PREPARATION OF SOME 3α,5-CYCLOANDROSTANE DERIVATIVES WITH EXPANDED RING B

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Reaction of 17β-hydroxy-3α,5-cyclo-5α-androstan-6-one-17-benzoate (*II*) with diazomethane is reported. From the complex reaction mixture compounds with eight-, nine- and ten-membered ring B were isolated. Their structures were established by means of spectroscopic methods. Some derivatives of these compounds are described.

Some time ago[1] we reported on the preparation of 3α,5-cyclocholestane derivatives with expanded ring B. In connection with our interest in structure–antiandrogenic activity relationships we decided to prepare analogous compounds of 3α,5-cyclo-5α--androstane series.

As starting material we used 17β-hydroxy-3α,5-cyclo-5α-androstan-6-one 17-benzoate (*II*) which was subjected to treatment with 7·5 equivalents of diazomethane under aluminum chloride catalysis. Under these conditions, all of the starting ketone reacted and chromatographic separation led to isolation of major reaction products *III*, *IV*, *V* and *VI* the structures of which were established by means of spectroscopic methods. The molecular formulas of these compounds were determined by mass spectrometry as $C_{29}H_{38}O_3$ for *III* and *V*, $C_{30}H_{40}O_3$ for *IV* and $C_{28}H_{36}O_3$ for *VI*. The IR spectra (Table I) of these compounds demonstrated the presence of a keto group in all three substances. In no case is the keto group conjugated with the cyclopropane ring. The presence of the cyclopropane ring in compounds *III*, *IV* and *VI* was also confirmed by ^{1}H-NMR spectrum (Table I). The nonconjugated character rules out the position 6 in any of these compounds.

The ^{1}H-NMR spectra of the substance *IV*, *V* and *VI* show the presence of an AB-system of the isolated CH_2-group (between the cyclopropane ring and the keto group) (Table I). The keto group could thus be located in position 7. On the basis of these data, the compound *IV* is formulated as 17β-hydroxy-3α,5-cyclo-B-tetrahomo--5α-androstan-7-one 17-benzoate, the compound *V* as 17β-hydroxy-3α,5-cyclo-B--trishomo-5α-androstan-7-one 17-benzoate and the compound *VI* as 17β-hydroxy--3α,5-cyclo-B-bishomo-5α-androstan-7-one 17 benzoate.

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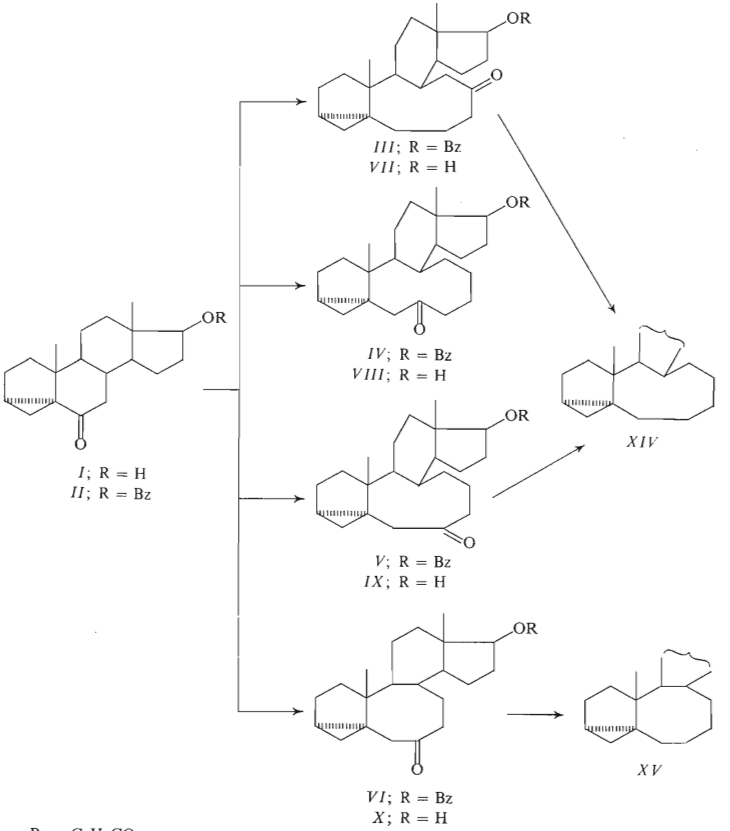
The spectroscopic data alone do not permit to decide whether the keto group in the compound *III* is located in position 7a or 7b. In order to establish the structure of *III*, the latter substance was brominated with Jacques' reagent to give a mixture of two bromo ketones *XI* and *XII*; both of them can be reconverted to the starting ketone *III* on reductive debromination. Dehydrobromination both of the bromo ketones



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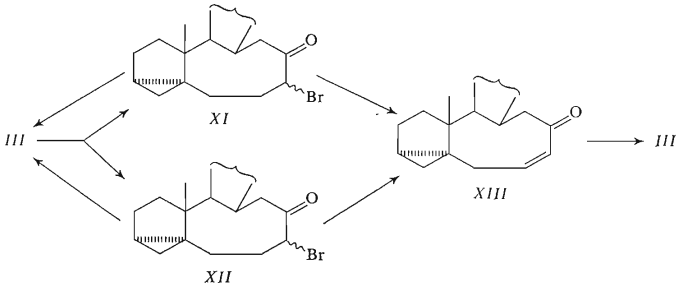

XI and *XII* with lithium carbonate and lithium bromide in dimethylformamide gives the same conjugated ketone *XIII* (ν(C=O) = 1 664 cm^{-1}) the structure of which was established by means of ^{1}H-NMR spectroscopy. Present in the ^{1}H-NMR spectrum of the compound *XIII* are signals of two olefinic protons of a conjugated *cis*-double

TABLE I

Characteristic Spectral Data of the Compounds *III*—*VI*

^{1}H-NMR spectra were measured in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts are given in δ-scale (ppm); the coupling constants in Hz. The following abbreviations are used for characterization of the signals: b broad, d doublet, dd doublet of doublets, m multiplet. IR spectra were measured in tetrachloromethane. Frequencies are given in cm^{-1}.

Compound	Mol. weight (mass spectra) calculated / found	^{1}H-NMR			IR
		19-H[a] / 18-H[a]	CH_2 (cyclopropane)	▽—CH_2[b]—CO	ν(cyclopropane)
III	434·6 / 434	1·07 / 0·95	0·23 (dd, J = 5·0; 8·0) / 0·65 (bt, J = 5·0)	—	3 065
IV	448·6 / 448	1·07 / 0·94	0·24 (m) / 0·58 (m)	1·78 (^2J = 18·5) / 3·74	3 070
V	434·6 / 434	0·95 / 0·88	—[c]	3·91 (bd, ^2J = 15·0)	3 075
VI	420·6 / 420	1·12 / 0·92	0·06 (dd, J = 8; 4·5) / 0·63 (m)	1·46 (^2J = 12·0) / 3·42	3 070

[a] Singlets; [b] AB system; [c] signals were not separated.

bond (δ = 6·01, d, 1 H, $J_{7a,7}$ = 12 Hz and δ = 6·45, ddd, 1 H, $J_{7,7a}$ = 12 Hz, $J_{7,6'}$ = 8·0 Hz, $J_{7,6}$ = 10·5 Hz) and signals of two allylic protons (δ = 3·45, dd, 1 H, $J_{6,6'}$ = 15 Hz, $J_{6,7}$ = 10·5 Hz and δ = 1·43, dd, 1 H, $J_{6',6}$ = 15 Hz, $J_{6',7}$ = = 8·0 Hz) in a fragment of the type —CO—CH=CH—CH_2—. The splitting pattern of the methylene protons is characteristic of a methylene group attached to a quaternary carbon. These arguments permit to locate the ketonic group in position 7b as expressed in formula *XIII*. In accord with this structure are also the signals of the methylene group at $C_{(7c)}$ (δ = 3·57, dd, 1 H, $J_{7c,7c'}$ = 15·0 Hz, $J_{7c,8}$ = 2·5 Hz, $J_{7c,7a} \neq 0$ and δ = 2·64, dd, 1 H, $J_{7c',7c}$ = 15·0 Hz, $J_{7c',8}$ = 5·5 Hz). Hydrogenation on a palladium–calcium carbonate catalyst converts the compound *XIII* into the ketone *III* which, therefore, has the structure 17β-hydroxy-3α,5-cyclo-B-trishomo--5α-androstan-7b-one 17-benzoate. Formation of the same conjugated ketone *XIII* from both *XI* and *XII* makes position 7a most probable for the bromine atom in these two bromo ketones. This assumption is proved by ^{1}H-NMR spectroscopy. In the ^{1}H-NMR spectrum of the compound *XII* the CH-Br proton appears as a doublet of doublets at δ = 4·71 (splitting 3·5 and 4·0 Hz) and in the spectrum of the bromo ketone *XI* it is present as a multiplet at δ = 4·06. The present results, however, do not permit any conclusion as to the configuration of the bromine atom in the compounds *XI* and *XII*.

Alkaline hydrolysis of the 17β-benzoyloxy group of the compounds *III*, *IV*, *V* and *VI* with potassium hydroxide in methanol afforded the corresponding 17β-hydroxy derivatives *VII*, *VIII*, *IX* and *X*. Removal of the keto group by Huang–Minlon reduction of the compounds *VII* and *IX* gave the deoxy derivative *XIV*. Similarly, the substance *X* afforded the deoxy derivative *XV*. Pharmacological properties of the compounds *VII*–*X*, *XIV* and *XV* are being investigated.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured in chloroform. The infrared spectra were measured on a Zeiss UR-20 spectrophotometer. The ^{1}H-NMR spectra were measured in deuteriochloroform on a Varian HA-100 apparatus using tetramethylsilane as internal standard. The chemical shifts are given in ppm. The mass spectra were measured on the double focussing mass spectrometer AEI 902 (Associated Electric Industries, Manchester) using the direct inlet system. All the precise masses were found to be within 3 ppm of the calculated values. The identity of samples prepared by different routes was checked by mixture melting points and by infrared spectra. The statement "worked up as usual" stands for: The solution was washed with 5% hydrochloric acid, 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*.

17β-Hydroxy-3α,5-cyclo-5α-androstan-6-one 17-Benzoate (*II*)

17β-Hydroxy-3α,5-cyclo-5α-androstan-6-one *I* (10 g) was benzoylated with benzoyl chloride (30 ml) in pyridine (100 ml) overnight. Ice was added to the mixture and the mixture was allowed

to stand at room temperature for 30 min. The product was extracted with ether and the ethereal extract was worked up as usual. The crude product (10 g) was crystallized from methanol to give 8 g of the benzoate *II*, m.p. 173–174°C, $[\alpha]_D^{20}$ +76° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1721, 1274, 1692 cm^{-1}. For $C_{26}H_{32}O_3$ (392·5) calculated: 79·55% C, 8·22% H; found: 79·38% C, 8·03% H.

Reaction of 17β-Hydroxy-3α,5-cyclo-5α-androstan-6-one 17-Benzoate (*II*) with Diazomethane

An ethereal solution (240 ml) containing 3·6 g of diazomethane was added to a solution of the ketone *II* (6·0 g) in benzene–ether (300 ml, 1 : 1). Aluminum chloride was added in catalytic amounts five times at five minutes intervals. After a further five minutes the mixture was poured into water and the product isolated with ether as usual. The oily residue (6·5 g) was chromatographed on a column of silica gel (300 g, $l = 2$ m, $\Phi = 2$ cm) in light petroleum–ether (99 : 1).

17β-Hydroxy-3α,5-cyclo-B-trishomo-5α-androstan-7b-one 17-Benzcate (*III*)

a) Working up of the corresponding fractions after separation of nonpolar products afforded 1·3 g of the ketone *III* which was crystallized from methanol, m.p. 137–139°C, $[\alpha]_D^{20}$ +64° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1722, 3065 cm^{-1}. ^{1}H-NMR spectrum: 0·23 (dd, 1 H, cyclopropane-H, $J = 5{\cdot}0$; 8·0 Hz); 0·65 (broad t, 1 H, cyclopropane-H, $J = 5{\cdot}0$ Hz); 0·95 (s, 3 H, 18-CH_3); 1·07 (s, 3 H, 19-CH_3); 4·86 (m, 1 H, $C_{(17)}$–H); 7·30–7·55 (m, 3 H, aromatic H); 7·90–8·00 (m, 2 H, aromatic H). Molecular weight (mass spectrometry): 434; for $C_{29}H_{38}O_3$ calculated: 434·6.

b) The bromo ketone *XI* (100 mg) in ethyl acetate (7 ml) and ethanol (3 ml) was shaken in a hydrogen atmosphere with a 5% palladium–calcium carbonate catalyst (300 mg) for 6 h. It was then diluted with ether, the catalyst filtered off, washed with ether and the filtrate concentrated *in vacuo*. The residue (86 mg) was chromatographed on two plates of silica gel (20 × 20 cm) in light petroleum–ether (99 : 1) with threefold development. The corresponding zones were collected, eluted with ether and the solvent evaporated *in vacuo*. The residue (65 mg) was crystallized from methanol to yield 47 mg of the ketone *III*; m.p. 137–139°C, $[\alpha]_D^{20}$ +63° (*c* 0·5).

c) The bromo ketone *XII* (100 mg) in ethyl acetate (7 ml) and ethanol (3 ml) was shaken in a hydrogen atmosphere with a 5% palladium–calcium carbonate catalyst (300 mg) for 6 h. The same working up as in case *b*) afforded 89 mg of the crude product which was preparatively chromatographed on two plates of silica gel (20 × 20 cm) in light petroleum–ether (99 : 1) with threefold development. The usual work-up afforded 70 mg of the ketone *III*, which was crystallized from methanol, m.p. 137–139°C, $[\alpha]_D^{20}$ +64 (*c* 0·5).

d) The ketone *XIII* (50 mg) in ethyl acetate (4 ml) and ethanol (2 ml) was shaken in a hydrogen atmosphere with a palladium–calcium carbonate catalyst (150 mg) for 10 h. The same working up as in case *b*) afforded 44 mg of the crude product which was preparatively chromatographed on one plate of silica gel (20 × 20 cm) in light petroleum–ether (99 : 1) with threefold development. The usual work-up afforded 35 mg of the ketone *III*, which was crystallized from methanol, m.p. 137–139°C, $[\alpha]_D^{20}$ +64° (*c* 0·5).

17β-Hydroxy-3α,5-cyclo-B-tetrahomo-5α-androstan-7-one 17-Benzoate (*IV*)

The following fractions afforded after working up 1·3 g of the crude ketone *IV* which was repeatedly crystallized from methanol to yield 800 mg of the ketone *IV*, m.p. 181–182·5°C, $[\alpha]_D^{20}$

−18° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1720, 3070 cm^{-1}. ^{1}H-NMR spectrum: 0·24 (m, 1 H, cyclopropane-H); 0·58 (m, 1 H, cyclopropane-H); 0·94 (s, 3 H, 18-CH_3); 1·07 (s, 3 H, 19-CH_3); 1·78 and 3·74 (AB-system, J = 18·5 Hz, —CH_2—CO); 4·82 (m, 1 H, $C_{(17)}$—H); 7·35—7·60 (m, 3 H, aromatic H); 7·95—8·10 (m, 2 H, aromatic H). Molecular weight (mass spectrometry); 448; for $C_{30}H_{40}O_3$ calculated: 448·6.

17β-Hydroxy-3α,5-cyclo-B-trishomo-5α-androstan-7-one 17-Benzoate (*V*)

a) Further corresponding fractions afforded after working up 760 mg of the crude ketone *V* which was repeatedly crystallized from methanol to yield 445 mg of the ketone *V*, m.p. 121 to 123°C, $[\alpha]_D^{20}$ +50° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1720, 1702, 3075 cm^{-1}. ^{1}H-NMR spectrum: 0·88 (s, 3 H, 18-CH_3); 0·95 (s, 3 H, 19-CH_3); 3·91 (broad d, 1 H, part of AB system, CH—CO); 4·86 (m, 1 H, $C_{(17)}$—H); Molecular weight (mass spectrometry): 434; for $C_{29}H_{38}O_3$ calculated: 434·6.

b) The alcohol *IX* (30 mg) in pyridine (2 ml) was benzoylated with two drops of benzoyl chloride overnight. The usual workup gave 30 mg of the crude product which was preparatively chromatographed on one plate of silica gel (20 × 20 cm) in light petroleum–ether (99 : 1) with twofold development. The corresponding zone was collected, eluted with ether and the solvent evaporated *in vacuo*. The residue (26·5) was crystallized from methanol to yield 16 mg of the benzoate *V*, m.p. 121—123°C, $[\alpha]_D^{20}$ +50° (*c* 0·5).

17β-Hydroxy-3α,5-cyclo-B-bishomo-5α-androstan-7-one 17-Benzoate (*VI*)

The working up of the corresponding fraction afforded 785 mg of the crude ketone *VI* which was repeatedly crystallized from methanol to yield 650 mg of the ketone *VI*, m.p. 178—180°C, $[\alpha]_D^{20}$ +104° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1721, 3070 cm^{-1}. ^{1}H-NMR spectrum: 0·06 (dd, 1 H, cyclopropane-H, J = 4·5; 8 Hz); 0·63 (m, 1 H, cyclopropane-H); 0·92 (s, 3 H, 18-CH_3); 1·12 (s, 3 H, 19-CH_3); 1·46 and 3·42 (AB system, CH_2—CO, J = 12·0 Hz); 4·82 (m, 1 H, $C_{(17)}$—H); Molecular weight (mass spectrometry): 420; for $C_{28}H_{36}O_3$ calculated: 420·6.

17β-Hydroxy-3α,5-cyclo-B-trishomo-5α-androstan-7b-one (*VII*)

Solid potassium hydroxide (220 mg) was added to a solution of the benzoate *III* (220 mg) in methanol (10 ml) and the mixture was refluxed for two hours. After being concentrated to one third of the original volume the mixture was poured into water and the product extracted with ether. The ethereal extract was washed with water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The residue (200 mg) was preparatively chromatographed on four plates of silica gel (20 × 20 cm) in light petroleum–ether (7 : 3) with twofold development. The working up of the corresponding zones gave 160 mg of the oily hydroxy derivative *VII* which resisted all attempts at crystallization, $[\alpha]_D^{20}$ +35° (*c* 0·5). Infrared spectrum (chloroform): 1705, 3065, 3470, 3620 cm^{-1}. Molecular weight (mass spectrometry): 330; for $C_{22}H_{34}O_2$ calculated: 330·5.

17β-Hydroxy-3α,5-cyclo-B-tetrahomo-5α-androstan-7-one (*VIII*)

The benzoate *IV* (200 mg) in methanol (10 ml) was treated with solid potassium hydroxide (200 mg) in the same manner as in the preceding case. The same workup afforded 200 mg of the oily produet which was preparatively chromatographed on four plates of silica gel (20 × 20 cm) in light petroleum–ether (7 : 3) with twofold development. The working up of the corresponding

zones gave 173 mg of the alcohol *VIII* which was crystallized from dioxane–heptane, m.p. 185 to 186°C, $[\alpha]_D^{20}$ −77° (*c* 0·5). Infrared spectrum (chloroform): 1697, 3070, 3480, 3620 cm^{-1}. Molecular weight (mass spectrometry) 344; for $C_{23}H_{36}O_2$ calculated: 344·5.

17β-Hydroxy-3α,5-cyclo-B-trishomo-5α-androstan-7-one (*IX*)

The benzoyloxy derivative *V* (150 mg) in methanol (8 ml) was treated with solid potassium hydroxide (150 mg) in the same manner as in the preceding cases. The oily product (150 mg) was chromatographed on three plates of silica gel (20 × 20 cm) in light petroleum–ether (7 : 3). The corresponding zones were collected, eluted with ether and the solvent evaporated *in vacuo*. The residue (134 mg) was crystallized from dioxane–heptane to yield 103 mg of the alcohol *IX*, m.p. 154—156°C, $[\alpha]_D^{20} = -34°$ (*c* 0·5). Infrared spectrum (chloroform). 1696, 3615, 3075 cm^{-1}. Molecular weight (mass spectrometry): 330; for $C_{22}H_{34}O_2$ calculated: 330·5.

17β-Hydroxy-3α,5-cyclo-B-bishomo-5α-androstan-7-one (*X*)

The benzoyloxy derivative *VI* (200 mg) in methanol (10 ml) was treated with solid potassium hydroxide (200 mg) in the same manner as in the preceding case. The oily product (190 mg) was chromatographed on three plates of silica gel (20 × 20 cm) in light petroleum–ether (7 : 3) with threefold development. The corresponding zones were collected, eluted with ether and the solvent evaporated *in vacuo*. The residue (169 mg) was crystallized from dioxane–heptane to yield 135 mg of the alcohol *X*, m.p. 150—152°C, $[\alpha]_D^{20}$ +64° (*c* 0·5). Infrared spectrum (chloroform): 1696, 1020, 3615, 3075 cm^{-1}. Molecular weight (mass spectrometry): 316; for $C_{21}H_{32}O_2$ calculated: 316·5.

Bromination of the 17β-hydroxy-3α,5-cyclo-B-trishomo-5α-androstan-7b-one 17-Benzoate (*III*)

The ketone *III* (1·08 g) in ethylene glycol dimethylether (15 ml) was treated with Jacques' reagent (1·00 g) for one hour. The mixture was then poured into water, taken up in ether and the ethereal extract was washed with 5% potassium hydrogen carbonate, water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The oily product (1·4 g) was chromatographed on a column of silica gel (800 g) in light petroleum–ether (9 : 1). Working up of the corresponding less polar fractions afforded 550 mg of the 17β-hydroxy-7aξ-bromo-3α,5-cyclo-B-trishomo-5α-androstan--7b-one 17-benzoate (*XI*) which was crystallized from ethanol, m.p. 141—143°C, $[\alpha]_D^{22}$ +122° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1722, 1275 cm^{-1}. ^{1}H-NMR spectrum: 0·26 (dd, 1 H, cyclopropane-H, J = 5·0; 8·0 Hz); 0·63 (m, 1 H, cyclopropane-H); 0·95 (s, 3 H, 18-CH_3); 1·19 (s, 3 H, 19-CH_3); 4·06 (m, 1 H, $C_{(7a)}$—H); 4·92 (m, 1 H, $C_{(17)}$—H). For $C_{29}H_{37}BrO_3$ (513·5) calculated: 67·82% C, 7·26% H, 15·56% Br; found: 67·98% C, 7·25% H, 16·12% Br.

Working up of the corresponding more polar fractions afforded 260 mg of the 17β-hydroxy--7aξ-bromo-3α,5-cyclo-B-trishomo-5α-androstan-7b-one 17-benzoate (*XII*) which was crystallized from ethanol, m.p. 166—168°C, $[\alpha]_D^{20}$ −12° (*c* 0·5). Infrared spectrum (tetrachloromethane): 1721, 1275 cm^{-1}. ^{1}H-NMR spectrum: 0·24 (dd, 1 H, cyclopropane-H, J = 4·5; 8·0 Hz); 0·64 (t, 1 H, cyclopropane-H, J = 4·5 Hz); 0·94 (s, 3 H, 18-CH_3); 1·10 (s, 3 H, 19-CH_3); 4·71 (dd, 1 H, $C_{(7a)}$—H, J = 3·5; 4·0 Hz); 4·91 (dd, 1 H, $C_{(17)}$—H, J = 7·0; 9·0 Hz). For $C_{29}H_{37}BrO_3$ (513·5) calculated: 67·82% C, 7·26% H, 15·56% Br; found: 67·38% C, 7·44% H, 16·13% Br.

17β-Hydroxy-3α,5-cyclo-B-trishomo-5α-androst-7-en-7b-one 17-Benzoate (*XIII*)

a) Lithium carbonate (210 mg) and lithium bromide (210 mg) were added to a solution of the bromo ketone *XI* (70 mg) in dimethylformamide (2·5 ml) and the mixture was refluxed for two hours in a nitrogen atmosphere. After cooling the mixture was diluted with benzene–light petroleum (1 : 1), the inorganic salts were filtered off and the filtrate was washed with water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The residue (70 mg) was chromatographed on two plates of silica gel (20 × 20 (cm) in light petroleum–ether (9·5 : 0·5). The corresponding zones were collected, eluted with ether and the solvent evaporated *in vacuo*. The residue (38 mg) was crystallized from ether to yield the conjugated ketone *XIII*, m.p. 188–190·5°C, $[\alpha]_D^{20}$ +245° (*c* 0·5). Infrared spectrum (chloroform): 1712, 1282, 1664 cm^{-1}. ^{1}H-NMR spectrum: 0·10 (m, 1 H, cyclopropane-H); 0·72 (m, 1 H, cyclopropane-H); 0·92 (s, 3 H, 18-CH_3); 1·13 (s, 3 H, 19-CH_3); 4·78 (dd, 1 H, $C_{(17)}$—H, J = 7; 8 Hz); 6·01 (d, 1H, $C_{(7a)}$—H, $J_{7a,7}$ = 12·0 Hz; $J_{7a,7c} \neq 0$), 6·45 (m, 1 H, $C_{(7)}$—H, $J_{7,7a}$ = 12·0 Hz, $J_{7,6'}$ = 8·0, $J_{7,6}$ = 10·5 Hz); 3·45 (dd, 1 H, $C_{(6)}$—H, $J_{6,7}$ = 10·5 Hz, $J_{6,6'}$ = 15·0 Hz); 1·43 (dd, 1 H, $C_{(6')}$—H, $J_{6',7}$ = 8·0 Hz, $J_{6',6}$ = 15·0 Hz); 3·57 (dd, 1 H, $C_{(7c)}$—H, $J_{7c,8}$ = 2·5 Hz, $J_{7c,7c'}$ = 15·0 Hz); 2·64 (dd, 1 H, $C_{(7c')}$—H, $J_{7c',8}$ = 5·5 Hz, $J_{7c',7c}$ = 15·0 Hz). Molecular weight (mass spectrometry): 432; for $C_{29}H_{36}O_3$ calculated: 432·5.

b) The bromo ketone *XII* (65 mg) in dimethylformamide (2·5 ml) was treated with lithium carbonate (200 mg) and lithium bromide (200 mg) in the same manner as in case *a*). The oily product (50 mg) was chromatographed on one plate of silica gel (20 × 20 cm) in light petroleum–ether (9·5 : 0·5). The corresponding zone was eluted with ether and the solvent evaporated *in vacuo*. The residue (25 mg) was crystallized from ether to yield 14 mg of the conjugated ketone *XIII*, m.p. 188–190°C, $[\alpha]_D^{20}$ +245° (*c* 0·5).

17β-Hydroxy-3α,5-cyclo-B-trishomo-5α-androstane (*XIV*)

a) The solution of the ketone *VII* (160 mg) in triethylene glycol (10 ml) was treated with hydrazine hydrate (1 ml, 96%) and solid sodium hydroxide (250 mg) and heated in an open flask. The temperature was allowed to rise to 140°C and the mixture was refluxed at this temperature for 30 min whereupon the condensor was removed until the temperature reached 200°C and refluxing was then continued for 3 h. The mixture was cooled, poured into water and the product extracted with ether. The ethereal extract was washed with water, dried over sodium sulfate and the solvent evaporated *in vacuo*. The oil (150 mg) was chromatographed on two plates of silica gel (20 × 20 cm) in light petroleum–ether (6 : 4). The corresponding zones were collected, eluted with ether and the solvent evaporated *in vacuo*. The residue (125 mg) was crystallized from methanol to give 98 mg of the hydroxy derivative *XIV*, m.p. 109–110·5°C, $[\alpha]_D^{20}$ +27° (*c* 0·5). Infrared spectrum (tetrachloromethane): 3625, 1032, 3065 cm^{-1}. ^{1}H-NMR spectrum: 0·31 (m, 1 H, cyclopropane-H), 0·72 (m, 1 H, cyclopropane-H); 0·83 (s, 3 H, 18-CH_3); 1·04 (s, 3 H, 19-CH_3); 3·62 (m, 1 H, $C_{(17)}$—H). For $C_{22}H_{36}O$ (316·5) calculated: 83·48% C, 11·47% H; found: 83·96% C, 11·69% H.

b) The solution of the ketone *IX* (63 mg) in triethylene glycol (3 ml) was treated with hydrazine hydrate (0·3 ml, 96%) and solid sodium hydroxide (95 mg) in the same manner as in case *a*). The crude product (60 mg) obtained by working up of the reaction mixture was preparatively chromatographed on one plate of silica gel (20 × 20 cm) in light petroleum–ether (6 : 4). The corresponding zone was eluted with ether and the solvent evaporated *in vacuo*. The residue (41 mg) was crystallized from methanol to give 35 mg of the hydroxy derivative *XIV*, m.p. 109 to 110°C, $[\alpha]_D^{20}$ +27° (*c* 0·5).

17β-Hydroxy-3α,5-cyclo-5-bishomo-5α-androstane (*XV*)

The solution of the ketone *X* (210 mg) in triethylene glycol (12 ml) was treated with hydrazine hydrate (1·5 ml, 96%) and solid sodium hydroxide (300 mg) in the same manner as in preceding procedure. The oily product obtained by working up of the mixture was crystallized from methanol to give 169 mg of the hydroxy derivative *XV*, m.p. 170·5–172°C, $[\alpha]_D^{20}$ −24° (*c* 0·5) Infrared spectrum (tetrachloromethane): 3630, 1072, 1057, 1041, 1025, 3070 cm^{-1}. For $C_{21}H_{34}O$ (302·5) calculated: 83·38% C, 11·32% H; found: 83·28% C, 11·53% H.

The analyses were carried out in the analytical laboratory of our Institute under the direction of Dr J. Horáček. The mass spectra were measured by Dr A. Trka, the IR *spectra were recorded by Mr P. Formánek (direction Dr J. Smolíková).*

REFERENCE

1. Gelhaus J., Černý V., Šorm F.: This Journal *37*, 1331 (1972).

Translated by the author (V. Č.).