BRASSINOLIDE ANALOGUES WITHOUT SIDE CHAIN*

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Received June 6, 1988
Accepted July 28, 1988

Dedicated to Prof. G. Snatzke on the occasion of his 60th birthday.

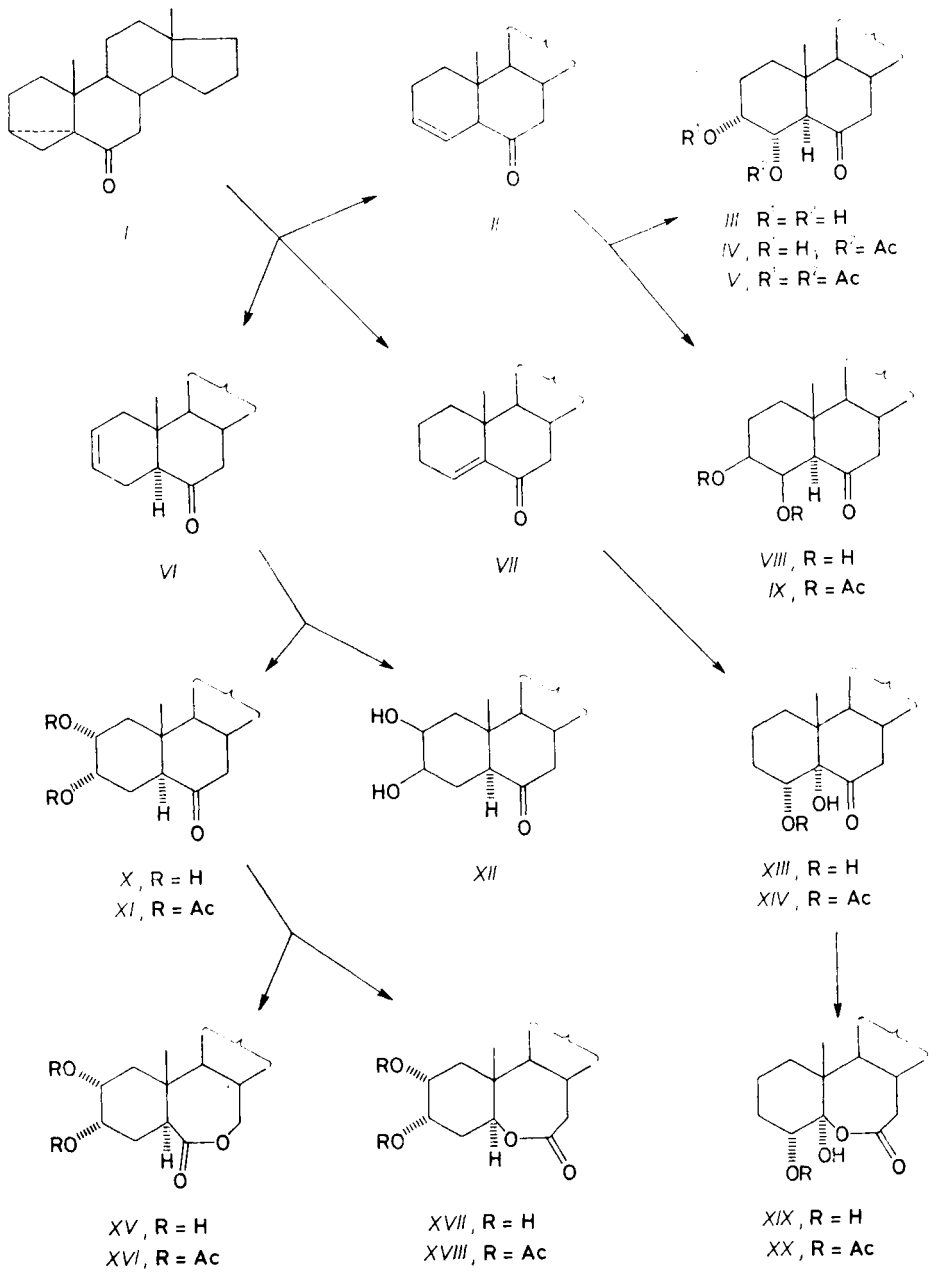
New brassinolide analogues, characterized by a modified androstane structure without substituent in position 17, were prepared. In the second internode assay, 2α,3α-dihydroxy-B-homo-6--oxa-5α-androstan-7-one (*XVII*) had the highest brassinoid activity.

In one of our preceding studies[1] we have found that 2β,3β-dihydroxy-5α-androstan--6-one (*XII*) exhibits an interesting activity in the bean second internode assay having two relatively high maxima at two different concentrations. Since in compound *XII* the substituents in positions 2 and 3 have configuration opposite to that in the natural brassinolide ((22*R*,23*R*,24*S*)-2α,3α,22,23-tetrahydroxy-24-methyl-B-homo-7--oxa-5α-cholestan-6-one; see ref.[2]), we prepared in this work an analogue with the 2α,3α-diol grouping.

Our synthesis started from the known[3] 3α,5-cyclo-5α-androstan-6-one (*I*) which was converted into the 2,3-olefin *VI* by heating with *p*-toluenesulfonic acid in sulfolane. The reaction also gave the isomeric olefins *VII* (see ref.[4]) and *II* (ref.[6]). On treatment with osmium tetroxide in the presence of N-methylmorpholine N-oxide, the 2,3-olefin *VI* afforded a mixture of the above-mentioned diol *XII* and its isomer *X*. The 2α,3α-diol *X* was acetylated and oxidized with trifluoroperoxyacetic acid to give a mixture of two isomeric lactones *XVI* and *XVIII*, the structure of which was derived from their ^{1}H NMR spectra. Whereas in the spectrum of the 7-oxa compound *XVI* the 7a-protons signals appear as a doublet at δ 4·11 (J = 4·5 Hz), the doublet due to 7a-protons of the 6-oxa derivative *XVIII* is located at δ 2·53 (J = 5 Hz). The shifts of the 5α-proton signal also differ considerably: in the spectrum of *XVI* it appears as a multiplet in the region 2·80–3·19 ppm whereas the spectrum of *XVIII* exhibits this signal at 4·29–4·65 ppm. Removal of the acetyl groups afforded 2α,3α-

* Part CCCXXXIX in the series On Steroids; Part CCCXXXVIII: Collect. Czech. Chem. Commun. *54*, 751 (1989).

-dihydroxy-B-homo-7-oxa-5α-androstan-6-one (*XV*) and the isomeric 2α,3α-dihydroxy-B-homo-6-oxa-5α-androstan-7-one (*XVII*).



Hydroxylation of 3,4-olefin *II* with osmium tetroxide in the presence of N-methylmorpholine N-oxide furnished further two isomers of compound *XII*: 3α,4α-diol *III* and 3β,4β-diol *VIII* which were characterized as the respective diacetates *V* and *IX*. Using the same hydroxylation reaction, we converted the 4,5-olefin *VII* into another isomer, 4α,5α-diol *XIII*. This diol was acetylated to give monoacetate *XIV* which on treatment with trifluoroperoxyacetic acid in dichloromethane gave lactone *XX*. Its structure was confirmed again by the ^{1}H NMR spectrum: the 7a-proton signals appeared as a doublet at about 2·3 ppm. Removal of the acetate group led to 4α,5α--dihydroxy-B-homo-6-oxa-5α-androstan-7-one (*XIX*).

The obtained diols with carbonyl functionality on the ring B (i.e. compounds *III*, *VIII*, *X* and *XIII*) and diols with lactone grouping (i.e. compounds *XV* and *XVII*) were subjected to the second bean internode bioassay. As seen from Table I, the activity of all the prepared brassinosteroids is lower than that of the epibrassinolide *XXI* ((22*R*,23*R*,24*R*)-2α,3α,22,23-tetrahydroxy-24-methyl-B-homo-7-oxa-5α-cholestan-6-one) used as a standard. Epibrassinolide is known[5] to be a very active analogue, nearly as active as the natural brassinolide. Lactone *XVII* was the most active of the studied compounds. Interestingly, both the lactone *XVII* and lactone *XV* exhibit two activity maxima, analogously to the compound *XII*.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured in chloroform solutions; error ±3°. Infrared spectra were recorded on a Zeiss UR 20 spectrometer in tetrachloromethane (unless stated otherwise), wavenumbers are given in cm^{-1}. Proton NMR spectra were obtained with a Tesla B 476 (60 MHz) or a Tesla BS 497·0 (100 MHz) instrument in deuterochloroform with tetramethylsilane as internal standard (unless stated otherwise). Chemical shifts are given in ppm (δ-scale), the coupling constants (*J*) and signal half-widths ($W_{1/2}$) in Hz. The spectra were interpreted as the first-order spectra. Mass spectra were measured on a ZAB-EG spectrometer at 70 eV. The identity of the prepared samples was checked by mixture melting points, thin-layer chromatography (TLC), IR and ^{1}H NMR spectra. Preparative TLC was carried out on 200 × 200 mm plates with a 0·7 mm layer of silica gel Woelm DC. „Usual work-up of a solution" denotes washing the solution with 5% hydrochloric acid, water, 5% aqueous solution of potassium hydrogen carbonate and water, drying over anhydrous sodium sulfate, filtration and evaporation of the solvent in vacuo. The light petroleum used was a fraction boiling between 40°C and 62°C.

Bean Second Internode Bioassay

Seeds of bean (*Phaseolus vulgaris* L., var. PINTO) were germinated for two days and selected germinated seeds were planted into pots containing perlite and modified Hoagland's solution (half concentration, pH 5·7). The pots were placed in a light-controlled cultivation room (25 to 27°C, light: 48 W/m^2, light/dark period: 16 h/8 h). Groups of eight 7-day-old bean seedlings with 1—2 mm long second internodes were treated with different amounts (mol) of the tested compounds in 2 μl lanolin. The control plants were treated with lanolin alone. The measurements were taken after 5 days. Difference in the length of the second internode of the treated and control plants was used as a measure of the activity.

TABLE I

Biological activities of brassinosteroids in the bean second internode bioassay

Compound	Elongation (mm) at dose (mol)							Maximal elongation at dose (mol)	24-Epibrassinolide equivalent[a] (mol)
	10^{-7}	10^{-8}	10^{-9}	10^{-10}	10^{-11}	10^{-12}	10^{-13}		
III	−5·1	−4·4	−1·6	2·7	−9·4	−3·7	–	10^{-10}	$<10^{-14}$
VIII	0	0·4	−0·9	−0·7	−1·2	−0·7	–	10^{-8}	$<10^{-14}$
X	–	−2·3	−2·4	−0·7	3·9	0·8	1·5	10^{-11}	$<10^{-14}$
XIII	–	3·2	6·8	2·0	−2·8	−2·7	−3·5	10^{-9}	$3 . 10^{-14}$
XV	–	0·3	1·0	4·3	3·2	−2·3	3·4	10^{-10}	$<10^{-14}$
XVII	–	7·6	3·7	5·5	9·2	6·6	7·5	10^{-11}	$3 . 10^{-13}$
XXI	–	20·4	30·8	32·3	18·6	12·9	7·2	10^{-10}	(10^{-10})

[a] Amount of epibrassinolide (*XXI*) necessary for inducing the same second internode elongation as the maximal elongation induced by the tested compound.

3-Androsten-6-one (*II*)

The title compound was obtained as further chromatographic fraction in the preparation of olefin *VI*. Yield 8·5 mg of oily *II*, $[\alpha]_D^{20}$ +23° (*c* 1·9). Mass spectrum (*m/z*): 272 (M^+). ^{1}H NMR spectrum: 0·71 s, 3 H (3 × H-18); 0·94 s, 3 H (3 × H-19); 5·10–6·10 m, 2 H (H-4 and H-3) (in accord with the published[6] values). IR spectrum: 3 020 (C=C), 1 710 (C=O).

3α,4α-Dihydroxy-5α-androstan-6-one (*III*)

A solution of osmium tetroxide (75 mg) in 2-methyl-2-propanol (2·6 ml) was added to a solution of olefin *II* (1·5 g) in acetone (75 ml). After addition of N-methylmorpholine N-oxide (1·50 g) and water (2·6 ml), the mixture was set aside at room temperature overnight. A 10% sodium sulfite solution (10 ml) was added, the reaction mixture was stirred overnight, poured into water and the product was taken up in chloroform. The usual work-up afforded 1·51 g of material which was chromatographed on a column of silica gel (200 g) in light petroleum–ether (3 : 1). After elution of the starting compound (800 mg), the chromatography gave diol *III* (202 mg), m.p. 150–157°C, $[\alpha]_D^{20}$ −33° (*c* 1·2). ^{1}H NMR spectrum: 0·70 s, 3 H (3 × H-18); 0·73 s, 3 H (3 × H-19); 3·57–4·37 m, 2 H (H-3β and H-4β). For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H; found: 74·42% C, 9·81% H.

3α,4α-Dihydroxy-5α-androstan-6-one 4-Acetate (*IV*)

Work-up of polar zones from preparative TLC in the preparation of diacetate *V* afforded 15·5 mg of monoacetate *IV*. ^{1}H NMR spectrum: 0·69 s, 3 H (3 × H-18); 0·78 s, 3 H (3 × H-19); 2·05 s, 3 H (CH_3COO); 2·48–2·86 m, 2 H (H-5 and H-7); 3·73 m, 1 H (H-3β, $W_{1/2}$ = 5 Hz); 4·95 m, 1 H (H-4β, $W_{1/2}$ = 21). IR spectrum: 3 610 (OH), 1 742, 1 239 (acetate), 1 712 (C=O). For $C_{21}H_{32}O_4$ (348·5) calculated: 72·38% C, 9·26% H; found: 71·94% C, 9·08% H.

3α,4α-Dihydroxy-5α-androstan-6-one 3,4-Diacetate (*V*)

A mixture of diol *III* (38 mg), pyridine (5 ml) and acetic anhydride (3 ml) was allowed to stand at room temperature for 2 days. After pouring into water, the product was extracted with ether and worked up in the usual manner. The residue consisted (TLC) of two compounds which were separated by preparative TLC in light petroleum–ether (3 : 1). Zones with the more lipophilic product afforded 9 mg of diacetate *V*, m.p. 107–110°C (ethanol). ^{1}H NMR spectrum: 0·70 s, 3 H (3 × H-18); 0·79 s, 3 H (3 × H-19); 2·01 s and 2·05 s, 6 H (2 × CH_3COO); 4·60–5·10 m, 2 H (H-3β and H-4β). IR spectrum: 1 746, 1 247, 1 230 (acetates), 1 716 (C=O). For $C_{23}H_{34}O_5$ (390·5) calculated: 70·74% C, 8·78% H; found: 70·72% C, 8·88% H.

2-Androsten-6-one (*VI*)

p-Toluenesulfonic acid monohydrate (35 mg) was added to a solution of compound *I* (300 mg) in tetramethylene sulfone (5 ml; Ventron). After heating under nitrogen to 155°C for 2 h, another portion of *p*-toluenesulfonic acid monohydrate (35 mg) was added and the temperature was kept at 185–190°C for 2 h. The reaction mixture was cooled, poured into water and the product was extracted with ether. The ethereal phase was washed with 10% potassium hydrogen carbonate solution and water, dried and the solvent was evaporated. The residue (300 mg) was chromatographed on a column of silica gel (100 g) in light petroleum–ether (19 : 1) to afford 170 mg of olefin *VI* which was crystallized from methanol–ethanol–water (18 : 1 : 2); m.p. 71–73°C, $[\alpha]_D^{20}$ +20° (*c* 2·2) (same as the published[3] values). ^{1}H NMR spectrum: 0·73 s, 6 H (3 × H-18

and 3 × H-19); 5·65 m, 2 H (H-2 and H-3, $W_{1/2}$ = 5). IR spectrum: 3 065, 3 025, 1 669 sh, 1 655, 671 (C=C), 1 711 (C=O).

4-Androsten-6-one (*VII*)

Further chromatographic fractions in the preparation of olefin *II* afforded 15 mg of material which on crystallization from methanol gave 6 mg of olefin *VII*, m.p. 140–141°C, $[\alpha]_D^{20}$ +20° (*c* 1·2) (in accord with the reported[4] data). Mass spectrum (*m/z*): 272 (M^+, base peak). ^{1}H NMR spectrum: 0·75 s, 3 H (3 × H-18); 0·98 s, 3 H (3 × H-19); 6·38 t, 1 H (H-4, *J* = 3·5). IR spectrum: 1 691, 1 628 (C=C—C=O).

3β,4β-Dihydroxy-5α-androstan-6-one (*VIII*)

Further chromatographic fractions in the preparation of diol *III* gave, after crystallization from aqueous ethanol, 161 mg of diol *VIII*, m.p. 198–200°C, $[\alpha]_D^{20}$ −112° (*c* 1·3). ^{1}H NMR spectrum: 0·70 s, 3 H (3 × H-18); 1·00 s, 3 H (3 × H-19); 3·80–4·21 m, 2 H (H-3α and H-4α). IR spectrum (chloroform): 3 625, 3 570, 1 061 (hydroxyls), 1 730 (ketone). For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H; found: 74·19% C, 9·81% H.

3β,4β-Dihydroxy-5α-androstan-6-one 3,4-Diacetate (*IX*)

A mixture of diol *VIII* (200 mg), pyridine (5 ml) and acetic anhydride (3 ml) was allowed to stand for 4·5 days at room temperature. After pouring into water, the product was extracted with ether and the extract was worked up in the usual manner. The residue (200 mg) was crystallized from ethanol to give 46 mg of diacetate *IX*, m.p. 129–130·5°C, $[\alpha]_D^{20}$ −61° (*c* 2·9). ^{1}H NMR spectrum: 0·69 s, 3 H (3 × H-18); 0·84 s, 3 H (3 × H-19); 5·07 m, 1 H (H-3α, $W_{1/2}$ = 13); 5·33 m, 1 H (H-4α, $W_{1/2}$ = 4·5). IR spectrum: 1 745, 1 247, 1 238 (acetates), 1 712 (C=O). For $C_{23}H_{34}O_5$ (390·5) calculated: 70·74% C, 8·78% H; found: 70·71% C, 8·88% H.

2α,3α-Dihydroxy-5α-androstan-6-one (*X*)

A solution of osmium tetroxide (78 mg) in 2-methyl-2-propanol (2·6 ml), followed by N-methylmorpholine N-oxide (1·57 g) in water (2·6 ml), was added to a solution of olefin *VI* (1·57 g) in acetone (78 ml). After stirring at room temperature for 4 h, 10% sodium sulfite solution (15 ml) was added, the mixture was stirred for 40 min and then poured into water. The product was taken up in chloroform, worked up in the usual manner and the residue (1·9 g) was chromatographed on a column of silica gel (300 g) in chloroform–ether (1 : 1). The obtained material (1·7 g) was crystallized from methanol to give 600 mg of diol *X*; further portions (360 mg and 238 mg) of *X* were obtained by crystallization of the mother liquors from ethanol–heptane; m.p. 151 to 155°C, $[\alpha]_D^{20}$ −18° (chloroform–methanol 1 : 1). ^{1}H NMR spectrum: 0·73 s and 0·76 s, 6 H (3 × H-18 and 3 × H-19); 3·17–4·20 m, 2 H (H-2β and H-3β). IR spectrum: 3 615, 3 572, 1 052 (hydroxyls), 1 711 (C=O). Mass spectrum (*m/z*): 306 (M^+). For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H; found: 74·64% C, 10·37% H.

2α,3α-Dihydroxy-5α-androstan-6-one 2,3-Diacetate (*XI*)

Acetic anhydride (6 ml) was added to a solution of diol *X* (1 g) in pyridine (10 ml) and the reaction mixture was allowed to stand at room temperature for 20 h. After pouring in water, the product was extracted with ether and worked up as usual. Crystallization of the residue gave 620 mg of diacetate *XI*, m.p. 181–183°C, $[\alpha]_D^{20}$ −21° (*c* 1·5). ^{1}H NMR spectrum: 0·69 s, 3 H

(3 × H-18); 0·825 s, 3 H (3 × H-19); 1·96 s and 2·05 s, 6 H (2 × CH_3COO); 4·92 m, 1 H (H-2β, $W_{1/2}$ = 21·5); 5·35 m, 1 H (H-3β, $W_{1/2}$ = 5·5). For $C_{23}H_{34}O_5$ (390·5) calculated: 70·74% C, 8·78% H; found: 71·21% C, 8·72% H.

2β,3β-Dihydroxy-5α-androstan-6-one (*XII*)

The mother liquors after crystallization of diol *X* were subjected to preparative TLC on six plates of silica gel in benzene–ether–2-propanol (99 : 99 : 1). Fractions, containing a slightly more lipophilic product than the diol *X*, afforded 70 mg of material which was crystallized from aqueous ethanol to give 5 mg of diol *XII*, m.p. 185–186°C, $[\alpha]_D^{20}$ −20° (*c* 1·3) (reported[3] m.p. 178–180°C and $[\alpha]_D^{20}$ −52°). ^{1}H NMR spectrum: 0·68 s, 3 H (3 × H-18); 0·96 s, 3 H (3 × H-19); 3·57 m, 1 H (H-3α, $W_{1/2}$ = 18); 4·00 m, 1 H (H-2α, $W_{1/2}$ = 7); (same values as reported[3]). For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H; found: 74·18% C, 9·82% H.

4α,5-Dihydroxy-5α-androstan-6-one (*XIII*)

Osmium tetroxide (150 mg) in 2-methyl-2-propanol (1·5 ml) was added to a solution of olefin *VII* (3 g) in acetone (150 ml). After addition of N-methylmorpholine N-oxide (3 g) in water (4 ml), the mixture was stirred under nitrogen for 4 h and set aside overnight. Further amount of N-methylmorpholine N-oxide (3 g) was added, the mixture was stirred for 60 min, 10% sodium sulfite solution (10 ml) was added and the stirring was continued for 1 h. The reaction mixture was poured into water, the product was extracted with ether and worked up in the usual manner. The residue (3·2 g) was chromatographed on a column of silica gel (200 g) in light petroleum–ether (9 : 1) to give 0·3 g of the starting compound *VII*. Elution with chloroform–ether (1 : 1) afforded material (1·2 g) which on crystallization from acetone gave 430 mg of diol *XIII*, m.p. 160–161°C, $[\alpha]_D^{20}$ −127° (*c* 1·4). ^{1}H NMR spectrum: 0·70 s, 3 H (3 × H-18); 0·80 s, 3 H (3 × H-19); 3·14 s, 1 H (OH); 4·26 m, 1 H (H-4β, $W_{1/2}$ = 15). IR spectrum: 3 570, 3 525, 1 080, 1 073, 993 (hydroxyls), 1 708 (carbonyl). For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H, found: 74·54% C, 9·85% H.

4α,5-Dihydroxy-5α-androstan-6-one 4-Acetate (*XIV*)

Acetic anhydride (3 ml) was added to a solution of diol *XIII* (1 g) in pyridine (5 ml). After standing for 3 days at room temperature, the mixture was poured into water, the product was taken up in ether and worked up as usual. Crystallization of the residue (1·05 g) from ethanol gave 540 mg of monoacetate *XIV*, m.p. 220–221°C, $[\alpha]_D^{20}$ −57° (*c* 1·2). ^{1}H NMR spectrum: 0·67 s, 3 H (3 × H-18); 0·79 s, 3 H (3 × H-19); 1·97 s, 3 H (CH_3COO); 2·55 s, 1 H (OH); 2·62 to 3·12 m, 1 H (H-7); 5·28 m, 1 H (H-4β, $W_{1/2}$ = 18). IR spectrum: 3 585 (hydroxyl), 1 721 (C=O), 1 756, 1 745, 1 252, 1 226, 1 213 (acetate). For $C_{21}H_{32}O_4$ (348·5) calculated: 72·38% C, 9·26% H; found: 71·83% C, 9·27% H.

2α,3α-Dihydroxy-B-homo-7-oxa-5α-androstan-6-one (*XV*)

A mixture of diacetate *XVI* (650 mg), methanol (30 ml), potassium hydroxide (1·3 g) and water (2 ml) was refluxed for 1·5 h and then concentrated under diminished pressure to about one third of the original volume. Tetrahydrofuran (30 ml) was added and the mixture was acidified with hydrochloric acid (pH < 2·5). After refluxing for 30 min, the mixture was poured into water, the product was extracted with chloroform and worked up as usual. The residue (520 mg) was dissolved in ethanol, filtered and the solvent was evaporated. Chromatography on a column of silica gel (200 g; elution with methanol–chloroform 1 : 49, then 1 : 24) afforded 320 mg of material

which was crystallized from aqueous ethanol to give 165 mg of diol *XV*, m.p. 186–188°C, $[\alpha]_D^{20}$ +36° (*c* 1·4; chloroform–methanol 1 : 1). ^{1}H NMR spectrum: 0·74 s, 3 H (3 × H-18); 0·92 s, 3 H (3 × H-19); 2·93–3·31 m and 3·50–4·25 m, 4 H (H-2β, H-3β and 2 × H-7a). IR spectrum: 1 730, 1 712 sh, 1 320, 1 188 (lactone), 3 430, 1 069, 1 034 (hydroxyls). For $C_{19}H_{30}O_4$ (322·4) calculated: 70·77% C, 9·38% H; found: 70·42% C, 9·21% H.

2α,3α-Dihydroxy-B-homo-7-oxa-5α-androstan-6-one 2,3-Diacetate (*XVI*)

A solution of ketone *XI* (1·35 g) in dichloromethane (15 ml) was added to a solution of trifluoroperoxyacetic acid (prepared by addition of trifluoroacetic anhydride (3·675 g) and 50% hydrogen peroxide (0·45 ml) into dichloromethane (37·5 ml) at 0–5°C). After standing at room temperature for 4 days, the reaction mixture was poured into water and the product was taken up in chloroform. The organic layer was washed with 10% potassium hydrogen carbonate solution and water, dried, and the solvent was evaporated. The obtained residue (1·5 g) consisted of two compounds (according to TLC) which were separated by column chromatography on silica gel (150 g; elution with light petroleum–ether 2 : 1 and then 1 : 1). The intermediate fractions were separated by preparative TLC (double elution with benzene–ether 2 : 1). The more lipophilic fractions gave 780 mg of product which on crystallization from aqueous ethanol afforded 352 mg of lactone *XVI*, m.p. 234–237°C, $[\alpha]_D^{20}$ +37° (*c* 1·5). ^{1}H NMR spectrum: 0·75 s, 3 H (3 × H-18); 0·985 s, 3 H (3 × H-19); 1·98 s and 2·09 s, 6 H (acetates); 2·80–3·19 m, 1 H (H-5α); 4·11 d, 2 H (2 × H-7a, J = 4·5); 4·86 dm, 1 H (H-2β, $W_{1/2}$ = 11; J = 12·5); 5·33 m, 1 H (H-3β, $W_{1/2}$ = 9·5). IR spectrum: 1 746, 1 256 (acetates), 1 746, 1 228, 1 185 (lactone). For $C_{23}H_{34}O_6$ (406·5) calculated: 67·95% C, 8·43% H; found: 68·19% C, 8·32% H.

2α,3α-Dihydroxy-B-homo-6-oxa-5α-androstan-7-one (*XVII*)

Diacetate *XVIII* (100 mg) was hydrolyzed as described for the preparation of compound *XV*. The usual work-up gave 85 mg of a residue which was purified by preparative TLC (4 plates) in chloroform–methanol (9 : 1). Crystallization of the crude product (35 mg) from aqueous ethanol afforded 21 mg of diol *XVII*, m.p. 228–233°C. ^{1}H NMR spectrum: 0·73 s, 3 H (3 × H-18); 0·95 s, 3 H (3 × H-19); 3·55–4·80 m, 3 H (H-2β, H-3β and H-5α). IR spectrum (KBr): 3 525 (hydroxyls), 1 715 sh, 1 703, 1 225, 1 085 (lactone). For $C_{19}H_{30}O_4$ (322·4) calculated: 70·77% C, 9·38% H; found: 70·41% C, 9·19% H.

2α,3α-Dihydroxy-B-homo-6-oxa-5α-androstan-7-one 2,3-Diacetate (*XVIII*)

Work-up of polar fractions in the preparation of lactone *XVI* afforded 130 mg of residue which was crystallized from aqueous ethanol to give 86 mg of lactone *XVIII*, m.p. 273–274°C. ^{1}H NMR spectrum: 0·74 s, 3 H (3 × H-18); 1·01 s, 3 H (3 × H-19); 1·98 s and 2·10 s, 6 H (2 × CH_3COO); 2·53 d, 2 H (2 × H-7a, J = 5); 4·29–4·65 m, 1 H (H-5α); 4·92 bd, 1 H (H-2β, $J \approx$ 12); 5·37 m, 1 H (H-3β, $W_{1/2}$ = 6·5). IR spectrum (chloroform): 1 738, 1 722, 1 274, 1 045 (lactone), 1 738, 1 727 sh, 1 253, 1 064 (acetates). For $C_{23}H_{34}O_6$ (406·5) calculated: 67·95% C, 8·43% H; found: 67·60% C, 8·41% H.

4α,5-Dihydroxy-B-homo-6-oxa-5α-androstan-7-one (*XIX*)

Diacetate *XX* (400 mg) was hydrolyzed as described in the preparation of compound *XV*. The usual work-up afforded 246 mg of material which was subjected to preparative TLC on silica gel (12 plates) in light petroleum containing 7% of 2-propanol. Yield 118 mg of noncrystalline diol *XIX*, $[\alpha]_D^{20}$ +13° (*c* 0·04). ^{1}H NMR spectrum: 0·72 s, 3 H (3 × H-18); 1·08 s, 3 H (3 × H-19);

3·30—3·78 m, 1 H (H-4, $W_{1/2}$ = 14). IR spectrum: 1 746, 1 730 (lactone), 3 540 (hydroxyls). For $C_{19}H_{30}O_4$ (322·4) calculated: 70·77% C, 9·38% H; found: 70·44% C, 9·32% H.

4α,5-Dihydroxy-B-homo-6-oxa-5α-androstan-7-one 4-Acetate (*XX*)

A solution of ketone *XIV* (0·8 g) in dichloromethane (9 ml) was added to a solution of trifluoroperoxyacetic acid, prepared by addition of trifluoroacetic anhydride (2·178 g) and 50% hydrogen peroxide (0·27 ml) into dichloromethane (22·2 ml) at 0—5°C. After standing at room temperature for 24 h, the reaction mixture was poured into water and the product was taken up in chloroform. The chloroform solution was washed with 10% potassium hydrogen carbonate solution and water, dried and the solvent was evaporated. The residue (0·65 g) was chromatographed on a column of silica gel (400 g) in light petroleum–ether (4 : 1). Yield 470 mg of noncrystalline acetate *XX*, $[\alpha]_D^{20}$ +33° (*c* 2·1). ^{1}H NMR spectrum: 0·75 s, 3 H (3 × H-18); 1·33 s, 3 H (3 × H-19); 2·10 s, 3 H (CH_3COO); 2·30 d, 2 H (H-7a, J = 5); 5·10—5·33 m (H-4β). IR spectrum: 3 585 (hydroxyl), 1 746, 1 241 (acetate), 1 721, 1 101 (lactone). Mass spectrum (*m/z*): 364 (M^+); high resolution: 305·2211 ($C_{19}H_{29}O_3$, i.e. M − $CH_3COO^•$), 304·2022 ($C_{19}H_{28}O_3$, i.e. M − CH_3COOH). For $C_{21}H_{32}O_5$ (364·5) calculated: 69·20% C, 8·85% H; found: 69·08% C, 8·64% H.

Elemental analyses were carried out in the Analytical Laboratory of this Institute by Mrs E. Sýkorová, Mrs E. Šípová and Mr V. Štěrba (Dr V. Pechanec, Head). The authors are indebted to Dr J. Smolíková for the interpretation of IR *spectra measured by Mrs K. Matoušková. Mass spectra were measured by Mrs P. Loudová, high resolution spectrum of compound* XX *by Dr V. Hanuš, the J. Heyrovský Institute of Physical Chemistry and Electrochemistry, Czechoslovak Academy of Sciences. The* ^{1}H NMR *spectra were measured by Mrs J. Jelínková and Mrs M. Snopková. The technical assistance of Mrs J. Mašková and Mrs J. Balounová is gratefully acknowledged.*

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Translated by M. Tichý.