ON STEROIDS. CXLIII.* B-HOMOSTEROIDS. VI.** SIMMONS-SMITH METHYLENATION OF Δ^5-STEROIDS

L.KOHOUT and J.FAJKOŠ

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 6

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A series of epimeric 5,7-cyclo-B-homosteroids has been prepared by Simmons–Smith methylenation of some 5-cholestene derivatives; their structures were established by spectral as well as chemical means.

In connection with our studies on B-homosteroids we became interested in the 5,7-cyclo-B-homosteroids. These compounds are expected to rearrange to a new type of B-homosteroids we liked to study. In this paper we describe the synthesis of the epimeric 5,7-cyclo-B-homosteroids using Simmons–Smith methylenation[1] of the 5,6 double bond in some cholestane derivatives.

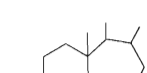
Surprisingly, this method has not yet been applied to a simple Δ^5-steroids though variously substituted 5,7-cyclo-B-homosteroids have been prepared by addition of dihalocarbenes[2–8], on catalysis with trichlorophenylmercury[9] or, by different types of rearrangements[10–21].

The methylenation has been carried out as described[22] in the B-norsteroid series only somewhat higher content of copper (0·7%) in the Zn–Cu couple has been found to give better yields. When 3β-acetoxy-5-cholestene (*II*) was treated with methylene iodide in ether under the presence of Zn–Cu couple for 7 hours at 100°C next to the starting material two new compounds were isolated after hydrolysis by chromatography in about equal quantities (14% and 19%). Spectroscopic evidence (NMR, IR and mass spectrometry) showed presence of the cyclopropane ring in both of these compounds. They are therefore evidently the epimers *III* and *V*. On acetylation they afforded the corresponding acetates *IV* and *VI* one melting at 120–121°C the other at 86–87°C.

The assignement of configurations was possible on the basis of the NMR spectra. It has been shown[23–25] that protons lying in conical regions extending above and below the plane of the cyclopropane ring are shielded and those lying outside of these conical regions – close enough to the cyclopropane ring – are deshielded. Fig. 1

* Part CXLII: This Journal *37*, 3483 (1972).

** Part V: This Journal *37*, 2227 (1972).



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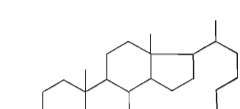
IV, R = Ac



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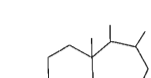
II, R = Ac



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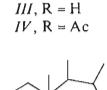
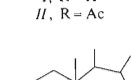
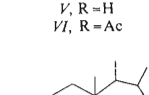


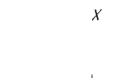
X



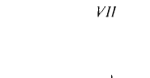
VII



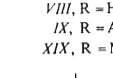
VIII, R = H
IX, R = Ac
XIX, R = Me



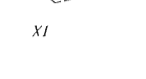
XI



XII, R = H *XIV*, R = Me
XIII, R = Ac *XV*, R = Et



XVI



XVII, R = H
XVIII, R = Ac

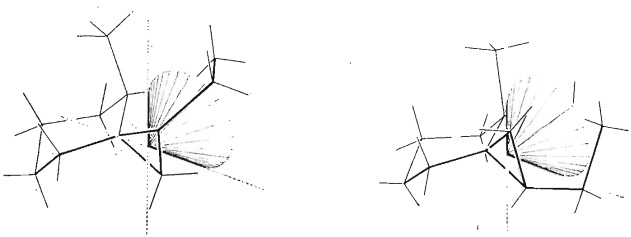
shows models of our two epimeric 5,7-cyclo derivatives. In the 5β,7β-epimer in which the cyclopropane ring itself has α-configuration the $C_{(19)}$ protons are evidently outside of the conical regions (Fig. 1*b*) and we may therefore expect a strong deshielding effect. On the other hand in the 5α,7α-epimer the $C_{(19)}$ protons are lying on the border of the conical regions (Fig. 1*a*) (the angle believed[23] to be about 110°) which should produce a weak shielding or deshielding effect. The NMR data are summarised in Table I related to the corresponding 5α-derivative. This seems to be a reasonable approximation as according to the models the conformation of the steroid skeleton in both epimeric cyclo derivatives is similar and close to the conformation of a 5α-steroid. This is in agreement with the ORD curves of the corresponding 3-oxo derivatives *VII* and *XI*, both showing a pronounced positive Cotton effect.

These considerations were applied on two epimeric cyclo derivatives obtained on methylenation of 3β-acetoxy-5-cholestene (*II*). The $C_{(19)}$ protons in the lower

melting epimer appear at 0·89 p.p.m. whereas in the higher melting compound we find the corresponding signal at 1·13 p.p.m. Compared with 3β-acetoxy-5α-cholestane in which the $C_{(19)}$ protons appear at 0·842 p.p.m. there is a downfield shift of 0·048 p.p.m. in the lower melting epimer and a much stronger downfield shift of 0·288 p.p.m. in the higher melting one. The lower melting compound is therefore 3β-acetoxy-5,7α-B-homo-5α-cholestane (*VI*) and the higher melting one is its 5,7β-epimer *IV*. Analogous shifts were detected also for the other derivatives in both of the epimeric series (Table I).

The acetates *IV* and *VI* were hydrolysed to the alcohols *III* and *V* which on oxidation with Jones' reagent afforded the oxo compounds *VII* and *XI*. Metal hydride reduction of these ketones gave mixtures of 3β- and 3α-alcohols from which the α-epimers *VIII* and *XII* were isolated by chromatography giving the corresponding acetates *IX* and *XIII* on acetylation. The parent hydrocarbons *X* and *XVI* were prepared from the ketones *VII* and *XI* by Huang-Minlon reduction.

These cyclo derivatives were also prepared directly by Simmons–Smith methylenation of the alcohols *I* and *XVII* and from the acetate *XVIII*. The results are summarised in Table II. Similarly to the findings in the B-norsteroid series[22] there seems to be no influence of the configuration of the 3-hydroxyl group on the relationship of the two isomers formed on methylation; much higher yields were obtained with the acetates than with the alcohols which is in contrast to the observations of Ginsig and Cross[27]. When 3α-hydroxy-5-cholestene (*XVII*) was submitted to the methylenation conditions the ethoxy derivative *XV* was isolated as the main product (20%). The methoxy derivatives *XIV* and *XIX* were not detected in the reaction mixture. They were prepared from the corresponding alcohols *VIII* and *XII* with diazomethane under catalysis with aluminium chloride.



a *b*

FIG. 1

Shielding-Deshielding of $C_{(19)}$ Protons in the Epimeric 5,7-Cyclo Derivatives

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 80°C/0·2 Torr. Optical measurements were carried out in chloroform with an error of ± 1°. The infrared spectra were recorded on the Zeiss UR 10 spectrometer in tetrachloromethane. The mass spectra were recorded on the mass spectrometer AEI MS 902. The NMR spectra were recorded on Varian HA-100 instrument in deuteriochloroform with tetramethylsilane as internal reference. The chemical shift is given in p.p.m. The identity of samples prepared by different routes was checked by mixture melting point determination, by thin layer chromatography and by infra-red spectra.

5,7α-Cyclo-B-homo-5α-cholestan-3β-ol (*V*)

a) *From 5-cholesten-3β-ol* (I): 0·7% Zn–Cu couple was prepared by adding zinc dust (52 g) into a solution of cupric acetate monohydrate (1 190 mg) in acetic acid (50 ml) at 50–60°C and shaking until the solution decolorised. Fresh acetic acid (50 ml) was added and the sedimented zinc was decanted with eight portions (50 ml each) of ether. The alcohol *I* (15 g) was dissolved in ether (150 ml) in a 500 ml autoclave, the solution was treated with methylene iodide (46 ml) in ether (100 ml) the couple was added and the mixture was heated for 7 h in a boiling water bath. The autoclave was set aside overnight at room temperature, the couple was filtered off, the ethereal solution was poured into a 5% sodium hydrogen carbonate solution, washed well with this solution, water, 5% hydrochloric acid again with a sodium hydrogen carbonate solution, with 10% sodium thiosulphate solution, water, dried, and evaporated. The residue was chromatographed on a silica gel column (150 g) in ether–light petroleum (b.p. 40–60°C) (1 : 4) and fractions corresponding in polarity to the starting material were combined and evaporated to yield 8·2 g of an oily product. The oil was dissolved in ether (100 ml) treated with a solution of per-

TABLE I

Chemical Shift Values (p.p.m.) for 19-Methyl Signals[a]

Compound	19-CH_3	Δ
5α-Cholestane[b]	0·77	0
X	0·86	+0·09
XVI	1·06	+0·29
5α-Cholestan-3α-ol[b]	0·77	0
VIII	0·82	+0·05
XII	1·05	+0·28
5α-Cholestan-3β-ol[b]	0·81	0
V	0·88	+0·07
III	1·21	+0·40
3β-Acetoxy-5α-cholestane[b]	0·84	0
VI	0·89	+0·05
IV	1·13	+0·29
5α-Cholestan-3-on[b]	0·99	0
VII	0·94	−0·05
XI	1·26	+0·27

[a] Solvent deuteriochloroform, tetramethylsilane as internal reference, Varian HA-100 instrument; [b] ref.[26].

phthalic acid (6·7 g) in ether (60 ml) allowed to stand at room temperature for 18 h. The excess peracid was removed with 5% sodium carbonate solution, washed with water, dried and evaporated. The residue was chromatographed on silica gel (200 g) in ether–light petroleum (b.p. 40—60°C) (1 : 9). Fractions containing the lipophilic component were combined and evaporated. The residue was crystallised from acetone to yield 820 mg of the alcohol *V*, m.p. 101—102°C, $[\alpha]_D^{20}$ —3°; Mass spectrum M^+ 400; IR: 3620, 3060, 1050, 1040, 1023 cm^{-1}; NMR: —0·08 (dd, J = 5 Hz, 8·5 Hz, 6α-H); 0·305 (t, J = 5 Hz, 6β-H), 0·63 (s, 18-H), 0·86 (d, J = 6 Hz, 26- and 27-H), 0·88 (s, 19-H), 0·88 (d, J = 6 Hz, 21-H), 3·86 (mt, 3α-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·46% C, 12·04% H.

b) *From* 3β-*acetoxy*-5-*cholestene* (II): The methylenation was carried out with 15 g of the acetate *II* as given in the foregoing experiment. The crude product was chromatographed on silica gel (150 g) in light petroleum (b.p. 40—60°C)–ether (19 : 1). Fractions corresponding in the polarity to the starting material were combined, evaporated and the oil (13·2) was dissolved in ether. The ethereal solution was treated with a solution of perphthalic acid (13 g) in ether (100 ml) and allowed to stand at room temperature for 18 h. The excess peracid was removed with a sodium carbonate solution, the solution was washed with water, dried, and evaporated. The residue was dissolved in methanol (900 ml) treated with a solution of potassium carbonate (10 g) in water (150 ml) and refluxed for 1 hour. Methanol was distilled off under reduced pressure, water was added and the product extracted into ether. The ethereal solution was washed with water, dried, and evaporated. The residue was chromatographed on silica gel (300 g) in light petroleum (b.p. 40—60°C)–ether (9 : 1) to yield after crystallisation from acetone 2·69 g of the alcohol *V*, m.p. 101—102°C, $[\alpha]_D^{20}$ —3° (*c* 1·39).

c) *From* 3β-*acetoxy*-5,7α-*cyclo*-B-*homo*-5α-*cholestane* (VI): The acetate *VI* (100 mg) in methanol (10 ml) was refluxed with a solution of potassium carbonate (100 mg) in water (1·5 ml) for 1 h. Methanol was distilled off under reduced pressure and the product isolated with ether. The ethereal solution was worked up as usual and evaporated. The residue (95 mg) was crystallised from acetone to give 68 mg of the alcohol *V*, m.p. 99—100°C, $[\alpha]_D^{20}$ —4·7° (*c* 1·35).

d) *From* 5,7α-*cyclo*-B-*homo*-5α-*cholestan*-3-*one* (VII): Continued elution of the chromatography after preparation of the 3α-epimer *VIII* from the ketone *VII* working up of the corresponding fractions and crystallisation from acetone gave 378 mg of the alcohol *V*, m.p. 102—103°C, $[\alpha]_D^{20}$ —2·8° (*c* 1·13).

5,7β-Cyclo-B-homo-5β-cholestan-3β-ol (*III*)

a) *From* 3β-*hydroxy*-5-*cholestene* (I): Continued elution of the chromatography of the foregoing experiment under *a*) working up of the corresponding fractions and crystallisation from acetone

TABLE II

The Yields (%) of Simmons–Smith Methylenation

Products	*XVII*	*XVIII*	*I*	*II*
5α,7α-cyclo	1	17	5	19
5β,7β-cyclo	4	9	6	14

yielded 980 mg of the alcohol *III*, m.p. 157–158°C, $[\alpha]_D^{20}$ −46° (*c* 1·14). Mass spectrum: M^+ 400; IR: 3615, 3060, 1039, 1058 cm^{-1}; NMR: 0·11 (dd, J = 9 Hz, 4 Hz, 6β-H), 0·32 (mt, 6α-H), 0·62 (s, 18-H), 0·86 (d, J = 7 Hz, 26-H and 27-H), 0·88 (d, J = 6 Hz, 21-H), 1·21 (s, 19-H), 3·72 (mt, 3α-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·97% C, 12·02% H.

b) *From* 3β-*acetoxy*-5-*cholestene* (II): Continued elution of the chromatography from the foregoing experiment under *b*) afforded after working up and crystallisation from acetone 1·94 g of the cyclo derivative *III*, m.p. 159–160°C, $[\alpha]_D^{20}$ −46° (*c* 1·43).

c) *From* 3β-*acetoxy*-5,7β-*cyclo*-B-*homo*-5β-*cholestane* (IV): The acetate *IV* (169 mg) in methanol (17 ml) was treated with a solution of potassium carbonate (170 mg) in water (2·5 ml) and refluxed for 2 h. Methanol was distilled off under reduced pressure, the residue diluted with water and the product taken into ether. Working up and crystallisation from acetone afforded 112 mg of the alcohol *III*, m.p. 156–158°C, $[\alpha]_D^{20}$ −45° (*c* 1·67).

d) *From* 5,7β-*cyclo*-B-*homo*-5β-*cholestan*-3-*one* (XI): Continued elution of the chromatography after preparation of the 3α-epimer *XII* under *a*) afforded fractions containing the 3β-epimer *III*. Working up and crystallisation from acetone yielded 254 mg of the alcohol *III*, m.p. 158–159°C, $[\alpha]_D^{20}$ −48° (*c* 4·36).

3β-Acetoxy-5,7β-cyclo-B-homo-5β-cholestane (*IV*)

The alcohol *III* (270 mg) was acetylated in pyridine (1·5 ml) with acetic anhydride (1 ml) at room temperature for 18 h. The reaction mixture was decomposed with ice, diluted with water, and the product extracted into ether. The ethereal solution was washed with dilute hydrochloric acid, a sodium hydrogen carbonate solution, water, dried and evaporated. The residue (275 mg) on crystallisation from methanol gave 170 mg of the acetate *IV*, m.p. 120–121°C, $[\alpha]_D^{20}$ −47·6° (*c* 1·46). IR: 3060, 1735, 1247, 1031 cm^{-1}; NMR: 0·1–0·5 (overlapping multiplets of two protons, 6-H), 0·61 (s, 18-H), 0·86 (d, J = 6·5 Hz, 26-H and 27-H), 0·89 (d, J = 6 Hz, 21-H), 1·13 (s, 19-H), 2·00 (s, 3β-acetate), 4·83 (broad mt, 3α-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·45% C, 11·39% H.

3β-Acetoxy-5,7α-cyclo-B-homo-5α-cholestane (*VI*)

The alcohol *V* (257 mg) was acetylated with acetic anhydride (1 ml) in pyridine (1·5 ml) for 18 h. Similar working up as given in the foregoing experiment afforded 260 mg of the crude product which on crystallisation from methanol gave 194 mg of the acetate *VI*, m.p. 86–87°C, $[\alpha]_D^{20}$ −1·1° (*c* 1·13). IR : 3060, 1735, 1248, 1030 cm^{-1}; NMR: −0·06 (dd, J = 5 Hz, 8 Hz, 6α-H), 0·29 (t, J = 5 Hz, 6β-H), 0·63 (s, 18-H), 0·86 (d, J = 6 Hz, 26-H and 27-H), 0·88 (d, J = 6 Hz, 21-H), 0·89 (s, 19-H), 2·00 (s, 3β-acetate), 4·90 (broad mt, 3α-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·16% C, 11·27% H.

5,7α-Cyclo-B-homo-5α-cholestan-3-one (*VII*)

a) *From* 5,7α-*cyclo*-B-*homo*-5α-*cholestan*-3β-*ol* (V): The alcohol *V* (220 mg) in acetone (15 ml) was treated with an excess of Jones' reagent and set aside at room temperature for 5 min. The excess oxidising agent was removed with methanol (1 ml), the reaction mixture was diluted with water and the product taken into ether. The ethereal solution was washed with water, a sodium hydrogen carbonate solution, water, dried, and evaporated. The residue (220 mg) was crystallised from methanol–acetone to yield 172 mg of the ketone *VII*, m.p. 76–77°C, $[\alpha]_D^{20}$ +80° (*c* 3·66). IR: 3065, 1724 cm^{-1}; NMR: 0·12 (dd, J = 5 Hz, 9 Hz, 6α-H), 0·35 (t, J = 6 Hz, 6β-H), 0·63

(s, 18-H), 0·84 (d, J = 6 Hz, 26-H and 27-H), 0·87 (d, J = 6 Hz, 21-H), 0·94 (s, 19-H), 2·21—2·45 (mt, 2-H), 2·78 and 1·36 (2d, 4-H); ORD: (*c* 0·164 in chloroform, +26°C), $[\Phi]_{400}$ +1160°, $[\Phi]_{314}$ +7560°, $[\Phi]_{307}$ +6300° (inflex), $[\Phi]_{277}$ −5530°, $[\Phi]_{250}$ −2910°, a = +131. For $C_{28}H_{46}O$ (398·7) calculated: 84·35% C, 11·63% H; found: 84·53% C, 11·61% H.

b) *From* 5,7α-*cyclo*-B-*homo*-5α-*cholestan*-3α-*ol* (VIII): The alcohol *VIII* (500 mg) was oxidised with Jones' reagent in acetone (250 ml) as given ad *a*). Crystallisation from methanol yielded 340 mg of the ketone *VII*, m.p. 75—77°C, $[\alpha]_D^{20}$ +79·5° (*c* 3·0).

5,7α-Cyclo-B-homo-5α-cholestan-3α-ol (*VIII*)

a) *From* 5,7α-*cyclo*-B-*homo*-5α-*cholestan*-3-*one* (VII): A solution of the ketone *VII* (1·66 g) in tetrahydrofuran (30 ml) was treated at room temperature with solid lithium tri-tert-butoxy-aluminium hydride (3·3 g) and allowed to stand for 30 min. The mixture was diluted with ether, decomposed with water, acidified with dilute HCl, and the ethereal solution was washed with water, a sodium hydrogen carbonate solution, dried, and evaporated. The crystalline residue (1·6 g) consisted of two components. It was chromatographed on a silica gel column (100 g) in light petroleum (b.p. 40—60°C)–ether (9 : 1). Fractions containing the lipophilic component were combined and evaporated to yield 1·150 g of the crude product which on crystallisation from methanol yielded 830 mg of the alcohol *VIII*, m.p. 124—125°C, $[\alpha]_D^{20}$ −23·7° (*c* 2·12). IR: 3610, 3060, 1045, 1021 cm^{-1}; NMR: −0·09 (dd, J = 5 Hz, 9 Hz, 6α-H), 0·24 (t, J = 5 Hz, 6β-H), 0·62 (s, 18-H), 0·82 (s, 19-H), 0·85 (d, J = 6 Hz, 26-H and 27-H), 0·88 (d, 21-H), 4·02 (broad mt, $W_{1/2}$ 16 Hz, 3β-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·63% C, 11·77% H.

b) *From* 3α-*acetoxy*-5,7α-*cyclo*-B-*homo*-5α-*cholestane* (*IX*): The acetate *IX* (140 mg) in methanol (10 ml) was refluxed with a solution of potassium carbonate (140 mg) in water (2 ml) for 2 hours. Methanol was distilled of under reduced pressure, the residue was diluted with water, and the product isolated with ether. The residue after evaporation (132 mg) was crystallised from methanol to yield 86 mg of the alcohol *VIII*, m.p. 123—125°C, $[\alpha]_D^{20}$ −24° (*c* 1·17).

c) *From* 5-*cholesten*-3α-*ol* (XVII): Continued elution of the chromatography in the preparation of *XII* under *c*) gave fractions containing the polar component. Working up and crystallisation from methanol yielded 16 mg of the alcohol *VIII*, m.p. 123—125°C, $[\alpha]_D^{20}$ −21° (*c* 1·17). Continued elution of the chromatography from the preparation of *XII* under *d*) gave after working up and crystallisation from methanol 12 mg of the 5α,7α-epimer *VIII*, m.p. 123—125°C, $[\alpha]_D^{20}$ −21° (*c* 0·81).

3α-Acetoxy-5,7α-cyclo-B-homo-5α-cholestane (*IX*)

a) *From* 5,7α-*cyclo*-B-*homo*-5α-*cholestan*-3α-*ol* (VIII): The alcohol *VIII* (137 mg) was acetylated with acetic anhydride (1·2 ml) in pyridine (2 ml) at room temperature for 20 h. Working up and crystallisation from methanol afforded 87 mg of the acetate *IX*, m.p. 68—69°C, $[\alpha]_D^{20}$ +5° (*c* 0·77). IR: 3060, 1738, 1249, 1025 cm^{-1}. For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·44% C, 11·37% H.

b) *From* 3α-*acetoxy*-5-*cholestene* (XVIII): The olefin *XVIII* (1·5 g) was treated as given for *V* under *a*). The crude product was chromatographed on silica gel (15 g) in light petroleum (b.p. 40—60°C)–ether (9 : 1). Fractions corresponding in polarity to the starting olefin (1·3 g) were dissolved in ether (50 ml) treated with perphthalic acid (1·2 g) in ether (11 ml) and allowed to stand for 20 hours at room temperature. The reaction mixture was diluted with ether, the excess peracid was extracted with a sodium carbonate solution and the ethereal solution was washed

with water, dried, and evaporated. The residue was dissolved in methanol (130 ml) and refluxed with a solution of potassium carbonate (1·3 g) in water (22 ml) for 2 h. Methanol was removed under reduced pressure, the residue diluted with water, and the product taken into ether. The ethereal solution was worked up and the residue after evaporation was chromatographed on a silica gel column (50 g) in light petroleum (b.p. 40—60°C)–ether (9 : 1). Fractions containing the lipophilic component were combined, evaporated, and the residue was acetylated with acetic anhydride (9 ml) in pyridine (15 ml) at room temperature for 16 hours. Working up and crystallisation from methanol gave 268 mg of the acetate *IX*, m.p. 66—68°C, $[\alpha]_D^{20}$ +4° (*c* 1·17).

5,7α-Cyclo-B-homo-5α-cholestane (*X*)

The ketone *VII* (480 mg) in ethylene glycol (40 ml) was refluxed with hydrazine hydrate (80%; 20 ml) for 2 hours. The reaction mixture was cooled to room temperature treated with a solution of potassium hydroxide (1·5 g) in water (1·5 ml) then heated to 195°C and kept at this temperature for additional 2 h. After cooling off the reaction mixture was poured into a saturated sodium chloride solution (40 ml) and the product was isolated with ether. The ethereal solution was washed with 5% HCl acid, a sodium hydrogen carbonate solution, water, dried, and evaporated. The residue was chromatographed on a silica gel column (35 g) in light petroleum (b.p. 40—60°C). Working up of the corresponding fractions and crystallisation from ethanol afforded 140 mg of the hydrocarbon *X*, m.p. 67—69°C, $[\alpha]_D^{20}$ −27° (*c* 1·55). IR: 3060 cm^{-1}; NMR: −0·12 (dd, J = 9 Hz, 4 Hz, 6α-H), 0·27 (t, J = 5 Hz, 6β-H), 0·62 (s, 18-H), 0·86 (s, 19-H), 0·86 (d, J = 6 Hz, 26-H and 27-H), 0·88 (d, J = 6 Hz, 21-H). For $C_{28}H_{48}$ (384·7) calculated 87·42% C, 12·58% H; found: 87·59% C, 12·46% H.

5,7β-Cyclo-B-homo-5β-cholestan-3-one (*XI*)

a) *From* 5,7β-*cyclo*-B-*homo*-5β-*cholestan*-3β-*ol* (III): The alcohol *III* (195 mg) in acetone (35 ml) was treated with excess Jones' reagent and set aside at room temperature for 5 min. The excess oxidising agent was removed with methanol (1 ml), the reaction mixture was diluted with water and the product was isolated with ether. The ethereal solution was washed with water, a sodium hydrogen carbonate solution, water, dried, and evaporated. The residue on crystallisation from methanol afforded 103 ml of the ketone *XI*, m.p. 149—150°C, $[\alpha]_D^{20}$ −2° (*c* 0·79). IR: 3006, 1716 cm^{-1}; NMR: 0·21 (dd, J = 5 Hz, 9 Hz, 6β-H), 0·32 (t, J = 5 Hz, 6α-H), 0·63 (s, 18-H), 0·85 (d, J = = 6 Hz, 26-H and 27-H), 0·88 (d, J = 6 Hz, 21-H), 1·26 (s, 19-H), 2·35—2·56 (m, 2-H), 3·00 (d, J = 15·5 Hz, 1-H and 4-H); ORD: (*c* 0·083 in chloroform; +25°C): $[\Phi]_{400}$ +216°, $[\Phi]_{313}$ +4200°, $[\Phi]_{271}$ −6144°, $[\Phi]_{250}$ −5570°. For $C_{28}H_{46}O$ (398·7) calculated: 84·35% C, 11·63% H; found: 84·36% C, 11·67% H.

b) *From* 5,7β-*cyclo*-B-*homo*-5β-*cholestan*-3α-*ol* (XII): The alcohol *XII* (100 mg) in acetone (15 ml) was oxidised with Jones' reagent as described in the foregoing experiment. Similar working up and crystallisation from methanol gave 65 mg of the ketone *XI*, m.p. 148—149°C, $[\alpha]_D^{20}$ −2° (*c* 1·25).

5,7β-Cyclo-B-homo-5β-cholestan-3α-ol (*XII*)

a) *From* 5,7β-*cyclo*-B-*homo*-5β-*cholestan*-3-*one* (XI): The ketone *XI* (360 mg) in tetrahydrofuran (50 ml) was treated with lithium tri-tert-butoxyaluminium hydride (1 g) and set aside at room temperature for 30 min. The reaction mixture was diluted with ether, decomposed with water and 2% HCl, the ethereal solution was washed with a sodium hydrogen carbonate solution, water, dried, and evaporated. The residue (360 mg) was chromatographed on a silica gel column in light

petroleum (b.p. 40—60°C)–ether (9 : 1) to yield after working up of the corresponding fractions and crystallisation from acetone 84 mg of the alcohol *XII*, m.p. 124—125°C, $[\alpha]_D^{20}$ −58° (*c* 1·91). IR: 3610, 3060, 1011 cm^{-1}; NMR: 0·49 (unresolved mt, 6α-H and 6β-H), 0·61 (s, 18-H), 0·86 (d, J = 6 Hz, 26-H and 27-H), 0·88 (d, J = 6 Hz, 21-H), 1·05 (s, 19-H), 3·96 (mt, $W_{1/2}$ 11 Hz, 3β-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 83·60% C, 11·91% H.

b) *From* 3α-*acetoxy*-5,7β-*cyclo*-B-*homo*-5β-*cholestane* (XIII): The acetate *XIII* (60 mg) in methanol (8·5 ml) was refluxed for 2 hours with a solution of potassium carbonate (80 mg) in water (1·5 ml). Methanol was distilled off, the residue diluted with water, and the product isolated with ether. The ethereal solution was washed with water, dried, and evaporated to yield after crystallisation from acetone 30 mg of the alcohol *XII*, m.p. 122—124°C, $[\alpha]_D^{20}$ −52° (*c* 1·11).

c) *From* 5-*cholesten*-3α-*ol* (XVII): The olefin *XVII* (1·5 g) was treated as given for *V* under *a*). The crude product was chromatographed on silica gel (20 g) in light petroleum (b.p. 40—60°C)–ether (9 : 1) to afford mixture of compounds similar in polarity to the starting material (*210 mg*). It was dissolved in ether (10 ml), treated with perphthalic acid (300 mg) in ether (2·5 ml) and allowed to stand at room temperature for 18 h. After dilution with ether the excess peracid was removed with a sodium carbonate solution, the ethereal solution was worked up, evaporated, and the residue was chromatographed on a silica gel column (20 g) in the same solvent mixture as given above. Working up and crystallisation from acetone gave 57 mg of the alcohol *XII*, m.p. 123—125°C, $[\alpha]_D^{20}$ −54° (*c* 1·31).

d) *From* 5-*cholesten*-3α-ol (*XVII*) *by modified procedure*: The olefin *XVII* (1 g) in ether (10 ml) was added drop by drop within 1 h to a boiling mixture of methylene iodide (18 g) and Zn–Cu couple (0·7% Cu; 6 g) in ether (30 ml). Half of the solvent was distilled off, the residue was transferred to an autoclave and heated to 100°C for 3 h. After cooling to 0°C the reaction mixture was poured into a saturated sodium hydrogen carbonate solution (150 ml) and the product was taken into ether. The ethereal solution was washed with 5% hydrochloric acid, water, a sodium hydrogen carbonate solution, water, dried and evaporated. The residue (0·84 g) was chromatographed on silica gel (10 g) in light petroleum (b.p. 40—60°C)–ether (4 : 1) to yield 220 mg of a mixture corresponding in polarity to the starting material. It was dissolved in ether (20 ml) treated with perphthalic acid (220 mg) in ether (2 ml) and set aside for 18 h. Working up gave a product which was chromatographed on a silica gel column (25 g) in light petroleum (b.p. 40—60°C)–ether (9 : 1) to yield after crystallisation from acetone 77 mg of the alcohol *XII*, m.p. 122—124°C, $[\alpha]_D^{20}$ −52° (*c* 0·71).

3α-Acetoxy-5,7β-cyclo-B-homo-5β-cholestane (*XIII*)

a) *From* 5,7β-*cyclo*-B-*homo*-5β-*cholestan*-3α-*ol* (XII): The alcohol *XII* (50 mg) was acetylated with acetic anhydride (0·6 ml) in pyridine (1 ml) for 24 h at room temperature. Working up and crystallisation from methanol gave 32 mg of the acetate *XIII*, m.p. 136—137°C, $[\alpha]_D^{20}$ −38° (*c* 1·47). IR: 3065, 1732, 1242, 1260, 1020 cm^{-1}; NMR: 0·15—0·50 (unresolved mt, 6α-H and 6β-H), 0·59 (s, 18-H), 0·83 (d, J = 6 Hz, 26-H and 27-H), 0·85 (d, J = 6 Hz, 21-H), 1·05 (s, 19-H), 1·98 (s, 3α-acetate), 4·98 (mt, 3β-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·42% C, 11·38% H.

b) *From* 3β-*acetoxy*-5-*cholestene* (XVIII): Continued elution of the chromatography after elution of *IX* under *b*) yielded 197 mg of the polar component which was acetylated with acetic anhydride (6 ml) in pyridine (10 ml) for 18 hours at room temperature. Working up and crystallisation from methanol afforded 140 mg of the acetate *XIII*, m.p. 136—137°C, $[\alpha]_D^{20}$ −36° (*c* 1·45).

3α-Methoxy-5,7β-cyclo-B-homo-5β-cholestane (*XIV*)

The alcohol *XII* (100 mg) in ether (10 ml) was treated with diazomethane (100 mg) in ether (5·5 ml) and aluminium chloride (30 mg) and allowed to stand at room temperature for 2 h. The excess diazomethane was decomposed with 5% HCl, the ethereal solution was washed with a sodium hydrogen carbonate solution, water, dried, and evaporated. The residue (100 mg) was chromatographed on two plates of silica gel (20 × 20 cm) in light petroleum (b.p. 40—60°C)–ether (33 : 1). Working up gave 78 mg of a product which on crystallisation from methanol yielded 52 mg of the methylester *XIV*, m.p. 111—112°C, $[\alpha]_D^{20}$ −37° (*c* 1·75). IR: 3070, 1101, 1089 cm^{-1}; NMR: 0·42 (mt, 6α-H and 6β-H), 0·60 (s, 18-H), 0·84 (d, J = 6 Hz, 26-H and 27-H), 0·87 (d, J = 6 Hz, 21-H), 1·03 (s, 19-H), 3·24 (s, 3α-methylether), 3·42 (mt, 3β-H). For $C_{29}H_{50}O$ (414·7) calculated: 84·00% C, 12·16% H; found: 84·39% C, 12·49% H.

3α-Ethoxy-5,7β-cyclo-B-homo-5β-cholestane (*XV*)

The olefin *XVII* (1·5 g) was treated as given for *V* under *a*). The product was chromatographed on a silica gel column (20 g) in light petroleum (b.p. 40—60°C)–ether (9 : 1). Fractions containing the lipophilic component were rechromatographed on silica gel (50 g) in light petroleum (b.p. 40—60°C)–ether (99 : 1) to yield after crystallisation from methanol 300 mg of the ethoxy derivative *XV*, m.p. 109—111°C, $[\alpha]_D^{20}$ −41° (*c* 1·25). Mass spectrum: M^+ 428; IR: 3070, 1129, 1104, 1084 cm^{-1}; NMR: 0·41 (mt, 6α-H and 6β-H), 0·59 (s, 18-H), 0·84 (d, J = 6 Hz, 26-H and 27-H), 0·87 (d, J = 6·5 Hz, 21-H), 1·03 (s, 19-H), 1·12 (t, J = 6 Hz, $C\underline{H}_3—CH_2—O$), 3·36 (q, $CH_3—C\underline{H}_2—O—$), 3·51 (mt, 3β-H). For $C_{30}H_{52}O$ (428·7) calculated: 84·04% C, 12·23% H; found: 84·30% C, 12·28% H.

5,7β-Cyclo-B-homo-5β-cholestane (*XVI*)

The ketone *XI* (275 mg) in ethylene glycol (20 ml) was refluxed with hydrazine hydrate (80%; 1·2 ml) for 2 h. The reaction mixture was cooled to room temperature, treated with a solution of KOH (750 mg) in water (0·75 ml), heated to 195°C and kept at this temperature for additional 2 h. The reaction mixture was decomposed with water and the product taken into ether. The ethereal solution was washed with 5% HCl, a sodium hydrogen carbonate solution, water, dried, and evaporated. The residue was chromatographed on silica gel (30 g) in light petroleum (b.p. 40—60°C) to afford after crystallisation from methanol 84 mg of the hydrocarbon *XVI*, m.p. 84—86°C, $[\alpha]_D^{20}$ −54° (*c* 0·85). IR: 3055 cm^{-1}; NMR: 0·05 (dd, J = 9 Hz, 4·5 Hz, 6β-H), 0·20—0·50 (mt, 6α-H and 7-H), 0·60 (s, 18-H), 0·85 (d, J = 6 Hz, 26-H and 27-H), 0·88 (d, J = 6 Hz, 21-H), 1·06 (s, 19-H). For $C_{28}H_{48}$ (384·7) calculated: 87·42% C, 12·58% H; found: 87·40% C, 12·44% H.

3α-Methoxy-5,7α-cyclo-B-homo-5α-cholestane (*XIX*)

A solution of diazomethane (30 mg) in ether (1·5 ml) was added to the alcohol *VIII* (85 mg) in ether (5 ml) and treated with aluminium chloride (20 mg). The reaction mixture was allowed to stand at room temperature for 10 min treated with additional 20 mg of aluminium chloride and set aside for 20 min. The solution was diluted with ether, washed with 5% HCl, a sodium hydrogen carbonate solution, water, dried, and evaporated. The product (90 mg) was chromatographed on two plates of silica gel (20 × 20 cm) in light petroleum (b.p. 40—60°C)–ether (33 : 1) to yield after crystallisation from methanol 38 mg of the methyl ester *XIX*, m.p. 35—37°C, $[\alpha]_D^{20}$ −15° (*c* 1·64). IR: 3075, 1098 cm^{-1}. For $C_{29}H_{50}O$ (414·7) calculated: 84·00% C, 12·16% H; found: 84·12% C, 12·18% H.

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