SOLVOLYTIC REACTIONS OF EPIMERIC 3-METHANESULFONYLOXY--7-BENZOYLOXY-5β,6β-CYCLOPROPANOCHOLESTANES*

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Acetolysis of 3-methanesulfonyloxy-7-benzoyloxy-5β,6β-cyclopropanocholestanes with various configurations in positions 3 and 7 is described and the products are asigned structure using spectral methods. The 7-substituted compounds show greater propensity to elimination reactions than the 7-unsubstituted ones.

In one of our previous communications[1] we described solvolysis of 3-methanesulfonyloxy-5,6-cyclopropanocholestanes. We have found that the solvolysis proceeds predominantly with participation of the cyclopropane ring under formation of B-homo derivatives. It was of interest whether, and how, the solvolysis is influenced by an oxygen-containing functionality next to the cyclopropane ring, *i.e.* in position 7. In this study we describe the synthesis of three isomeric 3-methanesulfonates (*IV*, *X*, and *XIV*) with a 7-benzoyl group, their behaviour under acetolysis conditions, isolation of the products and determination of their structure.

The methanesulfonate *IV* was obtained starting from the known[2] 5,6β-cyclopropano-5β-cholestane-3β,7β-diol 3-acetate (*I*) which was benzoylated in position 7 to give benzoate *II*. The acetoxy group in *II* was selectively saponified and the obtained monobenzoate *III* was converted to 3β-methanesulfonate *IV*. We did not succeed in obtaining the epimeric 3α-methanesulfonate since the ketone *V*, obtained from the 3β-alcohol *III* by Jones oxidation, was reduced with lithium tri-tert-butoxyaluminium hydride exclusively to the starting 3β-alcohol *III*.

The remaining two methanesulfonates were prepared from ketone *VI* which on reduction with lithium tri-tert-butoxyaluminium hydride afforded a mixture of 7α-alcohol *VII* and 7β-alcohol *I*, with the former predominating. The alcohol *VII* was benzoylated to 7α-benzoate *VIII* whose 3β-acetoxy group was selectively saponified to give alcohol *IX* which was converted to methanesulfonate *X* by treatment with methanesulfonyl chloride in pyridine. The epimeric methanesulfonate *XIV* was obtained from the 3α-alcohol *XII*, accessible by reduction of ketone *XII* with lithium tri-tert-butoxyaluminium hydride.

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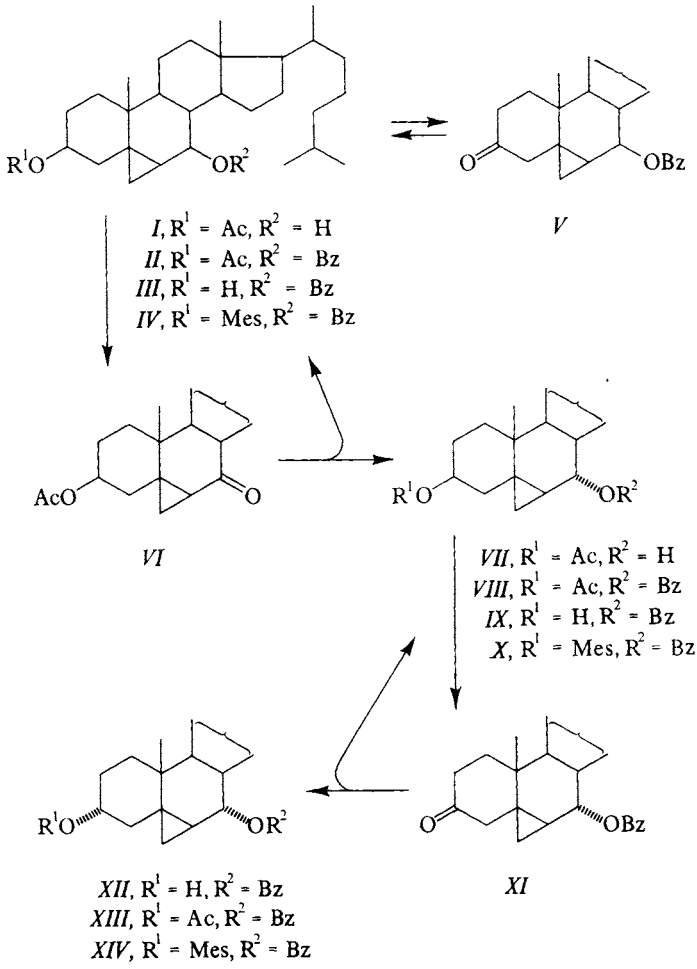
All the prepared methanesulfonates were subjected to acetolysis by 2 hours' reflux in a mixture of acetic acid, acetic anhydride and anhydrous sodium acetate.

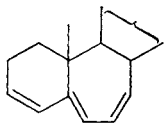
Acetolysis of methanesulfonate *IV* led to two products. The less polar product *XV* contained three conjugated double bonds (UV spectrum: λ_{max} 298 nm (log ε 4·14)) but no acetoxy or benzoyloxy group (according to IR spectrum) or a cyclopropane ring (no cyclopropane proton signals in the ^{1}H NMR spectrum). We can thus



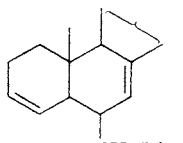
assume, that both the oxygen-containing functionalities were eliminated (which was confirmed also by the molecular peak in the mass spectrum) and the cyclopropane ring was cleaved under formation of B-homocholesta-3,5,7-triene *XV*. This structure was confirmed by the ^{1}H NMR and ^{13}C NMR spectra. The ^{13}C APT NMR spectrum exhibits six sp^2 carbon signals of which five are due to methine

carbons (δ 122·86, 122·88, 127·03, 132·43 and 136·68) and one due to a quaternary carbon (δ 148·14). In the region δ 5·4–6·1 ppm there are five proton signals in the ^{1}H NMR spectrum. The highest-field signal, a broad doublet at δ 5·54, corresponds to the 6-proton ($J_{6,7}$ = 7·3 Hz). Downfield, the doublet of doublets at δ 5·65 is due to the 7a-proton ($J_{7a,7}$ = 11·6 and $J_{7a,8}$ = 2·5 Hz). The 7-H-proton signal at 5·78 appears as a doublet of doublets of doublets with an allyl coupling (2·2 Hz) with the 8α-proton. The 3-proton multiplet occurs at about δ 5·75; at the lowest field (δ 5·98) there is the 4-proton multiplet showing a 9·6 Hz coupling with the 3-proton and allylic coupling of 2·1 and 0·8 Hz with the protons at $C_{(2)}$. Decoupling experiments revealed a long-range coupling (0·8 Hz) with the 6-proton.

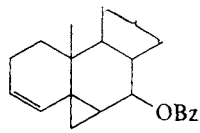
The second, more polar, acetolysis product arising from *IV* (compound *XVI*) contains an acetoxy group (IR bands at 1 743 and 1 244 cm^{-1}) and two double bonds but no cyclopropane ring (as shown by ^{1}H NMR spectrum). One of the double bonds is trisubstituted as shown by ^{13}C APT NMR signals of three methine sp^2 carbons at δ 124·61, 126·04, and 128·55 and one quaternary sp^2 carbon at δ 142·78. This, together with loss of 7-benzoyloxy group in the mass spectrum, indicates that the trisubstituted double bond is in the 7(8) position. The 7-proton signal in the ^{1}H NMR spectrum appears as a doublet at δ 5·31 with coupling constant of 3·5 Hz. The second double bond in the product *XVI* is disubstituted. The olefinic protons form multiplets at δ 5·67 ($\sum J$ = 17·2 Hz) and 5·95 ($\sum J$ = 14·0 Hz) with vicinal coupling of about 11·0 Hz. On the basis of greater $\sum J$, the multiplet at higher field (δ 5·67) is ascribed to the 3-proton (with two vicinal protons) whereas the multiplet at δ 5·95 to the 4-proton. The spectrum further contains two doublets of doublets at δ 3·79 and 4·31 due to a methylene, bearing an acetoxy group, with ^2J = −10·5 Hz and vicinal coupling constants ^3J = 7·5 and 3·3 Hz. We assume therefore that the CH_2OCOCH_3 group is in position 6β and that the polar acetolysis product has the structure *XVI*.



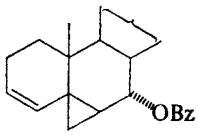
XV



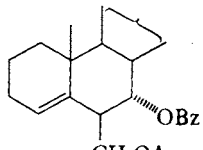
XVI



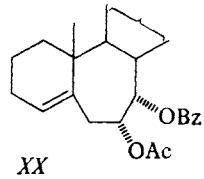
XVII



XVIII

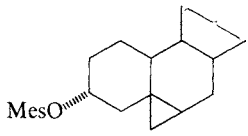


XIX

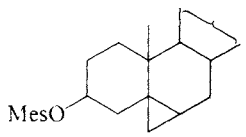


XX

Acetolysis of methanesulfonates *X* and *XIV* gave identical products and the reaction mixtures differed only in the product ratios (Table I). In addition to the compounds *XV* and *XVI*, already described in the solvolysis of *IV*, the acetolysis of *X* and *XIV* led to further five products. The most polar of them, acetates *XIII* and *VIII*, result from S_N1 and S_N2 substitution reaction of the methanesulfonate with the acetate anion. Elimination of the methanesulfonyl group gives rise to another product, the olefin *XVIII*. The remaining two compounds exhibited a very similar TLC behaviour and were separated only on 20% Ag-silica gel. Both contained an acetoxy and benzoyloxy group (IR and NMR spectra) and a double bond (NMR spectra). They have been assigned the structure *XIX* and *XX* on the basis of their ^{1}H NMR spectra: The more lipophilic compound *XIX* exhibits a triplet due to the 4-proton at δ 5·41 ($\sum J$ = 7·3 Hz). Another triplet at δ 5·13 is ascribed to the 7β-proton with the vicinal coupling constants $J_{7\beta,6\alpha} \doteq J_{7\beta,8\alpha} \doteq 2{\cdot}2$ Hz. The 6α-proton appears



XXI



XXII

TABLE I

Solvolyses of methanesulfonates *IV*, *X*, and *XIV*

Reaction	Product	Yield (%), from		
		IV	*X*	*XIV*
Elimination	*XVII*	0	—	—
	XVIII	—	33	9
Substitution	*VIII*	—	5	2
	XIII	—	9	2
Elimination with addition of acetic acid to cyclopropane ring	*XIX*	—	7	7
Double elimination with addition of acetic acid to cyclopropane ring	*XVI*	13	2	12
Double elimination with cleavage of cyclopropane ring	*XV*	67	23	55
Single elimination with participation of cyclopropane ring	*XX*	—	6	4

as a doublet of doublets of doublets at δ 2·72, its coupling constants with the $-CH_2OCOCH_3$ protons being 5·4 and 10·2 Hz. The doublets of doublets of the methylene protons (geminal coupling – 10·9 Hz) are at δ 4·00 and 4·34. In the spectrum of the more polar product *XX* the 4-proton gives rise to a triplet at δ 5·43 ($\sum J$ = 7·3 Hz), similarly as in the case of compound *XIX*. Since the doublet at δ 5·31 and the triplet of doublets at δ 4·67 have the same coupling constant (2·3 Hz), these signals correspond to the 7a and 7-protons, respectively. The triplet of the 7--proton signal is then a consequence of an approximately equal vicinal coupling with the 6α- and 6β-protons (8·3 and 8·5 Hz), as apparent from the corresponding doublet of doublets at δ 2·29 and 2·61 (^2J = −13·6 Hz).

The above-described experiments show that acetolysis of 3-methanesulfonyloxy--5β,6β-cyclopropanocholestanes is significantly influenced by the 7-benzoyloxy group. As compared with analogous compounds without any oxygen functionality in position 7, the described system shows a greater propensity to elimination reaction (Table II).

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical measurements were carried out in chloroform (experimental error ±3°). Infrared spectra were recorded on a Zeiss UR 20 instrument in tetrachloromethane, unless stated otherwise. ^{1}H NMR spectra were measured on Tesla B 476 (60 MHz) or Varian XL 200 (200 MHz) instruments, ^{13}C NMR spectra on a Varian XL 200 spectrometer. Unless otherwise stated, the spectra were taken in deuteriochloroform with tetramethylsilane as internal standard, chemical shifts are given in the δ-scale. The spectra were interpreted as first order spectra. The ultraviolet spectrum was obtained with a Specord instrument, mass spectra were taken on an AEI MS 902 spectrometer. Identity of the

TABLE II

Comparison of acetolyses of 7-benzoyloxy methanesulfonates *IV*, *X*, and *XIV* with acetolyses of the corresponding 7-H compounds *XXI*, *XXII*

Reaction	Yields (%)				
	IV	*X*	*XIV*	*XXI*	*XXII*
Substitution	0	14	4	13	47
Elimination	0	33	9	5	6
Elimination (with addition of acetic acid to cyclopropane ring or its cleavage)	80	32	74	0	0
Elimination with participation of cyclopropane ring	0	6	4	75	32

prepared samples was checked by mixture melting points, thin-layer chromatography (TLC), and IR and ^{1}H NMR spectra. Preparative TLC was performed on 200 × 200 mm plates, thickness of the silica gel layer 0·7 mm. The expression "the usual work-up" means that the solution was washed successively with 5% hydrochloric acid, water, 5% aqueous solution of potassium hydrogen carbonate, water, dried over sodium sulfate, filtered and the solvent was removed *in vacuo*. Light petroleum means a fraction boiling at 40–62°C.

5,6β-Cyclopropano-5β-cholestane-3β,7β-diol 3-Acetate 7-Benzoate (*II*)

Benzoyl chloride (14 ml) was added to a solution of 5,6β-cyclopropano-5β-cholestane-3β,7β-dio 3β-acetate[2] (*I*; 3·55 g) in pyridine. After standing overnight, the mixture was poured into an ice–water mixture, extracted with ether and the extract was processed in the usual manner. Crystallization from methanol afforded 2·6 g of acetoxy benzoate *II*, m.p. 132–135°C; $[\alpha]_D^{20}$ +85° (*c* 1·6). Another portion of *II* (0·15 g) was obtained from the mother liquors, raising the total yield to 2·75 g. IR Spectrum: 3 095, 3 075, 3 070, 3 035 (cyclopropane ring and benzoate), 1 735, 1 247 (acetate), 1 719, 1278 (benzoate) cm^{-1}. Mass spectrum: *m/z* 562 (M), 502 (M – CH_3COOH), 440 (M – C_6H_5COOH), 380 (base peak, M – CH_3COOH – C_6H_5COOH). ^{1}H NMR spectrum (60 MHz): 0·08 to 0·63 (mt, cyclopropane protons), 0·67 (s, 18-H), 0·93 (s, 19-H), 1·98 (s, 3β-acetate), 4·72–5·28 (mt, 3α-H and 6α-H), 7·37–7·64 and 7·91–8·17 (2 mt, 7β-benzoate). For $C_{37}H_{54}O_4$ (562·8) calculated: 78·96% C, 9·67% H; found: 78·80% C, 9·94% H.

5,6β-Cyclopropano-5β-cholestane-3β,7β-diol 7-Benzoate (*III*)

a) *By selective hydrolysis of* II: Hydrochloric acid (37%; 1 ml) was added to a solution of acetate *II* (1·06 g) in chloroform (15 ml) and methanol (100 ml). After standing for 20 h at 0°C, the mixture was poured in water and the product was extracted with ether. The ethereal extract was washed with saturated solution of potassium hydrogen carbonate and water, dried, and taken down. Crystallization of the residue from methanol gave 480 mg of pure product *III*, m.p. 132–133°C; $[\alpha]_D^{20}$ +89° (*c* 1·4). IR spectrum (Perkin–Elmer 580): 3 620 (hydroxyl), 1 710, 1 274 (benzoate), 3 070 (cyclopropane) cm^{-1}. Mass spectrum: *m/z* 398 (M – C_6H_5COOH), 380 (base peak, M – C_6H_5COOH – H_2O). ^{1}H NMR spectrum (60 MHz): 0·00–0·26 (mt, cyclopropane), 0·70 (s, 18-H), 0·95 (s, 19-H), 3·31 (s, 3β-OH), 3·93 (mt, 3α-H), 5·12 (mt, 7α-H), 7·40–7·65 and 7·96–8·26 (2 mt, benzoate). For $C_{35}H_{52}O_3$ (520·45) calculated: 80·71% C, 10·07% H; found: 79·97% C, 9·72% H.

b) *By reduction of* V: Lithium tri-tert-butoxyaluminium hydride (1 g) was added to a solution of ketone *V* (262 mg) in tetrahydrofuran (10 ml). After standing for 80 min at room temperature, the mixture was poured in water, extracted with ether and the extract was processed in the usual manner. Chromatography of the residue on silica gel (50 g) with light petroleum–ether (7 : 3) as eluent afforded 230 mg of product which on crystallization from methanol yielded 140 mg of *III*, m.p. 132–134°C, $[\alpha]_D^{20}$ +91° (*c* 1·9).

5,6β-Cyclopropano-5β-cholestane-3β,7β-diol 3-Methanesulfonate 7-Benzoate (*IV*)

Methanesulfonyl chloride (3 ml) was added to alcohol *III* (2·56 g) in pyridine (10 ml). The mixture was set aside at room temperature overnight, poured on a mixture of ice and water and extracted with ether. Usual work-up of the ethereal extract gave 2·6 g of the product which was crystallized from dichloromethane–light petroleum, m.p. 139–140°C; $[\alpha]_D^{20}$ +83° (*c* 1·5). IR Spectrum: 3 075 (cyclopropane), 1 712 ,1 276 (benzoate), 1 367, 1 243, 1 180 (methanesulfonate) cm^{-1}. ^{1}H NMR Spectrum: (60 MHz): –0·05–0·36 (mt, cyclopropane protons), 0·69 (s, 18-H), 0·96

(s, 19-H), 2·95 (s, methanesulfonate), 4·51—5·23 (3α-H and 7α-H), 7·30—7·59 and 7·89—8·15 (2 mt, benzoate). For $C_{36}H_{54}O_5S$ (598·9) calculated: 72·20% C, 9·09% H, 5·35% S; found: 72·40% C, 9·15% H, 5·27% S.

7β-Benzoyloxy-5,6β-cyclopropano-5β-cholestan-3-one (*V*)

Jones reagent[3] was added dropwise to alcohol *III* (80 mg) in acetone (5 ml) until the brown coloration persisted, and the mixture was set aside for five minutes at room temperature. Methanol (0·5 ml) was added and, after standing for further 5 min, the mixture was poured in water. The product was taken up in ether, the ethereal layer was washed with 5% solution of potassium hydrogen carbonate and water, dried over sodium sulfate and the solvent was evaporated. Crystallization of the residue from methanol gave 43 mg of ketone *V*, m.p. 152—153°C, $[\alpha]_D^{20}$ +178° (*c* 2·4). IR Spectrum: 3 080 (cyclopropane), 1 725, 1 274 (benzoate), 1 716 (ketone) cm^{-1}. Mass spectrum: *m/z* 518 (M), 500 (M — H_2O), 396 (base peak, M — C_6H_5COOH), 381 (M — C_6H_5COOH — CH_3). ^1H NMR Spectrum: (60 MHz): 0·28 (dd, J = 9 Hz, cyclopropane protons), 0·70 (s, 18-H), 1·02 (s, 19-H), 5·16 (dd, J = 5·5 Hz, J' = 8 Hz, 7α-H), 7·38—7·63 and 7·92—8·12 (2 mt, benzoate). For $C_{35}H_{50}O_3$ (518·4) calculated: 81·02% C, 9·72% H; found: 80·87% C, 9·50% H.

5,6β-Cyclopropano-5β-cholestane-3β,7α-diol 3β-Acetate (*VII*)

Lithium tri-tert-butylaluminium hydride (3 g) was added to a solution of 3β-acetoxy-5,6β-cyclopropano-5β-cholestan-7-one[2] (*VI*; 1·5 g) in tetrahydrofuran (100 ml). After standing for 4 h at room temperature, further hydride (3 g) was added. The mixture was set aside for 44 h, poured in water and extracted with ether. The usual work-up of the extract gave 1·5 g of a residue which contained 2 compounds (TLC) and was chromatographed on silica gel (300 g) in ether–light petroleum (1 : 4). The less polar fractions afforded 1·3 g of alcohol *VII*, m.p. 104—105°C; $[\alpha]_D^{20}$ −4° (*c* 2·0). IR Spectrum: 3 630 (hydroxyl), 3 075 (cyclopropane), 1 738, 1 251 (acetate) cm^{-1}. Mass spectrum: *m/z* 458 (M), 398 (M — CH_3COOH), 380 (M — CH_3COOH — H_2O), 365 (M — CH_3COOH — H_2O — CH_3). ^1H NMR Spectrum (60 MHz): 0·00—0·35 (mt, cyclopropane protons), 0·64 (s, 18-H), 0·90 (s, 19-H), 2·01 (s, 3β-acetate), 3·95 (mt, 7β-H), 4·67 (mt, 3α-H). For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·76% C, 11·01% H. Polar fraction gave 130 mg of 7β-alcohol *I*, identical in all respects with a standard.

5,6β-Cyclopropano-5β-cholestane-3β,7α-diol 3-Acetate 7-Benzoate (*VIII*)

a) *By benzoylation of* VII: Benzoyl chloride (20 ml) was added to a solution of alcohol *VII* (5 g) in pyridine (75 ml). After standing overnight at room temperature, the mixture was poured in an ice–water mixture, and processed in the usual manner (ether). Crystallization from methanol yielded 3·6 g of benzoate *VIII*, m.p. 112—117°C; $[\alpha]_D^{20}$ −29° (*c* 1·7). IR Spectrum: 3080 (cyclopropane), 1 740, 1 248, 1 029 (acetate), 1 721, 1 272 (benzoate) cm^{-1}. Mass spectrum: *m/z* 562 (M), 502 (M — CH_3COOH), 380 (base peak, M — CH_3COOH — C_6H_5COOH), 365 (380 — CH_3). ^1H NMR Spectrum (60 MHz): 0·05—0·54 (mt, cyclopropane protons), 0·65 (s, 18-H), 0·98 (s, 19-H), 1·98 (s, acetate), 4·81 (mt, 3α-H), 5·42 (br s, 7β-H), 7·39—7·76 and 7·96—8·28 (2 mt, benzoate). For $C_{37}H_{54}O_4$ (562·8) calculated: 78·96% C, 9·67% H; found: 79·32% C, 9·40% H.

b) *By acetolysis of* X: Continuation of the chromatography in the preparation of B-homo compound *XX* according to procedure *a*) (elution with light petroleum–ether 9 : 1) gave 69 mg of product *VIII*, m.p. 112—116°C; $[\alpha]_D^{20}$ −30° (*c* 1·2).

c) *By acetolysis of* XIV: Continuation of the chromatography in the preparation of *XX* ac-

cording to procedure *b*) (elution with light petroleum–ether 9 : 1) afforded 29 mg of *VIII*, m.p. 112–116°C; $[\alpha]_D^{20}$ −30° (*c* 1·2).

5,6β-Cyclopropano-5β-cholestane-3β,7α-diol 7-Benzoate (*IX*)

a) *By selective saponification of* VIII: Pulverized potassium hydroxide (15 g) was added at 20°C in one portion to a solution of acetate *VIII* (5 g) in ethanol (150 ml) the temperature being maintained at 20°C by cooling. After 2 min, the mixture was diluted with water and worked up in the usual manner (ether). The crude product (4·8 g) was crystallized from methanol to give 3·92 g of 3β-alcohol *IX*, m.p. 197–198°C; $[\alpha]_D^{20}$ −55° (*c* 2·2). IR Spectrum: 3 620 (hydroxyl), 3 075 (cyclopropane), 1 713, 1 275 (benzoate) cm^{-1}. Mass spectrum: *m/z* 398 (M − C_6H_5COOH), 383 (M − C_6H_5COOH − CH_3), 380 (M − C_6H_5COOH − H_2O). ^1H NMR Spectrum (60 MHz): 0·06–0·55 (mt, cyclopropane protons), 0·66 (s, 18-H), 0·98 (s, 19-H), 3·74 (mt, 3α-H), 5·38 (s, 7β-H), 7·38–7·71 and 7·99–8·24 (2 mt, benzoate). For $C_{35}H_{52}O_3$ (520·5) calculated: 80·71% C, 10·07% H; found: 80·63% C, 10·11% H.

b) *By reduction of* XI *with lithium tri-tert-butoxyaluminium hydride*: Continuation of the chromatography in the preparation of *XII* afforded 6·5 mg of *IX*, m.p. 197–199°C (methanol); $[\alpha]_D^{20}$ −49° (*c* 0·5).

5,6β-Cyclopropano-5β-cholestane-3β,7α-diol 3-Methanesulfonate 7-Benzoate (*X*)

Methanesulfonyl chloride (2 ml) was added to a solution of 3β-alcohol *IX* (2 g) in pyridine (10 ml) and the mixture was set aside at room temperature overnight. The usual work-up procedure (ether) afforded 2·1 g of a non-crystalline compound which, according to its spectra, was practically pure methanesulfonate *X*, $[\alpha]_D^{20}$ −10° (*c* 2·4). IR Spectrum: 3 075 (cyclopropane), 1 719, 1 273 (benzoate), 1 345, 1 366, 1 180 (methanesulfonate) cm^{-1}. ^1H NMR Spectrum (60 MHz): 0·09–0·50 (mt, cyclopropane protons), 0·65 (s, 18-H), 0·97 (s, 19-H), 4·73 (mt, 3α-H), 5·39 (mt, 7β-H), 7·37–7·73 and 8·00–8·25 (2 mt, benzoate). For $C_{36}H_{54}O_5S$ (598·9) calculated: 72·20% C, 9·09% H, 5·35% S; found: 72·31% C, 9·14% H, 5·27% S.

7α-Benzoyloxy-5,6β-cyclopropano-5β-cholestan-3-one (*XI*)

Alcohol *IX* (1·32 g) was dissolved in warm acetone (50 ml). After cooling to room temperature, the solution was oxidized with Jones reagent as described for the preparation of ketone *V*. Analogous work-up procedure gave 1·18 g of a residue which was crystallized from aqueous acetone to afford 0·85 g of the ketone *XI*, m.p. 171–172°C, $[\alpha]_D^{20}$ +33° (*c* 1·9). IR Spectrum: 3 080 (cyclopropane), 1 728, 1 270 (benzoate), 1 715 (ketone) cm^{-1}. Mass spectrum: *m/z* 518 (M), 396 (base peak, M − C_6H_5COOH). ^1H NMR Spectrum (60 MHz): 0·30–0·56 (cyclopropane protons), 0·67 (s, 18-H), 1·03 (s, 19-H), 5·38 (br mt, 7β-H), 7·42–7·69 and 7·90–8·18 (2 mt, benzoate). For $C_{35}H_{50}O_3$ (518·4) calculated: 81·02% C, 9·72% H; found: 80·88% C, 9·75% H.

5,6β-Cyclopropano-5β-cholestane-3α,7α-diol 7-Benzoate (*XII*)

Solid lithium tri-tert-butoxyaluminium hydride (1·5 g) was added to a solution of ketone *XI* (720 mg) in tetrahydrofuran (30 ml). After standing for 60 min at room temperature, the mixture was poured in water and processed in the usual manner (ether). The residue (650 mg) was subjected to chromatography on silica gel (150 g) in light petroleum–ether (4 : 1). The combined non-polar fractions afforded 492 mg of crude product which was crystallized from aqueous methanol to give 350 mg of 3α-alcohol *XII*, m.p. 146–147°C; $[\alpha]_D^{20}$ −56° (*c* 1·2). IR Spectrum: 3 620 (hydroxyl), 3 075 (cyclopropane), 1 717, 1 272 (benzoate) cm^{-1}. ^1H NMR Spectrum (60 MHz): 0·02

to 0·40 (mt, cyclopropane), 0·65 (s, 18-H), 0·92 (s, 19-H), 3·97 (mt, 3β-H), 5·44 (br s, 7β-H), 7·41–7·68 and 8·01–8·24 (2 mt, benzoate). For $C_{35}H_{52}O_3$ (520·5) calculated: 80·71% C, 10·07% H; found: 80·65% C, 10·01% H.

5,6β-Cyclopropano-5β-cholestane-3α,7α-diol 3-Acetate 7-Benzoate (*XIII*)

a) *By acetylation of* XII: Acetic anhydride (0·5 ml) was added to a solution of compound *XII* (132 mg) in pyridine (1 ml). After standing overnight at room temperature, the mixture was poured in water and ice, extracted with ether and worked up as usual; yield 140 mg of *XIII*; pure according to TLC; $[\alpha]_D^{20}$ −40° (*c* 0·9). IR Spectrum: 3 075 (cyclopropane), 1 733, 1 247, 1 030 (acetate), 1 728, 1 273 (benzoate). ^{1}H NMR Spectrum (60 MHz): 0·04–0·40 (mt, cyclopropane protons), 0·67 (s, 18-H), 0·79 (s, 19-H), 1·31 (s, 3β-acetate), 4·90 (mt, 3β-H), 5·35 (mt, 7β-H), 7·32–7·75 and 7·98–8·22 (2 mt, benzoate). For $C_{37}H_{54}O_4$ (562·8) calculated: 78·96% C, 9·67% H; found: 79·61% C, 9·04% H.

b) *By acetolysis of* X: Continuation of the chromatography in the preparation of *VIII* according to procedure *b*) afforded 129 mg of *XIII*; $[\alpha]_D^{20}$ −38° (*c* 1·1).

c) *By acetolysis of* XIV: Continuation of the chromatography in the preparation of *VIII* according to procedure *c*) gave 26 mg of *XIII*; $[\alpha]_D^{20}$ −35° (*c* 1·2).

5,6β-Cyclopropano-5β-cholestane-3β,7α-diol 3-Methanesulfonate 7-Benzoate (*XIV*)

Methanesulfonyl chloride (2·8 ml) was added to a solution of alcohol *IX* (2·8 g) in pyridine (15 ml). After standing overnight at room temperature, the mixture was worked up as usual (ether), giving 2·98 g of the product which was crystallized from methanol. Yield 1·6 g of *XIV*, m.p. 127–128°C; $[\alpha]_D^{20}$ −32° (*c* 1·38). IR Spectrum: 3 075 (cyclopropane), 1 713, 1 274 (benzoate), 1 341, 1 179 (methanesulfonate) cm^{-1}. ^{1}H NMR Spectrum (60 MHz): 0·07–0·46 (cyclopropane protons), 0·65 (s, 18-H), 0·92 (s, 19-H), 2·27 (s, methanesulfonate), 5·03 (mt, 3β-H), 5·40 (mt, 7β-H), 7·37–7·70 and 8·04–8·26 (2 mt, benzoate). For $C_{36}H_{54}O_5S$ (598·9) calculated: 72·20% C, 9·09% H, 5·35% S; found: 72·39% C, 9·09% H, 5·26% S.

B-Homo-3,5,7-cholestatriene (*XV*)

a) *By acetolysis of* IV: Anhydrous sodium acetate (2 g) was added to methanesulfonate *IV* (2 g) in acetic acid (50 ml) and acetic anhydride (5 ml). The mixture was refluxed under nitrogen for 2 h, cooled to room temperature, poured in water and extracted with ether. The ethereal layer was washed with water, saturated potassium hydrogen carbonate solution and again water, dried, and taken down. A part (300 mg) of the residue was chromatographed on a column of silica gel (50 g) in light petroleum, affording 140 mg of triene *XV*, m.p. 69–72°C (methanol); $[\alpha]_D^{20}$ −425° (*c* 1·0). IR Spectrum: 1 618, 1 587, 3 025 (double bonds) cm^{-1}. UV Spectrum (dichloromethane): λ_{max} 298 (log ε 4·14). Mass spectrum: *m/z* 380 (M). ^{1}H NMR Spectrum (200 MHz): 0·73 (s, 18-H), 0·90 (s, 19-H), 5·54 (bd, $J_{6,7}$ = 7·3 Hz, 6-H), 5·65 (bdd, $J_{7a,7}$ = 11·6 Hz, $J_{7a,8\alpha}$ = 2·5 Hz, 7a-H), 5·78 (ddd, $J_{7,8\alpha}$ = 2·2 Hz, 7-H), 5·75 (mt, 3-H), 5·98 (mt, $J_{4,3}$ = 9·6 Hz, $J_{4,6}$ = 0·8 Hz, $J_{4,2\alpha} + J_{4,2\beta}$ = 2·1 + 0·8 Hz, 4-H). For $C_{28}H_{44}$ (380·66) calculated: 88·35% C, 11·65% H; found: 88·60% C, 11·61% H.

b) *By acetolysis of* X: Methanesulfonate *X* (1·4 g) was treated with acetic acid (30 ml), acetic anhydride (3·0 ml) and sodium acetate (1·4 g) as described in procedure *a*). Analogous work-up procedure gave 1·2 g of a residue, containing (TLC) seven main products which were separated by chromatography on a column of silica gel (280 g). The compounds were eluted successively

by light petroleum and light petroleum–ether (49 : 1, 33 : 1, 20 : 1, and 10 : 1). The light petroleum fraction was taken down and the residue (223 mg) was crystallized from ethanol at −20°C to −60°C, affording triene *XV*, m.p. 68–72°C (unstable at room temperature); $[\alpha]_D^{20}$ −416° (*c* 1·1).

c) *By acetolysis of* XIV: A mixture of methanesulfonate *XIV* (1·25 g), acetic acid (31·2 ml), acetic anhydride (3·12 ml) and sodium acetate (1·25 g) was refluxed for 2 h under nitrogen. The mixture was worked up as described in procedure *a*), affording 980 mg of product which consisted of the compounds described under *b*) but their percentage was different. The residue was chromatographed essentially as described in experiment *b*). The least polar fractions gave 480 mg of the triene *XV*, m.p. 70–73°C; $[\alpha]_D^{20}$ −428° (*c* 1·2).

6β-Acetoxymethyl-5α-cholesta-3,7-diene (*XVI*)

a) *By acetolysis of* IV: Further fractions from the chromatography in the preparation of *XV* according to procedure *a*) afforded 31 mg of glassy diene *XVI* which resisted all crystallization attempts; $[\alpha]_D^{20}$ +57° (*c* 0·7). IR Spectrum: 1 743, 1 274 (acetate), 1 626 (double bonds) cm^{-1}. Mass spectrum: *m/z* 440 (M), 380 (M − CH_3COOH), 365 (M − CH_3COOH − CH_3). ^1H NMR Spectrum (200 MHz): 0·71 (s, 18-H), 0·90 (s, 19-H), 2·04 (s, acetate), 3·79 (dd, $J_{6\alpha,CH_2}$ = 7·5 Hz, J_{gem} = −10·5 Hz) and 4·31 (dd, $J_{6\alpha,CH_2}$ = 3·3 Hz) (together: 6-CH_2–OAc), 5·31 (d, $J_{7,6\alpha}$ = = 3·5 Hz, 7-H), 5·67 (mt, $\sum J$ = 17·2 Hz, 3-H), 5·95 (bd, $J_{4,3}$ = 11·0 Hz, $\sum J$ = 14·0 Hz, 4-H). For $C_{30}H_{48}O_2$ (440·7) calculated: 81·76% C, 10·98% H; found: 81·53% C, 10·73% H.

b) *By acetolysis of* X: Further fractions from the chromatography in preparation of *XVIII* according procedure *b*) gave 19 mg of diene *XVI*; $[\alpha]_D^{20}$ +54° (*c* 1·12).

c) *By acetolysis of* XIV: Further chromatographic fractions in the preparation of *XVIII* according to procedure *c*) yielded 118 mg of diene *XVI*; $[\alpha]_D^{20}$ +55° (*c* 1·2).

5,6β-Cyclopropano-5β-cholest-3-en-7β-ol 7-Benzoate (*XVII*)

A solution of methanesulfonate *IV* (100 mg) in collidine (2 ml) was refluxed for 2 h. After cooling, the mixture was poured in water, extracted with ether and the extract was processed as usual. The residue (85 mg) was purified by chromatography on a column of silica gel (50 g, eluent light petroleum–ether 48 : 1), affording 75 mg of the product which on crystallization from methanol melted at 160–161°C; $[\alpha]_D^{20}$ +53° (*c* 1·2). IR Spectrum: 3 080, 3 025 (cyclopropane and double bond), 1 652, 689 (double bond), 1 713, 1 276 (benzoate) cm^{-1}. ^1H NMR Spectrum (60 MHz): 0·12–0·42 (mt, cyclopropane protons), 0·70 (s, 18-H), 0·91 (s, 19-H), 4·60 (br d, *J* = 10 Hz, 4-H), 5·12 (mt, 7α-H), 5·63 (mt, 3-H), 7·30–7·58 and 7·85–8·13 (2 mt, benzoate). For $C_{35}H_{50}O_2$ (502·78) calculated: 83·61% C, 10·02% H; found: 83·40% C, 10·42% H.

5,6β-Cyclopropano-5β-cholest-3-en-7α-ol 7-Benzoate (*XVIII*)

a) *By elimination of methanesulfonyloxy group in* XIV: A solution of compound *XIV* (1·1 g) in collidine (10 ml) was refluxed for 2 h. After cooling to room temperature, the mixture was poured in water and processed in the usual manner, affording 900 mg of crude product. Purification by column chromatography on silica gel (100 g) in light petroleum–ether (49 : 1) gave 510 mg of olefin *XVIII*, m.p. 78–81°C (methanol); $[\alpha]_D^{20}$ −108° (*c* 0·7). IR Spectrum: 3 075, 3 025 (cyclopropane and double bond), 1 715, 1 273 (benzoate), 1 649 (double bond) cm^{-1}. ^1H NMR Spectrum (200 MHz): 0·40 (dd, J_{AB} = 5·1 Hz, $J_{A,6}$ = 9·3 Hz, H_A), 0·77 (t, $J_{B,6}$ = 5·6 Hz, H_B) (protons of the CH_2-part of the cyclopropane ring are denoted A and B), 0·67 (s, 18-H), 0·88 (s, 19-H), 4·65 (mt, $J_{3,4}$ = 10 Hz, $\sum J$ = 13·4 Hz, 4-H), 5·38 (bd, $J_{7\beta,8\alpha}$ = 2·3 Hz, 7β-H). For $C_{35}H_{50}O_2$ (502·8) calculated: 83·61% C, 10·02% H; found: 83·42% C, 10·07% H.

b) *By acetolysis of* X: Further chromatographic fractions in the preparation of *XV* according to procedure *b*) gave 374 mg of *XVIII*, m.p. 78–81°C; $[\alpha]_D^{20}$ −103° (*c* 1·1).

c) *By acetolysis of* XIV: Further chromatographic fractions in the preparation of *XV* according to procedure *c*) afforded 46 mg of *XVIII*, m.p. 76–80°C; $[\alpha]_D^{20}$ −106° (*c* 1·2).

6β-Acetoxymethylcholest-5-en-7α-ol 7-Benzoate (*XIX*)

a) *By acetolysis of* X: Further chromatographic fractions in the preparation of *XVI* according to procedure *b*) gave a mixture of two compounds of the same R_F (TLC on silica gel). They were separated by chromatography on 200 g of silica gel treated with 20% of silver nitrate (Ag-silica gel). Elution with light petroleum–ether (19 : 1) gave as a more polar fraction a non-crystallizable oil, $[\alpha]_D^{20}$ +47° (*c* 1·1). IR Spectrum: 1 743, 1 235 (acetate), 1 721, 1 274 (benzoate), 1 655 (double bond) cm^{-1}. Mass spectrum: *m/z* 562 (M), 502 (M − CH_3COOH), 440 (M − C_6H_5COOH), 380 (base peak, M − CH_3COOH − C_6H_5COOH). ^1H NMR Spectrum (200 MHz): 0·73 (s, 18-H), 1·07 (s, 19-H), 2·13 (s, acetate), 2·72 (ddd, 6α-H), 4·00 (dd, $J_{CH_2,6\alpha} = 5{\cdot}4$ Hz, $J_{gem} = -10{\cdot}9$ Hz) and 4·34 (t, $J_{CH_2,6\alpha} = 10{\cdot}2$ Hz) (6-CH_2–$OCOCH_3$), 5·13 (t, $J_{6\alpha,7\beta} \doteq J_{8\alpha,7\beta} \doteq 2{\cdot}2$ Hz, 7β-H), 5·41 (t, $\sum J = 7{\cdot}3$ Hz, 4-H). For $C_{37}H_{54}O_4$ (562·8) calculated: 78·96% C, 9·67% H; found: 78·82% C, 9·69% H.

b) *By acetolysis of* XIV: Further chromatographic fractions in the preparation of *XVI* according to procedure *c*) gave a mixture containing two products (TLC on 20% Ag-silica gel) which were separated by column chromatography on 20% Ag-silica gel in light petroleum–ether (19 : 1). Yield 94 mg of oily olefin *XIX*; $[\alpha]_D^{20}$ −42° (*c* 1·1).

B-Homo-cholest-5-en-7α,7aα-diol 7-Acetate 7a-Benzoate (*XX*)

a) *By acetolysis of X*: Further fractions from the chromatography on 20% Ag-silica gel in the preparation of *XIX* according to procedure *a*) gave 82 mg of the title compound *XX* as an oil, $[\alpha]_D^{20}$ +18° (*c* 0·79). IR Spectrum: 1 744, 1 235 (acetate), 1 721, 1 275 (benzoate), 1 658 (double bond) cm^{-1}. Mass spectrum: *m/z* 562 (M), 502 (M − CH_3COOH), 380 (base peak, M − CH_3·.COOH − C_6H_5COOH). ^1H NMR Spectrum (200 MHz): 0·74 (s, 18-H), 1·07 (s, 19-H), 2·08 (s, 7α-acetate), 2·29 (dd, $J_{gem} = -13{\cdot}6$ Hz, 6α-H), 2·61 (dd, 6β-H), 4·67 (td, $J_{7,6\gamma} = 8{\cdot}3$ Hz, $J_{7,6\beta} = 8{\cdot}5$ Hz, 7-H), 5·31 (d, $J_{7a,7} = 2{\cdot}4$ Hz, 7a-H), 5·43 (t, $\sum J = 7{\cdot}3$ Hz, 4-H). For $C_{37}H_{54}O_4$ (562·8) calculated: 78·96% C, 9·67% H; found: 78·60% C, 9·51% H.

b) *By acetolysis of* XIV: Further fractions from the chromatography on 20% Ag-silica gel in the preparation of *XIX* according to procedure *b*) afforded 53 mg of *XX*, $[\alpha]_D^{20}$ +19° (*c* 1·2).

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