonate, water, dried, and the solvents were distilled off under reduced pressure. The residue contained, according to the TLC, four products: The bromomethyl derivative *III* as the main product together with the bromoketones *II*, *IV*, and *VII*. The mixture was chromatographed on a silica gel column (100 g) in benzene. The corresponding fractions were worked up to yield 610 mg of the bromo ketone *III*, $[\alpha]_D^{20}$ 22° (*c* 1·2) resisting all attempts at crystallisation.

2α-Bromo-4α,5-cyclopropano-5α-cholestan-3-one (*IV*)

a) Elution of the chromatography after isolation of the dibromo ketone *II* with benzene afforded fractions with the polar component. Working up and crystallisation from ethanol yielded 1·1 g of the bromo ketone *IV*, m.p. 148–149°C, $[\alpha]_D^{20}$ −3° (*c* 1·4). IR spectrum: 3 084, 3 010 (cyclopropane), 1 700 cm^{-1} (carbonyl). CD spectrum: $\Delta\varepsilon_{307}$ = −2·61. ^{1}H NMR spectrum: 0·68 (s, 18-H), 1·08 (s, 19-H), 1·82 (dd, $J_{4\beta,cycl.}$ = 6·3 Hz, 4β-H), 2·36 (dd, J_{gem} = −14·3 Hz, 1β-H), 4·19 (ddd, $J_{2\beta,1\beta}$ = 8·7 Hz, $J_{2\beta,1\alpha}$ = 10·6 Hz, $J_{2\beta,4\beta}$ = 1·1 Hz, 2β-H). For $C_{28}H_{45}BrO$ (477·6) calculated: 70·42% C, 9·50% H, 16·73% Br; found: 71·07% C, 9·66% H, 17·15% Br.

b) Elution of the chromatographic column after isolation of the bromomethyl derivative *III* under *b*) with benzene afforded fractions with the more polar compound, working up and crystallisation from ethanol gave 220 mg of the bromo ketone *IV*, m.p. 148–149°C, $[\alpha]_D^{20}$ −2° (*c* 0·8).

c) A solution of the bromohydrin *VIII* (230 mg) in acetone (5 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 reaction mixture was diluted with water, and the product was

isolated with ether. Working up of the ethereal solution and crystallisation from ethanol afforded 185 mg of the bromo ketone *IV*, m.p. 149–150°C, $[\alpha]_D^{20}$ −3° (*c* 1·0).

d) A solution of the bromo ketone *VII* (100 mg) in methanol (3 ml) was treated at room temperature with 1 drop of 10% methanolic potassium hydroxide. After 5 min at room temperature the excess alkali was removed with acetic acid and solvents were distilled off *in vacuo*. The residue was taken into ether, and the ethereal solution was worked up. The product was crystallised from ethanol to yield 55 mg of the bromo ketone *IV*, m.p. 147–148°C, $[\alpha]_D^{20}$ −2° (*c* 0·7).

2β-Bromo-4α,5-cyclopropano-5α-cholestan-3β-ol (*V*)

A solution of the dibromo ketone *II* (2·3 g) in tetrahydrofuran (50 ml) was treated with lithium tri-tert-butoxyaluminium hydride (6 g) and allowed to stand at room temperature for 20 min. The mixture was diluted with ether and the ethereal solution was washed with 5% hydrochloric acid and worked up. The residue contained according to the TLC two products. The mixture was chromatographed over silica gel (200 g) in benzene. Fractions with the lipophilic component were worked up and the residue was crystallised from methanol to afford 1·05 g of the bromohydrin *V*, m.p. 131–132°C, $[\alpha]_D^{20}$ +34° (*c* 0·9). For $C_{28}H_{47}BrO$ (479·6) calculated: 70·12% C, 9·88% H, 16·66% Br; found: 70·21% C, 9·73% H, 16·51% Br.

2β-Bromo-4α,5-cyclopropano-5α-cholestan-3β-ol 3-Acetate (*VI*)

The bromohydrin *V* (350 mg) in pyridine (3 ml) was acetylated with acetic anhydride (2 ml) at 80°C for 5 h. The mixture was decomposed with ice and water and the product was extracted with ether. Usual working up and crystallization from ethanol gave 320 mg of the acetate *VI*, m.p. 154–155°C, $[\alpha]_D^{20}$ −8° (*c* 1·1). ^{1}H NMR spectrum: 0·28 (dd, $J_{gem} = -6{\cdot}0$ Hz, cyclopropane proton), 0·68 (s, 18-H), 1·36 (s, 19-H), 2·17 (s, acetate), 4·24 (ddd, $J_{2\alpha,1\alpha} = 10{\cdot}1$ Hz, $J_{2\alpha,1\beta} = 6{\cdot}6$ Hz, $J_{2\alpha,3\alpha} = 5{\cdot}0$ Hz, 2α-H), 5·46 (dd, $J_{3\alpha,4\beta} = 4{\cdot}0$ Hz, 3α-H). For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·07% C, 9·47% H, 15·32% Br; found: 69·03% C, 9·52% H, 15·63% Br.

2β-Bromo-4α,5-cyclopropano-5α-cholestan-3-one (*VII*)

The bromohydrin *V* (750 mg) in acetone (15 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 10 min. Methanol was added to destroy the excess reagent, the reaction mixture was diluted with water and the product was isolated with ether. Usual working up and crystallisation from ethanol afforded 615 mg of the bromo ketone *VII*, m.p. 145–146°C, $[\alpha]_D^{20}$ +8° (*c* 1·2). IR spectrum: 3 075, 3 010 (cyclopropane), 1 700 cm^{-1} (carbonyl). CD spectrum: $\Delta\varepsilon_{290}$ −4·53. ^{1}H NMR spectrum: 0·68 (s, 18-H), 1·20 (s, 19-H), 2·34 (dd, $J_{gem} = -16{\cdot}3$ Hz, 1α-H), 2·43 (dd, 1β-H), 4·61 (dd, $J_{2\alpha,1\alpha} = 7{\cdot}8$ Hz, $J_{2\alpha,1\beta} = 3{\cdot}6$ Hz, 2α-H). For $C_{28}H_{45}BrO$ (477·6) calculated: 70·42% C, 9·50% H, 16·73% Br; found: 70·48% C, 9·12% H, 16·55% Br.

2α-Bromo-4α,5-cyclopropano-5α-cholestan-3β-ol (*VIII*)

a) The bromo ketone *IV* (1 g) in tetrahydrofuran (50 ml) was cooled to −5°C and treated with lithium aluminium hydride (50 mg). After 5 min the mixture was diluted with wet ether and decomposed with ethyl acetate. The solution was washed with 2% hydrochloric acid and worked up in the usual way. The product was chromatographed over silica gel (50 g) in benzene to yield after working up of the corresponding fractions and crystallisation from methanol 745 mg of the bromohydrin *VIII*, m.p. 102–103°C, $[\alpha]_D^{20}$ +58° (*c* 1·3). For $C_{28}H_{47}BrO$ (479·6) calculated: 70·12% C, 9·88% H, 16·66% Br; found: 69·85% C, 9·74% H, 16·40% Br.

b) Elution of the column after isolation of the bromohydrin *V* with benzene gave fractions with the polar component. Working up and crystallisation from ethanol yielded 870 mg of the bromohydrin *VIII*, m.p. 103–104°C, $[\alpha]_D^{20}$ + 62° (*c* 1·8).

2α-Bromo-4α,5-cyclopropano-5α-cholestan-3β-ol 3-Acetate (*IX*)

The bromohydrin *VIII* (700 mg) was acetylated with acetic anhydride (3 ml) in pyridine (4 ml) at room temperature for 20 h. The mixture was decomposed with ice and water and the product was extracted with ether. Usual working up and crystallisation from ethanol afforded 640 mg of the acetate *IX*, m.p. 128–129°C, $[\alpha]_D^{20}$ + 31° (*c* 0·8). ^{1}H NMR spectrum: 0·34 (dd, $J_{gem} = -5{\cdot}5$ Hz, $J_{cycl.,4\beta} = 9{\cdot}8$ Hz, cyclopropane proton), 0·67 (s, 18-H), 1·19 (s, 19-H), 1·93 (dd, $J_{gem} = -13{\cdot}4$ Hz, 1β-H), 2·12 (s, acetate), 4·20 (ddd, $J_{2\beta,1\beta} = 5{\cdot}3$ Hz, $J_{2\beta,1\alpha} = 13{\cdot}6$ Hz, $J_{2\beta,3\alpha} = 7{\cdot}3$ Hz, 2β-H), 5·27 (d, $J_{3\alpha,4\beta} < 1$ Hz, 3α-H). For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·07% C, 9·47% H, 15·32% Br; found: 68·73% C, 9·39% H, 14·95% Br.

4α,5-Cyclopropano-5α-cholestan-3β-ol (*X*)

The bromohydrin *V* (110 mg) in benzene (3 ml) was treated with a molar solution of tri-n-butyltin hydride in benzene (0·8 ml) and refluxed with azobisisobutyronitrile (10 mg) for 1 h. After cooling off the solution was chromatographed over silica gel (10 g) in benzene. The corresponding fractions were worked up and the crude product was crystallised from methanol to yield 62 mg of the alcohol *X*, m.p. 130–131°C, $[\alpha]_D^{20}$ + 51° (*c* 1·6), identical with the authentic[3] sample.

2β,3β-Epoxy-4α.5-cyclopropano-5α-cholestane (*XI*)

The bromohydrin *VIII* (500 mg) in methanol (10 ml) w astreated at 0°C with 20% methanolic potassium hydroxide solution (5 ml) and allowed to stand at room temperature for 15 min. The mixture was diluted with ice cold water and the product was extracted into ether. The ethereal solution was washed well with water, dried, and ether distilled off *in vacuo*. The residue was crystallised from methanol to yield 285 mg of the epoxide *XI*, m.p. 100–101°C, $[\alpha]_D^{20}$ + 34° (*c* 1·4). IR spectrum: 3 065 (cyclopropane), 870, 830 cm^{-1} (epoxide). For $C_{28}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·65% C, 11·78% H.

4α,5-Cyclopropano-5α-cholestan-2-one (*XII*)

A benzene solution of the epoxide *XI* (110 mg) was passed through a silica gel column (20 g). The collected eluate was evaporated and the residue was crystallised from ethanol to yield 87 mg of the ketone *XII*, m.p. 148–149°C, $[\alpha]_D^{20}$ + 144° (*c* 1·2). IR spectrum: 3 065 (cyclopropane), 1 711 cm^{-1} (carbonyl). For $C_{28}H_{46}O$ calculated: 83·87% C, 11·99% H; found: 83·73% C, 11·67% H.

4β,5-Cyclopropano-5β-cholestan-3-one (*XIII*)

a) The dibromo ketone *XVI* (80 mg) in benzene was treated with a solution of tri-n-butyltin hydride in benzene (1 mol l^{-1}, 0·6 ml) and refluxed with azobisisobutyronitrile (10 mg) for 1 h. The mixture was passed through a silica gel column (10 g) and the product was eluted with benzene. Evaporation and crystallisation from ethanol gave 20 mg of the ketone *XIII*, m.p. 82–83°C, $[\alpha]_D^{20}$ + 70° (*c* 0·8), identical with the authentic[1] sample.

b) The bromo ketone *XV* (100 mg) was debrominated with tri-n-butyltin hydride as described above. Similar working up and crystallisation from ethanol afforded 65 mg of the ketone *XIII*, m.p. 80–82°C, $[\alpha]_D^{20}$ +71° (*c* 1·1).

c) The bromo ketone *XX* (90 mg) was treated with tri-n-butyltin hydride and the reaction mixture was worked up as described under *a*). Crystallisation from ethanol gave 54 mg of the ketone *XIII*, m.p. 82–83°C, $[\alpha]_D^{20}$ +72° (*c* 1·5).

d) The bromohydrin *XXIII* (165 mg) in methanol (4 ml) was refluxed with potassium hydroxide (80 mg) in methanol (1 ml) for 5 h. The alkali was removed with acetic acid and solvents were distilled off under reduced pressure. The residue was dissolved in ether and water and the ethereal solution was worked up in the usual way. The crude product was crystallised from ethanol to yield 102 mg of the ketone *XIII*, m.p. 83°C, $[\alpha]_D^{20}$ +68° (*c* 0·9).

e) The bromohydrin *XVIII* (140 mg) was treated with alkali and the reaction mixture was worked up as described in the previous experiment to yield 72 mg of the ketone *XIII*, m.p. 80–81°C, $[\alpha]_D^{20}$ +70° (*c* 1·3).

2β-Bromo-5-bromomethyl-5β-cholestan-3-one (*XIV*)

a) The ketone *XIII* (1·6 g) in chloroform (30 ml) was brominated with bromine (600 mg) under the presence of hydrobromic acid as described for preparation of the bromo ketone *III* under *b*). Similar working up afforded a mixture of the bromo ketones *XIV*, *XV*, and *XVI* in which the medium polar compound *XIV* predominated. Chromatography on a silica gel column (200 g) in benzene and working up of the corresponding fractions gave a crude product (1·2 g) which on on crystallisation from methanol yielded 930 mg of the bromomethyl derivative *XIV*, m.p. 133–115°C, $[\alpha]_D^{20}$ + 10° (*c* 1·2). IR spectrum: 1 739 cm^{-1} (carbonyl). CD spectrum: $\Delta\varepsilon_{293}$ −0·63. ^{1}H NMR spectrum: 0·68 (s, 18-H), 1·00 (s, 19-H), 2·11 (t, $J_{gem} = -14{\cdot}4$ Hz, 1β-H), 2·57 (dd, 1α-H), 2·77 (d, $J_{gem} = -14{\cdot}9$ Hz, 4β-H), 2·95 (dd, $J = 1{\cdot}6$ Hz, 4α-H), 3·42 and 3·48 (d and dd, $J_{gem} = -10{\cdot}5$ Hz, $-CH_2Br$), 4·66 (dd, $J_{2\alpha,1\beta} = 13{\cdot}8$ Hz, $J_{2\alpha,1\alpha} = 6{\cdot}2$ Hz, 2α-H). For $C_{28}H_{46}Br_2O$ (558·5) calculated: 60·21% C, 8·30% H, 28·62% Br; found: 60·15% C, 8·22% H, 28·55% Br.

b) The ketone *XIII* (4 g) in tetrahydrofuran (100 ml) was treated with Jacques' reagent (6·7 g) and allowed to stand at room temperature for 20 min. The mixture was diluted with ether and washed with 5% sodium thiosulphate, 5% sodium hydrogen carbonate, water, dried and solvents removed *in vacuo*. The bromomethyl derivative represented only the minor product in the reaction mixture. It was chromatographed on a silica gel column (500 g) in benzene. Fractions with the medium polar product afforded after working up 520 mg of a crude product which on crystallisation from methanol gave 410 mg of the bromo ketone *XIV*, m.p. 110–111°C, $[\alpha]_D^{20}$ +12° (*c* 0·9).

2β-Bromo-4β,5-cyclopropano-5β-cholestan-3-one (*XV*)

a) Fractions with the polar component from the chromatography of the foregoing experiment were combined and solvent removed. The residue (1·25 g) was crystallised from methanol to afford 980 mg of the bromo ketone *XV*, m.p. 112–114°C, $[\alpha]_D^{20}$ +75° (*c* 1·6). IR spectrum: 3 085, 3 015 (cyclopropane), 1 698 cm^{-1} (carbonyl). CD spectrum $\Delta\varepsilon_{307}$ +2·12. ^{1}H NMR spectrum 0·67 (s, 18-H), 1·10 (s, 19-H), 1·75 (dd, $J_{4\alpha,cycl.} = 11{\cdot}0$ Hz, $J_{4\alpha,cycl.} = 4{\cdot}4$ Hz, 4α-H), 1·87 (dd, $J_{gem} = -14{\cdot}9$ Hz, 1β-H), 2·33 (dd, 1α-H), 4·15 (ddd, $J_{2\alpha,1\alpha} = 7{\cdot}6$ Hz, $J_{2\alpha,1\beta} = 12{\cdot}3$ Hz, $J_{2\alpha,4\alpha} = 1{\cdot}0$ Hz, 2α-H). For $C_{28}H_{45}BrO$ (477·6) calculated: 70·42% C, 9·50% H, 16·73% Br; found: 70·35% C, 10·07% H, 17·08% Br.

b) Elution of the chromatographic column after isolation of the bromo ketone *XIV* under *a*) gave fractions with the polar component. Working up and crystallisation from methanol yielded 120 mg of the bromo ketone *XV*, m.p. 111–113°C, $[\alpha]_D^{20}$ + 72° (*c* 1·1).

c) The enol acetate *XVII* (5.2 g) was dissolved in tetrachloromethane (200 ml), calcium carbonate was added (10 g) and the mixture was treated at 0°C under stirring dropwise with bromine in tetrachloromethane until the yellow color persisted. The solution was washed with 5% sodium thiosulphate, 5% sodium hydrogen carbonate, water, dried, and solvent was distilled off *in vacuo*. The residue was crystallised from methanol to yield 5·5 g of the bromo ketone *XV*, m.p. 114 to 115°C, $[\alpha]_D^{20}$ + 73° (*c* 1·6).

d) The bromohydrin *XXI* (170 mg) in acetone (4 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 10 min. Methanol was added to remove the reagent, the mixture was diluted with water, and the product was isolated with ether. Usual working up and crystallisation from methanol gave 115 mg of the bromo ketone *XV*, m.p. 110–113°C, $[\alpha]_D^{20}$ + 72° (*c* 0·8).

e) The bromohydrin *XXIII* (65 mg) was oxidized and the reaction mixture was worked up as described in the foregoing experiment to yield 30 mg of the bromo ketone *XV*, m.p. 112–113°C, $[\alpha]_D^{20}$ + 70° (*c* 0·6).

f) The bromo ketone *XX* (115 mg) in methanol (4 ml) was treated at room temperature with 1 drop of 20% methanolic potassium hydroxide. After 5 min the alkali was removed with acetic acid, the mixture was diluted with water and the product was isolated with ether. Usual working up and crystallisation from methanol afforded 87 mg of the bromo ketone *XV*, m.p. 111–112°C, $[\alpha]_D^{20}$ + 73° (*c* 1·2).

2,2-Dibromo-4β,5-cyclopropano-5β-cholestan-3-one (*XVI*)

a) The bromo ketone *XV* (2 g) in tetrahydrofuran (60 ml) was treated with Jacques' reagent (2·5 g). After 20 min at room temperature the reaction mixture was diluted with ether and washed with 5% sodium thiosulphate, 5% sodium hydrogen carbonate, water, dried, and the solvent was distilled off. The residue was crystallised from ethanol to yield 1·7 g of the dibromo ketone *XVI*, m.p. 135–137°C, $[\alpha]_D^{20}$ + 92° (*c* 1·3). ^{1}H NMR spectrum: 0·68 (s, 18-H), 1·01 (s, 19-H), 2·87 (d, J_{gem} = −17·2 Hz, 1α-H), 3·39 (d, 1β-H). For $C_{28}H_{44}Br_2O$ (554·5) calculated: 59·75% C, 8·35% H, 29·32% Br; found: 59·43% C, 7·97% H, 28·72% Br.

b) Fractions with the lipophilic product obtained on preparation of the bromo ketone *XIV* under *a*) yielded after working up and crystallization from ethanol 110 mg of the bromo ketone *XVI*, m.p. 134–135°C, $[\alpha]_D^{20}$ + 90° (*c* 1·7).

c) Fractions with the lipophilic product obtained on preparation of the bromo ketone *XIV* under *b*) afforded similarly 1·7 g of the bromo ketone *XVI*, m.p. 135–136°C, $[\alpha]_D^{20}$ + 90° (*c* 1·2).

3-Acetoxy-4β,5-cyclopropano-5β-cholest-2-ene (*XVII*)

The ketone *XIII* (7 g) in isopropenyl acetate (150 ml) was treated with 5 drops of conc. sulphuric acid and in the course of two hours 100 ml of the distillate were collected. The remaining isopropenyl acetate was distilled off *in vacuo* and the residue was dissolved in ligroin. The solution was filtered through a column of alkaline aluminium oxide (200 g) and the collected filtrate was evaporated. The residue was chromatographed over silica gel (500 g) in ligroin–benzene (4 : 1). The corresponding fractions were worked up and the product was crystallised from ethanol to

yield 5·8 g of the enol acetate *XVII*, m.p. 116–117°C, $[\alpha]_D^{20}$ +27° (*c* 1·4). For $C_{30}H_{48}O_3$ (440·7) calculated: 81·76% C, 10·98% H; found: 81·69% C, 10·70% H.

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

A solution of the dibromo ketone *XVI* (1·3 g) in tetrahydrofuran (40 ml) was treated with solid lithium tri-tert-butoxyaluminium hydride (4·5 g) and set aside for 2 h. The mixture was poured into 1% hydrochloric acid and the product was taken into ether. The ethereal solution was worked up as usual and the residue was chromatographed over silica gel in benzene. The corresponding fractions were combined and evaporated to yield 720 mg of the oily bromohydrin *XVIII*, $[\alpha]_D^{20}$ +34° (*c* 2·6). For $C_{28}H_{47}BrO$ (479·6) calculated: 70·12% C, 9·88% H, 16·66% Br; found: 70·36% C, 9·65% H, 16·42% Br.

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

The bromohydrin *XVIII* (300 mg) was acetylated in pyridine (3 ml) with acetic anhydride (2·5 ml) at 80°C for 5 h. The mixture was decomposed with ice and water and the product was isolated with ether. Usual working up and crystallisation from ethanol yielded 265 mg of the acetate *XIX*, m.p. 88–89°C, $[\alpha]_D^{20}$ +69° (*c* 2·4). ^{1}H NMR spectrum: 0·23 and 0·35 (two dd, $J_{cycl.,4\alpha} = 9{\cdot}0$ Hz, $J_{cycl.,4\alpha} = 4{\cdot}7$ Hz, cyclopropane protons), 0·69 (s, 18-H), 1·03 (s, 19-H), 1·80 (ddd, $J_{gem} = -14{\cdot}3$ Hz, 1β-H), 2·17 (s, acetate), 4·23 (ddd, $J_{2\beta,1\alpha} = 12{\cdot}4$ Hz, $J_{2\beta,1\beta} = 6{\cdot}6$ Hz, $J_{2\beta,3\beta} = 2{\cdot}8$ Hz, 2β-H), 5·43 (t, $J_{3\beta,4\alpha} = 3{\cdot}4$ Hz, $J_{3\beta,1\beta} = 0{\cdot}8$ Hz, 3β-H). For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·07% C, 9·47% H, 15·32% Br; found: 69·31% C, 9·15% H, 15·46% Br.

2α-Bromo-4β,5-cyclopropano-5β-cholestan-3-one (*XX*)

The bromohydrin *XVIII* (860 mg) in acetone (12 ml) was treated with excess Jones' reagent and allowed to stand at room temperature for 15 min. The excess oxidizing agent was destroyed with methanol and the product was isolated with ether. Usual working up and crystallisation from methanol afforded 705 mg of the bromo ketone *XX*, m.p. 137–138°C, $[\alpha]_D^{20}$ +46° (*c* 1·7). IR spectrum: 3 080, 3 010 (cyclopropane), 1 696 cm^{-1} (carbonyl). CD spectrum: $\Delta\varepsilon_{295}$ +3·63). ^{1}H NMR spectrum: 0·68 (s, 18-H), 0·93 (dd, $J_{gem} = -5{\cdot}7$ Hz, one cyclopropane proton), 1·03 (s, 19-H), 1·80 (dd, $J_{4\alpha,cycl.} = 9{\cdot}4$ Hz, $J_{4\alpha,cycl.} = 4{\cdot}4$ Hz, 4α-H), 2·17 (dd, $J_{gem} = -17{\cdot}5$ Hz, 1α-H), 2·46 (dd, 1β-H), 4·48 (dd, $J_{2\beta,1\alpha} = 1{\cdot}2$ Hz, $J_{2\beta,1\beta} = 8{\cdot}8$ Hz, 2β-H). For $C_{28}H_{45}BrO$ (447·6) calculated: 70·42% C, 9·50% H, 16·73% Br; found: 70·15% C, 9·36% H, 16·82% Br.

2β-Bromo-4β,5-cyclopropano-5β-cholestan-3α-ol (*XXI*)

A solution of the bromo ketone *XV* (650 mg) in tetrahydrofuran (15 ml) was treated with solid lithium tri-tert-butoxyaluminium hydride and set aside for 30 min. The mixture was decomposed with acetic acid, diluted with water, and the product was extracted with ether. Usual working up gave a product consisting of two components in which the lipophilic one predominated. The mixture was chromatographed on a silica gel column (80 g) in benzene. Fractions with the lipophilic compound were worked up to yield 310 mg of the oily bromohydrin *XXI*, $[\alpha]_D^{20}$ +7° (*c* 1·0). For $C_{28}H_{47}BrO$ (479·6) calculated: 70·12% C, 9·88% H, 16·66% Br; found: 70·04% C, 9·75% H, 16·32% Br.

2β-Bromo-4β,5-cyclopropano-5β-cholestan-3α-ol 3-Acetate (*XXII*)

The bromohydrin *XXI* (340 mg) was acetylated with acetic anhydride (2 ml) in pyridine (3 ml) at room temperature for 18 h. Usual working up and crystallisation from methanol yielded 285 mg of the acetate *XXII*, m.p. 152°C, $[\alpha]_D^{20}$ +23° (*c* 0·8). ^{1}H NMR spectrum: 0·37 and 0·50 (two dd, $J_{cycl.,4\alpha} = 9{\cdot}7$ Hz, $J_{cycl.,4\alpha} = 5{\cdot}5$ Hz, $J_{gem} = -5{\cdot}2$ Hz, cyclopropane), 0·68 (s, 18-H), 0·78 (dd, $J_{cycl.,4\alpha}$ 4α-H), 1·00 (s, 19-H), 4·14 (ddd, $J_{2\alpha,1\beta} = 13{\cdot}9$ Hz, $J_{2\alpha,1\alpha} = 4{\cdot}0$ Hz, $J_{2\alpha,3\beta} = 8{\cdot}4$ Hz, 2α-H). For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·07% C, 9·47% H, 15·32% Br; found: 69·36% C, 9·31% H, 15·85% Br.

2β-Bromo-4β,5-cyclopropano-5β-cholestan-3β-ol (*XXIII*)

Elution of the chromatographic column after isolation of the 3α-isomer *XXI* with benzene yielded fractions with the polar component. Working up gave 175 mg of the oily bromohydrin *XXIII*, $[\alpha]_D^{20}$ −51°. For $C_{28}H_{47}BrO$ (479·6) calculated: 70·12% C, 9·88% H, 16·66% Br; found: 70·24% C, 9·65% H, 16·82% Br.

2β-Bromo-4β,5-cyclopropano-5β-cholestan-3β-ol 3-Acetate (*XXIV*)

The bromohydrin *XXIII* (470 mg) was acetylated with acetic anhydride (1·5 ml) in pyridine (2 ml) at 80°C for 6 h. Usual working up and crystallisation from methanol afforded 385 mg of the acetate *XXIV*, m.p. 114–115°C, $[\alpha]_D^{20}$ −58° (*c* 1·3). ^{1}H NMR spectrum: 0·67 (s, 18-H), 1·00 (s, 19-H), 2·11 (s, acetate), 4·30 (ddd, $J_{2\alpha,1\beta} = 13{\cdot}6$ Hz, $J_{2\alpha,1\alpha} = 3{\cdot}1$ Hz, $J_{2\alpha,3\alpha} = 5{\cdot}2$ Hz, 2α-H), 5·32 (ddd, $J_{3\alpha,4\alpha} = 8{\cdot}1$ Hz, $J_{3\alpha,1\alpha} = 1{\cdot}2$ Hz, 3α-H). For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·07% C, 9·47% H, 15·32% Br; found: 69·50% C, 9·36% H, 15·08% Br.

2α,3α-Epoxy-4β,5cyclopropano-5β-cholestane (*XXV*)

The bromohydrin *XXI* (400 mg) in ethanol (10 ml was treated at 0°C with a solution of potassium hydroxide (180 mg) in the minimum amount of water and ethanol (5 ml) and allowed to stand at room temperature for 15 min. The oily product which separated was taken into ether and the ethereal solution was worked up. Yield 290 mg of the epoxide *XXV* which resisted all attempts at crystallisation; $[\alpha]_D^{20}$ +62° (*c* 1·8). IR spectrum: 3 060 (cyclopropane), 989, 917, 862 cm^{-1} (epoxide). For $C_{28}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 84·23% C, 11·61% H.

4β,5-Cyclopropano-5β-cholestan-3α-ol (*XXVI*)

a) A solution of the bromohydrin *XXI* (80 mg) in benzene (3 ml) was treated with a molar solution of tri-n-butyltin hydride in benzene (0·4 ml) and refluxed under the presence of azobis-isobutyronitrile (10 mg) for 1 h. The mixture was adsorbed on a silica gel column (6 g) and the product was eluted with benzene. Evaporation of the solvent gave 45 mg of the non-crystalline alcohol *XXVI*, $[\alpha]_D^{20}$ +21° (*c* 1·1), identical in all respects with the authentic[3] sample.

b) The bromohydrin *XVIII* (110 mg) was dehalogenated and the reaction mixture was worked up as described in the previous experiment to afford 75 mg of the alcohol *XXVI*, $[\alpha]_D^{20}$ +23° (*c* 1·4).

4β,5-Cyclopropano-5β-cholestan-3β-ol (*XXVII*)

The bromohydrin *XXIII* (90 mg) afforded on treatment with tri-n-butyltin hydride as described in the foregoing experiment and after crystalliastion from methanol 50 mg of the alcohol *XXVII*, m.p. 81–83°C, $[\alpha]_D^{20}$ −8° (*c* 0·7), in accordance with the literature[1].

4β,5-Cyclopropano-5β-cholestan-2-one (*XXVIII*)

A benzene solution of the epoxide *XXV* (130 mg) was passed over a silica gel column (15 g) and the material was eluted with benzene. Evaporation of the solvent yielded TLC pure material which was crystallised from methanol to give 110 mg of the ketone *XXVIII*, m.p. 117–118°C, $[\alpha]_D^{20}$ −40° (*c* 1·2). IR spectrum: 3 060 (cyclopropane), 1 709 cm^{-1} (carbonyl). For $C_{28}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·92% C, 11·52% H.

5-Methyl-5α-cholestan-3-one (*XXIX*)

a) The dibromo ketone *III* (210 mg) in benzene (10 ml) was dehalogenated with molar benzene solution of tri-n-butyltin hydride (2·5 ml) as described for the preparation of the alcohol *XXVI*. Similar working up and crystallisation from methanol yielded 110 mg of the ketone *XXIX*, m.p. 167–168°C, $[\alpha]_D^{20}$ +42° (*c* 1·1) in accordance with the literature[2]. ^{1}H NMR spectrum: 0·68 (s, 18-H), 0·93 (d, $J_{5\alpha CH_3,4\beta}$ = 1 Hz, 5α-CH_3), 1·16 (19-H), 1·86 (dd, $J_{4\alpha,2\alpha}$ = 1·3 Hz, J_{gem} = = −15·2 Hz, 4α-H), 2·47 (dq, 4β-H).

b) The alcohol *XXXV* (85 mg) in acetone (3 ml) was oxidized with excess Jones' reagent for 10 min at room temperature. Methanol was added and the product was isolated with ether as usual. Crystallisation from methanol afforded 62 mg of the ketone *XXIX*, m.p. 166–168°C, $[\alpha]_D^{20}$ +39° (*c* 0·9).

2α-Bromo-5-bromomethyl-5α-cholestan-3α-ol (*XXX*)

The bromo ketone *III* (3·8 g) in tetrahydrofuran (80 ml) was treated at room temperature with lithium tri-tert-butoxyaluminium hydride (10 g) and allowed to stand for 30 min. The excess hydride was destroyed with acetic acid, the mixture was diluted with water and the product was taken into ether. Usual working up afforded a mixture of the bromo derivatives *XXX*, *XXXI*, and *XXXIV*. Chromatography over silica gel (500 g) in benzene yielded fractions with the lipophilic component. Evaporation of the solvent left 1·1 g of the oily bromohydrin *XXX*, $[\alpha]_D^{20}$ +16° (*c* 1·5). IR spectrum: 3 568 cm^{-1} (hydroxyl). For $C_{28}H_{48}Br_2O$ (560·5) calculated: 60·00% C, 8·63% H, 28·52% Br; found: 60·15% C, 8·28% H, 28·14% Br.

2α-Bromo-5-bromomethyl-5α-cholestan-3α-ol 3-Acetate (*XXXI*)

The bromohydrin *XXX* (105 mg) was acetylated with acetic anhydride (1 ml) in pyridine (1·5 ml) at 80°C for 6 h. Usual working up and crystallisation from ethanol yielded 95 mg of the acetate *XXXI*, m.p. 169–170°C, $[\alpha]_D^{20}$ +17° (*c* 0·8). ^{1}H NMR spectrum: 0·66 (s, 18-H), 1·15 (s, 19-H), 2·17 (s, acetate), 2·25 (dd, J_{gem} = −15·9 Hz, 4α-H), 4·07 and 4·20 (two dd, $J_{CH_2Br,4\beta}$ = 2·2 Hz, $J_{CH_2Br,6\beta}$ = 1·2 Hz, J_{gem} = −10·0 Hz, —CH_2Br, 4·47 (ddd, $J_{2,1\alpha}$ = 10·6 Hz, $J_{2\beta,1\beta}$ = 7·6 Hz, $J_{2\beta,3\beta}$ = 4·1 Hz, 2β-H), 5·23 (mt, $J_{3\beta,4\alpha}$ = 2·6 Hz, $J_{3\beta,4\beta}$ = 4·1 Hz, 3β-H). For $C_{30}H_{50}Br_2O_2$ (602·5) calculated: 59·80% C, 8·36% H, 26·53% Br; found: 59·46% C, 8·52% H, 26·90% Br.

5-Bromomethyl-5α-cholestan-3α-ol (*XXXII*)

Elution of the chromatographic column after isolation of the dibromo derivative *XXX* gave fractions with the most polar compound. Working up and crystallisation from methanol yielded 630 mg of the alcohol *XXXII*, m.p. 150–151°C, $[\alpha]_D^{20}$ +14° (*c* 1·2). IR spectrum: 3 600, 1 000 cm^{-1} (hydroxyl). For $C_{28}H_{49}BrO$ (481·6) calculated: 69·83% C, 10·26% H, 16·59% Br; found: 69·65% C, 10·04% H, 16·32% Br.

5-Bromomethyl-5α-cholestan-3α-ol 3-Acetate (*XXXIII*)

The alcohol *XXXII* (80 mg) was acetylated with acetic anhydride (1 ml) in pyridine (1·5 ml) at 80°C for 5 h. Usual working up and crystallisation from ethanol yielded 65 mg of the acetate *XXXIII*, m.p. 120—121°C, $[\alpha]_D^{20}$ +11° (*c* 0·7). ^{1}H NMR spectrum: 0·66 (s, 18-H), 1·08 (s, 19-H), 1·46 (ddd, $J_{4\beta,3\alpha}$ = 4·0 Hz, J_{gem} = −15·8 Hz, 4β-H), 2·09 (s, acetate), 4·08 and 4·23 (two dd, $J_{CH_2Br,4\beta}$ = 2·4 Hz, $J_{CH_2Br,6\beta}$ = 1·3 Hz, J_{gem} = −9·9 Hz, $-CH_2Br$), 5·06 (mt, ΣJ = 12·7 Hz, 3α-H). For $C_{30}H_{51}BrO_2$ (523·6) calculated: 68·81% C, 9·82% H, 15·26% Br; found: 68·73% C, 9·65% H, 15·82% Br.

2α-Bromo-3α,5-oxymethylene-5α-cholestane (*XXXIV*)

Elution of the chromatographic column after isolation of the bromohydrin *XXX* and working up of the corresponding fractions gave 830 mg of a crude product which on crystallisation from methanol yielded 705 mg of the bromo derivative *XXXIV*, m.p. 122—123°C, $[\alpha]_D^{20}$ +53° (*c* 1·3), IR spectrum: 1 020, 955, 833 cm^{-1} (ether). ^{1}H NMR spectrum: 0·65 (s, 18-H), 0·99 (d, $J_{19,1\alpha}$ = 0·6 Hz, 19-H), 1·80 (dd, J_{gem} = −13·4 Hz, 1α-H), 2·03 (dd, 1β-H), 3·46 and 4·32 (two d, J_{gem} = −8·6 Hz, $-OCH_2$), 4·15 (ddd, $J_{2\beta,1\alpha}$ = 11·5 Hz, $J_{2\beta,1\beta}$ = 5·8 Hz, $J_{2\beta,3\beta}$ = 0·8 Hz, 2β-H), 4·36 (d, $J_{3\beta,4\alpha}$ = 6 Hz, $J_{3\beta,4\beta}$ = 0 Hz, 3β-H). For $C_{28}H_{47}BrO$ (479·6) calculated: 70·12% C, 9·88% H, 16·66% Br; found: 70·06% C, 9·45% H, 16·42% Br.

5-Methyl-5α-cholestan-3α-ol (*XXXV*)

a) A solution of the acetate *XXXIV* (150 mg) in ethanol (5 ml) was refluxed with a solution of potassium hydroxide (100 mg) in ethanol (2 ml) for 6 h. Acetic acid was added to remove the alkali and solvents were distilled off *in vacuo*. The residue was diluted with water and the product was extracted with ether. Working up of the organic layer and crystallisation from methanol afforded 93 mg of the alcohol *XXXV*, m.p. 138—139 C, $[\alpha]_D^{20}$ +15° (*c* 1·2) For $C_{28}H_{50}O$ (402·7) calculated: 83·51% C, 12·52% H; found: 83·46% C, 12·38% H.

b) The ketone *XXIX* (210 mg) in tetrahydrofuran (6 ml) was reduced with lithium tri-tert-butoxyaluminium hydride (500 mg) at room temperature for 10 min. The mixture was poured into 2% hydrochloric acid and the product was taken into ether. Working up of the ethereal solution affored a product containing according to the TLC about 90% of the 3α-alcohol *XXXV* and 10% of the corresponding 3β-isomer. It was chromatographed on a silica gel column (12 g) in benzene to afford after working up of the fractions and crystallisation from methanol 132 mg of the alcohol *XXXV*, m.p. 138—140°C, $[\alpha]_D^{20}$ +17° (*c* 1·0).

5-Methyl-5α-cholestan-3α-ol 3-Acetate (*XXXVI*)

a) The dibromo derivative *XXXI* (180 mg) in benzene was treated with molar benzene solution of tri-n-butyltin hydride (1 ml) and refluxed under the presence of azobisisobutyronitrile (10 mg) for 1 h. The mixture was adsorbed on a silica gel column and the product was eluted with benzene. Evaporation of the solvent and crystallisation from methanol gave 75 mg of the acetate *XXXVI*, m.p. 131—132°C, $[\alpha]_D^{20}$ +24° (*c* 1·2). ^{1}H NMR spectrum: 0·65 (s, 18-H), 0·93 (s, 19-H), 1·11 (s, 5α-methyl), 2·02 (s, acetate), 5·03 (mt, ΣJ = 12·9 Hz, 3β-H equatorial). For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 80·78% C, 11·63% H.

b) The bromo derivative *XXXIII* (150 mg) was dehalogenated as described in the foregoing experiment. Similar working up and crystallisation yielded 82 mg of the acetate *XXXVI*, m.p. 130—131°C, $[\alpha]_D^{20}$ +24° (*c* 1·3).

3α,5-Oxymethylene-5α-cholestane (*XXXVII*)

The bromo derivative *XXXIV* (160 mg) was debrominated as described in the previous experiment. Working up and crystallisation from methanol afforded 105 mg of the epoxide *XXXVII*, m.p. 71–72°C, $[\alpha]_D^{20}$ +37° (*c* 1·6). ^{1}H NMR spectrum: 0·66 (s, 18-H), 0·97 (s, 19-H), 3·35 and 4·27 (two d, $J_{gem} = -8·2$ Hz, $-OCH_2$), 4·21 (d, $J_{3\beta,2\alpha} = 5·2$ Hz, $J_{3\beta,2\beta} = 0·5$ Hz, 3β-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·65% C, 11·91% H.

2β-Bromo-3β,5-oxymethylene-5β-cholestane (*XXXVIII*)

The bromo ketone *XIV* (400 mg) in tetrahydrofuran (20 ml) was reduced with lithium tri-tert-butoxyaluminium hydride for 15 min at room temperature. The mixture was poured into 2% hydrochloric acid and the product was taken into ether. Usual working up afforded after evaporation of ether a product which was uniform according to the TLC. Crystallisation from ethanol gave 485 mg of the epoxide *XXXVIII*, m.p. 125–127°C, $[\alpha]_D^{20}$ −22° (*c* 1·4). IR spectrum: 1 102, 1 018, 972, 891 cm^{-1} (ether). ^{1}H NMR spectrum: 0·65 (s, 18-H), 0·94 (s, 19-H), 1·82 (dd, $J_{gem} = -14·0$ Hz, 1β-H), 2·35 (d, $J_{gem} = -12·8$ Hz, 4α-H), 3·32 and 4·09 (d and dd, $J_{gem} = -8·6$ Hz, $-OCH_2$), 4·00 (dd, $J_{2\alpha,1\alpha} = 5·4$ Hz, $J_{2\alpha,1\beta} = 11·9$ Hz, $J_{2\alpha,3\alpha} = 0·8$ Hz, 2α-H), 4·38 (d, $J_{3\alpha,4\beta} = 6·5$ Hz, $J_{3\alpha,4\alpha} < 1$ Hz, 3α-H). For $C_{28}H_{47}BrO$ (479·6) calculated: 70·12% C, 9·88% H, 16·66% Br; found: 70·25% C, 9·52% H, 17·14% Br.

5-Methyl-5β-cholestan-3-one (*XXXIX*)

The bromo ketone *XIV* (115 mg) was dehalogenated with tri-n-butyltin hydride as described for preparation of the acetate *XXXVI*. Similar working up and crystallisation from methanol gave 45 mg of the ketone *XXXIX*, m.p. 89–90°C, $[\alpha]_D^{20}$ +32° (*c* 1·3) in accordance with the literature[5]. ^{1}H NMR spectrum: 0·68 (s, 18-H), 0·87 (s, 5β-methyl), 0·92 (s, 19-H).

3β,5-Oxymethylene-5β-cholestane (*XL*)

The bromo derivative *XXXVIII* (170 mg) was debrominated as described above for preparation of the acetate *XXXVI*. Working up and crystallisation from methanol afforded 95 mg of the epoxide *XL*, m.p. 53–54°C, $[\alpha]_D^{20}$ +28° (*c* 0·8). IR spectrum: 997, 901, 889, 884 cm^{-1} (ether). ^{1}H NMR spectrum: 0·66 (s, 18-H), 0·90 (s, 19-H), 2·24 (dd, $J_{gem} = -11·6$ Hz, 4α-H), 3·20 and 4·03 (d and dd, $J = 0·8$ Hz, $J_{gem} = -8·2$ Hz, $-OCH_2$), 4·26 (t, $J_{3\alpha,2\beta} = 5·3$ Hz, $J_{3\alpha,4\beta} = 5·3$ Hz, $J_{3\alpha,4\alpha} = 0$ Hz, 3α-H. For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·86% C, 12·25% H.

The analyses were carried out in the Analytical Laboratory of this Institute by Mrs E. Sýkorová and Mrs E. Šípová under the direction of Dr J. Horáček. The IR spectra were recorded by Mrs K. Matoušková under the direction of Dr J. Smolíková. The CD spectra were recorded and interpreted by Dr S. Vašíčková. Our thanks are due to Dr F. Tureček for recording and interpreting the mass spectra.

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