PARTICIPATION OF 19-ESTER GROUPS IN THE CLEAVAGE OF 2α,3α- AND 5α,6α-STEROID EPOXIDES. A CASE OF COMPETITION BETWEEN PARTICIPATION AND EXTERNAL NUCLEOPHILE ATTACK*

Pavel Kočovský and Václav Černý

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

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Acid cleavage of the acetoxy epoxide *IIIa* with aqueous perchloric acid or hydrobromic acid gave two types of products, *i.e.* the diol *Va* or the bromohydrin *VIa*, and the cyclic ether *VIII*. The latter compound arises by participation of ether oxygen of the ester group. On reaction with perchloric acid the epoxide *IVa* gave the diol *XIIIa* as a product of a normal reaction and the isomeric diol *Xa* as a product arising by intramolecular participation of the carbonyl oxygen of the 19-acetoxy group. Participation of the 19-ester group is confirmed by the formation of the cyclic carbonate *XI* when the 19-carbonate *IVb* is treated analogously. On reaction with hydrobromic acid, the epoxide *IVa* gave solely the bromohydrin *XIVa* as a product of the normal reaction course. Discussed is the similarity of these reactions with electrophilic additions to the related 19-acetoxy olefins *I* and *II*, the mechanism, the difference in behavior of both epoxides *III* and *IV*, the dependence of the product ratio on the nucleophility of the attacking species, and the competition between participation of an ambident neighboring group and an external nucleophile attack.

In our previous paper[1] we reported on the participation of the 19-acetoxy group in hypobromous acid addition to isomeric steroid olefins *Ia* and *IIa*. With regard to similarity in the opening of the cyclic halonium ion[2,3] and of the epoxide ring[4,5] it appeared of interest to investigate the behavior of analogous epoxides *IIIa* and *IVa* in acid catalyzed cleavage; particularly, the question arose whether or not participation of the 19-acetoxyl will also be operative and if so, whether or not such a process will be accompanied by the competitive attack of an external nucleophile. In another paper[5] we described the acid catalyzed cleavage of the two 19-methoxy epoxides *IIIc* and *IVc* and observed the competition between the attack of an external nucleophile (water or bromide anion) and intramolecular cyclization with participation of the methoxyl group.

In the present paper we report on the behavior of the related 19-acetoxy epoxides *IIIa* and *IVa*. Here, the number of possibilities of nucleophile attack is extended by potential intramolecular carbonyl oxygen participation. One obvious route to prove the

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last kind of participation appeared to be analogous experiments with ethyl carbonates *IIIb* and *IVb* that should yield stable cyclic carbonates[1,6]. We prepared model epoxides *IIIa*, *IIIb* and *IVb* by epoxidation of the corresponding olefins *Ia*, *Ib* and *IIb*; the epoxide *IVa* is a known compound[7].

On treatment with aqueous perchloric acid, the 2α,3α-epoxide *IIIa* was cleaved to give a mixture of the diol *Va* and the cyclic ether *VIII*. On treatment with hydrobromic acid, it gave the bromohydrin *VIa* and again the cyclic ether *VIII* (Table I). On treatment with aqueous perchloric acid the corresponding ethyl carbonate *IIIb* gave two diols, *Vb* and *VII*. In this case formation of the cyclic ether *VIII* was not observed. As reported earlier[5], the 19-methoxy derivative *IIIc* gave a mixture of the cyclic ether *VIII* and diol *Vc* or bromohydrin *VIc* on acidic fission (Table I).

TABLE I

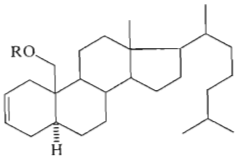
Yields and Ratios of Epoxide *IIIa*—*IIIc* Cleavage Products

Starting compound	Reagent	Products, % of the total yield				Total yield %	Ref.
		V	*VI*	*VII*	*VIII*		
IIIa	$HClO_4/H_2O$	40	—	—	60	95	—
IIIa	HBr/H_2O	—	85	—	15	89	—
IIIb	$HClO_4/H_2O$	63	—	37	—	90	—
IIIc	$HClO_4/H_2O$	32	—	—	68	91	5
IIIc	HBr/H_2O	—	52	—	48	90	5

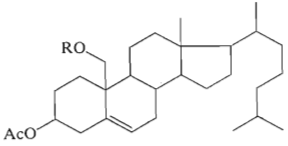
TABLE II

Yields and Ratios of Epoxide *IVa*—*IVc* Cleavage Products

Starting compound	Reagent	Products, % of the total yield					Total yield %	Ref.
		X	*XI*	*XII*	*XIII*	*XIV*		
IVa	$HClO_4/H_2O$	97	—	—	3	—	88	7
IVa	HBr/H_2O	—	—	—	—	100	92	—
IVb	$HClO_4/H_2O$	58	23	—	19	—	92	—
IVc	$HClO_4/H_2O$	—	—	27	73	—	87	5
IVc	HBr/H_2O	—	—	—	—	100	94	5



Ia, R = CH_3CO
Ib, R = C_2H_5OCO
Ic, R = CH_3



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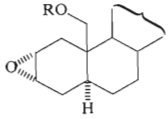
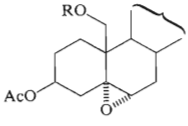
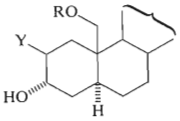
IIb, R = C_2H_5OCO
IIc, R = CH_3



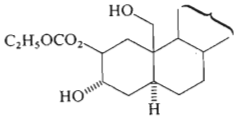
IIIa, R = CH_3CO
IIIb, R = C_2H_5OCO
IIIc, R = CH_3



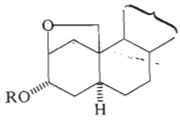
IVa, R = CH_3CO
IVb, R = C_2H_5OCO
IVc, R = CH_3



Va, Y = OH, R = CH_3CO
Vb, Y = OH, R = C_2H_5OCO
Vc, Y = OH, R = CH_3
VIa, Y = Br, R = CH_3CO
VIc, Y = Br, R = CH_3



VII

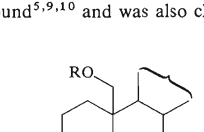


VIII, R = H
IX, R = Ac

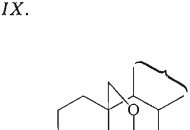
On cleavage with aqueous perchloric acid, the 5α,6α-epoxide *IVa* yields two isomeric diols, *Xa* and *XIIIa* (ref.[7,8]). Reaction with hydrobromic acid results in the exclusive formation of the bromohydrin *XIVa*. Upon the action of aqueous perchloric acid, the ethyl carbonate *IVb* gave analogous diols *Xb* and *XIIIb* and the cyclic carbonate *XI* (Table II).

The structure of the diol *Va* follows from its ^{1}H-NMR spectrum where the singlet of the acetate methyl and the unaffected position of the AB system of the two 19-protons demonstrate retention of the acetoxy group in position 19. The spectrum further

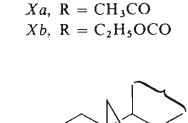
demonstrates the presence of equatorial 2α-H and 3β-H (Table III). The structure of the diol *Vb* was proved in the same manner. The structure of the bromohydrin *VIa* was also derived from its ^{1}H-NMR spectrum: Similarly as in the instance of the diol *Va*, the acetoxy group in position 19 remains preserved and in the spectrum are present signals of equatorial 2α- and 3β-protons. With regard to the α-configuration of the starting epoxide *IIIa* and assuming the chair conformation of the A-ring, the bromohydrin *VIa* must be a 2β-bromo-3α-hydroxy derivative. In accord with this alottment, the compound *VIa* is not identical with the previously prepared[1] 3α-bromo-5α-cholestan-2β,19-diol 19-acetate. The structure of the compound *VII* is also based on its ^{1}H-NMR spectrum retaining the signals of one ethoxyl group, and of two equatorial protons in positions 2α and 3β. The IR band of the carbonate group is present at 1744 cm^{-1}. The cyclic ether *VIII* is identical with the known compound[5,9,10] and was also characterized as the acetate *IX*.



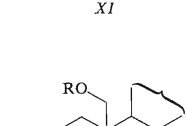
Xa, R = CH_3CO
Xb, R = C_2H_5OCO



XI



XII



XIIIa, X = OH, R = CH_3CO
XIIIb, Y = OH, R = C_2H_5OCO
XIIIc, Y = OH, R = CH_3
XIVa, Y = Br, R = CH_3CO
XIVc, Y = Br, R = CH_3

The ^{1}H-NMR spectrum of the diol *Xb* (Table III) proves retention of the ethyl carbonate group at $C_{(19)}$ since the chemical shift of the AB system of the 19-protons remains unaffected and the signals of the ethoxyl group are still present. The shape of the signal of the 6-proton reveals the α-configuration of the 6-hydroxyl. The fact that both hydroxyls react with trichloroacetyl isocyanate and only one proton signal is significantly shifted indicates that the second hydroxyl is tertiary. The multiplet

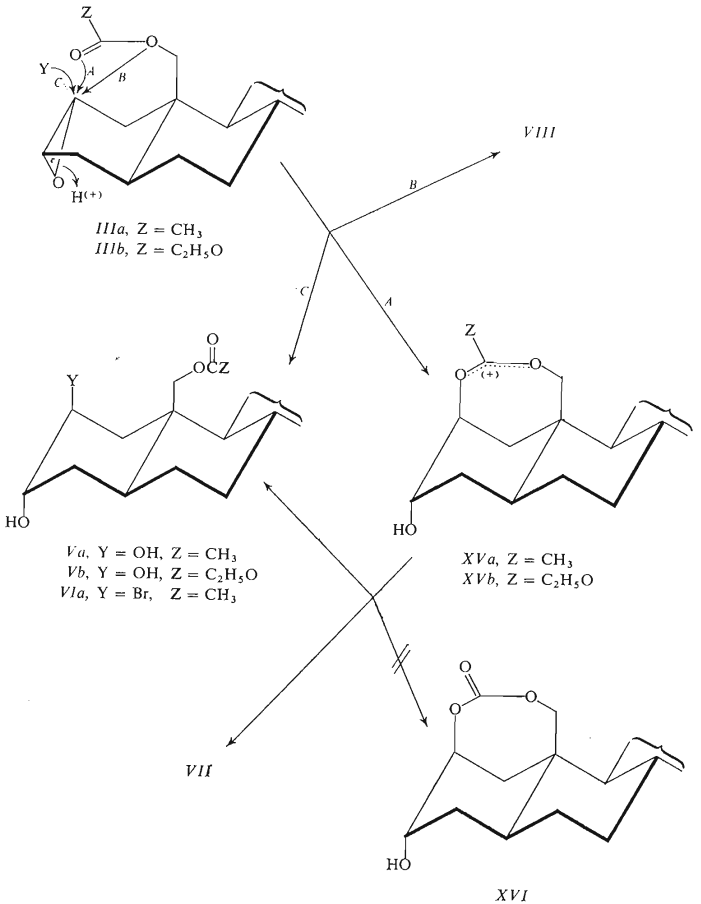
associated with 3α-H has $W_{1/2}$ = 8 Hz which is only compatible with axial conformation of the 3β-acetoxy group. This is only possible if the junction of the rings A and B is *cis*; the 5-hydroxyl group is therefore β-oriented. The ^{1}H-NMR spectrum of the cyclic carbonate *XI* (Table III) bears the same characteristic features as the spectra of both diols *Xa* and *Xb*. The compound is therefore characterized by 6α-configuration of the hydroxyl group and *cis* annelation of the A/B ring system. The compound reacts with only one molecule of trichloroacetyl isocyanate. The un-

TABLE III
^{1}H-NMR Data of Epoxide Cleavage Products

Compound	18-H	19-H[a]	2-H($W_{1/2}$)	3-H($W_{1/2}$)	6-H($W_{1/2}$)
Va	0·60	4·40	3·87 m (8)	3·87 m (8)	—
			5·12 m[b]	5·12 m[b]	—
Vb	0·65	4·42	3·88 m (7)	3·88 m (7)	—
		4·50[b]	5·13 m (7)[b]	5·13 m (7)[b]	—
Vc	0·67	3·51	3·88 m (7)	3·73 m (7)	—
VIa	0·63	4·30	4·30 m[c]	4·10 m[c]	—
			4·40 m[b,c]	5·30 m (8)[b]	—
VIc	0·67	3·53	4·40 m (8)	4·05 m (9)	—
VII	0·68	3·80	4·75 m (8)	3·96 m (7)	—
		4·50[b]	4·91 m (8)[b]	5·10 m (7)[b]	—
VIII	0·65	3·77	4·15 m (9)	3·92 m (8)	—
IX	0·62	3·68	4·20 m (12)	4·80 m (10)	—
Xa	0·66	4·34	—	5·28 m (8)	3·86 m (16)
Xb	0·62	4·40	—	5·28 m (8)	3·83 m (15)
				5·28 m[b]	5·28 m[b]
XI	0·60	4·24	—	5·06 m (9)	4·30 m
				5·06 m[b]	5·31 m (15)[b]
XII	0·70	3·82	—		3·70 m (5)
XIIIa	0·67	4·55	—	5·16 m (20)	3·54 m (6)
XIIIb	0·65	4·57	—	5·20 m (20)	3·51 m (7)
				5·20 m	6·02 m (7)[b]
XIIIc	0·68	3·71	—		4·64 m
XIVa	0·65	4·64	—	5·08 m (20)	3·95 m (7)
XIVc	0·73	3·86	—	—	[c]

[a] Center of AB system. [b] The values obtained after treatment with trichloroacetyl isocyanate. [c] Overlapped by other signals.

changed chemical shift of the 19-protons in its ^{1}H-NMR spectrum (relative to *IVb*), the absence of the ethoxyl group (^{1}H-NMR) but the presence of —O—CO—O— group (IR, 1767 cm^{-1}) prove that the oxygen atoms in the positions 5β and 19 form



part of a cyclic carbonate grouping. The ^{1}H-NMR spectrum of the diol *XIIIb* proves the presence of a 19-ester group and a 6β-hydroxyl, the latter being characterized by a narrow multiplet of the 6α-proton shifted toward the lower field after treatment with trichloroacetyl isocyanate. The second hydroxyl is tertiary *i.e.* located at $C_{(5)}$ as indicated also by trichloroacetyl isocyanate treatment. The 3α-proton has $W = 30$ Hz and the 3β-acetoxy group is therefore equatorial, the junction of the A/B ring is *trans* and the $C_{(5)}$-hydroxyl has the α-configuration. These characteristic spectral features are identical with those of the known acetate *XIIIa*. Analogous arguments lead to formula *XIVa* for the product of hydrogen bromide treatment.

The previously observed similarity in the opening of the cyclic halonium ion and of the epoxide ring[5] permitted the assumption of similar behavior of 19-acyloxy--2α,3α- and 5α,6α-epoxides *III* and *IV* in this respect when compared with 19-acyloxy-2,3- and 5,6-unsaturated steroids *I* and *II*. In fact, the similarity in reactivity is surprisingly close.

Acidic cleavage of the 2α,3α-epoxide *IIIa* should lead to a diaxial derivative as a product of steroelectronic control[11]. The fission should then occur at $C_{(2)}$ by an attack from the β-side. Similarly as in the case of the corresponding 2α,3α-bromonium ion[1], three potential reaction pathways can accommodate these requirements: *1*) Attack by the carbonyl oxygen of the 19-ester group with formation of the intermediate *XVa* containing a seven-membered ring, *i.e.* 7(O)$^{\pi,n}$ participation (path *A*); for notation *cf.* ref.[1]. Fission of this cation would yield the diol *Va*. *2*) Attack by ether oxygen of the ester grouping to form the cyclic ether *VIII*, *i.e.*5 (O)^n participation (path *B*). *3*) Attack by an external nucleophile (water or bromide anion) leading to the diol *Va* or bromohydrin *VIa* (path *C*).

When the 19-acetoxy epoxide *IIIa* was cleaved by aqueous perchloric acid, two products were isolated: The diol *Va* and the cyclic ether *VIII* in 2 : 3 proportion (Table I). Similarly as in the instance of the 2α,3α-bromonium ion[1] (generated by the addition of hypobromous acid to the 2,3-olefin *Ia*), 5(O)^n participation predominates over the two remaining pathways. It is also interesting to compare this result with the behavior of the analogous methoxy derivative *IIIc* on treatment with aqueous perchloric acid[5]. Here, a mixture of the diol *Vc* and the cyclic ether *VIII* is formed in c. 1 : 3 proportion (Table I). Thus, observed is a shift in the relative proportion of the cyclic ether to the product of the competing reaction in favor of the cyclic ether when passing from the 19-ester (*IIIa*) to the 19-ether (*IIIc*). This finding again parallels the differences found in hypobromous acid addition to 19-substituted olefins *Ia* and *Ic* where in the 19-acetoxy derivative *Ia* the 5(O)^n participation is somewhat suppressed in favor of the alternative product[1].

In view of the possibility that the diol *Va* can be a product of either of two pathways (*A* or *C*) the product analysis alone cannot provide information of the mode of its formation. In the hope of obtaining some evidence concerning this question we applied the same approach as already used[1] for solving a similar problem in the in-

Xa, Z = CH3
Xb, Z = C2H5O
IVa, Z = CH3
IVb, Z = C2H5O
XI
XII
XIIIa, Y = OH, Z = CH3
XIIIb, Y = OH, Z = C2H5O
XIVa, Y = Br, Z = CH3
XVIIa, Z = CH3
XVIIb, Z = C2H5O
A
B
C
A or C

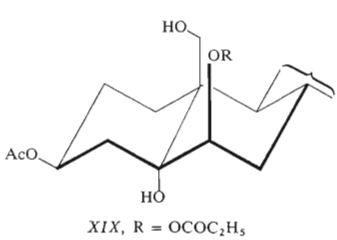
vestigation of hypobromous acid addition, *i.e.* the ethyl carbonate *IIIb* was taken as a substrate. For cleavage with aqueous perchloric acid, the following routes may be envisaged analogously to the acetate *IIIa*: $7(O)^{\pi,n}$ participation by carbonyl oxygen (path *A*), $5(O)^{n}$ participation of the methyleneoxy oxygen of the ester group (path *B*) and an attack by external nucleophile (water, path *C*). Owing to the character of the ester grouping there is the additional possibility of $7(O)^{n}$ participation of the ethoxyl oxygen. The following products were obtained: 19-carbonate *Vb* and isomeric 2β--carbonate *VII*. No products of $5(O)^{n}$ participation (cyclic ether *VIII*) or of $7(O)^{n}$ participation (cyclic carbonate *XVI*) were observed. Again, these results constitute

TABLE IV
Analytical and Physical Data of Epoxide Cleavage Products

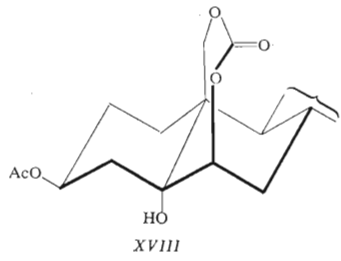
Compound	Formula (m. w.)	Calculated/Found			M. p., °C $[\alpha]_D^{20}$
		% C	% H	% Br	
Va	$C_{29}H_{50}O_4$	75·28	10·89	—	95—97
	(462·7)	75·14	10·76	—	+16°
Vb	$C_{30}H_{52}O_4$	73·13	10·64	—	oil
	(492·7)	73·05	10·51	—	+17°
VIa	$C_{29}H_{49}BrO_3$	67·03	9·50	15·38	138—140
	(519·6)	66·96	9·42	15·63	+28°
VII	$C_{30}H_{52}O_4$	73·13	10·64	—	oil
	(492·7)	72·98	10·47	—	+15°
VIII	$C_{27}H_{46}O_2$	80·54	11·51	—	188—190[a]
	(402·7)	80·63	11·38	—	+35°
IX	$C_{29}H_{48}O_3$	78·33	10·88	—	121—122[a]
	(444·7)	78·15	10·96	—	+38°
Xb	$C_{32}H_{54}O_7$	69·78	9·88	—	oil
	(550·8)	69·57	9·73	—	+36°
XI	$C_{30}H_{48}O_6$	71·39	9·59	—	116—118
	(504·7)	71·16	9·43	—	+19°
XIIIb	$C_{32}H_{54}O_7$	69·78	9·88	—	167—169
	(550·8)	69·53	9·94	—	−15°
XIVa	$C_{32}H_{53}BrO_6$	62·63	8·70	13·02	oil
	(613·7)	62·39	8·62	13·27	−33°

[a] In accordance with the literature[5,9].

strict analogy to those obtained with 2,3-olefins *Ia* and *Ib* on hypobromous acid addition[1]. Unfortunately, the reaction course leading exclusively to compounds *Vb* and *VII* does not permit a decision as to whether formation of the diol *Vb* is due to $7(O)^{\pi,n}$ participation or to an attack of water as external nucleophile (or whether both mechanisms are operative). For reasons outlined earlier[1] we prefer the assumption that formation of *Vb* (and also *Va*) is predominantly due to $7(O)^{\pi,n}$ participation *via* the cation *XVb* (path *A*). *A priori*, the diol *VII* could alternatively arise from *Vb* by intramolecular migration of the acyl group. However, this mode of formation was ruled out since the diol *Vb* was shown to be quite stable under conditions of epoxide cleavage. This behavior, once again, parallels the behavior of an analogous product in hypobromous acid additions to 2,3-olefin *Ib*.



XIX, R = $OCOC_2H_5$



XVIII

Cleavage of the 19-acetoxy-2α,3α-epoxide *IIIa* with hydrobromic acid yields a mixture of the bromohydrin *VIa* and cyclic ether *VIII* in 6 : 1 proportion. When compared with cleavage of the same compound with aqueous perchloric acid where the cyclic ether *VIII* slightly predominates in the reaction mixture, it is obvious that higher nucleophility of the bromide ion results in the increased importance of external nucleophile attack.

Another comparison may be made between hydrobromic acid cleavage of the 2α,3α-epoxide bearing a 19-acetoxy group (*IIIa*) and 2α,3α-epoxide bearing a 19--methoxy group (*IIIc*). The proportion of the participation product (cyclic ether *VIII*) to the product of external attack (bromohydrin *VIa* or *VIc*, respectively) is enhanced drastically when the 19-acetoxy group is replaced by the 19-methoxyl (Table I). This difference reflects decreased nucleophility of the ether oxygen in the acetoxy group.

The isomeric 5α,6α-epoxide *IVa* constitutes a more complicated model since its oxirane ring may be split at two sites[11]: Steric aspects require preferential cleavage at $C_{(6)}$ leading to 5α,6β-diaxial products whereas the electronic aspects favor cleavage at $C_{(5)}$. With common 19-unsubstituted steroids cleavage proceeds preferentially at $C_{(6)}$

but additional factors such as the nature of the substituent at $C_{(3)}$, of the reagent used *etc.*, play an important role. Particularly, treatment with Lewis acids in a non-polar medium (in the absence of external nucleophile) results in preferential cleavage at $C_{(5)}$ usually followed by skeletal rearrangements[11].

In the 19-acetoxy derivative *IVa* opening of the epoxide ring at $C_{(6)}$ with aqueous perchloric acid may proceed in three ways: *1*) With participation of the carbonyl oxygen of the ester group, *i.e.* with $7(O)^{\pi,n}$ participation (path *A*) yielding the diol *XIIIa*. *2*) By attack of the ether oxygen of the ester group to form the cyclic ether *XII* with a five-membered ring, *i.e.* involving $5(O)^n$ participation (path *B*). *3*) By attack of a molecule of water as external nucleophile (path *C*) to give the same diol *XIIIa* as by the path *A*. Actually, no cyclic ether *XII* was formed. The reason for this lack of $5(O)^n$ participation is presumably due to decreased electron density on the ether oxygen of the ester group. The only product of the epoxide cleavage at $C_{(6)}$ is the diol *XIII*; whether its formation is due to pathway *A* or *C* cannot be decided from the experimental data obtained by the product analysis of *IVa*. However, indirect evidence gained from analogy with the 19-carbonate *IVb* led us to the assumption that only the pathway *C* is responsible for the formation of *XIII*.

The only product of cleavage of the epoxide ring in *IVa* at $C_{(5)}$ is diequatorial 5β,6α-diol *Xa*. At the same time, with 86% yield the diol *Xa* is the main product of the overall cleavage reaction with 10% aqueous perchloric acid. This fission to the diol *Xa* is due to $6(O)^{\pi,n}$ participation of the carbonyl group *via* a six membered cyclic intermediate *XVIIa* (path *A'*).

In addition to the 19-acetoxy derivative *IVa*, analogous 19-ethyl carbonate *IVb* was subjected to treatment with aqueous perchloric acid since it was assumed that deeper insight into the reaction could be gained in this manner. The main products were 5β, 6α-diol *Xb* and the cyclic carbonate *XI*, the minor product being the 5α, 6β-diol *XIIIb* (Table II) analogous to the minor product *XIIIa* of the 19-acetoxy epoxide *IVa* cleavage. In view of the fact that no products were obtained arising by $7(O)^{\pi,n}$ participation (*i.e.* the cyclic 6β,19-carbonate *XVIII* with a seven-membered ring or the compound *XIX* with the $C_2H_5OCO_2$ – grouping at 6β-position), it is assumed that external nucleophile attack (path *C*) prevails in the formation of the 5α, 6β-diol *XIIIb*. Formation of the 5β,6α-diol *Xb* and cyclic carbonate *XI* is assumed to be due to $6(O)^{\pi,n}$ participation of the ester carbonyl. The assumption of this pathway is also supported by the high relative yield of *Xb* and *XI* (58% and 23%) from *IVb* which is comparable with the relative yield of the analogous diol *Xa* from the acetate *IVa* (97%) where only $6(O)^{\pi,n}$ participation is possible. The alternative $6(O)^n$ participation of the ethoxyl oxygen is thus less probable.

Cleavage of the epoxide *IVa* with perchloric acid demonstrates that $6(O)^{\pi,n}$ participation can change the "normal" direction of 5α,6α-epoxide cleavage in favor of the diequatorial product and that it is able to suppress $5(O)^n$ participation. In all these

respects, fission of the 5α,6α-epoxide *IVa* is quite analogous to cleavage of the 5α,6α--bromonium ion in the course of hypobromous acid addition to the olefin *IIa*.

Cleavage of the 5α,6α-epoxide *IVa* with hydrobromic acid affords solely the bromohydrin *XIVa*. The same exclusion of participation was observed earlier[5] with the 19-methoxy derivative *IVc* where the bromohydrin *XIVc* is also the sole reaction product. This uniform reaction is doubtlessly due to stronger nucleophility of the bromide anion.

When isomeric 19-methoxy derivatives with 2α,3α- or 5α,6α-epoxide group (*IIIc* and *IVc*) are compared a characteristic difference in their behavior towards both hydrobromic and perchloric acid is the absence of $5(O)^n$ participation in *IVc* as compared with *IIIc*. This difference is attributed to larger distance of the methoxyl oxygen in *IVc* from the reaction center at $C_{(6)}$ (ref.[5,10]). In the case of the acetate *IVa* an additional factor acting in the same direction is the decreased electron density on ether oxygen of the ester grouping. The $6(O)^{\pi,n}$ participation is not operative on hydrobromic acid cleavage presumably for marked steric compression about the reaction center which results in incapability to compete with the external attack of the strong nucleophile (Br^-). On the other hand, $6(O)^{\pi,n}$ participation is favored in competition with a weak nucleophile (H_2O).

It may be summarized that the reactions of 2α,3α- and 5α,6α-epoxides are thus closely analogous to those of the corresponding 2α,3α- and 5α,6α-bromonium ions and follow the same sequence of reactivities[1]:

$$6(O)^{\pi,n} > 5(O)^n > 7(O)^{\pi,n} \geqq \text{external attack of a weak nucleophile}$$

No evidence was found for $7(O)^n$ participation. If a strong external nucleophile (such as Br^-) is present, participation of the 19-ester (or ether) group is markedly (2α,3α-epoxide) or completely (5α,6α-epoxide) suppressed.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 50°C/0·2 Torr (26 Pa). Optical measurements were carried out in chloroform with an error of ±3°. The IR spectra were recorded on a Zeiss UR 20 spectrometer in tetrachloromethane. The ^{1}H-NMR spectra were recorded on a Tesla BS 467 instrument (60 MHz) in deuteriochloroform at 30°C with tetramethylsilane as internal reference. Chemical shifts are given in ppm. Apparent coupling constants (in Hz) were obtained from a first order analysis. 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. Usual work up of an ethereal solution means washing the solution with 5% aqueous hydrochloric acid solution, water, 5% aqueous potassium hydrogen carbonate solution, water, drying with sodium sulfate and evaporated of the solvent *in vacuo*.

Cleavage of Epoxides *IIIa*, *IIIb*, *IVa* and *IVb*

The epoxide (200 mg) was dissolved in dioxane (6—8 ml), water (0·5 ml) was added and the mixture was treated with acid, *i.e.* 72% aqueous perchloric acid (0·3 ml) or 48% aqueous hydrobromic acid (0·5 ml) for 1—2 h. The mixture was diluted with ether and water, the organic layer was washed ten times with water, dried with sodium sulfate and the solvent was evaporated. The residue was chromatographed on four preparative silica gel plates using a mixture of light petroleum, ether and acetone (80 : 10 : 10) for development. Corresponding zones were collected, eluted with ether, the solvent was evaporated and the residue dried in a vacuum desiccator overnight. The yields of products are given in Tables I and II. Their ^{1}H-NMR spectra, analytical data and physical constants are given in Tables III and IV.

2α,3α-Epoxy-5α-cholestan-19-ol 19-Acetate (*IIIa*)

The acetate[1] *Ia* (300 mg) was dissolved in a mixture of benzene (5 ml) and ether (5 ml) and treated with a solution of monoperoxyphthalic acid (3 ml; 110 mg/ml) at room temperature overnight. The mixture was diluted with ether and water, the organic layer was washed with water, 5% aqueous potassium hydrogen carbonate solution, aqueous sodium thiosulfate solution, water, dried with sodium sulfate and the solvent was evaporated. The residue was chromatographed on a silica gel column (30 g) using a mixture of light petroleum and ether (95 : 5) which separated a small amount of impurities. Subsequent elution with a mixture of light petroleum and ether (90 : 10) afforded the crude epoxide *IIIa* (245 mg), which on crystallization from a mixture of acetone, methanol and water gave the pure *IIIa* (183 mg), m.p. 80—81°C, $[\alpha]_D^{20}$ +27° (*c* 2·1). ^{1}H-NMR spectrum: 0·60 (3 H, s, 18-H), 4·15 (2 H, s, 19-H), 3·05 (2 H, m, $W_{1/2}$ = 5 Hz, 2β-H and 3β-H). For $C_{29}H_{48}O_3$ (444·7) calculated: 78·33% C, 10·88% H; found: 78·28% C, 10·96% H.

2α,3α-Epoxy-5α-cholestan-19-ol 19-Ethyl Carbonate (*IIIb*)

The carbonate[1] *Ib* (200 mg) was dissolved in a mixture of benzene (5 ml) and ether (5 ml) and treated with an ether solution of monoperoxyphthalic acid (2 ml; 110 mg/ml) at room temperature overnight. The mixture was diluted with ether and water, the organic layer was worked up as given for *IIIa*. The residue was chromatographed in the same manner as given for *IIIa* to yield the oily epoxide *IIIb* (182 mg), $[\alpha]_D^{20}$ +27° (*c* 2·9). ^{1}H-NMR spectrum: 0·65 (3 H, s, 18-H), 4·24 (2 H, s, 19-H), 3·17 (2 H, m, 2β-H and 3β-H), 1·30 (3 H, t, J = 7 Hz, C$\underline{H}_3$C$\underline{H}_2$), 4·19 (2 H, q, J = 7 Hz, C$\underline{H}_3$C$\underline{H}_2$). For $C_{30}H_{50}O_4$ (474·7) calculated: 75·90% C, 10·62% H; found: 75·72% C, 10·54% H.

5,6α-Epoxy-5α-cholestane-3β,19-diol 3-Acetate 19-Ethyl Carbonate (*IVb*)

The ethyl carbonate[1] *IIb* (400 mg) was dissolved in chloroform (5 ml) and treated with *m*-chloroperoxybenzoic acid (300 mg) at room temperature overnight. The mixture was diluted with ether and the organic layer was worked up as given for *IIIa*. The residue was chromatographed on a silica gel column (30 g) using a mixture of light petroleum and ether (96 : 4). Corresponding fractions were collected and evaporated to yield the crude epoxide *IVb* contamined with the isomeric 5β,6β-epoxide. The mixture was crystallized twice from a mixture of acetone, methanol and water, and the crystals of a minor component were mechanically separated. The pure 5α,6α-epoxide *IVb* had m.p. 106—108°C, $[\alpha]_D^{20}$ −31° (*c* 2·0). ^{1}H-NMR spectrum: 0·61 (3 H, s, 18-H), 4·42 (2 H, s, 19-H), 2·00 (3 H, s, CH_3CO_2), 1·31 (3 H, t, J = 7 Hz, C$\underline{H}_3$C$\underline{H}_2$), 4·62 (2 H, q, J = 7 Hz, $CH_3C\underline{H}_2$), 4·98 (1 H, m, W = 30 Hz, 3α-H), 2·98 (1 H, d, J = 3·9 Hz, 6β-H). For $C_{32}H_{52}O_6$ (532·8) calculated: 72·14% C, 9·84% H; found: 72·35% C, 10·02% H.

The analyses were carried out in the Analytical Laboratory of this Institute (under the direction of Dr J. Horáček). The IR spectra were recorded by Mrs K. Matoušková and Mr P. Formánek and interpreted by Dr S. Vašíčková. The ^{1}H-NMR *spectra were recorded and interpreted by Dr M. Synáčková.*

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Note added in proof: In considering cleavage of the 5α,6α-epoxide *IVa*, the question arises whether π or n orbitals of the carbonyl function are involved in $6(O)^{\pi,n}$ participation reaction. In a quantum chemistry study, undertaken in our laboratory, cleavage of protonated ethylene oxide by formic acid carbonyl is being used as a model reaction. The results as yet obtained indicate that n orbitals of the carbonyl oxygen take part in this reaction[12].