REARRANGEMENT OF THE 16,17-CYCLOPROPANO DERIVATIVES*

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Some reactions of the isomeric cyclopropano derivatives *II* and *V* leading to D-homo steroids are described and the mechanism of these reactions is discussed.

In our previous paper[1] we have studied the Simmons–Smith methylenation of the 16,17 double bond in acetate *I* and prepared the isomeric cyclopropano derivatives *II* and *V*. Whereas the structure of the α adduct *II* was well established by ^{1}H NMR spectroscopy, the spectrum of the isomeric β adduct *V* did not show presence of the cyclopropane protons. Therefore a final proof of structure was desirable in the case of the β adduct *V*.

In this paper we present new spectral as well as chemical evidence, which confirm the structures assigned previously[1]. The ^{13}C-NMR data are presented in Table I. They prove the structure of the α adduct *II* all the signals of the cyclopropane carbons being shifted to higher field: The methylene carbon shows as a triplet at 14·91 ppm, $C_{(16)}$ signal is presented by a doublet at 23·83 ppm, the $C_{(17)}$ signal by a singlet at 47·68 ppm. In the spectrum of the β isomer signals at 26·57 ppm and 27·22 ppm belong undoubtly to the carbon atoms in the cyclopropane ring. However, the doublet at 65·36 ppm is typical of a $H—C_{(17)}—CO—CH_3$ grouping which is not present in the adduct if the structure *V* is correct. We therefore carried out deuterium exchange experiments and obtained the fully deuterated derivative *IV* containing according to the mass spectral evidence three deuterium atoms. This proves absence of hydrogen atom at $C_{(17)}$ and position of the cyclopropane ring at $C_{(16)}$ and $C_{(17)}$. In addition, following reactions prove the configurations of the cyclopropane ring in both adducts.

In continuation of our recent work[2] on participation of the cyclopropane ring in solvolytic or similar reactions we extended our studies to the 16,17 cyclopropane derivatives *XI*, *XII*, *VI* and *VII*. The alcohols *XI* and *XII* were described in our previous paper[1] alcohols *VI* and *VII* were prepared by metal hydride reduction of the ketone *V*; Jones' oxidation gave back the starting ketone.

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Mesylation of the alcohol *XI* afforded mixture of three compounds. Analysis proved the polar compound to be a mesylate, one of the lipophilic compound a chloro derivative and the second one an olefin. Spectral evidence showed presence of the cyclopropane ring and a vinyl group in the olefin which is therefore a product of simple elimination of the 20α hydroxyl group and has structure *XIV*. ^{1}H NMR spectra of both the chloro derivative and the mesylate show absence of the cyclopropane ring. The multiplet of protons at $C_{(6)}$, $C_{(16)}$ and $C_{(20)}$ lying between 5·1 and 5·4 ppm shows a very similar pattern in the chloro derivative as well as in the mesylate. In ad-

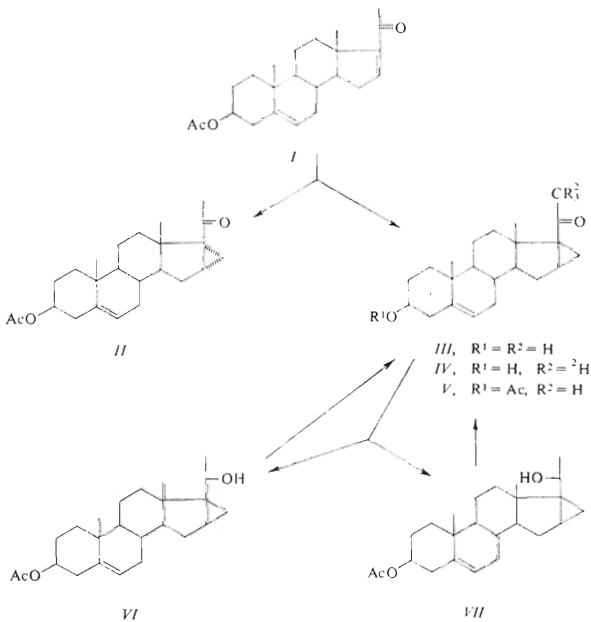
TABLE I

^{13}C NMR spectra of the isomeric cyclopropano derivatives *II* and *V*

Compound *II*		Compound *V*		
δ^a	assignment	δ^a	^1J (Hz)^a	assignment
207·87 (s)	CH_3—CO—C—	207·46 (s)	—	CH_3—CO—C—
170·39 (s)	CH_3—CO—O—	170·34 (s)	—	CH_3—CO—O—
140·18 (s)	$C_{(5)}$	140·08 (s)	—	$C_{(5)}$
122·03 (d)	$C_{(6)}$	122·11 (d)	147·3	$C_{(6)}$
73·90 (d)	$C_{(3)}$	73·84 (d)	151·6	$C_{(3)}$
50·55 (d)	$C_{(9)}$	65·36 (d)	124·2	$C_{(14)}$
47·78 (d)	$C_{(14)}$	51·22 (s)	—	$C_{(17)}$
47·68 (s)	$C_{(17)}$	49·87 (d)	124·2	$C_{(9)}$
40·76 (s)	$C_{(13)}$	41·08(s)	—	$C_{(13)}$
38·16 (t)	$C_{(4)}$	38·16 (t)	128·4	$C_{(4)}$
37·03 (t)	$C_{(1)}$	36·93 (t)^b	128·4	$C_{(1)} + C_{(12)}$
36·88 (s)	$C_{(10)}$	36·72 (s)	—	$C_{(10)}$
34·55 (t)	$C_{(12)}$	31·52 (t)	125·5	$C_{(7)}$
31·76 (t)	$C_{(7)}$	30·75 (d)	122·1	$C_{(8)}$
30·41 (d)	$C_{(8)}$	29·65 (t)	139·9	$C_{(15)}$
27·80 (t)	$C_{(2)}$	27·77 (t)	127·7	$C_{(2)}$
26·91 (q)	CH_3—CO—C—	27·82 (q)	127·0	CH_3—CO—C
26·05 (t)	$C_{(15)}$	27·22 (d)	168·4	$C_{(16)}$
23·83 (d)	$C_{(16)}$	26·57 (t)	163·1	$>CH_2$
21·33 (q)	CH_3—CO—O—	21·62 (t)	124·1	$C_{(11)}$
20·81 (t)	$C_{(11)}$	21·30 (q)	129·4	CH_3—CO—O—
19·24 (q)	$C_{(19)}$	19·16 (q)	128·3	$C_{(19)}$
17·02 (q)	$C_{(18)}$	16·79 (q)	126·3	$C_{(18)}$
14·91 (t)	$>CH_2$			

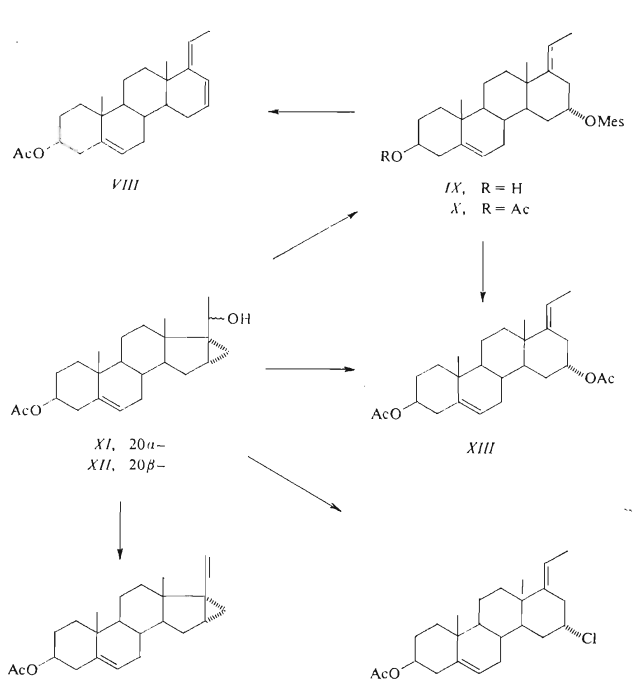
^{a} Bruker WH-300 instrument (75·47 MHz), $CDCl_3$ as internal standard, BB decoupling, ^1J constants determined from coupled spectra (±0·8 Hz). ^{b} The signal represents two carbon atoms.

dition, this multiplet resembles closely to the corresponding signals in the known[3] D-homo acetate *XIII* which we prepared from the alcohols *XI* and *XII* with thallium(III) acetate in acetic acid. We may conclude that the mesylate has structure *X* and the chloro derivative has structure *XV*. The 20β-hydroxy derivative *XII* gave on mesylation two products: The mesylate *X* and the chloro derivative *XV*. The olefin *XIV* was not detected. The alcohol *XI* when treated with acetic acid afforded the D-homo acetate *XIII* similarly, as described for the 20β isomer *XII*.



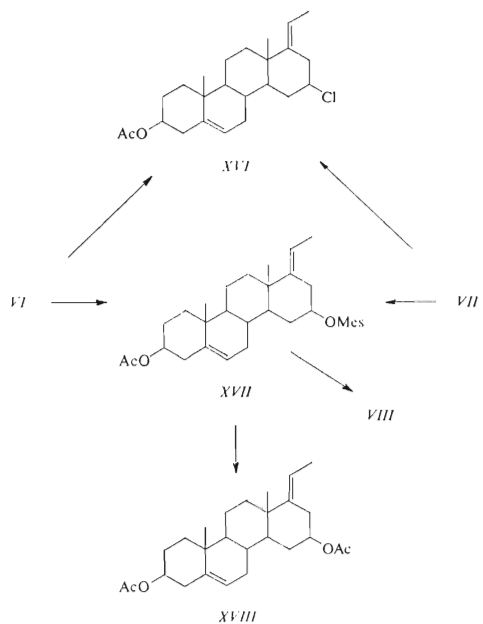
Solvolysis of the mesylate *X* led to a mixture of the D-homo acetate *XIII* (about 30%) and a lipophilic product (about 70%). This main product contained one isolated and two conjugated double bonds and no cyclopropane ring. Mass spectrum shows a molecular peak of 354 and a fragmentation which points to splitting off a two-carbon fragment. Identical triene was also obtained from the mesylate *X* with col-

lidine and from the chloride *XV* with potassium tert-butoxide. This triene is therefore 3β-acetoxy-D-homopregna-5,16,20-triene (*VIII*).



The epimeric alcohols *VI* and *VII* with the β-oriented cyclopropane ring afforded on mesylation an identical mixture of a chloro derivative (30%) and a mesylate (70%), the relationship being reversed in comparision with mesylation of the isomeric alcohols *II* and *V*. This mesylate is not identical with the mesylate *X* and on re-

action with collidine gave the triene *VIII*. This, together with spectral evidence points to structure *XVII*. Similar evidence proves the structure of the chloro derivative as a 16β-chloro compound *XVI* (Table II).



Acetolysis of the mesylate *XVII* gave a mixture of two products in about 1 : 1 relation. The lipophilic compound was again the triene *VIII*, the polar compound was the D-homo-16β-acetate *XVIII* as follows from spectral evidence. This acid-catalyzed rearrangement proceeds stereospecifically the configuration of the new substituent depending on the orientation of the cyclopropane ring. The electron deficient centre developed at $C_{(20)}$ on leaving of the substituent triggers the rearrangement. The stereospecificity is given by the different stereochemistry of the reaction at $C_{(16)}$ in the two isomeric cyclopropane structures.

EXPERIMENTAL

Melting points were determined on a Kofler block. Optical measurements were carried out in chloroform with an error of ±3°. The infrared spectra were recorded on the Zeiss UR 20 spectrometer in tetrachloromethane. The ^{1}H NMR spectra were recorded on the Tesla 60 MHz instrument in deuteriochloroform unless otherwise stated and corrected to tetramethylsilane. The chemical shift is given in ppm. The mass spectra were recorded on the mass spectrometer AEI MS 902. The identity of samples prepared by different routes was checked by mixture melting point determination, by thin layer chromatography (TLC), and by infrared and ^{1}H NMR spectra. Plates with 200 × 200 × 0·7 mm silica gel layer were used for preparative TLC. Usual working up of a solution implies washing the solution with 5% aqueous hydrochloric acid, water, 5% aqueous potassium hydrogen carbonate solution, water, drying with sodium sulphate, and evaporation of the solvent in vacuo. Ligroin refers to the fraction of b.p. 40–62°C.

TABLE II

^{1}H NMR spectra[a] of the dienes *XV* and *XVI* (Varian 200 MHz), deuteriobenzene)

δ	Multiplicity	Assignment
	Diene *XV*	
0·763	s	18-H
0·859	s	19-H
1·64	dd, $J_{20} = 6·7$, $J_{17} = 1·3$	21-H
1·756	s	3-OAc
2·12	dm, $J = 2·1$	17β-H
2·37	m, $J_6 = 2$	4β-H
2·48	ddd, $J_{gem} = 13·0$, $J_{3\alpha} = 5·3$, $J_2 = 2·0$	4α-H
2·79	dt, $J_{16\beta} = 2·5$, $J_{20} = 2·1$, $J_{gem} = 15$, $J_{15} = 1·8$	17α-H
4·25	q, $J_{17\alpha,17\beta} = 2·5-3·0$, $J_{15\alpha,15\beta} = 2·5-3·0$	16β-H
4·80	m, $J_{2\alpha,4\alpha} = 5·0$, $J_{2\beta,4\beta} = 10·0$	3α-H
5·24	m, $J_{4\alpha,4\beta} = 2·5$, $J_{7\alpha,7\beta} = 2·5$	6-H
5·43	dt, $J_{21} = 7·0$, $J_{17\alpha} = 1·5$, $J_{17\beta} = 1·0$	20-H
	Diene *XVI*	
0·793	s	18-H
0·817	s	19-H
1·463	dd, $J_{20} = 6·7$, $J_{17} = 1·5$	21-H
1·754	s	3-OAc
2·06	dt, $J_{gem} = 13·1$	15α-H
2·36	m	17α-H
2·49	ddd, $J_{gem} = 12·5$, $J_{3\alpha} = 5·3$, $J_2 = 2·0$	4α-H
3·1	ddd, $J_{gem} = 13·6$, $J_{16\alpha} = 4·8$, $J_{20} = 1·6$, $J_{21} = 1·4$	17β-H
3·6	m, $J_{15\beta,17\beta} = 12·2$, $J_{15\alpha,17\alpha} = 4·8$	16α-H
4·81	m, $J_{2\alpha,4\alpha} = 5·3$, $J_{2\beta,4\beta} = 11·4$	3α-H
5·2	m	6-H and 20-H

[a] Varian 200 MHz instrument; C_6D_6

3β-Hydroxy-16β,17β-cyclopropanopregn-5-en-20-one (*III*)

A solution of *V* (50 mg) in methanol (5 ml) was treated with a solution of potassium carbonate (50 mg) in water (0·5 ml) and refluxed for 5 min. After 20 h at room room temperature methanol was distilled off, the residue was diluted with water, and the product was taken into ether and worked up. Evaporation of the solvent and crystallization from methanol gave 16 mg of the alcohol *III*, m.p. 203–204°C (after sublimation), $[\alpha]_D^{20}$ −87° (*c* 0·84). IR spectrum: 3 625, 1 051 (hydroxyl), 3 085, 3 035 (cyclopropane and double bond), 1 680, 1 360 cm^{-1} (carbonyl). ^1H NMR spectrum: 0·83 (s, 18-H), 0·99 (s, 19-H), 2·00 (s, 21-H), 3·48 (mt, $W_{1/2}$ = 28 Hz, 3α-H), 5·31 (m, $W_{1/2}$ = 8 Hz, 6-H). For $C_{22}H_{32}O_2$ (328·5) calculated: 80·44% C, 9·82% H; found: 80·27% C, 9·42% H.

[21-$^2H_3$]3β-Hydroxy-16β,17β-cyclopropanopregn-5-en-20-one 3-Acetate (*IV*)

A solution of the ketone *III* (10 mg) in tetrahydrofuran (5 ml) was treated with a solution of lithiumdeuteroxide in deuterium oxide (1 ml) which was prepared by dissolving lithium (100 mg) in deuterium oxide (2·5 ml). One drop of the phase-transfer catalyst (Aliquat, Aldrich) was added and the mixture was stirred for 72 h at room temperature. The product was poured in water and isolated with ether in the usual way. Evaporation of the solvent afforded a residue pure on TLC which was submitted to mass spectroscopy. Mass spectrum: 85·5% *m/z* = 331, 14·5% *m/z* = 330.

16β,17β-Cyclopropanopregn-5-ene-3β,20α-diol 3-Acetate (*VI*)

The ketone *V* (100 mg) in tetrahydrofuran (6 ml) was treated with solid lithium tri-tert-butoxyaluminium hydride (200 mg) and allowed to stand at room temperature for 1 h. A new portion of the hydride (200 mg) was added and after 2 h at room temperature the mixture was decomposed with water and diluted hydrochlorid acid. The product was taken into ether and the ethereal solution was worked up as usual. The residue (80 mg) after evaporation of the solvent was chromatographed preparatively on 6 plates of silica gel (double developement in ligroin–ether 1 : 1). The zones with the lipophilic alcohol were collected, the product was extracted with ether, and ether was distilled off. The residue was crystallized from ether to yield 20 mg of the alcohol *VI*, m.p. 161–162°C, $[\alpha]_D^{20}$ −64° (*c* 1·85). Mass spectrum: *m/z* 312 (M−60). IR spectrum: 3 630 (hydroxyl), 3 075 (cyclopropane), 1 737, 1 247, 1 036 (acetate), 1 670, 3 025 cm^{-1} (double bond). ^1H NMR spectrum: 0·72 (s, 18-H), 1·02 (s, 19-H), 1·09 (d, *J* = 6·5 Hz, 21-H), 2·04 (s, 3β-acetate), 4·32 (q, *J* = 6·5 Hz, 20-H), 4·59 (m, $W_{1/2}$ = 21-Hz, 3α-H), 5·39 (m, $W_{1/2}$ = 9Hz, 6-H). For $C_{24}H_{36}O_3$ (372·5) calculated: 77·37% C, 9·74% H; found: 77·36% C, 9·68% H.

16β,17β-Cyclopropanopregn-5-ene-3β,20β-diol 3-Acetate (*VII*)

The zones with the polar alcohol from the chromatography in the foregoing experiment afforded after working up, extraction with ether and evaporation of the solvent a residue which on crystallization from ether gave 40 mg of the alcohol *VII*, m.p. 148–149°C, $[\alpha]_D^{20}$ −59·5° (*c* 1·86). Mass spectrum: *m/z* 312 (M−60). IR spectrum: 3 620, 3 605 (hydroxyl), 3 080 (cyclopropane), 1 738, 1 247, 1 036 (acetate), 1 670, 3 020 cm^{-1} (double bond). ^1H NMR spectrum: 0·77 (s, 18-H), 0·95 (d, *J* = 8 Hz, 21-H), 1·02 (s, 19-H), 2·04 (s, acetate), 4·24 (q, *J* = 6·5 Hz, 20-H), 4·57 (m, $W_{1/2}$ = 23 Hz, 3α-H), 5·43 (m, $W_{1/2}$ = 9 Hz, 6-H). For $C_{24}H_{36}O_3$ (372·5) calculated: 77·37% C, 9·74% H; found: 77·78% C, 9·65% H.

3β-Hydroxy-D-homopregna-5,16,17a-triene 3-Acetate (*VIII*)

a) The mesylate *X* (430 mg) and anhydrous sodium acetate (1·2 g) was refluxed in acetic acid (30 ml) and acetic anhydride (3 ml) for 8 h. After 18 h at room temperature the mixture was diluted with water, and the product was isolated with ether. Working up and evaporation of the solvent gave a residue which was chromatographed over silica gel (50 g) in ligroin–ether (2 : 1). Fractions with the lipophilic component yielded after working up and evaporation of the solvents 287 mg of a product which was crystallized from acetone to yield 165 mg of the triene *VIII*, m.p. 135–137°C, $[\alpha]_D^{20}$ −242° (*c* 1·09). IR spectrum: 3 085 sh, 3 040, 1 678, 1 645, 1 612 (double bonds), 1 740, 1 247, 1 036 cm^{-1} (acetate). ^1H NMR spectrum: 0·90 (s, 18-H), 1·02 (s, 19-H), 1·705 (d, J = 7 Hz, 21-H), 2·04 (s, acetate), 4·59 (mt, $W_{1/2}$ = 22 Hz, 3α-H), 5·11–5·94 (mts, 6-H, 16-H and 20-H), 6·40 (br d, J = 10 Hz, 17-H). Mass spectrum: m/z 354 (M^+), base peak 294 (M–60). For $C_{24}H_{34}O_2$ (354·5) calculated: 81·31% C, 9·67% H; found: 81·31% C, 9·29% H.

b) The chloro derivative *XV* (120 mg) was added to a solution of potassium (500 mg) in tert-butanol (15 ml) and allowed to stand at room temperature for 12 days. The mixture was diluted with water and the product was extracted into ether. Working up of the extract and evaporation of the solvent afforded a residue which was acetylated with acetic anhydride (0·6 ml) in pyridine (1 ml) at room temperature for 18 h. Working up gave a crude product which was purified by preparative TLC on 4 plates of silica gel in ligroin–ether (9 : 1) to yield 32 mg of the starting material and 65 mg of a lipophilic compound which on crystallization from acetone gave 39 mg of the triene *VIII*, m.p. 134–137°C, $[\alpha]_D^{20}$ −251° (*c* 1·3).

c) The mesylate *X* (106 mg) in *sym*-collidine (10 ml) was refluxed for 2 h in a nitrogen atmosphere. After cooling off the mixture was diluted with water, the product was taken into ether, and the ethereal solution was worked up. The residue after evaporation of the solvent was crystallized from ethanol to yield 41 mg of the triene *VIII*, m.p. 133–140°C, $[\alpha]_D^{20}$ −227° (*c* 1·2).

d) The mesylate *IV* (49 mg) in *sym*-collidine (5 ml) was refluxed for 150 min under nitrogen. After cooling off the mixture was worked up as described above. The residue was purified by preparative TLC on two plates of silica gel in ligroin–ether (9 : 1). Working up of the corresponding zones gave 25 mg of a crude product which was crystallized from acetone–water to give 12 mg of the triene *VIII*, m.p. 135–137°C, $[\alpha]_D^{20}$ −238° (*c* 0·6).

e) The mesylate *V* (100 mg) was refluxed with sodium acetate (250 mg) in acetic acid (7·5 ml) and acetic anhydride (0·75 ml) under nitrogen for 8 h. The mixture was diluted with water and the product was extracted with ether. Working up of the extract and evaporation of the solvent yielded 96 mg of a product which was chromatographed on two plates of silica gel in ligroin–ether (2 : 1). The zones with the lipophilic product afforded 42 mg of the triene *VIII*, m.p. 131–134°C (acetone–water), $[\alpha]_D^{20}$ −242° (*c* 0·7).

16α-Methanesulphonyloxy-D-homopregna-5,17a-dien-3β-ol (*IX*)

A solution of *X* (40 mg) in tetrahydrofuran (4 ml) was treated with lithium aluminiumhydride (40 mg) and allowed to stand at room temperature for 15 min. The excess hydride was decomposed with ethyl acetate and wet ether, diluted with water, and acidified with dilute hydrochloric acid. The ethereal layer was worked up as usual and ether removed. The residue was chromatographed on two plates of silica gel in ligroin–ether (3 : 2). The corresponding zones were collected and the product extracted with ether. Evaporation of the solvent and crystallization from chloroform–ligroin gave the alcohol *IX*, m.p. 125–127°C, $[\alpha]_D^{20}$ −135° (*c* 1·6). IR spectrum: 3 625 (hydroxyl), 3 065, 3 035 (double bonds), 1 342, 1 176 cm^{-1} (–SO_2–). ^1H NMR spectrum:

0·96 (s, 18-H), 1·01 (s, 19-H), 1·63 (d, J = 6·5 Hz, 21-H), 2·98 (s, mesylate), 3·53 (mt, $W_{1/2}$ = = 32 Hz, 3α-H), 5·28 (mt, 6β-H, 16α-H and 20β-H). For $C_{25}H_{38}O_5S$ (450·6) calculated: 66·63% C, 8·50% H, 7·12% S; found: 66·43% C, 8·50% H, 6·76% S.

3β,16α-Dihydroxy-D-homopregna-5,17a-diene 3-Acetate 16-Methanesulphonate (*X*)

a) A solution of *XI* (372 mg) in dichloromethane (10 ml) was cooled to 0°C and treated with triethylamine (1·1 ml) and methanesulphonyl chloride (1·43 ml). The mixture was kept at 0°C for 10 min, decomposed with water and ice and the product was taken into chloroform. The extract was worked up and the product was chromatographed on a silica gel column (50 g) in ligroin–ether (2 : 1). Fractions with the polar product were worked up and the crude product after evaporation of the solvents was crystallized from chloroform–ether to afford 120 mg of the mesylate *X*, m.p. 133–137°C (decomposition above 105°C), $[\alpha]_D^{20}$ −127° (*c* 1·2). IR spectrum: 3 070, 3 040, 1 679 (double bond), 1 740, 1 248 cm^{-1} (acetate). ^1H NMR spectrum: 0·92 (s, 18-H), 0·99 (s, 19-H), 1·60 (d, J = 7 Hz, 21-H), 2·00 (s, acetate), 2·95 (s, mesylate), 4·59 (mt, $W_{1/2}$ = 22·5 Hz, 3α-H), 5·28 (mt, 6-H, 16-H and 20-H). Mass spectrum: m/z 390 (M−HOAc), 354 (M−MesOH), 294 (basic peak; M−HOAc−MesOH), 279 (M−HOAc−MesOH−CH_3). For $C_{25}H_{38}O_5S$ (450·6) calculated: 66·63% C, 8·50% H, 7·12% S; found: 66·53% C, 8·55% H, 7·19% S.

b) The alcohol *XII* (180 mg) was esterified with methanesulphonyl chloride as described for *XI*. Similar working up and chromatography yielded 39 mg of the crude mesylate *X* which on crystallization from methanol gave needles, m.p. 130–135°C, $[\alpha]_D^{20}$ −116° (*c* 1·1).

3β,16α-Dihydroxy-D-homopregna-5,17a-diene 3,16-Diacetate (*XIII*)

a) A solution of *XII* (100 mg) in acetic acid (10 ml) was heated to 100°C for 2 h. After cooling off to room temperature the mixture was diluted with water and the product was taken into ether. Working up and evaporation gave 110 mg of an oily product which was chromatographed on a silica gel column (10 g) in ligroin–ether (9 : 1). The corresponding fractions were combined, solvents removed and the residual oil (82 mg) was crystallized from methanol to afford 45 mg of the diacetate *XIII*, m.p. 163–167°C. IR spectrum: 3 065, 3 040, 3 025, 1 654 (double bonds), 1 738, 1 247, 1 034 cm^{-1} (acetates). ^1H NMR spectrum (Varian 200 MHz instrument, in C_6D_6): 0·954 (s, 18-H), 1·017 (s, 19-H), 1·567 (dd, J = 7 Hz, J' = 1·4 Hz, 21-H), 1·995 (s, acetate), 2·034 (s, 3-acetate), 2·82 (dt, J = 15·3 Hz, J' = 1·8 Hz, J'' = 2·3 Hz, 17β-H), 4·59 (m, 3α-H), 5·11 (q, 16-H), 5·34 (m, 6-H, 20-H). Mass spectrum: m/z 354 (M−HOAc), 294 (M−2 HOAc). For $C_{26}H_{38}O_4$ (414·6) calculated: 75·32% C, 9·24% H; found: 75·38% C, 9·21% H.

b) The alcohol *XI* (100 mg) when treated with acetic acid as described in the foregoing experiment afforded after crystallization from ethanol 32 mg of the diacetate *XIII*, m.p. 167–169°C, $[\alpha]_D^{20}$ −136° (*c* 1·3).

c) A solution of *XII* (250 mg) and thallium(III) acetate (500 mg) in acetic acid (2·5 ml) was heated in a sealed tube to 75°C for 80 h. After cooling off the mixture was diluted with water and the product was extracted into ether. Working up yielded a residue (250 mg) which was chromatographed on 15 plates of silica gel in benzene–ether (19 : 1, double developement). Working up of the corresponding zones and crystallization from methanol gave 150 mg of the diacetate *XIII*, m.p. 167–168°C, $[\alpha]_D^{20}$ −132° (*c* 1·2).

d) The alcohol *XI* (250 mg) was treated with thallium(III) acetate in acetic acid as described above. Similar working up and crystallization from methanol afforded 190 mg of the diacetate *XIII*, m.p. 167–169°C, $[\alpha]_D^{20}$ −134° (*c* 0·8).

e) Elution of the chromatography after isolation of the triene *VIII* under *a*) afforded fractions with the polar component. Working up gave 85 mg of a product which on crystallization from methanol yielded 30 mg of the diacetate *XIII*, m.p. 163—158°C, $[\alpha]_D^{20}$ —121° (*c* 1·2).

3β-Hydroxy-16α,17α-cyclopropanopregna-5,20-diene 3-Acetate (*XIV*)

Fractions with the lipophilic component from the chromatography of the mesylate *X* under *a*) were worked up and solvent removed; the residue (160 mg) consisted of two components according to TLC. They were separated by preparative TLC on 8 plates of silica gel in ligroin–ether (9 : 1). Zones with the lipophilic component were collected and the product was extracted with ether. Evaporation of the solvent left 5 mg of the acetate *XIV*, m.p. 119—120°C (methanol), $[\alpha]_D^{20}$ —20° (*c* 1·5). IR spectrum: 3 085, 3 030, 3 005, 1 635, 992, 904 (CH_2=CH—), 3 070 (cyclopropane), 3 030, 1 670 (>C=CH—), 1 737, 1 246, 1 034 cm^{-1} (acetate). ^1H NMR spectrum: 0·26—0·73 (unresolved mt, cyclopropane protons), 0·87 (s, 18-H), 1·045 (s, 19-H), 2·03 (s, 3β-acetate), 5·38 (broad d, $W_{1/2}$ = 8 Hz, J = 4·5 Hz, 6-H), 4·68—5·22 and 5·98—6·49 (two mt, vinyl protons). For $C_{24}H_{34}O_2$ (354·5) calculated: 81·31% C, 9·67% H; found: 81·19% C, 9·52% H.

3β-Hydroxy-16α-chloro-D-homopregna-5,17a-diene 3-Acetate (*XV*)

a) Zones with the polar component from the preparative TLC from the foregoing experiment gave after working up 80 mg of a product which on crystallization from methanol yielded 55 mg of the chloro derivative *XV*, m.p. 194—196°C, $[\alpha]_D^{20}$ —145° (*c* 1·22). IR spectrum: 1 749, 1 248, 1 037 (acetate), 3 085, 3 035 cm^{-1} (double bond). Mass spectrum: *m/z* 390 (M). For $C_{24}H_{35}ClO_2$ (391·0) calculated: 73·73% C, 9·02% H, 9·07% Cl; found: 74·16% C, 8·80% H, 8·97% Cl.

b) Fractions with the lipophilic component from the chromatography of the mesylate *X* under *b*) were worked up, solvent removed, and the residue was purified by preparative TLC on two plates of silica gel in ligroin–ether (9 : 1). The zones with the chloro derivative were separated, extracted with ether, and ether was distilled off to yield after crystallization from acetone 17 mg of the chloro derivative *XV*, m.p. 193—195°C, $[\alpha]_D^{20}$ —156° (0·7).

3β-Hydroxy-16β-chloro-D-homopregna-5,17a-dien 3-Acetate (*XVI*)

a) A solution of the alcohol *VI* (240 mg) in dichloromethane (12 ml) was cooled to 0°C and treated with triethylamine (1·2 ml) and then with methanesulphonyl chloride (0·24 ml). After 10 min at 0°C the mixture was allowed to stand at room temperature for 30 min. Ice and water were added and the product was taken into chloroform. The extract was washed with a 1% sodium hydrogen carbonate solution, water, dried, and the solvent was removed. The residue (220 mg) was chromatographed on eight plates of silica gel in ligroin–ether (1 : 1). The zones with the lipophilic product afforded after working up 62 mg of the crude product which after crystallization from 95% acetone gave 29 mg of the chloro derivative *XVI*, m.p. 123—125°C, $[\alpha]_D^{20}$ —152° (*c* 0·8). IR spectrum (Perkin–Elmer 580): 3 058, 3 045, 1 676, 1 655, 829 (double bonds), 1 736, 1 243, 1 032 cm^{-1} (acetate). Mass spectrum: *m/z* 330, 2 115 ($C_{22}H_{31}Cl$; M—60). For $C_{24}H_{35}ClO_2$ (391·0) calculated: 73·73% C, 9·02% H; found: 73·45% C, 8·97% H.

b) The alcohol *VII* (108 mg) in dichloromethane (6 ml) was treated with triethylamine (0·6 ml) and methanesulphonyl chloride (0·12 ml) as described above. Similar working up and chromatography on three plates of silica gel in ligroin–ether (2 : 3) yielded 37 mg of a product. Crystallization from 95% acetone gave 16 mg of the chloro derivative *XVI*, m.p. 121—124°C, $[\alpha]_D^{20}$ —144° (*c* 1·2).

3β,16β-Dihydroxy-D-homopregna-5,17a-diene 3-Acetate 16-Methanesulphonate (*XVII*)

a) The zones with the polar component after isolation of the chloro derivative *XVI* under *a*) were worked up, extracted with ether, and solvent removed. The residue (115 mg) was crystallized from chloroform–ether to yield 72 mg of the mesylate *XVII*, m.p. 146–148°C, $[\alpha]_D^{20}$ (*c* 1·3). Mass spectrum: *m/z* 390 (M–HOAc), 354 (M–MesOH), 294 (basic peak, M–HOAc–MesOH), 279 (M–MesOH–HOAc–CH_3). IR spectrum: 3 090, 3 070, 3 030, 1 677, 1 659 (double bonds), 1 738, 1 246 (acetate), 1 345, 1 179 cm^{-1} (mesylate). ^1H NMR spectrum: 0·94 (s, 18-H), 1·02 (s, 19-H), 1·63 (d, J = 6·5 Hz, 21-H), 2·02 (s, acetate), 3·02 (s, mesylate), 5·45 (mt, $W_{1/2}$ = 28 Hz, 3α-Z and 20-H), 5·36 (unresolved doublet of met, $W_{1/2}$ = 11 Hz, J = 6 Hz, 6-H and 16-H). For $C_{25}H_{38}O_5S$ (450·6) calculated: 66·63% C, 8·50% H; found: 66·40% C, 8·42% H.

b) The zones with the polar component from the chromatography of the chloro derivative *XVI* under *b*) afforded after working up 66 mg of a crude product which was crystallized from chloroform–ether to yield 35 mg of the mesylate *XVII*, m.p. 149–151°C, $[\alpha]_D^{20}$ −121° (*c* 1·16).

3β,16β-Dihydroxy-D-homopregna-5,17a-diene 3,16-Diacetate (*XVIII*)

The zones with the polar component after isolation of the diene *VIII* under *e*) were worked up to yield 42·5 mg of a product which on crystallization from methanol gave 29 mg of the diacetate *XVIII*, m.p. 182–184°C, $[\alpha]_D^{20}$ −156° (*c* 0·6). IR spectrum (Perkin–Elmer 580): 3 060, 3 035 sh, 1 675, 1 655 (double bonds), 1 736, 1 242, 1 031, 1 025 cm^{-1} (acetates). ^1H NMR spectrum (Varian 200 MHz, C_6D_6): 0·987 (s, 19-H), 1·032 (s, 19-H), 1·63 (ddd, J = 6·6 Hz, J' = 1·4 Hz, J'' = 2 Hz, 21-H), 2·046 (s, 16-acetate), 2·067 (s, 3-acetate), 2·88 (ddd, J = 13·2 Hz J' = 5·3 Hz, J'' = 1·7 Hz, 17α-H), 4·61 (m, J = 11·4 Hz, J' = 5·3 Hz, 16α-H), 5·27–5·50, (mt, 3α-H, 6-H and 20-H). For $C_{26}H_{38}O_4$ (414·6) calculated: 75·32% C, 9·24% H; found: 75·63% C, 9·11% H.

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