ELECTROPHILIC ADDITIONS TO 10β-VINYL CHOLESTANE DERIVATIVES*

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Dedicated to Academician O. Wichterle on the occassion of his 70th birthday.

Hypobromous acid addition to steroid dienes *I*—*VI* proceeds in four steps. The reaction commences by the attack on more reactive endocyclic double bond from the α-side yielding intermediary diaxial bromohydrins *XXVIII*, *XXXIV*, *XL*, *XLIV*, *L* and *LVI via* corresponding α-bromonium ions. The 10β-vinyl group of the bromohydrins then reacts with a second equivalent of the reagent forming transient 19-epimeric bromonium ions. The ions generated from *I*, *II*, *V* and *VI* are cleaved intramolecularly by the hydroxyl group, in accordance with the Markovnikov rule, giving rise to 19-epimeric dibromo epoxides *XXXIa* and *XXXIIa*, *XXXVII* and *XXXVIII*, *LIIIa* and *LIVa*, *LIX* and *LX*. By contrast, the ions generated from *III* and *IV* are cleaved in an anti-Markovnikov manner to yield dibromo epoxides *XLII*, *XLVII* and *XLVIII*. Products due to formation of a new C—C bond were not observed. The reaction mechanism and differences in the behavior of the dienes *I*—*VI* are discussed.

The course of electrophilic addition to a double bond can be substantially altered by intramolecular participation of functional groups located in the vicinity of the reaction center[1,2]. In previous papers we have investigated the effect of $C_{(19)}$ hydroxyl, methoxyl and acetoxyl groups on the regio- and stereospecificity of electrophilic addition to double bonds placed at 1, 2, 3, 4, 5 or 6 positions of the steroid skeleton[3–7]. The intramolecular participation by oxygen substituents has been invariantly observed to some extent[4,5], which led us to some conclusions concerning the distance of the participating group from the reaction center, angle of approach and competition between possible participating atoms in ambident groups[4,5].

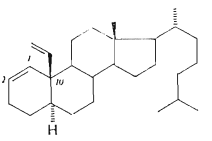
Due to donating properties of the bonding π-orbital, a suitably oriented carbon–carbon double bond can also serve as a participating group[8], forming thus a new carbon–carbon bond. Such an example is the facile cyclization in germacratriene[9] (Scheme 1) which was explained by favorable orientation of the double bonds enabling a colinear overlap of the π-orbitals[8,9]. Recently we have examined hypobromous acid addition to a different system *IV* in which the π-orbitals of the double

* Part CCXC in the series On Steroids; Part CCLXXXIX: Tetrahedron, in press.

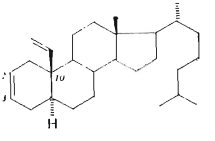
bonds were fixed perpendicular to each other[10,11]. Since no carbon–carbon bond was formed in *IV*, it was of particular interest to vary the position of the endocyclic double bond and investigate behavior of such modified systems. This paper deals with the hypobromous acid addition to model dienes *I – VI* and 10β-vinylcholestanes *VII*, *VIII*.

Syntheses of Model Compounds I – VI

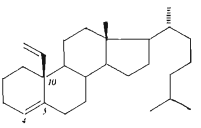
The compounds *I – VI* were prepared according to a general procedure (Schemes 2 and 3): Unsaturated 19-hydroxy derivatives with double bonds in desired positions



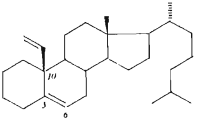
I



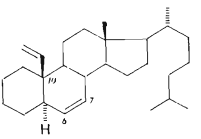
II



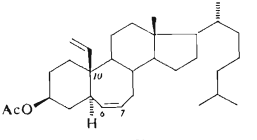
III



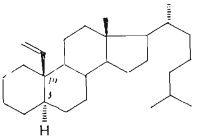
IV



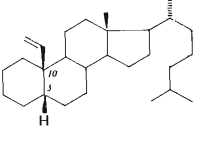
V



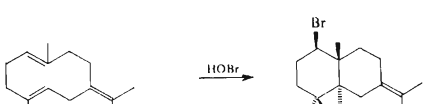
VI



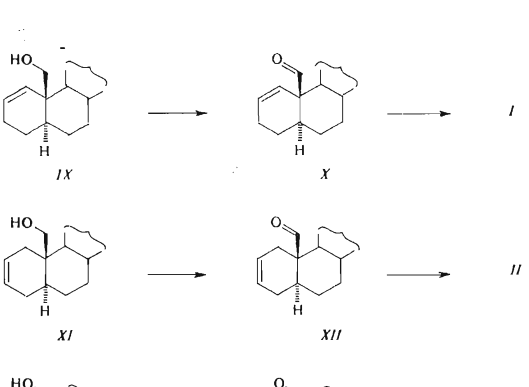
VII



VIII

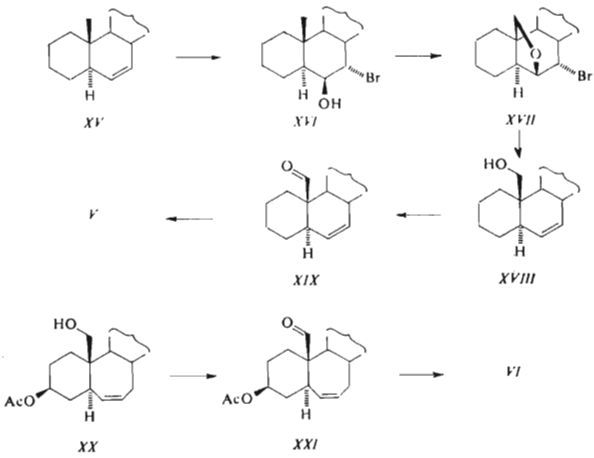


SCHEME 1



SCHEME 2

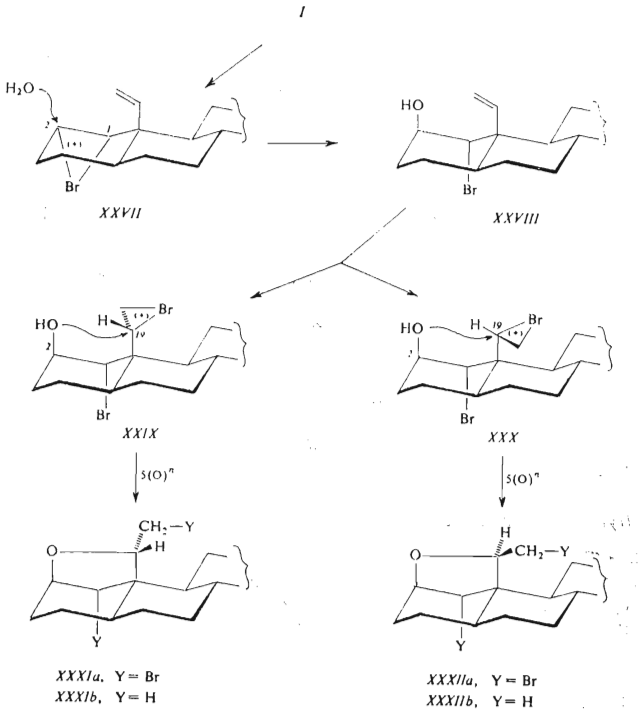
were oxidized to the corresponding aldehydes in which the 10β-vinyl group was formed by the Wittig reaction. The alcohol[12] *IX* was oxidized with Jones' reagent to the aldehyde *X* and the latter treated with triphenylphosphonium-methylide to yield the diene *I*. In a similar reaction sequence the alcohols *XI* (ref.[13]) and *XIII* (ref.[14]) gave dienes *II* and *III*, respectively. The alcohol *XVIII* was prepared as follows: Hypobromous acid addition to the olefin[15,16] *XV* afforded the bromohydrin *XVI* which was cyclized with lead tetraacetate to the ether *XVII*. Reduction of the latter with zinc and acetic acid yielded *XVIII*. Further steps comprised oxidation of the $C_{(19)}$-hydroxyl group (aldehyde *XIX*) and Wittig reaction yielding the target diene *V*. In an analogous sequence, the unsaturated alcohol[4] *XX* was converted, *via* the aldehyde *XXI*, to the diene *VI*.



SCHEME 3

Hypobromous Acid Addition to I–VI

The diene *I* was treated with an excess of hypobromous acid (generated *in situ* from N-bromoacetamide and perchloric acid in aqueous dioxane) yielding a mixture of cyclic ethers *XXXIa* (56%) and *XXXIIa* (44%) (Scheme 4). The relative amounts of the products (Table I) were determined from the ^{1}H NMR spectrum of the mixture. The structure for *XXXIa* and *XXXIIa* followed from the mass and ^{1}H NMR spectra. The mass spectrum of the mixture of *XXXIa* and *XXXIIa* displays weak molecular ions *m/z* 556, 558, 560 showing the presence of two bromine atoms after a formal addition of (2 Br + O) to the diene *I*. The fragment ions $C_{27}H_{44}BrO$, $(M-CH_2Br)^+$, are indicative of a CH_2Br grouping in *XXXIa* and *XXXIIa* which confirms ring formation bridging $C_{(19)}$ with the skeleton. The ^{1}H NMR spectra of both *XXXIa* and *XXXIIa* display ABX systems corresponding to O—CH—CH_2Br subunits, doublets of 1β-H and multiplets of 2α-H. On reduction of *XXXIa* + + *XXXIIa* with tri-n-butyltin hydride we obtained the ethers *XXXIb* and *XXXIIb*, the ^{1}H NMR spectra of which showed doublets of the newly formed methyl groups (δ = 1·27 and 1·46 for *XXXIb* and *XXXIIb*, respectively) coupled to 19-H methines (quadruplets, δ = 4·12 (*XXXIb*) and δ = 4·13 (*XXXIIb*)). Furthermore, *XXXIb* and *XXXIIb* were found to be identical with the products obtained by debromination of *XXXVII* and *XXXVIII*, respectively, which definitively confirmed the 2β-19



SCHEME 4

bridging in the former compounds. The assignment of the $C_{(19)}$-configuration in *XXXIa* and *XXXIIa* is based on the different chemical shifts of the $C_{(19a)}$ protons only and therefore should be regarded as tentative.

Hypobromous acid addition to the diene *II* (Scheme 5) furnished a mixture of $C_{28}H_{46}Br_2O$ isomers *XXXVII* and *XXXVIII* as evidenced by molecular ions *m/z* 556, 558, 560 in the mass spectrum. The structure for *XXXVII* and *XXXVIII* followed again from their spectra. Abundant fragment ions $(M-CH_2Br)^+$ in the mass spectrum indicate the presence of a CH_2Br group in both isomers which is

consistent with two distinct ABX systems (O—CH—CH_2Br) found in the ^1H NMR spectrum of the mixture. Reduction of *XXXVII* + *XXXVIII* with tri-n-butyltin hydride gave a mixture of *XXXIb* and *XXXIIb*, providing thus a conclusive proof for the 2β-19 bridging in both *XXXVII* and *XXXVIII*.

The reaction of the diene *III* (Scheme 6) with hypobromous acid was not so clean as in the cases of *I* and *II*: the main product *XLII* was accompanied by a mixture of unstable minor by-products which have not been characterized. The mass spectrum of *XLII* displays very weak molecular ions *m/z* 556, 558, 560 and fragments arising by combined losses of bromine, hydrogen bromide and water, while $(M-CH_2Br)^+$ ions are absent. This points to the structure with an oxygen bridge connecting $C_{(4)}$ and $C_{(19a)}$. The ^1H NMR spectrum of *XLII* brings further support, showing an ABX system with the $C_{(19)}$ proton shifted downfield[10] and a doublet of the $C_{(4)}$ proton. The vicinal coupling constants reveal that both the A ring and the heterocycle must be flattened, possibly to release the steric repulsion between 2β and 19a-*endo* hydrogen atoms. Inspection of Dreiding models indicates that the tetrahydropyran ring should assume a half-chair conformation with *R* configuration at $C_{(19)}$, while an alternative 19*S* configuration would be incompatible with the spectral data. The preferred formation of the 19*R* isomer is understandable as it results from the reagent approach from the better accessible "back" side of the skeleton.

Addition of hypobromous acid to the 5,6-unsaturated 10β-vinyl derivative *IV* resulted in formation of a mixture of epimeric tetrahydropyrane derivatives *XLVII*

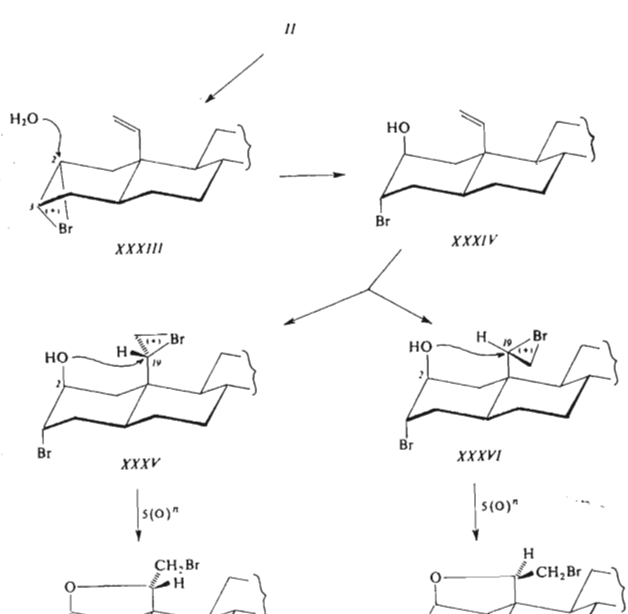
TABLE I

Yields and ratios of products of hypobromous acid addition to the compounds *I*—*VI*, *LXI* and *LXXII*

Starting compound	Mode of reaction	Relative yield, %		Total yield %
		(19*S*)	(19*R*)	
I	5(0)[n]	56 (*XXXIa*)	44 (*XXXIIa*)	88
II	5(0)[n]	55 (*XXXVII*)	45 (*XXXVIII*)	87
III	6(0)[n]	—	<95 (*XLII*)	⟨2
IV[b]	6(0)[n]	83 (*XLVII*)	17 (*XLVIII*)	93
V	5(0)[n]	61 (*LIIIa*)	39 (*LIVa*)	89
VI	6(0)[n]	71 (*LIX*)	29 (*LX*)	90
LXI	5(0)[n]	47 (*LXIV*)	53 (*LXV*)	92
LXXII[b]	6(0)[n]	90 (*LXXV*)	10 (*LXXVI*)	90

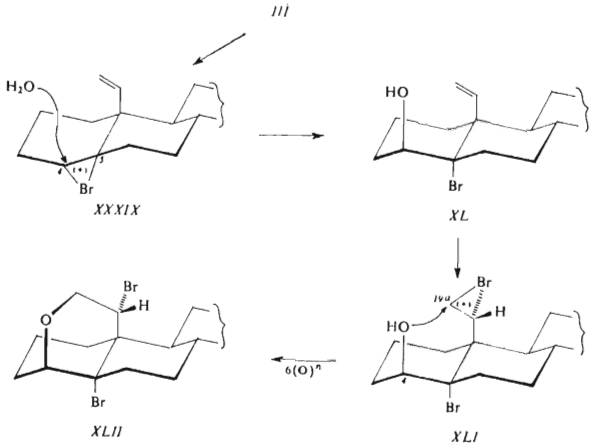
[a] Determined from ^1H NMR spectra of mixtures of the diastereoisomers; [b] ref.[11].

and *XLVIII*. The mechanism of their formation is summarized in Scheme 7 (for discussion *cf.* ref.[11]).



SCHEME 5

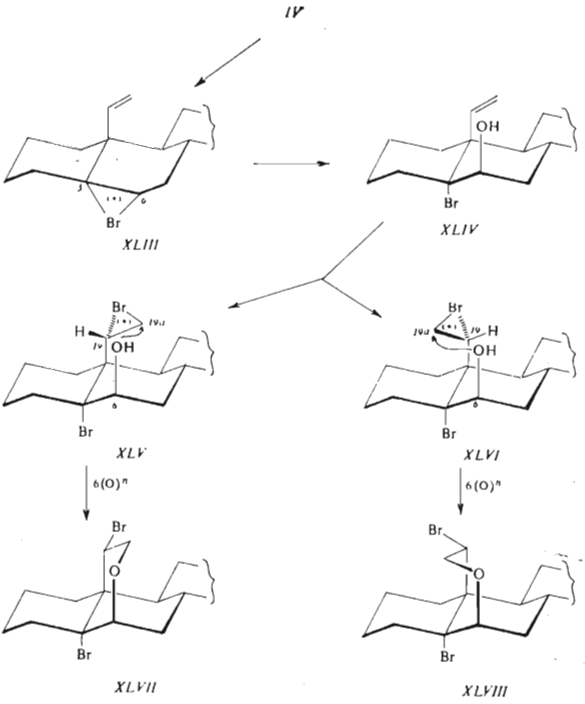
Hypobromous acid addition to the diene *V* (Scheme 8) afforded a mixture of dibromo ethers *LIIIa* and *LIVa*. The mass spectrum of the mixture (*m/z* 556, 558, 560, M^+; 463, 465, $(M-CH_2Br)^+$) shows again the presence of a CH_2Br group corresponding to an oxygen link between $C_{(19)}$ and the skeleton. The position of substituents on the B-ring follows unambiguously from the ^1H NMR spectra. Beside the ABX patterns corresponding to the O—CH—CH_2Br subsystems, the spectra show vicinal coupling constants $J_{6,7} = 4{\cdot}5$ Hz and $J_{7,8} = 4{\cdot}5$ Hz which can be expected



SCHEME 6

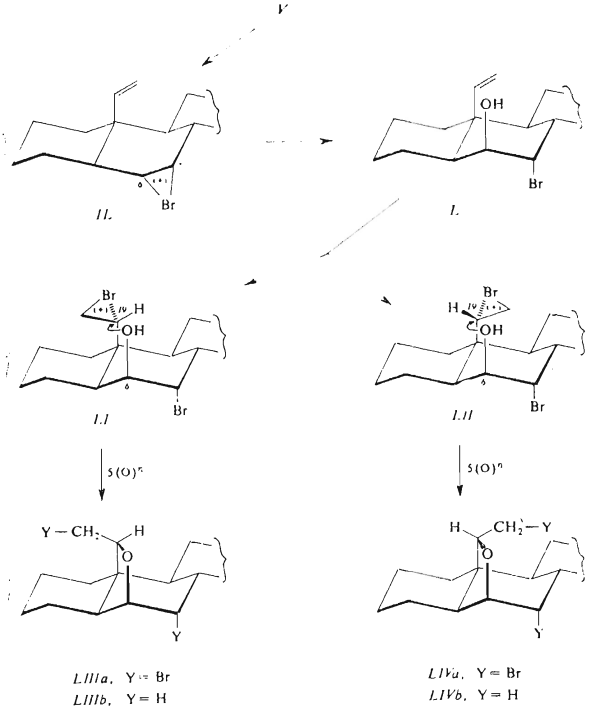
for 6β-19 bridging, while excluding alternative structures with a 7β-19 oxygen ring. The five-membered heterocycle in *LIIIa* and *LIVa* imposes strain on the B-ring in which the dihedral angle between 5α-H and 6α-H is close to 90°. Hence the coupling constant $J_{5,6}$ is very small and the signal of the 6α-H appears as a doublet. In order to obtain further structural information, the mixture of *LIIIa* and *LIVa* was reduced with tri-n-butyltin hydride affording epimeric 19-methyl derivatives *LIIIb* and *LIVb*. The presence of the O—CH—CH_3 grouping is apparent from both the mass spectra (ions $(M-C_2H_4O)^+$) and ^{1}H NMR spectra (quartets of 19-H coupled to doublets of 19-CH_3) of *LIIIb* and *LIVb*. On the other hand, the spectral data gave no definite clue for the configurational assignment at $C_{(19)}$, so the presented configurations in *LIIIa*, *LIVa*, *LIIIb* and *LIVb* are only tentative.

The diene *VI* (Scheme 9) reacted with hypobromous acid in a similar way as did *I*, *II* and *V*, giving a mixture of isomers *LIX* and *LX*. The structural evidence for the products stems from the spectral data: The loss of CH_2Br radical from the molecular ions in the mass spectrum indicates the $C_{(19)}$—O connection supported by ABX systems found in the ^{1}H NMR spectra. The vicinal coupling constant $J_{5,6}$ = 9·1 and 9·2 Hz for *LIX* and *LX*, respectively, corroborates the structure with a tetrahydropyran ring, while an alternative with a reversed position of the bromine and oxygen substituents should show a much smaller value for $J_{5,6}$.



SCHEME 7

Finally, addition of hypobromous acid to the unsaturated diol *LXI* (Scheme 10) gave rise to a mixture of epimeric ethers *LXIV* and *LXV* in which the formation of a tetrahydrofuran ring was established from the spectral data. Comparison of the ^{1}H NMR spectra of *LXIV* and *LXV* with those of the acetates *LXVI*, *LXVII* made it possible to assign the signals of the $C_{(2)}$ and $C_{(3)}$ protons. The mixture of *LXIV* + + *LXV* was reduced with tri-n-butyltin hydride to yield ethers *LXVIII* and *LXIX* in which the presence of a O—CH—CH_3 grouping was established through their ^{1}H NMR spectra, giving thus additional evidence for the 2β-19 bridging in the starting bromo-



LIIIa, Y = Br
LIIIb, Y = H

LIVa, Y = Br
LIVb, Y = H

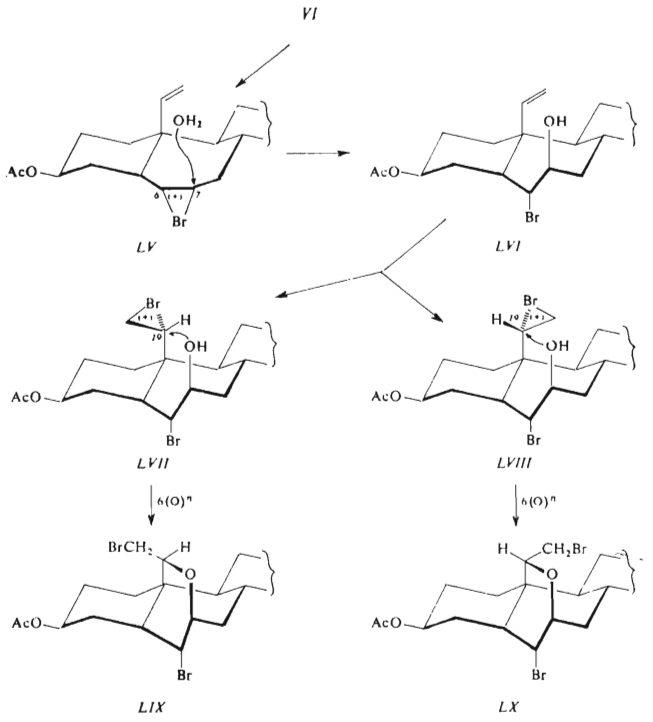
SCHEME 8

ethers *LXIV* and *LXV*. The proton signals in *LXVIII* and *LXIX* were assigned after acetylation (compounds *LXX* and *LXXI*).

Hypobromous acid addition to the unsaturated diol *LXXII* gave a mixture of epimeric tetrahydropyrane derivatives *LXXV* and *LXXVI* (Scheme 11)[11].

Mechanism of Addition

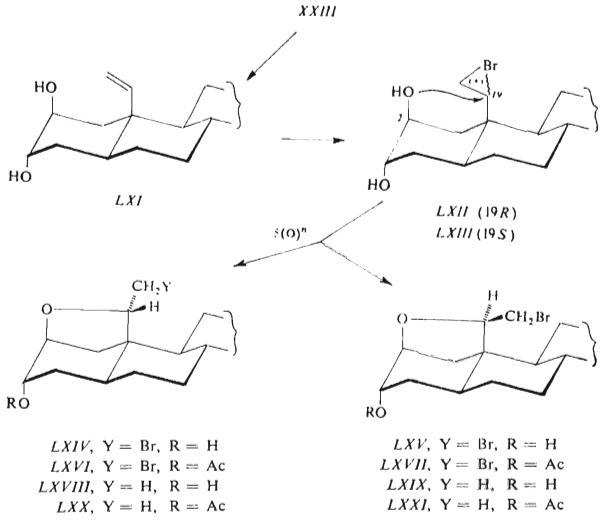
As noted above, all the model dienes *I*–*VI* react with two equivalents of hypobromous acid. Since we were unable to stop the reaction after the first addition step,



SCHEME 9

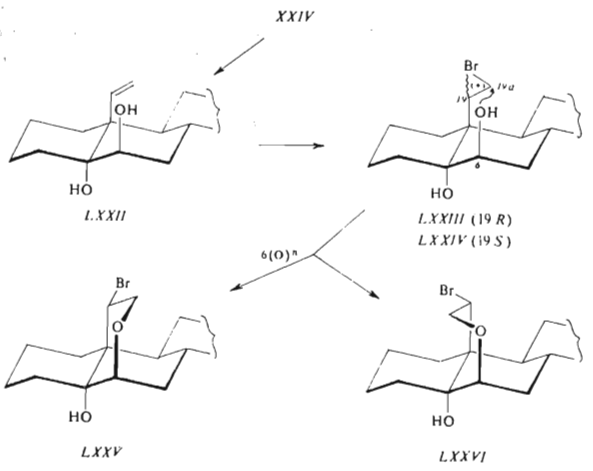
the reaction course furnished only indirect evidence as to which of the two double bonds had been attacked first. To answer this question we treated the dienes with an excess of 3-chloroperoxybenzoic acid obtaining only monoepoxides in all cases (Scheme 12). The epoxidation takes place from the α-side of the skeleton yielding 1α,2α-epoxide *XXII*, 2α,3α-epoxide *XXIII*, 5α,6α-epoxide *XXIV* (ref.[11]) and 6α,7α--epoxides *XXV* and *XXVI* from *I*, *II*, *IV*, *V* and *VI*, respectively. This shows that the endocyclic double bonds are more reactive than the 10β-vinyl group (for discussion

see ref.[11]), probably due to steric hindrance of the reagent approach to the latter. While the endocyclic double bonds are easily accessible from direction perpendicular to the skeleton, the attack of the vinyl group by an electrophile should occur



SCHEME 10

in a plane parallel with the AB rings and so it would be impaired by axial hydrogen atoms. By analogy, we therefore assume that the formation of intermediary bromonium ions occurs at the α-side of the endocyclic double bonds, as well. Further fate of these bromonium ions is depicted in Schemes 4–9. The 1α,2α-bromonium ion *XXVII* arising from *I* is cleaved by water as an external nucleophile at $C_{(2)}$, according to the Fürst–Plattner rule, giving rise to non-isolable bromohydrin *XXVIII* (Scheme 4). The vinyl group of the latter reacts with the second equivalent of the reagent forming a pair of epimeric bromonium ions *XXIX* and *XXX* which are further cleaved at $C_{(19)}$ by intramolecular attack of the $C_{(2)}$-hydroxyl group, yielding the final products *XXXIa* and *XXXIIa*. This cleavage with 5(0)^n participation of the hydroxyl conforms with the Markovnikov rule.



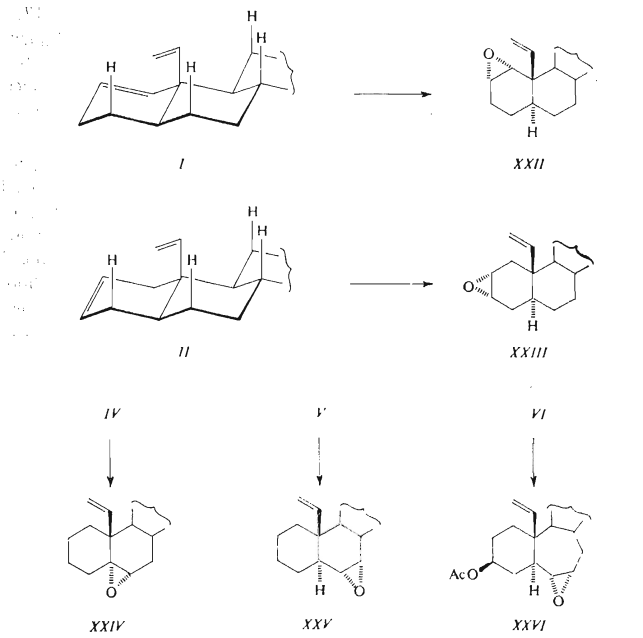
SCHEME 11

The diene *II* behaves similarly (Scheme 5) giving subsequently the 2α,3α-bromonium ion *XXXIII*, bromohydrin *XXXIV*, intermediary ions *XXXV* and *XXXVI* and final epoxides *XXXVII* and *XXXVIII*. Since the transient species *XXXIII* and *XXXIV* could not be isolated, we simulated[17–21] the reaction course *II*→*XXXVII*, *XXXVIII* by employing the stable 2α,3α-epoxide *XXIII* as a starting compound (Scheme 10). The oxirane ring in *XXIII* was cleaved with aqueous perchloric acid to afford the diaxial diol *LXI*, an analog of the bromohydrin *XXXIV*. Hypobromous acid addition to *LXI* shows the same regiospecificity as with *XXXIV* proceeding *via* epimeric bromonium ions *LXII* and *LXIII* (analogs of *XXXV* and *XXXVI*) which are cleaved by intramolecular attack of the 2β-hydroxyl at $C_{(19)}$ to yield ethers *LXIV* and *LXV*.

The reaction sequence starting from the diene *III* is shown in Scheme 6. In this case the stereoselectivity of the reagent approach is not so pronounced as with *I* and *II*. Nevertheless, the endocyclic double bond is attacked preferentially from the α-side and the intermediate *XXXIX* is then cleaved by water to give diaxial bromohydrin *XL*. The lesser specificity of the addition to *III* has an analogy in the behavior of 4-cholestene which gives a mixture of non-polar products possibly arising as a result of an extensive backbone rearrangement[14,18]. The intermediary bromohydrin

XL further reacts with the second equivalent of the reagent, however, the reaction course is different from those of *I* and *II*. The vinyl group in *XL* is preferentially attacked from the less hindered side and the transient (19*R*)-bromonium ion *XLI* is cleaved by the 4β-hydroxyl at $C_{(19a)}$ ($6(0)^n$ participation) to yield *XLII*, a product of anti-Markovnikov addition.

The reaction of the diene *IV* with hypobromous acid leading again to anti-Markovnikov products *XLVII* and *XLVIII* (Scheme 7) was discussed in the preceding paper[11] in which we have also presented further evidence for preferential reactivity of the endocyclic double bond. In order to check the earlier conclusions we made use of the epoxide *XXIV* as a stable analog of the corresponding 5α,6α-bromonium ion[21]. Acid cleavage of the epoxide ring in *XXIV* gave the diaxial diol[11] *LXXII* (Scheme 11), an analog of the unstable 5α,6β-bromohydrin *XLIV* (Scheme 7). Hypobromous



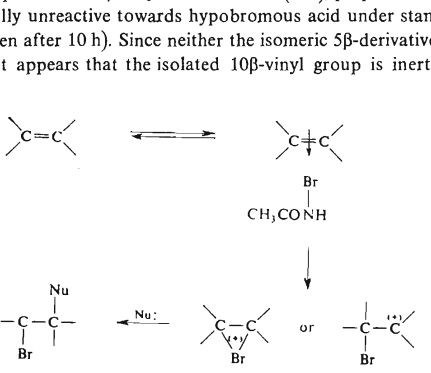
SCHEME 12

acid addition to *LXXII* resembles the second addition step to the diene *IV*: Bromonium ions *LXXIII* and *LXXIV* obtained from *LXXII* (Scheme 11) are cleaved by the 6β-hydroxyl at $C_{(19a)}$ (anti-Markovnikov mode)[11] yielding ethers *LXXV* and *LXXVI*.

The diene *V* gives 6α,7α-bromonium ion *IL* upon addition of hypobromous acid (Scheme 8) which is cleaved externally by water to give the non-isolated bromohydrin *L*. Further addition proceeds *via* epimeric ions *LI* and *LII* which are opened by intramolecular attack of the 6β-hydroxyl ($5(0)^n$ participation) at $C_{(19)}$ to yield isomers *LIIIa* and *LIVa*.

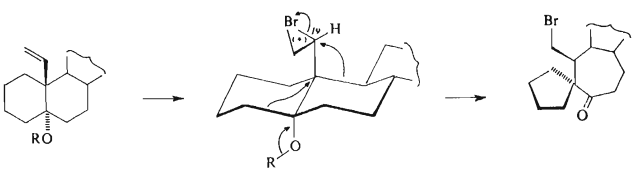
An analogous reaction course can be assumed for hypobromous acid addition to the diene *VI* which contains the endocyclic double bond in the seven-membered B-homo ring (Scheme 9). The postulated mechanism can be distinguished from alternatives owing to the known mode of participation of the 19-hydroxyl group in B-homo-5α-cholest-6-en-3β,19-diol 3-acetate[4]. Should we suppose Markovnikov addition of the first equivalent of hypobromous acid to the vinyl group in *VI*, the newly formed 19-hydroxyl would participate in the next addition step at $C_{(6)}$ giving isomers with a reversed position of the bromine and oxygen substituents on the B-homo ring[4]. Hence the regiochemistry of the addition (Scheme 9) is further evidence for the preferential attack of the endocyclic double bond in *VI*, in line with the results of epoxidation.

In the previous text we have analyzed the regio- and stereochemistry of separate addition steps to *I* – *VI*. Since the substituents introduced by addition to the endocyclic double bonds served as control elements in the addition to the 10β-vinyl group, it was of interest to examine the reactivity of the latter in the absence of any other functional group. 19-Nor-10β-vinyl-5α-cholestane (*VII*), prepared for this purpose[22], was found totally unreactive towards hypobromous acid under standard conditions (no reaction even after 10 h). Since neither the isomeric 5β-derivative[22] *VIII* showed any reaction, it appears that the isolated 10β-vinyl group is inert in the absence



SCHEME 13

of a participating group. This points our that the first step of the addition must be reversible, so that the concept of bromonium ions as sole primary intermediates is in fact an oversimplification. In a detailed mechanistic description[2] one has to consider formation of a reversible complex of the reagent and the olefin (Scheme 13) further reactivity of which will depend on the nucleophile counterpart. If the access of the latter is impaired as in *VII* and *VIII*, the complex dissociates back to the reactants, while intramolecular participation by a suitable nucleophilic group traps the intermediate and thus drives the addition into completion. It is noteworthy that the participation can also be exerted by a suitably oriented and reactive carbon–carbon single bond as documented by rearrangement in 10β-vinyl-5α-hydroxy and methoxy derivatives[10,23] *LXXVII* (Scheme 14).



LXXVIIa, R = H
LXXVIIb, R = CH_3

LXXVIIIa, R = H
LXXVIIIb, R = CH_3

LXXIX

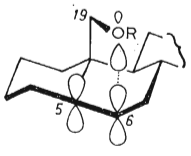
SCHEME 14

Structural Factors

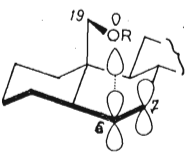
The regiospecific formation of the bromoethers posed further questions as to the Markovnikov or anti-Markovnikov course of addition to the 10β-vinyl group depending on the position of the endocyclic double bond. The different behaviour of 19,19a-bromonium ions *XLV*, *XLVI* and *LI*, *LII* generated from *IV* and *V*, respectively, (Schemes 7 and 8) is especially striking, for the participating hydroxyl is located in the 6β-position in both cases. The species differ only in the location of the bromine atom which is in a homoallylic (*XLV*, *XLVI*) or δ-position (*LI*, *LII*) with respect to the 10β-vinyl and this difference has very dramatic effect on the reaction course. One of possible rationalizations would invoke the inductive effect of the homoallylic bromine atom in *XLV* and *XLVI* which would decrease the electron density at $C_{(19)}$ prefering thus the anti-Markovnikov addition (ref.[2,21,24–31]). Note, however, that a similar pair of bromonium ions *XXIX*, *XXX* and *XXXV*, *XXXVI* generated from *I* and *II*, respectively (Schemes 4 and 5), in which the positions of bromine atoms also differ, gives exclusively products of Markovnikov addition. It seems therefore more probable that the different course of addition in *IV* and *V* is due to conformational effects, *e.g.* B-ring deformation in *IV* which may alter the distance and

angle of approach of the 6β-hydroxyl to $C_{(19)}$, preferring thus the attack at $C_{(19a)}$. The behavior of the diene *III* is in line with this concept.

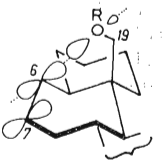
The last topic deserving comment is the non-occurence of $(C)^{\pi}$ participation which would have led to carbon–carbon bond formation. It is well established[4] that compounds having 19-hydroxyl or methoxyl and an endocyclic double bond in the A or B ring, such as *LXXX*–*LXXXII* (Fig. 1), react with hypobromous acid with intra-



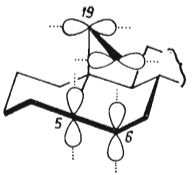
LXXX



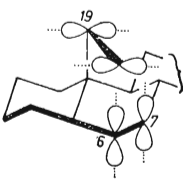
LXXXI



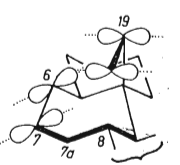
LXXXII



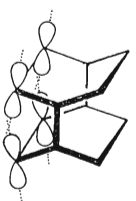
IV



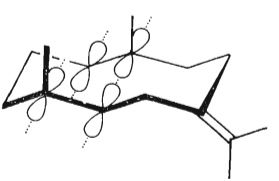
V



VI



LXXXIII



LXXXIV

FIG. 1

Stereoelectronic Effects in Hypobromous Acid Addition

molecular participation and formation of carbon–oxygen bond. Inspection of Dreiding models shows that both the methylene terminus of the 10β-vinyl and the 19-hydroxyl can approach endocyclic double bonds to a distance *a priori* enabling intramolecular participation (Fig. 1, *IV*–*VI*). Their different reactivity is due to stereoelectronic factors: while the participating p_z-orbital on oxygen can be suitably oriented by rotating the OR group about the $C_{(19)}$—O bond, the bonding π-orbital of the rigid vinyl group points out of the molecule, preventing an effective participation. Thus, despite the favorable distance between $C_{(19a)}$ and an electron-deficient center in *I*–*V* (0·25 to 0·30 nm), the nucleophilicity of π-electrons is impaired by unfavorable orbital orientation. On the other hand in the diene *VI*, the vinyl group and the B-homo ring can assume conformation in which the π-orbitals of both double bonds are nearly coplanar. A similar arrangement of double bonds in tricyclic diene[32,34] *LXXXIII* favors $(C)^{\pi}$ participation and leads to carbon–carbon bond formation upon attack of an electrophile. Inspection of models shows, however, that the distance between $C_{(6)}$ and $C_{(19a)}$ in *VI* (ca 0·30 nm) is too long to promote carbon–carbon bond formation. Moreover, in conformation with coplanar double bonds the 19a-methylene hydrogen atom comes too close to the 8β-hydrogen. The resulting steric repulsion decreases population of this conformer and impairs the participation propensity of the vinyl group. It appears that ideal conditions for $(C)^{\pi}$ participation are met in germacratriene *LXXXIV* (*cf.* Fig. 1 and Scheme 1): the molecular conformation maintains both the coplanarity of the π-orbitals and favorable distance between $C_{(5)}$ and $C_{(10)}$.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 20°C/26 Pa or at 50°C/26 Pa. Optical rotation measurements were carried out in chloroform with an error of ±3°. The infrared spectra were recorded on a Zeiss UR 20 or on a Perkin–Elmer spectrometers in tetrachloromethane unless stated otherwise. The ^{1}H NMR spectra were measured on a Bruker WH-300 apparatus (300·15 MHz, FT mode) or on a Varian XL-200 apparatus (200·05 MHz, FT-mode) and on a Tesla B 476 (60 MHz) instrument at 25°C in deuteriochloroform with tetramethylsilane as internal reference. Chemical shifts are given in δ (ppm) scale. Coupling constants of ABX systems were obtained from the second-order analysis, the others were taken from the first-order analysis; in all cases they were checked by double resonance experiments. Mass spectra were recorded on a JEOL JMS D-100 spectrometer at 75 eV. The samples were introduced using a direct inlet heated to 120–150°C, the ion source was maintained at 150°C. Elemental composition of all reported ions was determined by peak matching method using perfluorokerosene as a reference. The identity of the samples prepared by different routes was checked by thin-layer chromatography (TLC), infrared, ^{1}H NMR and mass spectra. Usual workup 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*.

19-Nor-10β-vinyl-5α-cholest-1-ene (*I*)

Sodium hydride (300 mg) was dissolved in dimethyl sulfoxide (10 ml) with stirring and heating

at 65°C for 3 h. Triphenylmethylphosphonium iodide (1·5 g) was added at 15°C and the mixture was stirred at room temperature for 1 h. A solution of the aldehyde *X* (800 mg) in tetrahydrofuran (10 ml) was added at room temperature and the mixture was stirred at 70°C for 5 h. The mixture was cooled, diluted with ether and water and the ethereal layer was worked up as usual. The residue was dissolved in a mixture of light petroleum and benzene (9 : 1) and filtered through a column of aluminum oxide. The eluate was evaporated and the residue was crystallized from acetone to yield the diene *I* (530 mg), m.p. 74—76°C. IR spectrum (film): 920, 999, 1 406, 1 622, 1 642, 3 020, 3 078, cm^{-1}. For $C_{28}H_{46}$ (382·7) calculated: 87·88% C, 12·12% H; found: 87·73% C, 12·20% H.

19-Nor-10β-vinyl-5α-cholest-2-ene (*II*)

Triphenylmethylphosphonium iodide (5 g) was added to a solution of sodium hydride (1 g) in dimethyl sulfoxide (30 ml) and the mixture was stirred at room temperature for 30 min. A solution of the aldehyde[13] *XII* (2 g) in tetrahydrofuran (25 ml) was added at room temperature, the mixture was stirred at 65°C for 1 h and then worked up as given in previous experiment. After filtration through a column of aluminum oxide the residue was crystallized from a mixture of acetone and methanol to afford the diene *II* (1·3 g), m.p. 54—55°C, $[\alpha]_D^{20}$ +134° (*c* 1·6). ^1H NMR spectrum: 0·62 (3 H, s, 18-H), 5·00 (1 H, m, $W = 40$ Hz, 19-H), 5·58 (2 H, m, $W = 10$ Hz, 2-H, 3-H), 6·00 (2 H, m, $W = 35$ Hz, 19a-H). IR spectrum: 659, 678, 914, 999, 1 412, 1 633, 1 657, 3 022, 3 080 cm^{-1}. For $C_{28}H_{46}$ (382·7) calculated: 87·88% C, 12·12% H; found: 88·61% C, 12·34% H.

19-Nor-10β-vinyl-cholest-4-ene (*III*)

Triphenylmethylphosphonium iodide (4 g) was added to a solution of sodium hydride (600 mg) in dimethyl sulfoxide (24 ml) and the mixture was stirred at room temperature for 30 min. A solution of the aldehyde *XIV* (700 mg) in tetrahydrofuran (15 ml) was added at 75°C for 2 h. The mixture was worked up as given for *I*. The filtrate from aluminum oxide column was evaporated and the residue was crystallized from a mixture of acetone and methanol to give the diene *III* (420 mg), m.p. 63—65°C, $[\alpha]_D^{20}$ +78° (*c* 1·7). IR spectrum: 922, 998, 1 408, 1 630, 3 085 cm^{-1}. For $C_{28}H_{46}$ (382·7) calculated: 87·88% C, 12·12% H; found: 87·64% C, 12·19% H.

19-Nor-10β-vinyl-5α-cholest-6-ene (*V*)

Triphenylmethylphosphonium iodide (600 mg) was added to a solution of sodium hydride (150 mg) in dimethyl sulfoxide (5 ml) and the mixture was stirred at room temperature for 1 h. A solution of the aldehyde *XIX* (320 mg) in tetrahydrofuran (5 ml) was added at room temperature and the mixture was stirred at 70°C for 5 h. The mixture was worked up as given for *I*. The residue was crystallized from a mixture of acetone and methanol to yield the diene *V* (160 mg), m.p. 89—90°C, $[\alpha]_D^{20}$ −60° (*c* 1·6). IR spectrum: 914, 1 419, 1 630, 1 640, 3 015, 3 080 cm^{-1}. For $C_{28}H_{46}$ (382·7) calculated: 87·88% C, 12·12% H; found: 87·93% C, 12·09% H.

19-Nor-10β-vinyl-B-homo-5α-cholest-6-en-3β-ol 3-Acetate (*VI*)

Triphenylmethylphosphonium iodide (500 mg) was added to a solution of sodium hydride (55 mg) in dimethyl sulfoxide (5 ml) and the mixture was stirred at room temperature for 30 min. A solution of the aldehyde *XXI* (300 mg) in tetrahydrofuran (5 ml) was added at room temperature and the mixture was stirred at 70°C for 5 h. The mixture was then worked up as given for *I*. The residue containing *VI* contaminated with a product of saponification of the acetoxy group

was dissolved in pyridine (5 ml) and treated with acetic anhydride (2 ml) at room temperature for 6 h. The mixture was then decomposed with ice and water, the product extracted with ether and the etheral phase was worked up. The residue was dissolved in a mixture of benzene and light petroleum (1 : 4) and filtered through a column of aluminum oxide. The eluate was evaporated and the residue by crystallization from aqueous acetone furnished the diene *VI* (60 mg), m.p. 125–126°C, $[\alpha]_D^{20}$ +65° (*c* 1·8). IR spectrum: 918, 989, 1 245, 1 414, 1 632, 1 668, 1 733, 3 020, 3 075 cm^{-1}. For $C_{31}H_{50}O_2$ (454·7) calculated: 81·88% C, 11·08% H; found: 81·66% C, 11·10% H.

5α-Cholest-1-en-19-al (*X*)

The alcohol[12] *IX* (1 g) was dissolved in acetone (20 ml) and treated with Jones' reagent at 0°C for 10 min. The excess reagent was decomposed with methanol, the mixture was diluted with ether and water, the ethereal layer was washed with water, a 5% aqueous potassium hydrogen carbonate solution, water, dried with sodium sulfate and the solvent was evaporated. The residue was crystallized from aqueous ethanol to afford the aldehyde *X* (810 mg), m.p. 68–69°C, $[\alpha]_D^{20}$ −67° (*c* 2·3). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 5·82 (2 H, m, W = 12 Hz, 1-H and 2-H), 9·87 (1 H, s, 19-H). For $C_{27}H_{44}O$ (384·7) calculated: 84·31% C, 11·53% H; found: 84·19% C, 11·62% H.

4-Cholesten-19-al (*XIV*)

The alcohol[14] *XIII* (400 mg) in acetone (10 ml) was oxidized with Jones' reagent to yield after crystallization from aqueous acetone the aldehyde *XIV* (180 mg), m.p. 57–59°C, $[\alpha]_D^{20}$ +68° (*c* 4·4). ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 5·67 (1 H, m, W = 12 Hz, 4-H), 9·83 (1 H, s, 19-H). For $C_{27}H_{44}O$ (384·7) calculated: 84·31% C, 11·53% H; found: 84·16% C, 11·65% H.

7α-Bromo-5α-cholestan-6β-ol (*XVI*)

The olefin[15,16] *XV* (700 mg) was dissolved in dioxane (50 ml), water (2 ml) and a 10% aqueous perchloric acid (3 ml) were added and the mixture was treated with N-bromoacetamide (280 mg) at room temperature for 1 h. Then the mixture was diluted with ether and water, the ethereal 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 a column of silica gel (30 g) using a mixture of light petroleum and ether (95 : 5) as eluent. The corresponding fraction was evaporated to afford the unstable oily bromohydrin *XVI* (*c.* 450 mg) which was directly used in further experiment. ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 0·98 (3 H, s, 19-H), 3·93 (1 H, m, W = 11 Hz, 6α-H), 4·25 (1 H, t, J = 2·5 Hz, 7β-H).

6β,19-Epoxy-7α-bromo-5α-cholestane (*XVII*)

The bromohydrin *XVI* (1 g) was dissolved in benzene (15 ml) and refluxed while stirring with calcium carbonate (0·5 g), lead tetraacetate (1 g) and iodine (100 mg) for 1 h. The inorganic material was filtered off, the solution was diluted with ether and water and the organic phase was washed with water, 5% aqueous hydrochloric acid, 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 a column of silica gel using a mixture of light petroleum and benzene (85 : 15) as eluent. Corresponding fraction was evaporated to yield the oily epoxide *XVII* (600 mg), $[\alpha]_D^{20}$ −48° (*c* 2·3). ^{1}H NMR spectrum: 0·71 (3 H, s, 18-H), 3·63 (1 H, d, J = 8·5 Hz, 19-H), 3·83 (1 H, d, J = 8·5 Hz, 19-H), 4·05 (2 H,

m, $W = 22$ Hz, 6α-H and 7β-H). For $C_{27}H_{45}BrO$ (465·6) calculated: 69·66% C, 9·74% H, 17·16% Br; found: 69·48% C, 9·82% H, 17·29% Br.

5α-Cholest-6-en-19-ol (*XVIII*)

Powdered zinc (2 g) was added in 10 portions to a stirred refluxing solution of the epoxide *XVII* (570 mg) in a mixture of dioxane (2 ml) and acetic acid (3 ml) in a period of 10 min. The hot mixture was filtered, the inorganic material was washed with hot acetic acid, the eluate was diluted with water and set aside overnight. The product *XVIII* (460 mg) was filtered off, m.p. 101—102°C, $[\alpha]_D^{20} = -79°$ (*c* 1·6). ^{1}H NMR spectrum: 0·72 (3 H, s, 18-H), 3·87 (2 H, s, 19-H), 5·42 (2 H, m, $W = 30$ Hz, 6-H and 7-H). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·74% C, 12·02% H.

5α-Cholest-6-en-19-al (*XIX*)

The alcohol *XVIII* (400 mg) in acetone (10 ml) was oxidized with Jones' reagent as given for *X* to yield after crystallization from aqueous acetone the aldehyde *XIX* (340 mg), m.p. 93—94°C $[\alpha]_D^{20} = -44°$ (*c* 2·1). ^{1}H NMR spectrum: 0·62 (3 H, s, 18-H), 5·60 (2 H, m, $W = 8$ Hz, 6-H and 7-H), 9·88 (1 H, s, 19-H). IR spectrum: 1 640, 1 712, 2 730, 3 020 cm^{-1}. For $C_{27}H_{44}O$ (384·7) calculated: 84·31% C, 11·53% H; found: 84·14% C, 11·57% H.

3β-Acetoxy-B-homo-5α-cholest-6-en-19-ol (*XXI*)

The alcohol[4] *XX* (300 mg) in acetone (5 ml) was oxidized with Jones' reagent as given for *X*. The crude product was dissolved in a mixture of benzene and light petroleum (4 : 1) and filtered through a column of aluminum oxide. The eluate was evaporated to yield the oily aldehyde *XXI* (267 mg), $[\alpha]_D^{20} = +53°$ (*c* 1·9). ^{1}H NMR spectrum: 0·58 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 4·62 (1 H, m, $W \approx 30$ Hz, 3α-H), 5·35 (1 H, m, $W = 25$ Hz) and 5·93 (1 H, m, $W = 25$ Hz) 6-H and 7-H. For $C_{30}H_{48}O_3$ (456·7) calculated: 78·90% C, 10·59% H; found: 78·69% C, 10·76% H.

1α,2α-Epoxy-19-nor-10β-vinyl-5α-cholestane (*XXII*)

The diene *I* (40 mg) was dissolved in chloroform (2 ml) and treated with 3-chloroperoxybenzoic acid (29 mg) at room temperature for 30 min. The mixture was diluted with ether and water, the ethereal layer was washed with water, a 5% aqueous potassium hydrogen carbonate, a 5% aqueous sodium thiosulfate solution, water, dried with sodium sulfate and the solvent was evaporated. The residue was chromatographed on a silica gel plate (20 × 20 cm) using a mixture of light petroleum, ether and acetone (94 : 3 : 3) as eluent. The corresponding zone was separated, eluted with ether and the eluate was evaporated to afford the oily epoxide *XXII* (22 mg), $[\alpha]_D^{20} = -1°$ (*c* 2·6). ^{1}H NMR spectrum: 0·63 (3 H, s, 18-H), 2·23 (2 H, m, W = 18 Hz, 1β-H and 2β-H), 5·20 (2 H, m, $W = 40$ Hz, 19a-H), 6·10 (1 H, m, $W = 40$ Hz, 19-H). For $C_{28}H_{46}O$ (398·7) calculated: 84·36% C, 11·63% H; found: 84·22% C, 11·79% H.

2α,3α-Epoxy-19-nor-10β-vinyl-5α-cholestane (*XXIII*)

The diene *II* (1 g) was dissolved in chloroform (10 ml) and treated with 3-chloroperoxybenzoic acid (700 mg) at room temperature for 1 h. The mixture was worked up as in the previous experiment. 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 give the oily epoxide *XXIII* (850 mg), $[\alpha]_D^{20} = +101°$ (*c* 1·2), ^{1}H NMR spectrum: 0·58 (3 H, s, 18-H), 3·12 (2 H, m, $W = 20$ Hz,

2-H and 3-H), 5·15 (2 H, m, $W = 40$ Hz, 19a-H), 5·90 (1 H, m, $W = 30$ Hz, 19-H). For $C_{28}H_{46}O$ (398·7) calculated: 84·36% C, 11·63% H; found: 84·19% C, 11·84% H.

6α,7α-Epoxy-19-nor-10β-vinyl-5α-cholestane (*XXV*)

The diene *V* (28 mg) in chloroform (1 ml) was treated with 3-chloroperoxybenzoic acid (20 mg) at room temperature for 30 min. The mixture was worked up as given for *XXII*. Crystallization of the crude product from a mixture of acetone, methanol and water gave the epoxide *XXV* (19 mg), m.p. 78–79°C, $[\alpha]_D^{20}$ −6° (*c* 1·6). ^{1}H NMR spectrum: 0·62 (3 H, s, 18-H), 2·77 (1 H, d, $J = 4$ Hz, 6β-H), 3·02 (1 H, m, $W = 10$ Hz, 7β-H), 5·35 (3 H, m, $W = 70$ Hz, $CH{=}CH_2$). For $C_{28}H_{46}O$ (398·7) calculated: 84·36% C, 11·63% H; found: 84·22% C, 11·69% H.

6α,7α-Epoxy-19-nor-10β-vinyl-B-homo-5α-cholestan-3β-ol 3-Acetate (*XXVI*)

The diene *VI* (30 mg) in chloroform (2 ml) was treated with 3-chloroperoxybenzoic acid (25 mg) at room temperature for 1 h. The mixture was worked up as given for *XXII*. The residue was dissolved in a mixture of benzene and light petroleum (1 : 4) and filtered through a column of aluminum oxide. Elution with the same mixture removed impurities, elution with a mixture of light petroleum, benzene and ether (5 : 3 : 1) gave the pure product, which on crystallization from a mixture of acetone, methanol and water furnished the epoxide *XXVI* (12·1 mg), m.p. 163–164°C, $[\alpha]_D^{20}$ +42° (*c* 1·5). ^{1}H NMR spectrum: 0·58 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 2·60 (1 H, m, $W = 15$ Hz) and 2·88 (1 H, m, $W = 15$ Hz, 6β-H and 7β-H), 4·60 (1 H, m, $W = 30$ Hz, 3α-H), 5·40 (3 H, m, $W = 70$ Hz, $CH{=}CH_2$). IR spectrum: 918, 982, 1 245, 1 418, 1 632, 1 735 cm^{-1}. For $C_{31}H_{50}O_3$ (470·7) calculated: 79·10% C, 10·71% H; found: 79·01% C, 10·83% H.

Addition of Hypobromous Acid to Compounds *I*–*III* and *V*–*VI*

The unsaturated compound (0·5 mmol) was dissolved in dioxane (5 ml) and water (0·5 ml) and treated with 10% perchloric acid (0·4 ml) and N-bromoacetamide (80 mg, 0·6 mmol or 160 mg, 1·2 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 the solvent was evaporated. The residue was chromatographed on three preparative silica gel plates (20 × 20 cm) using a mixture of light petroleum and ether (90 : 10) or a mixture of light petroleum ether and acetone (85 : 10 : 5) as eluent. Zones containing the desired compound were collected, eluted with ether and evaporated. The yields are given in Table I

^{1}H NMR and Mass Spectral Data of the Products of Hypobromous Acid Addition and Reduction with tri-n-Butyltin Hydride

(19*S*)-1α-*Bromo*-19-*bromomethyl*-2β,19-*epoxy*-5α-*cholestane* (XXXIa): ^{1}H NMR spectrum: 0·64 (3 H, s, 18-H), 3·49 (1 H, dd, $J = 11·0$ and 9·9 Hz, 19a-H), 3·76 (1 H, dd, $J = 9·9$ and 1·5 Hz, 19a-H), 4·20 (1 H, dd, $J = 11·0$ and 1·5 Hz, 19-H), 4·32 (1 H, d, $J = 5·5$ Hz, 1β-H), 4·37 (1 H, m, 2α-H). Mass spectrum (in a mixture with *XXXIIa*): *m/z* 556, 558, 560 ($M^{+\cdot}$), 477, 479 $(M-Br)^+$ 463, 465 $(M-CH_2Br)^+$.

(19*R*)-2β,19-*Epoxy*-19-*methyl*-5α-*cholestane* (XXXIb): ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 1·27 (3 H, d, $J = 6·9$ Hz, 19a-H), 4·12 (1 H, q, $J = 6·9$ Hz, 19-H), 4·24 (1 H, m, 2α-H). Mass spectrum (in a mixture with *XXXIIb*): *m/z* 400 ($M^{+\cdot}$), 398 $(M-2H)^{+\cdot}$, 356 $(M-CH_3.CHO)^{+\cdot}$, base peak), 341 $(356-CH_3)^+$, 314 $(356-C_3H_6)^{+\cdot}$, 243 $(356-C_8H_{17})^+$, 201 $(356-C_{11}H_{23})^{+\cdot}$.

(19*R*)-1α-*Bromo*-2β,19-*epoxy*-19-*bromomethyl*-5α-*cholestane* (XXXIIa): ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 3·87 (1 H, m, J = 10·3 and 2·2 Hz, 19a-H), 3·93 (1 H, m, J = 10·6 and 10·3 Hz, 19a-H), 4·37 (2 H, m, 2α-H and 19-H), 4·48 (1 H, d, J = 5·9 Hz, 1β-H).

(19*S*)-2β,19-*Epoxy*-19-*methyl*-5α-*cholestane* (XXXIIb): ^{1}H NMR spectrum: 0·66 (3 H, s, 18-H), 1·46 (3 H, d, J = 7·10 Hz, 19a-H), 4·13 (1 H, q, J = 7·0 Hz, 19-H), 4·21 (1 H, m, 2α-H).

(19*R*)-3α-*Bromo*-19-*bromomethyl*-2β,19-*epoxy*-5α-*cholestane* (XXXVII): ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 3·79 (1 H, A part of the ABX system, J_{AB} = 10·6 Hz, 19a-H), 3·81 (1 H, B part of ABX system, J_{AB} = 10·6 Hz, 19a-H), 4·27 (1 H, m, 3β-H), 4·37 (m, 2α-H, 19-H, overlapped by signals of *XXXVIIIa*.) Mass spectrum (in a mixture with *XXXVIII*): m/z 556, 558, 560 ($M^{+\cdot}$), 477, 479 $(M-Br)^+$, 463, 465 $(M-CH_2Br)^+$.

(19*S*)-2β,19-*Epoxy*-3α-*bromo*-19-*bromomethyl*-5α-*cholestane* (XXXVIII): ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 3·46 (1 H, dd, J = 11·2 Hz and 9·7 Hz, 19a-H), 3·68 (1 H, dd, J = 9·7 and 1·8 Hz, 19a-H), 4·17 (1 H, dd, J = 11·2 and 1·8 Hz, 19-H), 4·32–4·38 (m, 2α-H, and 3β-H overlapped by signals of *XXXVIIa*).

(19*R*)-4β,10β-(*Epoxyethano*)-5,19-*dibromo*-5α-*cholestane* (XLII): ^{1}H NMR spectrum: 3·67 (1 H, dd, J = 10·7 and 1·5 Hz, 19a-*exo*-H), 3·75 (1 H, dd, J = 10·7 and 9·5 Hz, 19a-*endo*-H), 4·13 (1 H, d, J = 29 Hz, 4α-H), 4·53 (1 H, dd, J = 9·4 and 1·5 Hz, 19-H). Mass spectrum: m/z 541, 543, 545 $(M-CH_3)^+$, 477, 479 $(M-Br)^+$, 459, 461 $(M-Br-H_2O)^+$, 397 $(M-Br-HBr)^+$, 379 $(M-Br-HBr-H_2O)^+$.

(19*S*)-6β,19-*Epoxy*-7α-*bromo*-19-*bromomethyl*-5α-*cholestane* (LIIIa): ^{1}H NMR spectrum: 0·71 (3H, s, 18-H), 3·66 (1 H, dd, J = 10·2 and 2·8 Hz, 19a-H), 3·86 (1 H, dd, J = 10·2 and 10·2 Hz, 19a-H), 4·01 (1 H, d, J = 4·5 Hz, 6α-H), 4·27 (1 H, dd, J = 4·5 and 4·5 Hz, 7β-H), 4·62 (1 H, dd, J = 10·1 and 2·8 Hz, 19-H). Mass spectrum (in a mixture with *LIVa*): m/z 541, 543, 545 $(M-CH_3)^+$), 477, 479 $(M-Br)^+$, 463, 465 $(M-CH_2Br)^+$, 445, 447 $(M-CH_2Br-H_2O)^+$, 459, 461 $(M-Br-H_2O)^+$, 397 $(M-Br-HBr)^+$, 379 $(M-Br-HBr-H_2O)^+$, 383 $(M-CH_2Br-HBr)^+$, 365 $(M-CH_2Br-HBr-H_2O)^+$.

(19*R*)-6β,19-*Epoxy*-19-*methyl*-5α-*cholestane* (LIIIb): ^{1}H NMR spectrum: 0·71 (3 H, s, 18-H), 1·36 (3 H, d, J = 6·9 Hz, 19a-H), 3·88 (1 H, m or d, J = 4·5 Hz, 6α-H), 4·36 (1 H, q, J = 6·9 Hz, 19-H). Mass spectrum: m/z 400 $(M)^{+\cdot}$, 356 $(M-CH_3CHO)^{+\cdot}$, 341 $(356-CH_3)^+$, 243 $(356-C_8H_{17})^+$, 217 $(356-C_{10}H_{19})^+$, 201 $(356-C_{11}H_{23})^+$.

(19*R*)-6β,19-*Epoxy*-7α-*bromo*-19-*bromomethyl*-5α-*cholestane* (LIVa): ^{1}H NMR spectrum: 0·73 (3 H, s, 18-H), 2·42 (1 H, dd, J = 11·8 and 5·3 Hz, 5α-H), 3·51 (1 H, dd, J = 10·0 and 3·3 Hz, 19a-H), 3·70 (1 H, dd, J = 9·6 and 9·8 Hz, 19a-H), 4·08 (1 H, dd, J = 9·6 and 3·3 Hz, 19-H), 4·09 (1 H, d, J = 4·4 Hz, 6α-H), 4·23 (1 H, dd, J = 4·4 and 4·4 Hz, 7β-H).

(19*S*)-6β,19-*Epoxy*-19-*methyl*-5α-*cholestane* (LIVb): ^{1}H NMR spectrum: 0·69 (3 H, s, 18-H), 1·32 (3 H, d, J = 6·7 Hz, 19a-H), 3·94 (1 H, m, J = 4·4, 0·8 and 0·8 Hz, 6α-H), 4·03 (1 H, q, J = 6·7 Hz, 19-H).

(19*S*)-6α-*Bromo*-7β,19-*epoxy*-19-*bromomethyl*-B-*homo*-5α-*cholestan*-3β-*ol acetate* (LIX): ^{1}H NMR spectrum: 0·71 (3 H, s, 18-H), 2·05 (3 H, s, CH_3CO_2), 3·53 (1 H, J = 10·9 and 1·5 Hz, 19a-H), 3·59 (1 H, dd, J = 10·1 and 10·9 Hz, 19a-H), 3·94 (1 H, dd, J = 10·9 and 1·5 Hz, 19-H), 4·02 (1 H, dd, $J_{7\alpha,6\beta}$ = 3·7 Hz, $J_{7\alpha,7\beta}$ = 9·5 Hz, $J_{7\alpha,7a\alpha}$ < 0·6 Hz, 7α-H), 4·37 (1 H, dd, $J_{6\beta,7\alpha}$ = = 3·7 Hz, $J_{6\beta,5\alpha}$ = 9·1 Hz, 6β-H), 4·99 (1 H, m, 3α-H). Mass spectrum (in mixture with LX): m/z 628, 630, 632 ($M^{+\cdot}$), 549, 551 $(M-Br)^+$, 535, 537 $(M-CH_2Br)^+$, 505, 507 $(M-CH_2Br-CH_2O)^+$, 489, 491 $(M-Br-CH_3CO_2H)^+$, 475, 477 $(M-CH_2Br-CH_3CO_2H)^+$, 469 $(M-Br-HBr)^+$, 445, 447 $(475-CH_2O)^+$, 409 $(M-Br-HBr-CH_3CO_2H)^+$.

(19*R*)-6α-*Bromo*-7β,19-*epoxy*-19-*bromomethyl*-B-*homo*-5α-*cholestan*-3β-*ol Acetate* (LX): ^{1}H NMR spectrum: 0·73 (3 H, s, 18-H), 2·05 (3 H, s, CH_3CO_2), 3·37 (1 H, dd, J = 10·4 and 10·9 Hz, 19a-H), 3·70 (1 H, dd, J = 10·4 and 3·2 Hz, 19a-H), 4·086 (1 H, dd, $J_{7\alpha,6\beta}$ = 3·5 Hz, $J_{7\alpha,7a\beta}$ = 10 Hz, $J_{7\beta,7a\alpha}$ < 0·6 Hz, 7β-H), 4·092 (1 H, dd, J = 9·5 and 3·2 Hz, 19-H), 4·32 (1 H, dd, $J_{6\beta,7\alpha}$ = 3·5 Hz, $J_{6\beta,5\alpha}$ = 9·2 Hz, 6β-H), 4·91 (1 H, m, 3α-H).

19-Nor-10β-vinyl-5α-cholestane-2β,3α-diol (*LXI*)

The epoxide *XXIII* (800 mg) was dissolved in dioxane (15 ml) and treated with a mixture of 70% perchloric acid (0·5 ml) in water (1 ml) at room temperature for 2 h. The mixture was diluted with ether and water, the ethereal phase was washed with water, a 5% aqueous potassium hydrogen carbonate solution, water, dried with sodium sulfate and the solvent was evaporated. The residue was crystallized from a mixture of acetone and n-heptane to give the diol *LXI* (420 mg), m.p. 142–144°C. ^{1}H NMR spectrum: 0·64 (3 H, s, 18-H), 3·82 (2 H, m, W = 20 Hz, 2α-H and 3β-H), 5·40 (2 H, m, W = 30 Hz, 19a-H), 6·30 (1 H, m, W = 40 Hz, 19-H). IR spectrum: 1 622, 1 630, 3 080, 3 410, 3 580, 3 625 cm^{-1}. For $C_{28}H_{48}O_2$ (416·7) calculated: 80·71% C, 11·61% H; found: 80·50% C, 11·47% H.

Addition of Hypobromous Acid to the Compound *LXI*

The unsaturated compound *LXI* (0·5 mmol) was dissolved in a mixture of dioxane (5 ml) and water (0·5 ml) and treated with 10% perchloric acid (0·4 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 successively 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) as eluent. Zone containing the desired product was eluted with ether and evaporated to yield a mixture of cyclic ethers *LXIV* and *LXV*.

(19*S*)-2β,19-*Epoxy*-19-*bromomethyl*-5α-*cholestan*-3α-*ol* (LXIV): ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 3·80 (2 H, m, AB part of ABX system, 19a-H), 3·99 (1 H, m, 3β-H), 4·24 (1 H, m, 2α-H), 4·32 (1 H, X part of ABX system, J = 7·6 and 5·2 Hz, 19-H). Mass spectrum (in a mixture with *LXV*): m/z 494, 496 $(M)^{+\cdot}$, 415 $(M-Br)^+$, 401 $(M-CH_2Br)^+$.

(19*R*)-2β,19-*Epoxy*-19-*bromomethyl*-5α-*cholestan*-3α-*ol* (LXV): ^{1}H NMR spectrum: 0·69 (3 H, s, 18-H), 3·47 (1 H, dd, J = 11·3 and 9·6 Hz, 19a-H), 3·72 (1 H, dd, J = 9·6 and 1·8 Hz, 19a-H) 4·06 (1 H, m, 3β-H), 4·13 (1 H, dd, J = 11·3 and 1·8 Hz, 19-H), 4·19 (1 H, dd, J = 5·9 and 5·1 Hz, 2α-H).

Acetylation of the Mixture of the Alcohols *LXIV* and *LXV*

The mixture of the alcohols *LXIV* and *LXV* (300 mg) was dissolved in pyridine (2 ml) and treated with acetic anhydride (1 ml) at room temperature for 12 h. The mixture was then decomposed with ice, the product was extracted with ether and the ethereal phase was worked up as usual. The residue was dissolved in a mixture of light petroleum and ether (3 : 1) and filtered through a column of aluminum oxide. The filtrate was evaporated to afford the mixture of acetates *LXVI* and *LXVII* (290 mg).

(19*S*)-2β,19-*Epoxy*-19-*bromomethyl*-5α-*cholestan*-3α-*ol Acetate* (LXVI): ^{1}H NMR spectrum: 0·69 (3 H, s, 18-H), 2·03 (3 H, s, CH_3CO_2), 3·79 (2 H, AB of ABX system 19a-H), 4·28 (1 H, m, 2α-H), 4·33 (1 H, m, 19-H), 4·99 (1 H, m, 3β-H). Mass spectrum (in a mixture with *LXVII*):

m/z 526, 528 ($M^{+\cdot}$), 447 $(M-Br)^+$, 433 $(M-CH_2Br)^+$, 387 $(M-Br-CH_3CO_2H)^+$, 353 $(M-CH_2BrCHOH-CH_3CO_2H)^+$.

(19*R*)-2β,19-*Epoxy*-19-*bromomethyl*-5α-*cholestan*-3α-*ol Acetate* (LXVII): ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 2·04 (3 H, s, CH_3CO_2), 3·45 (1 H, dd, J = 11·0 and 9·6 Hz, 19a-H), 3·71 (1 H, dd, J = 9·7 and 1·6 Hz, 19a-H), 4·14 (1 H, dd, J = 11·0 and 1·6 Hz, 19-H), 4·35 (1 H, m, 2α-H), 4·90 (1 H, m, 3β-H).

Reduction of the Dibromo Derivatives *XXXIa*, *XXXIIa*, *XXXVIIa*, *XXXVIIIa*, *LIIIa*, *LIVa*, *LXIV* and *LXV* with Tri-n-butyltin Hydride

The dibromo derivative (40 mg) in benzene (4 ml) was refluxed with a 1 mol l^{-1} benzene solution of tri-n-butyltin hydride (0·2 ml) and a catalytic amount of 2,2'-bis(azo-2-methylpropionitrile) for 30 min. The solvent was evaporated, the residue was dissolved in light petroleum and filtered through a column of aluminum oxide. The filtrate was evaporated and the residue was chromatographed on one preparative silica gel plate (20 × 20 cm) using a mixture of light petroleum, ether and acetone (90 : 5 : 5) as eluent. The corresponding zone was collected, washed with ether and the eluate evaporated. The spectral data of the product are given in the text.

(19*R*)-2β,19-*Epoxy*-19-*methyl*-5α-*cholestan*-3α-*ol* (LXVIII): ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 1·44 (3 H, d, J = 7·0 Hz, 19a-H), 3·99 (1 H, m, 3β-H), 4·14 (1 H, q, J = 7·0 Hz, 19-H), 4·12 (1 H, m, 2α-H). Mass spectrum (in a mixture with *LXIX*): *m/z* 416 $(M)^{+\cdot}$, 372 $(M-CH_3CHO)^{+\cdot}$, 318 $(372-C_4H_6)^{+\cdot}$.

(19*S*)-2β,19-*Epoxy*-19-*methyl*-5α-*cholestan*-3α-*ol* (LXIX): ^{1}H NMR spectrum: 0·66 (3 H, s, 18-H), 1·29 (3 H, d, J = 6·4 Hz, 19a-H), 3·88 (1 H, m, 3β-H), 4·07 (1 H, q, J = 6·4 Hz, 19-H), 4·09 (1 H, m, 2α-H).

Acetylation of a Mixture of the Alcohols *LXVIII* and *LXIX*

The mixture of the alcohols *LXVIII* and *LXIX* (30 mg) was dissolved in pyridine (1 ml) and treated with acetic anhydride (0·5 ml) at room temperature overnight. The mixture was then decomposed with ice, the product was taken up in ether and the ethereal layer was worked up as usual to give a mixture of the acetates *LXX* and *XLXI*.

(19*R*)-2β,19-*Epoxy*-19-*methyl*-5α-*cholestan*-3α-*ol Acetate* (LXX): ^{1}H NMR spectrum: 0·67 (3 H, s, 18-H), 1·45 (3 H, d, J = 6·9 Hz, 19a-H), 2·04 (3 H, s, CH_3CO_2), 4·16 (1 H, q, J = 6·9 Hz, 19-H), 4·21 (1 H, m, 2α-H), 4·81 (1 H, m, 3β-H). Mass spectrum (in a mixture with *LXXI*): *m/z* 458 $(M)^{+\cdot}$, 398 $(M-CH_3CO_2H)^{+\cdot}$, 354 $(M-CH_3CO_2H-CH_3CHO)^{+\cdot}$, 300 $(M-CH_3CO_2H-CH_3CHO-C_4H_6)^{+\cdot}$.

(19*S*)-2β,19-*Epoxy*-19-*methyl*-5α-*cholestan*-3α-*ol Acetate* (LXXI): ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 1·29 (3 H, d, J = 6·7 Hz, 19a-H), 2·03 (3 H, s, CH_3CO_2), 4·10 (1 H, q, J = 6·7 Hz, 19-H), 4·16 (1 H, m, 2α-H), overlapped by the signal of *LXX*, 4·93 (1 H, m, 3β-H).

The elemental analyses were carried out in the Analytical Laboratory of this Institute (under the direction of Dr J. Horáček). The 60 MHz ^{1}H NMR *spectra were recorded by Mrs J. Jelinková and Mrs M. Snopková. The* IR *spectra were recorded by Mrs K. Matoušková and interpreted by Dr S. Vašíčková.*

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