ON STEROIDS. CLVIII.* A-HOMOSTEROIDS. IV.**

A-RING CONFORMATION OF SOME A-HOMO-5α-CHOLESTAN-4A-ONE DERIVATIVES

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Synthesis of a series of A-homo-5α-cholestan-4a-one derivatives is reported and conformation of the A-homo-ring is discussed on the basis of the IR, ORD and NMR-data.

In previous papers of this series[1-3], we reported on the preparation and structure proof of some 6β-acetoxy-A-homo-5α-cholestan-4-one derivatives. This paper deals with the preparation, structure and conformation of certain derivatives of 6β-acetoxy-A-homo-5α-cholestan-4a-one.

Oxidation of the previously reported[3] A-homo-5α-cholestan-4aα,6β-diol 6-acetate (*I*) with Jones' reagent furnished the 4a-ketone *II* in 80% yield which on bromination in acetic acid was converted to the bromo ketone *III* in 50% yield. In the NMR-spectrum the signal of the C<u>H</u>—Br proton appears as a doublet of doublet (δ = = 4·09 p.p.m., J = 10 Hz and 8·5 Hz). This fact indicates the presence of two neighboring protons and localizes the bromine atom in the position 4. Oxidation of the previously described[3] 4β-bromo-A-homo-5α-cholestan-4aα,6β-diol 6-acetate (*VI*) resulted in the formation of the bromo ketone *VII*. The NMR-spectrum of this compound shows the signal of the C<u>H</u>—Br proton as a triplet (δ = 4·83 p.p.m., J = = 5·6 Hz and 5·6 Hz), which also is only compatible with the position 4. Thus, compound *III* and *VII* are epimeric 4α- and 4β-bromo ketones, respectively. The presence of an asymmetric center at $C_{(5)}$ in the neighborhood of the 4a-keto group makes it desirable to check that no isomerization at $C_{(5)}$ occurred in the course of the oxidation process. This possibility was ruled out in the following manner. The bromo ketone *VII* was reduced with lithium tri-tert-butoxyaluminum hydride to give the bromohydrin *VIII* in 80% yield. This latter compound was subjected to reduction with zinc in acetic acid to furnish 6β-acetoxy-A-homo-5α-cholest-4-ene (*X*) with the known[2] configuration at $C_{(5)}$. The bromohydrin *VIII* is thus shown to be an A-homo-

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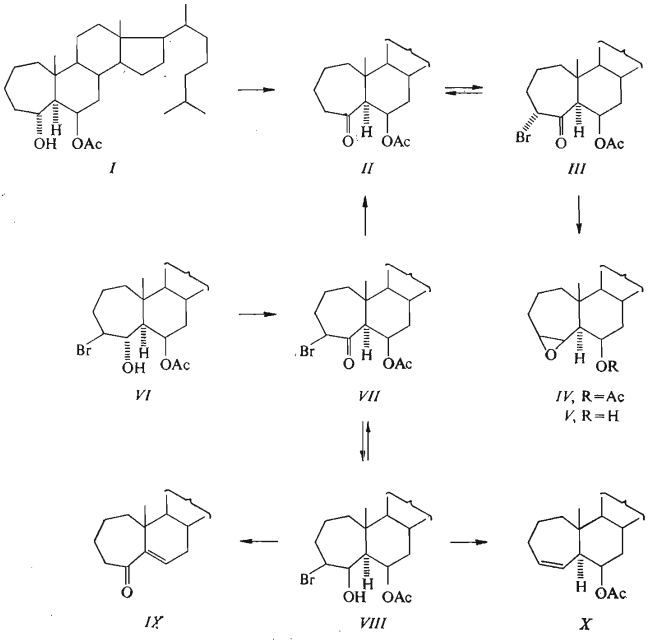
5α-cholestane derivative. The same conclusion must also be made for the bromo ketone *VII* since this compound can be recovered from *VIII* on Jones' oxidation. Moreover, correlation of the keto derivatives *II* and *III* with the bromo ketone *VII* proves the 5α-configuration also for these two compounds. The correlation was performed in the following manner. Palladium catalyzed hydrogenolysis of the bromo ketone *VII* leads to the ketone *II*. Bromination of the latter results in the formation of the bromo ketone *III*. Retention of the configuration at $C_{(5)}$ in the course of this reaction was proved by converting the bromo ketone *III* to the ketone *II* on hydrogenolysis.

When treated with methanolic potassium hydroxide, the bromohydrin *VIII* is converted to α,β-unsaturated ketone *IX* arising by splitting off one molecule of water from the primarily formed 6β-hydroxy-A-homo-5α-cholestan-4a-one. Formation



of a 4a-ketone shows that the starting bromohydrin is a *cis* derivative in agreement with its formulation as *VIII*.

On reduction with lithium tri-tert-butoxyaluminum hydride in tetrahydrofuran, the bromo ketone *III* gives the epoxide *IV* in 78% yield. It is assumed that the primarily formed *trans* bromohydrin is easily converted to epoxide *IV* in the alkaline reaction medium. The epoxide was also characterized as the hydroxy derivative *V*.

Spectral data together with examination of the Dreiding models offer the possibility of making some conclusions concerning preferred conformations of the A-ring in A-homo-5α-cholestan-4aα, 6β-diol 6-acetate[3] (*I*), in the bromohydrins *VI*[3] and *VIII* and in the bromo ketones *III* and *VII*. In the case of the compounds *I*, *VI* and *VIII* the stereochemical conclusions are further supported by hydrogen bond measurements in the IR-region. This method provides direct information about the orientation of both hydrogen-bonded groups and permits, by indirect evidence, to make conclusions about geometry of the respective ring system. In A-homo-5α-cholestan-4aα,6β-diol 6-acetate (*I*) there was found a strong intramolecular hydrogen bond ($\Delta_{\nu(OH)} = 116\ cm^{-1}$). From the shift in carbonyl frequency (Table I) it is evident that the hydrogen is bonded to the carbonyl oxygen of the acetoxy grouping. Examination of Dreiding models shows that in two conformations formation of a hydrogen bond is impossible, *i.e.* in one chair form with a plane of symmetry passing through the $C_{(2)}$-atom ($C_{(2)}$-chair) and in one twist chair form with the axis of symmetry passing through $C_{(5)}$-atom ($C_{(5)}$-twist chair).* A very weak bond of the free hydroxyl in the IR-spectrum shows that at least one of these forms also participates to a small extent in the mixture of conformers. With regard to a strong interaction between 4β-hydrogen and 19-methyl in the $C_{(2)}$-chair form, it may be concluded that the predominating conformation (of those with a nonbonded hydroxyl group) is the $C_{(5)}$-twist chair form. In the remaining conformations, *i.e.* $C_{(1)}$, $C_{(4)}$, $C_{(4a)}$, $C_{(5)}$, $C_{(10)}$-chair and $C_{(1)}$, $C_{(2)}$, $C_{(3)}$, $C_{(4)}$, $C_{4a)}$, $C_{(10)}$-twist chair there are good

TABLE I

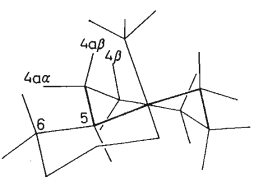
IR Spectroscopic Characteristics (cm^{-1}) of Some Hydroxy Derivatives.

Structure	Formula	$\nu(OH)_{bonded}$	$\nu(OH)_{free}$	$\nu(OAc)_{free}$	$\nu(OAc)_{bonded}$
4aα-Hydroxy	*I*	3 516	3 632	1 736	1 716
4β-Bromo-4aα-hydroxy[3]	*VI*	3 568	—	1 738	—
4β-Bromo-4aβ-hydroxy	*VIII*	3 577	—	1 738	—

* In the following text we will designate the ring conformations according to the carbon atom lying in the plane or axis of symmetry.

conditions for the formation of a hydrogen bond between the hydroxyl hydrogen and carbonyl oxygen of the acetoxy group. In all cases the distance between the respective groups is favourable and all three atoms involved can achieve linearity. From consideration of the nonbonded interactions inside the A-ring the $C_{(10)}$-twist chair conformer appears to be the least strained one and is therefore likely to be an important component in the equilibrated mixture of conformers of the hydroxy derivative *I*.

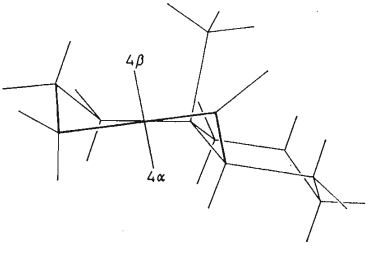
In bromohydrins *VI* and *VIII*, the IR spectrum demonstrated the presence of a strong hydrogen bonding whereas no band for the free hydroxyl was found (Table I). Examination of various conformations of the 4β-bromo-4aα-hydroxy derivative *VI* on Dreiding models showed that in the $C_{(1)}$- and $C_{(2)}$-chair and in the $C_{(4a)}$ and $C_{(5)}$-twist chair forms the dihedral angle between the C—OH and C—Br linkages is larger than 90° and thus excludes formation of hydrogen bonding; moreover, in the $C_{(2)}$-chair, $C_{(4a)}$ and $C_{(5)}$-twist chair forms there is a very strong non-bonded interaction between the 4β-bromine and 19-methyl group. Strong interactions are also present in the following conformations: $C_{(4)}$-chair (4aβ-hydrogen-19-methyl and 2α-5α-hydrogen interactions), $C_{(4a)}$-chair (strong 3β-hydrogen-19-methyl and 4aβ-hydrogen-19-methyl interactions), $C_{(5)}$-chair (2β-hydrogen-19-methyl and 4aβ-hydrogen-19-methyl interactions), $C_{(10)}$-chair (2β-hydrogen-19-methyl and 4aβ-hydrogen-19-methyl interactions), $C_{(1)}$-twist chair (4aβ-hydrogen-19-methyl interaction), $C_{(2)}$-twist chair (3β-hydrogen-19-methyl and 4aβ-hydrogen-19-methyl interactions), $C_{(3)}$-twist chair (2β-hydrogen-19-methyl and 4aβ-hydrogen-19-methyl interactions), $C_{(4)}$-twist chair (4aβ-hydrogen-19-methyl interaction). These interactions are relatively small in the $C_{(10)}$-twist chair and it therefore appears to be the favored conformation (Fig. 1).



$C_{(10)}$-twist chair

Fig. 1

Conformation of Ring A in Bromohydrins *VI* and *VIII*



$C_{(4)}$-twist chair

FIG. 2

Conformation of Ring A in 6β-Acetoxy-4α--bromo-A-homo-5α-cholestan-4a-one (*III*)

Similar considerations may be applied to the bromohydrin *VIII*. Steric interactions destabilize (and decrease the population of) the following conformation: $C_{(1)}$-chair (strong 4aβ-hydroxyl-19-methyl interaction), $C_{(2)}$-chair (4β-bromine-19-methyl interaction), $C_{(4)}$-chair (4aβ-hydroxyl-19-methyl and 2α-5α-hydrogen interactions), $C_{(4a)}$-chair (strong 3β-hydrogen-19-methyl and 4aβ-hydroxyl-19-methyl interactions), $C_{(5)}$-chair (strong 4aβ-hydroxyl-19-methyl interaction), $C_{(10)}$-chair (4aβ-hydroxyl--19-methyl and 2β-hydrogen-19-methyl interactions), $C_{(1)}$-twist chair (4aβ-hydroxyl--19-methyl interaction), $C_{(2)}$-twist chair (3β-hydrogen-19-methyl and 4aβ-hydroxyl--19-methyl interactions), $C_{(3)}$-twist chair (strong 4aβ-hydroxyl-19-methyl interaction), $C_{(4)}$-twist chair (4aβ-hydroxyl-19-methyl interaction), $C_{(4a)}$-twist chair (4β-bromine-19-methyl and 4aβ-hydroxyl-19-methyl interactions) and $C_{(5)}$-twist chair (4β-bromine-19-methyl interaction). For similar reasons as above, it is assumed that the favored conformation for the bromohydrin *VIII* is the $C_{(10)}$-twist chair (Fig. 1).

Combined IR, NMR and ORD-data (Table II) provided valuable information about the stereochemistry of the bromo ketones *III* and *VII*. A small shift in the IR-carbonyl frequency of the bromo ketone *III* as compared with the parent ketone *II* ($\Delta_{(CO)} + 8\ cm^{-1}$) coupled with a bathochromic shift of the first extremum in the ORD-curve of the bromo ketone *III* ($\Delta\lambda + 21$ nm) shows that the angle between both dipoles is in the range corresponding to axial conformation of the bromine substituent in six-membered α-bromo ketones. The ORD-curve of the bromo ketone *III* exhibits a very strong negative Cotton effect ($a = -256$) whereas a large value of the vicinal coupling constant ($J_{4,3} = 10$ Hz) shows that the dihedral angle between the 4β-hydrogen and one of the $C_{(3)}$-hydrogens must have a value near to 180°. All these facts are consistent with only two conformations, *i.e.* the $C_{(1)}$-chair and $C_{(4)}$-twist chair forms. Consequently, both conformers should be present in significant

TABLE II
Spectroscopic Characteristic of Ketones

Structure Formula	IR ν(CO) (cm^{-1})	ORD a	NMR δ (p.p.m.)
4a-One *II*	1 702	−100	—
4α-Bromo-4a-one *III*	1 710	−256	1 H, CH—Br: 4·09 (dd, $J = 10 + 8{\cdot}5$ Hz) 1 H, $C_{(5)}$—H: 3·055 (d, $J = 2{\cdot}0$ Hz)
4β-Bromo-4a-one *VII*	1 730	− 97	1 H, CH—Br: 4·83 (t, $J = 5{\cdot}6 + 5{\cdot}6$ Hz) 1 H, $C_{(5)}$—H: 2·71 (d, $J = 2{\cdot}4$ Hz)

proportions in the equilibrium. With respect to the known facts[4,5], the $C_{(4)}$-twist chair-conformer is likely to be the main component of the mixture of conformers (Fig. 2).

In the bromo ketone *VII*, a large shift in the IR-carbonyl frequency ($\Delta\nu_{(CO)}$ +28 cm^{-1}) together with a small bathochromic shift of the first extremum in the ORD-curve ($\Delta\lambda$ +7 nm) demonstrate the presence of a small angle between both dipoles. In line with these data is the practically unchanged Cotton effect of the bromo ketone *VII* ($a = -97$) as compared with that of the starting ketone *II* ($a = -100$). The requirements given by the above facts are met by the following six conformations: $C_{(5)}$-chair, $C_{(10)}$-chair, $C_{(2)}$-twist chair, $C_{(3)}$-twist chair, $C_{(4)}$-twist chair and $C_{(10)}$-twist chair. However, the available facts do not warrant unequivocal selection between the conformations.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Unless stated otherwise, optical rotations were measured in chloroform. The infrared spectra were measured on a Zeiss UR-10 spectrophotometer. The NMR-spectra were measured in deuteriochloroform on Varian HA-100 apparatus using tetramethylsilan as internal standard. The ORD-measurements were done on a Jasco Model ORD/UV-5. The identity of samples prepared by different routes was checked by mixture melting point determination and by infrared spectra.

6β-Acetoxy-A-homo-5α-cholestan-4a-one (*II*)

a) From 6β-acetoxy-A-homo-5α-cholestan-4aα-ol[3] (*I*): The alcohol *I* (50 mg) in acetone (3 ml) was treated with excess Jones' reagent and agitated at room temperature for 8 min. The excess reagent was removed with methanol, the reaction mixture diluted with water and the product extracted with ether. The ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and evaporated *in vacuo*. After repeated crystallization from methanol the residue (40 mg) afforded 24 mg of the ketone *II*, m.p. 112–114°C, $[\alpha]_D^{26}$ −25·8° (methanol, *c* 0·1). Infrared spectrum (tetrachloromethane): 1740, 1708, 1252, 1037 cm^{-1}. Infrared spectrum (KBr): 1702, 1738, 1758, 1036 cm^{-1}. ORD (methanol, *c* 0·1, 26°C): $[\Phi]_{400}$ −340°, $[\Phi]_{350}$ −750°, $[\Phi]_{330}$ −3400°, $[\Phi]_{318}$ −4400°, $[\Phi]_{310}$ −3260°, $[\Phi]_{300}$ ±0°, $[\Phi]_{285}$ +4620°, $[\Phi]_{275}$ +5570°, $[\Phi]_{260}$ +4760°, *a* −100. For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·54% C, 10·82% H.

b) From 6β-acetoxy-4β-bromo-A-homo-5α-cholestan-4a-one (*VII*). The bromo ketone *VII* (55 mg) in ethyl acetate (5 ml) and ethanol (5 ml) was agitated in a hydrogen atmosphere over 5% palladium–calcium carbonate catalyst (110 mg) for 8 h. The mixture was then diluted with ether, the catalyst was filtered off, washed with ether and the filtrate evaporated *in vacuo*. The residue (50 mg) was chromatographed preparatively on one plate of silica gel (20 × 20 cm) in benzene–ether (95 : 5). The corresponding zone was collected, eluted with ether and the solvent evaporated *in vacuo*. The residue (35 mg) was crystallized from methanol to yield 19·8 mg of the ketone *II*, m.p. 111–114°, $[\alpha]_D^{22}$ −25° (methanol, *c* 1·0).

c) From 6β-acetoxy-4α-bromo-A-homo-5α-cholestan-4a-one (*III*): The bromo ketone *III* (60 mg) in ethyl acetate (5 ml) and ethanol (5 ml) was agitated in a hydrogen atmosphere over a 5% palladium–calcium carbonate catalyst (120 mg) for 7 h. The mixture was diluted with ether, the catalyst was filtered off, washed with ether and the filtrate evaporated *in vacuo*. The residue

(54 mg) was chromatographed on one plate of silica gel (20 × 20 cm) in benzene–ether (95 : 5). The corresponding zone was collected, eluted with ether and the solvent evaporated *in vacuo*. The residue (43 mg) was crystallized from methanol to yield 28 mg of the ketone *II*, m.p. 112 to 114°C, $[\alpha]_D^{22}$ −26° (*c* 1·0, methanol).

6β-Acetoxy-4α-bromo-A-homo-5α-cholestan-4a-one (*III*)

A solution of bromine (100 mg) in acetic acid (1·0 ml) was added to a solution of the ketone *II* (130 mg) in acetic acid (5·0 ml) containing one drop of hydrobromic acid. The reaction mixture was allowed to stand at room temperature overnight and then poured into ice-water and the product extracted with ether. The ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The residue (135 mg) was chromatographed preparatively on two plates of silica gel (20 × 20 cm) in light petroleum–acetone (98 : 2). The corresponding zones were collected, eluted with ether and the solvent evaporated *in vacuo*. After crystallization from methanol the residue (66 mg) afforded 45 mg of the bromo ketone *III*, m.p. 121—123°C, $[\alpha]_D^{25}$ −118·0° (methanol, *c* 0·1). Infrared spectrum (KBr): 1710, 1739, 1250, 1033 cm^{-1}. ORD (methanol, *c* 0·1, 26°C): $[\Phi]_{400}$ −3000°, $[\Phi]_{360}$ −8180°, $[\Phi]_{345}$ −11840°, $[\Phi]_{335}$ −9960°, $[\Phi]_{321}$ ±0°, $[\Phi]_{310}$ +8180°, $[\Phi]_{293}$ +13720°, $[\Phi]_{275}$ +10900°, *a* −256. NMR: 0·995 (s, 3 H, 19-CH_3); 0·70 (s, 3 H, 18-CH_3); 0·855 (d, J = 6 Hz, 6 H, 26,27-CH_3); 0·90 (d, J = 6 Hz, 3 H, 21-CH_3); 2·11 (s, 3 H, OAc); 5·37 (broad unresolved signal, $W_{1/2}$ ~7 Hz, 1 H, $J_{5,6}$ = 2 Hz, C<u>H</u>—OAc); 4·09 (dd, $J_{4,3}$ = 10 Hz, $J_{4,3'}$ = 8·5 Hz, 1 H, C<u>H</u>—Br); 3·055 (d, $J_{5,6\alpha}$ = 2 Hz, 1 H, $C_{(5)}$—H). For $C_{30}H_{49}BrO_3$ (537·5) calculated: 67·03% C, 9·19% H; found: 66·80% C, 9·16% H.

4β,4aβ-Epoxy-A-homo-5α-cholestan-6β-yl Acetate (*IV*)

To a solution of the bromo ketone *III* (50 mg) in tetrahydrofuran (2 ml) lithium tri-tert-butoxyaluminum hydride (130 mg) was added and the mixture was allowed to stand at room temperature for 2 h. The reaction mixture was poured into ice-5% hydrochloric acid and the product was extracted with ether. The ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The residue (57 mg) was chromatographed preparatively on one plate of silica gel (20 × 20 cm) in light petroleum–acetone (95 : 5). The corresponding zone was collected, eluted with ether and the solvent evaporated *in vacuo*. After crystallization from methanol the residual substance (40 mg) afforded 32 mg of the epoxide *IV*, m.p. 74—75·5°C. Infrared spectrum (tetrachloromethane): 1737, 1240, 1030 cm^{-1}. NMR: 0·69 (s, 3 H, 18-CH_3); 1·14 (s, 3 H, 19-CH_3); 0·85 (d, J = 6·5 Hz, 6 H, 26,27 CH_3); 0·89 (d, J = 6·0 Hz, 3 H, 21-CH_3); 2·1 (s, 3 H, OAc); 2·86 (d, J = 4·4 Hz, 1 H, epoxidic); 2·97 (q, epoxidic); 5·23 (mt, J = 10 Hz, C<u>H</u>—OAc). For $C_{30}H_{50}O_3$ (456·7) calculated: 78·55% C, 10·99% H; found: 78·19% C, 11·29% H.

4β,4aβ-Epoxy-A-homo-5α-cholestan-6β-ol (*V*)

The epoxide *IV* (30 mg) was added to a solution of potassium hydroxide (600 mg) in methanol (10 ml) and refluxed for one hour. The methanol was distilled off under reduced pressure, the residue was diluted with water and the product extracted with ether. The ethereal extract was washed with water, dried over sodium sulfate and the solvent evaporated *in vacuo*. After recrystallization from methanol the residue (30 mg) afforded 16·5 mg of the epoxy alcohol *V*, m.p. 159—161°C. Infrared spectrum (tetrachloromethane): 3610 cm^{-1}. For $C_{28}H_{48}O_2$ (416·7) calculated: 80·71% C, 11·61% H; found: 80·99% C, 11·63% H.

6β-Acetoxy-4β-bromo-A-homo-5α-cholestan-4a-one (*VII*)

a) The alcohol *VI* (60 mg) in acetone (6 ml) was treated with excess Jones' reagent and agitated at room temperature for 8 min. The excess reagent was removed with methanol, the reaction mixture diluted with water and the product extracted with ether. The ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The residual oil (60 mg) was chromatographed preparatively on one plate of silica gel (20 × 20 cm) in light petroleum–acetone (99 : 1). The corresponding zone was collected, eluted with ether and the solvent evaporated *in vacuo*. After recrystallization from methanol the residue afforded the bromo ketone *VII*, m.p. 149–151°C, $[\alpha]_D^{25}$ +10·6° (methanol, *c* 0·1). Infrared spectrum (tetrachloromethane): 1740, 1730 (inflex), 1244, 1028, 1037 cm^{-1}. ORD (methanol, *c* 0·1, 25°C): $[\Phi]_{400}$ −110°, $[\Phi]_{350}$ −990°, $[\Phi]_{335}$ −2200°, $[\Phi]_{328}$ −2530°, $[\Phi]_{325}$ −2420°, $[\Phi]_{320}$ −1290°, $[\Phi]_{307}$ ±0°, $[\Phi]_{290}$ +5510°, $[\Phi]_{275}$ +7160°, $[\Phi]_{260}$ +6940°, *a* −97. NMR: 0·72 (s, 3 H 18-CH_3); 0·87 (d, 6 H, J = 6·0 Hz, 26,27-CH_3); 0·91 (d, 3 H, J = 6·0 Hz, 21-CH_3); 1·04 (s, 3 H, 19-CH_3); 2·12 (s, 3 H, OAc); 2·71 (d, 1 H, $J_{5,6}$ = 2·4 Hz, $C_{5\alpha}$—H); 4·83 (t, $J_{4,3}$ = 5·6 + 5·6 Hz, 1 H, CH—Br); 5·27 (q, $J_{6,5}$ = 2·4 Hz c. = $J_{6,7\alpha} + J_{6,7\beta}$, 1 H, CH—OAc). For $C_{30}H_{49}BrO_3$ (537·5) calculated: 67·03% C, 9·19% H; found: 67·47% C, 9·26% H.

b) The alcohol *VIII* (40 mg) in acetone (6 ml) was treated with excess Jones' reagent in the same manner as in the case *a*). The usual workup gave 40 mg of the crude product which was crystallized from methanol, m.p. 149–151°C, $[\alpha]_D^{22}$ +10° (methanol, *c* 1·0).

4β-Bromo-A-homo-5α-cholestan-4aβ,6β-diol 6-Acetate (*VIII*)

To a solution of the bromo ketone *VII* (75 mg) in tetrahydrofuran (2 ml) lithium tri-tert-butoxyaluminum hydride (160 mg) was added and the mixture was allowed to stand at room temperature for 4 h. The reaction mixture was then poured into ice–5% hydrochloric acid and the product was extracted with ether. The ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. After repeated crystallization from methanol the residue (61 mg) afforded 41 mg of the bromohydrin *VIII*, m.p. 163·5 to 165°C, $[\alpha]_D^{23}$ +10·7° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1738, 1250, 3577 cm^{-1}. For $C_{30}H_{51}BrO_3$ (539·5) calculated: 66·77% C, 9·52% H; found: 65·91% C, 9·96% H.

A-Homo-cholest-5-en-4a-one (*IX*)

The bromohydrin *VIII* (35 mg) was added to a solution of potassium hydroxide (600 mg) in methanol (10 ml) and refluxed for 1 h. Methanol was distilled off under reduced pressure, the residue was diluted with water and the product extracted with ether. The ethereal extract was washed with water, dried over sodium sulfate and the solvent evaporated *in vacuo*. After repeated crystallization from methanol the residue (19·5 mg) afforded 10 mg of the ketone *IX*, m.p. 78–80°. Infrared spectrum (tetrachloromethane): 1694, 1680, 1610 cm^{-1}. NMR: 1·04 (s, 3 H, 19-CH_3); 0·79 (s, 3 H, 18-CH_3); 0·86 (d, J = 6·2 Hz, 6 H, 26,27-CH_3); 0·91 (d, J = 6·0 Hz, 3 H, 21-CH_3); 2·50 (mt, 2 H); 6·12 (mt, 1 olefinic H). For $C_{28}H_{46}O$ (398·7) calculated: 84·35% C, 11·63% H; found: 84·00% C, 11·70% H.

6β-Acetoxy-A-homo-5α-cholest-4-ene (*X*)

The bromohydrin *VIII* (50 mg) in glacial acetic acid (10 ml) was refluxed with zinc dust (50 mg) for 5 h. Zinc was filtered off, washed with ether and the filtrate was poured into water. The ethereal extract was washed with 5% sodium hydrogen carbonate solution, water, dried over sodium

sulfate and the solvent evaporated under reduced pressure. The residue (35 mg) was preparatively chromatographed on one plate of silica gel in light petroleum, the corresponding zone was collected, eluted with ether and the solvent was evaporated under reduced pressure. The purified product *X* (20 mg) was still an oil resisting all attempts at crystallization. Infrared spectrum (tetrachloromethane): 1 736, 1 245, 1 655, 3 020 cm^{-1} is identical with that of the authentic sample[2].

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