68. 5,10:8,9-Disecosteroids (= Steroklastanes): A New Type of Modified Steroids

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Dedicated to Dr. *Günther Ohloff* on the occasion of his 65th birthday

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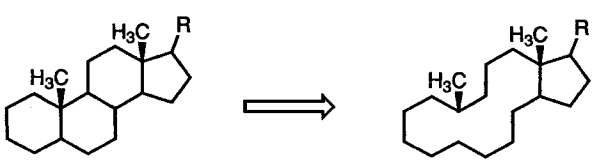
Thermolysis of steroidal 5α,8α-peroxides of type **3a–d** generates as major products the corresponding diseco compounds containing a 14-membered ring instead of the standard A-B-C-ring skeleton. Depending on the reaction conditions, either the primary products of type **9** or the α,β-unsaturated ketones of type **4**, formed by subsequent elimination of AcOH, are isolated. The latter, configurationally uniform compounds undergo epoxidation of the C(9)=C(10) bond followed by a *Baeyer-Villiger* oxidation to give, as final products, the 15-membered cyclic epoxyenol lactones of type **20** and **21**. The structures of the various products were determined by ^{1}H- and ^{13}C-NMR spectroscopy. The conformations of the 14- and 15-membered rings were established by X-ray structure analyses of **7** and **21a**. A reaction mechanism for the above transformations is discussed.

Introduction. – The possibility that steroids, by suitable chemical transformations involving bis-fragmentation of the C(5)–C(10) and C(8)–C(9) bonds as the key step (*Scheme 1*), could be correlated with some other naturally occurring products containing a 14-membered ring (*e.g.* cembrenoids [1], some derivatives of which, isolated from marine organisms, possess significant cytotoxic and antineo-plastic activity) or compounds of the prostaglandine type containing a substituted 5-membered ring prompted us to investigate synthetic ways by which these bonds could be cleaved. However, although there are several efficient methods for the single cleavage of the steroidal C(5)–C(10) [2] and C(8)–C(9) [3] bond, most of these methods cannot be effectively applied to induce fragmentation of both these bonds in the same molecule [4].

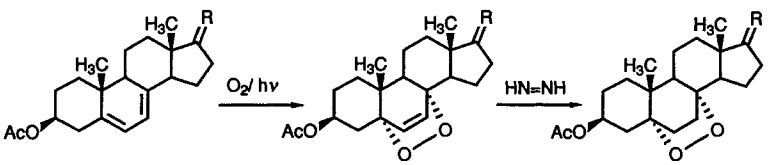
Scheme 1



In preliminary communications [5][6], we reported that a successful C(5)–C(10) and C(8)–C(9) bis-fragmentation was accomplished in steroidal 5α,8α-peroxides which, under thermal conditions, underwent the known cycloreversion-type reaction [7] to produce the desired bicyclic system containing a 14-membered ring (fused to ring D) instead of the three 6-membered rings A, B, and C[1]). In the present paper, we wish to give more detailed information on our synthesis of these modified 5,10:8,9-disecosteroids (= steroklastanes[2])), and also to describe some chemical transformations of these compounds.

Synthesis of the 5α,8α-Peroxides 3a–c. – The peroxides used as substrates in this study, *i.e.* 5,8α-epidioxy-5α-androstane-3β,17β-diol diacetate (**3a**), 5,8α-epidioxy-17-oxo-5α-androstan-3β-ol acetate (**3b**), and 5,8α-epidioxy-5α-cholestan-3β-ol acetate (**3c**), were prepared by oxygenation of the corresponding 5,7-dienes **1a–c** with singlet oxygen and subsequent diimide reduction of the olefinic double bond in the resulting 6-unsaturated peroxides (**2a–c**)[3]) as described in [7] (*Scheme 2*).

Scheme 2



Thermolysis of the 5α,8α-Peroxides 3a–c. – Thermolysis of **3a–c** was carried out in boiling AcOH or diglyme solution under N_2, until practically all starting material was consumed. The reaction mixtures were separated by column chromatography on silica gel or by prep. TLC. The following comments can be made about the results:

i) When subjected to thermolysis in AcOH, **3a**[4]) afforded the desired bis-fragmentation derivative (*E,E*)-17β-hydroxyandroklasta-3,9-diene-5,8-dione acetate (=(*E,E*)-17β-hydroxy-

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[1]) Recently, a similar 5,10:8,9-bis-fragmentation leading to another type of modified 'ansa-steroids' was described [8].

[2]) The name 'steroklastanes' for the modified 5,10:8,9-disecosteroids in which the whole hydrophenanthrene system of the steroid moiety is destroyed is suggested. The use of this name has been shown to be practical, particularly for compounds obtained from 5,10:8,9-disecosteroids by further chemical reactions, the naming of which according to the steroid nomenclature is rather awkward.

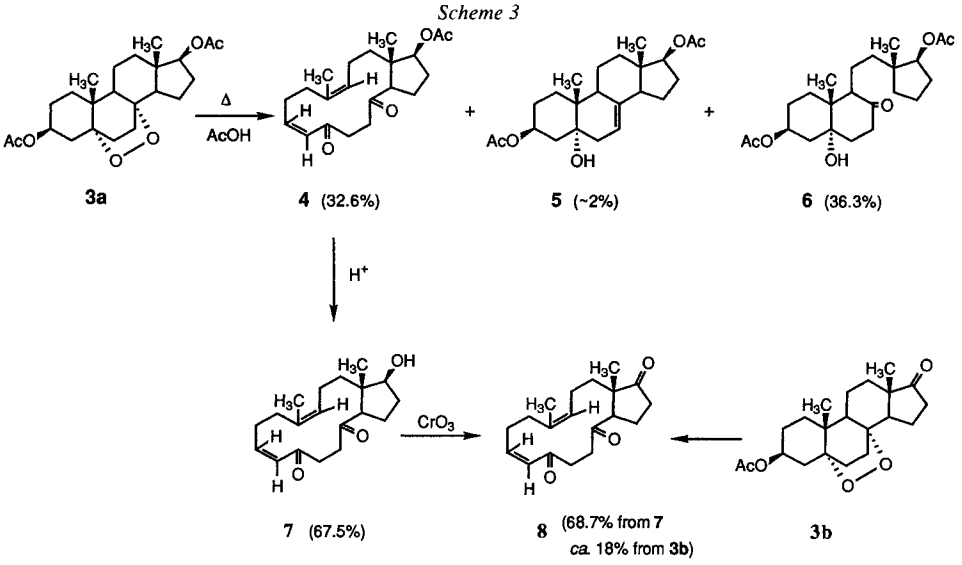
[3]) By this procedure, the 17-oxo peroxide **3b** was obtained in very poor yield, due to reaction of the 17-oxo function under conditions of diimide reduction. For that reason, the starting 17-oxo-5,7-diene **1b** was first reduced with $NaBH_4$, and the photo-oxygenation and diimide reduction were performed on the 17-hydroxy compound **1d** thus obtained; the saturated 17β-hydroxy peroxide **3d** was eventually transformed to **3b** by oxidation with the CrO_3-Py complex (see *Exper. Part*).

[4]) For the thermolysis of the 5α,8α-peroxide **3a** in AcOH, see also [9].

5,10:8,9-disecoandrosta-3,9-diene-5,8-dione acetate; **4**) in 32.6% yield, besides two products arising from the reductive dehydration and 8,14-mono-fragmentation, *i.e.* 5α-androst-7-ene-3β,5,17β-triol 3,17-diacetate (**5**; *ca.* 2%), and 3β,5,17β-trihydroxy-8,14-seco-5α-androstan-8-one 3,17-diacetate (**6**; 36.3%), while the rest was a complex mixture from which no characterized product could be isolated (*Scheme 3*)[5]).

Acid hydrolysis of the diseco compound **4** afforded crystalline (*E,E*)-17β-hydroxyandroklasta-3,9-diene-5,8-dione (= (*E,E*)-17β-hydroxy-5,10:8,9-disecoandrosta-3,9-diene-5,8-dione; **7**; 67.5%) whose structure was confirmed by X-ray structure analysis (see below) and which, upon subsequent oxidation (with *Kiliani* acid or CrO_3/pyridine complex) gave the corresponding 17-oxo derivative **8** (68.7%; *Scheme 3*).

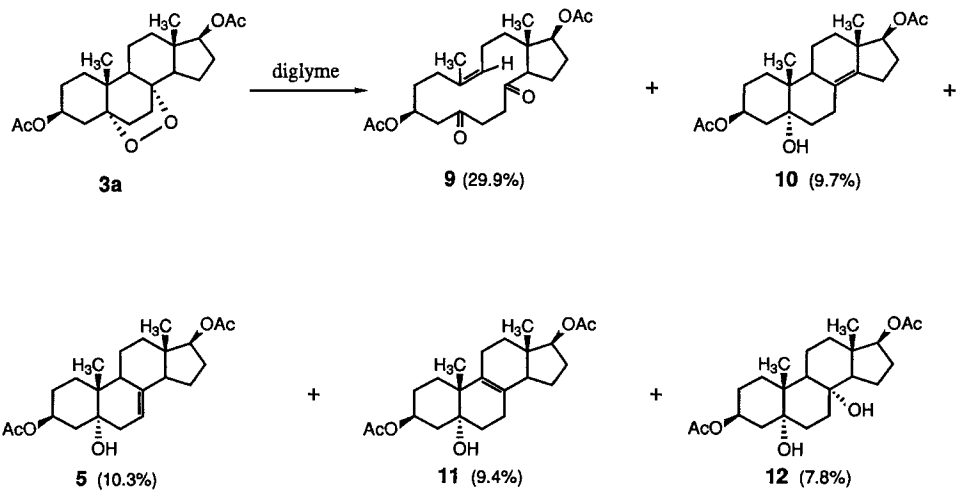
Scheme 3



On the other hand, when thermolysis of the 17β-acetoxy peroxide **3a** was performed in anhydrous diglyme solution, it gave products different from those obtained in AcOH (*Scheme 4*). In this case, spectral data revealed that the main reaction product contained 2 AcO groups (^{1}H-NMR: *s* at 2.02 and 2.04 ppm), 1 olefinic proton (^{1}H-NMR: *dd* at 5.11 ppm), and 1 Me group attached to the olefinic double bond (^{1}H-NMR: br. *s* at 1.62 ppm), and 2 keto functions (^{13}C-NMR (^{1}H-decoupled): 209.3 and 207.1 ppm). From this and from elemental microanalysis ($C_{23}H_{24}O_6$), it was concluded that, in diglyme solution, bis-fragmentation of **3a** took place without AcOH elimination to produce the hitherto unknown (*E*)-3β,17β-dihydroxyandroklast-9-ene-5,8-dione diacetate (= (*E*)-3β,17β-dihydroxy-5,10:8,9-disecoandrost-9-ene-5,8-dione diacetate; **9**; 29.9%), the other isolated products being the tetrol diacetate **12**, formed by reductive cleavage of the peroxide bridge, and the corresponding 7-, 8(14)-, and 8(9)-unsaturated 5α-alcohols (**5**, **10**, and **11**), obviously arising from the 5α,8α-diol **12** by loss of the 8α-OH group as H_2O molecule (*Scheme 4*).

[5]) All yields given in *Schemes 3–6* refer to crude products (see *Exper. Part*).

Scheme 4



To correlate the diseco diketones **4** and **9**, the 3β-acetoxy derivative **9** was heated in boiling AcOH for 4 h. In this solvent, it was quantitatively transformed to the 3-unsaturated diseco diketone **4**, showing, thus, that both compounds have the same geometry of the 9-olefinic bond.

ii) Thermolysis of the 17-oxo 5α-peroxide **3b** was carried out in AcOH; it was found that it also proceeded by C(5)–C(10) and C(8)–C(9) bis-fragmentation along with AcOH elimination to give, as the only isolable derivative, (*E,E*)-androklasta-3,9-diene-5,8,17-trione (= (*E,E*)-5,10:8,9-disecoandrosta-3,9-diene-5,8,17-trione; **8**, *ca.* 18%; *Scheme 3*), while the rest was a complex mixture from which no identifiable product could be isolated. The triketone **8** was identical in all respects with the 17-oxo derivative obtained from the 17β-hydroxy compound **7** by CrO_3 oxidation, indicating that in both androstane series (17β-AcO and 17-oxo) the bis-fragmentation follows the same stereochemical course.

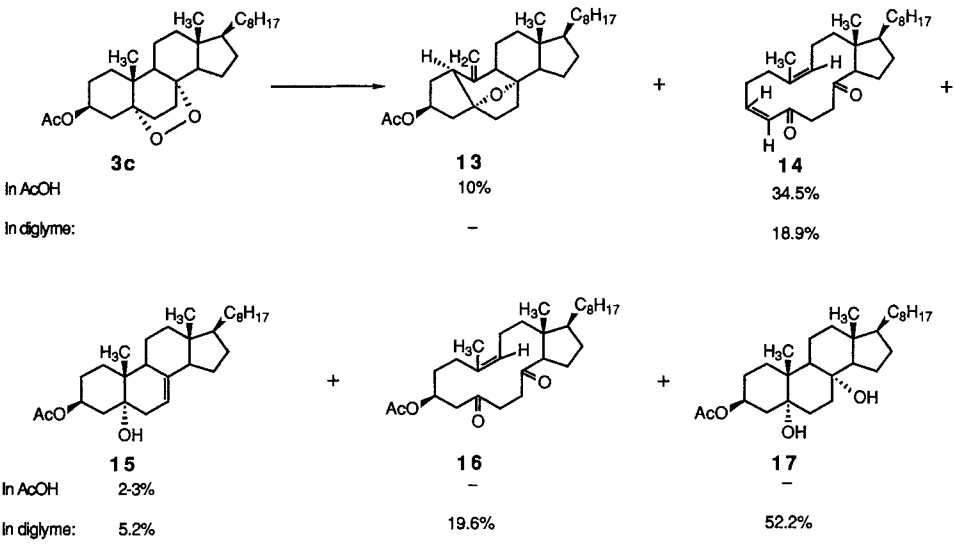
iii) Thermolysis of the cholestane 5α,8α-peroxide **3c** in AcOH afforded as the main product the expected (*E,E*)-choleklasta-3,9-diene-5,8-dione (= (*E,E*)-5,10:8,9-disecocholesta-3,9-diene-5,8-dione; **14**; 34.5%) and two minor components, *i.e.* the rearranged product 5,8α-epoxy-5(10→1)*abeo*-1β(H),5α-cholest-10(19)-en-3β-yl acetate (**13**; *ca.* 10%) and 5α-cholest-7-ene-3β,5-diol 3-acetate (**15**; 2–3%), the latter arising from reductive dehydration of **3c** (*Scheme 5*)[6]).

On the other hand, thermolysis of the peroxide **3c** in diglyme, which also resulted in C(5)–C(10) and C(8)–C(9) bis-fragmentation, afforded both the 3-unsaturated diseco diketone **14** (18.9%) and the 3β-acetoxydiseco diketone **16** (19.6%). The correlation of these two products was accomplished by quantitative transformation of the 3β-acetate **16** to the

[6]) For the thermolysis of the 5α,8α-peroxide **3c** in AcOH, see also [6].

3-unsaturated analogue **14** upon heating in boiling AcOH for 2 h. However, the main thermal reaction of **3c** in diglyme was reductive opening of the peroxide bridge which led to the 5α,8α-diol **17** (52.2%) and its dehydration product **15** (5.2%)[7]).

Scheme 5



The configuration at the C(3)=C(4) bond in the 5,10:8,9-diseco compounds **4**, **8**, and **14** was determined on the basis of ^{1}H-NMR data (J (3,4) = 17 Hz; see also *Table 1*, below), while the (*E*)-configuration at the C(9)=C(10) bond was deduced from mechanistic considerations (*i.e.* assuming that the thermal decomposition of the 5α,8α-peroxides **3a–c** proceeded as a concerted, allowed $[_{\pi}2_s+_{\pi}2_s+_{\pi}2_s]$ process)[8]).

Chemistry. – Treatment of the diseco diketones **4** and **14** with 3 mol-equiv. of 3-chloroperbenzoic acid in the presence of $NaHCO_3$ in CH_2Cl_2/Et_2O 1:1 at room temperature resulted, first, in non-stereospecific epoxidation of the C(9)=C(10) bond leading to the formation of the stereoisomeric (9*R*,10*R*)- and (9*S*,10*S*)-epoxides **18a** and **18c**, and **19a** and **19c**, respectively[9]), which subsequently underwent *Baeyer-Villiger* oxidation to give the 15-membered cyclic (9*R*,10*R*)- and (9*S*,10*S*)-epoxy-enol lactones **20a** and **20c**, and **21a** and **21c**, respectively (*Scheme 6*).

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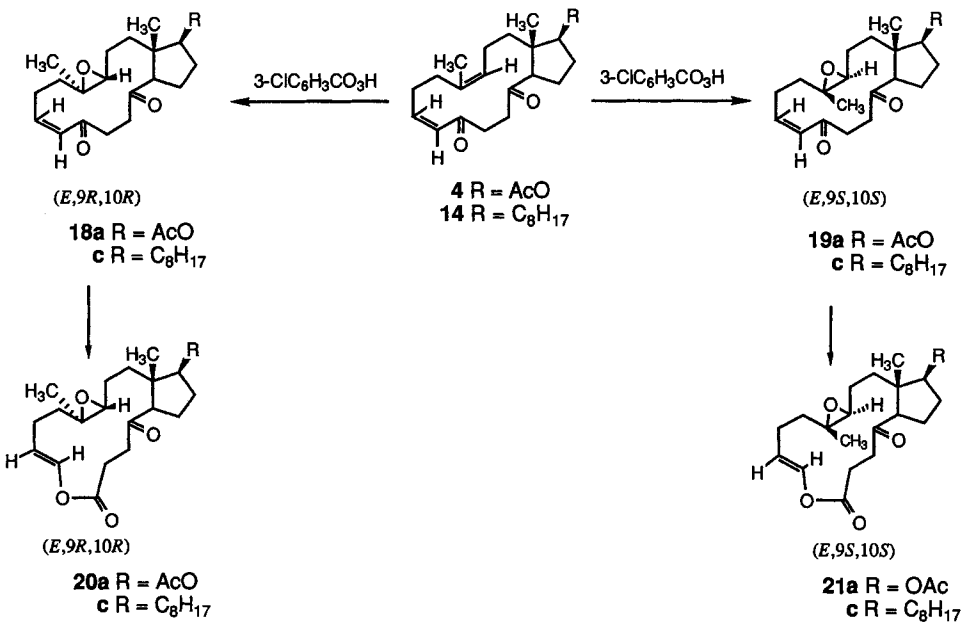
[7]) Actually, the dehydration of **17** gave a mixture of 7-, 8(9)-, and 8(14)-unsaturated stereoisomers, in which the 7-ene **15** prevailed. Thus, after recrystallization, only **15** could be obtained in pure state (see *Exper. Part*) [4].

[8]) This configuration for the compounds of the androstane series was confirmed by X-ray structure analysis carried out on the 17β-hydroxy derivative **7** (*cf.* also [10]).

[9]) In the 17β-acetoxyandrostane series, it was possible to separate the epoxides **18a** and **19a** by column chromatography and to correlate them with the corresponding epoxy-enol lactones **20a** and **21a**, respectively, while in the cholestane series, the epoxides **18c** and **19c** could not be separated (see *Exper. Part*).

Scheme 6



Structures and Conformations of 4, 8, 14, and 18–21. – In an attempt to gain more insight concerning the configurational and conformational features of the large ring system just described, detailed ^{1}H-NMR and ^{13}C-NMR analyses were performed on the 14-membered-ring diene-diones **4**, **8**, and **14**, and epoxides **18a** and **19a**, as well as on the 15-membered-ring epoxy-enol lactones **20** and **21**.

^{1}H-NMR Spectra of **4**, **8**, **14**, **18a**, *and* **19a**. The data listed in *Table 1* are in good agreement with the proposed strutures of the 5,10:8,9-disecosteroids. Beside the (3*E*)-configuration, no other details can actually be extracted from these data. Especially, no specific informations about the conformation of the 14-membered rings can be deduced.

Table 1. *^{1}H-NMR of Selected 14-Membered-Ring Protons of* **4**, **8**, **14**, **18a**, *and* **19a**[a])

Proton	Chemical shifts[b]) and coupling patterns[c])				
	4	**8**	**14**	**18a**	**19a**
H–C(3)	6.58 (*dt*)	6.60 (*dt*)	6.52 (*dt*)	6.75 (*ddd*)	6.72 (*ddd*)
H–C(4)	5.95 (*dm*)	5.95 (*dt*)	5.92 (*dm*)	6.21 (*dm*)	6.14 (*dm*)
H_α–C(6)	2.96 (*dt*)	– [c])	– [c])	– [c])	– [c])
H_β–C(6)	2.51 (*dt*)	– [c])	– [c])	– [c])	– [c])
H_α–C(7)	2.61 (*dt*)	– [c])	– [c])	– [c])	– [c])
H_β–C(7)	2.70 (*dt*)	– [c])	– [c])	– [c])	– [c])
H–C(9)	5.2 (br. *t*)	5.2 (br. *t*)	5.2 (*dd*)	2.54 (*dd*)	2.76 (*dd*)
CH_3(18)	0.85 (*s*)	0.85 (*s*)	0.75 (*s*)	0.98 (*s*)	0.90 (*s*)
CH_3(19)	1.59 (br. *s*)	1.59 (br. *s*)	1.60 (br. *s*)	1.21 (br. *s*)	1.24 (br. *s*)

[a]) ^{1}H-NMR spectra were recorded in $CDCl_3$ at r.t. and 360 MHz.
[b]) δ in ppm rel. to TMS.
[c]) Signal masked or ill-resolved due to overlap with other resonances.

The ^{1}H-NMR data of the epimeric 9,10-epoxides **18a** and **19a** are also scarcely different. Only the signals of H–C(9) and H–C(18) show a characteristic difference, but no information about the overall conformation of the large ring can be deduced (*Table 1*).

^{1}H-NMR Spectra of **20** *and* **21**. The ^{1}H-NMR signals of the protons of the 15-membered ring in these epoxy-enol lactones (see *Table 2*) are much better resolved in the high-field region: for **21a** and **21c**, one can find the signals of 2 H–C(6), 2 H–C(7), H–C(9), and H–C(14) clearly separated. The resonances of CH_3(18) are different for the epimeric epoxy-enol lactones in both pairs **20a/21a** and **20c/21c**. An X-ray structure analysis of **21c** showed the overall conformation of the 15-membered ring in the solid state (see below). Assuming that the geometry of the molecule is similar in solution and in the solid state, one can understand the observed coupling patterns in the ^{1}H-NMR spectra and assign the resonances. The small but characteristic chemical-shift differences for CH_3(18) can be rationalized as well (*cf. Table 2*, $\Delta\delta(CH_3(18)) \approx 0.1$ ppm).

Table 2. *^{1}H-NMR Data of Selected 15-Membered-Ring Protons of Epoxy-enol Lactones* **20** *and* **21**[a])

Proton	Chemical shifts[b]) and coupling patterns			
	20a	**20c**	**21a**	**21c**
H–C(3)	5.28 (*ddd*)	5.30 (*ddd*)	5.21 (*td*)	5.21 (*td*)
H–C(4)	7.06 (*dd*)	7.0 (*dd*)	7.03 (*dd*)	7.03 (*dd*)
H_α–C(6)	– [c])	– [c])	2.42 (*ddd*)	2.40 (*ddd*)
H_β–C(6)	– [c])	– [c])	3.19 (*ddd*)	3.10 (*ddd*)
H_α–C(7)	– [c])	– [c])	2.92 (*ddd*)	2.80 (*ddd*)
H_β–C(7)	– [c])	– [c])	2.59 (*dd*)	2.60 [c])
H–C(9)	– [c])	– [c])	2.53 (*dd*)	2.50 (*t*)
H–C(14)	– [c])	– [c])	2.75 (*dd*)	2.70 [c])
CH_3(18)	1.12 (*s*)	1.02 (*s*)	0.99 (*s*)	0.90 (*s*)
CH_3(19)	1.18 (*s*)	1.20 (*s*)	1.18 (*s*)	1.17 (*s*)

[a]) ^{1}H-NMR spectra were recorded in $CDCl_3$ at r.t. and 360 MHz.
[b]) δ in ppm rel. to TMS.
[c]) Signal masked or ill-resolved due to overlap with other resonances.

^{13}C-NMR Spectra for **4**, **8**, **14**, **18a**, *and* **19a**. The chemical shifts of the same C-atoms in the different substitution at C(17) (AcO, =O, C_8H_{17}) or by the presence of an epoxide ring instead of the double bond at C(9). Small differences between the chemical shifts of C(14) and C(17) in the two epimeric epoxides **18a** and **19a** are probably due to a different spatial arrangement of the C-atoms in the 14-membered ring. However, the shift differences are so small that one cannot propose two different conformations for the two epimers (*Table 3*).

^{13}C-NMR Spectra for **20** *and* **21**. In comparison to the small differences of the corresponding ^{13}C-NMR shifts in the epimeric epoxides **18a/19a** containing a 14-membered ring (see above), one can find quite reasonable shift differences for C(14) and C(17) in both epimeric epoxy-enol lactone pairs **20a/21a** and **20c/21c** (15-membered ring). Most likely, these differences of *ca.* 4–5 ppm for the epimers **20c** and **21c** with a cholestane side chain can be attributed to a different spatial arrangement of C(12) and C(11). In **21c** with a β-oriented CH_3(19), the bond C(12)–C(11) is in a *cis*-arrangement to CH_3(18) (confirmed by X-ray structure analysis of **21a**), while in **20c** with an α-oriented CH_3(19), the bond C(12)–C(11) is oriented parallel to H–C(17) and H–C(14). The upfield shift of the resonances of C(14) from 62.4 to 58.8 ppm and of C(17) from 55.7 to 50.2 ppm can be explained by the γ shift of the C(12)–C(11) bond in the substances with an α-oriented CH_3(19) group (*Table 4*).

Since the usual physical methods (^{1}H-NMR and ^{13}C-NMR spectroscopy) have shown to be inadequate for a complete configurational assignment at C(9) and C(19) in **18–21**, the *trans*-(9*S*,10*S*)-configuration at the epoxide ring of the epoxy-enol lactone **21a** was established by X-ray structure analysis (which also revealed the (3*E*)-configuration; see below). In this way, indirectly, the proposed (3*E*,9*E*)-configuration at the two double bonds of the 14-membered ring in the diseco compounds was unequivocally confirmed.

Table 3. *^{13}C-NMR Chemical Shifts*[a]) of **4**, **8**, **14**, **18a**, *and* **19a**[b])

C-atom	**4**	**8**	**14**	**18a**	**19a**
C(1)	34.6	35.2	34.8	37.1	37.1
C(2)	29.3	29.2	29.2	29.4	29.2
C(3)	148.1	148.8	147.7	147.2	147.3
C(4)	130.2	129.6	129.8	130.1	130.7
C(5)	200.7	200.3	201.3	198.0	199.5
C(6)	37.7	37.9	37.9	35.9	35.4
C(7)	40.4	39.8	41.8	40.0	40.7
C(8)	208.2	208.6	209.8	209.4	210.9
C(9)	128.2	127.8	128.4	64.2	64.7
C(10)	133.0	133.3	132.8	59.2	59.2
C(11)	22.6	23.8	24.4	23.5	24.2
C(12)	37.7	35.2	38.8	36.1	37.0
C(13)	47.1	52.6	48.4	47.1	47.7
C(14)	54.6	54.7	57.7	55.9	57.7
C(15)	22.0	21.0	21.6	23.2	23.8
C(16)	27.2	36.7	26.6	27.5	27.2
C(17)	78.4	220.0	50.2	79.5	80.2
C(18)	16.5	19.1	17.5	15.8	16.1
C(19)	15.5	15.5	15.8	14.1	13.0

[a]) δ in ppm rel. to TMS.
[b]) Spectra measured in $CDCl_3$ at r.t. and 90 MHz.

Table 4. *^{13}C-NMR Chemical Shifts*[a]) of **20** *and* **21**[b])

C-atom	**20a**	**20c**	**21a**	**21c**
C(1)	38.8	37.5	37.8	38.1
C(2)	23.2	23.0	23.8	25.2
C(3)	114.8	115.1	114.1	113.6
C(4)	135.8	135.7	134.9	135.3
C(5)	169.3	170.1	167.8	168.2
C(6)	30.3	30.1	28.3	28.4
C(7)	38.8	38.6	41.1	40.5
C(8)	209.8	210.5	209.6	211.6
C(9)	64.9	66.0	64.7	65.8
C(10)	59.4	59.4	59.5	59.8
C(11)	23.2	23.0	24.2	24.4
C(12)	36.2	36.6	37.0	39.5
C(13)	46.0	46.1	47.5	49.4
C(14)	58.4	58.8	58.2	62.4
C(15)	23.8	25.9	23.8	25.4
C(16)	27.7	28.0	27.9	27.7
C(17)	79.7	50.2	80.4	55.7
C(18)	15.2	16.0	15.1	15.8
C(19)	13.3	16.0	12.9	14.0

[a]) δ in ppm rel. to TMS.
[b]) Spectra measured in $CDCl_3$ at r.t. and 90 MHz.

X-Ray Structure Analyses of **7** *and* **21a**. The results of X-ray structure analyses are shown in *Figs. 1* and *2* (PLUTO program) [12]. Crystal data for both compounds are given in *Table 5*.

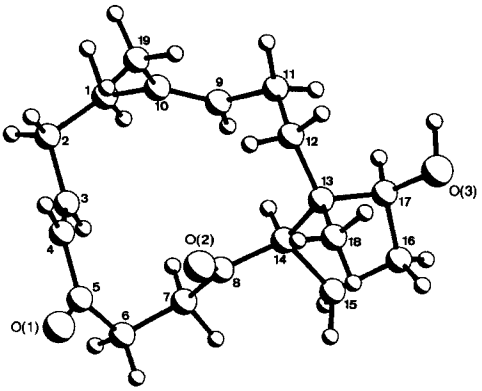


Fig. 1. *PLUTO plot of* **7**

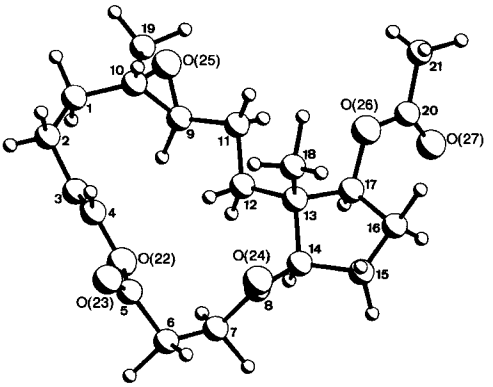


Fig. 2. *PLUTO plot of* **21a**

Table 5. *Crystal Data for* **7** *and* **21**

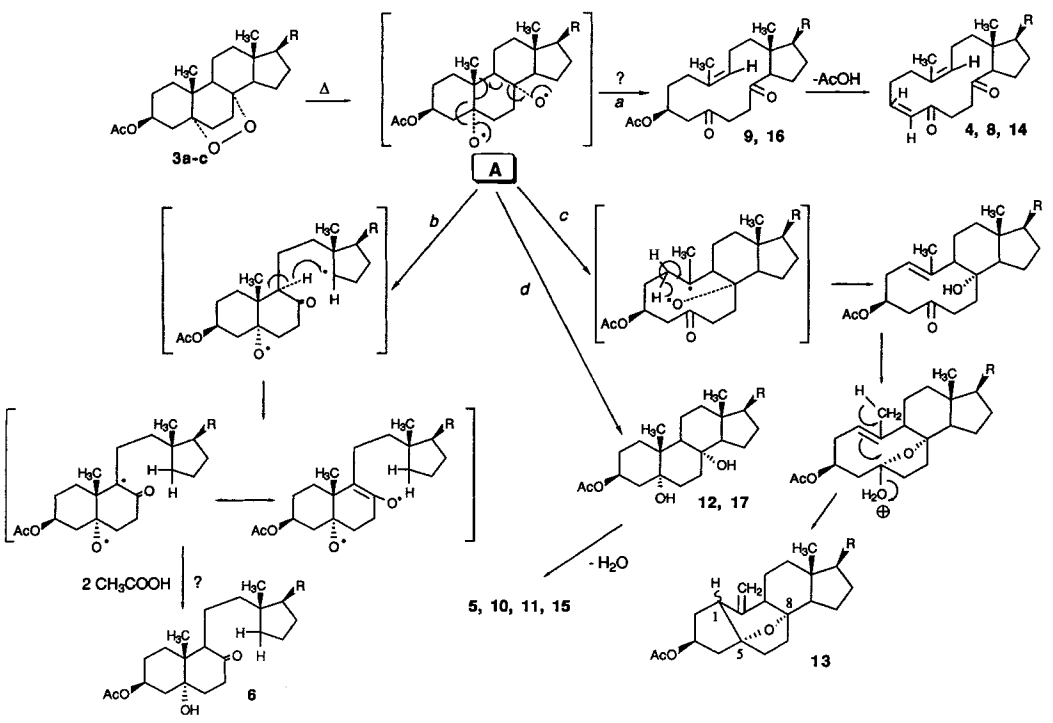
Compound	**7**	**21a**
Formula	$C_{19}H_{28}O_3$	$C_{21}H_{30}O_6$
Crystal system	monoclinic	monoclinic
Space group	$P2_1$	$P2_1$
a [Å]	8.773(1)	6.162(2)
b [Å]	10.290(2)	8.174(3)
c [Å]	9.878(1)	20.274(2)
β [°]	106.35(1)	94.40(2)
V [Å^3]	856	1018
Z	2	2
Calc. density [g/cm^3]	1.181	1.182
No. of reflections	1961	2018
No. of non-zero reflections ($I > 2\,\sigma(I)$)	1863	1729
No. of parameters	310	334
Final R factor	0.069	0.049
Max. residual electron density [e/Å^3]	0.280	0.187

Intensity measurements were made on a *Philips PW 1100* automatic diffractometer with monochromated CuK_α radiation. The structures were solved by direct methods (MULTAN 80) [13]. All H-atoms were found from difference *Fourier* maps. Least-squares refinements were carried out with anisotropic thermal parameters for non-H-atoms and isotropic ones for H-atoms. Final fractional coordinates with their standard deviations and bond lengths are deposited with the *Cambridge Crystallographic Data Center*. The latter agree, in general, with the standard values quoted in the literature.

The main structural feature of the 15-membered ring of **21a** is the dihedral angle of 19° between the C(3)=C(4) and the C(5)=O(23) bonds. In **7**, the dihedral angle between the C(3)=C(4) bond and the adjacent keto group amounts to 17°.

Mechanistic Considerations (*Scheme 7*). – Although the stereospecific bis-fragmentation of the steroidal 5α,8α-peroxides **3a–c** producing diseco diketones with (9*E*)-configuration could be interpreted in terms of a concerted symmetry-allowed [$_\pi2_s+_\pi2_s+_\pi2_s$] process, participation of a biradical of type **A** cannot be excluded on the basis of present evidence. Such an intermediate could undergo (see *Scheme 7*): *i*) bis-fragmentation (*Path a*) to give the diseco compounds **9**, **16**, and/or **4**, **8**, **14**; *ii*) rearrangement prior to H-abstraction (*Path b*) to afford the 8,14-mono-fragmentation product **6**; *iii*) rearrangement with subsequent H_2O elimination (*Path c*) to produce product **13**; *iv*) H-abstraction (to **12** and **17**; *Path d*) followed by loss of H_2O to give the products **5**, **10**, **11**, and **15**. Since (in *Path b*) there is no chemical evidence that H-atoms are extracted from AcOH, a probable source of H-atoms could be the substrate molecule.

Scheme 7



The authors from Yugoslavia are grateful to the *Serbian Academy of Sciences and Arts* and to the *Serbian Research Fund* for financial support.

Experimental Part

1. *General*[10]). All evaporations of solvents were carried out under reduced pressure. Prep. column chromatography: silica gel 0.063–0.200 mm. TLC: control of reactions and separation of products on silica gel *G* (*Stahl*) with benzene/AcOEt 9:1 or 7:3, detection with 50% aq. H_2SO_4 soln. M.p.: uncorrected. UV spectra: *Varian UV Super Scan 3* spectrophotometer: λ_{max} in nm (ε). IR spectra: *Perkin-Elmer-337* spectrophotometer; $\tilde{\nu}$ in cm^{-1}. NMR spectra: *Bruker AM-360* (^1H at 360 MHz, ^{13}C at 90.55 MHz), $CDCl_3$ soln. at r.t., TMS as internal standard; chemical shifts in ppm as δ values. MS: *Varian-CH7* instrument; in *m/z*.

2. *5,8α-Epidioxy-5α-androstane-3β,17β-diol Diacetate* (**3a**). To a stirred mixture of *5,8α-epidioxy-5α-androst-6-ene-3β,17β-diol diacetate* [14] (**2a**; 6.824 g) in CH_2Cl_2 (70 ml) and dipotassium azodicarboxylate (10 g) in abs. MeOH (180 ml) cooled in an ice bath, a soln. of AcOH (6.5 ml) in abs. MeOH (30 ml) was added dropwise within *ca.* 1 h. Stirring was continued at r.t. for additional 6 h, when the yellow color disappeared. Most of the solvent was evaporated, the residue taken up in 300 ml of H_2O, extracted twice with CH_2Cl_2/Et_2O 1:1, the combined org. extract washed with sat. aq. $NaHCO_3$ soln. and H_2O, dried (Na_2SO_4), evaporated, and the solid residue (6.769 g, 98.7%) recrystallized from acetone/MeOH to give 5.822 g (84.9%) of **3a**. M.p. 238°. $[\alpha]^{20}$ = –118.7 (*c* = 1.02, $CHCl_3$). IR (KBr): 2940*s*, 1738*s*, 1245*s*, 1035*m*, 1015*m*, 965*w*. ^1H-NMR: 0.83 (*s*, CH_3(18)); 1.02 (*s*, CH_3(19)); 2.00, 2.04 (2 *s*, AcO–C(3), AcO–C(17)); 4.60 (*q*, H–C(17)); 4.80 (*m*, H–C(3)). Anal. calc. for $C_{23}H_{34}O_6$ (406.525): C 67.95, H 8.43; found: C 67.95, H 8.49.

3. *5,8α-Epidioxy-17-oxo-5α-androstan-3β-yl Acetate* (**3b**). 3.1. *$NaBH_4$ Reduction of 17-Oxoandrosta-5,7-dien-3β-yl Acetate* (**1b**) [15]. To a stirred soln. of **1b** (22.0 g) in MeOH (500 ml) cooled in an ice bath, $NaBH_4$ (3.5 g) was added portionwise. The mixture was stirred at 5° for 1 additional h, diluted with H_2O, and cooled in a refrigerator. The resulting precipitate was filtered off, thoroughly washed with H_2O, and air-dried to give 21.3 g (96.2%) of *androsta-5,7-diene-3β,17β-diol 3-acetate* (**1d**). M.p. 129° (from acetone/light petroleum). $[\alpha]^{20}$ = –119.8 (*c* = 1.00, $CHCl_3$). IR (KBr): 3540*m*, 3280*s* (br.), 2925*s*, 2850*s*, 1760*s*, 1655*w*, 1605*w*, 1245*s*, 1020*m*. ^1H-NMR: 0.69 (*s*, CH_3(18)); 0.96 (*s*, CH_3(19)); 2.04 (*s*, AcO–C(3)); 3.76 (*q*, H–C(17)); 4.73 (*m*, H–C(3)); 5.38, 5.58 (2 *d*, *J* ≈ 5.5, H–C(6), H–C(7)). Anal. calc. for $C_{21}H_{30}O_3$ (330.471): C 76.32, H 9.15; found: C 76.43, H 9.08.

3.2. *Photooxygenation of* **1d**. The uncrystallized **1d** (5.004 g) and eosine (75 mg) were dissolved in benzene/MeOH 9:1 (250 ml) and irradiated under O_2 with a high-pressure Hg lamp *TQ 150 Z2* for 90 min. After filtration through alumina (5 g, *Brockmann I*, neutral), the solvents were removed, and the residue (5.430 g) was chromatographed on silica gel (250 g). Elution with benzene and benzene/Et_2O 19:1 and 9:1 afforded a complex mixture (1.783 g) which was not further investigated. Elution with benzene/Et_2O 17:3 and 4:1 gave 2.530 g (46.1%) of *5,8α-epidioxy-5α-androst-6-ene-3β,17β-diol 3-acetate* (**2d**). M.p. 195° (from acetone/light petroleum). $[\alpha]^{20}$ = +19.0 (*c* = 0.93, $CHCl_3$). IR (KBr): 3505*m*, 3420*s*, 2960*s*, 1730*s*, 1720*s*, 1255*s*, 1245*s*, 1030*m*. ^1H-NMR: 0.78 (*s*, CH_3(18)); 0.85 (*s*, CH_3(19)); 1.94 (*s*, AcO–C(3)); 3.65 (*m*, H–C(17)); 4.82 (*m*, H–C(3)); 6.18, 6.48 (2 *d*, *J* ≈ 8.5, H–C(6), H–C(7)). Anal. calc. for $C_{21}H_{30}O_5$ (362.471): C 69.59, H 8.34; found: C 69.41, H 8.19.

3.3. *Diimide Reduction of* **2d**. To a stirred mixture of **2d** (6.08 g) in CH_2Cl_2 (70 ml) and dipotassium azodicarboxylate (10 g) in 180 ml of abs. MeOH cooled in an ice bath, a soln. of AcOH (6.5 ml) in abs. MeOH (30 ml) was added dropwise within *ca.* 1 h. Stirring was continued at r.t. for additional 6 h, when the yellow color disappeared. The mixture was worked up as described above for **3a** to give 6.004 g (98.2%) of *5,8α-epidioxy-5α-androstane-3β,17β-diol 3-acetate* (**3d**). Recrystallization from acetone/light petroleum yielded 5.321 g (86.8%). M.p. 196°. $[\alpha]^{20}$ = –107.7 (*c* = 0.47, $CHCl_3$). IR (KBr): 3490*s*, 2950*s*, 1700*s*, 1255*s*, 1035*m*. ^1H-NMR: 0.78 (*s*, CH_3(18)); 1.04 (*s*, CH_3(19)); 1.98 (*s*, AcO–C(3)); 3.65 (*m*, H–C(17)); 4.82 (*m*, H–C(3)). Anal. calc. for $C_{21}H_{32}O_5$ (364.487): C 69.20, H 8.85; found: C 69.20, H 9.08.

3.4. *Oxidation of* **3d**. A soln. of **3d** (4.620 g) in pyridine (46 ml) was added to a slurry of CrO_3 (4.62 g) in pyridine (46 ml) [16]. The mixture was left overnight at r.t., diluted with Et_2O and filtered, and the soln. washed twice with H_2O, twice with sat. aq. $CuSO_4 \cdot H_2O$ soln., H_2O, dried (Na_2SO_4), and evaporated: 4.620 g (100%) of **3b**. M.p. 241° (from acetone; 3.442 g, 74.9%). $[\alpha]^{20}$ = –37.4 (*c* = 0.92, $CHCl_3$). IR (KBr): 2960*s*, 1740*s*, 1728*s*, 1250*s*, 1035*m*. ^1H-NMR: 0.86 (*s*, CH_3(18)); 0.98 (*s*, CH_3(19)); 1.96 (*s*, AcO–C(3)); 4.75 (*m*, H–C(3)). Anal. calc. for $C_{21}H_{30}O_5$ (362.471): C 69.58, H 8.34; found: C 69.69; H 8.44.

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[10]) UV and IR measurements as well as elemental microanalyses were carried out in the Laboratories for Instrumental Analysis of the Institute of Chemistry, Belgrade. NMR and MS measurements and X-ray structure analyses were performed at *Ciba-Geigy Ltd.*, Basel, Switzerland.

4. *5,8α-Epidioxy-5α-cholestan-3β-yl Acetate* (**3c**) [6]. M.p. 183° (from acetone/MeOH). $[\alpha]^{20} = -40.2$. IR (KBr): 2930*s* (br.), 1725*s*, 1240*s*, 1025*m*. ^{1}H-NMR: 0.69 (*s*, CH_3(18)); 0.86 (*s*, CH_3(19)); 2.00 (*s*, AcO); 4.81 (*m*, H–C(3)). Anal. calc. for $C_{29}H_{48}O_4$ (460.703): C 75.61, H 10.50; found: C 75.72, H 10.50.

5. *Thermolysis of 5α,8α-Peroxides* **3a–c**. 5.1. *General Procedures*. 5.1.1. *In AcOH*. A soln. of the saturated peroxide (**3a–c**) in AcOH/H_2O (0.65–1 ml H_2O per 100 ml AcOH) was refluxed with stirring under N_2, until practically all starting material was consumed (*ca.* 16–28 h). The soln. was concentrated and diluted with Et_2O, the org. layer washed with H_2O, sat. aq. $NaHCO_3$ soln., and H_2O, dried (Na_2SO_4), evaporated, and the residue separated by column chromatography (SiO_2).

5.1.2. *In Diglyme*. A soln. of the peroxide **3a** or **3c** in diglyme was refluxed with stirring until the substrate was consumed (3–10 h). The mixture was diluted with H_2O and extracted several times with CH_2Cl_2/Et_2O 1:1. The org. layer was thoroughly washed with H_2O, dried (Na_2SO_4), and evaporated. The oily mixtures thus obtained were chromatographed on silica gel.

5.2. *Thermolysis of* **3a**. 5.2.1. *In AcOH*[11]). A soln. of **3a** (5.50 g) in AcOH (250 ml) and H_2O (2.5 ml) was heated for 28 h and worked up as described above. The residue (*ca.* 4.50 g) was chromatographed on silica gel (180 g). Elution with benzene/Et_2O 9:1 gave a fraction consisting mainly of *(3E,9E)-5,8-dioxo-5,10:8,9-disecoandrosta-3,9-dien-17β-yl acetate* [5] (**4**; 1.252 g, 32.6%), which was rechromatographed on a SiO_2 column to afford a chromatographically (TLC) pure sample (984 mg, 25.7%). Oil. $[\alpha]^{20} = -39.8$ (*c* = 0.92, $CHCl_3$). UV (MeOH): 225 (8650). IR (film): 2920*s* (br.), 1770*m*, 1725*s*, 1705*s*, 1660*s*, 1620*m*, 1238*s*. ^{1}H-NMR: 0.85 (*s*, CH_3(18)); 1.59 (br. *s*, CH_3(19)); 2.05 (*s*, AcO–C(17)); 2.51 (*dt*, *J* = 13.5, 7, H_β–C(6)); 2.61 (*dt*, *J* = 17.5, 7, H_α–C(7)); 2.70 (*dt*, *J* = 17.5, 7, H_β–C(7)); 2.96 (*dt*, *J* = 13.5, 7, H_β–C(6)); 4.88 (*t*, H–C(17)); 5.2 (br. *t*, H–C(9)); 5.95 (*dm*, *J* = 17, H–C(4)); 6.58 (*dt*, *J* = 17, 8, H–C(3)). ^{13}C-NMR: 208.2 (*s*, C(8)); 200.7 (*s*, C(5)); 170.6 (*s*, CH_3COO); 148.1 (*d*, C(3)); 133.0 (*s*, C(10)); 130.2 (*d*, C(4)); 128.2 (*d*, C(9)); 78.4 (*d*, C(17)); 54.6 (*d*, C(14)); 47.1 (*s*, C(13)); 40.4 (*t*, C(7)); 37.7 (*t*, C(6), C(12)); 34.6 (*t*, C(1)); 29.3 (*t*, C(2)); 27.2 (*t*, C(16)); 22.6 (*t*, C(11)); 22.0 (*t*, C(15)); 21.1 (*q*, CH_3COO); 16.5 (*q*, C(18)); 15.5 (*q*, C(19)). MS (70 eV): 346 ($M^{+\cdot}$), 331 ($M^{+\cdot}$ – 15), 328 ($M^{+\cdot}$ – 18), 286 ($M^{+\cdot}$ – 60). Anal. calc. for $C_{21}H_{30}O_4$ (345.471): C 72.80, H 8.73; found: C 72.86, H 8.68.

Benzene/Et_2O 4:1 eluted a complex mixture (214 mg) which was not further investigated. Elution with benzene/Et_2O 7:3 afforded *5α-androst-7-ene-3β,5,17β-triol 3,17-diacetate* (**5**; 113 mg, 2.6%). M.p. 187–188° (from Et_2O; 57 mg, 1.3%). $[\alpha]^{20} = -8.4$ (*c* = 0.98, $CHCl_3$). IR (KBr): 3510*s*, 2960*s*, 2940*s*, 1735*s*, 1720*s*, 1710*s*, 1255*s*, 1240*s*, 1030*s*. ^{1}H-NMR: 0.67 (*s*, CH_3(18)); 0.95 (*s*, CH_3(19)); 2.03, 2.06 (2 *s*, 2 AcO); 4.73 (*q*, H–C(17)); 5.10 (*m*, H–C(3), H–C(7)). ^{13}C-NMR: 171.6 (*s*, CH_3COO); 171.0 (*s*, CH_3COO); 139.8 (*s*, C(8)); 115.5 (*d*, C(7)); 83.3 (*d*, C(17)); 74.5 (*s*, C(5)); 71.3 (*d*, C(3)); 49.8 (*d*, C(14)); 44.2 (*s*, C(13)); 44.1 (*d*, C(9)); 39.7 (*t*, C(4)); 38.6 (*s*, C(10)); 37.9 (*t*, C(12)); 37.2 (*t*, C(6)); 31.7 (*t*, C(2)); 28.0 (*t*, C(1)); 27.6 (*t*, C(16)); 22.7 (*t*, C(15)); 21.9 (*q*, CH_3COO); 21.6 (*q*, CH_3COO); 21.5 (*t*, C(11)); 18.9 (*q*, C(19)); 12.7 (*q*, C(18)). MS (70 eV): 390 ($M^{+\cdot}$), 372 ($M^{+\cdot}$ – 18), 312 (372 – 60), 297 (312 – 15), 252 (312 – 60), 237 (297 – 60). Anal. calc. for $C_{23}H_{34}O_5$ (390.525): C 70.74, H 8.78; found: C 70.81, H 8.69.

Further elution with benzene/Et_2O 7:3 and 3:2 gave *3β,5,17β-trihydroxy-8,14-seco-5α-androstan-8-one 3,17-diacetate* (**6**; 1.64 g, 36.3%). Oil. MS (70 eV): 408 ($M^{+\cdot}$), 393 ($M^{+\cdot}$ – 15), 390 ($M^{+\cdot}$ – 18), 348 ($M^{+\cdot}$ – 60), 333 (393 – 60), 330 (390 – 60), 315 (333 – 18) ([9]: oil; MS: 408 ($M^{+\cdot}$)).

Acid Hydrolysis of **4**. A soln. of **4** (670 mg) in acetone (100 ml) and H_2O (45 ml) containing 50% aq. H_2SO_4 soln. (0.6 ml) was refluxed, until the substrate was consumed (*ca.* 3 d). The mixture was diluted with H_2O, neutralized with sat. aq. $NaHCO_3$ soln., and extracted with $CHCl_3$. The org. layer was washed with H_2O, dried (Na_2SO_4), and evaporated leaving an oily mixture (520 mg) which was chromatographed on silica gel (15 g). Elution with benzene/Et_2O 7:3 and 3:2 gave *(3E,9E)-17β-hydroxy-5,10:8,9-disecoandrosta-3,9-diene-5,8-dione* (**7**; 387 mg, 67.5%). M.p. 93° (from Et_2O; 188 mg, 31.9%). $[\alpha]^{20} = -79.7$ (*c* = 0.92, $CHCl_3$). UV (MeOH): 223 (7850). IR (KBr): 3400*s*, 2440–2400*s* (br.), 2370*s*, 1700*s*, 1670*s*, 1645*s*, 1625*s*, 1080*s*. ^{1}H-NMR: 0.80 (*s*, CH_3(18)); 1.55 (*s*, CH_3(19)); 3.67 (*t*, H–C(17)); 5.12 (br. *t*, *J* = 6.4, H–C(9)); 5.90 (*d*, *J* = 16, H–C(4)); 6.45 (*dt*, *J* = 16, 7.6, H–C(3)). ^{13}C-NMR: 211.3 (*s*, C(8)); 200.3 (*s*, C(5)); 148.2 (*d*, C(3)); 132.8 (*s*, C(10)); 129.6 (*d*, C(4)); 128.1 (*d*, C(9)); 78.8 (*d*, C(17)); 54.7 (*d*, C(14)); 48.2 (*s*, C(13)); 40.6 (*t*, C(7)); 37.7 (*t*, C(6)); 37.5 (*t*, C(12)); 34.8 (*t*, C(1)); 30.6 (*t*, C(16)); 29.1 (*t*, C(2)); 22.8 (*t*, C(11)); 22.1 (*t*, C(15)); 15.4 (*q*, C(18)); 15.3 (*q*, C(19)). Anal. calc. for $C_{19}H_{28}O_3$ (304.433): C 74.96, H 9.27; found: C 74.82, H 9.24.

Oxidation of **7**. a) *With* Kiliani *Acid*. To a cooled (0–5°) soln. of **7** (271 mg) in acetone (30 ml), a slight excess of *Kiliani's* CrO_3 soln. [17] was added with constant stirring. After 10 min, ice-cold H_2O was added and the mixture extracted twice with Et_2O/CH_2Cl_2 1:1. The combined org. extracts were washed with sat. aq. $NaHCO_3$ soln. and H_2O, dried (Na_2SO_4), and evaporated. The oily residue (236 mg) was chromatographed on silica gel (10

[11]) See also [9].

g) with benzene/Et_2O 17:3 and 4:1 affording *(3E,9E)-5,10;8,9-disecoandrosta-3,9-diene-5,8,17-trione* (**8**; 185 mg, 68.7%) as an oil which solidified on standing. M.p. 63–64°. $[\alpha]^{20} = +30.1$ ($c = 0.79$, $CHCl_3$).

b) *With CrO_3/Pyridine.* A mixture of **7** (106 mg) in pyridine (1 ml) and CrO_3 (106 mg) in pyridine (1 ml) was left overnight at r.t. [16], diluted with Et_2O, and filtered. The soln. was worked up in the usual way leaving an oily residue (110 mg) which was chromatographed on silica gel (5 g). Elution with benzene/Et_2O 17:3 afforded **8** (49 mg, 46.5%) as an oil which solidified on standing. M.p. 59–63°. $[\alpha]^{20} = +29.2$ ($c = 1.00$, $CHCl_3$). UV (MeOH): 223 (3400). IR (KBr): 2900*s*, 1730*s*, 1700*s*, 1660*s*, 1620*m*, 975*m*. ^{1}H-NMR: 0.85 (*s*, CH_3(18)); 1.59 (*s*, CH_3(19)); 5.2 (br. *t*, $J = 6$, H–C(9)); 5.95 (*d*, $J = 17$, H–C(4)); 6.60 (*dt*, $J = 17, 7$, H–C(3)). ^{13}C-NMR: 220.0 (*s*, C(17)); 208.6 (*s*, C(8)); 200.3 (*s*, C(5)); 148.8 (*d*, C(3)); 133.3 (*s*, C(10)); 129.6 (*d*, C(4)); 127.8 (*d*, C(9)); 54.7 (*d*, C(14)); 52.6 (*s*, C(13)); 39.8 (*t*, C(7)); 37.9 (*t*, C(6)); 36.7 (*t*, C(16)); 35.2 (*t*, C(1)); 35.1 (*t*, C(12)); 29.2 (*t*, C(2)); 23.8 (*t*, C(11)); 21.0 (*t*, C(15)); 19.1 (*q*, C(18)); 15.5 (*q*, C(19)). Anal. calc. for $C_{19}H_{26}O_3$ (302.417): C 75.46, H 8.67; found: C 75.27, H 8.84.

5.2.2. *Thermolysis of* **3a** *in Diglyme.* A soln. of **3a** (2.20 g) was thermolyzed in diglyme (100 ml) for 4 h and the mixture worked up as described above. The residue (*ca.* 2.5 g) was chromatographed on silica gel (80 g). Elution with benzene/Et_2O 9:1 gave a fraction consisting mainly of *(E)-3β,17β-dihydroxy-5,10:8,9-disecoandrost-9-ene-5,8-dione diacetate* (**9**; 659 mg, 29.9%) which was rechromatographed on a SiO_2 column to afford a chromatographically (TLC) pure sample (481 mg, 29.9%). Oil. $[a]^{20} = -22.1$ ($c = 1.00$, $CHCl_3$). IR (film): 2930*s*, 1735*s*, 1710*s*, 1245*s*, 1030*s*. ^{1}H-MNR: 0.87 (*s*, CH_3(18)); 1.60 (*s*, CH_3(19)); 2.02, 2.04 (2 *s*, 2 AcO); 4.92 (*t*, H–C(17)); 4.95 (*m*, H–C(3)); 5.11 (*q*, H–C(9)). ^{13}C-NMR: 209.3 (*s*, C(8)); 207.1 (*s*, C(5)); 170.7 (*s*, CH_3COO); 170.6 (*s*, CH_3COO); 133.8 (*s*, C(10)); 127.6 (*d*, C(9)); 72.2 (*d*, C(17)); 69.4 (*d*, C(3)); 53.1 (*d*, C(14)); 46.5 (*s*, C(13)); 46.4 (*t*, C(4)); 37.9 (*t*, C(6), C(7)); 35.8 (*t*, C(12)); 34.2 (*t*, C(1)); 30.6 (*t*, C(2)); 26.4 (*t*, C(16)); 22.2 (*t*, C(11)); 21.8 (*t*, C(15)); 21.2 (*q*, CH_3COO); 21.1 (*q*, CH_3COO); 16.5 (*q*, C(18)); 16.1 (*q*, C(19)). Anal. calc. for $C_{23}H_{34}O_6$ (406.525): C 67.95, H 8.43; found: C 67.78, H 8.38.

Elution with benzene/Et_2O 4:1 afforded *5α-androst-8(14)-ene-3β,5,17β-triol 3,17-diacetate* (**10**; 205 mg, 9.7%). M.p. 180° (from Et_2O; 146 mg, 6.9%). $[\alpha]^{20} = -23.9$ ($c = 0.56$, $CHCl_3$). IR (KBr): 3520*s*, 2970*s*, 2940*s*, 2860*m*, 1740*s*, 1715*s*, 1255*s*, 1245*s*, 1040*s*, 1028*s*. ^{1}H-NMR: 0.89 (*s*, CH_3(18)); 0.95 (*s*, CH_3(19)); 2.03, 2.07 (2 *s*, 2 AcO); 4.57 (*q*, H–C(17)); 5.18 (*m*, H–C(3)). ^{13}C-NMR: 170.6 (*s*, CH_3COO); 170.2 (*s*, CH_3COO); 135.9 (*s*, C(14)); 128.7 (*s*, C(8)); 82.5 (*d*, C(17)); 74.5 (*s*, C(5)); 70.4 (*d*, C(3)); 41.9 (*s*, C(13)); 41.0 (*d*, C(9)); 40.0 (*t*, C(4)); 39.8 (*s*, C(10)); 34.3 (*t*, C(12)); 34.2 (*t*, C(6)); 30.0 (*t*, C(2)); 26.7 (*t*, C(16)); 26.0 (*t*, C(1)); 23.4 (*t*, C(15)); 23.3 (*t*, C(7)); 21.0 (*q*, CH_3COO); 20.8 (*q*, CH_3COO); 19.2 (*t*, C(11)); 18.0 (*q*, C(19)); 16.8 (*q*, C(18)). MS (70 eV): 390 (M^+), 372 ($M^+ - 18$), 312 (372 – 60), 297 (312 – 15), 252 (312 – 60), 237 (297 – 60). Anal. calc. for $C_{23}H_{34}O_5$ (390.525): C 70.74, H 8.78; found: C 70.82, H 8.66.

Benzene/Et_2O 7:3 eluates gave *5α-androst-7-ene-3β,5,17β-triol 3,17-diacetate* (**5**; 218 mg, 10.3%). M.p. 187–188° (from Et_2O; 155 mg, 7.3%). See *5.2.1*.

Elution with benzene/Et_2O 3:2 afforded *5α-androst-8(9)-ene-3β,5,17β-triol 3,17-diacetate* (**11**; 198 mg, 9.4%). M.p. 163–164° (from Et_2O; 139 mg, 6.6%). $[\alpha]^{20} = +4.5$ ($c = 1.00$, $CHCl_3$). IR (KBr): 3520*s*, 2950*s*, 2930*s*, 1735*s*, 1728*s*, 1265*s*, 1245*s*, 1050*s*, 1030*s*. ^{1}H-NMR: 0.76 (*s*, CH_3(18)); 1.16 (*s*, CH_3(19)); 2.03, 2.06 (2 *s*, 2 AcO); 4.66 (*q*, H–C(17)); 5.17(*m*, H–C(3)). ^{13}C-NMR: 171.1 (*s*, CH_3COO); 170.4 (*s* CH_3COO); 133.1 (*s*, C(9)); 128.3 (*s*, C(8)); 81.6 (*d*, C(17)); 74.0 (*s*, C(5)); 70.5 (*d*, C(3)); 46.1 (*d*, C(14)); 42.3 (*s*, C(13)); 40.9 (*s*, C(10)); 38.1 (*t*, C(4)); 33.8 (*t*, C(12)); 30.7 (*t*, C(6)); 29.2 (*t*, C(1)); 28.3 (*t*, C(16)); 26.9 (*t*, C(2)); 23.5 (*q*, C(19)); 22.9 (*t*, C(15)); 22.8 (*t*, C(7), C(11)); 21.4 (*q*, CH_3COO); 21.1(*q*, CH_3COO); 11.4 (*q*, C(18)). MS (70 eV): 390 (M^+), 372 ($M^+ - 18$), 312 (372 – 60), 297 (312 – 15), 252 (312 – 60), 237 (297 – 60). Anal. calc. for $C_{23}H_{34}O_5$ (390.525): 70.74, H 8.78; found: C 70.64, H 8.69.

Elution with Et_2O/benzene 1:1, 3:2, and 7:3 gave a complex mixture (311 mg) which was not further investigated. Elution with Et_2O/benzene 4:1 afforded *5α-androstane-3β,5,8α,17β-tetrol 3,17-diacetate* (**12**; 173 mg, 7.8%). M.p. 151–152° (from MeOH; 118 mg, 5.3%). $[\alpha]^{20} = -52.4$ ($c = 1.00$, $CHCl_3$). IR (KBr): 3490–3190*s* (br.), 2980*s*, 2940*s*, 1735*s*, 1725*s*, 1245*s*, 1025*s*, 965*s*. ^{1}H-NMR: 0.80 (*s*, CH_3(18)); 1.06 (*s*, CH_3(19)); 2.02, 2.05 (2 *s*, 2 AcO); 4.60 (*q*, H–C(17)); 5.12 (*m*, H–C(3)). MS (70 eV): 390 ($M^+ - 18$), 372 (390 – 18), 312 (372 – 60), 297 (312 – 15), 237 (297 – 60). Anal. calc. for $C_{23}H_{36}O_6$ (408.541): C 67.62, H 8.88; found: C 67.40, H 8.99.

Thermolysis of **9**. A soln. of **9** (100 mg) in AcOH (10 ml) and H_2O (0.1 ml) was refluxed under N_2 for 4 h. The mixture was worked up as described above to give an oily product identified (MS, IR, ^{1}H-NMR) as **4** (80 mg, 93.7%).

5.3. *Thermolysis of* **3b**. A soln. of **3b** (1.00 g) in AcOH and H_2O (1 ml) was refluxed with stirring under N_2 for 20 h. The residue (*ca.* 1 g), obtained after the usual workup, was chromatographed on silica gel (50 g). Benzene/Et_2O 17:3 and 4:1 eluted fractions consisting mostly of **8** (148 mg, 17.7%) which was purified by prep. TLC with light petroleum/AcOEt 3:2 (72 mg, 8.6%). Spectral data (IR, ^{1}H-NMR, ^{13}C-NMR) of this product were identical with those observed for the 17-keto derivative formed by CrO_3 oxidation of **7** (see *5.2.1*).

5.4. *Thermolysis of* **3c**. 5.4.1. *In AcOH* [6]. A soln. of **3c** (5.00 g) in AcOH (1350 ml) and H_2O (8.75 ml) was refluxed with stirring under N_2 for 22 h. The usual workup gave an oily residue (*ca.* 5.1 g) which was chromatographed on silica gel (150 g). Elution with light petroleum/AcOEt 19:1 afforded first an unresolvable mixture (286 mg) and then *5,8α-epoxy-5(10 →1)*abeo-*1α(H),5α-cholest-10(19)-en-3β-yl acetate* (**13**; 535 mg, 10.7%). M.p. 120–123° (from acetone; 428 mg, 8.6%; [6]: m.p. 120–123°). Light petroleum/AcOEt 9:1 eluted *(3*E,9E*)-5,10:89-disecocholesta-3,9-diene-5,8-dione* (**14**) as an oil (1.33 g, 30.60%; [6]: oil). Further fractions obtained with light petroleum/AcOEt 9:1 contained **14** mixed with *5α-cholest-7-ene-3β,5-diol 3-acetate* (**15**; 430 mg). This mixture was subjected to prep. TLC with benzene/AcOEt 18:1 to give 170 mg (3.9%) of **14** (total yield of **14**, 34.5%) and 143 mg (2.9%) of **15**, m.p. 188° (from acetone/MeOH; 102 mg, 2.1%; [16]: m.p. 188–190°). Elution with benzene/AcOEt 4:1 afforded a complex mixture (*ca.* 2.4 g) which was not further investigated.

5.4.2. *In Diglyme*. A soln. of **3c** (500 mg) in diglyme (60 ml) was refluxed with stirring for 3 h. The mixture was worked up as described above to give an oily residue (590 mg) which was chromatographed on silica gel (15 g). Elution with light petroleum/AcOEt 9:1 gave **14/15** (128 mg) which was separated by prep. TLC with benzene/AcOEt 18:1 affording 82 mg (18.9%) of **14** (oil; [6]: oil) and 25 mg (5.2%) of **15**, m.p. 188° (from acetone/MeOH; 16 mg, 3.3%; [16]: m.p. 188–190°). Elution with light petroleum/AcOEt 17:3 gave *(*E*)-3β-hydroxy-5,10:8,9-disecocholest-9-ene-5,8-dione acetate* (**16**; 98 mg, 19.6%) which was rechromatographed on a SiO_2 column to give a chromatographically (TLC) pure sample (63 mg, 12.6%) as an oil. $[\alpha]^{20} = -30.2$ ($c = 1.00$, $CHCl_3$). IR (film): 2960–2870*s* (br.), 1735*s*, 1710*s*, 1235*s*. ^{1}H-NMR: 0.77 (*s*, CH_3(18)); 0.86 (*d*, CH_3(26), CH_3(27)); 0.89 (*d*, CH_3(21)); 1.69 (*s*, CH_3(19)); 2.0 (*s*, AcO); 5.25 (2 *m*, H–C(3), H–C(9)). MS (70 eV): 460 ($M^{+\cdot}$), 400 ($M^{+\cdot} - 60$). Anal calc. for $C_{29}H_{48}O_4$ (460.703): C 75.61, H 10.50; found: C 75.28, H 10.73.

Elution with AcOEt gave *5α-cholestane-3β,5,8α-triol 3-acetate* (**17**; 262 mg, 52.2%) which, after recrystallization from acetone, had m.p. 150–151° (219 mg, 43.6%; [4]: m.p. 151°).

6. *Oxidation of* **4** *with* m-*Chloroperbenzoic Acid*. To a stirred soln. of **4** (1.969 g) in CH_2Cl_2/Et_2O 1:1 (100 ml) cooled to 0°, $NaHCO_3$ (1.6 g) and *m*-chloroperbenzoic acid (90%; 3.27 g) in CH_2Cl_2/Et_2O 1:1 (20 ml) were added, and the mixture was allowed to warm to r.t. After 4 h, it was diluted with Et_2O, the org. layer washed with H_2O, 10% aq. KI soln., aq. $Na_2S_2O_3$ soln., H_2O, sat. aq. $NaHCO_3$ soln., and H_2O, dried (Na_2SO_4), and evaporated, leaving an oily mixture (*ca.* 2.2 g) which was chromatographed on silica gel (100 g). Elution with benzene/Et_2O 86:14 afforded *(*E,9R,*10*R*)-9,10-epoxy-17β-hydroxy-4a-oxa*-A-*homo-5,10:8,9-disecoandrost-3-ene-5,8-dione acetate* (**20a**; 140 mg, 6.5%). M.p. 110° (from acetone/light petroleum; 103 mg, 4.8%). [a]^{20} = – 61.1 ($c = 0.68$, $CHCl_3$). UV (MeOH): 213 (2600). IR (KBr): 2920*s*, 2850*m*, 1730*s*, 1725*s*, 1720*s*, 1690*s*, 1245*s*, 1235*s*, 1150*s*. ^{1}H-NMR: 1.12 (*s*, CH_3(18)); 1.18 (*s*, CH_3(19)); 2.04 (*s*, AcO); 4.67 (*t*, H–C(17)); 5.28 (*ddd*, $J = 13, 11, 5$, H–C(3)); 7.06 (*dd*, $J = 13, 2$, H–C(4)). ^{13}C-NMR: 209.8 (*s*, C(8)); 170.6 (*s*, C(5)); 169.3 (*s*, CH_3COO); 135.3 (*d*, C(4)); 114.8 (*d*, C(3)); 79.7 (*d*, C(17)); 64.9 (*d*, C(9)); 59.4 (*s*, C(19)); 58.3 (*d*, C(14)); 46.0 (*s*, C(13)); 38.8 (*t*, C(7)); 38.3 (*t*, C(6)); 36.1 (*t*, C(1)); 30.3 (*t*, C(12)); 27.7 (*t*, C(16)); 23.8 (*t*, C(2), C(11)); 23.2 (*t*, C(15)); 21.2 (*q*, CH_3COO); 15.2 (*q*, C(18)); 13.3 (*q*, C(19)). MS (70 eV): 378 ($M^{+\cdot}$), 360 ($M^{+\cdot} - 18$), 318 ($M^{+\cdot} - 60$). Anal calc. for $C_{21}H_{30}O_6$ (378.471): C 66.64, H 7.99; found: C 66.50, H 7.83.

Elution with benzene/Et_2O 21:4 afforded *(*E,9S,*10S*)-9,10-epoxy-17β-hydroxy-4a-oxa*-A-*homo-5,10:8,9-disecoandrost-3-ene-5,8-dione acetate* (**21a**; 234 mg, 10.9%). M.p. 207–208° (from acetone/light petroleum; 191 mg, 8.9%). $[\alpha]^{20} = +20.2$ ($c = 1.00$, $CHCl_3$). UV (MeOH): 207 (1950). IR (KBr): 2920*s*, 1745*s*, 1740*s*, 1730*s*, 1695*s*, 1235*s*, 1150*s*. ^{1}H-NMR: 0.99 (*s*, CH_3(18)); 1.18 (*s*, CH_3(19)); 2.03 (*s*, AcO); 2.42 (*ddd*, $J = 16.5, 6, 3$, H_α–C(6)); 2.53 (*dd*, $J = 10.5, 3.6$, H–C(9)); 2.59 (*ddd*, $J = 18.5, 6, 3$, H_β–C(7)); 2.75 (*dd*, $J = 12, 8$, H–C(14)); 2.92 (*ddd*, $J = 16.5, 13.5, 3$, H_α–C(7)); 3.19 (*ddd*, $J = 18.5, 13.5, 3$, H_β–C(6)); 4.69 (*t*, H–C(17)); 5.00 (*td*, $J = 13, 4$, H–C(3)); 6.95 (*dd*, $J = 13, 2.5$, H–C(4)). ^{13}C-NMR: 209.6 (*s*, C(8)); 170.5 (*s*, CH_3COO); 167.8 (*s*, C(5)); 134.9 (*d*, C(4)); 114.1 (*d*, C(3)); 80.4 (*d*, C(17)); 64.7 (*d*, C(9)); 59.5 (*s*, C(10)); 58.2 (*d*, C(14)); 47.5 (*s*, C(13)); 41.1 (*t*, C(7)); 37.8 (*t*, C(1)); 37.0 (*t*, C(12)); 28.3 (*t*, C(6)); 27.9 (*t*, C(16)); 24.2 (*t*, C(11)); 23.8 (*t*, C(2), C(15)); 21.2 (*q*, CH_3COO); 15.1 (*q*, C(18)); 12.9 (*q*, C(19)). MS (70 eV): 378 ($M^{+\cdot}$), 360 ($M^{+\cdot} - 18$), 318 ($M^{+\cdot} - 60$). Anal. calc. for $C_{21}H_{30}O_6$ (378.471): C 66.64, H 7.99; found: C 66.85, H 7.81.

Elution with benzene/Et_2O 4:1 gave *(*E,9S,*10S*)-9,10-epoxy-17β-hydroxy-5,10:8,9-disecoandrost-3-ene-5,8-dione acetate* (**19a**; 337 mg, 16.0%) as an oil which was purified by rechromatography (286 mg, 13.9%). $[\alpha]^{20} = -8.9$ ($c = 1.71$, $CHCl_3$). IR (film): 2910*s*, 1725*s*, 1705*s*, 1660*s*, 1615*m*, 1240*s*. ^{1}H-NMR: 0.90 (*s*, CH_3(18)); 1.24 (br. *s*, CH_3(19)); 2.03 (*s*, AcO); 2.76 (*dd*, $J = 12, 8$, H–C(9)); 4.73 (*t*, H–C(17)); 6.14 (*dm*, $J = 16.5$, H–C(4)); 6.72 (*ddd*, $J = 16.5, 9, 7.5$, H–C(3)). ^{13}C-NMR: 210.9 (*s*, C(8)); 199.5 (*s*, C(5)); 170.5 (*s*, CH_3COO); 147.3 (*d*, C(3)); 130.7 (*d*, C(4)); 80.2 (*d*, C(17)); 64.7 (*d*, C(9)); 59.2 (*s*, C(10)); 57.7 (*d*, C(14)); 47.7 (*s*, C(13)); 40.7 (*t*, C(7)); 37.1 (*t*, C(1)); 30.7 (*t*, C(12)); 35.4 (*t*, C(6)); 29.2 (*t*, C(2)); 27.2 (*t*, C(16)); 24.2 (*t*, C(11)); 23.8 (*t*, C(15)); 21.1 (*q*, CH_3COO); 16.1 (*q*, C(18)); 13.0 (*q*, C(19)). MS (70 eV): 362 ($M^{+\cdot}$), 344 ($M^{+\cdot} - 18$), 302 ($M^{+\cdot} - 60$). Anal. calc. for $C_{21}H_{30}O_5$ (362.471): C69.59, H 8.34; found: C 69.38, H 8.17.

Further benzene/Et_2O 4:1 and the first benzene/Et_2O 3:1 fractions afforded a mixture of **19a** and **18a** (223 mg, 10.8%). Further elution with benzene/Et_2O 3:1 gave *(E,9R,10R)-9,10-epoxy-17β-hydroxy-5,10:8,9-disecoandrost-3-ene-5,8-dione acetate* (**18a**; 392 mg, 19%). M.p. 100° (from Et_2O/light petroleum; 304 mg, 14.8%). $[\alpha]^{20} = -59.1$ ($c = 0.95$, $CHCl_3$). IR (KBr): 2930*s*, 2910*s*, 1730*s*, 1725*s*, 1698*s*, 1620*m*, 1235*s*. ^{1}H-NMR: 0.98 (*s*, CH_3(18)); 1.21 (*s*, CH_3(19)); 2.03 (*s*, AcO); 2.54 (*dd*, $J = 8.5, 5.5$, H–C(9)); 4.75 (*t*, H–C(17)); 6.21 (*dm*, $J = 16.5$, H–C(4)); 6.75 (*ddd*, $J = 16.5, 10.5, 6.0$, H–C(3)). ^{13}C-NMR: 209.4 (*s*, C(8)); 198.0 (*s*, C(5)); 170.5 (*s*, CH_3COO); 147.2 (*d*, C(3)); 130.1 (*d*, C(4)); 79.5 (*d*, C(17)); 64.2 (*d*, C(9)); 59.2 (*s*, C(10)); 55.9 (*d*, C(14)); 47.1 (*s*, C(13)); 40.0 (*t*, C(7)); 37.1 (*t*, C(1)); 36.1 (*t*, C(12)); 35.9 (*t*, C(6)); 29.4 (*t*, C(2)); 27.5 (*t*, C(16)); 23.5 (*t*, C(11)); 23.2 (*t*, C(15)); 21.2 (*q*, CH_3COO); 15.8 (*q*, C(18)); 14.1 (*q*, C(19)): MS (70 eV): 362 ($M^{+\cdot}$), 344 ($M^{+\cdot} - 18$), 302 ($M^{+\cdot} - 60$) Anal. calc. for $C_{21}H_{30}O_5$ (362.471): C 69.59, H 8.34; found: C 69.35, H 8.12.

7. Baeyer-Villiger *Oxidation of* **18a**. A soln. of **18a** (288 mg) in CH_2Cl_2/Et_2O 1:1 (50 ml) was treated with *m*-chloroperbenzoic acid (*ca.* 90%; 460 mg) and $NaHCO_3$ (225 mg) for 48 h as described above. The usual workup afforded **20a** (294 mg, 97.7%). M.p. 108–110° (from acetone/light petroleum; 247 mg, 82.1%).

8. Baeyer-Villiger *Oxidation of* **19a**. A soln. of **19a** (227 mg) in CH_2Cl_2/Et_2O 1:1 (50 ml) was treated with *m*-chloroperbenzoic acid (*ca.* 90%; 370 mg) and $NaHCO_3$ (180 mg) for 12 h as above to give, after the usual workup, **21a** (223 mg, 94.1%). M.p. 207° (from acetone/light petroleum, 192 mg, 81.0%).

9. *Oxidation of* **14** *with* m-*Chloroperbenzoic Acid.* To a stirred soln. of **14** (1.120 g) in CH_2Cl_2/Et_2O 1:1 (80 ml) cooled to 0°, $NaHCO_3$ (780 mg) and *m*-chloroperbenzoic acid (*ca.* 90%; 1.61 g) in CH_2Cl_2/Et_2O 1:1 (10 ml) were added, and the mixture was allowed to stand at r.t. for 6 h. It was diluted with Et_2O, the org. layer washed with aq. $NaHSO_3$ soln., H_2O, sat. aq. $NaHCO_3$ soln., H_2O, dried (Na_2SO_4), and evaporated to give an oily mixture (1.236 g) which was chromatographed on silica gel (40 g). Elution with light petroleum/AcOEt 17:3 afforded *(E,9R,10R)-9,10-epoxy-4a-oxa*-A-*homo-5,10:8,9-disecocholest-3-ene-5,8-dione* (**20c**; 225 mg, 18.6%) as an oil, which was purified by rechromatography (189 mg, 15.6%). $[\alpha]^{20} = -8.8$ ($c = 1.00$, $CHCl_3$). UV (MeOH): 205 (1600). IR (film): 2920*s*, 1735*s*, 1700*s*, 1668*m*, 1230*s*, 1155*s*. ^{1}H-NMR: 0.87 (*d*, CH_3(26), CH_3(27)); 0.92 (*d*, CH_3(21)); 1.02 (*s*, CH_3(18)); 1.20 (*s*, CH_3(19)); 5.30 (*ddd*, $J = 13, 11, 6$, H–C(3)); 7.0 (*dd*, $J = 13, 2$ H–C(4)). ^{13}C-NMR: 210.5 (*s*, C(8)); 170.1 (*s*, C(5)); 135.7 (*d*, C(4)); 115.1 (*d*, C(3)); 66.0 (*d*, C(9)); 59.4 (*s*, C(10)); 58.8 (*d*, C(14)); 50.2 (*d*, C(17)); 46.1 (*s*, C(13)); 39.5 (*t*, C(24)); 38.6 (*t*, C(7)); 37.5 (*t*, C(6)); 36.6 (*t*, C(1)); 35.4 (*t*, C(22)); 33.7 (*d*, C(20)); 30.1 (*t*, C(12)); 28.0 (*d*, C(25)); 25.9 (*t*, C(16)); 24.6 (*t*, C(11)); 24.2 (*t*, C(2)); 23.8 (*t*, C(23)); 23.0 (*t*, C(15)); 22.8 (*q*, C(27)); 22.6 (*q*, C(26)); 19.3 (*q*, C(21)); 16.0 (*q*, C(18), C(19)). Anal. calc. for $C_{27}H_{44}O_4$ (432.649): C 74.96, H 10.25; found: C 74.78, H 10.06.

Further elution with light petroleum/AcOEt 17:3 afforded first a complex mixture (156 mg) and then *(E,9S,10S)-9,10-epoxy-4a-oxa*-A-*homo-5,10:8,9-disecocholest-3-ene-5,8-dione* (**21c**; 246 mg, 20.3%). M.p. 78–79° (from acetone/MeOH; 194 mg, 16.0%). $[\alpha]^{20} = +41.2$ ($c = 1.00$, $CHCl_3$). UV (MeOH): 207 (2000). IR (KBr): 2920*s*, 1750*s*, 1700*s*, 1665*m*, 1230*s*, 1150*s*. ^{1}H-NMR: 0.85 (*d*, CH_3(26), CH_3(27)); 0.89 (*d*, CH_3(21)); 0.90 (*s*, H–C(18)); 1.17 (*s*, CH_3(19)); 2.40 (*ddd*, $J = 16, 5, 3$, H_α–C(6)); 2.50 (*t*, $J = 12$, H–C(9)); 2.60 (*m*, H_β–C(7)); 2.70 (*m*, H–C(14)); 2.80 (*ddd*, $J = 16, 13, 3$, H_α–C(7)); 3.10 (*ddd*, $J = 19, 13, 3$, H_β–C(6)); 5.21 (*td*, $J = 12.5, 4$, H–C(3)); 7.03 (*dd*, $J = 12.5, 2.5$, H–C(4)). ^{13}C-NMR: 211.6 (*s*, C(8)); 168.2 (*s*, C(5)); 135.3 (*d*, C(4)); 113.6 (*d*, C(3)); 65.8 (*d*, C(9)); 62.4 (*d*, C(14)); 59.8 (*s*, C(10)); 55.7 (*d*, C(17)); 49.4 (*s*, C(13)); 40.5 (*t*, C(7)); 39.9 (*t*, C(24)); 39.5 (*t*, C(12)); 38.1 (*t*, C(1)); 34.4 (*t*, C(22)); 33.0 (*d*, C(20)); 28.4 (*t*, C(6)); 28.0 (*d*, C(25)); 27.7 (*t*, C(16)); 25.4 (*t*, C(15)); 25.2 (*t*, C(2)); 24.4 (*t*, C(11)); 23.9 (*t*, C(23)); 22.7 (*q*, C(27)); 22.6 (*q*, C(26)); 21.3 (*q*, C(21)); 15.8 (*q*, C(18)); 14.0 (*q*, C(19)). Anal. calc. for $C_{27}H_{44}O_4$ (432.649): C 74.96, H 10.25; found: C 75.06, H 10.19.

Elution with light petroleum/AcOEt 1:1 gave an unresolvable mixture of *(E,9R,10R)-* and *(E,9S,10S)-9,10-epoxy-5,10:8,9-disecocholest-3-ene-5,8-dione* (**18c** and **19c**, resp.; 273 mg, 23.4%). M.p. 85–86° (from acetone). ^{1}H-NMR: 0.82 (*s*, CH_3(18)); 0.86 (*d*, CH_3(26), CH_3(27)); 0.92 (*d*, CH_3(19)); 1.28, 1.29 (2 *s*, H–C(9) of **18c** and **19c**, resp.); 6.01 (*d*, $J = 16.5$, H–C(4) of **19c**); 6.16 (*d*, $J = 16.5$, H–C(4) of **18c**); 6.70 (*m*, H–C(3)). Anal. calc. for $C_{27}H_{44}O_3$ (416.649): C 77.83, H 10.65; found: C 77.98, H 10.48.

Baeyer-Villiger *Oxidation of the Mixture* **18c/19c**. A soln. **18c/19c** (200 mg) in CH_2Cl_2/Et_2O 1:1 (50 ml) was treated with *m*-chloroperbenzoic acid (90%; 280 mg) and $NaHCO_3$ (135 mg) for 16 h as described above. The mixture was worked up in the usual way leaving an oil (*ca.* 220 mg) which was chromatographed on silica gel (10 g). Elution with light petroleum/AcOEt 17:3 afforded first **20c** (48 mg, 23.1%) as an oil and then **21c** (55 mg, 26.4%). M.p. 78–79° (from acetone/MeOH).

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