CYCLOPROPYL→CYCLOBUTYL REARRANGEMENT IN INTRAMOLECULAR CYCLIZATION OF 3,5-BRIDGED B-SECOANDROSTANE-6,7(OR 5,7)-DIOLS AND MASS SPECTRA OF PRODUCTS*

Helena VELGOVÁ, Jorga SMOLÍKOVÁ, Antonín TRKA and Antonín VÍTEK

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6

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Acid-catalyzed intramolecular cyclization of 6,7-dihydroxy-3α,5-cyclo-6,7-seco-5α-androstan-17-one (*VII*), 5,7-dihydroxy-3,5-methylene-5,7-secoandrostan-17-one and 5,7-dihydroxy-3β,5-cyclo-5,7-seco-A-homo-5β-androstan-17-one (*XIII*) in benzene and dioxane was investigated. The main cyclization products were 3,5-methylene-6-oxaandrostan-17-one (*I*) and/or 3β,5-cyclo-6-oxa-A-homo-5β-androstan-17-one (*VIII*). In the case of *VI* and *VII* the ratio of *I* and *VIII* was solvent-dependent: in benzene more *VIII* was formed than in dioxane. The mass spectra of *I* and *VIII* were almost identical and corresponded to the structure *VIII*.

The facility of the cyclopropylmethyl-cyclobutyl interconversion is well known and the character of the intermediary cations has been studied both from the experimental and theoretical point of view[1,2]. Although the question of classical or non-classical nature of the intermediary cations has not been solved as yet, it is assumed that cyclopropylmethyl derivatives are primarily transformed into cyclopropylmethyl cations which can undergo either a degenerate cyclopropylmethyl-cyclopropylmethyl rearrangement or a rearrangement to homoallyl or cyclobutyl derivatives. Ionization of primary and secondary cyclobutyl derivatives is usually accompanied by a disrotatory opening to give cyclopropylmethyl cations. Only in some cases, particularly those of tertiary cyclobutyl derivatives, formation of a stable cyclobutyl cation is assumed. In connection with our previous work[3], dealing with intramolecular cyclization of 17-ethylenedioxy-6,7-seco-3α,5-cyclo-5α-androstane-6,7-diol by action of *p*-toluenesulfonyl chloride in pyridine, we were interested in the outcome of an acid-catalyzed intramolecular cyclization of 3α,5-cyclo-6,7-seco-5α-androstane, 3,5-methylene-5,7-secoandrostane and 3β,5-cyclo-5,7-seco-A-homo-5β-androstane diols. We can assume that under these conditions cyclobutyl derivatives give rise to cyclobutyl cations whereas the cyclopropylmethyl derivative is transformed to cyclopropylmethyl cation. The cyclizations of 6,7-dihydroxy-3α,5-cyclo-6,7-seco-5α-andro-

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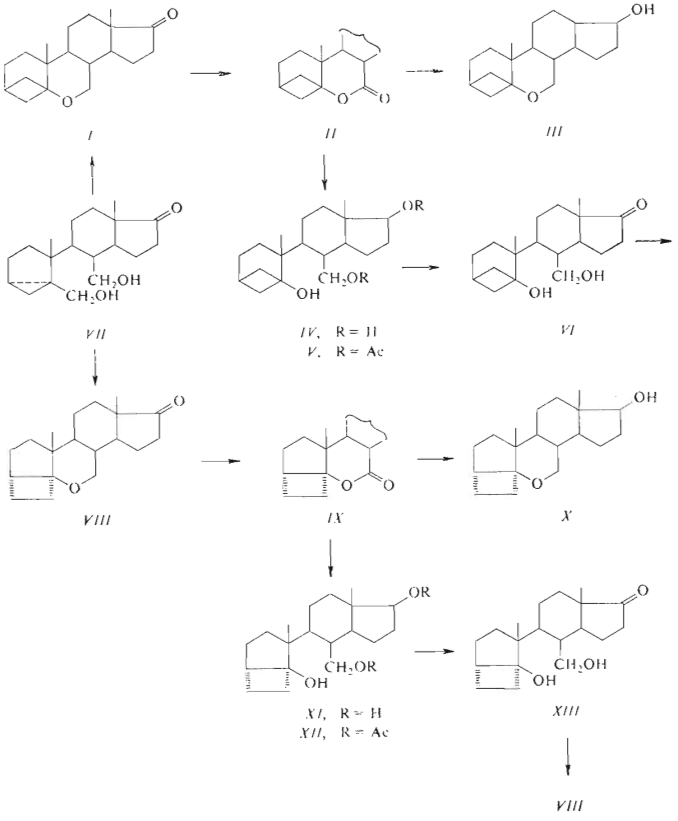
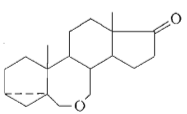
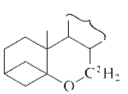
stan-17-one (*VII*), 5,7-dihydroxy-3,5-methylene-5,7-seco-androstan-17-one (*VI*) and 5,7-dihydroxy-3β,5-cyclo-5,7-seco-A-homo-5β-androstan-17-one (*XIII*) were performed at 30°C with aqueous perchloric acid in benzene and dioxane, *i.e.* in solvents of different polarity. The yields of the principal cyclization products are given in Table I.



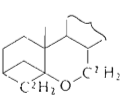
Synthesis of the diol *VII* was described already previously[4]. The diols *VI* and *XIII* were prepared as follows: Oxidation of the cyclic ether *I* (ref.[3]) with chromium trioxide in a mixture of acetic acid and acetic anhydride (1 : 1) afforded in 67% yield the lactone *II*. As expected for a 7-keto derivative, its ^{1}H NMR spectrum exhibited no $C_{(7)}$ proton signals. Compound *II* was reduced with diborane *in situ* to give the alcohol *III* whose structure was confirmed by oxidation with chromium trioxide to the starting ketone *I*. Reduction of the lactone *II* with lithium aluminium hydride in boiling dioxane gave the triol *IV*, characterized as its diacetate *V*. The triol was oxidized with N-bromosuccinimide in aqueous tert-butyl alcohol to give the desired ketone *VI* in 35% yield (besides 30% of the lactone *II*). Oxidation of the ether *VIII* (ref.[3]) with chromium trioxide in acetic acid–acetic anhydride (1 : 1) afforded in 52% yield the lactone *IX*, which, according to the ^{1}H NMR spectrum, had the keto group in the position 7. On reduction with diborane, the lactone *IX* was transformed into the alcohol *X* the structure of which was confirmed by oxidation with chromium trioxide in pyridine to the starting ketone *VIII*. The lactone *IX* was reduced with lithium aluminium hydride in boiling dioxane to the triol *XI*, characterized as its diacetate *XII*. Oxidation of *XI* with N-bromosuccinimide in aqueous tert-butyl alcohol afforded the desired ketone *XIII* in 60% yield.



XIV



XV



XVI

TABLE I

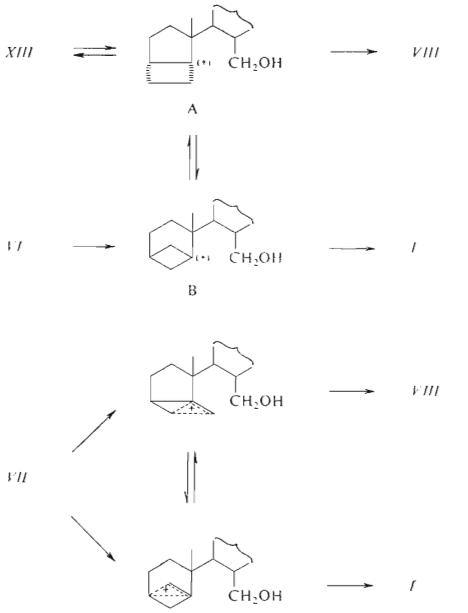
Yields and ratios of products of cyclization of diols *VI*, *VII* and *XIII*

Compound	Solvent	*I*	*VIII*	*XIII*	Total yield, %
VI	benzene	81·1 ± 1·1[a]	18·9 ± 1·6[a]	—	65
	dioxane	97·2 ± 2·6	2·8 ± 3·7	—	76
VII	benzene	28·2 ± 0·8	71·8 ± 1·1	—	79
	dioxane	58·4 ± 0·4	41·6 ± 0·6	—	75
XIII	benzene	0·0 ± 0·0	100·0 ± 0·0	—	86
	dioxane	—	—	100	91

[a] Given as % of the total yield; the error is expressed as estimated standard deviation.

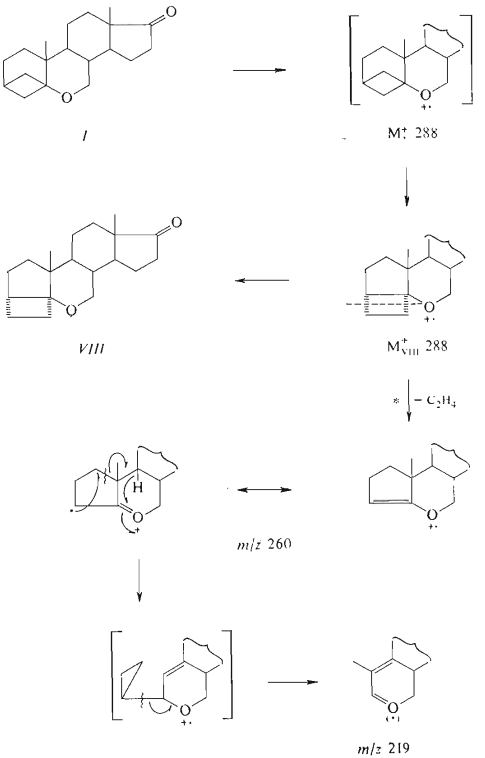
Acid-catalyzed intramolecular cyclization of the diols *VI*, *VII* and *XIII* afforded mixtures of products which, however, did not contain (according to thin-layer chromatography) substantial amounts of 3%-cyclo-7-oxa-B-homo-5α-androstan-17-one[3] (*XIV*) which could be expected to arise, particularly from the diol *VII*. The reaction mixtures consisted mainly of the chromatographically unseparable cyclic ethers *I* and *VIII*. Their proportions were quantitatively determined by IR spectral analysis[5,6]. Under assumption that in dilute solutions the molar extinction coefficients of *I* and *VIII* do not influence each other, we may write the following relationship for the total absorbancy of the reaction mixture in solution, at a wavenumber ν:

$$D(\tilde{\nu}) = D_0 + c_I \,.\, d \,.\, \varepsilon_I(\tilde{\nu}) + c_{VIII} \,.\, d \,.\, \varepsilon_{VIII}(\tilde{\nu}), \qquad (I)$$



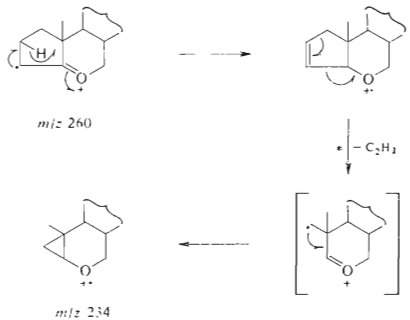
SCHEME 1

where D_0 is the background absorbancy, d cell thickness, c_I and c_{VIII} are concentrations of the components and $\varepsilon_I(\tilde{\nu})$ and $\varepsilon_{VIII}(\tilde{\nu})$ molar extinction coefficients of the pure compounds *I* and *VIII* at the wavenumber $\tilde{\nu}$. The proportions of compounds *I* and *VIII* in the analyzed cyclization mixtures, calculated from the found values of c_I and c_{VIII}, are given in Table I.



SCHEME 2

As seen, the outcome of the acid-catalyzed intramolecular cyclization of the diols *VI*, *VII* and *XIII* depends on character of the solvent. In benzene, the diol *XIII* afforded practically exclusively the ether *VIII*, the diol *VI* gave the unrearranged *I* as the main product besides a small amount of the rearranged ether *VIII*, whereas reaction of the diol *VII* led to a 1 : 3 mixture of *I* and *VIII*. In dioxane, the proportion of the ether *VIII* in the reaction mixtures from *VI* and *VII* dropped in favour of the ether *I* whereas the diol *XIII* did not cyclize under these conditions. Although complete analysis of the cyclization mixtures was not carried out and minor components were not identified, some partial mechanistic conclusions about the cyclization of the diols *VI*, *VII* and *XIII* can be made. Thus, we can assume that ionization of the diol *XIII* leads to a relatively stable tertiary cyclobutyl cation *A* (Scheme 1). Ionization of the diol *VI* affords obviously primarily the tertiary cyclobutyl cation *B* which, however, under the given reaction conditions, to some extent rearranges to the more stable cation *A* (Scheme 1). This rearrangement, which probably proceeds by a disrotatory opening *via* a cyclopropyl methyl cation, is more facile in a less solvating and ionizing solvent, *i.e.* in benzene. The higher stability of the cyclobutyl cation *A* in comparison with that of the cation *B* is in accord with the fact that bicyclo[3,2,0]heptane is more stable than bicyclo[3,1,1]heptane[7]. The formation of both the ethers *I* and *VIII* in the cyclization of the diol *VII* indicates that the developing *p*-orbital interacts with both the neighbouring cyclopropane bonds. In a less solvating and ionizing solvent, such as benzene, interaction of the *p*-orbital with the $C_{(4)}$—$C_{(5)}$ bond is much more advantageous than interaction with the $C_{(3)}$—$C_{(5)}$ bond (Scheme 1)



m/z 260

$-C_2H_2$

m/z 234

SCHEME 3

Mass spectrum of compound *I* displays a dominant ion *m/z* 260, arising from the molecular ion by loss of ethylene molecule. Mass spectra of deuterated analogues of compound *I* (compounds *XV* and *XVI*, ref.[3]) prove that the eliminated species C_2H_4 contains the $C_{(4)}$ carbon atom. It follows therefore that, immediately after its formation, the molecular ion of compound *I* rearranges into the structure M^+_{VIII} which only then undergoes further decomposition (Scheme 2). Compounds *I* and *VIII* have almost identical mass spectra, corresponding to the structure *VIII*, and thus the fragmentation of M_I^+ proceeds *via* the structure M^+_{VIII}. The other abundant ions in the mass spectra of *I* and *VIII* are formed by decomposition of the ion *m/z* 260: loss of CH_3 affords an ion *m/z* 245, elimination of C_3H_5 species (the corresponding metastable peak m* 186·4 was observed) leads to an ion *m/z* 219 (Scheme 2). Also the concurrent loss of acetylene molecule (Scheme 3) is accompanied by a metastable transition (*m** 210·5).

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Unless stated otherwise, the optical rotations were measured in chloroform. The IR spectra were taken on a Zeiss UR 20 spectrophotometer, the ^{1}H NMR spectra were measured on a Tesla B 476 (60 MHz) instrument in deuteriochloroform with tetramethylsilane as internal standard; chemical shifts are given in ppm (δ-scale). The identity of samples prepared by different routes was proved by IR spectra and mixture melting points. The expression "usual work-up procedure" means that the solution was washed successively with 5% hydrochloric acid, 5% solution of sodium hydrogen carbonate and water, dried over sodium sulfate and taken down *in vacuo*. Unless stated otherwise, the crude reaction mixtures were chromatographed preparatively on plates of silica gel (20 × 20 cm) in light petroleum–ether–acetone (9 : 0·5 : 0·5). The corresponding zones were combined, the compound was eluted with ether and the solvent evaporated *in vacuo*.

3,5-Methylene-6-oxaandrostane-7,17-dione (*II*)

Chromium trioxide (4·5 g) was added portionwise at 0°C to a stirred solution of 3,5-methylene--6-oxaandrostan-17-one[1] (*I*) (4 g) in an acetic acid–acetic anhydride mixture (1 : 1; 80 ml). After standing overnight at room temperature, the mixture was poured into water and set aside for 30 min. The product was taken up in ether, the ethereal extract washed with 5% sodium hydrogen carbonate solution and water, dried over sodium sulfate and taken down *in vacuo*. The residue (3·5 g) was chromatographed on a column of silica gel (350 g) in light petroleum--ether–acetone (9 : 0·5 : 0·5). The pertinent fractions afforded 2·8 g of the lactone *II* which after crystallization from heptane melted at 199–201°C (1·6 g); $[\alpha]_D^{20}$ +79° (*c* 0·5). IR spectrum (chloroform): 1 735 cm^{-1}; ^{1}H NMR spectrum: 0·98 (s, 3 H, 18-CH_3), 1·09 (s, 3 H, 19-CH_3). For $C_{19}H_{26}O_3$ (302·4) calculated: 75·46% C, 8·67% H; found: 75·45% C, 8·62% H.

3,5-Methylene-6-oxaandrostan-17β-ol (*III*)

A solution of the lactone *II* (60 mg) in freshly distilled boron trifluoride etherate (1·7 ml) was added dropwise at 0°C during 5 min to a solution of sodium borohydride (100 mg) in diglym (1·7 ml). The solution was set aside at 0°C for 1 h and then at room temperature overnight.

After decomposition with a 5% aqueous solution of potassium hydrogen carbonate the product was taken up in ether, the ethereal extract washed with water, dried over sodium sulfate and taken down *in vacuo*. Crystallization of the residue (58 mg) from ligroin afforded 30 mg of the hydroxy derivative *III*, m.p. 198–198·5°C, $[\alpha]_D^{20}$ +50°C (*c* 0·5); IR spectrum (chloroform), cm^{-1}: 3 620, 1 248, 1 140, 1 053; ^1H NMR spectrum: 0·74 (s, 3 H, 18-CH_3), 0·99 (s, 3 H, 19-CH_3), 2·98 (t, 1 H, $C_{(7)}$—H, $J_{7,7}$ = 11 Hz), 3·58 (dd, 1 H, $C_{(7)}$—H, $J_{7,8}$ = 4 Hz, $J_{7,7}$ = 11 Hz), 3·56 (center of mt, 1 H, $C_{(17)}$—H). For $C_{19}H_{30}O_3$ (290·4) calculated: 78·57% C, 10·41% H; found: 78·33% C, 10·40% H.

3,5-Methylene-5,7-secoandrostane-5,7,17-triol (*IV*)

Lithium aluminium hydride (150 mg) was added to a solution of the lactone *II* (60 mg) in dioxane (5 ml) and the mixture was refluxed for 4 h. The excess hydride was destroyed with a saturated aqueous solution of sodium sulfate and the mixture was filtered through a short column of sodium sulfate. The solvent was evaporated *in vacuo* and the residue (58 mg) chromatographed on one plate of silica gel in light petroleum–ether–acetone (6 : 2 : 2). The corresponding zone afforded 45 mg of the triol *IV* which on crystallization from heptane melted at 87–89°C; $[\alpha]_D^{20}$ +24° (*c* 0·5); yield 22 mg. IR spectrum (KBr pellet), cm^{-1}: 3 610, 3 400, 1 138, 1 110, 1 071, 1 049, 1 022. For $C_{19}H_{32}O_3$ (308·5) calculated: 73·98% C, 10·46% H; found: 73·58% C, 10·13% H.

7·17β-Diacetoxy-3,5-methylene-5,7-secoandrostan-5-ol (*V*)

The triol *IV* (30 mg) was acetylated with acetic anhydride (0·3 ml) in pyridine (3 ml) overnight. The usual work-up procedure afforded an oily product (30 mg) which was subjected to preparative thin-layer chromatography on one plate of silica gel in light petroleum–ether–acetone (8 : 1 : 1). The corresponding zone afforded 24 mg of the diacetoxy derivative *V* which on crystallization from ligroin melted at 66–68°C; $[\alpha]_D^{20}$ +37° (*c* 0·5); yield 12 mg. IR spectrum (chloroform), cm^{-1}: 3 610, 1 738, 1 728, 1 714, 1 260; ^1H NMR spectrum: 0·835 (s, 3 H, 18-CH_3); 0·935 (s, 3 H, 19-CH_3); 2·025 (s, 6 H, 2× —OAc); 3·47 (dd, 1 H, $C_{(7)}$—H, $J_{7,8}$ = 7 Hz, $J_{7,7}$ = 13·5 Hz); 4·135 (dd, 1 H, $C_{(7)}$—H, $J_{7,8}$ = 3 Hz, $J_{7,7}$ = 13·5 Hz); 4·57 (mt, 1 H, $C_{(17)}$—H). For $C_{23}H_{36}O_5$ (392·5) calculated: 70·34% C, 9·52% H; found: 70·83% C, 9·52% H.

5·7-Dihydroxy-3,5-methylene-5,7-secoandrostan-17-one (*VI*)

N-Bromosuccinimide (1·4 g) was added to a solution of the triol *IV* (1 g) in aqueous tert-butyl alcohol (24 ml, 10% H_2O). After standing for 3 h at room temperature, the mixture was decomposed with 10% aqueous sodium hydrogen carbonate solution, concentrated *in vacuo* and the product taken up in ether. The ethereal extract was washed with water, dried over sodium sulfate and taken down *in vacuo*. The residue (1 g) was chromatographed on a column of silica gel (100 g) in light petroleum–ether–acetone (7 : 1·5 : 1·5). The less polar fractions afforded 300 mg of the lactone *II* which on crystallization from methanol melted at 199–201°C; $[\alpha]_D^{20}$ +79° (*c* 0·5); yield 220 mg. The more polar fractions gave the ketone *VI* (345 mg) which was crystallized from ether, m.p. 154–155°C; $[\alpha]_D^{20}$ +106° (*c* 0·5); yield 274 mg. IR spectrum (chloroform), cm^{-1}: 3 615, 3 610, 1 732; ^1H NMR spectrum: 0·82 (s, 3 H, 18-CH_3); 1·13 (s, 3 H, 19-CH_3); 3·615 (d, 1 H, $C_{(7)}$—H, $J_{7,7}$ = 11·5 Hz); 3·99 (d, 1 H, $C_{(7)}$—H, $J_{7,7}$ = 11·5 Hz). For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H; found: 74·30% C, 10·09% H.

3β,5-Cyclo-A-homo-6-oxa-5β-androstan-17-one[1] (*VIII*)

a) Perchloric acid (72%, 0·6 ml) was added to a solution of 3α,5-cyclo-6,7-seco-5α-androstane-6,7-diol[1] (*VII*) (1 g) in benzene (200 ml). The mixture was shaken for 5 min, then poured into water and the product was taken up in ether. The ethereal extract was washed with 5% aqueous potassium hydrogen carbonate solution, water, dried over sodium sulfate and taken down *in vacuo*. The residue (1 g) was chromatographed on a column of silica gel (100 g) in light petroleum–ether–acetone (9 : 0·5 : 0·5). Corresponding fractions afforded 820 mg of the crude product which was crystallized from methanol to give 150 mg of the ether *VIII*, m.p. 156–157°C, $[\alpha]_D^{20}$ +142° (*c* 0·5); reported[1] m.p. 156–157°C, $[\alpha]_D^{20}$ +142°.

b) Chromium trioxide (20 mg) was added to a solution of the hydroxy derivative *X* (28 mg) in pyridine (3 ml) and the mixture was allowed to stand at room temperature overnight. The usual work-up afforded 20 mg of the crude product which was chromatographed on one plate of silica gel. The corresponding zone gave 15 mg of the ether *VIII* which was crystallized from methanol, m.p. 156–157°C, $[\alpha]_D^{20}$ +142° (*c* 0·5); yield 8 mg.

3β,5-Cyclo-A-homo-6-oxa-5β-androstane-7,17-dione (*IX*)

Chromium trioxide (600 mg) was added portionwise at 0°C to a stirred solution of the cyclic ether *VIII* (600 mg) in a mixture of acetic acid and acetic anhydride (1 : 1, 12 ml). After standing overnight at room temperature the mixture was poured into ice-cold water and set aside for 30 min. The product was taken up in ether, the ethereal extract was washed with 5% aqueous potassium hydrogen carbonate solution and water, dried over sodium sulfate and taken down *in vacuo*. Chromatography of the residue (600 mg) on a column of silica gel (60 g) in light petroleum–ether–acetone (92 : 4 : 4) afforded 324 mg of product which on crystallization from heptane gave 215 mg of the lactone *IX*, m.p. 140–141°C, $[\alpha]_D^{20}$ +63° (*c* 0·5). IR spectrum (chloroform): 1 738 cm^{-1}; ^1H NMR spectrum: 0·885 (s, 3 H, 18-CH_3), 1·025 (s, 3 H, 19-CH_3). For $C_{19}H_{20}O_3$ (302·4) calculated: 75·46% C, 8·67% H; found: 75·40% C, 8·92% H.

3β,5-Cyclo-A-homo-6-oxa-5β-androstan-17β-ol (*X*)

A solution of the lactone *IX* (62 mg) in freshly distilled boron trifluoride etherate (1·7 ml) was added dropwise at 0°C during 5 min to a solution of sodium borohydride (100 mg) in diglyme (1·7 ml). The mixture was set aside at 0°C for 1 h and then at room temperature overnight. After decomposition with 5% aqueous potassium hydrogen carbonate solution the product was taken up in ether. The ethereal solution was washed with water, dried over sodium sulfate and taken down *in vacuo*. Chromatography of the residue on one plate of silica gel afforded 51 mg of the hydroxy derivative *X* which was crystallized from heptane; m.p. 111–112°C; yield 40 mg. IR spectrum (chloroform), cm^{-1}: 3 615, 1 113, 1 094, 1 061, 1 012. For $C_{19}H_{30}O_2$ (290·4) calculated: 78·57% C, 10·41% H; found: 78·07% C, 10·88% H.

3β,5-Cyclo-A-homo-5,7-seco-5β-androstane-5,7,17β-triol (*XI*)

Lithium aluminium hydride (500 mg) was added to a solution of the lactone *IX* (200 mg) in dioxane (15 ml) and the mixture was refluxed for 4 h. After decomposition of excess hydride with saturated aqueous solution of sodium sulfate, the mixture was filtered through a short column of sodium sulfate. The filtrate was taken down *in vacuo* and the residue (196 mg) crystallized from dioxane–heptane, affording 110 mg of the triol *XI*, m.p. 254–245°C; $[\alpha]_D^{20}$ +10° (*c* 0·5).

IR spectrum (chloroform), cm^{-1}: 3 620, 3 610. For $C_{19}H_{32}O_3$ (308·5) calculated: 73·98% C, 10·46% H; found: 73·44% C, 10·41% H.

3β,5-Cyclo-7,17β-diacetoxy-A-homo-5,7-seco-5β-androstan-5-ol (*XII*)

The triol *XI* (300 mg) was acetylated with acetic anhydride (2 ml) in pyridine (6 ml) overnight. The usual work-up procedure afforded 300 mg of the crude product which on crystallization from methanol gave 180 mg of the diacetoxy derivative *XII*, m.p. 113–115°C, $[\alpha]_D^{20}$ +43° (*c* 0·5). IR spectrum (tetrachloromethane), cm^{-1}: 3 615, 3 550, 1 753, 1 740, 1 248, 1 225, 1 041, 1 030. For $C_{23}H_{36}O_5$ (392·5) calculated: 70·37% C, 9·25% H; found: 69·86% C, 9·27% H.

5,7-Dihydroxy-3β,5-cyclo-A-homo-5,7-seco-5β-androstan-17-one (*XIII*)

N-Bromosuccinimide (330 mg) was added to a solution of the triol *XII* (300 mg) in aqueous tert-butyl alcohol (18 ml; 10% H_2O) and the mixture was set aside at room temperature overnight. The same work-up procedure as described for the preparation of the ketone *VI* afforded 300 mg of crude product which was crystallized from methanol to give 180 mg of the ketone *XIII*, m.p. 224–226°C, $[\alpha]_D^{20}$ +56° (*c* 0·5); IR spectrum (chloroform), cm^{-1}: 1 730, 3 605; ^1H NMR spectrum: 0·87 (s, 3 H, 18-CH_3); 1·00 (s, 3 H, 19-CH_3); 3·57 (bs, 1 H, $C_{(7)}$—H); 4·02 (mt, 1 H, $C_{(7)}$—H). For $C_{19}H_{30}O_3$ (306·4) calculated: 74·47% C, 9·87% H; found: 74·24% C, 9·65% H.

Reaction of Diols *VI*, *VII* and *XIII* with Perchloric Acid

A) Perchloric acid (0·05 ml; 72%) was added at 30°C to a stirred solution of the diol (60 mg) in benzene (3 ml) and the mixture was stirred at 30°C for 2 h. After pouring into water the product was taken up in ether. The ethereal extract was washed with 5% aqueous solution of potassium hydrogen carbonate and water, dried over sodium sulfate and taken down *in vacuo*. The residue (60 mg) was chromatographed on one plate of silica gel. The corresponding zone gave crude product which was analyzed by IR spectroscopy. The yields and ratios of the cyclic ethers *I* and *VIII* are given in Table I.

B) Perchloric acid (0·05 ml; 72%) was added at 30°C to a stirred solution of the diol (60 mg) in dioxane (3 ml). The mixture was stirred at 30°C for 2 h and worked up as described under *A*), yielding 60 mg of material which was chromatographed on one plate of silica gel. The corresponding zone afforded a mixture which was analyzed by IR spectroscopy: the pure standards *I* and *VIII*, their mixtures of known composition and the mixtures obtained according to the procedures *A*) and *B*) were measured in 4% tetrachloromethane solutions. The measurements were performed on a Perkin–Elmer 580 instrument (10fold expansion of abscissa, calibration by gaseous ammonia, 0·1 mm cells). For the quantitative evaluation the region 1 300–1 050 cm^{-1} was chosen. The respective molar extinction coefficients, ε_I and ε_{VIII}, of the pure compounds *I* and *VIII* were determined at seven wavenumbers: 1 081·5, 1 140·0, 1 156·0 and 1 243·0 cm^{-1} (analytical bands of compound *I*), 1 092·5 and 1 262·0 cm^{-1} (analytical bands of compound *VIII*) and 1 220·0 cm^{-1} (weak absorption of both the compounds *I* and *VIII* for background determination). Substitution into the relationship (1) afforded a set of seven equations with three unknowns (D_0, c_I and c_{VIII}) which was solved by the least squares method. From the thus-calculated values of c_I and c_{VIII} the relative amounts of compounds *I* and *VIII* in the analyzed mixtures were determined, together with the standard deviations of these quantities. The method was checked using artificial mixtures of *I* and *VIII* of known composition; the deviation did not exceed ±2%.

Mass Spectra

Mass spectra were taken on a double focusing AEI MS 902 instrument (Associated Electric Industries, Manchester, G.B.). The samples were introduced by direct inlet probe into the ion source heated at 120°C. Low resolution mass spectra were recorded using resolving power 1 000 and electron energy 70 eV. High-resolution measurements were carried out at the resolving power $m_1/(m_1 - m_2) = 10\,000$ (10% valley definition). The determined accurate masses were within the theoretical error limits (±3 ppm). The 7,7-dideuterio analogue of the compound *I* (*i.e.* compound *XV*) was prepared by a procedure analogous to the preparation of compound *I*, described previously[3,4]: Methyl 17-ethylenedioxy-6-hydroxy-3α,5-cyclo-6,7-seco-5α-androstan-7-oate[4] was reduced with lithium aluminium deuteride in boiling dioxane to give 7,7-dideuterio-17-ethylenedioxy-3α,5-cyclo-6,7-seco-5α-androstane-6,7-diol[4] which was converted by reaction with *p*-toluenesulfonyl chloride in pyridine into 7,7-dideuterio-17-ethylenedioxy-3,5-methylene-6-oxaandrostane[3]. Acid-catalyzed removal of the protecting group afforded the desired compound *XV*.

Partial mass spectra of compounds *I* and *VIII*; *m/z*, elemental composition and (in parentheses) the respective relative abundances for *I* and *VIII*: 219, $C_{14}H_{19}O_2$ (45 and 39); 234, $C_{15}H_{22}O_2$ (50 and 30); 245, $C_{16}H_{21}O_2$ (19 and 12); 260, $C_{17}H_{24}O_2$ (100 and 100); M^+ 288, $C_{19}H_{28}O_2$ (9 and 7).

Elemental analyses were carried out in the Analytical Laboratory of this Institute (Dr J. Horáček, Head). Infrared spectra were taken by Mrs K. Matoušková and Mr P. Formánek and interpreted by Dr J. Smolíková, ^{1}H NMR *spectra were measured by (the late) Dr M. Synáčková and Mrs J. Jelínková. Thanks are due to Mrs M. Bárová for technical assistance.*

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