4,4-DIMETHYL-A-HOMOCHOLESTANE DERIVATIVES*

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The synthesis of epimeric bromo ketones *VII*, *VIII*, *XXV* and *XXVI*, derived from 4,4-dimethyl--A-homo-4a-cholesten-3-one (*I*) and 4,4-dimethyl-A-homo-5-cholesten-3-one (*XIII*) is described in this paper. In the case of bromo ketones *VII*, *VIII* and *XXV* the IR data demonstrate the presence of conformers both with a quasi-axial and a quasi-equatorial bromine atom in the equilibrium mixture, the quasi-equatorial conformer being the predominant component. On the basis of IR, CD and ^{1}H-NMR data the conformation of the ring A in compounds *VII*, *VIII*, *XXV* and *XXVI* is discussed.

In the preceding paper[1] of this series we have described the preparation of 4,4-dimethyl-A-homocholestane derivatives carrying an oxygen-containing substituent in the position 3. In this paper we describe the preparation of epimeric bromoketones derived from 4,4-dimethyl-A-homo-4a-cholesten-3-one (*I*), ref.[1], and 4,4-dimethyl-A-homo-5-cholesten-3-one (*XIII*), ref.[1], and discuss spectral properties of these bromo ketones in the IR region. On the basis of physical studies the conformation of the A-ring of these compounds is also discussed.

Bromination of 4,4-dimethyl-A-homo-4a-cholesten-3-one (*I*), ref.[1], with the Jacques reagent in tetrahydrofuran afforded 2α,2β-dibromo-4,4-dimethyl-A-homo-4a-cholesten-3-one (*II*) in 6% yield, and a mixture of two epimeric bromoketones *VII* and *VIII* as the main product. The reduction of this mixture and subsequent acetylation afforded a chromatographically more easily separable mixture of bromohydrin acetates *III* and *IV*, which were obtained in a 1 : 2 ratio. Bromohydrin acetate *III* gave the known[1] 3β-acetoxy-4,4-dimethyl-A-homo-4a-cholestene (*IX*) on catalytic debromination, while bromohydrin *V* which was obtained on reduction of bromohydrin acetate *III* with lithium aluminum hydride, gave with methanolic potassium hydroxide ketone *I*. These reactions demonstrate that both the bromine atom at $C_{(2)}$ and the hydroxyl group at $C_{(3)}$ are *cis*-oriented and β, and hence bromohydrin *V* must have the structure of 2β-bromo-4,4-dimethyl-A-homo-4a-cholesten-3β-ol. On oxidation with chromium trioxide–pyridine complex bromohydrin *V* gave bromo ketone *VII*. Catalytic debromination of bromohydrin acetate *IV* led to the known[1]

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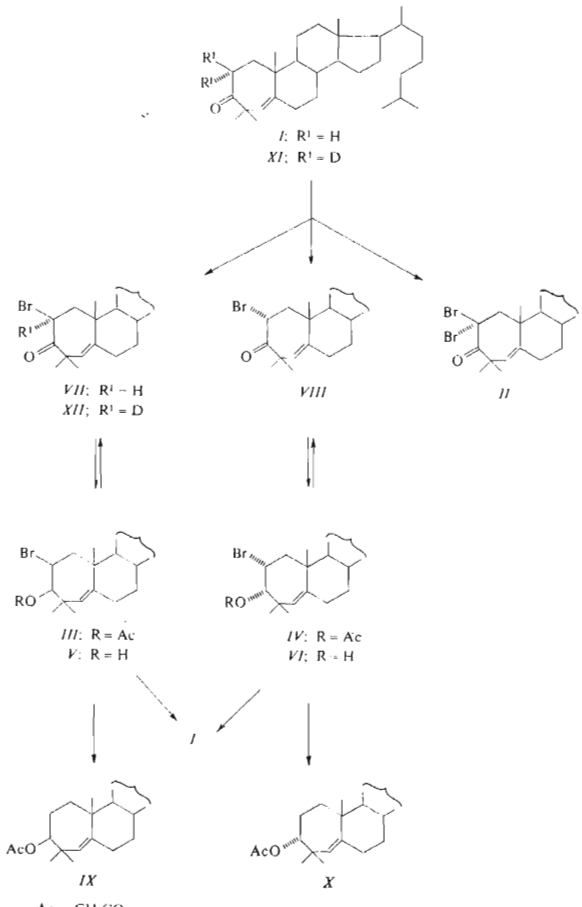
3α-acetoxy-4,4-dimethyl-A-homo-4a-cholesten (*X*), while bromohydrin *VI*, which was obtained on reduction of bromohydrin acetate *IV* with lithium aluminum hydride,



gave ketone *I* on reaction with methanolic potassium hydroxide. These reactions demonstrate that both the bromine atom at $C_{(2)}$ and the hydroxyl group at $C_{(3)}$ are *cis*-oriented and α, and therefore bromohydrin *VI* has the structure of 2α-bromo-4,4-dimethyl-A-homo-4a-cholesten-3α-ol. Oxidation of bromohydrin *VI* with chromium trioxide–pyridine complex gave bromo ketone *VIII*.

Bromination of 4,4-dimethyl-A-homo-5-cholesten-3-one (*XIII*), ref.[1], with the Jacques reagent in ethylene glycol dimethyl ether afforded a mixture of bromo ketones *XXV* and *XXVI* in 73% yield. The reduction of this mixture with lithium aluminum hydride afforded a chromatographically more easily separable mixture of three bromohydrins, *XIV*, *XV* and *XVI*, in an approximate 2 : 1 : 1 ratio, which were characterized as acetates *XVII*, *XVIII* and *XIX*. Catalytic debromination of bromohydrin acetate *XVII* afforded acetoxy derivative *XXI* which was converted by alkaline hydrolysis to the known[1] 4,4-dimethyl-A-homo-5-cholesten-3α-ol (*XXIII*). On reaction with methanolic potassium hydroxide bromohydrin acetate *XVII* gave α-epoxide *XX*, which demonstrates that bromohydrin acetate *XVII* is a *trans* derivative and has therefore the structure of 3α-acetoxy-2β-bromo-4,4-dimethyl-A-homo-5-cholestene. The reaction of bromohydrin acetate *XVIII* and *XIX* with methanolic potassium hydroxide led in both cases to the starting ketone *XIII* which means that both bromohydrin acetates *XVIII* and *XIX* are *cis*-derivatives. Catalytic debromination of bromohydrin acetate *XVIII* afforded acetoxy derivative *XXII* which was converted by alkaline saponification to the known[1] 4,4-dimethyl-A-homo-5-cholesten-3β-ol (*XXIV*). Hence, bromohydrin acetate *XVIII* has the structure of 3β-acetoxy-2β-bromo-4,4-dimethyl-A-homo-5-cholestene. Bromohydrin acetate *XIX* gave acetoxy derivative *XXI* on catalytic debromination, which means that bromohydrin acetate *XIX* has the structure of 3α-acetoxy-2α-bromo-4,4-dimethyl-A-homo-5-cholestene. Oxidation of bromohydrins *XIV* and *XV* afforded the same bromo ketone *XXV* and oxidation of bromohydrin *XVI* gave epimeric bromo ketone *XXVI*.

All the bromo ketones *VII*, *VIII*, *XXV* and *XXVI* were studied from the point of view of their spectral properties in the infrared region. In the infrared spectrum of bromoketone *XXVI* a single carbonyl group band was found at 1729 cm^{-1}. In the infrared spectra of bromo ketones *VII*, *VIII* and *XXV*, however, two bands were found in the carbonyl region after measurement in solution. When the non-polar solvent (tetrachloromethane) was substituted by the more polar chloroform, a change in the ratio of the intensities of the two bands took place in all instances (Table I). In order to eliminate the effect of Fermi's resonance, which is often operative in substances of this type[2], as the cause of the occurrence of two maxima in the carbonyl frequency, we also investigated the fingerprint regions in both solvents. In all the substances investigated (*VII*, *VIII* and *XXV*) relative changes in the band intensities were found in this region as well, which proves that a change of solvent causes a change in the proportion of the conformations in solution[3–5] (Table II). From this it follows that in these substances Fermi's resonance is not the sole reason for the

appearance of a doublet in the carbonyl frequency region. In order to further determine the possible effect of association of the substance[5,6] on the shape of the carbonyl region spectra at the 0·2M concentration used in our measurements, we also measured for each substance the concentration dependence in tetrachloromethane. The doublet in the carbonyl region did not disappear, but the ratio of the band intensities did change a little: In the case of bromo ketones *VIII* and *XXV* the band with the lower frequency is somewhat stronger in dilute solutions in comparison with the concentrated solutions (Table I) – in agreement with the literature[5,6]. However, bromo ketone *VII* displays a reversed change of the intensities of the carbonyl bands at the same change of concentration. In dilute solution the proportion of the conformer displaying the ν(C=O) band at lower frequency is lower than in concentrated solution. In all three bromo ketones, *VII*, *VIII* and *XXV*, the change in the ratio of the intensities of the carbonyl bands corresponding to individual conformers, is much stronger on passage from a non-polar solvent (tetrachloromethane) to a more polar one (chloroform) than on a mere change in concentration in non-polar solvent, and it is easily explicable by the presence of a conformational equilibrium[2,3,6].

In the case of bromo ketone *VII* in which anomalous behaviour has been observed during concentration changes we carried out deuteration in the α-position to the carbonyl group, so that we might consider the appearance of the carbonyl region of the spectrum and check the behaviour of this substance during the concentration dependence. The corresponding deuterated bromo ketone *XII* was prepared in a similar manner as bromo ketone *VII*: The bromination of 2α,2β-dideuterio-4,4-dimethyl--A-homo-4a-cholesten-3-one (*XI*) with the Jacques reagent in ethylene glycol dimethyl ether afforded a mixture of two epimeric bromo ketones, which was reduced with lithium aluminum deuteride and the product acetylated. The reduction of the less polar bromohydrin acetate with lithium aluminum deuteride and the oxidation of the resulting bromohydrin gave the required 2β-bromo-2α-deuterio-4,4-dimethyl--A-homo-4a-cholesten-3-one (*XII*). In the infrared spectrum of bromo ketone *XII* in tetrachloromethane solution two bands were again found in the carbonyl region. The maximum of the band with the lower frequency was not shifted in comparison with the non-deuterated compound *VII*; however, the maximum of the band with the higher frequency was shifted up to 3 cm^{-1}. The change of the ratio of the intensities of both bands on concentration change in non-polar solution (tetrachloromethane) is indeed small, but it is in agreement with the literature data[5,6] (Table I); hence, even here we have to do with the equilibrium of two conformers differing in polarity. In chloroform solution of the deuterated substance *XII* a third, less strong, band appeared between the two investigated bands in the carbonyl region, largely overlapping them.

In view of the small shifts of the carbonyl bands of the deuterated bromo ketone *XII* in comparison with the non-deuterated bromo ketone, and in view of the fact

that the behaviour of all bromo ketones investigated (*i.e. VII, VIII, XII* and *XXV*) during the change of the polarity of the solvent is in agreement with the literature data[2] (Tables I and II) we consider that the observed frequency values of the carbonyl bands can provide approximate information on the spacial relationship of the C—Br bond and the carbonyl group. As follows from Table III in all bromo ketones studied

TABLE I

Stretching Vibrations of the Carbonyl Group of Compounds *VII, VIII, XII* and *XXV*

Compound	Solvent concentration mol l^{-1}	ν(CO) cm^{-1}	A_a^a A_e^a	$\frac{A_e}{A_a}$
VII	CCl_4	1 704·5	0·295	1·89
	0·002[b]	1 729·1	0·558	
	CCl_4	1 704·8	0·2825	1·87
	0·2[c]	1 729·1	0·5285	
	$CHCl_3$	1 699·6	0·2245	2·28
	0·2[c]	1 723·0	0·5125	
VIII	CCl_4	1 706·0	0·4965	0·9426
	0·002[b]	1 729·8	0·4680	
	CCl_4	1 706·5	0·4838	0·9964
	0·2[c]	1 730·8	0·4820	
	$CHCl_3$	1 701·0	0·3275	1·3634
	0·2[c]	1 723·8	0·4465	
XII	CCl_4	1 704·5	0·321	1·33
	0·002[b]	1 732·4	0·427	
	CCl_4	1 704·6	0·3195	1·34
	0·2[c]	1 732·0	0·4285	
	$CHCl_3$[d]	1 701·2	0·2665	—
	0·2[c]	1 727·2	0·4465	
XXV	CCl_4	1 701·4	0·3135	1·4577
	0·002[b]	1 723·5	0·457	
	CCl_4	1 701·9	0·378	1·4815
	0·2[c]	1 723·4	0·560	
	$CHCl_3$	1 697·4	0·2808	1·8305
	0·2[c]	1 717·5	0·514	

[a] Absorbance of bands in the carbonyl region were calculated by the baseline method, A_a absorbance of the conformer with the quasi-axial bromine atom, A_e absorbance of the conformer with the quasi-equatorial bromine atom; [b] cell width 10 mm; [c] cell width 0·1 mm; [d] another band was observed in the carbonyl region, at 1 713·7 cm^{-1} ($A = 0·3025$).

(*VII*, *VIII* and *XXV*) the bands with lower frequency may be assigned to conformers in which the angle between the two dipoles corresponds to the angle of the axial bromine atom in α-bromo ketones with a six-membered ring, while the bands with higher frequency may be assigned to conformers in which the angle between the two dipoles corresponds to the equatorial conformation of the bromine atom. In bromo ketones *VII*, *VIII* abd *XXV* the conformer with a quasi-equatorial bromine atom predominates in the equilibrium mixture, the amount of the quasi-axial conformer being higher in the case of bromo ketone *VIII* (Table I). For bromo ketones *VII*, *VIII* and *XXV* it applies that the change in the proportion of individual conformers in dependence of the solvent used is small in comparison with substances with a cyclohexane ring[2].

TABLE II

Changes in the Wave-frequency Values (cm^{-1}) of the Bands in the Fingerprint Region of Compounds *VII*, *VIII*, *XII* and *XXV* in Passage from Tetrachloromethane to Chloroform

The spectra were measured at 0·2M concentration in tetrachloromethane and chloroform, respectively. Cell width 0·1 mm. The values of the wave-frequency of bands are from tetrachloromethane solution; the observed changes in passage to chloroform solution are given in brackets.

Compound	Decreasing values	Increasing values
VII	1 329, 1 262, 1 031 (+2), 512	1 335, 1 304, 1 045 (+2), 912, 538
VIII	1 440, 1 260, 1 175 (+1), 1 169 (+1), 933 (+3), 512	1 372, 1 301, (+1), 1 151 (+1), 969, 535
XII	1 084, 910, 612, 516	1 102 (+1), 1 080, 1 010, 540
XXV	1 261, 1 111 (+1), 929, 908, 522	1 255, 1 132, 1 000, 965, 897, 860

TABLE III

Differences (in cm^{-1}) of the Carbonyl Bands of Compounds *I*, *VII*, *VIII*, *XIII* and *XXV*, Measured in Tetrachloromethane

Compound	*VII*	*VIII*	*XXV*
$\Delta\nu$(C=O)[a]	—0·6[b], 23·7[b]	1·1[b], 25·4[b]	0·5[c], 22·0[c]

[a] Wave-numbers of compounds *VII*, *VIII* and *XXV*, see Table I; [b] shift of the wave-number of the carbonyl band in comparison with that of ketone *I*, ν(C=O) 1 705·4 cm^{-1}; [c] shift of the wave-number of the carbonyl band in comparison with ketone *XIII* ν(C=O) 1 701·4 cm^{-1}.

The spectral data together with the inspection of Dreiding models enable some conclusions on the preferred conformations of the ring A in bromo ketones *VII*, *VIII*, *XXV* and *XXVI*. In the case of bromo ketones *VII* and *VIII* the Dreiding models show that if the ring B is in the chair conformation, then the seven-membered ring A may assume four conformations *A*, *B*, *C* and *D* (Fig. 1). The boat conformation of the ring B, proposed for A-homo-$\Delta^{4a,5}$-3-keto derivatives on the basis of CD data[10] does not seem to be probable in the case of analogous 4,4-dimethyl derivatives considering the strong interactions between $C_{(4\beta)}$ and 19-methyl groups in all unstrained conformations of the ring A. The positive Cotton effect ($\Delta\varepsilon = +2{\cdot}00$) observed in bromo ketone *VII* is consistent with all the proposed conformations *A*, *B*, *C* and *D*, equally as the negative Cotton effect ($\Delta\varepsilon = -1{\cdot}86$) observed in bromo ketone *VII*. However, the conformation *B* is somewhat strained. Further, in the case of bromo ketone *VII* the conformation *D* may be excluded since the dihedral angle between the C–Br bond and the carbonyl group is about 70°C, which does not correspond to the IR data (Table III). Hence, we consider that in the case of bromo ketone *VII* the ring A of the quasi-equatorial conformer, prevailing in the equilibrium mixture (Table I), probably assumes the conformations *A* and *C*, respectively. The presence of the conformer with the quasi-axial bromine atom, with the ring A in con-

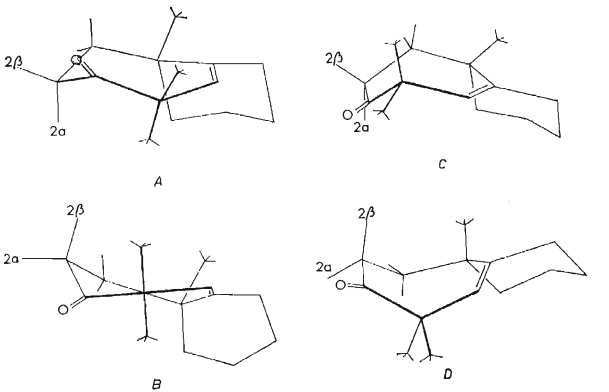


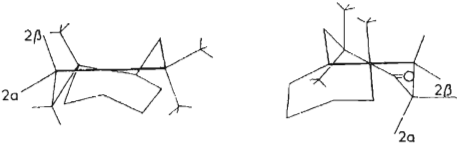
FIG. 1
Conformation of Ring A of Bromo Ketones *VII* and *VIII*

formation *B* – which is less favourable from the point of view of strain, is probably given by the strong preference of the axial conformation of the bromine atom, observed in cyclic α-bromo ketones[7–11].

In the case of bromo ketone *VIII* conformation *C* may be excluded since the dihedral angle between the C–Br bond and the carbonyl group is about 70°, which again does not correspond to the IR data (Table III). We consider that conformations *A* (quasi-axial bromine atom) and *D* (quasi-equatorial bromine atom) are preferred conformations of bromo ketone *VIII*.

In the case of bromo ketone *XXV* the study of Dreiding models showed that the conformations $C_{(1)}$-chair, $C_{(2)}$-chair, $C_{(4a)}$-twist chair and $C_{(5)}$-twist chair are very improbable in view of the strong steric interactions between $C_{(4\beta)}$ and 19-methyl groups; the conformations $C_{(3)}$-chair and $C_{(5)}$-chair are also very improbable in view of the substantial strain in such molecules. In the remaining conformations the bromine atom would assume quasi-axial conformation in the ring A conformations, *i.e.* $C_{(10)}$-chair, $C_{(4)}$-twist chair and $C_{(3)}$-twist chair, and quasi-equatorial conformation in the conformations $C_{(4)}$-chair, $C_{(4a)}$-chair, $C_{(1)}$-twist chair, $C_{(2)}$-twist chair and $C_{(10)}$-twist chair. The observed positive Cotton effect ($\Delta\varepsilon = +1{\cdot}31$) is consistent with the conformations $C_{(10)}$-chair, $C_{(4a)}$-chair, $C_{(4)}$-twist chair, $C_{(3)}$-twist chair, $C_{(2)}$-twist chair and $C_{(10)}$-twist chair, but after estimating the non-bonding interactions within the ring A the conformations $C_{(3)}$-twist chair (quasi-axial bromine atom) and $C_{(10)}$-twist chair (quasi-equatorial bromine atom) seem to be the least strained ones. We consider that these conformations (Fig. 2) are predominant in the equilibrium mixture of bromo ketone *XXV*.

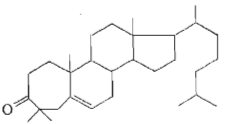
The strong shift of the IR-carbonyl frequency of bromoketone *XXVI*, resulting after the introduction of one bromine atom into position α to the carbonyl of the keto derivative *XIII* ($\Delta\nu$ *m* 28 cm^{-1}), as well as the weak shift of the CD maximum of this bromo ketone *XXVI* in comparison with the parent ketone *XIII* ($\Delta\lambda = +2$ nm) shows that the angle between both dipoles corresponds to the equatorial conformation of the bromine substituent in α-bromo ketones with the six-membered ring. The large value of the vicinal coupling constant ($J_{2,1} = 12$ Hz) further shows that



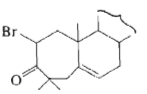
TC_3-twist chair TC_{10}-twist chair

FIG. 2

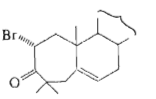
Conformation of Ring A of Bromo Ketones *XXV* and *XXVI*



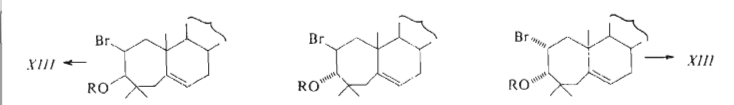
XIII



XXV



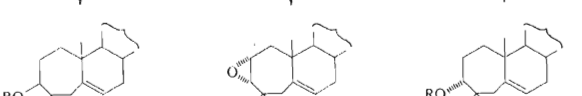
XXVI



XV; R = H
XVIII; R = Ac

XIV; R = H
XVII; R = Ac

XVI; R = H
XIX; R = Ac



XXII; R = Ac
XXIV; R = H

XX

XXI; R = Ac
XXIII; R = H

the dihedral angle between the 2β-hydrogen and one of the hydrogens on $C_{(1)}$ must be close to 180°. All these facts are fulfilled in the following conformations of the A-ring: $C_{(1)}$-chair, $C_{(2)}$-chair, $C_{(3)}$-chair, $C_{(10)}$-chair, $C_{(3)}$-twist chair, $C_{(4)}$-twist chair, $C_{(4a)}$-twist chair and $C_{(5)}$-twist chair. However, the conformations $C_{(1)}$-chair, $C_{(2)}$-chair, $C_{(4a)}$-twist chair and $C_{(5)}$-twist chair seem to be very improbable in view of the strong steric interactions between $C_{(4\beta)}$ and 19-methyl groups, and the conformation $C_{(3)}$-chair in view of the substantial strain in such a molecule. Further, the conformations $C_{(1)}$-chair, $C_{(10)}$-chair and $C_{(4)}$-twist chair are not consistent with the strong negative Cotton effect ($\Delta\varepsilon = -3{\cdot}12$) which was observed in bromo ketone *XXVI*. Hence, the $C_{(3)}$-twist chair conformation seems to be the preferred conformation in the equilibrium mixture of the conformers of bromo ketone *XXVI*.

EXPERIMENTAL

The melting points were measured on a Kofler melting point apparatus and they are not corrected. Optical rotations were measured in chloroform. The infrared spectra were measured on a Perkin–Elmer, model 621, spectrophotometer, calibrated with water vapour and, in some regions, with indene, and on a UR-20 (Zeiss, Jena) instrument. The ^{1}H-NMR spectra were measured on a Varian HA-100 instrument, in deuteriochloroform, using tetramethylsilane as internal reference. The chemical shifts are given in ppm. The CD curves were measured on a Roussel Jouan CD 185 dichrograph in dioxane. The identity of the samples prepared in various ways was checked by mixture melting point determinations and infrared spectra measurements. The phrase "worked up as usual" means the following procedure: The solution was washed with 5% hydrochloric acid, 5% potassium hydrogen carbonate solution and water, dried over sodium sulfate and concentrated in a vacuum.

Bromination of 4,4-Dimethyl-A-homo-4a-cholesten-3-one[1] (*I*)

Jacques reagent (800 mg) was added to a solution of ketone *I* (650 mg) in tetrahydrofuran (12 ml) and the mixture was allowed to stand at room temperature for 4 h. After pouring into water the product was extracted with ether and the extract washed with a 5% solution of potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent was evaporated in a vacuum. The residue (800 mg) was chromatographed on a column of silica gel (80 g) with light petroleum–ether (9·5 : 0·5). The less polar fractions were combined and worked up affording 51 mg of 2α,2β-dibromo-4,4-dimethyl-A-homo-4a-cholesten-3-one (*II*) which was crystallized from methanol, m.p. 103—105°C, $[\alpha]_D^{21}$ —15° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1712 cm^{-1}. ^{1}H-NMR spectrum: 0·70 (s, 3 H, 18-CH_3); 0·865 (d, 6 H, 26 + 27-CH_3, $J = 6$ Hz); 0·905 (d, 3 H, 21-CH_3, $J = 6$ Hz); 1·255 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 1·48 (s, 19-CH_3 or $C_{(4)}$—CH_3); 1·58 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 3·36 (s, 2 H, $C_{(1)}$—H); 5·05 (broad s, 1 H, $C_{(4a)}$—H). For $C_{30}H_{48}Br_2O$ (584·3) calculated: 61·65% C, 8·29% H, 27·32% Br; found: 61·42% C, 8·14% H, 26·48% Br.

The more polar fractions were worked up affording 510 mg of an oily product which was pure according to TLC, but — as will be shown below — it represented a mixture of two inseparable bromo ketones *VII* and *VIII*. Infrared spectrum (nujol): 1732, 1709 cm^{-1}. CD spectrum: $\Delta\varepsilon_{303} = -0{\cdot}74$. For $C_{30}H_{49}BrO$ (505·5) calculated: 71·33% C, 9·74% H, 15·80% Br; found: 70·88% C, 9·56% H, 16·10% Br.

3β-Acetoxy-2β-bromo-4,4-dimethyl-A-homo-4a-cholestene (*III*)

a) Lithium aluminum hydride (120 mg) was added to a solution of the unseparable mixture of bromo ketones *VII* and *VIII* (220 mg) in ether (10 ml) at 0°C and the mixture was allowed to stand at this temperature for 10 min. The excess of the hydride was decomposed with a saturated aqueous solution of sodium sulfate and the mixture was filtered through a small column of sodium sulfate. The filtrate was evaporated in a vacuum and the residue (220 mg) was acetylated with acetic anhydride (1·2 ml) in pyridine (6 ml) overnight. The mixture was poured into water and the product was extracted with ether. The ethereal extract was worked up as usual, affording 220 mg of an oily product which was chromatographed on five silica gel plates (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The polar zones were combined, eluted with ether and the solvent evaporated in a vacuum. The residue (72 mg) was crystallized from methanol, affording 50·5 mg of compound *III*, m.p. 85—86°C, $[\alpha]_D^{21}$ —53° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1753, 1235, 1039, 1647 cm^{-1}. ^{1}H-NMR spectrum: 0·66 (s, 3 H, 18-CH_3); 0·86 (d, 6 H, 26 + + 27-CH_3, J = 6 Hz); 0·89 (d, 3 H, 21-CH_3, J = 6 Hz); 1·06 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 1·11 (s, 6 H, 19-CH_3 + $C_{(4)}$—CH_3 or $C_{(4)}$—CH_3 + $C_{(4)}$—CH_3); 2·14 (s, 3 H, —OAc); 4·64 (mt, 1 H, $C_{(2)}$—H, $J_{2,3}$ = 3·5 Hz, $J_{2,1}$ = 10 + 3·0 Hz); 4·92 (broad s, 1 H, $C_{(4a)}$—H); 5·13 (d, 1 H, $C_{(3)}$—H, $J_{3,2}$ = 3·5 Hz). For $C_{32}H_{53}BrO_2$ (545·6) calculated: 69·71% C, 9·79% H; found: 69·01% C, 9·18% H.

b) Bromohydrin *V* (25 mg) was acetylated with acetic anhydride (two drops) in pyridine (1 ml) overnight. After the usual working up an oily product was obtained (20 mg) which was chromatographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The required zone was eluted with ether and the solvent was evaporated in a vacuum. The residue (15 mg) was crystallized from methanol, affording 8 mg of bromohydrin acetate *III*, m.p. 85—86°C, $[\alpha]_D^{21}$ —53° (*c* 0·3).

3α-Acetoxy-2α-bromo-4,4-dimethyl-A-homo-4a-cholestene (*IV*)

a) The working up of the more polar zones after the isolation of bromohydrin acetate *III* in the preceding procedure *a*) afforded 130·5 mg of bromohydrin acetate *IV* which was crystallized from methanol, m.p. 126—126·5°C, $[\alpha]_D^{21}$ +60° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1750, 1232, 1030 cm^{-1}. ^{1}H-NMR spectrum: 0·68 (s, 3 H, 18-CH_3); 0·865 (d, 6 H, 26 + 27-CH_3, J = 6 Hz); 0·90 (d, 3 H, 21-CH_3, J = 6 Hz); 1·09 (s, 6 H, 19-CH_3 + $C_{(4)}$—CH_3 or $C_{(4)}$—CH_3 + + $C_{(4)}$—CH_3); 1·11 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 2·165 (s, 3 H, —OAc); 4·80 (broad mt, 1 H, $C_{(2)}$—H); 4·90 (broad s, 1 H, $C_{(4a}$—H); 5·18 (d, 1 H, $C_{(3)}$—H, $J_{3,2}$ = 3·0 Hz). For C_{32}· $.H_{53}BrO_2$ (545·6) calculated: 69·71% C, 9·79% H; found: 69·93% C, 9·67% H.

b) Bromohydrin *VI* (80 mg) was acetylated with acetic anhydride (0·4 ml) in pyridine (2 ml) overnight. The usual working up gave 80 mg of an oily product, which was chromatographed on two silica gel plates (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). Corresponding zones were combined, eluted with ether and the solvent evaporated under reduced pressure. The residue (52 mg) was crystallized from methanol, affording 43 mg of bromohydrin acetate *IV*, m.p. 126—126·5, $[\alpha]_D^{21}$ +59° (*c* 0·5).

2β-Bromo-4,4-dimethyl-A-homo-4a-cholesten-3β-ol (*V*)

a) Lithium aluminum hydride (30 mg) was added to a solution of bromohydrin acetate *III* (60 mg) in ether (5 ml) at 0°C and the mixture was allowed to stand at the same temperature for 10 min. The excess of hydride was decomposed with a saturated aqueous sodium sulfate solution and the mixture was filtered through a small bed of sodium sulfate in a column. The

filtrate was concentrated under reduced pressure affording 50 mg of an oily product which was chromatographed on one plate of silica gel (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The required zone was eluted with ether, the solvent was evaporated in a vacuum. The resulting bromohydrin *V* (40 mg) was pure according to TLC but it would not crystallize, $[\alpha]_D^{21}$ —49° (*c* 0·5). Infrared spectrum (tetrachloromethane): 3 589, 3 549 cm^{-1}. For $C_{30}H_{51}BrO$ (507·3) calculated: 70·99% C, 10·12% H; found: 71·24% C, 10·21% H.

b) Lithium aluminum hydride (15 mg) was added to a solution of bromo ketone *VII* (33 mg) in ether (4 ml) at 0°C and the mixture was allowed to stand at this temperature for 10 min. The same working up as in the preceding case (*a*) afforded 30 mg of an oily product which was chromatographed on one plate of silica gel (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The required zone was eluted with ether and the solvent was evaporated under reduced pressure. The resulting bromohydrin *V* (22 mg) was reluctant to crystallize in all attempts at crystallization, $[\alpha]_D^{21}$ —49° (*c* 0·5).

2α-Bromo-4,4-dimethyl-A-homo-3a-cholesten-3α-ol (*VI*)

a) Lithium aluminum hydride (50 mg) was added to a solution of bromohydrin acetate *IV* (120 mg) in ether (8 ml) at 0°C and the mixture was allowed to stand at this temperature for 10 min. The same working up as in the preceding experiments afforded 120 mg of a crude product, which was chromatographed on two silica gel plates (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). Corresponding zones were combined, eluted with ether and the solvent was evaporated under reduced pressure. The resulting bromohydrin *VI* (110 mg) was homogenous according to TLC, but it could not be obtained in crystalline form, $[\alpha]_D^{21}$ +60° (*c* 0·5). Infrared spectrum (tetrachloromethane): 3 589, 3 550 cm^{-1}. For $C_{30}H_{51}BrO$ (507·3) calculated: 70·99% C, 10·12% H; found: 70·71% C, 10·21% H.

b) Lithium aluminum hydride (25 mg) was added to a solution of bromo ketone *VIII* (50 mg) in ether (5 ml) at 0°C and the mixture was allowed to stand at the same temperature for 10 min. The same working up as under *a*) afforded 50 mg of a crude product which was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The required zone was eluted with ether and the solvent was evaporated in a vacuum. The resulting bromohydrin *VI* (31 mg) was not crystalline, $[\alpha]_D^{21}$ +60° (*c* 0·5).

2β-Bromo-4,4-dimethyl-A-homo-4a-cholesten-3-one (*VII*)

A solution of bromohydrin *V* (65 mg) in pyridine (4 ml) was added to the chromium trioxide–pyridine complex (40 mg in 1 ml) and the mixture was allowed to stand at room temperature overnight. After the usual working up 48 mg of a crude product were obtained which was chromatographed on a 20 × 20 cm silica gel plate in light petroleum–ether (0·5 : 0·5). The required zone was eluted with ether, the solvent was evaporated in a vacuum. The resulting bromo ketone *VII* was pure according to TLC, but it would not crystallize, $[\alpha]_D^{21}$ +13° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1 731, 1 709 cm^{-1}. ^{1}H-NMR spectrum: 0·675 (s, 3 H, 18-CH_3); 0·85 (d, 6 H, 26 + 27-CH_3, J = 6 Hz); 1·00 (d, 3 H, 21-CH_3, J = 6 Hz); 1·20 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 1·42 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 1·25 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 4·71 (dd, 1 H, $C_{(2)}$—H, $J_{2,1}$ = 10 + 3 Hz); 5·07 (broad s, 1 H, $C_{(4a)}$—H). CD spectrum: $\Delta\varepsilon_{288}$ = +2·00. For $C_{30}H_{49}BrO$ (505·5) calculated: 71·33% C, 9·74% H; found: 71·20% C, 9·72% H.

2α-Bromo-4,4-dimethyl-A-homo-4a-cholesten-3-one (*VIII*)

Bromohydrin *VI* (40 mg) was reacted with the chromium trioxide–pyridine complex (20 mg in 1 ml) in the same manner as in the preceding experiment. The crude product (40 mg) was chrom-

atographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The working up of the required zone gave 35 mg of bromo ketone *VIII* which was crystallized from methanol, at —10°C, m.p. 64—66°C. Infrared spectrum (tetrachloromethane): 1 730, 1 706 cm^{-1}. ^{1}H-NMR spectrum: 0·68 (s, 3 H, 18-CH_3); 0·86 (d, 6 H, 26 + 27-CH_3, J = 6 Hz); 0·89 (d, 3 H, 21-CH_3, J = 6 Hz); 1·15 (s, 3 H, $C_{(4)}$—CH_3 or 19-CH_3); 1·195 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 1·44 (s, 3 H, $C_{(4)}$—CH_3 or 19-CH_3); 4·78 (dd, 1 H, $C_{(2)}$—H, $J_{2,1}$ = 10 + 2·5 Hz); 5·50 (broad s, 1 H, $C_{(4a)}$—H). CD spectrum: $\Delta\varepsilon_{295}$ = —1·86. For $C_{30}H_{49}BrO$ (505·5) calculated: 71·33% C, 9·74% H, 15·80% Br; found: 71·13% C, 9·72% H, 16·30% Br.

3β-Acetoxy-4,4-dimethyl-A-homo-4a-cholestene (*IX*)

Raney nickel was added in excess to a solution of bromohydrin acetate *III* (18 mg) in ethanol and the mixture was refluxed under stirring for 5 h. The Raney nickel was filtered off and the filtrate evaporated in a vacuum. The residue (10 mg) was crystallized from methanol affording 5 mg of acetate *IX*, m.p. 83—85°C, $[\alpha]_D^{21}$ +60° (*c* 0·5); literature[1] gives m.p. 84—85°C and $[\alpha]_D^{22}$ +62°.

3α-Acetoxy-4,4-dimethyl-A-homo-4a-cholestene (*X*)

Bromohydrin acetate *IV* (33 mg) was reacted with Raney nickel in the same manner as in the preceding experiment. The crude product (30 mg) was crystallized from methanol, affording 10 mg of acetate *X*, m.p. 101—102°C, $[\alpha]_D^{22}$ +27° (*c* 0·5); literature[1] gives m.p. 101—102°C, $[\alpha]_D^{22}$ +27°.

4,4-Dimethyl-A-homo-4a-cholesten-3-one (*I*)

a) Bromo ketone *VII* (40 mg) in ethyl acetate (5 ml) and ethanol (3 ml) was shaken under hydrogen with 5% palladium on calcium carbonate (150 mg) for 4 h. The mixture was diluted with ether, the catalyst was filtered off and the filtrate evaporated in a vacuum. The residue (40 mg) was crystallized from methanol, affording 23 mg of ketone *I*, m.p. 76—78°C, $[\alpha]_D^{22}$ +13° (*c* 0·5) in accordance with literature[1].

b) Bromo ketone *VIII* (50 mg) in ethyl acetate (6 ml) and ethanol (3 ml) was shaken under hydrogen with 5% palladium on calcium carbonate (150 mg) for 4 h. The same working up as under *a*) afforded 50 mg of a crude product, which was crystallized from methanol affording 30 mg of ketone *I*, m.p. 76—78°C, $[\alpha]_D^{22}$ +13° (*c* 0·5), in accordance with the literature[1].

c) Solid potassium hydroxide (40 mg) was added to a solution of bromohydrin *V* (40 mg) in methanol (3·5 ml) and the mixture was refluxed for 1 h, then poured into water and the product extracted with ether. The extract was washed with water, dried over sodium sulfate and the solvent was evaporated under reduced pressure. The residue (30 mg) was chromatographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The required zone was eluted with ether and the solvent evaporated under reduced pressure. The residue (18 mg) was crystallized from methanol affording 11 mg of ketone *I*, m.p. 76—78°C, $[\alpha]_D^{22}$ +13° (*c* 0·5) in accordance with literature[1].

d) Solid potassium hydroxide (40 mg) was added to bromohydrin *VI* (40 mg) in methanol (2 ml) and the mixture was refluxed for 1 h. The same working up as in experiment *c*) afforded 31 mg of a crude product which was chromatographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The corresponding zone was eluted with ether and the solvent was

evaporated under reduced pressure. The residue (18·5 mg) was crystallized from methanol affording 11 mg of ketone *I*, m.p. 76–78°C, $[\alpha]_D^{22}$ +13° (*c* 0·5) in accordance with literature[1].

2α,2β-Dideuterio-4,4-dimethyl-A-homo-3a-cholesten-3-one (*XI*)

Sodium (350 mg) was added to a solution of deuterium oxide (10 ml) in dioxane (30 ml), followed by a solution of ketone *I* (350 mg) in dioxane (18 ml) and the mixture was refluxed for 2 h under nitrogen. After concentration under reduced pressure dioxane (10 ml) was added, followed by deuterium oxide (2 ml) and the mixture was refluxed under nitrogen for another 2 h. This procedure was repeated once more and the residue was extracted with ether, washed with deuterium oxide, dried over sodium sulfate and the solvent was evaporated in a vacuum. The residue (350 mg) was chromatographed on a silica gel column (30 g, 10% D_2O) in benzene. The required fractions were worked up affording 325 mg of ketone *XI*, m.p. 78–80°C. Mass spectrometry demonstrated the presence of 2 atoms of deuterium in the molecule. Infrared spectrum (tetrachloromethane): 1 701·9 cm^{-1}.

2β-Bromo-2α-deuterio-4,4-dimethyl-A-homo-4a-cholesten-3-one (*XII*)

Bromo ketone *XII* was prepared from the deuterated ketone *XI* in the same manner as bromo ketone *VII* from ketone *I* (*i.e. via* bromination with the Jacques reagent, reduction with lithium aluminum deuteride, acetylation with acetic anhydride in pyridine, reduction of the less polar bromohydrin acetate with lithium aluminum deuteride and oxidation with the chromium trioxide–pyridine complex). Infrared spectrum (tetrachloromethane): 1 704·6, 1 732·0 cm^{-1}. Content of deuterium (mass spectrometry): 83%.

Bromination of 4,4-Dimethyl-A-homo-5-cholesten-3-one[1] (*XIII*)

Jacques reagent (300 mg) was added to a solution of ketone *XIII* (500 mg) in ethylene glycol dimethyl ether (4 ml) and the mixture was allowed to stand at room temperature for 5 h. It was poured into water and the product extracted with ether. The extract was washed with 5% potassium hydrogen carbonate solution and water, dried over sodium sulfate and the solvent was evaporated in a vacuum. The residue (500 mg) was chromatographed on a silica gel column (50 g) in light petroleum–ether (9·5 : 0·5). The working up of the required fractions afforded 433 mg of a crystalline product which gave a single spot on TLC, but which consisted, as will be shown below, of a mixture of two inseparable bromo ketones *XXV* and *XXVI*. Infrared spectrum (tetrachloromethane): 1 725, 1 703 cm^{-1}. CD spectrum: $\Delta\varepsilon_{284} = +1·06$. For $C_{30}H_{49}BrO$ (505·5) calculated: 71·33% C, 9·74% H, 15·80% Br; found: 71·29% C, 9·75% H, 15·70% Br.

2β-Bromo-4,4-dimethyl-A-homo-5-cholesten-3α-ol (*XIV*)

a) Lithium aluminum hydride (80 mg) was added at 0°C to a solution of the inseparable mixture of bromo ketones *XXV* and *XXVI* (150 mg) in ether and the mixture was allowed to stand at this temperature for 15 min. The excess of the hydride was decomposed with a saturated sodium sulfate solution and the mixture was filtered through a small column of sodium sulfate. The filtrate was concentrated in a vacuum and the crude product obtained (150 mg) was chromatographed on four silica gel plates (20 × 20 cm) in light petroleum–ether (25 : 1). The corresponding less polar zones were combined, eluted with ether and the solvent was evaporated in a vacuum. The residue (75 mg) was crystallized from methanol affording 35 mg of bromo-

hydrin *XIV*, m.p. 74·5—75°C, $[\alpha]_D^{21}$ —12° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1665, 3040, 3575 cm^{-1}. For $C_{30}H_{51}BrO$ (507·3) calculated: 70·99% C, 10·12% H; found: 71·08% C, 9·99% H.

b) Lithium aluminum hydride (50 mg) was added to a solution of bromo ketone *XXV* (100 mg) in ether (4 ml) at 0°C and the mixture was allowed to stand at the same temperature for 15 min. Identical working up as in experiment *a*) afforded 100 mg of a crude product which was chromatographed on two silica gel plates (20 × 20 cm) in light petroleum–ether (25 : 1) using double elution. The corresponding less polar zones were combined, eluted with ether and the solvent was evaporated in a vacuum. The residue (60 mg) was crystallized from methanol affording 30 mg of bromohydrin *XIV*, m.p. 74·5—75°C, $[\alpha]_D^{22}$ —12° (*c* 0·5).

c) Lithium aluminum hydride (80 mg) was added to a solution of acetate *XVII* (180 mg) in ether (5 ml) at room temperature and the mixture was allowed to stand for 30 min. Working up of the mixture as under *a*) afforded 170 mg of a crude product which was crystallized from methanol to give 100 mg of bromohydrin *XIV*, m.p. 74·5—75°C, $[\alpha]_D^{22}$ —12° (*c* 0·5).

2β-Bromo-4,4-dimethyl-A-homo-5-cholesten-3β-ol (*XV*)

a) The working up of corresponding more polar zones after the isolation of bromohydrin *XIV* (see under *a*) in the preceding experiment) afforded 32 mg of bromohydrin *XV* which was crystallized from methanol, m.p. 83—58°C, $[\alpha]_D^{22}$ —22° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1662, 3035, 3585 cm^{-1}. For $C_{30}H_{51}BrO$ (507·3) calculated: 70·99% C, 10·12% H; found: 70·68% C, 10·05% H.

b) The working up of the corresponding more polar zones after the isolation of bromohydrin *XIV* (see under *b*) in the preceding experiment) afforded 28 mg of bromohydrin *XV* which was crystallized from methanol, m.p. 83—95°C, $[\alpha]_D^{22}$ —22° (*c* 0·5).

c) Lithium aluminum hydride (40 mg) was added to a solution of acetate *XVIII* (90 mg) in ether (3 ml) and the mixture was allowed to stand at room temperature for 20 min. Working up of the mixture as in case *c*) of the preceding experiment gave 85 mg of a crude product which was crystallized from methanol, m.p. 83—85°C, $[\alpha]_D^{22}$ —22° (*c* 0·5).

2α-Bromo-4,4-dimethyl-A-homo-5-cholesten-3α-ol (*XVI*)

a) The working up of the corresponding most polar zones after the isolation of bromohydrin *XIV* and *XV* (see under *a*) in the preceding experiments) afforded 25 mg of bromohydrin *XVI* which was crystallized from methanol, m.p. 124—126°C, $[\alpha]_D^{20}$ —15° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1662, 3035, 3575 cm^{-1}. For $C_{30}H_{51}BrO$ (507·3) calculated: 70·99% C, 10·12% H; found: 70·68% C, 10·65% H.

b) Lithium aluminum hydride (5 mg) was added to a solution of bromo ketone *XXVI* (10 mg) in ether (2 ml) at room temperature and the mixture was allowed to stand at this temperature for 10 min. The excess of hydride was decomposed with a saturated aqueous sodium sulfate solution and the mixture was filtered through a small column of sodium sulfate. The filtrate was concentrated in a vacuum and the crude product obtained (9·5 mg) was chromatographed on a silica gel plate (7·5 × 10 cm) in light petroleum–ether (25 : 1), using double elution. The required zone was eluted with ether and the solvent was evaporated under reduced pressure. The residue (6·6 mg) was crystallized from methanol affording 3 mg of bromohydrin *XVI*, m.p. 124—126°C.

c) Lithium aluminum hydride (20 mg) was added to a solution of acetate *XIX* (40 mg) in ether (2 ml) at room temperature and the mixture was allowed to stand at this temperature for 20 min. The same working up as under *b*) gave 38 mg of a crude product which was crystallized from methanol, affording 21 mg of bromohydrin *XVI*, m.p. 124—126°C, $[\alpha]_D^{22}$ —15° (*c* 0·5).

3α-Acetoxy-2β-bromo-4,4-dimethyl-A-homo-5-cholestene (*XVII*)

Bromohydrin *XIV* (90 mg) was acetylated with acetic anhydride (0·5 ml) in pyridine (3 ml) overnight. The conventional working up gave 90 mg of a crude product which was crystallized from methanol affording 78·5 mg of acetate *XVII*, m.p. 154—155°C, $[\alpha]_D^{21}$ —19° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1 748, 1 232 cm^{-1}. For $C_{32}H_{53}BrO_2$ (545·6) calculated: 69·71% C, 9·79% H; found: 70·21% C, 9·46% H.

3β-Acetoxy-2β-bromo-4,4-dimethyl-A-homo-5-cholestene (*XVIII*)

Bromohydrin *XV* (50 mg) was acetylated with acetic anhydride (0·3 ml) in pyridine (3 ml) overnight. The conventional working up afforded 50 mg of a crude product which was crystallized from methanol to give 28·5 mg of acetate *XVIII*, m.p. 148—149°C, $[\alpha]_D^{21}$ —23° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1 752, 1 232, 1 047, 1 665 cm^{-1}. For $C_{32}H_{53}BrO_2$ (545·6) calculated: 69·71% C, 9·79% H; found: 70·35% C, 9·70% H.

3α-Acetoxy-2α-bromo-4,4-dimethyl-A-homo-5-cholestene (*XIX*)

Bromohydrin *XVI* (50 mg) was acetylated with acetic anhydride (0·3 ml) in pyridine (3 ml) overnight. The mixture was worked up as usual, affording 50 mg of a crude product which was chromatographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (99 : 1). The corresponding zone was eluted with ether and the solvent evaporated under reduced pressure. The residue (41 mg) was homogeneous according to TLC but it resisted all attempts at crystallization, $[\alpha]_D^{21}$ —19° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1 751, 1 232, 1 034 cm^{-1}. For $C_{32}H_{53}BrO_2$ (545·6) calculated: 69·71% C, 9·79% H; found: 70·11% C, 9·66% H.

4,4-Dimethyl-2α,3α-epoxy-A-homo-5-cholestene (*XX*)

A solution of acetate *XVII* (40 mg) and potassium hydroxide (50 mg) in methanol (5 ml) was refluxed for 3 h, then poured into water and the product extracted with ether. The ethereal extract was washed with water, dried over sodium sulfate and the solvent was evaporated in a vacuum. The residue (38 mg) was chromatographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (99 : 1). The less polar zone was eluted with ether and the solvent evaporated under reduced pressure. The residue (25 mg) was crystallized from methanol affording 15 mg of epoxide *XX*, m.p. 156—157·5°C, $[\alpha]_D^{21}$ —5° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1 670, 3 035 cm^{-1}. ^{1}H-NMR spectrum: 0·655 (s, 3 H, 18-CH_3); 0·79 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 0·84 (d, 6 H, 26 + 27-CH_3, J = 6 Hz); 0·89 (d, 3 H, 21-CH_3, J = 6 Hz); 1·038 (s, 6 H, 19-CH_3 + + $C_{(4)}$—CH_3 or $C_{(4)}$—CH_3 + $C_{(4)}$—CH_3); 2·53 (d, 1 H, $C_{(3)}$—H, $J_{3,2}$ = 4·5 Hz); 3·00 (dd, 1 H, $C_{(2)}$—H, $J_{2,1}$ = 4·5 + 9 Hz); 5·26 (broad d, 1 H, $C_{(6)}$—H, $J_{6,7}$ = 4·5 + 2 Hz). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·81% H; found: 84·32% C, 11·80% H. The working up of the more polar zone gave 6 mg of the starting acetate *XVII*, m.p. 154—155°C, $[\alpha]_D^{21}$ —19° (*c* 0·5).

3β-Acetoxy-4,4-dimethyl-A-homo-5-cholestene (*XXII*)

a) Lithium aluminum hydride (100 mg) was added to a solution of ketone *XIII* (200 mg) in ether (10 ml) and the mixture was allowed to stand at room temperature for 2 h. The excess of hydride was decomposed with a saturated aqueous sodium sulfate solution and the mixture was filtered through a small column of sodium sulfate. The filtrate was concentrated in a vacuum and the residue (200 mg) acetylated with acetic anhydride (0·6 ml) in pyridine (5 ml) overnight. After working up in the usual manner 180 mg of a crude product were obtained, which was chromatographed on five silica gel plates (20 × 20 cm) in light petroluem–ether (97 : 3), using triple elution. The corresponding less polar zones were combined, eluted with ether and the solvent evaporated in a vacuum. The residue (35 mg) was crystallized from methanol, affording 20 mg of acetate *XXII*, m.p. 134—136°C, $[\alpha]_D^{21}$ +24° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1 739, 1 250, 1 031, 1 663 cm^{-1}. For $C_{32}H_{54}O_2$ (470·7) calculated: 81·64% C, 11·56% H; found: 82·02% C, 11·77% H.

b) An excess of Raney nickel was added to a solution of bromohydrin acetate *XVIII* (18 mg) in ethanol (4 ml) and the mixture was refluxed under stirring for 4 h. The Raney nickel was filtered off and the filtrate evaporated in a vacuum. The residue (13 mg) was crystallized from methanol, giving 5 mg of acetate *XXII*, m.p. 134—136°C, $[\alpha]_D^{21}$ +24° (*c* 0·5).

c) 4,4-Dimethyl-A-homo-5-cholesten-3β-ol (*XXIV*), ref.[1], (50 mg), was acetylated with acetic anhydride (0·2 ml) in pyridine (2 ml) overnight. Working up of the reaction mixture in the usual manner gave. 50 mg of a crude product which was crystallized from methanol, affording 35 mg of acetate *XXII*, m.p. 134—136°C, $[\alpha]_D^{21}$ +24° (*c* 0·5).

3α-Acetoxy-4,4-dimethyl-A-homo-5-cholestene (*XXI*)

a) The working up of the corresponding more polar zones after the isolation of the 3β-isomer *XXII* from the preceding experiment *a*) afforded 140 mg of acetate *XXI* which was crystallized from ethanol, m.p. 132—134°C, $[\alpha]_D^{21}$ —7° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1 739, 1 248, 1 027, 1 663 cm^{-1}. For $C_{32}H_{54}O_2$ (470·7) calculated: 81·64% C, 11·56% H; found: 81·24% C 11·37% H.

b) An excess of Raney nickel was added to a solution of bromohydrin acetate *XVII* (150 mg) in ethanol (10 ml) and the mixture was refluxed for 10 h. The Raney nickel was filtered off and the filtrate evaporated under reduced pressure. The residue (150 mg) was chromatographed on three silica gel plates (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The corresponding zones were combined, washed with ether and the solvent was evaporated under reduced pressure. The residue (130 mg) was crystallized from ethanol to yield 100 mg of acetate *XXI*, m.p. 132 to 134°C, $[\alpha]_D^{21}$ —7° (*c* 0·5).

c) An excess of Raney nickel was added to a solution of bromohydrin acetate *XIX* (20 mg) in ethanol (7·5 ml) and the mixture was refluxed for 5 h. Identical working up as under *b*) afforded 20 mg of a crude product which was chromatographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The required zone was eluted with ether and the solvent evaporated in a vacuum. The residue (15 mg) was crystallized from ethanol to give 6 mg of acetate *XXI*, m.p. 132—134°C, $[\alpha]_D^{21}$ —7° (*c* 0·5).

d) 4,4-Dimethyl-A-homo-5-cholesten-3α-ol (*XXIII*), ref.[1], (50 mg) was acetylated with acetic anhydride (0·2 ml) in pyridine (2 ml) overnight. The mixture was worked up as usual, giving 50 mg of a crude product which was crystallized from ethanol to yield 32 mg of acetate *XXI*, m.p. 132—134°C, $[\alpha]_D^{21}$ —7° (*c* 0·5).

2β-Bromo-4,4-dimethyl-A-homo-5-cholesten-3-one (*XXV*)

a) Jones reagent (0·3 ml) was added to a solution of bromohydrin *XIV* (90 mg) in acetone (9 ml) and the mixture was shaken for 8 min and poured into water. The mixture was extracted with ether and the extract washed with 5% potassium hydrogen carbonate solution and water. After drying over sodium sulfate and filtration the solvent was evaporated in a vacuum. The residue (90 mg) was crystallized from methanol, affording 61 mg of bromo ketone *XXV*, m.p. 105 to 107°C, $[\alpha]_D^{20}$ —5° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1 725, 1 704, 3 040, 1 664 cm^{-1}. ^{1}H-NMR spectrum: 0·675 (s, 3 H, 18-CH_3); 0·85 (d, 6 H, 26 + 27-CH_3, J = 6 Hz); 0·94 (s, 3 H, 19-CH_3 or $C_{(4)}$ CH_3); 1·12 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 1·275 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3 —CH_3); 4·42 (dd, 1 H, $C_{(2)}$ -H, $J_{2,1}$ = 3 + 12 Hz); 5·54 (broad d, 1 H, $C_{(6)}$—H). CD spectrum: $\Delta\varepsilon_{290}$ = +1·31. For $C_{30}H_{49}BrO$ (505·5) calculated: 71·33% C, 9·74% H, 15·80% Br; found: 71·15% C, 8·99% H, 15·90% Br.

b) Jones reagent (0·15 ml) was added to a solution of bromohydrin *XV* (50 mg) in acetone (3 ml) and the mixture was shaken for 8 min. The same working up as under *a*) afforded 50 mg of a crude product which was crystallized from methanol to yield 30 mg of bromoketone *XXV*, m.p. 105—107°C, $[\alpha]_D^{20}$ —5° (*c* 0·5).

2α-Bromo-4,4-dimethyl-A-homo-5-cholesten-3-one (*XXVI*)

Jones reagent (0·1 ml) was added to a solution of bromohydrin *XVI* (30 mg) in acetone (2 ml) and the mixture was shaken for 8 min. The same working up as in the preparation of bromo ketone *XXV* gave 30 mg of a crude product which was chromatographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The corresponding less polar zone was washed with ether and the solvent evaporated under reduced pressure. The residue (20 mg) was crystallized from methanol, yielding 15 mg of bromo ketone *XXVI*, m.p. 174—175°C. Infrared spectrum (tetrachloromethane): 1 729, 1 660, 3 040 cm^{-1}. ^{1}H-NMR spectrum: 0·52 (s, 3 H, 18-CH_3); 0·89 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 0·85 (d, 6 H, 26 + 27-CH_3, J = 6 Hz); 0·905 (d, 3 H, 21-CH_3, J = 6 Hz); 1·105 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 1·16 (s, 3 H, 19-CH_3 or $C_{(4)}$—CH_3); 5·23 (dd, 1 H, $C_{(2)}$—H, $J_{2,1}$ = 3 + 12 Hz); 5·46 (centre of mt, 1 H, $C_{(6)}$—H). CD spectrum: $\Delta\varepsilon_{293}$ = —3·12. For $C_{30}H_{49}BrO$ (505·5) calculated: 71·33% C, 9·74% H, 15·80% Br; found: 71·04% C, 9·86% H, 15·95% Br. The working up of the more polar zone afforded 6 mg of ketone *XIII* which was crystallized from methanol, m.p. 152—154°C, $[\alpha]_D^{21}$ —3° in agreement with the literature[1].

Reaction of Bromohydrin Acetate *XVIII* and *XIX* with Potassium Hydroxide

Potassium hydroxide (50 mg) was added to a solution of acetate *XVIII* (50 mg) in methanol (4 ml) and the mixture was refluxed for 2 h. After pouring into water the product was extracted with ether and the extract washed with water, dried over sodium sulfate and the solvent evaporated in a vacuum. The residue (50 mg) was chromatographed on a silica gel plate (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The corresponding zone was eluted with ether and the solvent evaporated under reduced pressure. The residue (40 mg) was crystallized from methanol to yield 29 mg of ketone *XIII*, m.p. 152—154°C, $[\alpha]_D^{21}$ —3° (*c* 0·5) in agreement with the literature[1].

In the same manner the reaction of acetate *XIX* (50 mg) with potassium hydroxide (50 mg) was carried out and the mixture worked up. The crude product (50 mg) was submitted to preparative chromatography to yield 42 mg of ketone *XIII* which was crystallized from methanol, m.p. 152—154°C, $[\alpha]_D^{21}$ —3° (*c* 0·5), in agreement with literature[1].

The analyses were carried out in the analytical laboratories of this Institute by V. Štěrba, V. Rusová and E. Sýkorová (under the direction of Dr J. Horáček), the IR *spectra were measured by P. Formánek (under the direction of Dr J. Smolíková), the* ^{1}H-NMR *spectra were measured by Dr M. Synáčková and the* CD *spectra by Dr S. Vašíčková.*

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