NEIGHBORING GROUP PARTICIPATION IN ELECTROPHILIC ADDITIONS: THE ROLE OF MARKOVNIKOV AND FÜRST–PLATTNER RULE IN HYPOBROMOUS ACID ADDITION TO 5,6-UNSATURATED CHOLESTANE DERIVATIVES*

Pavel Kočovský

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

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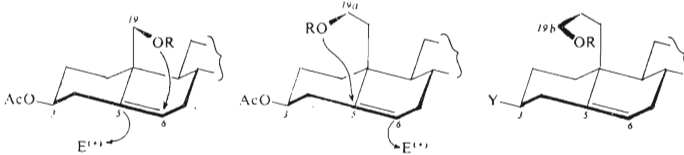
On reaction with hypobromous acid, the unsaturated alcohol *IIIa* yields the diequatorial bromo epoxide *XIX* arising from the 5α,6α-bromonium ion *XVIIIa* on cleavage at $C_{(5)}$ by 19b-hydroxyl group with $6(O)^n$ participation. By contrast, the bromonium ion *XVIIIb* generated from the unsaturated methyl ether *IIIb* is cleaved by water as external nucleophile to yield the unstable diaxial bromohydrin *XX* which undergoes cyclization to the oxirane derivative *XXI*. A comparison with the reaction course in homologs of the type *I* and *II* permits the conclusion that the change in regioselectivity, generally possible outcome of the $5(O)^n$ participation, is only possible for the $6(O)^n$ process if the participating group is a hydroxyl.

In our earlier papers[1–4] we dealt with participation of the neighboring groups (hydroxyl and methoxyl) in the addition of hypobromous acid to double bond in the 5,6-position of the steroid skeleton. The participating group was located either at $C_{(19)}$ (*Ia* and *Ib*) (ref.[1–3]) or at $C_{(19a)}$ (*IIa* and *IIb*) (ref.[4]). In both types of compounds we observed the preference of $5(O)^n$ participation (Scheme 1; for notation *cf.* ref.[5])



Ia, R = H
Ib, R = CH_3
} $5(O)^n$

IIa, R = H
IIb, R = CH_3
} $5(O)^n$

IIIa, R = H, Y = CH_3O
IIIb, R = CH_3, Y = AcO

SCHEME 1

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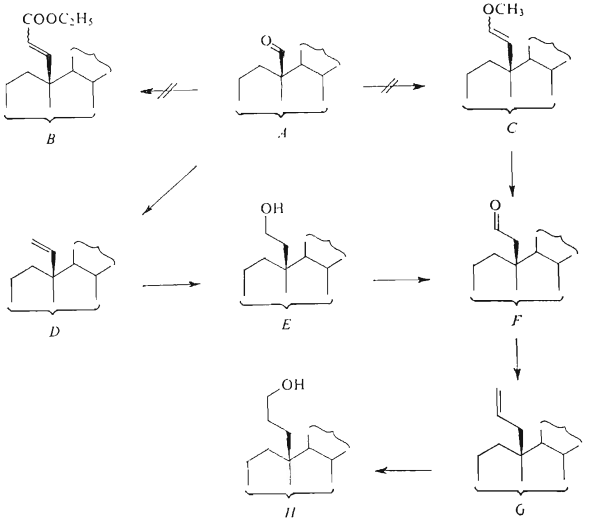
With 19-substituted derivatives *I* this reaction course follows the Fürst–Plattner rule and leads to anti-Markovnikov product; competition of a 4(O)^n participation, which would proceed in accordance with the Markovnikov rule, was not observed. By contrast, the homologous 19a-substituted derivatives *II* strictly follow the Markovnikov rule in a 5(O)^n participation. Competition of a 6(O)^n process would follow the Fürst–Plattner rule to give a diaxial product but it does not proceed at all. Comparison of the both homologs *I* and *II* led us to the conclusion[4] that the 5(O)^n participation is here the preferred process and if it is (in unsymmetrically substituted olefins) assisted by the inductive effect of the substituents (in accordance with Markovnikov rule) it may cause that the electrophilic addition proceeds in conflict with Fürst–Plattner rule to yield a diequatorial product. This is accompanied by a change in the regioselectivity of the addition as compared with the normal reaction course (*i.e.* in compounds without a participating group and in derivatives of the type *I*).

Therefore, it appeared desirable to establish whether or not similar regularities will be valid for 6(O)^n participation. To this end, it was needed to prepare higher homologs bearing a suitable substituent at $C_{(19b)}$, *i.e.* the alcohol *IIIa* and the methyl

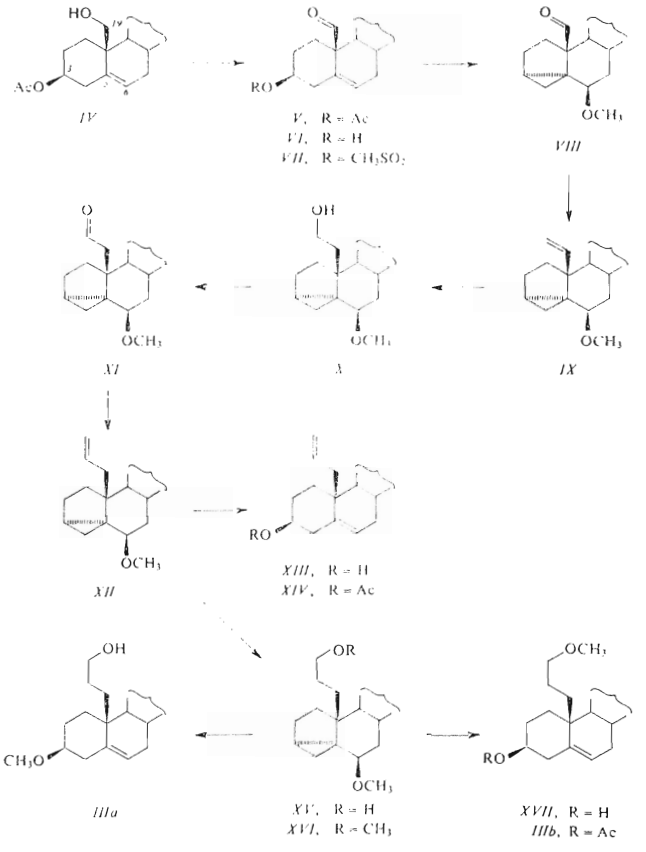


SCHEME 2

ether *IIIb* (Scheme 2). We intended to perform the homologization by application of the Wittig reaction to a readily accessible aldehyde of the type *A* (Scheme 2) while using a suitable reagent with two carbon atoms. Unfortunately, 3β-acetoxycholest-5-en-19-al (type *A*) does not react *e.g.* with triphenylphosphonoacetate ($A \nrightarrow B$). Also failed an attempt at introducing a substituted one-carbon fragment, as demonstrated by attempted reaction with methoxymethyltriphenylphosphonium chloride and sodium salt of dimethyl sulfoxide ($A \nrightarrow C$). In these circumstances, we had to choose a longer and less elegant route. As we have reported earlier[4,5–8], the aldehydes of the type *A* yield 10β-vinyl derivatives ($A \rightarrow D$) on reaction with triphenylphosphonium methylide which is the simplest Wittig reagent of comparatively low steric requirement. The 10β-vinyl group can be hydroborated[6] ($D \rightarrow E$) and the alcohol thus obtained can be oxidized to an aldehyde. Repeating this sequence ($F \rightarrow G \rightarrow H$) was thought to furnish the required derivatives of the type *H*.

This procedure, however, requires protection of both the 3β-oxygen function and the 5,6-double bond. As we have demonstrated earlier, this goal may be suitably achieved by application of i-steroid rearrangement which provides a 3α,5α-cyclo-6β-methoxy derivative[6]. A problem of the synthetic tacticts remained in which step this rearrangement should be performed. In the earlier papers[6] we described two of three possible procedures starting from the derivative *IV*. In the first route, the diacetate of the compound *IV* was hydrolyzed selectively in position 3, subjected to *i*-steroid rearrangement followed by hydrolysis of the 19-acetoxy group, oxidation to the 19-aldehyde and application of the Wittig reaction. The product *IX* could be then hydroborated on the vinylic double bond with retention of the latent 5,6-double bond[6]. In the second procedure, the alcohol *IV* was first oxidized to the aldehyde[6,9] and by application of the Wittig reaction converted into a vinyl derivative which, after hydrolysis of the acetoxy group and mesylation, was rearranged to the corresponding cyclosteroid *IX*. This procedure is by two steps shorter but its disadvantage lies in extreme reluctance to i-steroid rearrangement resulting in lower yield than in the first procedure. For this reason, we chose the third route which, at last, turned out to be the most suitable procedure (Scheme 3): The diol monoacetate *IV* was oxidized with Jones' reagent (chromium trioxide in 8M-H_2SO_4) in acetone to the aldehyde *V*, following alkaline hydrolysis yielded the hydroxy aldehyde *VI* the mesylate of which (*VII*) was easily rearranged by means of buffered methanolysis to yield the cyclosteroid *VIII* in which the aldehyde group remains unaffected. This compound was subjected to a Wittig reaction with the ylide generated from triphenylmethylphosphonium iodide by sodium salt of dimethyl sulfoxide to give in excellent yield the vinyl derivative *IX* (*cf.* ref.[6]) which on hydroboration[6] was converted to the alcohol *X* and oxidized to the aldehyde *XI*. The latter was subjected to the Wittig reaction with triphenylphosphonium methylide to yield the homolog *XII* the structure of which was corroborated by its conversion to the 3β-acetoxy-5,6-unsaturated derivative *XIV* (*via XIII*).

Hydroboration of the vinyl derivative *XII* provided the alcohol *XV* which was converted to the methyl ether *XVI*. The last step involved recovery of the 3β-oxygen function and 5,6-double bond. It was desirable to differentiate the functional groups

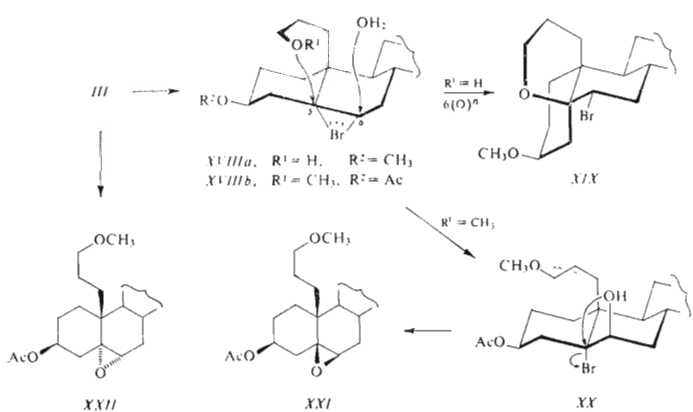


SCHEME 3

in the positions 3 and 19b. To this end, the treatment of the alcohol *XV* with acid was conducted in methanol which procedure led to introduction of a methoxyl group into 3β-position (*XV*→*IIIa*). On the other hand, the methyl ether *XVI* was rearranged in aqueous acidic medium to the 3β-hydroxy derivative *XVII* which on acetylation provided the second model compound *IIIb*.

Hypobromous Acid Addition

The 19b-alcohol *IIIa*, when treated with hypobromous acid (generated in situ from N-bromoacetamide and perchloric acid in aqueous dioxane), gave the diequatorial cyclic bromo ether *XIX* in quantitative yield (Scheme 4). The reaction proceeds *via*



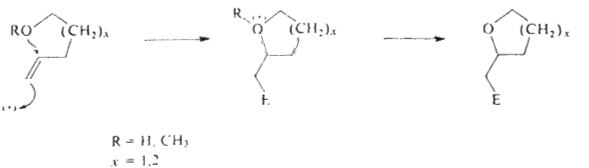
SCHEME 4

the 5α,6α-bromonium ion *XVIIIa* which is cleaved by the 19b-hydroxyl with 6(0)ⁿ participation. The structure of the product follows from the IR, mass and ^{1}H NMR spectra. In the IR-spectrum the band of the hydroxyl group is absent and the molecular ion in the mass spectrum is consistent with the structure *XIX*. The width of the multiplet of 3α-H (J = 15 Hz) demonstrates the *cis* annellation of the rings A and B. The coupling of CHBr proton shows that this grouping is adjacent to a methylene group, *i.e.* demonstrates the presence of a —CH_2—CH—Br grouping and equatorial conformation of the bromine atom. These facts prove the structure *XIX* conclusively.

The methyl ether *IIIb* yields the 5β,6β-epoxide *XXI* when treated with hypobromous acid under the same conditions. Formation of this epoxide is due to cleavage of the 5α,6α-bromonium ion *XVIIIb* at $C_{(6)}$ with water as external nucleophile to give the unstable diaxial bromohydrin *XX* which cyclizes spontaneously (*XX* → → *XXI*). The structure of the epoxide *XXI* is corroborated mainly by the ^{1}H NMR spectrum, namely by the shape and width of the 6-H signal. For comparison, the diastereoisomeric 5α,6α-epoxide *XXII* was prepared by epoxidation of *IIIb* with 3-chloroperoxybenzoic acid. In the ^{1}H NMR spectrum of this epoxide, the multiplet related to 6-H has a different shape. Since in the series of 5α,6α- and 5β,6β-epoxides the corresponding multiplets of 6-H show characteristic differences, the configuration of the epoxides *XXI* and *XXII* should be considered proved.

General Considerations

For 19-substituted derivatives *Ia* and *Ib* and their homologs *IIa* and *IIb*, the 5(O)^n participation is the dominant process in reactions with hypobromous acid and other electrophilic reagents[1–4,10]. However, some difference may be noted in the readiness to participate: Whereas the alcohol *Ia* yields the corresponding cyclic product quantitatively, with the methyl ether *Ib* competing processes occur to some extent[2]. This may be explained by easier conversion of the intermediary oxonium ion (Scheme 5) to the stable cyclic product if R = H. When a five-membered ring is involved (x = 1), *i.e.* in the case of a 5(O)^n participation, the difference in the reactivity between the hydroxyl and methoxyl groups is not great (the pairs *I* and *II*). However, in homo-



SCHEME 5

logs *IIIa* and *IIIb* only 6(O)^n participation (x = 2) is possible for structural reasons and this difference in reactivity is reflected in a dramatic change of the reaction course: While the alcohol *IIIa* cyclizes quantitatively, in the methoxy derivative *IIIb* the participation is completely suppressed in favor of external attack. The entropic factors associated with the introduction of the second methylene group appear to be still counterbalanced in *IIIa* by the high reactivity of the hydroxyl group which is no more valid for the less reactive methoxyl in *IIIb*.

As we have demonstrated earlier [4] $6(O)^n$ participation by hydroxyl and methoxyl groups proceeds readily if it is not in conflict with the Fürst–Plattner rule. The results reported in the present paper show that participation by hydroxyl group can proceed even with violation of the Fürst–Plattner rule when this participation is favored by inductive effect (Markovnikov rule). However, in compounds with the less reactive methoxyl group, the $6(O)^n$ process is suppressed in such a case and external attack is preferred.

The observed facts lead to the conclusion that the $5(O)^n$ participation takes precedence over the $6(O)^n$ process and that the both processes can change the regioselectivity of bromonium ion cleavage (with respect to the normal reaction course).

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*.

3β-Methoxy-19-bishomocholest-5-en-19b-ol (*IIIa*)

The 3α,5-cyclo derivative *XV* (200 mg) was dissolved in a mixture of acetone (10 ml) and methanol (15 ml) and refluxed with *p*-toluensulfonic acid (25 mg) for 1 h. The solution was cooled, diluted with water and the product was extracted with ether. The ethereal solution was washed with water, a 5% aqueous potassium hydrogen carbonate solution, water, dried with sodium sulfate and the solvent was evaporated. The crude material was dissolved in a mixture of benzene and light petroleum (1 : 4) and the solution was filtered through a column of aluminum oxide. The eluate was evaporated to yield the oily product *IIIa* (145 mg), $[\alpha]_D^{20}$ −18° (*c* 2·2). ^{1}H NMR spectrum: 0·70 (3 H, s, 18-H), 3·10 (1 H, m, W = 30 Hz, 3α-H), 3·33 (3 H, s, CH_3O), 3·57 (2 H, m, W = = 15 Hz, 19b-H), 5·53 (1 H, m, W = 12 Hz, 6-H). For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 80·79% C, 11·84% H.

19b-Methoxy-19-bishomocholest-5-en-3β-ol 3-Acetate (*IIIb*)

The alcohol *XVII* (200 mg) was dissolved in pyridine (1·2 ml) and refluxed with acetic anhydride (0·8 ml) for 10 min. The mixture was cooled and decomposed by ice and water, the product 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 give the acetate *IIIb* (115 mg), m.p. 99—100°C,

$[\alpha]_D^{20}$ −43° (*c* 2·1). ^{1}H NMR spectrum: 0·69 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 3·32 (3 H, s, CH_3O), 3·33 (2 H, m, W = 18 Hz, 19b-H), 4·60 (1 H, m, W = 30 Hz, 3α-H) 5·55 (1 H, m, W = 10 Hz, 6-H). For $C_{32}H_{54}O_3$ (486·8) calculated: 78·96% C, 11·18% H; found: 78·74% C, 11·32% H.

3β-Methanesulfonyloxy-cholest-5-en-19-al (*VII*)

The hydroxy aldehyde *VI* (4 g) was dissolved in pyridine (40 ml) and treated with methanesulfonyl chloride (4 ml) at 0°C for 1 h. The mixture was then decomposed with ice and water, the product extracted with ether and the ethereal solution was worked up as usual to afford the crude mesylate *VII* (*c.* 4·1 g), m.p. 78–81°C which was used without purification in further step. ^{1}H NMR spectrum: 0·60 (3 H, s, 18-H), 2·95 (3 H, s, CH_3SO_3), 4·50 (1 H, m, W = 30 Hz, 3α-H), 5·92 (1 H, m, W = 11 Hz, 6-H), 9·63 (1 H, s, 19-H).

6β-Methoxy-3α,5-cyclo-5α-cholestan-19-al (*VIII*)

The crude mesylate *VII* (15 g) was dissolved in a mixture of dioxane (70 ml) and methanol (300 ml) and refluxed with anhydrous sodium acetate (10 g) for 12 h. The volume of the solution was then reduced to about 1/5 by evaporation *in vacuo*, the residue was treated with ether and water, the ethereal layer was washed with water, a 5% aqueous potassium hydrogen carbonate solution, water, dried with sodium sulfate and evaporated. The residue was dissolved in light petroleum and filtered through a column of aluminum oxide. The eluate was evaporated to furnish the oily aldehyde *VIII* (11 g), $[\alpha]_D^{20}$ +63° (*c* 2·0) identical with an authentic sample[6]. ^{1}H NMR spectrum: 0·73 (3 H, s, 18-H), 2·85 (1 H, m, W = 8 Hz, 6α-H), 3·27 (3 H, s, CH_3O), 10·00 (1 H, s, 19-H).

6β-Methoxy-3α,5-cyclo-19-homo-5α-cholestan-19a-al (*XI*)

The alcohol[6] *X* (2 g) was dissolved in dichloromethane (40 ml) potassium acetate (1 g) and sodium sulfate (4 g) were added, and pyridinium chlorochromate (5 g) was added in portions over a period of 2 h while stirring at room temperature. The mixture was filtered through a column of aluminum oxide, the eluate evaporated, the residue dissolved in ether and the ethereal solution was washed 5 times with water, dried with sodium sulfate and evaporated to yield the oily aldehyde *XI* (1·4 g), $[\alpha]_D^{20}$ +6° (*c* 2·2). ^{1}H NMR spectrum: 0·82 (3 H, s, 18-H), 2·90 (1 H, m, W = 10 Hz, 6α-H), 3·43 (3 H, s, CH_3O), 10·08 (1 H, m, W = 10 Hz, 19a-H). For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·12% C, 11·34% H.

6β-Methoxy-19-vinyl-3α,5-cyclo-5α-cholestane (*XII*)

Sodium hydride (150 mg) was dissolved in dimethyl sulfoxide (20 ml) with stirring and heating at 65°C for 2 h. Triphenylmethylphosphonium iodide (3 g) was then added at 10°C and the mixture was stirred at room temperature for 30 min. A solution of the aldehyde *XI* (2 g) in tetrahydrofuran (15 ml) was added, the mixture was stirred at room temperature for 1 h and then at 65°C for 4 h. The mixture was then cooled, diluted with water and the product was extracted with ether. The ethereal layer was washed with water, a 5% aqueous potassium hydrogen sulfate, a 5% aqueous sodium thiosulfate, water, dried with sodium sulfate and evaporated. The residue was dissolved in benzene and treated with light petroleum. The solid was separated by suction, the filtrate was evaporated, the residue dissolved in light petroleum and the solution was filtered through a column of aluminum oxide. The eluate was evaporated to yield the oily olefin *XII* (1·6 g), $[\alpha]_D^{20}$ +34° (*c* 2·7). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 2·68 (1 H, m, W = 9 Hz,

6α-H), 3·30 (3 H, s, CH_3O), 4·80 (1 H, m, $W = 8$ Hz, 19b-H), 5·03 ((1 H, m, $W = 14$ Hz, 19b-H), 6·15 (1 H, m, $W = 45$ Hz, 19a-H). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·81% H; found: 84·29% C, 11·90% H.

19-Vinyl-cholest-5-en-3β-ol 3-Acetate (*XIV*)

The 3α,5-cyclo derivative *XII* (500 mg) was dissolved in a mixture of acetone (50 ml) and water (2 ml) and refluxed with 10% aqueous perchloric acid (3 ml) for 20 min. The solution was concentrated by evaporation *in vacuo*, diluted with water and the product was extracted with ether. The ethereal layer was successively washed with water, a 5% aqueous potassium hydrogen carbonate solution, water, dried with sodium sulfate and evaporated to yield the crude alcohol *XIII* (*c.* 450 mg). The alcohol *XIII* was dissolved in pyridine (10 ml) and heated with acetic anhydride (3 ml) at 100°C for 15 min. The mixture was then cooled, decomposed with ice and water, the product was taken up into ether and the ethereal solution was worked up as usual. The residue was chromatographed on a column of silica gel (30 g) using a mixture of light petroleum and ether (99 : 1) which eluted the impurities and then with a mixture of the same solvents (98 : 2) to elute the desired product. This fraction was evaporated and the residue crystallized from a mixture of methanol, acetone and water to give the acetate *XIV* (180 mg), m.p. 81–82°C, $[\alpha]_D^{20}$ −32° (*c* 1·4). ^{1}H NMR spectrum: 0·64 (3 H, s, 18-H), 2·02 (3 H, s, CH_3CO_2), 4·60 (1 H, m, $W = 30$ Hz, 3α-H), 5·13 (3 H, m, $W = 35$ Hz, —CH=CH_2), 5·60 (1 H, m, $W = 13$ Hz, 6-H). For $C_{31}H_{50}O_2$ (454·7) calculated: 81·88% C, 11·08% H; found: 81·69% C, 11·15% H.

6β-Methoxy-3α,5-cyclo-19-bishomo-5α-cholestan-19b-ol (*XV*)

Boron trifluoride etherate (1·63 ml) in ether (3 ml) was added dropwise to a stirred mixture of the olefin *XII* (1·6 g) dissolved in tetrahydrofuran (20 ml) and sodium borohydride (400 mg) at 0°C in the period of 30 min under argon and the mixture was stirred for an additional 2 h. The excess of reagent was decomposed with water, the mixture was stirred with a solution of potassium hydroxide (1 g) in water (10 ml) and 30% hydrogen peroxide (5 ml) at 0°C for 1·5 h. and then refluxed for 1 h while stirring. The volume of the mixture was reduced to about 1/4 by evaporation *in vacuo*, the residue was treated with water and ether, the ethereal layer was washed with water, a 5% aqueous sodium thiosulfate, water, dried with sodium sulfate and evaporated. The residue was chromatographed on a column of silica gel (70 g) impregnated with ammonia using a mixture of light petroleum, ether and acetone (88 : 10 : 2). The fraction containing the desired compound was evaporated to afford the oily alcohol *XV* (1·1 g), $[\alpha]_D^{20}$ +36° (*c* 2·1). ^{1}H NMR spectrum: 0·70 (3 H, s, 18-H), 2·68 (1 H, m, $W = 9$ Hz, 6α-H), 3·30 (3 H, s, CH_3O), 3·60 (2 H, m, $W = 30$ Hz, 19b-H). For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 80·84% C, Y11·82% H.

6β,19b-Dimethoxy-3α,5-cyclo-19-bishomo-5α-cholestane (*XVI*)

A solution of the alcohol *XV* (250 mg) in tetrahydrofuran (15 ml) was refluxed with sodium hydride (100 mg) while stirring under argon for 30 min. Methyl iodide (1 ml) was then added and the mixture was refluxed while stirring for 1 h. The mixture was then cooled, the excess of sodium hydride was decomposed with water, 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 evaporated. The residue was dissolved in a mixture of benzene and light petroleum (1 : 9) and filtered through a column of aluminum oxide. The filtrate containing partially purified product was evaporated and the residue was chromatographed on a column of silica gel (20 g) impregnated with ammonia

using a mixture of light petroleum and benzene (95 : 5) which eluted lipophilic impurities. Elution with a mixture of light petroleum, benzene and ether (93 : 5 : 2) furnished the fraction containing the pure desired product. This fraction was evaporated to give the oily ether *XVI* (160 mg), $[\alpha]_D^{20}$ +42° (*c* 2·2). ^{1}H NMR spectrum: 0·72 (3 H, s, 18-H), 2·65 (1 H, m, W = 9 Hz, 6α-H), 3·32 (3 H, s, CH_3O), 3·40 (2 H, m, W = 30 Hz, 19b-H). For $C_{31}H_{54}O_2$ (458·8) calculated: 81·16% C, 11·86% H; found: 81·03% C, 11·95% H.

19b-Methoxy-19-bishomo-cholest-5-en-3β-ol (*XVII*)

The 3α,5-cyclo derivative *XVI* (120 mg) was dissolved in a mixture of acetone (10 ml) and water (0·5 ml) and refluxed with 10% aqueous perchloric acid (1 ml) for 10 min (checked by TLC). The mixture was then concentrated by evaporation *in vacuo*, the residue was diluted with water, the product was extracted with ether, the ethereal phase was washed with water, a 5% aqueous potassium hydrogen carbonate, water, dried with sodium sulfate and evaporated. The residue was dissolved in a mixture of benzene and light petroleum (1 : 2) and filtered through a column of aluminum oxide. The filtrate was evaporated to afford the oily alcohol *XVII* (85 mg), $[\alpha]_D^{20}$ −41° (2·1). ^{1}H NMR spectrum: 0·69 (3 H, s, 19-H), 3·30 (3 H, s, CH_3O), 3·42 (3 H, m, W = = 30 Hz, 3α-H and 19b-H), 5·50 (1 H, m, W = 12 Hz, 6-H). For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 80·86% C, 11·92% H.

Addition of Hypobromous Acid to Compounds *IIIa* and *IIIb*

The unsaturated compound (0·5 mmol) was dissolved in dioxane (5 ml) and water (0·5 ml) and treated with 10% aqueous perchloric acid (0·4 ml) and N-bromoacetamide (80 mg, 0·6 mmol) for 30 min at room temperature. The mixture was then diluted with ether and water, the ethereal phase was washed successively with water, a 5% aqueous potassium hydrogen carbonate solution, a 5% sodium thiosulpfate solution, water, dried with sodium sulfate and 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 were collected, eluted with ether and evaporated. The yields are given in the text.

3β-Methoxy-5,10β-(epoxypropano)-6α-bromo-19-nor-5β-cholestane (*XIX*)

$[\alpha]_D^{20}$ +4° (*c* 2·0). ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 3·40 (3 H, s, CH_3O), 3·54 (1 H, m, W = 15 Hz, 3α-H), 3·75 (2 H, m, W = 50 Hz, 19b-H), 5·17 (1 H, dd, J = 4 and 12 Hz, 6β-H). For $C_{30}H_{51}BrO_2$ (523·6) calculated: 68·81% C, 9·82% H, 15·26% Br; found: 68·64% C, 9·90% H, 15·37% Br.

5,6β-Epoxy-19b-methoxy-19-bishomo-5β-cholestan-3β-ol 3-Acetate (*XXI*)

$[\alpha]_D^{20}$ −1° (*c* 2·0). ^{1}H NMR spectrum: 0·63 (3 H, s, 19-H), 2·02 (3 H, s, CH_3CO_2), 2·90 (1 H, m, W = 7 Hz, 6α-H), 3·33 (2 H, m, W = 15 Hz, 19b-H), 3·35 (3 H, s, CH_3O), 5·10 (1 H, m, W = 30 Hz, 3α-H). For $C_{32}H_{54}O_4$ (502·8) calculated: 76·45% C, 10·83% H; found: 76·28% C, 11·04% H.

5,6α-Epoxy-19b-methoxy-19-bishomo-5α-cholestan-3β-ol 3-Acetate (*XXII*)

The olefin *IIIb* (50 mg) was dissolved in chloroform (3 ml) and treated with 3-chloroperoxybenzoic acid (35 mg) at room temperature for 3 h. The mixture was then 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 evaporated. The residue was dissolved in a mixture of benzene and light petroleum (1:5) and filtered through a column of aluminum oxide. The eluate was evaporated to afford the oily epoxide *XXII* (28 mg), $[\alpha]_D^{20}$ −37° (*c* 2·0). ^{1}H NMR spectrum: 0·62 (3 H, s, 18-H), 1·99 (3 H, s, CH_3CO_2), 2·49 (1 H, d, J = 2·5 Hz, 6β-H), 3·33 (2 H, m, W = 15 Hz, 19b-H), 3·35 (3 H, s, CH_3O), 4·95 (1 H, m, W = 30 Hz, 3α-H). For $C_{32}H_{54}O_4$ (502·8) calculated: 76·45% C, 10·83% H; found: 76·21% C, 10·97% H.

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

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