SYNTHESIS OF SOME ALLYLIC ACETOXY DERIVATIVES IN THE STEROID SERIES

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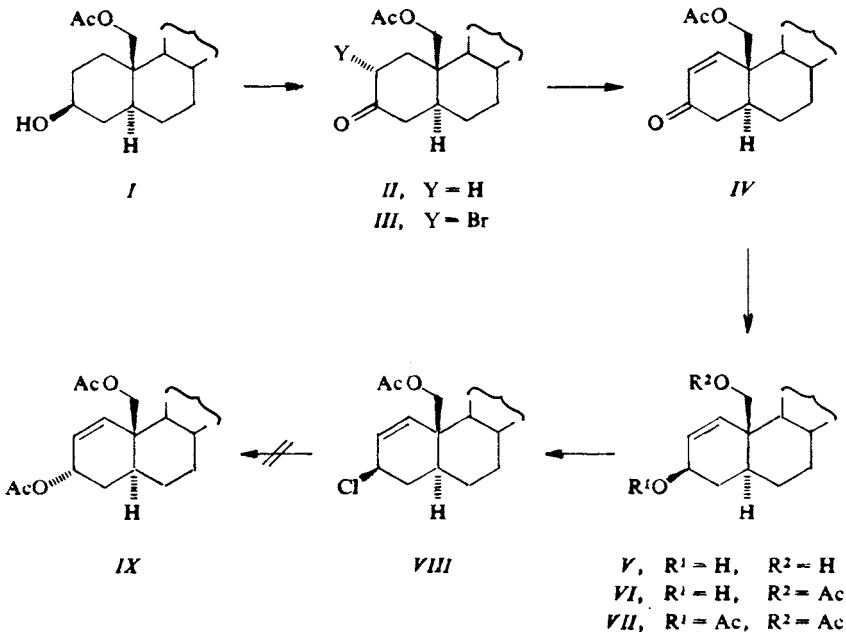
A synthesis is reported of 1,2- and 5,6-unsaturated cholestane derivatives bearing an acetoxy group in allylic position (*i.e.* 3 and 7) and containing further functional groups. A simple strategy for synthesis of 3α-substituted 5-cholestenes is devised.

For a study of participation of ambident ester groups in electrophilic additions we needed a series of steroid olefins bearing an acetoxy group in allylic position and possibly also containing one or two further acetoxy groups potentially capable to participate in electrophilic additions. In the present paper we report a synthesis of an 1,2-unsaturated diacetoxy derivative (*VII*), 5,6-unsaturated 3,7-diacetoxy (*XV*, *XVIII*, *XXVII* and *XXIX*), and 3,7,19-triacetoxy derivatives (*XXXIII* and *XXXV*).

The compounds *XV* and *XVIII* were described earlier[1-3]. Here, we report some modifications of their preparation. Furthermore, the synthesis of 5,6-unsaturated cholestane derivatives with a 3α-oriented oxygen function has been a long-standing problem in the steroid chemistry.

Following the procedure used in the preparation of 19-unsubstituted derivative[4-7], synthesis of the 1,2-unsaturated 3,19-diacetoxy derivative *VII* set out from the known[8] monoacetate of the 3,19-diol *I* (Scheme 1). The double bond was introduced into the position 1,2 in the usual manner. The alcohol *I* was oxidized with pyridinium chlorochromate and the resulting ketone *II* was brominated selectively to give the bromo ketone *III* which on dehydrobromination under controlled conditions furnished the enone *IV* as the major product. Lithium aluminum hydride reduction of the latter yielded the diol *V* which was acetylated to give the diacetate *VII*. In contrast to the 19-unsubstituted ketone[5-7], reduction of the keto group proceeds stereoselectively to give *V*, while the epimeric 3α-alcohol could not be detected in the reaction mixture. We therefore tried to prepare the 3α-acetate by another route that requires presence of 3 and 19 oxygen functions possessing different reactivity. Reduction of the ketone *IV* with sodium borohydride in a medium buffered with boric acid (for the method ref.[9]) led to the 3β-alcohol *VI* accompanied by a smaller amount

of the compound *I* arising by double bond reduction. It was intended to use the pure alcohol *VI* for the synthesis of its epimer by inversion of configuration at $C_{(3)}$ using the known[10] method. However, reaction of *VI* with thionyl chloride in ether, followed by acetolysis of the crude chloro derivative *VIII*, did not give the desired 3α-acetoxy derivative but furnished a mixture of lipophilic products which was not further examined.

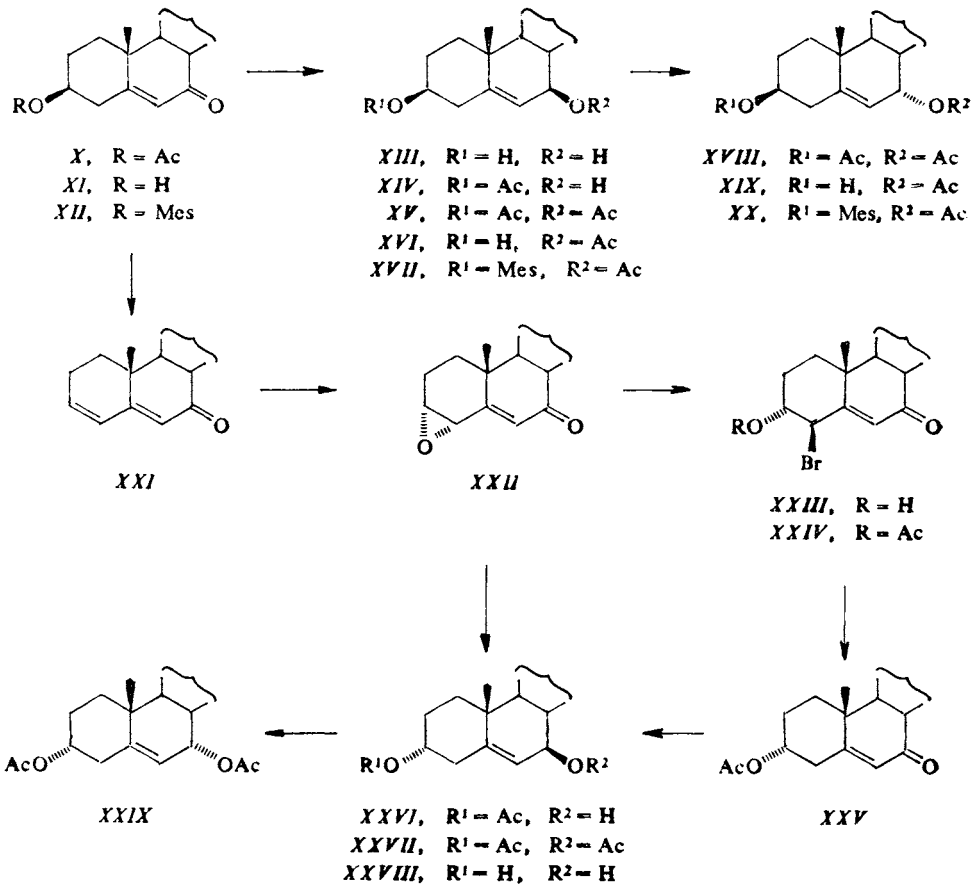


SCHEME 1

Synthesis of 5,6-unsaturated 3β-acetoxy derivatives with an additional acetoxy group in the position 7β and 7α is well known. The 7β-derivative can be prepared by lithium aluminum hydride reduction of the 7-oxo derivative *X* to yield the diol *XIII* which was then acetylated to the diacetyl derivative[11] *XV* (Scheme 2). For the preparation of its 7α-epimer *XVIII* the British authors[10] worked out a two-step method based on replacement of the hydroxyl group in *XIV* by chlorine (with retention of configuration) and subsequent S_N2-inversion by acetolysis. The alcohol *XIV* we prepared by a selective reduction of the ketone *X* with sodium borohydride buffered with boric acid.

For the synthesis of 3α-acetoxy derivatives *XXVII* and *XXIX* a possibility may be considered consisting of inversion of configuration in 3β-substituted derivatives that are currently available. However, it is well known[12] that 3β-mesyloxy and other

suitable substrates, containing a 5,6-double bond, react with retention of configuration due to participation of the homoallylic double bond. In a buffered medium the reaction proceeds with an *i*-steroid rearrangement to give a 3α,5α-cyclo-6β-substituted derivative[12]. Not even the diethyl azodicarboxylate method[13] leads to a preparatively usable yield of 3α-substituted 5,6-unsaturated steroids[14]. Our experiments have



SCHEME 2

shown that not even introduction of an additional substituent into the position 7 inhibits the double bond participation. Thus, unbuffered acetolysis of the mesylates *XVII* and *XX* yields 3β-acetoxy derivatives *XV* and *XVIII* as major products. No effect on the reaction course in the desired direction has also conjugation of the 5,6-double bond with a carbonyl group; thus, acetolysis of the mesylate[15] *XII* leads again mostly to the 3β-acetoxy derivative *X*. The mesylates *XII*, *XVII* and *XX* were

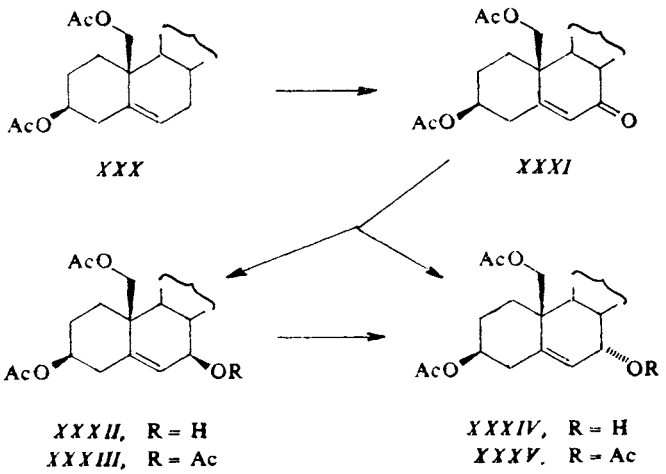
prepared by mesylation of the corresponding alcohols *XI*, *XVI* and *XIX* with methanesulphonyl chloride in pyridine. The requisite alcohols *XVI* and *XIX* were obtained by selective hydrolysis of the diacetates *XV* and *XVIII* with potassium hydrogen carbonate in methanol (for the method ref.[8]), the alcohol *XI* by hydrolysis of the acetate *X* with potassium hydroxide in methanol.

It was therefore necessary to seek another route for preparation of 3α-substituted derivatives. It has been known from the literature[12,16] that *e.g.* 3α,4α-epoxides are cleaved according to the Fürst–Plattner rule to yield 3α-hydroxy-4β-substituted derivatives. It turned out that this approach solved ultimately the problem of the synthesis of our 5,6-unsaturated 3α-acetoxy derivatives. Elimination of the acetoxy group in the acetate *X* by treatment with hydrochloric acid in boiling ethanol[4] gave the dienone[15,17] *XXI* which on reaction with 3-chloroperoxybenzoic yielded selectively the 3α,4α-epoxide *XXII* (Scheme 2). Apart from the analogy[18], this structure is supported by retention of the conjugated system (UV detection TLC), singlet of one olefinic proton (6-H) and presence of two oxirane ring protons in the ^{1}H NMR spectrum. The NMR spectrum did not permit to establish the configuration of the oxirane ring unequivocally but this question was solved in favor of the 3α,4α-configuration (*XXII*) by following chemical transformations: Lithium aluminum hydride reduction of the unsaturated epoxy ketone *XXII* yielded predominantly the diol *XXVIII* which was converted into the diacetate *XXVII* on treatment with acetic anhydride in pyridine. The 3α-configuration of the hydroxyl group in the diol *XXVIII* is confirmed by the width of the 3-H multiplet (W = 11 Hz) in the ^{1}H NMR spectrum and further reactions of the epoxide *XXII* specified below. The 7β-configuration of the second hydroxyl group follows from the shape of the 6-H signal.

The strategy involving inversion of configuration of the allylic group was again chosen for preparation of the 3α,7α-diacetoxy derivative *XXIX* (Scheme 2). This required a procedure and reagents differentiating the reactivity of the oxirane ring and keto group in the ketone *XXII*. The oxirane ring in this compound was cleaved with hydrobromic acid at −5°C to give the diaxial bromohydrin *XXIII*. Reduction of this compound with tributyltin hydride gave, however, a mixture of elimination products instead of the expected 3α-hydroxy-5-cholesten-7-one. An attempted preparation of the corresponding chlorohydrin was unsuccessful since cleavage of the epoxide *XXII* with hydrochloric acid leads also to products of complex elimination. On the other hand, the acetate *XXIV* prepared from the bromohydrin *XXIII* could be reduced with tributyltin hydride to give the compound *XXV* in a relatively good yield.

^{1}H NMR spectra of the bromohydrin *XXIII*, its acetate *XXIV* and reduction product *XXV* corroborate conclusively the configuration of the oxirane ring in the parent epoxide *XXII* and also the structure of all compounds prepared from it: The 3α,4α-epoxide *XXII* should be cleaved to a diaxial derivative (following the Fürst–Plattner rule) with 3α-OH, 4β-Br arrangement whereas the diastereoisomeric 3β,4β-epoxide

should give the isomeric diaxial derivative with 3α-Br, 4β-OH arrangement. The half-widths of the 3-H and 4-H signals in the ^{1}H NMR spectra of the compounds *XXIII* and *XXIV* are indeed in accord with the axial substitution at these positions. The shift of one of the signals resulting after acetylation (*XXIII* →*XXIV*) allowed the conclusion that the broader multiplet (*i.e.* 3β-H) corresponds to the group CH—OR. This is in favor of the first structure. Moreover, also significant is the change in chemical shift of the 10β-methyl singlet accompanying the transformation *XXIII*→ →*XXIV*→*XXV*. Acetylation (*XXIII*→*XXIV*) does not change the value of its chemical shift, thus indicating a large distance of the 10β-methyl group from the hydroxyl group. On the other hand, removal of the bromine atom (*XXIV*→*XXV*) results in the shift of the singlet toward high field ($\Delta\delta$ = 0·35 ppm). This means that the bromine atom must be located at the 4β-position. The structure 3α-Br,4β-OR is thus ruled out. The structure *XXII* follows unambiguously for the parent epoxide from which the above compounds were prepared.



SCHEME 3

The ketone *XXV* was reduced with sodium borohydride in a medium buffered with boric acid and yielded the 7β-hydroxy derivative *XXVI* with the acetoxy group preserved at the position 3. Thionyl chloride in ether under standard conditions (ref.[10]) converted it into the corresponding 7β-chloro derivative which was subjected to acetolysis with inversion of configuration to yield the unsaturated 7α-acetoxy derivative *XXIX*.

The remaining two model compounds, the 5-unsaturated triacetoxy derivatives *XXXII* and *XXXV*, were prepared (Scheme 3) from the known[19] diacetate *XXX* which on allylic oxidation gave the ketone *XXXI*. Subsequent reduction with sodium

borohydride buffered with boric acid yielded a mixture of epimeric alcohols *XXXII* and *XXXIV* (8 : 1). The acetate *XXXIII* was prepared from the alcohol *XXXII* by acetylation. A larger quantity of the 7α-acetoxy derivative *XXXV* was obtained from the 7β-alcohol *XXXII* again in two steps *via* corresponding allyl chloride.

A series of model olefins with one or more acetoxy groups was prepared in this manner and a method of synthesis of 3α-substituted 5,6-unsaturated steroids was found at the same time.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 20°C/26 Pa. Optical rotation measurements were carried out in chloroform with an error of ±3°. The infrared spectra were recorded on a Zeiss UR 20 or on a Perkin–Elmer spectrometer in tetrachloromethane unless stated otherwise. The ^{1}H NMR spectra were measured on a Tesla B 476 (60 MHz) instrument at 25°C in deuteriochloroform with tetramethylsilane as internal reference. Chemical shifts are given in δ (ppm) scale. Apparent coupling constants were obtained from the first-order analysis. The identity of the samples prepared by different routes was checked by thin-layer chromatography (TLC), infrared and ^{1}H NMR spectra. Usual workup of an ethereal solution means washing the solution with 5% aqueous hydrochloric acid, water, a 5% aqueous potassium hydrogen carbonate solution, water, drying with sodium sulfate and evaporation of the solvent *in vacuo*.

19-Acetoxy-5α-cholestan-3-one (*II*)

Pyridinium chlorochromate (6 g) was added over a period of 15 min to a stirred mixture of alcohol *I* (3 g), dry potassium acetate (1·5 g) and sodium sulfate (6 g) in dichloromethane (50 ml) at room temperature. Stirring was continued for one hour at the same temperature, then the mixture was diluted with ether, decanted and the residue extracted with ether four times. Organic portions were combined, filtered through a column of alumina and the ethereal solution worked up as usual to give the crude ketone *II* (2·9 g), $[\alpha]_D^{20}$ +30° (*c* 1·8). ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 2·07 (3 H, s, CH_3CO_2), 4·43 (2 H, s, 19-H). IR spectrum: 1 233 and 1 740 (CH_3CO_2), 1 718 (C=O) cm^{-1}. For $C_{29}H_{48}O_3$ (444·7) calculated: 78·33% C, 10·88% H; found: 78·14% C, 11·02% H.

19-Acetoxy-2α-bromo-5α-cholesten-3-one (*III*)

To a stirred solution of the ketone *II* (1·7 g) in tetrahydrofuran (20 ml) was added trimethylanilinium hydrobromide perbromide (1·7 g) at room temperature in several portions in a period of 15 min, the mixture was then stirred at room temperature for 1 h, then diluted with water and the product was extracted with ether. The ethereal phase was worked up as usual and the crude product was chromatographed on a column of silica gel (^{SiH} Merck) using a mixture of light petroleum, ether and acetone (89 : 10 : 1) as eluent. Fraction corresponding to the bromo ketone was evaporated to afford the bromo ketone *III* (1·10 g), $[\alpha]_D^{20}$ +43° (*c* 2·6). The NMR spectrum: 0·67 (3 H, s, 18-H), 2·10 (3 H, s, CH_3CO_2), 4·42 (2 H, s, 19-H), 4·80 (1 H, brq, $J_{1\alpha-H,2\beta-H}$ = = 12 Hz, $J_{1\beta-H,2\beta-H}$ = 6·5 Hz, 2β-H). For $C_{29}H_{47}BrO_3$ (523·6) calculated: 66·52% C, 9·05% H, 15·26% Br; found: 66·37% C, 9·21% H, 15·08% Br.

19-Acetoxy-5α-cholest-1-en-3-one (*IV*)

A solution of the bromo ketone *III* (1·07 g) in dioxane (6 ml) was added in a course of 5 min to a stirred refluxing mixture of lithium carbonate (600 mg) and calcium carbonate (600 mg) in dimethylformamide (30 ml) and the mixture was refluxed while stirring for 2 h under argone. Then the mixture was cooled, diluted with ether, filtered and the filtrate was worked up as usual. The residue was chromatographed on a column of silica gel (60 g) using a mixture of light petroleum and ether (92 : 8) as eluent. Corresponding fraction was evaporated to furnish *IV* (400 mg), $[\alpha]_D^{20}$ +17° (*c* 2·5). ^{1}H NMR spectrum: 0·69 (3 H, s, 18-H), 1·93 (3 H, s, CH_3CO_2), 4·38 (2 H, d, AB system, J_{gem} = 2·5 Hz, 19-H), 6·02 (1 H, d, A-part of the AB system, J = 11 Hz, 2-H), 7·00 (1 H, d, B-part of the AB system, J = 11 Hz, 1-H). IR spectrum: 1 226, 1 682, 1 746 cm^{-1}. For $C_{29}H_{46}O_3$ (442·7) calculated: 78·68% C, 10·47% H; found: 78·51% C, 10·59% H.

5α-Cholest-1-ene-3β,19-diol 19-Acetate (*VI*)

A solution of trihydrogen boric acid (1·5 g) in ethanol (150 ml) was added to a solution of the ketone *IV* (380 mg) in benzene (30 ml) and to this mixture was added while stirring at room temperature sodium borohydride (600 mg) in several portions in the course of 30 min. The mixture was stirred at room temperature for 6 h, the excess of reagent was then decomposed with 5% hydrochloric acid and the mixture was concentrated to *c.* 1/5 by evaporation *in vacuo*. The residue was diluted with ether and worked up as usual. The residue was chromatographed on a column of silica gel (30 g) using a mixture of light petroleum, ether and acetone (87 : 10 : 3) as eluent. The lipophilic fraction was evaporated to yield *VI* (230 mg). $[\alpha]_D^{20}$ +14° (*c* 2·4). ^{1}H NMR spectrum: 0·67 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 4·22 (1 H, m, W = 24 Hz, 3α-H), 4·25 (2 H, s, 19-H), 5·62 (1 H, dd, A-part of the AB system, $J_{1-H,2-H}$ = 11 Hz, $J_{2-H,3\alpha-H}$ = 2 Hz, 2-H), 5·85 (1 H, brd, B-part of the AB system, $J_{1-H,2-H}$ = 11 Hz, 1-H). For $C_{29}H_{48}O_3$ (444·7) calculated: 78·33% C, 10·88% H; found: 78·18% C, 11·06% H. Evaporation of the polar fraction furnished the 5α-cholestane-3β,19-diol 19-acetate (*I*) (50 mg), m.p. 61–62°C, identical with an authentic sample[8].

5α-Cholest-1-ene-3β,19-diol Diacetate (*VII*)

A solution of the ketone *IV* (245 mg) in ether (10 ml) was treated with lithium aluminum hydride (100 mg) at room temperature for 1 h. The excesss of reagent was decomposed with water and 5% hydrochloric acid, the product was extracted with ether and the ethereal solution was worked up as usual. The residue (230 mg) was dissolved in pyridine (4 ml) and treated with acetic anhydride (2 ml) at room temperature for 5 h. The mixture was poured into ice and water, the product was extracted with ether and the ethereal solution was worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to afford *VII* (192 mg), m.p. 88–89°C, $[\alpha]_D^{20}$ +10° (*c* 2·1). ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 2·03 (6 H, s, two CH_3CO_2), 4·12 and 4·45 (2 H, d, AB system, J_{gem} = 11·5 Hz, 19-H), 5·30 (1 H, m, W = 27 Hz, 3α-H), 5·60 (1 H, dd, A-part of the AB system $J_{1-H,2-H}$ = 10 Hz, $J_{2-H,3\alpha-H}$ = 2 Hz, 2-H), 5·97 (1 H, brd, B-part of the AB system $J_{1-H,2-H}$ = 10 Hz, 1-H). For $C_{31}H_{50}O_4$ (486·7) calculated: 76·50% C, 10·35% H;

5-Cholestene-3β,7β-diol 3-Acetate (*XIV*)

A solution of boric acid (15 g) in ethanol (1 000 ml) was added to a stirred solution of the ketone *X* (3 g) in benzene (40 ml) and sodium borohydride (3·9 g) was added to this mixture in several portions while stirring in the course of 30 min. The mixture was stirred at room temperature

for 6 h, the excess of the reagent was decomposed with 5% hydrochloric acid, the mixture was concentrated by evaporation *in vacuo* to *c* 1/5 of its volume, diluted with water and ether and the ethereal phase was worked up as usual. A part (120 mg) of the obtained crude alcohol *XIV* (2·84 g) was chromatographed on two plates of silica gel (20 × 20 cm) using the mixture of light petroleum, ether and acetone (80 : 10 : 10) as eluent. Zone containing the desired product was eluted with ether to give *XIV* (110 mg), $[\alpha]_D^{20}$ −15·1° (*c* 1·9) (lit.: −22° (ref.[20]) and −5° (ref.[21])). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 1·05 (3 H, s, 19-H), 2·00 (3 H, s, CH_3CO_2), 3·83 (1 H, m, W = 16 Hz, 7α-H), 4·58 (1 H, *m*, W = 31 Hz, 3α-H), 5·32 (1 H, brs, 6-H) (in agreement with ref.[20]). For $C_{29}H_{48}O_3$ (444·7) calculated: 78·33% C, 10·88% H; found: 78·20% C, 11·03% H.

3α,4α-Epoxy-5-cholesten-7-one (*XXII*)

The dienone[17] *XXI* (1·4 g) in dichloromethane (80 ml) was treated with 3-chloroperoxybenzoic acid (1·2 g) at room temperature for 24 h. Another portion of the reagent was added (100 mg) and after additional 2 h the mixture was concentrated *in vacuo* to about 1/5, the residue was diluted with ether and water and the organic layer was worked up as usual to afford the crude epoxide *XXII* (1·46 g) which was directly used in further experiment. A sample (80 mg) was chromatographed on a preparative plate of silica gel (20 × 20 cm) using a mixture of light petroleum, ether and acetone (80 : 10 : 10). The zone containing the desired compound was collected, washed with ether and the eluate was evaporated to give *XXII* (34 mg), $[\alpha]_D^{20}$ −105° (*c* 5·1). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 1·07 (3 H, s, 19-H), 3·37 (1 H, brs, 3β-H), 3·40 (1 H, brs, 4β-H), 5·18 (1 H, s, 6-H). For $C_{27}H_{42}O_2$ (398·6) calculated: 81·35% C, 10·62% H; found: 81·02% C, 10·71% H.

4β-Bromo-3α-hydroxy-5-cholesten-7-one (*XXIII*)

The crude epoxide *XXII* (4·2 g) in chloroform (100 ml) was stirred with a 48% aqueous hydrogen bromide (40 ml) at −5°C for 20 min. The cold mixture was diluted with water and ether, the organic phase was washed five times with water, one time with a 5% aqueous potassium hydrogen carbonate solution, water, dried and evaporated at 20°C *in vacuo* to give the crude bromohydrin which was used in further experiment. A sample (80 mg) was purified by preparative thin-layer chromatography on one silica gel plate (20 × 20 cm) using a mixture of light petroleum, ether and acetone (80 : 10 : 10) as eluent to afford *XXIII* (35 mg), $[\alpha]_D^{20}$ −111° (*c* 5·0). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 1·35 (3 H, s, 19-H), 4·23 (1 H, m, W = 13 Hz, 3β-H). 4·52 (1 H, m, W = 10 Hz, 4α-H), 5·88 (1 H, s, 6-H). For $C_{27}H_{43}BrO_2$ (479·6) calculated: 67·63% C, 9·04% H, 16·66% Br; found: 67·48% C, 9·13% H, 16·50% Br.

3α-Acetoxy-4β-bromo-5-cholesten-7-one (*XXIV*)

The bromohydrin *XXIII* (289 mg) in pyridine (5 ml) was treated with acetic anhydride (2·5 ml) at 0°C for 3 h and then at room temperature for 12 h. The mixture was poured into ice and water, the product was taken up into ether and the ethereal solution was worked up as usual to yield the crude acetate which was immediately used in further operation. A sample (100 mg) was chromatographed on two preparative plates of silica gel (20 × 20 cm) using a mixture of light petroleum, ether and acetone (80 : 10 : 10) as eluent to obtain *XXIV* (37 mg), $[\alpha]_D^{20}$ −84° (*c* 2·3). ^{1}H NMR spectrum: 0·69 (3 H, s, 18-H), 1·53 (3 H, s, 19-H), 2·00 (3 H, s, CH_3CO_2), 4·58 (1 H, m, W = 10 Hz, 4α-H), 5·19 (1 H, m, W = 12 Hz, 3β-H), 5·87 (1 H, s, 6-H). For $C_{29}H_{45}BrO_3$ (521·6) calculated: 66·78% C, 8·70% H, 15·32% Br; found: 66·59% C, 8·83% H, 15·10% Br.

3α-Acetoxy-5-cholesten-7-one (*XXV*)

A solution tri-n-butyltin hydride (1 ml, 1 mol l^{-1}) in benzene was added to a solution of *XXIV* (220 mg) in benzene (15 ml), the mixture was heated up to reflux, then a catalytic amount of 2,2'--bis(azo-2-methylpropionitrile) (*c* 5 mg) was added and the mixture was refluxed for 30 min. After cooling the mixture was diluted with ether and water and the organic phase was worked up as usual. The residue was chromatographed on three plates of silica gel (20 × 20 cm) using a mixture of light petroleum, ether and acetone (80 : 10 : 10) as eluent. Zones containing the desired product were collected, washed with ether and the eluate evaporated to give *XXV* (49 mg), $[\alpha]_D^{20}$ −44·8° (*c* 5·3). ^{1}H NMR spectrum: 0·67 (3 H, s, 18-H), 1·18 (3 H, s, 19-H), 1·99 (3 H, s, CH_3CO_2), 5·13 (1 H, m, W = 12 Hz, 3β-H), 5·67 (1 H, brs, 6-H). For $C_{29}H_{46}O_3$ (442·7) calculated: 78·68% C, 10·47% H; found: 78·53% C, 10·59% H.

5-Cholestene-3α,7β-diol 3-Acetate (*XXVI*)

A solution of boric acid (2·5 g) in ethanol (180 ml) was added to a stirred solution of the ketone *XXV* (600 mg) in benzene (30 ml) and sodium borohydride (1·2 g) was added in several portions to this mixture at room temperature in the course of 30 min. The mixture was stirred at room temperature for 2 h, the excess of the reagent was decomposed with 5% hydrochloric acid and the mixture was concentrated by partial evaporation *in vacuo*. The residue was diluted with ether and water and the ethereal layer was worked up as usual. The residue was dissolved in a mixture of light petroleum and benzene (5 : 1) and filtered through a column of aluminum oxide. The eluate was evaporated to give *XXVI* (575 mg), $[\alpha]_D^{20}$ +10° (*c* 2·6). ^{1}H NMR spectrum: 0·72 (3 H, s, 18-H), 1·03 (3 H, s, 19-H), 1·97 (3 H, s, CH_3CO_2), 3·83 (1 H, m, W = 19 Hz, 7α-H), 5·00 (1 H, m, W = 15 Hz, 3β-H), 5·20 (1 H, m, W = 8 Hz, 6-H). For $C_{29}H_{48}O_3$ (444·7) calculated: 78·33% C, 10·88% H; found: 78·14% C, 10·97% H.

5-Cholestene-3α-7β-diol Diacetate (*XXVII*)

The crude diol *XXVIII* (520 mg) was dissolved in pyridine (20 ml) and treated with acetic anhydride (7 ml) at room temperature for 12 h. The mixture was decomposed with ice and water, the product was extracted with ether and the ethereal layer was worked up as usual. The residue was chromatographed on a column of silica gel (30 g) using a mixture of light petroleum and ether (90 : 10). Fraction containing the desired product was evaporated to afford *XXVII* (280 mg), $[\alpha]_D^{20}$ +24° (*c* 2·8). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 1·07 (3 H, s, 19-H), 2·00 (6 H, s, two CH_3CO_2), 5·00 (2 H, m, W = 17 Hz, 3β-H and 7α-H), 5·13 (1 H, s, 6-H). For $C_{31}H_{50}O_4$ (486·7) calculated: 76·50% C, 10·35% H; found: 76·24% C, 10·39% H.

5-Cholestene-3α,7β-diol (*XXVIII*)

The crude epoxide *XXII* (550 mg) in ether (30 ml) was treated with lithium aluminum hydride (300 mg) at room temperature for 1 h. The excess of the reagent was decomposed with water and 5% hydrochloric acid, the product was extracted with ether and the ethereal solution was worked up as usual to afford the crude diol (519 mg) which was directly used in further preparation. A sample (60 mg) was chromatographed on a plate of silica gel (20 × 20 cm) using a mixture of light petroleum, ether and acetone (75 : 10 : 15) to furnish *XXVIII* (20 mg), $[\alpha]_D^{20}$ −2° (*c* 2·8). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 1·02 (3 H, s, 19-H), 3·87 (1 H, m, W = 15 Hz, 7α-H), 4·03 (1 H, m, W = 11 Hz, 3β-H), 5·33 (1 H, brs, 6-H). For $C_{27}H_{46}O_2$ (402·7) calculated: 80·54% C, 11·31% H; found: 80·39% C, 11·46% H.

5-Cholestene-3α,7α-diol Diacetate (*XXIX*)

A solution of thionyl chloride (0·60 ml) in ether (4 ml) was added at 0°C to a stirred solution of the alcohol *XXVI* (520 mg) in ether (20 ml) under argone and the mixture was stirred at 0°C for 20 min. The solvent was removed by evaporation *in vacuo* at 20°C. To the resulting crude 7β-chloro derivative was added at room temperature a solution of anhydrous sodium acetate (290 mg) in acetic acid (25 ml), the mixture was stirred at room temperature for 24 h, then diluted with water and the product was extracted with ether. The ethereal layer was washed with water, a 5% aqueous potassium hydrogen carbonate solution, water, dried and evaporated. The residue was chromatographed on a column of silica gel (30 g) using a mixture of light petroleum and ether (90 : 10). Fraction containing the desired compound was evaporated to afford *XXIX* (158 mg), $[\alpha]_D^{20}$ −112° (*c* 1·8). ^{1}H NMR spectrum: 0·67 (3 H, s, 18-H), 0·98 (3 H, s, 19-H), 1·93 (3 H, s, CH_3CO_2), 1·98 (3 H, s, CH_3CO_2), 4·97 (2 H, m, W = 20 Hz, 3β-H and 7β-H), 5·50 (1 H, brd, $J_{6-H,7\beta-H}$ = 6 Hz, 6-H). For $C_{31}H_{50}O_4$ (486·7) calculated: 76·50% C, 10·35% H; found: 76·29% C, 10·48% H.

3β,19-Diacetoxy-5-cholesten-7-one (*XXXI*)

A solution of chromium trioxide (2·5 g) in a mixture of water (2·5 ml) and acetic acid (2·5 ml) was added to a stirred solution of the unsaturated diacetate[19] *XXX* (2·5 g) in acetic acid (35 ml) at 55°C in the course of 90 min. The mixture was then stirred at 55°C for 3 h, cooled, treated with methanol (10 ml) and water (10 ml), set aside for 15 min and then extracted with ether. The organic phase was washed with water, a 5% aqueous solution of potassium hydrogen carbonate, water, dried with sodium sulfate and evaporated. The residue was chromatographed on a column of silica gel (120 g) using a mixture of light petroleum and ether (90 : 10) which eluted lipophilic impurities and then with a mixture of light petroleum, ether and acetone (87 : 10 : 3) which eluted the desired product. This fraction was evaporated to afford *XXXI* (900 mg), $[\alpha]_D^{20}$ −114° (*c* 2·6). ^{1}H NMR spectrum: 0·69 (3H, s, 18-H), 2·01 (6 H, s, two CH_3CO_2), 4·07 and 4·70 (2 H, two dd, AB system, J_{gem} = 12 Hz, 19-H), 4·75 (1 H, m, W = 30 Hz, 3α-H), 5·88 (1 H, s, 6-H). For $C_{31}H_{48}O_5$ (500·7) calculated: 74·36% C, 9·66% H; found: 74·07% C, 9·75% H.

5-Cholestene-3β,7β,19-triol 3,19-Diacetate (*XXXII*)

Continued elution (after isolation of *XXIV*) with a mixture of light petroleum, ether and acetone (89 : 10 : 1) and then (87 : 10 : 3) afforded *XXXII* (308 mg), m.p. 110—112°C (aqueous acetone), $[\alpha]_D^{20}$ −29° (*c* 2·1). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 1·97 (3 H, s, CH_3CO_2), 2·00 (3 H, s, CH_3CO_2), 3·75 (1 H, m, W = 25 Hz, 7α-H), 3·90 and 4·47 (2 H, two d, AB system, J_{gem} = = 12 Hz, 19-H), 4·55 (1 H, m, W = 36 Hz, 3α-H), 5·52 (1 H, brs, 6-H). For $C_{31}H_{50}O_5$ (502·7) calculated: 74·06% C, 10·02% H; found: 73·89% C, 10·08% H.

5-Cholestene-3β,7β,19-triol Triacetate (*XXXIII*)

The alcohol *XXXII* (100 mg) in pyridine (3 ml) was treated with acetic anhydride (1·5 ml) at room temperature for 6 h. The mixture was then decomposed with ice and water and the product was extracted with ether. The organic phase was worked up as usual to yield *XXXIII* (115 mg), $[\alpha]_D^{20}$ +16° (*c* 2·0). ^{1}H NMR spectrum: 0·70 (3 H, s, 18-H), 1·99 (3 H, s, CH_3CO_2), 2·00 (3 H, s, CH_3CO_2), 2·03 (3 H, s, CH_3CO_2), 3·92 and 4·60 (2 H, two d, AB system, J_{gem} = 12 Hz, 19-H), 4·58 (1 H, m, W = 30 Hz, 3α-H), 4·96 (1 H, brd, $J_{7\alpha-H,8\beta-H}$ = 8 Hz, 7α-H), 5·47 (1 H, brs, 6-H). For $C_{33}H_{52}O_6$ (544·8) calculated: 72·76% C, 9·62% H; found: 72·61% C, 9·84% H.

5-Cholestene-3β,7α,19-triol 3,19-Diacetate (*XXIV*)

A solution of boric acid (2·0 g) in ethanol (150 ml) was added to a stirred solution of the ketone *XXXI* (500 mg) in benzene (30 ml) and sodium borohydride (800 mg) was added to the stirred mixture in several portions in the course of 30 min. The mixture was stirred at room temperature for 6 h, the excess of the reagent was decomposed with 5% hydrochloric acid, the mixture was concentrated by evaporation *in vacuo* to *c* 1/5 of its volume, diluted with ether and water and the ethereal phase was worked up as usual. The residue was chromatographed on a column of silica gel (30 g) using a mixture of light petroleum, ether and acetone (88 : 10 : 2) as eluent. The lipophilic fraction was evaporated to afford *XXXIV* (35 mg), $[\alpha]_D^{20}$ −88° (*c* 1·9). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 2·00 (6 H, s, two CH_3CO_2), 3·87 (1 H, m, W = 16 Hz, 7β-H), 3·93 and 4·57 (2 H, two d, AB system, J_{gem} = 12 Hz, 19-H), 4·72 (1 H, m, W = 30 Hz, 3α-H), 5·88 (1 H, brd, $J_{6-H,7\beta-H}$ = 5·5 Hz, 6-H). For $C_{31}H_{50}O_5$ (502·7) calculated: 74·06% C, 10·02% H; found: 73·89% C, 10·17% H.

5-Cholestene-3β,7α,19-triol Triacetate (*XXXV*)

A solution of thionyl chloride (0·20 ml) was added under argon to a stirred solution of *XXXII* (170 mg) in ether (8 ml) in a period of 5 min at 0°C and the mixture was stirred at 0°C for 20 min. The solvent was evaporated *in vacuo* at 20°C. A solution of anhydrous sodium acetate (100 mg) in acetic acid (10 ml) was added at room temperature to the resulting crude 7β-chloro derivative, the mixture was stirred for 18 h at room temperature, then diluted with water and the product was extracted with ether. The ethereal solution was washed with water, a 5% aqueous potassium hydrogen carbonate solution, dried and evaporated. The residue was chromatographed on two plates of silica gel (20 × 20 cm) using a mixture of light petroleum, ether and acetone (80 : 10 : : 10) as eluent. Zone containing the desired product was eluted with ether to give *XXXV* (37 mg), $[\alpha]_D^{20}$ −22° (*c* 1·9). ^{1}H NMR spectrum: 0·67 (3 H, s, 18-H), 1·98 (9 H, s, three CH_3CO_2), 3·90 and 4·58 (2 H, two d, AB system J_{gem} = 12 Hz, 19-H), 4·57 (1 H, m, W = 34 Hz, 3α-H), 4·98 (1 H, m, W = 18 Hz, 7β-H), 5·83 (1 H, brd, $J_{6-H,7\beta-H}$ = 5 Hz, 6-H). For $C_{33}H_{52}O_6$ (544·8) calculated: 72·76% C, 9·62% H; found: 72·70% C, 9·68% H.

The elemental analyses were carried out in the Analytical Laboratory of this Institute (under the direction of Dr J. Horáček). The 60 MHz ^{1}H NMR *spectra were recorded by Mrs J. Jelínková and Mrs M. Snopková. The* IR *spectra were recorded by Mrs K. Matoušková and interpreted by Dr S. Vašíčková.*

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