TRANSANNULAR PARTICIPATION OF THE HYDROXYL GROUP IN THE ADDITION OF HYPOBROMOUS ACID TO SOME 5-HYDROXY-5α-CHOLEST-2-ENES

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Addition of hypobromous acid to 5-hydroxy-5α-cholest-2-enes *Ia—Id* gives three types of products *i.e.* bromohydrins *IVa—IVd* as products of normal reaction course, and epoxides *IIa—IId* as well as *IIIa—IIId* formed by participation of 5α-hydroxy group. The mechanism of this reaction is discussed.

As a part of a program aimed at the preparation of Westphalen-type steroids, a route to 2β,5-dihydroxy-5α-cholestanes with or without an oxygen function at position 6 was sought. To this end, we investigated the addition of hypobromous acid to 2,3-unsaturated 5-hydroxy-5α-cholest-2-enes *Ia—Id* the preparation of which was reported in one of our previous papers[1].

In our experiments, hypobromous acid was generated *in situ* from N-bromoacetamide and aqueous perchloric acid in dioxane solution; its addition to the double bond in *Ia—Id* afforded a complex mixture of *IIa—IId*, *IIIa—IIId* and *IVa—IVd*. All products were separable chromatographically except for *IIc* and *IIIc*, but the separation of the latter compounds could be achieved after their conversion into free alcohols *IIe* and *IIIe* by treatment with lithium aluminum hydride (Table I).

Whereas type *IV* corresponds to normal addition, formation of the cyclic ethers *II* and *III* is due to participation of the 5α-hydroxyl. These results show close similarity to those observed with unsaturated compounds *Ia—Id* under conditions of Woodward hydroxylation.[2] As could be anticipated, this similarity is not confined to analogy in the structure of the products but is also expressed in the dependence of the ratio of both reaction types on substitution at $C_{(6)}$. In the instance of 6-unsubstituted 2-cholestene *Ia*, the ratio of the cyclized products to the normal ones is 1 : 1, in the presence of a 6-benzoyloxy grouping as in *Ic* and *Id* the normal addition products prevail slightly (3 : 2) whereas in the 6-oxo derivative *Ib* participation of the 5α-hydroxyl is considerably suppressed and the ratio becomes 4 : 1 in favor of the normal addition. And again, as before[2], a normal reaction course

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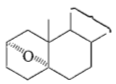
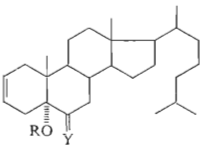
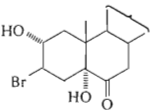
could easily be ensured by acetylation of the 5α-hydroxyl in the starting compound. Thus addition of hypobromous acid to the 5α-acetoxy derivative *Ie* resulted in the exclusive formation of the bromohydrin *IVe*. The latter compound was acetylated to give the diacetate *IVf* identical with the acetylation product of *IVb*.



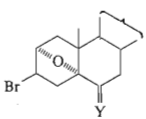
VI



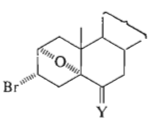
Ia, R = H, Y = H_2
Ib, R = H, Y = O
Ic, R = H, Y = 
Id, R = H, Y = 
Ie, R = Ac, Y = O



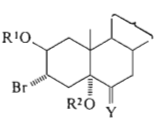
V



IIa, Y = H_2
IIb, Y = O
IIc, Y = 
IId, Y = 
IIe, Y = 



IIIa, Y = H_2
IIIb, Y = O
IIIc, Y = 
IIId, Y = 
IIIe, Y = 



IVa, R^1 = H, R^2 = H, Y = H_2
IVb, R^1 = H, R^2 = H, Y = O
IVc, R^1 = H, R^2 = H, Y = 
IVd, R^1 = H, R^2 = H, Y = 
IVe, R^1 = H, R^2 = Ac, Y = O
IVf, R^1 = Ac, R^2 = Ac, Y = O
IVg, R^1 = H, R^2 = H, Y = 

The ether *IIIa* is identical with a known compound prepared in a different manner[3]. The structure of the remaining ethers of the type *III* follows from comparing their ^{1}H-NMR spectra with those of *IIIa*. As shown in Table II, the spectra of *IIIb*–*IIId* show similarity in relevant spectroscopic features due to A-ring protons at $C_{(2)}$

TABLE I

Yield of Products of Hypobromous Acid Addition

Starting compound	Products, %				Ratio (*II* + *III*) : : (*IV* + *V*)	Total yield %
	II	*III*	*IV*	*V*		
Ia	16	32	48	—	50 : 50	96
Ib	2	20	66	10	22 : 78	98
Ic	13[a]	27[a]	56	—	42 : 58	96
Id	14	23	56	—	40 : 60	93

[a] Isolated as free alcohols *IIe* and *IIIe*.

TABLE II

^{1}H-NMR Data of 2α,5α-Epoxides

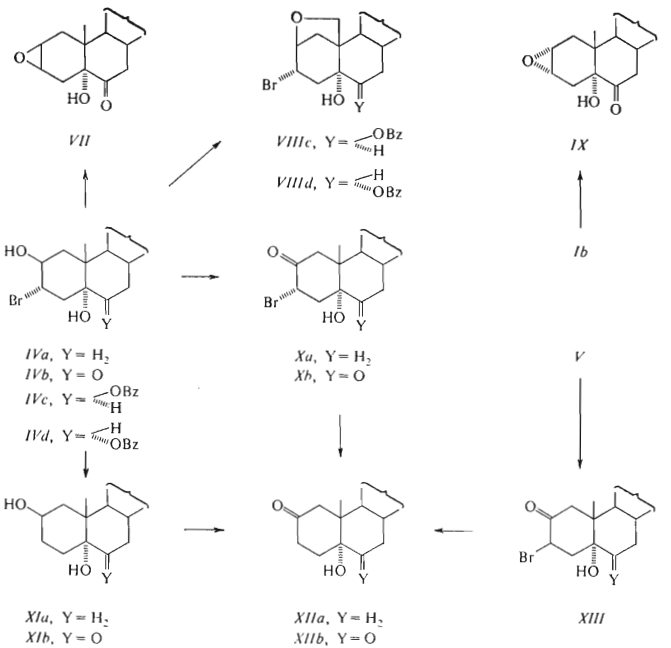
Compound	18-H	19-H	2β-H ($J_{2\beta,1\alpha}$)	3-H ($J_{3\beta,4\beta}$, $J_{3\beta,4\alpha}$)
IIa	0·68	1·04	4·36 m	4·15 m
IIb	0·67	1·04	4·63 m	4·10 m
IIc	0·69	1·33	4·45 m	4·20 m
IId	0·70	1·14	4·50 m	4·15 m
IIe	0·71	1·20	4·40 m	4·16 m
IIIa	0·68	0·91	4·45 d (6·0)	4·00 dd (7·0, 3·0)
IIIb	0·66	0·92	4·70 d (5·8)	4·00 dd (6·6, 3·6)
IIIc	0·68	1·20	4·54 d (7·2)	4·01 d (7·8, 3·4)
IIId	0·68	1·00	4·59 d (7·0)	4·05 dd (7·0, 3·0)
IIIe	0·70	1·06	4·50 d (6·2)	4·05 dd (7·6, 3·4)

and $C_{(3)}$. The shape of the signals in all compounds *IIIa–IIId* is very similar to the shape of the signals of analogous ethers bearing an 3α-acetoxy group.

Structure proof of the cyclic ethers of the type *II* is based on the fact that hydrogenation of the bromo compound *IIa* afforded the epoxide *VI* which is identical with the epoxide[3] also prepared in the same manner from the bromo compound *IIIa*. By implication, the bromo atom in *IIa* must have the 3β-configuration. Additional evidence for this conclusion is provided by the ^{1}H-NMR spectrum: The shapes of the multiplets due to $C_{(2)}$ and $C_{(3)}$-protons in all compounds of the type *II* are virtually identical with analogous multiplets in the spectra of the 3β-acetoxy and 3β-hydroxy compounds described in our preceding paper[2]. The assigned 3β-configuration is further supported by shifts of 19-H signals in 3-epimeric bromo derivatives as compared with 3-epimeric acetoxy (or hydroxy) derivatives: The difference in shifts of protons $(19\text{-H})_{II} - (19\text{-H})_{III}$ remain in the same range (0·12 to 0·14 ppm) as in analogous epimeric acetoxy and hydroxy derivatives (0·10 to 0·14 ppm).

The products of simple addition *IVa–IVd* may be expected to have the structure of a 2β-hydroxy-3α-bromo (or possibly 2β-bromo-3α-hydroxy) derivatives. ^{1}H-NMR spectra show that the substituents at $C_{(2)}$ and $C_{(3)}$ in *IVa–IVd* are axial. The structure of the bromohydrin *IVa* follows from the conversion of this compound to the known[3] 2,5-diol *XIa* by reductive removal of the bromine atom. In the case of the bromohydrin *IVb*, treatment with alkali affords a β-epoxide *VII* which result (coupled with the ^{1}H-NMR evidence[4]) proves the structure *IVb*. The validity of this structure proof may be extended to all compounds of the type *IV*. Corroboration of this conclusion was achieved by the formation of transannular epoxides *VIIIc* and *VIIId* from *IVc* and *IVd* on treatment with lead tetraacetate. For the 6-oxo derivative *IVb*, the lead tetraacetate procedure was not feasible since its application led to fragmentation but even here the possibility of an alternative structure with a hydroxyl at $C_{(3)}$ was excluded in the following manner: Oxidation of the bromohydrin *IVb* followed by reductive removal of bromine atom from *Xb* afforded a diketone *XIIb* not identical with known[5,6] 5-hydroxy-5α-cholestan-3,6-dione.

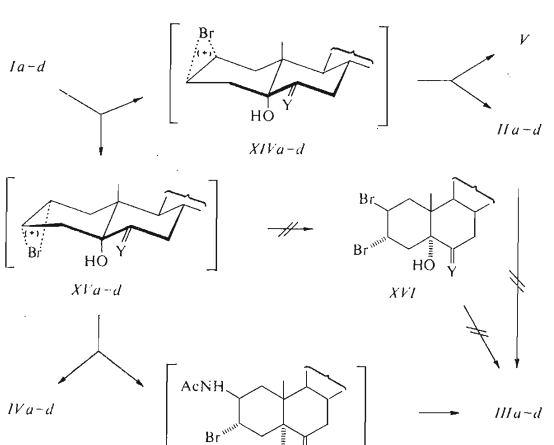
In addition to the three products, the addition of hypobromous acid to the 6-oxo derivative *Ib* yields a small amount of another bromohydrin in which the ^{1}H-NMR spectrum reveals both 2 and 3 substituents to be axial. This finding suggested a 2β-bromo-3α-hydroxy structure and was further supported by the result of alkali treatment giving rise to the α-epoxide *IX*. However, oxidation of the bromohydrin gave a bromo ketone which on hydrogenation on palladized calcium carbonate afforded the ketone *XIIb* already obtained from *Xb*. Thus, the original assumption of 2β-bromo-3α-hydroxy structure was shown to be incorrect; all these facts are only compatible with the 2α-hydroxy-3β-bromo structure *V* for the bromohydrin in which the ring A occupies a boat conformation stabilized by a hydrogen bridge between the 2α- and 5α-hydroxyls. If the hydroxyl groups are esterified by trichloroacetyl isocyanate treatment, the A-ring assumes the chair conformation (Table III).



Similarly as in the Woodward hydroxylation of the unsaturated steroids *Ia*–*Id*, both 2α,3α- and 2β,3β-halonium ions *XIV* and *XV* are involved in the reactions. Formation of the 2β,3β-bromonium ions *XIVa*–*XIVd* is assumed[2] in the reactions yielding 2α,5α-epoxides of the type *II*. The bromohydrin *V* could be isolated only in low yield and only when an oxo group was present at position 6, *i.e.* under conditions unfavorable for participation of the 5α-hydroxyl. In the remaining cases *Ia*, *Ic*, *Id* no 2α-hydroxy-3β-bromo steroid could be found. The intermediacy of 2α,3α--bromonium ions *XVa*–*XVd* in the formation of *IVa*–*IVd* needs no commentary but somewhat puzzling is the mode of formation of substances belonging to type *III*. Several possibilities were considered to explain this result: One of them was the primary addition of bromine to *I* giving rise to a 2β,3α-dibromo derivative of the type *XVI* and subsequent displacement of the 2β-bromo substituent by the 5α-hydroxyl. However, we disproved this assumption experimentally since the dibromo

derivative[3] *XVIa* remains unchanged under the reaction conditions (perchloric acid in aqueous dioxane solution). Another possibility was equilibration of the axial 3β-bromo derivative to yield the equatorial 3α-epimer. However, treatment of *IIe* in aqueous dioxane with perchloric acid and sodium bromide (both in the presence and absence of N-bromoacetamide) did not change the starting compound.

We believe that a plausible rationalization may be intermediary formation of the N-bromoacetamide adduct *XVII* in which the CH_3CONH group is then displaced by the 5α-hydroxyl. Evidence for the addition of N-bromo acylamides to the double bond was reported[7,8] and some adducts were isolated[9,10].



EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 50°C/0·2 Torr. Optical measurements were carried out in chloroform with an error of ±1°. The infrared spectra were recorded on a Zeiss UR 20 spectrometer in tetrachloromethane unless stated otherwise. The ^{1}H-NMR spectra were recorded on a Varian HA-100 instrument in deuteriochloroform with tetramethylsilane as internal reference at 30°C. Chemical shifts are given in ppm. Apparent coupling constants were obtained from the first order analysis. The mass spectra were recorded on an AEI MS 907 mass spectrometer. The CD spectra were recorded on a Dichrograph II (Jouan-Roussel) in methanol. The identity of samples prepared by different routes was checked by mixture melting point determination, by thin-layer chromatography (TLC) and by in-

frared and ^{1}H-NMR spectra. Usual work up of an etheral solution means washing the solution with 5% aqueous hydrochloric acid, water, 5% aqueous potassium hydrogen carbonate solution, water, drying with sodium sulfate and evaporation of the solvent *in vacuo*.

Addition of Hypobromous Acid to Olefins *Ia—Id*

The unsaturated compound (1 mmol) was dissolved in dioxane (20 ml) and water (4 ml), treated with 10% perchloric acid (1 ml) and N-bromoacetamide (165 mg; 1·2 mmol) and set aside for 1 h at room temperature. The mixture was then diluted with water and the product extracted with ether. The ethereal solution was washed with water, aqueous sodium thiosulfate solution, a potassium hydrogen carbonate solution, water, dried and evaporated. The residue was chromatographed on seven silica gel preparative plates (20 × 20 cm) using double development with a mixture of benzene and ether (97 : 3) as eluent. The lipophilic components were *IIa—IId* and *IIIa—IIId*. The polar components were bromohydrins *IVa—IVd*. In the case of the hydroxy ketone *Ib* two more polar compounds *Vb* and *VII* were isolated. The yields of the products are given in Table I. Analytical and physical data of the isolated compounds are recorded in Table IV.

2α,5-Epoxy-3β-bromo-5α-cholestan-6-one (*IIb*)

The alcohol *IIe* (50 mg) was dissolved in dichloromethane (5 ml) and oxidized with Corey's oxidant[11] (100 mg) at room temperature overnight. The mixture was filtered through a column of aluminum oxide, the solvent was evaporated and the residue was crystallized from a mixture

TABLE III

^{1}H-NMR Data of Bromohydrins and their Derivatives

Compound	18-H	19-H	2-H (*W*)	3-H (*W*)
IVa	0·67	1·06	4·40 m (22)	4·40 m
		1·20[a]	5·44 m (13)[a]	4·38 m (11)[a]
IVb	0·66	0·97	4·40 m (18)	4·40 m
		1·05[a]	5·43 m (12)[a]	4·45 m (12)[a]
IVc	0·68	1·39	4·40 m (26)	4·40 m
		1·53[a]	5·45 m (10)[a]	4·43 m (13)[a]
IVd	0·68	1·16	4·40 m (28)	4·40 m
		1·19[a]	5·55 m (14)[a]	4·42 m (16)[a]
IVe	0·65	1·00	4·34 m (18)	4·34 m
IVf	0·69	0·95	5·30 m (11)	4·31 m (13)
V	0·66	0·91	4·40 m (20)	4·40 m
		0·91[a]	5·50 m (30)[a]	4·45 m (25)[a]

[a] The values obtained after treatment with trichloroacetyl isocyanate.

of acetone, methanol and water to yield the ketone *IIb* (26 mg), m.p. 93–95°C, $[\alpha]_D^{20}$ −13° (*c* 1·4). For $C_{27}H_{43}BrO_2$ (479·6) calculated: 67·63% C, 9·04% H, 16·66% Br; found: 67·72% C, 9·12% H, 16·30% Br.

2α,5-Epoxy-3β-bromo-5α-cholestan-6β-ol (*IIe*)

The mixture of the benzoates *IIc* and *IIIc* (195 mg) in ether (10 ml) was refluxed with lithium aluminum hydride (50 mg) for 15 min. The mixture was decomposed with saturated aqueous sodium sulfate solution, the product extracted with ether and the ethereal solution worked up as usual. The residue was chromatographed on two preparative silica gel plates (20 × 20 cm)

TABLE IV

Analytical and Physical Data of Products of Hypobromous Acid Treatment of Compounds *Ia–Id*

Compound	Formula (m.w.)	Calculated/Found			M.p., °C $[\alpha]_D^{20}$
		% C	% H	% Br	
IIa	$C_{27}H_{45}BrO$	69·67	9·74	17·16	80–82
	(465·6)	69·73	9·91	17·28	
IIb	$C_{27}H_{43}BrO_2$	67·63	9·04	16·66	92–94
	(479·6)	67·52	9·03	16·45	−12°
IId	$C_{34}H_{49}BrO_3$	69·73	8·43	13·64	oil
	(585·7)	69·82	8·35	13·55	+60°
IIIa	$C_{27}H_{45}BrO$	69·67	9·74	17·16	121–122[a]
	(465·6)	69·72	9·66	17·21	+23°
IIIb	$C_{27}H_{43}BrO_2$	67·63	9·04	16·66	181–182
	(479·6)	67·59	9·11	16·38	−20°
IIId	$C_{34}H_{49}BrO_3$	69·73	8·43	13·64	176–177
	(585·7)	69·71	8·39	13·51	−45°
IVa	$C_{27}H_{47}BrO_2$	67·06	9·80	16·52	133–135
	(483·6)	67·15	9·91	16·58	+71°
IVb	$C_{27}H_{45}BrO_3$	65·17	9·12	16·06	190–191
	(497·6)	65·24	9·18	15·93	−10°
IVc	$C_{34}H_{51}BrO_4$	67·65	8·52	13·24	165–170
	(603·7)	67·56	8·63	13·07	−2°
IVd	$C_{34}H_{51}BrO_4$	67·65	8·52	13·24	oil
	(603·7)	67·71	8·49	13·32	+67°
V	$C_{27}H_{45}BrO_3$	65·17	9·12	16·06	oil
	(497·6)	65·13	9·11	16·01	+18°

[a] In accordance with the literature[3].

with a mixture of benzene and ether (90 : 10). The zones with polar component were collected and eluted to yield the noncrystalline alcohol *IIe* (34 mg), $[\alpha]_D^{20}$ +8° (*c* 1·4). IR spectrum: 3500, 3633 cm^{-1}. For $C_{27}H_{45}BrO_2$ (481·6) calculated: 67·34% C, 9·42% H, 16·59% Br; found: 67·25% C, 9·31% H, 16·45% Br.

2α,5-Epoxy-3α-bromo-5α-cholestan-6-one (*IIIb*)

The alcohol *IIIe* (27 mg) was dissolved in dichloromethane (5 ml) and oxidized with Corey's oxidant[11] (50 mg) at room temperature overnight, worked up as given for *IIb*, and the residue was crystallized from a mixture of acetone, methanol and water to yield the ketone *IIIb* (18 mg), m.p. 182—183°C. IR spectrum: 1720 cm^{-1}. For $C_{27}H_{43}BrO_2$ (479·6) calculated: 67·63% C, 9·04% H, 16·66% Br; found: 67·62% C, 9·15% H, 16·78% Br.

2α,5-Epoxy-3α-bromo-5α-cholestan-6β-ol (*IIIe*)

Elution of the zones containing a lipophilic fraction obtained from the chromatography, after isolation of the 3β-compound (*IIe*) and evaporation of the eluents gave the 3α-compound *IIIe* (68 mg), m.p. 232—234°C (ether), $[\alpha]_D^{20}$ +6° (*c* 1·4). IR spectrum (chloroform): 3625 cm^{-1}. Found: 67·21% C, 9·35% H, 16·71% Br.

2α,5-Diacetoxy-3α-bromo-5α-cholestan-6-one (*IVf*)

a) *From* 2β,5-*dihydroxy*-3α-*bromo*-5α-*cholestan*-6-*one* (IVb): The dihydroxy compound *IVb* (150 mg) was dissolved in acetic acid (5 ml) and acetylated with acetic anhydride (1 ml) in the presence of *p*-toluenesulfonic acid (50 mg) at room temperature for 2 h. The mixture, was decomposed with ice, the product extracted with chloroform, the organic layer washed with 5% aqueous potassium hydrogen carbonate, water, dried and the solvent evaporated to yield the noncrystalline diacetate *IVf* (152 mg), $[\alpha]_D^{20}$ +30° (*c* 1·5). For $C_{31}H_{49}BrO_5$ (581·7) calculated: 64·02% C, 8·49% H, 13·73% Br; found: 64·18% C, 8·53% H, 13·81% Br.

b) *From* 2β-*hydroxy*-3α-*bromo*-5-*acetoxy*-5α-*cholestan*-6-*one* (IVe): Alcohol *IVe* (50 mg) was acetylated with acetic anhydride (0·2 ml) in pyridine (1 ml) at room temperature overnight. The mixture was decomposed with ice, the product taken up in ether and the ethereal solution worked up as usual to yield the diacetate *IVf* (43 mg).

3α-Bromo-5α-cholestan-2β,5,6β-triol (*IVg*)

a) *From* 2β,5-*dihydroxy*-3α-*bromo*-5α-*cholestan*-6-*one* (IVb): The ketone *IVb* (80 mg) was dissolved in dimethylformamide (2 ml) and reduced with sodium borohydride (50 mg) at room temperature for 2 h. The mixture was decomposed with 5% aqueous hydrochloric acid, the product taken up in ether and the ethereal solution worked up as usual. The residue was crystallized from a mixture of n-heptane and ethyl acetate to afford the triol *IVg* (59 mg), m.p. 182—184°C, $[\alpha]_D^{20}$ +8° (*c* 1·6). For $C_{27}H_{47}BrO_3$ (499·6) calculated: 64·91% C, 9·47% H, 16·00% Br; found: 65·03% C, 9·52% H, 15·88% Br.

b) *From* 3α-*bromo*-5α-*cholestan*-2β,5,6β-*triol* 6-*monobenzoate* (IVc): The benzoate *IVc* (70 mg) in ether (10 ml) was refluxed with lithium aluminum hydride (50 mg) for 30 min, the mixture was decomposed with saturated aqueous sodium sulfate solution, the product extracted with ether, and the ethereal solution worked up as usual. The residue was crystallized from a mixture of n-heptane and ethyl acetate to yield the triol *IVg* (32 mg).

2α,5-Epoxy-5α-cholestane (*VI*)

The mixture of compounds *IIa* and *IIIa* (40 mg) was dissolved in a mixture of methanol (4 ml) and ethyl acetate (2 ml), 5% $Pd/CaCO_3$ catalyst (60 mg) was added and the mixture was agitated in a hydrogen atmosphere for 30 h. It was then diluted with ether, the catalyst was filtered off and the filtrate was evaporated under reduced pressure. The residue was dissolved in ether and the ethereal solution was worked up as usual. The residue was crystallized from aqueous ethanol to yield, as a single product, the epoxide *VIa*, m.p. 103–104°C, $[\alpha]_D^{20}$ +26° (*c* 2·0) in accordance with the literature[3].

2β,3β-Epoxy-5-hydroxy-5α-cholestan-6-one (*VII*)

A solution of bromohydrin *IVb* (40 mg) and potassium hydroxide (100 mg) in methanol (5 ml) was refluxed for 2 h. Methanol was distilled off under reduced pressure, the residue treated with ether and water, the organic layer washed with water, dried and evaporated. The residue was crystallized from n-heptane to afford the epoxide *VII* (23 mg), m.p. 161–162°C, $[\alpha]_D^{20}$ −34° (*c* 2·1). IR spectrum: 1714, 3485, 3603 cm^{-1}, ^{1}H-NMR spectrum: 0·64 (3 H, s, 18-H), 0·81 (3 H, s, 19-H). For $C_{27}H_{44}O_3$ (416·6) calculated: 77·84% C, 10·64% H; found: 77·92% C, 10·68% H.

2β,19-Epoxy-3α-bromo-5α-cholestan-5,6β-diol 6-Monobenzoate (*VIIIc*)

The alcohol *IVc* (100 mg) was dissolved in benzene (6 ml) and about 1 ml of the solvent was removed by distillation. The solution was treated with lead tetraacetate (200 mg) and refluxed while stirring for 4 h, and diluted with ether; the ethereal solution was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and the solvent evaporated. The residue was chromatographed on one preparative silica gel plate using a mixture of benzene and ether (95 : 5) as eluent. Corresponding zones were collected, eluted, the solvent was evaporated and the residue was crystallized from a mixture of acetone, methanol and water to yield the epoxide (*VIIIc*) (38 mg), m.p. 168–170°C, $[\alpha]_D^{20}$ −47° (*c* 1·6). IR spectrum (chloroform): 1275, 1716, 3590 cm^{-1}. ^{1}H-NMR spectrum: 0·66 (3 H, s, 18-H), 3·59 and 4·57 (2 H, 2 d, J = 9 Hz, 19-H). For $C_{34}H_{49}BrO_4$ (601·7) calculated: 67·87% C, 8·21% H, 13·28% Br; found: 67·93% C, 8·19% H, 13·34% Br.

2β,19-Epoxy-3α-bromo-5α-cholestan-5,6α-diol 6-Monobenzoate (*VIIId*)

The alcohol *IVd* (60 mg) was dissolved in benzene (6 ml), and about 1 ml of the solvent was removed by distillation. The solution was treated with lead tetraacetate (200 mg) and refluxed while stirring for 4 h. The mixture was worked up as given for *VIIIc*. The residue was chromatographed on one silica gel plate (20 × 20 cm) using a mixture of benzene and ether (95 : 5) as eluent. Corresponding zones were collected and eluted to yield the noncrystalline epoxide *VIIId* (43 mg), $[\alpha]_D^{20}$ +11° (*c* 2·8) ^{1}H-NMR spectrum: 0·65 (3 H, s, 18-H), 3·91 (2 H, s, 19-H). For $C_{34}H_{49}BrO_4$ (601·7) calculated: 67·87% C, 8·21% H, 13·28% Br; found: 67·90% C, 8·33% H, 13·09% Br.

2α,3α-Epoxy-5-hydroxy-5α-cholestan-6-one (*IX*)

a) *From 5-hydroxy-5α-cholest-2-en-6-one* (1b): The olefin *Ib* (100 mg) in chloroform (5 ml) was treated with *m*-chloroperbenzoic acid (100 mg) and allowed to stand at room temperature overnight. The mixture was diluted with ether and the ethereal solution was washed with 5%

aqueous potassium hydrogen carbonate, water, dried and evaporated. The residue was crystallized from aqueous methanol to yield the epoxide *IX* (38 mg), m.p. 154—156°C, $[\alpha]_D^{20}$ +5° (*c* 1·5). IR spectrum: 1723, 3480 cm^{-1}. ^{1}H-NMR spectrum: 0·63 (3 H, s, 18-H), 0·73 (3 H, s, 19-H). For $C_{27}H_{44}O_3$ (416·6) calculated: 77·84% C, 10·64% H; found: 77·80% C, 10·59% H.

b) *From* 3β-*bromo*-2α,5-*dihydroxy*-5α-*cholestan*-6-*one* (V): A solution of bromohydrin *V* (45 mg) and potassium hydroxide (100 mg) in methanol (4 ml) was refluxed for 2 h. The mixture was worked up as given for *VII*, and the residue was crystallized from aqueous methanol to give the epoxide *IX* (14 mg), m.p. 154—156°C, identical with the product decsribed under *a*).

3α-Bromo-5-hydroxy-5α-cholestan-2-one (*Xa*)

The bromohydrin *IVa* (17 mg) in acetone (2 ml) was treated with excess Jones' reagent at room temperature for 10 min. The excess reagent was destroyed with methanol, ether was added and the mixture was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and evaporated. The residue was crystallized from a mixture of acetone, methanol and water to yield the bromo ketone *Xa* (11 mg), m.p. 171—175°C, $[\alpha]_D^{20}$ +125° (*c* 1·3). IR spectrum: 1720, 3598 cm^{-1}. ^{1}H-NMR spectrum: 0·66 (3 H, s, 18-H), 0·91 (3 H, s, 19-H), 4·34 (1 H, m, 3β-H). For $C_{27}H_{45}BrO_2$ (481·6) calculated: 67·34% C, 9·42% H, 16·59% Br; found: 67·22% C, 9·47% H, 16·38% Br.

3α-Bromo-5-hydroxy-5α-cholestan-2,6-dione (*Xb*)

The bromohydrin *IVb* (100 mg) dissolved in acetone (3 ml) was treated with excess Jones' reagent at room temperature for 5 min. The mixture was worked up as given for *Xa*, and the residue was crystallized from a mixture of acetone, methanol and water to yield the bromo ketone *Xb* (58 mg), m.p. 214—215°C, $[\alpha]_D^{20}$ +116° (*c* 1·8). IR spectrum (chloroform): 1716, 3587 cm^{-1}. ^{1}H-NMR spectrum: 0·66 (3 H, s, 18-H), 0·72 (3 H, s, 19-H), 4·39 (1 H, broad d, J = 5·6 Hz, 3β-H). For $C_{27}H_{43}BrO_3$ (495·6) calculated: 65·44% C, 8·76% H, 16·12% Br; found: 65·31% C, 8·76% H, 16·20% Br.

5α-Cholestane-2β,5-diol (*XIa*)

The bromohydrin *IVa* (35 mg) was dissolved in methanol (5 ml), 5% $Pd/CaCO_3$ catalyst (50 mg) was added and the mixture was agitated in a hydrogen atmosphere for 9 h. It was then worked up as given for *VI*, and the residue was crystallized from a mixture of acetone, methanol and water to yield the diol *XIa*, (17 mg), m.p. 173—175°C, $[\alpha]_D^{20}$ +23° (*c* 2·0) in accordance with the lit.[3]. ^{1}H-NMR spectrum: 0·66 (3 H, s, 18-H), 1·20 (3 H, s, 19-H).

2β,5-Dihydroxy-5α-cholestan-6-one (*XIb*)

The bromohydrin *IVb* (20 mg) was dissolved in methanol (5 ml), 5% $Pd/CaCO_3$ catalyst (25 mg) was added and the mixture was agitated in hydrogen atmosphere for 4 h. It was worked up as given for *VI* and the residue was crystallized from aqueous methanol to yield the alcohol *XIb* (6 mg), m.p. 203—206°C. IR spectrum (chloroform): 1711, 3450, 3595 cm^{-1}. For $C_{27}H_{46}O_3$ (418·7) calculated: 77·46% C, 11·07% H; found: 77·49% C, 11·03% H.

5-Hydroxy-5α-cholestan-2-one (*XIIa*)

The alcohol *XIa* (14 mg) was dissolved in acetone (2 ml) and treated with excess Jones' reagent at room temperature for 5 min. The mixture was worked up as given for *Xa*, and the residue was crystallized from aqueous ethanol to yield the ketone *XIIa* (11 mg), m.p. 186–187°C in accordance with the literature[7].

5-Hydroxy-5α-cholestane-2,6-dione (*XIIb*)

a) *From* 3α-*bromo*-5-*hydroxy*-5α-*cholestan*-2,6-*dione* (Xb): The bromo ketone *Xb* (21 mg) was dissolved in a mixture of methanol (2 ml) and ethyl acetate (3 ml), 5% $Pd/CaCO_3$ catalyst (70 mg) was added and the mixture was agitated in a hydrogen atmosphere for 2 h. It was then worked up as given for *VI*, and the residue was crystallized from a mixture of acetone, methanol and water to yield the dione *XIIb* (13 mg), m.p. 202–204°C, $[\alpha]_D^{20}$ −36° (*c* 1·5). IR spectrum (chloroform): 1711, 3535, 3596 cm^{-1}. ^{1}H-NMR spectrum: 0·66 (3 H, s, 18-H), 0·74 (3 H, s, 19-H). For $C_{27}H_{44}O_3$ (416·6) calculated: 77·84% C, 10·64% H, found: 77·91% C, 10·65% H.

b) *From* 3β-*bromo*-5-*hydroxy*-5α-*cholestan*-2,6-*dione* (XIII): The bromo ketone *XIII* (100 mg) was dissolved in a mixture of methanol (5 ml) and ethyl acetate (3 ml), 5% $Pd/CaCO_3$ catalyst (150 mg) was added and the mixture was agitated in a hydrogen atmosphere for 4 h. It was then worked up as given for *VI*, and the residue was crystallized from a mixture of acetone, methanol and water to yield the dione *XIIb* (33 mg), m.p. 201–203°C, identical with the product described under *a*).

3β-Bromo-5-hydroxy-5α-cholestane-2,6-dione (*XIII*)

The bromohydrin *V* (200 mg) was dissolved in acetone (5 ml) and treated with excess Jones' reagent at room temperature for 5 min. The mixture was worked up as given for *Xa*, and the residue was crystallized from a mixture of acetone, methanol and water to yield the bromo ketone *XIII* (120 mg), m.p. 185–186°C, $[\alpha]_D^{20}$ −27° (*c* 1·3). IR spectrum (chloroform): 1717, 3591, 3635 cm^{-1}. ^{1}H-NMR spectrum: 0·66 (3 H, s, 18-H), 0·76 (3 H, s, 19-H), 4·92 (1 H, dd, $J_{3\alpha,4\xi} = 8$ Hz, $J_{3\alpha,4\xi} = 11$ Hz). For $C_{27}H_{43}BrO_3$ (495·6) calculated: 65·44% C, 8·76% H, 16·13% Br; found: 65·38% C, 8·82% H, 16·35% Br.

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