ACETOXYL GROUP AS CONTROL ELEMENT IN ELECTROPHILIC ADDITION: PARTICIPATION BY ACETOXY GROUP AND ITS COMPETITION WITH OTHER PARTICIPATING GROUPS IN HYPOBROMOUS ACID ADDITION TO SOME 5-CHOLESTENE DERIVATIVES*

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The 3β-acetoxy cholestene *II* (with nonparticipating group at the position 19) is known to be attacked with hypobromous acid predominantly from α-site which results in formation of the diaxial bromohydrin *XIV*. By contrast, inversion of configuration of the 3-acetoxy group leads to a dramatic change in the reaction course: the 3α-acetoxycholestene derivative *VIII* is preferentially approached by the electrophile from β-site to give the corresponding 5β,6β-bromonium ion *XXVII* which on cleavage with $6(O)^{\pi,n}$ participation by the 3α-acetoxyl yields two products *XXIX* and *XXXI*. When hydroxy and acetoxy groups can compete in $5(O)^n$ or $6(O)^{\pi,n}$ processes, only hydroxyl group participation takes place (*IX* → *XXV* and *XI* → *XXXIV*). Two acetoxy groups in *X* compete successfully in $6(O)^{\pi,n}$ processes (*X* → *XXXVII* + *XLI*).

The presence of other functionalities in a molecule of an olefinic substrate may considerably influence the course of electrophilic addition[1]. This effect may be particularly dramatic when participation of a neighboring group involves a covalent bonding in transition state of the reaction[2]. These effects were often utilized in synthetic strategy for stereo- and regioselective introduction of substituents into defined positions[3–6], specific ring closure reactions[7], selective protection of certain groups[6,8], and to other purposes[9]. The aim of the present paper is to demonstrate on several examples how purposeful introduction of participating group as a control element can influence the course of electrophilic addition or change or direct its regio- or stereoselectivity in the demanded way.

In our previous papers on neighboring group participation we studied the course of hypobromous acid addition to 5,6-unsaturated steroid derivatives bearing a functional group (Z) in position 19 (*III*, *IV*) (ref.[10–13]) and 19a (*V*, *VI*; Scheme 1) (ref.[14]). It is known[15,16] that hypobromous acid addition to the 5,6-unsaturated 3β-acetoxy derivative *II* (as well as to *I*) proceeds (Scheme 2) preferentially *via* the 5α6α-bromonium ion *XIII* which on reaction with water as nucleophile follows Fürst–Plattner

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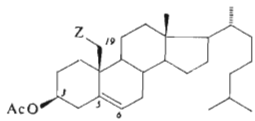
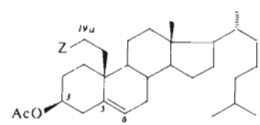
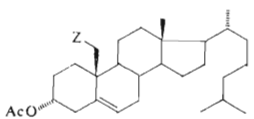
rule, and gives the diaxial bromohydrin *XIV* against Markovnikov rule. In the 19-hydroxy derivative *III* the cleavage of the corresponding 5α,6α-bromonium ion *XV* is controlled by stereoelectronic factors (Fürst–Plattner rule)[10]; the 19-hydroxyl



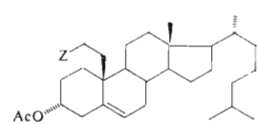
I, Z = H
II, Z = O_2NO
III, Z = OH
IV, Z = AcO



V, Z = OH
VI, Z = AcO



VII, Z = H
VIII, Z = O_2NO
IX, Z = OH
X, Z = AcO



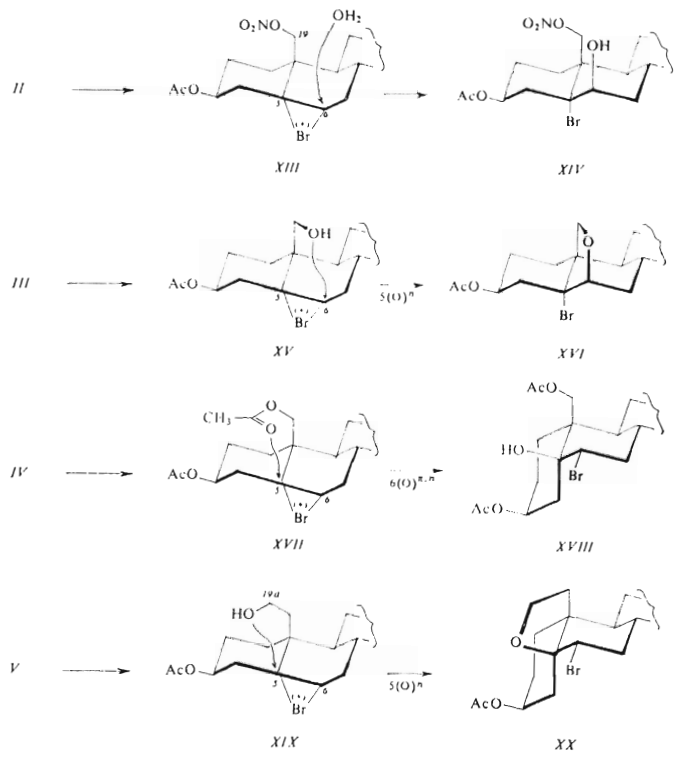
XI, Z = OH
XII, Z = AcO

SCHEME 1

acts as a nucleophile to yield the cyclic bromo ether *XVI*. By contrast, the 5α,6α--bromonium ion generated from the 19-acetoxy derivative *IV* is split at $C_{(5)}$ by carbonyl oxygen of the 19-acetoxy group[11–13] which leads to the diequatorial bromohydrin *XVIII*. In a similar manner, the 19a-hydroxy derivative *V* reacts with violation of Fürst–Plattner rule to give the Markovnikov-like product *XX*. The above reactions show clearly how pronounced influence exerts the participating group on the regioselectivity of the process.

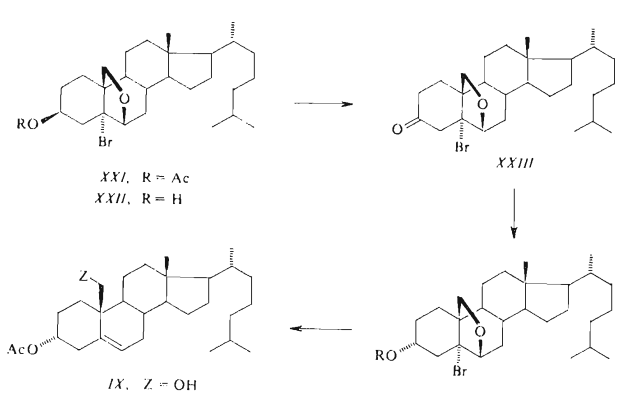
In this paper we concentrated on a study of influence of the acetoxy group in position 3 on the course of the addition. The aim has been to evaluate the capability of the 3α-acetoxy group to participate as a control element in addition to 5,6-double bond or its possible competition with a participating group located in position 19 or 19a. To this purpose we prepared a series of 5,6-unsaturated acetoxy derivatives *VII*–*XII*.

As starting material for the synthesis of the 3α-acetoxy derivatives we utilized the known[17] epoxide *XXI* which was saponified to the alcohol[17] *XXII* and the latter oxidized with Jones' reagent to the unstable ketone *XXIII* (Scheme 3). This ketone



SCHEME 2

was reduced with lithium tri-sec-butylborohydride (L-Selectride) in tetrahydrofuran to give a high yield of the axial alcohol *XXIV* which was converted into the acetate *XXV*. Reduction of this compound with zinc in boiling acetic acid provided the 5,6-unsaturated 19-hydroxy derivative *IX* which gave the acetate *X*, nitrate *VIII* and mesylate *XXVI* in the usual manner. Reduction of the mesylate *XXVI* by zinc--sodium iodide method[18,19] in wet 1,2-dimethxoyethane led to the 19-deoxy derivative *VII*.



SCHEME 3

Hypobromous Acid Addition

Reaction of 19-unsubstituted 3α-acetoxy derivative *VII* with hypobromous acid gave a mixture of two products which could not be obtained in pure condition and characterized for their unstability. We therefore turned our attention to the 19-nitrate *VIII* as equivalent of the 19-unsubstituted derivative *VII* since it is known that the 19-nitrate group does not participate in the course of addition to the 5,6-double bond[16]. The 5,6-unsaturated 19-nitrate *VIII* when treated with hypobromous acid (generated *in situ* from N-bromoacetamide and perchloric acid in aqueous dioxane) afforded two major products (Scheme 4): The diaxial bromohydrin *XXIX* and the 5α,6α-epoxide *XXXI* (Table I). The structure of both compounds follows mainly from their ^{1}H NMR spectra (Table II): The spectrum of *XXIX* indicates retention of the nitrate group in position 19, presence of a tertiary acetoxy group, axial bromine atom in position 6 and a 3α-hydroxyl (proved by treatment with trichloroacetyl isocyanate). The width of the 3β-H multiplet is in accord with *trans*-annelation of A and B rings. The spectrum of *XXXI* proves that it is a 5α,6α-epoxy derivative with a preserved nitrate group in the position 19. The width of 3β-H multiplet reveals the axial conformation of the 3β-acetoxy group, the configuration of the oxirane ring follows from the shape of the 6-H signal.

The both compounds are formed from the 5β,6β-bromonium ion *XXVII* which is cleaved with $6(O)^{\alpha,\alpha}$ participation by the 3α-acetoxy group *via* the acyloxonium ion *XXVIII*. The latter is hydrated to an *ortho* ester hydrolysis of which gives two diaxial products *XXIX* and *XXX*. On working up the reaction mixture the bromohydrin *XXX* cyclizes to the epoxide *XXXI*. Formation of the bromohydrin *XXX* could also be explained by cleavage of the bromonium ion *XXVII* by water as external nucleophile but we consider this possibility extremely unlikely on the basis of our earlier work[11-13,20-22]. If at all, this pathway is likely to be operative only to a negligible extent. Formation of the compound *XXIX* could be alternatively explained

TABLE I

Yields and ratios of products of hypobromous acid addition to the compounds *VIII*–*XI*

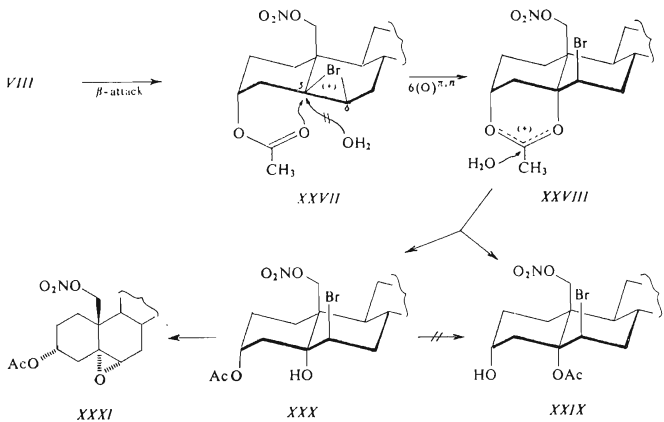
Starting compound	Relative yield, % (product)			Total yield, %
	participation of Cα-OAc	participation of 19-OR	others	
VIII	36 (*XXIX*) 55 (*XXXI*)		~10[a]	91
IX	—	≥98 (*XXV*)	≤ 2	96
X	39 (*XL*)	36 (*XXXVII*)	~25[b]	92
XI	—	≥99 (*XXXIV*)	≤ 1	95

[a] Mixture of at least two nonidentified compounds. [b] Mixture of two highly unstable compounds in c. 2 : 1 ratio

TABLE II

^{1}H NMR data of the products of hypobromous acid addition

Compound	18-H	19-H (*J* or *W*)	3-H (*W*)	6-H (*J* or *W*)
XXV	0·68	3·65 d + 3·85 d (9)	5·03 m (14)	3·92 d (4)
XXIV	0·70	4·77 d + 5·16 d (10)	4·24 m (14)	5·25 m (8)
XXXI	0·59	4·67 s	5·26 m (10)	2·86 d (3·4)
XXXIV	0·65	4·00 m (20)	4·95 m (30)	4·32 m (25)
XXXVII	0·63	4·13 s	5·17 m (30)	4·75 dd (4 + 12)
XLI	0·59	4·33 s	5·10 m (12)	2·82 d (2·5)



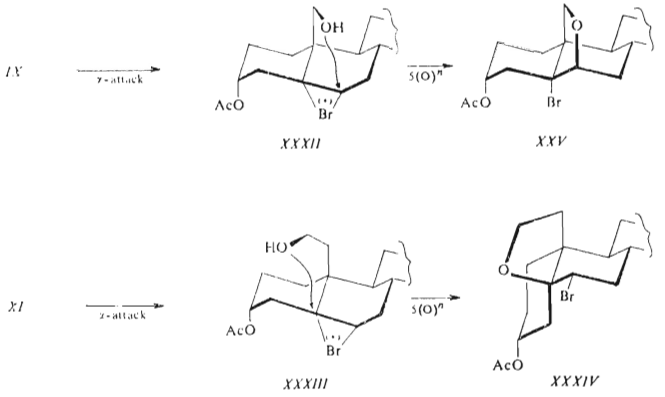
SCHEME 4

to arise from the isomer *XXX* by acetate group transfer. However, we know from analogous cases that this transfer does not occur under the conditions of addition[11,13,22]. Unfortunately, unstability of both products precluded to present a direct proof of the mechanism by carrying out the reaction in water enriched in ^{18}O isotop and by identification of the label position by mass spectrometry[13,22,26].

The 3α-acetoxy alcohols *IX* and *XI* react in the same manner as their 3β-epimers, *i.e.* by way of the 5α,6α-bromonium ions *XXXII* and *XXXIII* (Scheme 5) which are opened with $5(O)^n$ participation by the hydroxyl group to yield the corresponding cyclic ethers *XXV* and *XXXIV*. Their structure is inferred from the identity with compounds prepared in a different way (for *XXV* see the text above, for *XXXIV* see ref.[23]). No intervention of 3α-acetoxy group occurs.

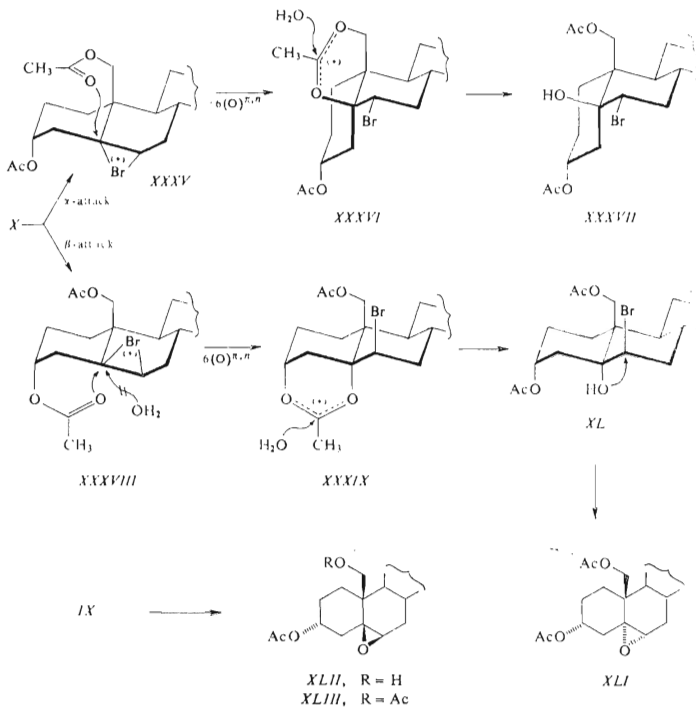
Finally, reaction of hypobromous acid with the diacetate *X* gives rise to two major products (Scheme 6), namely the diequatorial bromohydrin *XXXVII* and the epoxide *XLI* (Table I). Structure of both products was again established mainly on the basis of their ^1H NMR spectra: The spectrum of *XXXVII* reveals the presence of two acetoxy groups in positions 3 and 19 and presence of a $—CH_2CH—Br$ group. From coupling constants of CHBr follows the 6α-configuration of the bromine atom. The width of 3β-H multiplet proves the equatorial character of the 3α-acetoxy group which is only possible for *cis* annellation of the A and B rings. This informa-

tion proves the structure *XXXVII* unequivocally. The spectrum of the second product shows it to be a 5,6-epoxide. Its configuration was established by comparing its spectrum with that of the epoxide *XLIII* prepared by epoxidation of the unsaturated alcohol *IX* followed by acetylation. In the alcohol *IX* is the direction of epoxidation controlled by the 19-hydroxyl the product of this stereoselective reaction being the 5β,6β-epoxide *XLII*, as follows from the existence of a strong intramolecular hydrogen bond (3 545 cm^{-1} in the IR spectrum). Acetylation of this hydroxy epoxide provided the compound *XLIII* and the shape of the 6-H signals permitted unequivocal assignment of 5α,6α-configuration for the epoxide in question (*XLI*).



SCHEME 5

The product analysis leads to the conclusion that the reaction of the diacetate *X* with hypobromous acid involves intermediary formation of both diastereoisomeric bromonium ions *XXXV* and *XXXVIII*. In the same manner as in the series of 3β-acetoxy derivatives *IV*, the 5α,6α-bromonium ion *XXXV* is opened at $C_{(5)}$ by 19-acetoxyl with $6(O)^{\pi,n}$ participation and yields the diequatorial bromohydrin *XXXVII via* the acyloxonium ion *XXXVI*. Two mechanisms of cleavage can be proposed for the 5β,6β-bromonium ion *XXXVIII*: by 3α-acetoxyl with $6(O)^{\pi,n}$ participation or by water as an external nucleophile. From the reasons discussed above for the reaction of the nitrate *VIII* the second pathway is likely to play an unimportant part, if proceeding at all. The first path leads to the intermediary ion *XXXIX* which is hydrated and hydrolyzed to the diaxial bromohydrin *XL* cyclizing then to the 5α,6α-epoxide

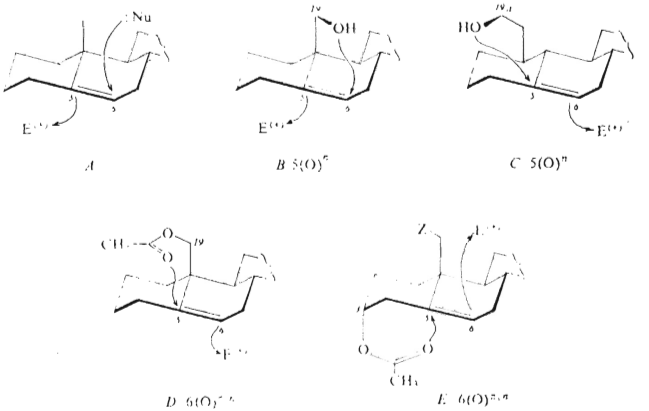


SCHEME 6

XLI. The diacetate *XI*, when treated with hypobromous acid, yields un untractable mixture of unstable products which was not further investigated.

Structure – Reactivity Relationship

The Scheme 7 presents a summary of the influence of neighboring groups on the course of electrophilic additions to 5,6-unsaturated steroids. The parent compound of the type A lacks functional groups capable to participate and is preferentially



A *B* 5(O)[5] *C* 5(O)[n]

D 6(O)[5,n] *E* 6(O)[n,n]

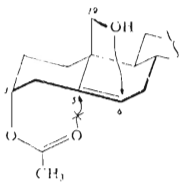
SCHEME 7

attacked by an electrophile from the more accessible α-face[15]. The following nucleophile attack occurs in accord with Fürst–Plattner and violates Markovnikov rule[15]. In the product is then the electrophilic component attached to position 5α, the nucleophilic part to position 6α. In similar manner proceeds addition of the electrophilic reagent to a hydroxy derivative of the type B where the role of nucleophile plays the 19-hydroxyl[10].

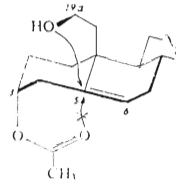
A 5,6-unsaturated 19a-homoalcohol of the type C is again attacked by an electrophile from the α-face but the participating hydroxyl changes the regioselectivity of the reaction. In conflict with Fürst–Plattner and in accord with Markovnikov rule a diequatorial product[14] arises with the electrophile attached to 6α and nucleophile bonded to 5β-position. Analogously, in compounds of the type D, the 6(O)[n,n] participation by the 19-acetoxyl changes the regioselectivity of the reaction as compared with the normal course (*A*) and the product is again a diequatorial derivative[11–13].

Stereoselectivity of the reaction is changed in 3α-acetoxy derivative of the type *E*. Contrasting with the preceding cases the electrophile approach occurs from the β-face; the driving force of this change is evidently 6(O)[n,n] participation by the 3α-acetoxyl since steric accessibility of all derivatives mentioned above should be about the same. In the product the electrophile is attached to 6β- and the nucleophile to 5α-position. These examples demonstrate how purposeful introduction of a specific

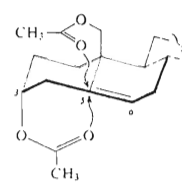
functional group as a control element can direct the regio- and stereoselectivity of a given reaction.



F 5(O)^n



G 5(O)^n



H 6(O)$^{\pi,n}$

SCHEME 8

It follows further from our experiments (Scheme 8) that 5(O)^n participation by a hydroxyl group takes precedence over 6(O)$^{\pi,n}$ process independently whether or not participation by the hydroxyl is in accord with or contradicts Fürst–Plattner or Markovnikov rule (*cf.* *F* and *G*). If 6(O)$^{\pi,n}$ participation of two acetoxyl groups comes into consideration in the course of addition to the same double bond (as in *H*) both processes may proceed yielding a mixture of products corresponding to the both pathways.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 50°C/26 Pa (0·2 Toorr). Optical rotations were measured 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 Varian XL-200 apparatus (FT mode) and 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*.

5-Cholesten-3α-ol 3-Acetate (*VII*)

The mesylate *XXVI* (400 mg) was dissolved in a mixture of 1,2-dimethoxyethane (10 ml), dioxane (20 ml) and water (2 ml) and stirred with sodium iodide (1 g) and powdered zinc[16,19] (1 g)

at 80°C for 3 h. The inorganic material was filtered off, the filtrate was concentrated by evaporated *in vacuo*, the residue was diluted with ether and water and the ethereal layer was successively washed with water, 5% aqueous hydrochloric acid, water, a 5% aqueous potassium hydrogen carbonate solution, water, dried with sodium sulfate and evaporated. The residue was dissolved in a mixture of benzene and light petroleum (1 : 4) and filtered through a column of aluminum oxide. The filtrate was evaporated and the residue was crystallized from a mixture of chloroform and methanol to afford *VII* (190 mg), m.p. 83–85°C (literature[24] gives 84–86°C). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 1·00 (3 H, s, 19-H), 2·00 (3 H, s, CH_3CO_2), 5·00 (1 H, m, W = = 11 Hz, 3β-H), 5·27 (1 H, m, W = 12 Hz, 6-H).

5-Cholestene-3α-19-diol 3-Acetate 19-Nitrate (*VIII*)

A solution of the alcohol[25] *IX* (300 mg) in chloroform (5 ml) was added drop-by-drop into a reagent prepared from acetic anhydride (1·2 ml) and 65% nitric acid (0·3 ml) in chloroform (2 ml) at −30°C in the period of 15 min, the mixture was stirred at −30°C for 3 h and at −10°C for 2 h, then poured onto ice and aqueous ammonium hydroxide and stirred for 1 h. The product was extracted with ether and the ethereal phase was worked up as usual. The residue was crystallized from aqueous ethanol to give the nitrate *VIII* (136 mg), m.p. 136–137°C. ^{1}H NMR spectrum: 0·70 (3 H, s, 18-H), 2·03 (3 H, s, CH_3CO_2), 4·37 (1 H, d, J = 11 Hz, 19-H), 4·72 (1 H, d, J = 11 Hz, 19-H), 5·00 (1 H, m, W = 15 Hz, 3β-H), 5·55 (1 H, m, W = 11 Hz, 6-H). For $C_{29}H_{47}NO_5$ (489·7) calculated: 71·13% C, 9·67% H, 2·86H N; found: 70·98% C, 9·75% H.

5-Cholestene-3α,19-diol 3,19-Diacetate (*X*)

The alcohol[25] *IX* (500 mg) was dissolved in pyridine (6 ml) and treated with acetic anhydride (2 ml) at room temperature overnight. The mixture was decomposed with ice and water, the product taken up into ether and the ethereal solution was worked up as usual. The residue by crystallization from a mixture of acetone, methanol and water furnished the diacetate *X* (360 mg), m.p. 75–76°C, $[\alpha]_D^{20}$ −34° (*c* 5·0), identical with an authentic sample[25]. ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 3·93 (1 H, d, J = 12 Hz, 19-H), 4·43(1 H, d, J = = 12 Hz, 19-H), 5·03 (1 H, m, W = 16 Hz, 3β-H), 5·50 (1 H, m, W = 13 Hz, 6-H).

19-Homo-cholest-5-ene-3α,19a-diol 3,19-Diacetate (*XII*)

The alcohol[23] *XI* (40 mg) in pyridine (2 ml) was treated with acetic anhydride (0·5 ml) at room temperature for 6 h and then worked up as usual. The residue was dissolved in a mixture of benzene and light petroleum (1 : 4) and filtered through a column of aluminum oxide. The filtrate was evaporated to yield the oily diacetate *XII* (32 mg), $[\alpha]_D^{20}$ −19° (*c* 4·1). ^{1}H NMR spectrum: 0·73 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 4·02 (2 H, m, W = 50 Hz, 19a-H), 4·97 (1 H, m, W = 14 Hz, 3β-H), 5·45 (1 H, m, W = 14 Hz, 6-H). For $C_{32}H_{54}O_4$ (502·8) calculated: 76·45% C, 10·83% H; found: 76·33% C, 10·92% H.

5-Bromo-6β,19-epoxy-5α-cholestan-3-one (*XXIII*)

The alcohol[17] *XXII* (9 g) was dissolved in acetone (200 ml) and treated with Jones' reagent (7 ml) at 0°C for 5 min. The excess of reagent was decomposed with methanol, the mixture was diluted with ether and water and the ethereal solution was worked up as usual to yield the crude unstable ketone *XXIII* (8·5 g). Crystallization of a sample from a mixture of acetone, methanol and water afforded the pure *XXIII*, m.p. 86–87°C (dec.), $[\alpha]_D^{20}$ +50° (*c* 1·7). ^{1}H NMR spectrum: 0·73 (3 H, s, 18-H), 3·47 (1 H, d, J = 8 Hz, 19-H), 4·20 (1 H, d, J = 8 Hz, 19-H),

4·65 (1 H, d, $J = 4$ Hz, 6α-H). For $C_{27}H_{43}BrO_2$ (379·6) calculated: 67·63% C, 9·04% H, 16·66% Br; found: 67·48% C, 9·06% H, 16·81% Br.

5-Bromo-6β,19-epoxy-5α-cholestan-3α-ol (*XXIV*)

The ketone *XXIII* (5 g) in tetrahydrofuran (30 ml) was treated with 1 mol l^{-1} solution of lithium tri-sec-butylborohydride (L-Selectride) in tetrahydrofuran (13 ml) at −78°C for 1 h, then at −40°C for 30 min and at 0°C for 3 h. The excess of reagent was decomposed with water and the mixture was treated with 30% hydrogen peroxide (30 ml) and potassium hydroxide (5 g) in water (20 ml) at 0°C for 2 h. The mixture was diluted with ether and water and the ethereal solution was worked up as usual. The residue was dissolved in a mixture of benzene and light petroleum (1 : 4) and filtered through a column of aluminum oxide. The filtrate was evaporated and the residue crystallized from aqueous acetone to give the alcohol *XXIV* (3·7 g), m.p. 146−147°C, $[\alpha]_D^{20}$ +6° (*c* 2·1), identical with an authentic sample[25]. ^{1}H NMR spectrum: 0·70 (3 H, s, 18-H), 3·70 (1 H, d, $J = 8$ Hz, 19-H), 3·88 (1 H, d, $J = 8$ Hz, 19-H), 4·00 (1 H, m, $W = 10$ Hz, 6α-H), 4·16 (1 H, m, $W = 15$ Hz, 3β-H).

5-Bromo-6β,19-epoxy-5α-cholestan-3α-ol 3-Acetate (*XXV*)

The alcohol *XXIV* (3 g) was dissolved in pyridine (20 ml) and treated with acetic anhydride (7 ml) at room temperature overnight. The mixture was decomposed with ice and water, the product was taken up into ether and the ethereal solution was worked up as usual. The residue was crystalized from a mixture of acetone, methanol and water to yield the acetate *XXV* (2·1 g), m.p. 145−146°C, identical with an authentic samples[25]. ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 2·03 (3 H, s, CH_3CO_2), 3·65 (1 H, d, $J = 9$ Hz, 19-H), 3·85 (1 H, d, $J = 9$ Hz, 19-H), 3·92 (1 H, d, $J = 4$ Hz, 6α-H), 5·03 (1 H, m, $W = 14$ Hz, 3β-H). IR spectrum: 1 240, 1 739 cm^{-1}.

TABLE III

Analytical and physical data of products of hypobromous acid addition

Compound	Formula (m.w.)	Calculated/Found			M.p., °C $[\alpha]_D^{20}$
		% C	% H	% Br	
XXIV	$C_{29}H_{48}BrNO_6$	59·38	8·25	13·62	oil
	(586·6)	59·21	8·36	13·48	+ 8°
XXXI	$C_{29}H_{47}NO_6$	68·88	9·37	—	foam
	(505·7)	68·63	9·45	—	−20°
XXXVII	$C_{31}H_{51}BrO_5$	63·79	8·81	13·69	oil
	(583·7)	63·51	8·92	13·94	+25
XLI	$C_{31}H_{50}O_5$	74·06	10·02	—	101−102
	(502·7)	74·18	9·86	—	−19°

5-Cholestene-3α,19-diol 3-Acetate 19-Methanesulfonate (*XXVI*)

The alcohol *IX* (400 mg) was dissolved in pyridine (4 ml) and treated with methanesulfonyl chloride (0·4 ml) at 0°C for 30 min. The mixture was 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 mesylate *XXVI* (375 mg), m.p. 126–128°C (dec.). ^{1}H NMR spectrum: 0·71 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 2·98 (3 H, s, CH_3SO_3), 4·15 (1 H, d, J = 10 Hz, 19-H), 4·40 (1 H, d, J = 10 Hz, 19-H), 5·00 (1 H, m, W = 14 Hz, 3β-H), 5·55 (1 H, m, W = 13 Hz, 6-H). For $C_{30}H_{50}O_5S$ (522·8) calculated: 68·92% C, 9·64% H, 6·13% S; found: 68·74% C, 9·91% H, 6·39% S.

5,6β-Epoxy-5β-cholestane-3α,19-diol 3,19-Diacetate (*XLIII*)

The olefin *IX* (50 mg) was dissolved in chloroform (5 ml) and treated with 3-chloroperoxybenzoic acid (40 mg) in the presence of potassium acetate (50 mg) at room temperature for 1 h. The mixture was then diluted with ether and water and the ethereal phase was washed with water, a 5% aqueous potassium hydrogen carbonate solution, a 5% sodium thiosulfate solution, water, dried with sodium sulfate and evaporated to afford the crude unstable epoxide *XLIII* (*c.* 50 mg), IR spectrum: 1 242, 1 739, 3 545 cm^{-1}, 30 mg of which was immediately dissolved in pyridine (2 ml) and treated with acetic anhydride (0·8 ml) at room temperature for 3 h. The mixture was decomposed with ice and water, the product extracted with ether, the ethereal layer was washed ten times with water, three times with a 5% aqueous potassium hydrogen carbonate solution, water, dried with sodium sulfate and evaporated. The residue was dissolved in a mixture of benzene and light petroleum (1 : 4) and filtered through a column of aluminum oxide. The filtrate was evaporated to yield the epoxide *XLIII* (19 mg), $[\alpha]_D^{20}$ +12° (*c* 2·0). ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 2·03 (3 H, s, CH_3CO_2), 2·06 (3 H, s, CH_3CO_2), 2·90 (1 H, m, W = 7 Hz, 6α-H), 4·05 (1 H, d, J = 11 Hz, 19-H), 4·37 (1 H, d, J = 11 Hz, 19-H), 5·13 (1 H, m, W = 15 Hz, 3β-H). For $C_{31}H_{50}O_5$ (502·7) calculated: 74·06% C, 10·02% H; found: 73·97% C, 10·06% H.

Addition of Hypobromous Acid to the Compounds *VIII*–*XII*

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 then 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 evaporated. The residue was chromatographed on three preparative silica gel plates using a mixture of light petroleum, ether and acetone (85 : 10 : 5) or (80 : 10 : 10) with eventual double development. Zones containing products were collected, washed with ether and the eluate was evaporated. The yields are given in Table I, ^{1}H NMR data in the Table II, physical and analytical data of new compounds in the Table III.

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 M. Zimová and interpreted by Dr S. Vašíčková. The* ^{1}H NMR *spectra were recorded by Dr J. Zajíček, Mrs J. Jelínková and Mrs M. Snopková. Mass spectra were recorded and interpreted by Dr F. Tureček.*

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