ON STEROIDS. CL.*
BROMO AND CYANO DERIVATIVES OF 5α-CHOLESTAN-3β-OL

A. KUREK,** L. KOHOUT, J. FAJKOŠ and F. ŠORM
Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 6

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The syntheses of the 6- and 7-substituted bromo and cyano derivatives in the 5α-cholestane series are described and the chemical as well as spectral evidence for the structure of the compounds prepared are presented.

In connection with our studies of the stereochemistry of the steroid skeleton we were interested in the B-ring substituted bromo and cyano derivatives. In this paper we describe the syntheses of these compounds and prove their structures.

The epimeric 7-bromo derivatives *IV* and *VI* were prepared by two unambiguous routes either by Hunsdiecker reaction from the 7-carboxylic acids *I* and *II*, the syntheses of which have recently been described by us[1], or from the corresponding alcohols *VII* and *VIII* with phosphorus pentabromide. All these experiments led to a 1 : 1 mixture of the two at $C_{(7)}$ epimeric bromo derivatives *IV* and *VI* which were separated by chromatography. The configurations were assigned on the basis of the NMR measurements. The half-band width of the protons adjacent to the bromine atom in the two epimers differ considerably showing 8 Hz in the higher melting epimer and 26 Hz in the lower melting one. From this it follows the equatorial conformation and β-configuration for the $C_{(7)}$-proton in the higher melting epimer (structure *IV*) and axial conformation and α-configuration of this proton in the lower melting compound (structure *VI*). The downfield shift of the $C_{(19)}$-protons in the 7β-bromo compound *VI* when compared with its 7α-epimer *IV* is also in agreement with this assignment. When the 6β-carboxylic acid *IX* was submitted to the Hunsdiecker reaction only one bromo derivative was obtained. It was not identical with 3β-acetoxy-6β-bromo-5α-cholestane and in comparison with this known[2,3] compound our bromo derivative showed an upfield shift for the $C_{(19)}$-protons (−0·27 p.p.m.) as well as for the $C_{(18)}$-protons (−0·11 p.p.m.). Our bromo compound is therefore the 6α-epimer *X*.

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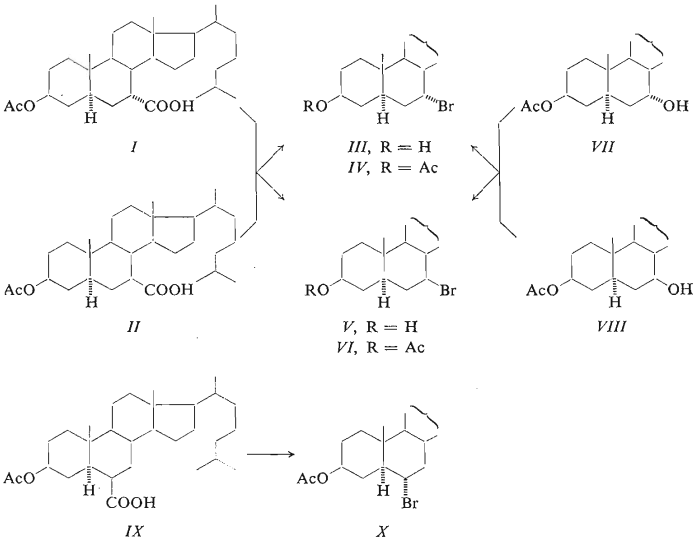
** Present address: Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, Poland.

Our next concern were the cyano derivatives. They were prepared either from the ketones *via* the cyanohydrins or from the corresponding carboxylic acids. The 7-oxo compound *XI* was transformed to the cyanohydrin *XII* which on reaction with phosphorus oxychloride afforded a mixture of three compounds. According to the analytical and spectral evidence two of them were the isomeric nitriles *XIII* and *XV*, the third compound was the chloronitrile *XIV*. Positions of the double bonds in nitriles *XIII* and *XV* follows from the NMR spectra where only the 6,7-unsaturated derivative shows one olefinic proton at 6·25 p.p.m. The structure of the chloronitrile *XIV* was proved by its conversion to a mixture of the nitriles *XIII* and *XV* on reaction with lithium carbonate and lithium chloride in dimethylformamide. The 6,7-unsaturated nitrile *XV* afforded on catalytic hydrogenation the 7β-cyano derivative *XVII*. This structure follows from its unambiguous synthesis from the 7β-carboxylic acid *II*. The acid was transformed to the corresponding amide *XIX* which on reaction with methanesulphonyl chloride in pyridine gave the nitrile *XVII*. The 7α-cyano derivative *XXII* was obtained similarly from the 7α-carboxylic acid *I*.

For the synthesis of a 6-substituted nitrile we used again the cyanohydrin method. The ketone *XXIII* gave quantitatively the cyanohydrin *XIV* which on dehydration with phosphorus oxychloride in pyridine yielded one unsaturated nitrile. Its structure



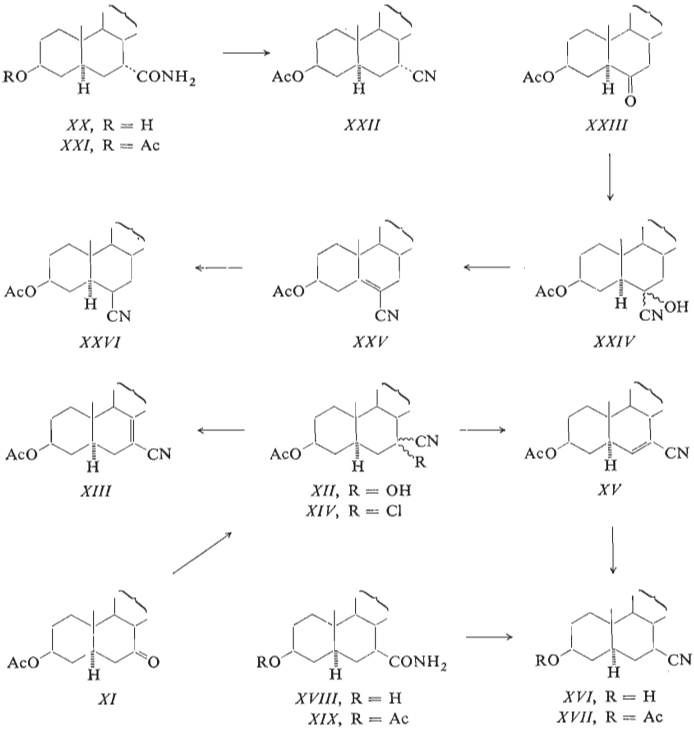


TABLE I

18-H and 19-H Chemical Shifts (p.p.m.) of 6- and 7-Cyano-3β-acetoxy-5α-cholestanes

Nitrile	Predicted[4]		Found	
	18-H	19-H	18-H	19-H
6α-	0·65	0·71	—	—
6β- (*XXVI*)	0·68	1·13	0·70	1·13
7α- (*XXII*)	0·66	0·86	0·66	0·83
7β- (*XVII*)	0·69	0·87	0·71	0·86

follows again from spectral evidence (presence of the double bond and absence of the olefinic proton). Catalytic hydrogenation led to the saturated derivative *XXVI*. The 6β-configuration of the cyano group follows from the NMR measurements. The data are summarised in Table I and are in excellent agreement with the calculated[4] values.

EPXERIMENTAL

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 unless otherwise stated with an error of ±1°. The infrared spectra were recorded on the Zeiss UR 10 Spectrometer in tetrachloromethane unless otherwise stated. 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 specific rotation, by thin-layer chromatography and by IR spectra. Ligroin, b.p. 40—60°C, was used in chromatography.

7α-Bromo-5α-cholestan-3β-ol (*III*)

Methanolic KOH (1M, 2 ml) was added to a solution of the acetate *IV* (40 mg) in methanol (25 ml) and refluxed for 2 h. Methanol was distilled off under reduced pressure, the residue was diluted with water, and the product taken into ether. The ethereal solution was washed with a saturated solution of ammonium sulphate, dried, and evaporated. The residue on crystallisation from methanol gave 25 mg of the alcohol *III*, m.p. 189—191°C, $[\alpha]_D^{20}$ −27·3° (*c* 1·19); IR (nujol): 3460, 1043 cm^{-1}. For $C_{27}H_{47}BrO$ (467·6) calculated: 69·36% C, 10·13% H, 17·09% Br; found: 69·18% C, 10·47% H, 17·29% Br.

3β-Acetoxy-7α-bromo-5α-cholestane (*IV*)

a) To a solution of the acid *I* (504 mg) in ethanol (30 ml) and water (8·5 ml) 2M-NaOH was added to alkaline reaction (phenolphthalein). One drop of conc. HNO_3 was then added and the solution was treated with a solution of silver nitrate (235 mg) in water (12 ml). After 1 h at room temperature the precipitate was collected by succion and dried at 90°C and 0·2 Torr for 8 h over P_2O_5. The silver salt was suspended in tetrachloromethane (20 ml), a solution of bromine (280 mg) in the same solvent (6 ml) was added and refluxed for 1 h. The precipitate was separated, washed with ether, the filtrate was diluted with ether (100 ml) and washed with 5% $NaHCO_3$, with a saturated ammonium sulphate solution, dried, and evaporated. The residue (473 mg) was chromatographed over silica gel (50 g) in ligroin–ether (49 : 1). Fractions containing the lipophilic bromo derivative were combined, evaporated, and the product crystallised from methanol to yield 110 mg of the bromo derivative *IV*, m.p. 117—118°C, $[\alpha]_D^{20}$ −37° (*c* 0·97); IR: 1738, 1244, 1029 cm^{-1}. For $C_{29}H_{49}BrO_2$ (509·6) calculated: 68·35% C, 9·68% H, 15·68% Br; found: 68·45% C, 9·19% H, 15·50% Br. *b*) From the acid *II* (340 mg) the silver salt (309 mg) was prepared similarly as ad *a*). The salt was suspended in tetrachloromethane (15 ml), treated with bromine (160 mg) in the same solvent (7 ml) and refluxed for 1 h. The mixture was worked up as ad *a*) to yield 274 mg of an oily residue. Chromatography over silica gel (40 g) in ligroin–ether (99 : 1), working up of the corresponding fractions, and crystallisation from methanol afforded 74 mg of the bromo derivative *IV*, m.p. 119—120°C, $[\alpha]_D^{20}$ −35° (*c* 0·99). *c*) A solution of the diol monoacetate *VII* (200 mg) in tetrachloromethane (3 ml) was treated with phosphorus pentabromide (270 mg) and allowed to stand at room temperature for 40 min. The mixture was decomposed with water, the product taken into ether, and the

ethereal solution was washed with 5% $NaHCO_3$, a saturated ammonium sulphate solution, water, dried, and evaporated. The residual oil (185 mg) which consisted according to the thin-layer chromatography from two components was chromatographed on a silica gel column (19 g) in ligroin–ether (199 : 1) to yield after working up and crystallisation from methanol 81 mg of the bromoderivative *IV*, m.p. 115–117°C, $[\alpha]_D^{20}$ −40° (*c* 1·95); NMR: 0·68 (s, 18-H), 0·85 (s, 19-H), 0·86 (d, J = 6 Hz, 26-H and 27-H), 0·89 (d, J = 6 Hz, 21-H), 2·00 (s, 3β-acetate), 4·48 (mt, $W_{1/2}$ = 8 Hz, 7β-H), 4·76 (broad mt, 3α-H). *d*) The diol monoacetate *VIII* (120 mg) in tetrachloromethane (2 ml) was treated with phosphorus pentabromide (190 mg) as given in the foregoing experiment. Similar working up and chromatography over silica gel in the same solvent mixture gave after crystallisation from methanol 50 mg of the bromo derivative *IV*, m.p. 117–118°C, $[\alpha]_D^{20}$ −37° (*c* 1·11).

7β-Bromo-5α-cholestan-3β-ol (*V*)

A solution of KOH in methanol (1M, 2 ml) was added to a solution of the acetate *VI* (35 mg) in methanol (20 ml) and allowed to stand at room temperature for 20 h. The solvent was removed under reduced pressure, the residue treated with water, and the product was isolated with ether. The ethereal solution was washed with 5% HCl, 5% $NaHCO_3$, with a saturated ammonium sulphate solution, dried, and evaporated. The residue on crystallisation from methanol gave 20 mg of the bromo derivative *V*, m.p. 137–138·5°C, $[\alpha]_D^{20}$ +88·8° (*c* 1·21); IR: 1737, 1245, 1048, 1028 cm^{-1}. For $C_{27}H_{47}BrO$ (467·6) calculated: 69·36% C, 10·13% H, 17·09% Br; found: 69·04% C, 10·11% H, 17·40% Br.

3β-Acetoxy-7β-bromo-5α-cholestane (*VI*)

a) Continued elution of the chromatography after isolation of the bromo derivative *IV* under *a*) yielded next to the starting acid *I* (140 mg) 85 mg of the bromo derivative *VI*, m.p. 97–98°C (methanol), $[\alpha]_D^{20}$ +51·3° (*c* 1·18); IR: 1726, 1258, 1030 cm^{-1}; NMR: 0·69 (s, 18-H), 0·86 (d, J = 6·0 Hz, 26-H and 27-H), 0·89 (s, 19-H), 0·91 (d, J = 6 Hz, 21-H), 2·00 (s, 3β-acetate), 3·82 (mt, $W_{1/2}$ = 26 Hz, 7α-H), 4·63 (broad mt, 3α-H). For $C_{29}H_{49}BrO$ (509·6) calculated: 68·35% C, 9·68% H, 15·68% Br; found: 68·16% C, 9·67% H, 15·70% Br. *b*) Elution of the chromatography after preparation of the bromo derivative *IV* under *b*) gave 110 mg of the starting acid *II* and 40 mg of the bromo derivative *VI*, m.p. 94–95°C (methanol), $[\alpha]_D^{20}$ +53° (*c* 0·96). *c*) Elution of the chromatography after isolation of the bromo derivative *IV* under *c*) and crystallisation from methanol gave 62 mg of the 7β-bromo derivative *VI*, m.p. 97–98°C, $[\alpha]_D^{20}$ +54° (*c* 1·13). *d*) Elution of the chromatography after preparation of the bromo derivative *IV* under *d*) with the same solvent mixture, working up of the corresponding fractions, and crystallisation from methanol yielded 36 mg of the bromo derivative *VI*, m.p. 94–96°C, $[\alpha]_D^{20}$ +57·6° (*c* 1·39).

3β-Acetoxy-6α-bromo-5α-cholestane (*X*)

A solution of the acid *IX* (220 mg) in ethanol (35 ml) and water (10 ml) was treated with 2M-KOH to alkaline reaction (phenolphthalein). A solution of silver nitrate (190 mg) in water (20 ml) was then added and after 1 h at room temperature the mixture was diluted with water (75 ml), the precipitate was collected by succion and dried at 90°C and 0·02 Torr for 8 h. The salt was suspended in tetrachloromethane (10 ml) and treated under stirring with a solution of bromine (200 mg) in tetrachloromethane (5 ml). After reflux for 1·5 h the precipitate was filtered off, washed with chloroform, and the combined filtrates were washed with 5% $NaHCO_3$, with a saturated ammonium sulphate solution, water, dried, and evaporated. The residue was chromatographed on six plates of silica gel (20 × 20 cm) in ligroin–ether (19 : 1). The corresponding zones were

separated, the product was eluted with ether, and the ethereal solution was evaporated. Crystallisation from methanol yielded 120 mg of the bromo derivative *X*, m.p. 86—88°C and 102—104°C, $[\alpha]_D^{20}$ +36·5° (*c* 0·78); IR: 3610, 1033 cm^{-1}; NMR: 0·64 (s, 18-H), 0·86 (s, 19-H), 0·86 (d, J = = 6·0 Hz, 26-H and 27-H), 0·89 (d, J = 6 Hz, 21-H), 2·02 (s, 3β-acetate), 4·01 (broad mt, 6β-H), 4·68 (broad mt, 3α-H). For $C_{29}H_{49}BrO_2$ (509·6) calculated: 68·35% C, 9·68% H, 15·68% Br; found: 68·70% C, 9·72% H, 15·88% Br.

3β-Acetoxy-7ξ-cyano-5α-cholestan-7ξ-ol (*XII*)

A solution of the ketone *XI* (5 g) in dioxane (50 ml) and ethanol (50 ml) was cooled to 0°C and treated under stirring successively with powdered potassium cyanide (7·3 g) and glacial acetic acid (8 ml). The stirring was continued for 1·5 h at 0°C and then for additional 2 h at room temperature. The reaction mixture was poured into an ice-water mixture and after standing for 1 h the precipitate was collected by succion. The product was dissolved in ether, the ethereal solution was washed with a $NaHCO_3$ solution, water, dried, and evaporated. The solid residue (5·1 g) was crystallised from ethyl acetate (30 ml) to yield 2·8 g of the cyanohydrin *XII*, m.p. 164 to 167°C, $[\alpha]_D^{20}$ +8·7° (*c* 1·32); IR (chloroform): 3595, 2230, 1723, 1245 cm^{-1}; NMR: 0·67 (s, 18-H), 0·84 (s, 19-H), 0·85 (d, J = 6 Hz, 26-H and 27-H), 0·90 (d, J = 6 Hz, 21-H), 2·00 (s, 3β-acetate), 4·68 (broad mt, 3α-H). For $C_{30}H_{49}NO_3$ (471·7) calculated: 76·38% C, 10·47% H, 2·97% N; found: 76·60% C, 10·20% H, 2·99% N.

3β-Acetoxy-7-cyano-5α-cholest-7-ene (*XIII*)

a) Protracted elution of the chromatography after isolation of the nitrile *XV* under *a*) gave fractions with the less lipophilic component. Working up and crystallisation from methanol yielded 417 mg of the nitrile *XIII*, m.p. 131·5—132·5°C, $[\alpha]_D^{20}$ −52·8° (*c* 1·09); IR: 2210, 1738, 1627, 1245, 1030 cm^{-1}; NMR: 0·64 (s, 18-H), 0·80 (s, 19-H), 0·85 (d, J = 6 Hz, 26-H and 27-H), 0·91 (d, J = 6 Hz, 21-H), 2·01 (s, 3β-acetate), 4·68 (broad mt, 3α-H). For $C_{30}H_{47}NO_2$ (453·7) calculated: 79·42% C, 10·44% H, 3·09% N; found: 79·37% C, 10·56% H, 3·05% N. *b*) Elution of the chromatography after preparation of the unsaturated nitrile *XV* under *b*) and crystallisation from methanol afforded 450 mg of the nitrile *XIII*, m.p. 131—133°C, $[\alpha]_D^{20}$ −51° (*c* 1·08).

3β-Acetoxy-7ξ-chloro-7ξ-cyano-5α-cholestane (*XIV*)

The alcohol *XII* (6 g) in pyridine (80 ml) was treated with phosphorus oxychloride (16 ml) and refluxed for 3 h. The reaction mixture was then poured on ice, and the product extracted into ether. The ethereal solution was washed with 5% hydrochloric acid, 5% $NaHCO_3$, water, dried, and evaporated. The residue (5·8 g) was chromatographed over silica gel (600 g) in ligroin–ether (19 : 1). Fractions containing the most lipophilic component were combined, evaporated, and the residue was crystallised from methanol to yield 3·83 g of the chloro derivative *XIV*, m.p. 142—144°C, $[\alpha]_D^{20}$ −5·8° (*c* 1·89); mass spectrum: $(M-1)^+$ 489; IR: 1738, 1245, 1031 cm^{-1}; NMR: 0·69 (s, 18-H), 0·84 (d, J = 6 Hz, 26-H and 27-H), 0·85 (s, 19-H), 0·89 (d, J = 6 Hz, 21-H), 2·00 (s, 3β-acetate), 4·72 (broad mt, 3α-H). For $C_{30}H_{48}ClNO_2$ (490·2) calculated: 73·51% C, 9·87% H, 7·23% Cl, 2·86% N; found: 73·14% C, 9·89% H, 7·34% Cl, 2·74% N.

3β-Acetoxy-7-cyano-5α-cholest-6-ene (*XV*)

a) Continued elution of the chromatography from the foregoing experiment with the same solvent mixture, working up of the corresponding fractions, and crystallisation from methanol gave 371 mg of the nitrile *XV*, m.p. 126·5—127·5°C, $[\alpha]_D^{20}$ −48° (*c* 1·68); IR: 2220, 1738, 1619, 1245,

1 030 cm^{-1}; NMR: 0·71 (s, 18-H), 0·77 (s, 19-H), 0·84 (d, J = 6 Hz, 26-H and 27-H), 0·89 (d, J = = 6 Hz, 21-H). 2·01 (s, 3β-acetate), 4·72 (broad mt, 3α-H), 6·25 (broad s, 6-H). For $C_{30}H_{47}NO_2$ (453·7); calculated: 79·42% C, 10·44% H, 3·09% N; found: 79·72% C, 10·65% H, 3·02% N. *b*) The nitrile *XIV* (1 g) in dimethylformamide (45 ml) was heated with lithium chloride (1 g) and lithium carbonate (1 g) for 8 h to 110—120°C. The reaction mixture was cooled off, diluted with water, and the product taken into ether. The ethereal solution was washed with 5% HCl, 5% $NaHCO_3$, saturated ammonium sulphate solution, dried, and evaporated. The residue (1 g) consisted according to thin-layer chromatography of two components. It was chromatographed on a silica gel column (100 g) in ligroin–ether (15 : 1). Fractions containing the lipophilic component were combined, evaporated, and the residue was crystallised from methanol to yield 350 mg of the nitrile *XV*, m.p. 126—128°C, $[\alpha]_D^{20}$ —48·1° (c 1·24).

7β-Cyano-5α-cholestan-3β-ol (*XVI*)

A solution of the acetate *XVII* (40 mg) in ethylene glycol (8 ml) was treated with a solution of NaOH (200 mg) in water (2 ml) and heated to 200°C for 5 h. The reaction mixture was diluted with water, the product extracted with chloroform, and worked up. The residue after evaporation of the solvent (35 mg) was crystallised from acetone to yield 22 mg of the alcohol *XVI*, m.p. 216—217°C, IR (nujol): 3 460, 2 230, 1 048 cm^{-1}. For $C_{28}H_{47}NO$ (413·7) calculated: 81·29% C, 11·45% H, 3·38% N; found: 81·42% C, 11·60% H, 3·30% N.

3β-Acetoxy-7β-cyano-5α-cholestane (*XVII*)

a) The olefin *XV* (130 mg) in ethyl acetate (4 ml) was hydrogenated over 5% $Pd/CaCO_3$ catalyst (130 mg) for 3 h. Catalyst was filtered off, washed with ether, the filtrate was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column (20 g) in ligroin–ether (17 : 1). Working up of the corresponding fractions and crystallisation from methanol afforded 82 mg of the acetate *XVII*, m.p. 130·5—132°C, $[\alpha]_D^{20}$ +38·1° (*c* 1·10); IR: 2 235, 1 735, 1 245, 1 029 cm^{-1}; NMR: 0·71 (s, 18-H), 0·86 (s, 19-H), 0·86 (d, J = 6 Hz, 26-H and 27-H), 0·90 (d, J = 6 Hz, 21-H), 2·00 (s, 3β-acetate), 4·66 (broad mt, 3α-H). For $C_{30}H_{49}NO_2$ (455·7) calculated: 79·07% C, 10·84% H, 3·07% N; found: 78·74% C, 10·73% H, 3·51% N. *b*) The amide *XIX* (60 mg) in pyridine (3 ml) was treated with methanesulphonyl chloride (0·25 ml) and allowed to stand at room temperature for 30 min. The reaction mixture was then decomposed with ice and the product taken into ether. The ethereal solution was washed with 5% HCl, 5% $NaHCO_3$, water, dried, and evaporated. The crystalline residue (60 mg) was chromatographed preparatively on one silica gel plate (20 × 20 cm) in ligroin–ether (4 : 1). The corresponding zone was collected, eluted with ether, and the solvent was evaporated. The residue on crystallisation from methanol yielded 45 mg of the nitrile *XVII*, m.p. 130—131°C, $[\alpha]_D^{20}$ +38·9° (*c* 1·04).

3β-Hydroxy-5α-cholestane-7β-carboxamide (*XVIII*)

A solution of the amide *XIX* (148 mg) in methanol (10 ml) was treated with 1M methanolic potassium carbonate (1 ml), heated to 60°C, and allowed to stand at room temperature for 1 h. The solution was diluted with water, the product taken into chloroform, and the extract was washed with water, dried, and evaporated. The product (125 mg) was crystallised from methanol to yield 88 mg of the alcohol *XVIII*, m.p. 292—295°C, $[\alpha]_D^{20}$ +43·3° (*c* 0·78 in chloroform–methanol 1 : 1); IR (KBr): 3 360, 3 185, 1 662, 1 609, 1 039 cm^{-1}; NMR: 0·66 (s, 18-H), 0·80 (s, 19-H), 0·83 (d, J = 6 Hz, 26-H and 27-H), 0·87 (d, J = 6 Hz, 21-H), 3·40 (broad mt, 3α-H), 4·17 (mt, 7α-H). For $C_{28}H_{49}NO_2$ (431·7) calculated: 77·90% C, 11·44% H; found: 77·93% C, 11·12% H.

3β-Acetoxy-5α-cholestane-7β-carboxamide (*XIX*)

The acid *II* (120 mg) was dissolved in thionyl chloride (6 ml) and allowed to stand at room temperature 3 days. Thionyl chloride was then removed by repeated distillation with benzene, the residue was dissolved in ether (5 ml) and the solution was saturated with ammonia. After 30 min. at room temperature the reaction mixture was diluted with ether (100 m) washed with a saturated solution of ammonium sulphate, and ether was evaporated. The product was chromatographed on a silica gel column (12 g) in benzene–ether (8 : 1). Working up and crystallisation from acetone gave 85 mg of the amide *XIX*, m.p. 108—112°C, $[\alpha]_D^{20}$ +20·3° (*c* 1·19 in chloroform–methanol 1 : 1); IR (chloroform): 3520, 3410, 1723, 1680, 1589, 1258, 1030 cm^{-1}. For $C_{30}H_{51}NO_3$ (473·7) calculated: 76·06% C, 10·85% H, 2·95% N; found: 74·63% C, 10·84% H, 2·69% N.

3β-Hydroxy-5α-cholestane-7α-carboxamide (*XX*)

A solution of the acetate *XXI* (190 mg) in methanol (11 ml) was treated with 1M methanolic KOH (2 ml), heated to 60°C and left at room temperature for 1 h. Water was then added, the product taken into chloroform, and the extract worked up. The residue after evaporation of the solvent was crystallised from methanol to yield 125 mg of the amide *XX*, m.p. 278—280°C, $[\alpha]_D^{20}$ +12° (*c* 0·78 in chloroform–methanol 1 : 1); IR (KBr): 3400, 3330, 3185, 1660, 1615, 1034 cm^{-1}; NMR: 0·60 (s, 18-H), 0·78 (d, $J = 6$ Hz, 26-H and 27-H), 0·87 (s, 19-H), 0·88 (d, $J = 6$ Hz, 21-H), 3·40 (broad mt, 3α-H), 4·14 (mt, 7β-H). For $C_{28}H_{49}NO_2$ (431·7) calculated: 77·90% C, 11·44% H, 3·25% N; found: 78·07% C, 11·06% H, 3·30% N.

3β-Acetoxy-5α-cholestane-7α-carboxamide (*XXI*)

The acid *I* (280 mg) in thionyl chloride (6 ml) was allowed to stand at room temperature for 24 h. The excess thionyl chloride was then removed by distillation with benzene, the residue was dissolved in ether (10 ml) and treated with a solution of liquid ammonia (1 ml) in ether (2 ml). After 3 h at room temperature the reaction mixture was diluted with ether, the ethereal solution was washed with 5% HCl, 5% $NaHCO_3$, a saturated ammonium sulphate solution, dried, and evaporated. The residue was chromatographed over silica gel in benzene–ether (7 : 1) to yield after working up and crystallisation from methanol 190 mg of the amide *XX*, m.p. 185 to 190°C, $[\alpha]_D^{20}$ −6·6° (*c* 1·70 in chloroform–methanol 1 : 1); IR (chloroform): 3520, 3405, 1724, 1678, 1589, 1260, 1029 cm^{-1}. For $C_{30}H_{51}NO_3$ (473·7) calculated: 76·06% C, 10·85% H, 2·95% N; found: 76·07% C, 10·84% H, 2·69% N.

3β-Acetoxy-7α-cyano-5α-cholestane (*XXII*)

The amide *XXI* (200 mg) in pyridine (6 ml) was treated with methanesulphonyl chloride (0·6 ml) and allowed to stand at room temperature for 30 min. The reaction mixture was decomposed with ice, diluted with water, and the product was isolated with ether. Working up and evaporation left 200 mg of a crude product which was chromatographed on a silica gel column (10 g) in benzene. Combination and evaporation of the corresponding fractions gave 170 mg of the product which after crystallisation from methanol yielded 140 mg of the nitrile *XXII*, m.p. 169 to 170°C, $[\alpha]_D^{20}$ −20·6° (*c* 1·39); IR: 2235, 1735, 1245, 1030 cm^{-1}; NMR: 0·66 (s, 18-H), 0·83 (s, 19-H), 0·87 (d, $J = 6$ Hz, 26-H and 27-H), 0·89 (d, $J = 6$ Hz, 21-H), 2·00 (s, 3β-acetate), 2·82 (mt, 7β-H), 4·74 (broad mt, 3α-H). For $C_{30}H_{49}NO_2$ (455·7) calculated: 79·07% C, 10·84% H, 3·07% N; found: 79·02% C, 10·80% H, 3·41% N.

3β-Acetoxy-6ξ-cyano-5α-cholestan-6ξ-ol (*XXIV*)

Potassium cyanide (4·4 g) was added to a solution of the ketone *XXIII* (3 g) in ethanol (30 ml) and dioxane (30 ml) and cooled to 0°C. Acetic acid (4·8 ml) was then added drop by drop under

stirring within 30 min. and the reaction mixture was allowed to stand for 1 h at 0°C and for additional 2 h at room temperature. Water was then added, the product taken into ether, and the ethereal solution was washed with water, 5% $NaHCO_3$, dried, and evaporated. The residue was chromatographed on a silica gel column in benzene–ether (49 : 1). Next to the starting ketone (1·8 g) 1·2 g of the desired product were obtained which on crystallisation from ethyl acetate yielded 800 mg of the nitrile *XXIV*, m.p. 170—175°C, $[\alpha]_D^{20}$ +8·8° (*c* 1·82); IR: 3590, 2230, 1736, 1713, 1245 cm^{-1}; NMR: 0·67 (s, 18-H), 0·84 (d, J = 6·5 Hz, 26-H and 27-H), 0·89 (d, J = = 6 Hz, 21-H), 1·07 (s, 19-H), 2·02 (s, 3β-acetate), 2·55 (s, 6-OH), 4·70 (mt, 3α-H). For $C_{30}H_{49}NO_3$ (471·3) calculated: 76·38% C, 10·47% H, 2·97% N; found: 76·40% C, 10·42% H, 2·61% N.

3β-Acetoxy-6-cyano-5-cholestene (*XXV*)

The cyanohydrin *XXIV* (1 g) in pyridine (9 ml) was refluxed with phosphorus oxychloride (5 ml) for 1 h. The mixture was poured on ice, diluted with water, and the product was extracted with ether. The ethereal solution was washed with 5% HCl ,5% $NaHCO_3$, water, dried, and evaporated. The residue (890 mg) was chromatographed on a silica gel column (45 g) in benzene to yield after working up of the corresponding fractions and crystallisation from methanol 550 mg of the unsaturated nitrile *XXV*, m.p. 142·5—143·5°C, $[\alpha]_D^{20}$ −10·5° (*c* 2·03); IR: 2210, 1740, 1637, 1240, 1039 cm^{-1}; NMR: 0·68 (s, 18-H), 0·87 (d, J = 6 Hz, 26-H and 27-H), 0·91 (d, J = 6 Hz, 21-H), 1·08 (s, 19-H), 2·05 (s, 3β-acetate), 3·08 (three d, J = 2 Hz [homoallylic], J' = 5·5 Hz [vic.], J'' = 13·5 Hz [gem.], 4-H), 4·68 (broad mt, 3α-H). For $C_{30}H_{47}NO_2$ (453·7) calculated: 79·42% C, 10·44% H, 3·09% N; found: 79·27% C, 10·58% H, 3·65% N.

3β-Acetoxy-6β-cyano-5α-cholestane (*XXVI*)

The olefin *XXV* (120 mg) in ethanol (20 ml) was hydrogenated over 5% $Pd/CaCO_3$ (120 mg) for 12 h at 70°C. Cazalyst was filtered off, washed with ether and the solvent removed. The residue was chromatographed preparatively on 3 silica gel plates (20 × 20 cm) in ligroin–ether (4 : 1). The corresponding zones were collected, eluted with ether, and the ethereal solution was evaporated. Next to some starting olefin (20 mg) 105 mg of the hydrogenated product were obtained as an oil which after crystallisation from methanol gave 82 mg of the nitrile *XXVI*, m.p. 153—154°C, $[\alpha]_D^{20}$ −42·6° (*c* 0·41); IR: 2235, 1734, 1243, 1031 cm^{-1}; NMR: 0·70 (s, 18-H), 0·86 (d, J = = 6·0 Hz, 26-H and 27-H), 0·90 (d, J = 6 Hz, 21-H), 1·13 (s, 19-H), 2·02 (s, 3β-acetate), 2·69 (mt, $W_{1/2}$ = 6·0 Hz, 6α-H), 4·70 (broad mt, 3α-H). For $C_{30}H_{49}NO_2$ (455·7) calculated: 79·07% C, 10·84% H, 3·07% N; found: 79·13% C, 10·90% H, 3·13% N.

The analyses were carried out in the Analytical Laboratories of this Institute by Mr V. Štěrba, Mrs V. Rusová and Mrs E. Sýkorová under the direction of Dr J. Horáček. The IR spectra were recorded by Mrs K. Matoušková and by Mr P. Formánek under the direction Dr J. Smolíková, the mass spectrum was recorded by Dr L. Dolejš, NMR spectra were recorded and interpreted by Dr P. Sedmera.

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