COMPETITION OF 5(O)^n AND 6(O)^n PARTICIPATION BY 19a-SUBSTITUENT IN HYPOBROMOUS ACID ADDITION TO 2,3- AND 5,6-UNSATURATED 19-HOMOCHOLESTANE DERIVATIVES*

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19-Substituted 2,3-unsaturated cholestane derivatives *IIIa*—*IIIc* react with hypobromous acid to give the cyclic bromo ether *VI* as sole or major product arising by cleavage of the 2α,3α-bromonion *V* with 6(O)^n participation by the 19a-group. The 5,6-unsaturated alcohol *IVa* reacts with hypobromous acid to yield the cyclic bromo ether *X* as product of 5(O)^n participation. Under the same conditions, the methoxy derivative *IVb* yields two products, *X* and *XI*, with violation of Fürst–Plattner rule. In similar manner as in the preceding case, the products arise by cleavage of the bromonium ion *IXb* with 5(O)^n participation by the 19a-methoxyl. In contrast, the 5,6-unsaturated acetoxy derivative *IVc* reacts without participation *via* two diastereoisomeric bromonium ions *VIIIc* and *XV* to give the corresponding diaxial bromohydrins *XVI* and *XVII* which undergo spontaneous cyclization to the epoxides *XVIII* and *XIX*. The course of these reactions, comparison with the lower homologs of the type *I* and *II*, the role of Markovnikov and Fürst–Plattner rules and capability of the particular functional groups to participate in 5(O)^n and 6(O)^n processes are discussed.

One of the factors that may dramatically influence the course of electrophilic addition[1] is neighboring group participation[2]. This has been well documented by application of intramolecular participation for synthetic purposes in stereoselective halolactonization[3,4], stereo- and regioselective introduction of new substituents[5,6] into a substrate molecule, stereoselective ring closure *etc*[7]. In our previous papers[8–12] we dealt with participation by neighboring group (OH, OCH_3, $OCOCH_3$) located in the position 19 of the steroid skeleton whereby a 2,3 (*Ia*–*Ic*) or 5,6-double bond (*IIa*–*IIc*) (Scheme 1) was involved. The compounds *Ia*–*IIb* react preferentially with 5(O)^n participation by a 19-OR group (for notation *cf.* ref.[10]). We rationalized certain quantitative differences in the reactivity of the particular derivatives by influence of steric and stereoelectronic factors differing from case to case (distance of the OR group from the reaction center, the angle of approach *etc.*)[12,13]. The acetate *IIc* reacted differenly[10,12], the main reaction pathway being a 5(O)$^{\pi,n}$ participation.

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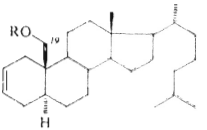
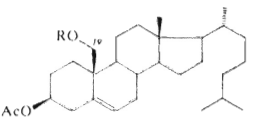


Ia, R = H
Ib, R = CH_3
Ic, R = Ac



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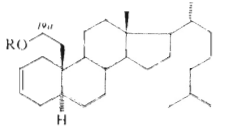
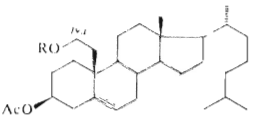
IIc, R = Ac



IIIa, R = H
IIIb, R = CH_3
IIIc, R = Ac



IVa, R = H
IVb, R = CH_3
IVc, R = Ac

SCHEME 1

In continuation of these studies it appeared desirable to investigate the reactivity of homologous derivatives *IIIa–IIIc* and *IVa–IVc* (Scheme 1; for synthesis *cf.* ref.[14,15]) as complementary models to the earlier studied compounds. For structural reasons, these homologs could be expected to undergo 6(O)^n participation (type *III*) possibly accompanied by competition of 5(O)^n participation (type *IV*).

The 2.3-unsaturated alcohol *IIIa*, as well as the methyl ether *IIIb*, when treated with hypobromous acid (generated *in situ* from N-bromoacetamide and perchloric acid in aqueous dioxane) furnish the cyclic bromo ether *VI* quantitatively. The acetate *IIIc* yields the ether *VI* along with the bromohydrin *VII* as a minor product (Table I). The structures of both products follow mainly from ^{1}H NMR spectra. In the bromo epoxide *VI*, no olefinic protons could be observed. Instead, the spectrum contains multiplets corresponding to equatorial 2α-H and 3β-H by their shape and width, similarly to a homolog with a tetrahydrofuran ring[8,9]. In addition, the molecular peak in the mass spectrum is consistent with the structure *VI* and in the IR-spectrum no band of a hydroxy group is present. The ^{1}H NMR spectrum of the bromohydrin *VII* shows a multiplet due to equatorial 2α-H and 3β-H (analogously to the homolog with a 19-acetoxy group[10]) and reveals retention of the acetoxy group in position 19a (Table II). On the basis of these facts the structure of these products may be considered as proved.

Under the same conditions, the 5,6-unsaturated alcohol *IVa* (Scheme 3) gives the cyclic bromo ether *X*. The methyl ether *IVb* gives the same bromo ether which is,

TABLE I

Yields and ratios of products of hypobromous acid addition to the compounds *IIIa—IVc*

Starting compound	Relative yields in % (product)			Total yield (%)	Ref.
	$(O)^n$ participation	external attack	others		
Ia	100	—	—	95	8
Ib	100	—	—	96	9
Ic	88	12	—	90	10
IIa	100	—	—	97	8
IIb	65	—	35[a]	88	9
IIc	—	12	88[b]	86	10
IIIa	100 (*VI*)	—	—	96	—
IIIb	100 (*VI*)	—	—	95	—
IIIc	56 (*VI*)	43 (*VII*)	—	91	—
IVa	>98 (*X*)	—	<2	90	—
IVb	84 (*X*)	16 (*XI*)	—	87	—
IVc	—	66 (*XVI*)	34 (*XVIII*)[a]	81	—

[a] Product of 5β,6β-bromonium ion cleavage. [b] Sum of products arizing from 5α,6α-bromonium ion cleavage with $6(O)^{\pi,n}$ particioation and from 5β,6β-bromonium ion.

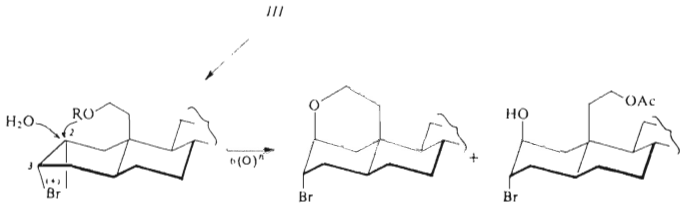
TABLE II

^{1}H NMR Data of the products of hypobromouns acid addition

Compound	19-H	19a-H (*W*)[a]	CH—O (*W*)[a]	CH—Br (*W*)[a]	3α-H (*W*)[a]
VI	0·64	3·70 m (20)	4·18 m (12)	4·28 m (10)	—
VII	0·70	4·20 m (35)	4·25 m (*W* = 17)		—
X	0·65	4·00 m (20)	—	4·20 dd[b]	5·08 m (14)
XI	0·63	3·70 m (20)	—	4·63 dd[c]	5·15 m (13)
XI[d]	0·65	4·40 dt[e] 4·68 dt[f]	—	4·57 dd[g]	5·12 m (13)
XVI	0·67	4·20 m (40)	4·10 m (9)	—	5·40 m (30)
XVIII	0·65	4·25 m (25)	2·95 d[h]	—	5·00 m (30)

[a] The values are given in Hz. [b] J = 5·5 and 12·0 Hz. [c] J = 5·4 and 12·1 Hz. [d] The values obtained after treatment with trichloroacetyl isocyanate. [e] J = 4·8, 10·6 and 10·6 Hz; [f] J = 6·0, 10·4 and 10·4 Hz. [g] J = 5·0 and 12·0 Hz. [h] J = 3·5 Hz.

however, accompanied by a small amount of the derivative *XI* (Table I). The structure of the compound *X* was established from its ^{1}H NMR spectrum (Table II). The spectrum shows absence of a methoxy group, the half width of the 3α-H signal discloses *cis*-annellation of the A and B rings, and finally the coupling of the CH—Br moiety reveals the 6α-configuration of the bromine atom. The molecular peak in the mass spectrum is in agreement with the structure *X*.



Va, R = H
Vb, R = CH_3
Vc, R = Ac

VI *VII*

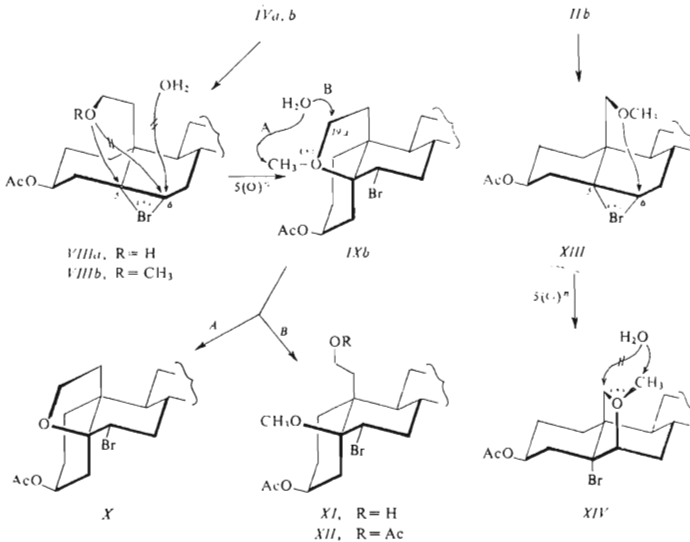
SCHEME 2

The structure determination of *XI* was somewhat more complicated. Similar to the preceding case, the ^{1}H NMR spectrum shows a multiplet of 3α-H, the shape and width of which is again in conformity with *cis*-annellation of the A and B rings and the signal of the CH—Br grouping shows 6α-position of the bromine atom. Finally, there is present a multiplet of the CH_2—O grouping and, in addition, a singlet of a methoxy group at 3·62 ppm. The molecular peak in the mass spectrum is in agreement with a product of simple hypobromous acid addition. Based on these data, two structures may be proposed: the structure *XI* and a positional isomer in which the positions of the OH and methoxy groups are interchanged, *i.e.* 5β-hydroxy-19a-methoxy structure. A definite decision could be made after acetylation which resulted in a strong shift of the CH_2O group. This fact permits to formulate the acetate as *XII* and the parent alcohol as *XI*. The same conclusion follows from treatment of the alcohol in question with trichloroacetyl isocyanate (Table II).

On reaction with hypobromous acid, the acetate *IVc* yields a mixture of diastereoisomeric epoxides *XVIII* and *XIX*. We proved their structures by chemical correlation with the products of epoxidation of *IVc* with 3-chloroperoxybenzoic acid. The configuration at $C_{(5)}$ and $C_{(6)}$ in these epoxides follows from the shape and width of the signals corresponding to the 6-H (Table II).

Mechanism of Additions

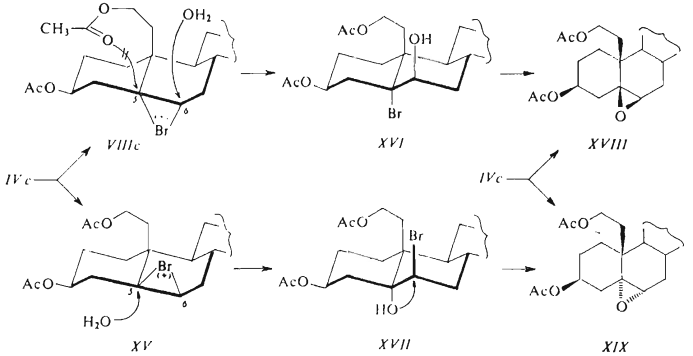
Reactions of 2,3-unsaturated derivatives *IIIa–IIIc* commence by formation of 2α,3α--bromonium ions *Va–Vc*. Products corresponding to formation of 2β,3β-bromonium ions could not be found in the reaction mixture. The bromonium ion of the type *V* is cleaved by the 19a-oxygen in a 6(O)^n process to yield the diaxial cyclic bromo ether *VI* (Scheme 2). This reaction route is exclusive for the alcohol *IIIa* and methyl ether *IIIb* while 2α,3α-bromonium ion derived from the acetate *IIIc* is attacked also by water as external nucleophile which leads to the diaxial bromohydrin *VII*. This behavior is in line with generally smaller disposition of the ester groups to (O)^n participation[13].



SCHEME 3

Similar to preceding case, the 5,6-unsaturated alcohol *IVa* and methyl ether *IVb* suffer solely attack by the electrophilic reagent from the α-side to give rise to 5α,6α-bromonium ions *VIIIa* and *VIIIb*, respectively (Scheme 3). The bromonium ion

VIIIa, thus generated from the alcohol *IVa*, is cleaved solely by the 19a-hydroxyl with $5(O)^n$ participation in conflict with the Fürst–Plattner rule to yield the cyclic Markovnikov-type product *X*. The bromonium ion *VIIIb* generated from the methoxy derivative *IVb* is also split with $5(O)^n$ participation to yield the oxonium ion *IXb*. This ion suffers loss of the methyl group (path *A*) to give the cyclic bromo ether *X*. To a small extent, however, this ion undergoes a competitive cleavage at $C_{(19a)}$ (path *B*) which leads to transfer of the methoxy group to the 5-position and formation of the 5β-methoxy-19a-alcohol *XI*. A comparison with the lower homolog *IIb* (ref.[9]), is of interest. This homolog gives also rise to the 5α,6α-bromonium ion *XIII* that undergoes $5(O)^n$ participation and is cleaved at $C_{(6)}$ to the oxonium ion *XIV*. However, the sole product of the reaction of this ion with water is the corresponding cyclic ether arising by loss of a methyl (analogously to the pathway *A* on cleavage of the oxonium ion *IXb*). An attack by water at $C_{(19)}$ in the ion *XIV*, corresponding to pathway *B*, was not observed. Obviously, this difference is due to steric factors: The accessibility of the methyl group of both oxonium ions *IXb* and *XIII* is about the same (as seen from Dreiding models) and is attacked by water as nucleophile preferentially. Cleavage of the oxonium ion at the methylene carbon (path *B*) can occur in the ion *IXb* due to better accessibility whereas in the ion *XIV* and analogous S_N2-like approach of water to $C_{(19)}$ is hindered by axial protons in positions 2β and 11β.



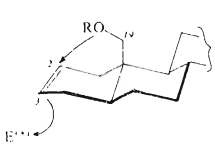
SCHEME 4

With the 5,6-unsaturated acetate *IVc* (Scheme 4) no participation occurs at all. The reaction with hypobromous acid proceeds through the both bromonium ions

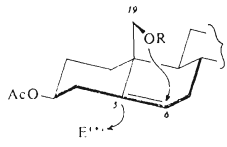
VIIIc and *XV* which, in the same manner as in 19-unsubstituted steroids, are cleaved by attack of water as external nucleophile to yield the diaxial bromohydrins *XVI* and *XVII* undergoing cyclization to the corresponding epoxides *XVIII* and *XIX* on working up the reaction mixture.

General Considerations

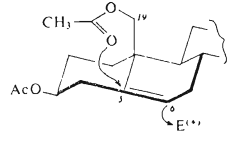
Additions of electrophilic reagents to 2,3-unsaturated 19-unsubstituted steroids are controlled by stereoelectronic factors and formation of the products follows the Fürst–Plattner rule[16]. Also the 2,3-unsaturated 19-substituted derivatives *Ia–Ic* follow this rule and undergo solely an axial attack at $C_{(2)}$ (Scheme 5) (ref.[8–10]).



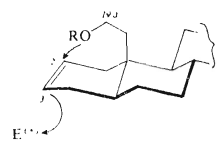
Ia, R = H
Ib, R = CH_3
Ic, R = Ac



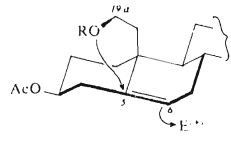
IIa, R = H
IIb, R = CH_3



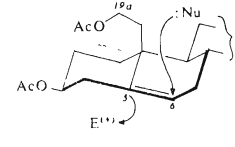
IIc



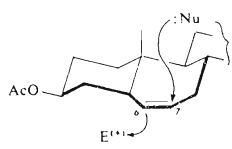
IIIa, R = H
IIIb, R = CH_3
IIIc, R = Ac



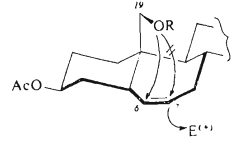
IVa, R = H
IVb, R = CH_3



IVc



XX



XXIa, R = H
XXIb, R = CH_3
XXIc, R = Ac

SCHEME 5

In the alcohol *Ia* and methyl ether *Ib* solely the 19-substituent acts as a nucleophile giving rise to a tetrahydrofuran ring by 5(O)^n participation (Scheme 5). Due to decreased nucleophilicity of the ether oxygen atom in the acetoxy derivative *Ic* the 5(O)^n participation is here accompanied by attack of water as external nucleophile and by 7(O)^{n,n} participation[12] (Table I). In homologs *IIIa* and *IIIb*, the attacking nucleophile is again and exclusively the OR group giving rise to a tetrahydropyran ring by a homologous 6(O)^n process (Scheme 5). With the acetoxy derivative *IIIc*, the cyclic ether is still the major product of the reaction but the competing external attack is more pronounced than with *Ic*. This demonstrates that the 6(O)^n participation by the ether oxygen atom of the ester group obviously occurs less readily than the 5(O)^n participation[10,13].

Again, on reaction with electrophilic reagents, the 5,6- unsaturated steroids are preferentially attacked from the sterically more accessible α-site. The addition is governed by stereoelectronic factors (Fürst-Plattner rule) leading, in conflict with Markovnikov rule, to a nucleophile attack at $C_{(6)}$ to form a 5α,6β-diaxial product[16]. In 19-hydroxy and 19-methoxy derivatives *IIa* and *IIb* the 19-substituent plays the role of the nucleophile cleaving the bromonium ion. Here again, the position 6 is attacked in a 5(O)^n process[8,9]. However, this type of participation by the 19-substituent is less favored in 5,6- than in 2,3-unsaturated compounds (this preference is still more pronounced in analogous epoxides[13]). We attributed[12,13] this difference to a larger distance of the participating atom from the reaction center and to a larger angle of approach in *II* than in *I*. All these factors, coupled with the lesser disposition of the ether oxygen in the ester group to participate, are reflected in the reactivity of the 19-acetoxy derivative *IIc* so that the competing 6(O)^{n,n} process[10,12] is preferred and the 5(O)^n participation does not proceed at all in *IIc*. On the other hand, the 6(O)^{n,n} participation in *IIc* is in conflict with the stereoelectronic factors (Fürst–Plattner rule) but is favored by the inductive effect according to Markovnikov rule. As we have demonstrated recently[17], without this support the 6(O)^{n,n} process could not prevail in competition with the 5(O)^n process.

In homologs *IVa* and *IVb* an axial attack by the internal nucleophile should be directed toward the $C_{(6)}$ position and should require a 6(O)^n participation. However, the both compounds equally prefer cleavage at $C_{(5)}$ (Scheme 5) with 5(O)^n participation. Similar to 19-acetoxy derivative *IIc* the participating group changes the regioselectivity of the reaction. The 5(O)^n participation predominates here over the 6(O)^n process under similar conditions in which the 6(O)^{n,n} process prevails over 5(O)^n participation (see above). In this case the 5(O)^n process, though in conflict with the stereoelectronic effect (Fürst–Plattner rule), is supported by the inductive effect (Markovnikov rule). Further experiments are necessary to show whteher or not assistance by the inductive effect (as in *IIc*) is necessary.

In B-homocholestane derivatives *XXI* is the 5(O)^n preferred to the 6(O)^n process[13] and the reaction is thus accompanied by a change of regioselectivity (as compared

with a normal course[18] in *XX*) without being assisted by the inductive effect. However, 19-substituted derivatives *XX1a*–*XX1c* are likely to react in a different conformation than *XX*, which is extremely favorable for 5(O)^n participation (due to favorable distance and angle of approach)[13].

In the acetoxy derivative *IVc*, the nucleophilicity of the ether oxygen atom is decreased, no (O)^n process takes place and the compound reacts without participation. In the case of *IIc*, the 5(O)^n process was suppressed by a competing 6(O)$^{\pi,n}$ reaction, whereas in the case of *IVc* 5(O)^n process should be in conflict with Fürst-Plattner rule and was suppressed by the attack of an external nucleophile proceeding in accord with this rule. The 6(O)^n participation is here not operative (in contrast to *IIIc*), obviously for the same reason why in the type *II* the 5(O)^n process proceeds less readily than in the type *I*. Another route, which could be considered for the acetoxy derivative *IVc*, should be (homologous to *IIc*) a 7(O)$^{\pi,n}$ participation requiring a cleavage of the corresponding bromonium ion at $C_{(5)}$. Neither this pathway is operative. It may be concluded that both the 5(O)^n and 6(O)$^{\pi,n}$ participation can suppress the stereoelectronic control (Fürst–Plattner rule), if assisted by the inductive effect (Markovnikov rule), but the 7(O)$^{\pi,n}$ participation proceeds only (*cf.* ref.[12]) if it is not in conflict with the Fürst–Plattner rule and even so is accompanied by competing external attack to considerable extent.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 50°C/26 Pa (0·2 Torr). Optical measurements were carried out in chloroform with an error of ±3°. The infrared spectra were recorded on a Zeiss UR 20 spectrometer in tetrachloromethane unless otherwise stated. The ^{1}H NMR spectra were recorded on a Tesla BS 476 instrument (60 MHz) in deuteriochloroform at 30°C with tetramethylsilane as internal reference. Chemical shifts are given in ppm. Apparent coupling constants were obtained from the first order analysis. The mass spectra were recorded on a Jeol JMS D-100 spectrometer operating at 14–75 eV. The samples were introduced using a direct inlet at lowest temperature enabling evaporation. The elemental composition of ions was determined by accurate mass measurements. The identity of the 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, water, a 5% aqueous potassium hydrogen carbonate solution, water, drying with sodium sulfate and evaporation of the solvent *in vacuo*.

Addition of Hypobromous Acid to Compounds *IIIa*–*IVc*

The unsaturated compound (0·5 mmol) was dissolved in dioxane (5 ml) and treated with 10% perchloric acid (0·5 ml) and N-bromoacetamide (80 mg, 0·6 mmol) at room temperature for 30 min. The mixture was diluted with ether and water, the organic phase was washed with water a 5% aqueous potassium hydrogen carbonate solution, a 5% aqueous sodium thiosulfate solution, water, dried with sodium sulfate, and the solvent was evaporated. The residue was chromatographed on three preparative silica gel plates (20 × 20 cm) using a mixture of light petroleum.

ether and acetone (85 : 10 : 5 or 80 : 10 : 10) as eluent. Zones containing the desired compound were collected, eluted with ether and evaporated. The yields are given in Table I, ^{1}H NMR data in Table II and physical and analytical data in Table III.

19-Homo-5α-cholest-2-en-19a-ol (*IIIa*)

Powdered zinc (1·5 g) was added in 10 portions to a stirred refluxing solution of the epoxide[15] *VI* (500 mg) in a mixture of dioxane (4 ml) and acetic acid (8 ml) in a period of 10 min. The hot mixture was filtered, the inorganic material was washed with hot acetic acid, the hot filtrate was diluted with water and set aside overnight. The product *IIIa* (315 mg) was isolated by suction; m.p. 108–109°C, $[\alpha]_D^{20}$ +64° (*c* 1·1). ^{1}H NMR spectrum: 0·67 (3 H, s, 18-H), 3·68 (2 H, brd. t, J = 8 Hz, 19a-H), 5·63 (2 H, d, J = 2 Hz, 2-H and 3-H). IR spectrum: 1 012, 1 635, 3 020, 3 340, 3 470, 3 627 cm^{-1}. For $C_{28}H_{48}O$ (400·7) calculated: 80·93% C, 12·07% H; found: 80·75% C, 12·14% H.

19-Homo-5α-cholest-2-en-19a-ol Acetate (*IIIc*)

The alcohol *IIIa* (160 mg) was dissolved in pyridine (2 ml) and treated with acetic anhydride (0·4 ml) at room temperature overnight. The mixture was then decomposed by ice, the product was taken up in ether and the ethereal solution was worked up as usual. The residue was crystallized from aqueous acetone to yield the acetate *IIIc* (130 mg), m.p. 62–64°C, $[\alpha]_D^{20}$ +46° (*c* 3·9). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 4·08 (2 H, m, W = 35 Hz, 19a-H), 5·60 (2 H, d, J = 2 Hz, 2-H and 3-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·27% C, 11·40% H.

TABLE III

Analytical and physical data of products of hypobromous acid addition to olefins *IIIa*–*IVc*

Compound	Formula (m.w.)	Calculated/Found			M.p., °C $[\alpha]_D^{20}$
		% C	% H	% Br	
VI	$C_{28}H_{47}BrO$	70·12	9·88	16·66	102–103
	(479·6)	70·04	9·90	16·85	+49°
VII	$C_{30}H_{51}BrO_3$	66·77	9·53	14·81	180–181
	(539·7)	66·60	9·58	14·96	−44°
X	$C_{30}H_{49}BrO_3$	67·02	9·19	14·86	106–107
	(537·6)	66·87	9·13	14·95	− 1°
XI	$C_{31}H_{53}BrO_4$	65·36	9·38	14·03	foam
	(569·7)	65·19	9·45	14·25	+11°
XVI	$C_{32}H_{53}BrO_5$	64·31	8·94	13·37	143–144
	(597·7)	64·12	9·02	13·64	−16°
XVIII	$C_{32}H_{52}O_5$	74·38	10·14	—	122–124
	(516·8)	74·21	10·23	—	−47°

19-Homo-5-cholestene-3β,19a-diol 3-Monoacetate (*IVa*)

A) *From 6α-bromo-5,19a-epoxy-19-homo-5β-cholestan-3β-ol acetate* (X): Powdered zinc 2 g) was added in 10 portions to a stirred refluxing solution of *X* (300 mg) in a mixture of dioxane (3 ml) and acetic acid (7 ml) in a period of 10 min. The hot mixture was filtered, the ionorganic material was washed with hot acetic acid, the hot filtrate was diluted with water and the mixture was set aside overnight. The product *IVa* (195 mg) was isolated by suction; m.p. 146–148°C, $[\alpha]_D^{20}$ −42° (*c* 2·8). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 3·75 (2 H, m, W = 30 Hz, 19a-H), 4·58 (1 H, m, W = 30 Hz, 3α-H), 5·58 (1 H, brd d, J = 4 Hz, 6-H). For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·16% C, 11·19% H.

B) *From 5-methoxy-6α-bromo-19-homo-5β-cholestane-3β,19a-diol 3-monoacetate* (XI): *XI* (150 mg) was reduced with zinc (1 g) in a mixture of dioxane (1 ml) and acetic acid (3 ml) and worked up as given in the prelious experiment to afford *IVa* (64 mg), m.p. 143–145°C identical with the compound prepared under *A*.

5-Methoxy-6α-bromo-19-homo-5β-cholestane-3β,19a-diol 3,19a-Diacetate (*XII*)

The alcohol *XI* (50 mg) was dissolved in pyridine (3 ml) and treated with acetic anhydride (1 ml) at room temperature overnight. The mixture was then decomposed with ice and water, the product was extracted with ether and the ethereal phase was worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to yield the diacetate *XII* (38 mg), m.p. 66–68°C, $[\alpha]_D^{20}$ + 20° (*c* 6·1). ^{1}H NMR spectrum: 0·64 (3 H, s, 18-H), 2·03 (6 H, s, 2 × × CH_3CO_2), 3·48 (3 H, s, CH_3O), 4·25 (2 H, m, W = 20 Hz, 19a-H), 4·60 (1 H, dd, J = 4·5 and 11·0 Hz, 6β-H), 5·08 (1 H, m, W = 12 Hz, 3α-H). For $C_{33}H_{55}BrO_5$ (611·7) calculated: 64·80% C, 9·06% H, 13·06% Br; found: 64·66% C, 9·10% H, 13·35% Br.

5,6β-Epoxy-19-homo-5β-cholestane-3β,19a-diol 3,19-Diacetate (*XVIII*)

The olefin[14] *IVc* (350 mg) was dissolved in chloroform (5 ml) and treated with 3-chloroperoxybenzoic acid (270 mg) at room temperature for 30 min. The mixture was then diluted with ether, washed with water, a 5% aqueous potassium hydrogen carbonate solution, a 5% aqueous sodium thiosulfate solution, water, dried with sodium sulfate and evaporated. The residue was chromatographed on a column of silica gel (30 g) using a mixture of light petroleum and ether (90 : 10) which eluted impurities and then with a mixture of light petroleum, ether and acetone (89 : 10 : 1) which eluted the oily 5β,6β-epoxide *XVIII* (48 mg), $[\alpha]_D^{20}$ −4° (*c* 4·2). ^{1}H NMR spectrum: 0·67 (3 H, s, 18-H), 2·02 (3 H, s, CH_3CO_2), 2·07 (3 H, s, CH_3CO_2), 2·88 (1 H, d, J = 2·0 Hz, 6α-H), 4·50 (3 H, m, W = 50 Hz, 3α-H and 19a-H). For $C_{32}H_{52}O_5$ (516·8) calculated 74·38% C, 10·14% H; found: 74·19% C, 10·21% H.

5,6α-Epoxy-19-homo-5α-cholestane-3β,19a-diol 3,19-Diacetate (*XIX*)

Continued elution with the same mixture of solvents after isolation of *XVIII* afforded the 5α,6α-epoxide *XIX* (220 mg), m.p. 123–125°C (from a mixture of acetone, methanol and water). $[\alpha]_D^{20}$ −46° (*c* 1·8). ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 2·07 (3 H, s, CH_3CO_2), 2·95 (1 H, d, J = 3·5 Hz, 6β-H), 5·00 (1 H, m, W = 30 Hz, 3α-H). For $C_{32}H_{52}O_5$ (516·8) calculated: 74·38% C, 10·14% H; found: 74·35% C, 10·18% H.

The elemental analyses were carried out in the analytical laboratory of this Institute (head Dr J. Horáček). The IR *spectra were recorded by Mrs K. Matoušková and interpretedt by Dr S. Vašíčková. The* ^{1}H NMR *spectra were recorded by (the late) Dr M. Synáčková Dr J. Zajíček,*

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