STRUCTURAL REQUIREMENTS IN WESTPHALEN REARRANGEMENT*

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The relative importance of steric and electronic influence in Westphalen rearrangement was investigated on compounds 1) with or without an electron-withdrawing substituent at $C_{(6)}$ incapable of steric interaction with angular 10β-methyl group (*i.e.* keto group or α-benzoyloxy group), 2) with or without an axial 2β-substituent (steric compression by 1,3-*syn*-diaxial interaction with 10β-methyl). The presence of an electron-withdrawing group at $C_{(4)}$ or $C_{(6)}$ is essential but its configuration is not important provided the 10β-methyl is in steric compression with a 2β-substituent or another suitably located group. Some other aspects of the reaction are discussed.

In the Westphalen rearrangement of 5α-hydroxy steroids two factors are of importance. First, the presence of an electron-withdrawing substituent at $C_{(4)}$ or $C_{(6)}$ (*i.e.* adjacent to the reaction center at $C_{(5)}$; electronic effect). Secondly, β-configuration of a substituent present at $C_{(4)}$ or $C_{(6)}$ (steric effect). All hitherto available data show that the reaction takes a different course if these conditions are not fulfilled[1].

The following relevant results from literature illustrate this point: Whereas 3β,6β-diacetoxy-5α-cholestan-5-ol undergoes readily the rearrangement being the substance on which the reaction was observed for the first time[2,3], its 6α-epimer reacts in a different manner[4]. However, introduction of a 4β-methyl group into the molecule of the latter makes the rearrangement possible[5,6]. Introduction of 4β-methyl into 6β-acetoxy-5α-cholestan-5-ol increases the rearrangement rate by about two orders whereas introduction of a 4α-methyl group does not markedly influence the reaction rate[6]. These facts show the importance of the steric factor. They may be confronted with other facts demonstrating the role of electronic effect: 3β-Acetoxy-6β-methyl-5α-cholestan-5-ol, with its bulky but non-polar 6β-substituent, does not undergo Westphalen rearrangement[7]. On the other hand, the presence of a strongly electron-withdrawing 6β-fluorine atom makes the rearrangement possible despite the small size of the fluorine atom[3]. This last example is evidence for the essential

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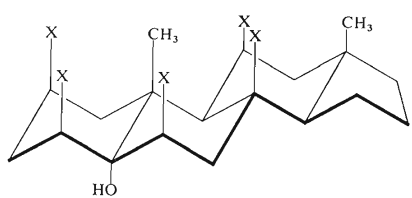
importance of the electronic factor; it indicates that if the electron-withdrawing power of the 6-substituent is strong, it may be *per se* a sufficient condition for the Westphalen rearrangement. On the other hand, there is no case known where suitable steric orientation of the appropriate substituents could substitute their electron--withdrawing capability.

In spite of this knowledge there remains some uncertainty about the necessity of the steric factor and it is not yet clear to what extent the steric and electronic effects may be separated; doubtlessly, additional information is desirable.

Generally, in all cases as yet investigated, the study of the steric factor has been limited to evaluating of the influence of 4β- or 6β-substituents that are in 1,3-*syn*-diaxial interaction with the angular methyl group at $C_{(10)}$. It is probable that the function of the steric factor is a steric acceleration of the rearrangement. It may be anticipated that the steric compression of the angular methyl group, exerted by a 4β- or 6β-substituent, could be successfully replaced by such an effect of a substituent located at another position (2β, 8β or 11β) enabling a 1,3-*syn*-diaxial interaction with the 10β-methyl group (A). This should also make β-orientation of the negative substituent at $C_{(4)}$ or $C_{(6)}$ unnecessary.



A

In order to verify this assumption we subjected to standard Westphalen dehydration several model compounds: 1) Containing an axial 2β-substituent and, at the same time, an electron-withdrawing substituent at $C_{(6)}$ incapable of steric interaction with angular 10β-methyl (*I*, *XVIa*); 2) Containing the same electron-withdrawing substituent but bearing no substituent at $C_{(2)}$ (*VIIIb*, *XXII*); 3) Bearing an axial 2β-substituent and unsubstituted at position 6 (*XXVI*, *XXXIIIb*, *XXXIIIc*).

Preparation of compounds *I*, *XVIa*, *XXII* and *XXVI* was reported from this laboratory in an earlier paper[8]. The substance *VIIIb* was prepared from cholesteryl acetate (*VII*) by osmium tetroxide hydroxylation followed by benzoylation. In the preparation of compounds *XXXIIIa*–*XXXIIIc*, we set out from the unsaturated alcohol[9] *XXVIII*, which on epoxidation with *m*-chloroperoxybenzoic acid furnished a mixture of two epimeric epoxides *XXIX* and *XXX* in 1 : 2 proportion. Reductive cleavage of the α-epoxide *XXX* with lithium aluminum hydride afforded the diol

XXXI which was oxidized to the hydroxy ketone *XXXII*. Reduction of the latter compound gave a mixture of 2α- and 2β-epimers *XXXI* and *XXXIIIa* in 2 : 3 relation; the required acyl derivatives were obtained in the conventional manner.

The compounds *I*, *VIIIb*, *XVIa*, *XXII*, *XXVI*, *XXXIIIb* and *XXXIIIc* were treated with potassium hydrogen sulfate in acetic anhydride under standard conditions. The results are summarized in Table I.

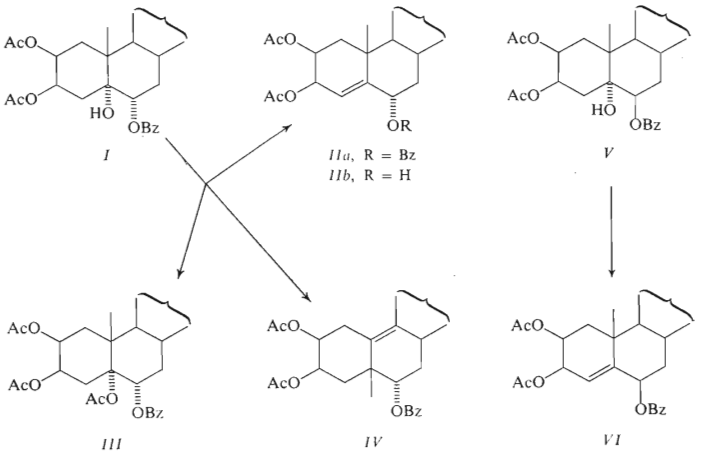


TABLE I

Yields of Dehydration Products of 5-Hydroxy-5α-cholestanes with $KHSO_4$ and Acetanhydride

Starting compound	Products, %				Total yield, %
	5β-CH_3-9-ene	5-acetate	4-ene	other	
I	87	5	3	—	95
VIIIb	—	38	32	19 (*XIa*)	89
XVIa	29	65	2	—	96
XXII	10	76	2	—	88
XXXIIIb	—	—	39	56 (*XXXVa*)	95
XXXIIIc	—	—	44	39 (*XXXVa*)	89

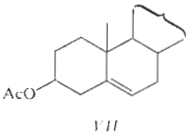
The substance *I* gives products of simple elimination (*IIa*), acetylation[8] (*III*) and Westphalen rearrangement (*IV*). An attempt was made to confirm the structure *IIa* by dehydration of the 5α-hydroxy derivative *I* with thionyl chloride, but this experiment led to a complex mixture of products. Therefore, the unsaturated substance *IIa* was synthesized from the ketone *XIXa* by sodium borohydride reduction followed by benzoylation of the reduction product *IIb*. For purposes of comparison, the 6-epimeric benzoate *VI* was prepared by dehydration of the derivative[8] *V* with thionyl chloride. The ^{1}H-NMR spectrum of compound *IV* has the typical features of the spectra of analogous Westphalen-type substances. It confirms this structure particularly by the characteristic 5β-methyl signal and absence of olefinic proton signals (Table II).

Potassium hydrogen sulfate dehydration of another model substance, *VIIIb*, furnished, along with the 5α-acetate *IX*, also two dehydration products, *Xa* and *XIa*. Formation of the olefin *Xa* is due to simple dehydration, as was corroborated by an independent synthesis from the ketone *XXIIIa via* the alcohol *Xb*. The dehydration process leaves the configuration of the 6α-benzoyloxy group unaffected; the epimeric 6β-benzoyloxy derivative *XV* was obtained by dehydration of the 5α-alcohol[10] *XIV* with thionyl chloride. Formation of the second dehydration product *XIa* was accompanied by epimerization of the 3-acetoxy group. This fact was proved in the following manner. Saponification of the product *XIa* led to the diol *XIb* which was oxidized to the known[11] dione *XIII* that can be also prepared *a*) from the compound *Xa via* the diol *Xc* by oxidation of the latter *b*) from the hydroxydione *XII* by dehydration and *c*) from the alcohol *XXIIIb* by oxidation. These conversions

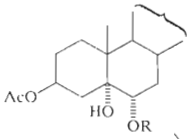
TABLE II

^{1}H-NMR Data of Prepared Westphalen-Type Steroids

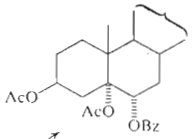
Compound	18-H	5β-CH_3	2α-H	3α-H	6-H	$J_{6,7}$, Hz
IV	0·72	1·27	5·60 m	5·60 m	5·20 dd	(8·0 and 4·0)
XVIIIa	0·82	1·27	4·63 m	5·32 m	4·96 dd	(10·5 and 5·0)
XVIIIb	0·82	1·18	4·78 m	5·20 m	3·51 dd	(11 and 4)
XXIa	0·79	1·39	4·60 m	5·37 m	—	—
XXIb	0·78	1·43	3·55 m	4·07 m	—	—
XXIc	0·77	1·40	5·30 m	5·82 m	—	—
XXVa	0·74	1·36	—	5·10 m	—	—
XXXIXa	0·81	1·18	4·75 m	—	4·75 m	—
XXXIXb	0·82	1·14	4·80 m	—	3·56 dd	(10·6 and 4·2)
XL	0·78	1·32	4·80 m	—	—	—
XLI	0·79	1·07	3·40 m	—	—	—



VII

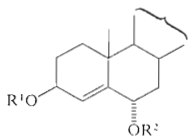


VIIIa, R = H
VIIIb, R = Bz

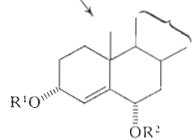


IX

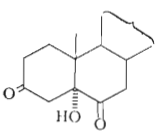
XXIIIa ⟶



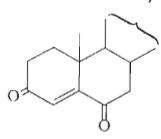
Xa, R¹ = Ac, R² = Bz
Xb, R¹ = Ac, R² = H
Xc, R¹ = H, R² = H



XIa, R¹ = Ac, R² = Bz
XIb, R¹ = H, R² = H

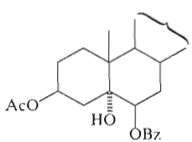


XII

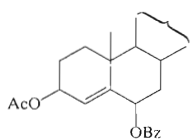


XIII

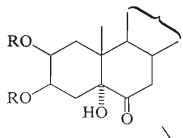
XXIIIb ⟵



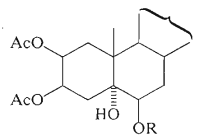
XIV



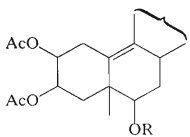
XV



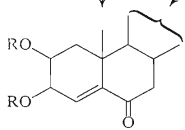
XVIa, R = Ac
XVIb, R = Bz



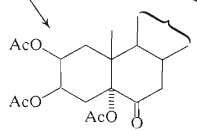
XVIIa, R = H
XVIIb, R = NO_2



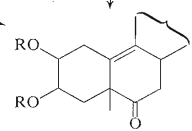
XVIIIa, R = NO_2
XVIIIb, R = H



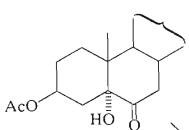
XIXa, R = Ac
XIXb, R = Bz



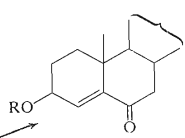
XX



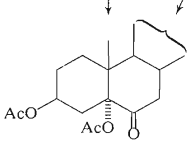
XXIa, R = Ac
XXIb, R = H
XXIc, R = Bz



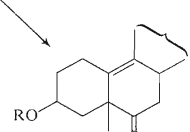
XXII



XXIIIa, R = Ac
XXIIIb, R = H



XXIV



XXVa, R = Ac
XXVb, R = Bz
XXVc, R = H

demonstrate both the positions of the substituents and the presence of the normal steroid skeleton. The retention of the α-configuration of the benzoyloxy group is demonstrated by the presence in ^{1}H-NMR spectrum of a broad multiplet associated with the 6β-proton. Epimerization of the 3β-acetoxy group under "Westphalen conditions" was observed in an analogous case[3].

The next substance, *XVIa*, gave a normal dehydration product *XIXa*, the 5α-acetate[8] *XX* and the product of Westphalen rearrangement *XXIa*. The substance *XIXa* was alternatively prepared from the alcohol *XVIa* with thionyl chloride. The product of rearrangement *XXIa* was prepared by alternative synthesis: Reduction of the hydroxy ketone *XVIa* with sodium borohydride gave the diol *XVIIa* in which the 6β-hydroxyl group was protected by conversion into a nitrate group. In one of our previous papers[10] we demonstrated the suitability of this protective group under Westphalen conditions. The nitrate *XVIIb* was smoothly rearranged to *XVIIIa* in which the hydroxyl group was recovered with zinc in acetic acid to give the alcohol *XVIIIb* that was oxidized to a ketone identical with *XXIa*.

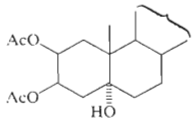
A further model compound, *XXII*, likewise furnished products of the following three types: Products of simple elimination[12] *XXIIIa*, of acetylation[13] *XXIV* and of Westphalen rearrangement *XXVa*. The structure of the rearranged product was proved by independent synthesis from the benzoate[10] *XXVb* by way of the hydroxy derivative *XXVc*.

Treatment of the compound *XXVI* with potassium hydrogen sulfate in acetic anhydride led exclusively to normal dehydration with formation of the 5,6-unsaturated steroid[9] *XXVIIa*.

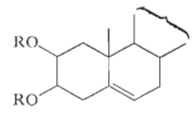
The same treatment of the last model compounds, *XXXIIIb* and *XXXIIIc*, afforded mixtures of 4,5- and 5,6-unsaturated steroids *XXXIVb* with *XXXVb* and *XXXIVc* with *XXXVc*. Since the corresponding pairs of 4,5- and 5,6-unsaturated acyl derivatives could not be separated by the usual chromatographic methods, they were converted into separable alcohols *XXXIVa* and *XXXVa* which were described in an earlier paper[9].

Since the Westphalen steroid *XLI* was not accessible in this manner, we prepared this compound for purposes of comparison in a different manner. We set out from the bromohydrin[14] *XXXVIa*. After protection of the 2β-hydroxyl by benzoylation, the 6-keto group was reduced with sodium borohydride to furnish stereospecifically the 6β-hydroxy derivative *XXXVII*. Hydrogenolytic removal of the bromine atom followed by Westphalen rearrangement gave the diester *XXXIXa*. Treatment of this diester with ethanolic hydrogen chloride gave the alcohol *XXXIXb* which was oxidized to the 6-keto derivative *XL* to give the required alcohol *XLI* after Huang–Minlon reduction.

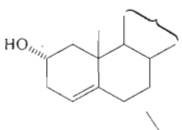
Further, conformation of the A-ring in 4,5-unsaturated compounds *IIa*, *IIb*, *VI*, *Xa–Xc*, *XIa*, *XIb*, *XV*, *XIXa*, *XIXb*, *XXIIIa*, *XXIIIb* and *XXXIVa* should be briefly commented on here. Several studies on 4,5-unsaturated steroids disclosed



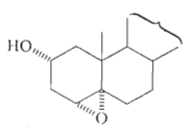
XXVI



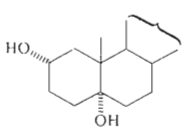
XXVIIa, R = Ac
XXVIIb, R = H
XXVIIc, R = Bz



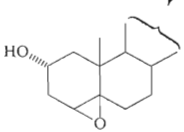
XXVIII



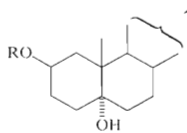
XXX



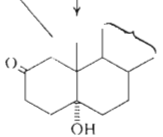
XXXI



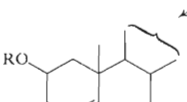
XXIX



XXXIIIa, R = H
XXXIIIb, R = Ac
XXXIIIc, R = $(CH_3)_3CCO$



XXXII



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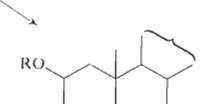
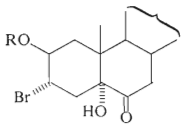
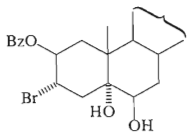
XXXIVb, R = Ac
XXXIVc, R = $(CH_3)_3CCO$



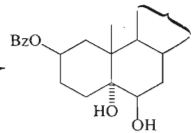
XXXVa, R = H
XXXVb, R = Ac
XXXVc, R = $(CH_3)_3CCO$



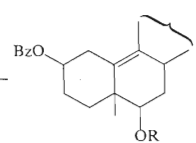
XXXVIa, R = H
XXXVIb, R = Bz



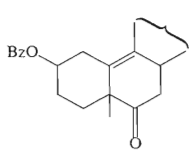
XXXVII



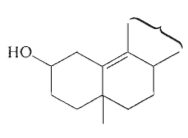
XXXVIII



XXXIXa, R = Ac
XXXIXb, R = H

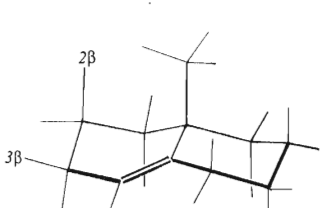


XL

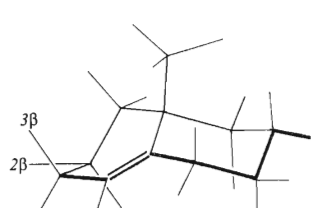


XLI

that conformation of 4,5-unsaturated steroids depends on substitution of the A-ring[15–19]. Generally, the A-ring assumes either "normal" (*B*) or "inverted" (*C*) half-chair form. In the case of 4,5-unsaturated steroids bearing no substituent at the



B



C

position 2, the A-ring adopts the normal (*B*) conformation. Accordingly, in the 3β-substituted derivatives of this type (*Xa–Xc*, *XV*, *XXIIIa* and *XXIIIb*) the 3β-substituent assumes the pseudoequatorial conformation. This conclusion can be made from the half-width of the $C_{(4)}$-H multiplet in the ^{1}H-NMR spectrum. In the normal (*B*) conformation of the A-ring, dihedral angle of 3α-H with $C_{(4)}$-proton is 78°

and is associated with a small coupling constant (≤ 2 Hz). Due to the homoallylic coupling, $W_{1/2}$ was found to be 3·2–5·2 Hz. If the A-ring assumed the inverted half-chair conformation (*C*) with an 4-H and 3α-H dihedral angle of 42°, the value of $J_{4,3}$ should be considerably larger.

The same conformation (*B*) must be attributed to 3α-substituted derivatives *XIa* and *XIb* in which the 3α-substituent is pseudo-axial. The dihedral angle between 4-H and 3β-H (42°) is expected to be associated with $J_{4,3} = 6$ Hz (homoallylic coupling leads to broadening of the signal, $W_{1/2}$ being 9 Hz).

In the ^{1}H-NMR spectra of 2β,3β-disubstituted derivatives *IIa*, *IIb*, *VI*, *XIXa* and *XIXb* the half-width of the 4-H multiplet could not be reliably estimated due to overlapping with 2α-H and 3α-H signals. However, a negative Cotton effect of the dibenzoate *XIXb* demonstrates a levorotatory helical arrangement[20] compatible only with conformation (*C*). By adopting this conformation, the compounds *IIa*, *IIb*, *VI*, *XIXa* and *XIXb* can avoid 1,3-*syn*-diaxial interaction of the 2β-substituent with the angular methyl. The same behavior was observed earlier[19] in 2β--substituted-4,5-unsaturated steroids lacking substitution at position 3 (*XXXIVa*).

The results of the experiments on model compounds will be briefly commented on at this point. Let us first consider the group of models which are 2β-substituted steroids lacking an electron-withdrawing substituent adjacent to 5α-hydroxyl. In these compounds the steric factor (1,3-*syn*-diaxial interaction of a 2β-substituent with the angular 10β-methyl group) is present whereas no electronic influence is operative in the immediate neighborhood of the incipient $C_{(5)}$-carbonium ion. In contrast with previous experiments where the steric compression was due to a 4β- or 6β-substituent, the present model compounds leave the space around the $C_{(5)}$ reaction center free for the migrating methyl group. It can be assumed that this circumstance may favorably influence the Westphalen rearrangement in such compounds. However, our experiments demonstrated that not even in such models could the steric influence counterbalance the lack of the electronic one. Of the corresponding compounds neither the models bearing a 2β-acetoxy group (*XXVI*, *XXXIIIb*) nor the substance containing a bulkier pivaloyl group (*XXXIIIc*) undergo the Westphalen rearrangement.

Each of the remaining model compounds contains an electron-withdrawing substituent at $C_{(6)}$ not interfering sterically with the 10β-methyl (6α-benzoyloxy or 6-oxo derivatives). They constitute pairs of identical structural types (*I*, *VIIIb*, *XVIa*, *XXII*) with or without a 2β-axial substituent (acetoxy group). The 6-keto derivative *XXII*, which lacks the 2β-substituent, afforded the corresponding Westphalen-type product in 10% yield. This result is of interest, since up to now it was generally believed that the 6-keto derivatives do not undergo the Westphalen rearrangement unless steric compression of the angular methyl is operative at the same time[1]. The case is also exceptional in that here the presence of the steric factor is not a necessary condition for the rearrangement[23]. To our knowledge, the only such known case

may be the above mentioned rearrangement of 6β-fluoro-5α-cholestan-3β,5-diol 3-acetate[3]. However, the importance of the steric factor is obvious from the fact that introduction of a 2β-acetoxy group into the molecule of the ketone *XXII* (compound *XVIa*) enhances the yield of the Westphalen-type product from 10% to 29%. This effect is particularly pronounced in the 6α-benzoyloxy derivative *VIIIb* where no Westphalen rearrangement occurs but introduction of a 2β-acetoxy group into its molecule (*I*) gives the corresponding Westphalen product (*IV*) in 87% yield.

In addition, our experiments further confirm the view that if the combination of electronic and steric effects is necessary for Westphalen rearrangement, both effects need not be localized in the same substituent[5,6]. They also demonstrate that the group exhibiting the steric influence need not be localized in position 4β or 6β but may also be present in 2β-position. Our findings do not support the view of Kirk and Hartshorn[1] that the direction of the dipole induced by the 6-substituent plays an important role in Westphalen rearrangement.

From the above and earlier results it may be concluded that for Westphalen rearrangement the combination of steric and electronic effects is normally required. The steric effect may be defined as steric compression of the 10β-methyl group by a suitably oriented grouping (1,3-*syn*-diaxial interaction) at position 2, 4 or 6. The electronic effect may be defined as electron-withdrawing capability (−I effect) of a substituent adjacent to 5α-hydroxyl (4 or 6 position). Presence of the electronic effect is essential; the steric effect is less important. If the electron-withdrawing power of the 4- or 6-substituent is strong, it may be *per se* a sufficient condition for the Westphalen rearrangement. In cases where the substituent at $C_{(4)}$ or $C_{(6)}$ has a medium electron-withdrawing capability, the steric factor becomes important as a necessary supplement of the electronic factor. If the electron-withdrawing substituent at $C_{(4)}$ or $C_{(6)}$ is lacking the rearrangement cannot be enforced even by a strong steric effect.

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 ±3°. The infrared spectra were recorded on a Zeiss UR 20 spectrometer in tetrachloromethane unless otherwise stated. The ^{1}H-NMR spectra were recorded on a Varian HA-100 instrument (100 MHz), or Tesla B 467 (60 MHz) in deuteriochloroform at 30°C with tetramethylsilane as internal reference. Chemical shifts are given in δ scale in ppm. Apparent coupling constants were obtained from the first order analysis. The mass spectra were recorded on a AEI MS 907 mass spectrometer. The CD spectra were recorded on a Dichrographe 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 infrared and ^{1}H-NMR spectra. Usual work up of an ethereal 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*.

Dehydration of 5α-Hydroxy Derivatives *I*, *VIIIb*, *XVIa*, and *XXII* with a Mixture of Acetic Anhydride and Potassium Hydrogen Sulfate

Powdered potassium hydrogen sulfate (100 mg) was added to a stirred solution of the 5α-alcohol (200 mg) in acetic anhydride (5 ml) at 90°C, and the mixture was stirred for 45 min at the same temperature. The solution was poured onto ice and pyridine, the product was extracted with ether and the ethereal solution was worked up as usual. The residue was chromatographed on four silica gel preparative plates (20 × 20 cm) with benzene or a mixture of benzene and ether (96 : 5) as eluent. The yields of products are given in Table I. Analytical and physical data of the isolated compounds are recorded in Table III.

Cholest-4-ene-2β,3β,6α-triol 2,3-Diacetate 6-Benzoate (*IIa*)

The alcohol *IIb* (90 mg) in pyridine (1 ml) was benzoylated with benzoyl chloride (0·1 ml) at room temperature overnight. The mixture was decomposed with ice, the product taken up in ether, the ethereal layer worked up as usual and the residue was chromatographed on one silica gel preparative plate (20× 20 cm) using a mixture of benzene and ether (95 : 5) as eluent. Corresponding zones were separated and eluted with ether to yield the oily benzoate *IIa* (85 mg), $[\alpha]_D^{20}$ +28° (*c* 3·8). ^{1}H-NMR spectrum: 0·72 (3 H, s, 18-H), 1·26 (3 H, s, 19-H), 2·06 (3 H, s, CH_3·.COO—). For $C_{38}H_{54}O_6$ (606·9) calculated: 75·21% C, 8·97% H; found: 75·22% C, 9·10% H.

Cholest-4-ene-2β,3β,6α-triol 2,3-Diacetate (*IIb*)

The ketone *XIXa* (200 mg) in ethanol (10 ml) was reduced with sodium borohydride (100 mg) at room temperature for 2 h. The mixture was decomposed with 5% aqueous hydrochloric acid, the product extracted with ether and the ethereal solution worked up as usual. The residue was crystallized from a mixture of acetone and light petroleum to afford *IIb* (110 mg), m.p. 81—83°C, $[\alpha]_D^{20}$ −31° (*c* 1·8). ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·12 (3 H, s, 19-H). For $C_{31}H_{50}O_5$ (502·7) calculated: 74·06% C, 10·02% H; found: 73·90% C, 9·96% H.

5α-Cholestan-2β,3β,5,6α-tetraol 2,3,5-Triacetate 6-Benzoate (*III*)

The alcohol[8] *I* (25 mg) in acetic acid (1 ml) was acetylated with acetic anhydride (0·1 ml) in the presence of *p*-toluenesulfonic acid (10 mg) at room temperature overnight. The mixture was decomposed with ice, the product taken up in ether, the organic layer washed with 5% aqueous potassium hydrogen carbonate solution, water, dried and the solvent evaporated. The residue was crystallized from a mixture of acetone, methanol and water to give *III* (9 mg), m.p 199 to 201°C, $[\alpha]_D^{20}$ +31° (*c* 1·1). For $C_{40}H_{58}O_8$ (666·9) calculated: 72·04% C, 8·77% H; found: 72·13% C, 8·79% H.

Cholest-4-ene-2β,3β,6β-triol 2,3-Diacetate 6-Benzoate (*VI*)

The hydroxy derivative[10] *V* (30 mg) was dissolved in pyridine (2 ml), and treated with thionyl chloride (0·1 ml) at 0°C for 10 min. The mixture was decomposed with ice, the product taken up in ether and the ethereal solution worked up as usual, to yield the oily compound *VI*, (23 mg) $[\alpha]_D^{20}$ −51° (*c* 2·7). ^{1}H-NMR spectrum: 0·71 (3 H, s, 18-H), 1·37 (3 H, s, 19-H). For $C_{38}H_{54}O_6$ (606·9) calculated: 75·21% C, 8·97% H; found: 75·29% C, 9·06% H.

TABLE III

Analytical and Physical Data of Products of Westphalen Dehydration of Compounds *I*, *VIIIb*, *XVIa* and *XXII*

Compound	Formula (M.w.)	Calculated/Found		M.p., °C	$[\alpha]_D^{20}$
		% C	% H		
IIa	$C_{38}H_{54}O_6$ (606·9)	75·21 75·33	8·97 8·96	oil	+26°
III	$C_{40}H_{58}O_8$ (666·9)	72·04 72·15	8·77 8·73	198—200	+33°
IV	$C_{38}H_{54}O_6$ (606·9)	75·21 75·38	8·97 8·85	oil	+ 7°
IX	$C_{38}H_{56}O_6$ (608·9)	74·96 74·82	9·27 9·03	218—221	+29°
Xa	$C_{36}H_{52}O_4$ (548·8)	78·79 78·93	9·55 9·62	oil	+60°
XIa	$C_{36}H_{52}O_4$ (548·8)	78·79 78·62	9·55 9·53	oil	+80°
XIXa	$C_{31}H_{48}O_5$ (500·7)	74·36 74·51	9·66 9·67	129—130	−69°
XX	$C_{33}H_{52}O_7$ (560·8)	70·68 70·56	9·35 9·33	132—134	− 5°
XXIa	$C_{31}H_{48}O_5$ (500·7)	74·36 74·29	9·66 9·72	oil	−35°
XXIIIa	$C_{29}H_{46}O_3$ (442·7)	78·68 78·53	10·47 10·44	107—109	−55°
XXIV	$C_{31}H_{50}O_5$ (502·7)	74·06 73·92	10·02 9·55	172—173	−13°
XXVa	$C_{29}H_{46}O_3$ (442·7)	78·68 78·54	10·47 10·51	93—95	−50°

5α-Cholestane-3β,5,6α-triol 3-Monoacetate (*VIIIa*)

Cholesteryl acetate *VII* (1·56 g) was dissolved in pyridine (10 ml) and treated with osmium tetroxide (1 g) at room temperature overnight. The adduct was decomposed with a solution of sodium hydrogen sulfide (2 g) in water (20 ml) and pyridine (20 ml), the mixture was diluted with water,

and the product taken up in ether. The ethereal solution was worked up as usual and the residue was crystallized from a mixture of acetone, methanol and water to afford *VIIIa* (1·22 g), m.p. 175–176°C, $[\alpha]_D^{20}$ +9° (*c* 1·8). ^{1}H-NMR spectrum: 0·64 (3 H, s, 18-H), 0·96 (3 H, s, 19-H), 5·10 (1 H, brd m, 3α-H), 3·60 (1 H, brd m, 6β-H). For $C_{29}H_{50}O_4$ (462·7) calculated: 75·28% C, 10·89% H; found: 75·33% C, 10·93% H.

5α-Cholestane-3β,5,6α-triol 3-Acetate 6-Benzoate (*VIIIb*)

The diol *VIIIa* (1·1 g) was dissolved in pyridine (6 ml) and benzoylated with benzoyl chloride (1 ml) at room temperature for 3 h. The mixture was decomposed with ice and worked up as in the case of *IIa*. The residue was crystallized from a mixture of acetone, methanol and water to yield *VIIIb* (0·8 g), m.p. 262–263°C, $[\alpha]_D^{20}$ +32° (*c* 1·6). ^{1}H-NMR spectrum: 0·67 (3 H, s, 18-H), 1·11 (3 H, s, 19-H). For $C_{36}H_{54}O_5$ (566·8) calculated: 76·28% C, 9·60% H; found: 76·15% C, 9·58% H.

5α-Cholestane-3β,5,6α-triol 3,5-Diacetate 6-Benzoate (*IX*)

The alcohol *VIIIb* (50 mg) in acetic acid (2 ml) was acetylated with acetic anhydride (1 ml) in the presence of *p*-toluenesulfonic acid (10 mg) at room temperature overnight. The mixture was worked up as in the case of *III*. The residue was crystallized from a mixture of acetone, methanol and water to afford *IX* (19 mg), m.p. 219–223°C, $[\alpha]_D^{20}$ +31° (*c* 4·2). ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·20 (3 H, s, 19-H), 1·97 (3 H, s, CH_3COO—$C_{(3)}$), 2·18 (3 H, s, CH_3COO—$C_{(5)}$). For $C_{38}H_{56}O_6$ (608·9) calculated: 74·96% C, 9·27% H; found: 75·01% C, 9·25% H.

Cholest-4-ene-3β,6α-diol 3-Acetate 6-Benzoate (*Xa*)

The alcohol *Xb* (150 mg) was dissolved in pyridine (1 ml) and benzoylated with benzoyl chloride (0·1 ml) at room temperature for 4 h. The mixture was worked up as in the case of *IIa* to yield the oily benzoate *Xa* (145 mg), $[\alpha]_D^{20}$ +59° (*c* 1·9). ^{1}H-NMR spectrum: 0·69 (3 H, s, 18-H), 1·16 (3 H, s, 19-H), 2·00 (3 H, s, CH_3COO—), 5·25 (1 H, m, 3α-H), 5·55 (1 H, m, $W_{1/2}$ = 4·6 Hz, 4-H), 5·60 (1 H, m, 6β-H). For $C_{36}H_{52}O_4$ (548·8) calculated: 78·79% C, 9·55% H; found: 78·96% C, 9·64% H.

Cholest-4-ene-3β,6α-diol 3-Monoacetate (*Xb*)

The ketone *XXIIIa* (300 mg) was dissolved in ethanol (6 ml) and reduced with sodium borohydride (100 mg) at room temperature for 3 h. The mixture was worked up as in the case of *IIb* to afford the amorphous alcohol *Xb* (270 mg), $[\alpha]_D^{20}$ +7° (*c* 1·3). ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·05 (3 H, s, 19-H), 2·01 (3 H, s, CH_3COO—), 5·25 (1 H, m, 3α-H), 5·57 (1 H, m, $W_{1/2}$ = 5·2 Hz, 4-H), 4·05 (1 H, brd m, 6α-H). For $C_{29}H_{48}O_3$ (444·7) calculated: 78·33% C, 10·88% H; found: 78·40% C, 10·91% H.

Cholest-4-ene-3β,6α-diol (*Xc*)

A solution of the diester *Xa* (100 mg) in a mixture of methanol (7 ml) and acetone (3 ml) was refluxed with a solution of potassium hydrogen carbonate (100 mg) in water (1 ml) for 2 h. The solvents were removed by distillation *in vacuo*, the residue was diluted with ether and water, the organic layer was washed with water, dried and the ether evaporated. The residue was crystallized from ether to afford *Xc* (42 mg), m.p. 184–186°C, $[\alpha]_D^{20}$ +52° (*c* 1·8). ^{1}H-NMR spectrum:

0·67 (3 H, s, 18-H), 1·02 (3 H, s, 19-H). For $C_{27}H_{46}O_2$ (402·7) calculated: 80·54% C, 11·51% H; found: 80·42% C, 11·45% H.

Cholest-4-ene-3α,6α-diol (*XIb*)

A solution of the diester *XIa* (18 mg) in a mixture of methanol (3 ml) and acetone (1 ml) was treated with a solution of potassium hydrogen carbonate (50 mg) in water (0·5 ml) at reflux temperature for 2 h. The mixture was worked up as in the case of *Xc*. The residue was crystallized from ether to yield *XIb* (6 mg), m.p. 189–191°C, $[\alpha]_D^{20}$ +70° (*c* 1·2). ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 0·97 (3 H, s, 19-H), 4·20 (2 H, m, 3β-H and 6β-H), 5·80 (1 H, m, $W_{1/2}$ = 9 Hz, 4-H). For $C_{27}H_{46}O_2$ (402·7) calculated: 80·54% C, 11·51% H; found: 80·55% C, 11·62% H.

Cholest-4-ene-3,6-dione (*XIII*)

a) *From cholest-4-ene-3β,6α-diol* (Xc): Powdered manganese dioxide (100 mg) was added to a stirred solution of the diol *Xc* (50 mg) in chloroform (5 ml), the mixture was stirred for 3 h at room temperature, filtered and the solvent evaporated. The residue was crystallized from a mixture of acetone, methanol and water to afford *XIII* (16 mg), m.p. 121–124°C, $[\alpha]_D^{20}$ −41° (*c* 2·0) in accordance with the literature[11].

b) *From cholest-4-ene-3α,6α-diol* (XIb): The diol *XIb* (9 mg) in chloroform (3 ml) was oxidized with manganese dioxide (30 mg) as in *a*) to yield the identical diketone *XIII*.

c) *From 5-hydroxy-5α-cholestane-3,6-dione*[21] (*XII*:) The hydroxy derivative *XII* (300 mg) was erfluxed with a mixture of methanol (20 ml), dioxane (5 ml) and 35% aqueous hydrochloric acid (0·1 ml) for 2 h. The solvents were removed by distillation under reduced pressure, the residue was dissolved in ether, the ethereal solution 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 *XIII* (115 mg), identical with the compound described in *a*) and *b*).

d) *From 3β-hydroxycholest-4-ene-6-one* (XXIIIb): The alcohol *XXIIIb* (100 mg) was oxidized with manganese dioxide (300 mg) in chloroform (7 ml) as in *a*) to yield the identical diketone *XIII* (29 mg) after crystallization.

Cholest-4-ene-3β,6β-diol 3-Acetate 6-Benzoate (*XV*)

The alcohol[10] *XIV* (30 mg) was dissolved in pyridine (1 ml) and treated with thionyl chloride (0·05 ml) at 0°C for 5 min. The mixture was worked up as in the case of *VI* to yield the oily compound *XV* (24 mg), $[\alpha]_D^{20}$ −40° (*c* 3·7). ^{1}H-NMR spectrum: 0·70 (3 H, s, 18-H), 1·31 (3 H, s, 19-H), 2·01 (3 H, s, CH_3COO—), 5·25 (1 H, m, 3α-H), 5·68 (1 H, m, $W_{1/2}$ = 3·2 Hz, 4-H), 5·55 (1 H, t, 6α-H). For $C_{36}H_{52}O_4$ (548·8) calculated: 78·79% C, 9·55% H; found: 78·76% C, 9·48% H.

5α-Cholestane-2β,3β,5,6β-tetraol 2,3-Diacetate (*XVIIa*)

The ketone[8] *XVIa* (950 mg) was dissolved in dimethylformamide (15 ml) and reduced with sodium borohydride (30 mg) at room temperature for 2 h. The mixture was diluted with ether, decomposed with 5% aqueous hydrochloric acid, the organic layer was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and the solvent evaporated. The residue was crystallized from a mixture of acetone and n-heptane to give the 6β-hydroxy derivative

XVIIa (810 mg), m.p. 231–232°C, $[\alpha]_D^{20}$ −1° (*c* 2·3). IR spectrum (chloroform): 1238, 1256, 1722 sh, 1742, 3470, 3635 cm^{-1}. ^{1}H-NMR spectrum: 0·70 (3 H, s, 18-H), 1·90 (3 H, s, 19-H), 5·32 (2 H, m, 2α-H and 3α-H), 3·69 (1 H, 6α-H). For $C_{31}H_{52}O_6$ (520·8) calculated: 71·50% C, 10·07% H; found: 71·33% C, 10·12% H.

5α-Cholestane-2β,3β,5,6β-tetraol 2,3-Diacetate 6-Nitrate (*XVIIb*)

A solution of the diol *XVIIa* (770 mg) in chloroform (10 ml) was treated at −30 to −20°C with a reagent prepared from acetic anhydride (6 ml) and 65% nitric acid (1·4 ml) at −30°C. The mixture was kept at −15 to −10°C for 1 h. The solution was poured onto ice and neutralized with potassium hydrogen carbonate solution. The organic layer was washed with 5% aqueous potassium hydrogen carbonate solution, water, dried, and the solvent evaporated. The residue was crystallized from a mixture of acetone, methanol and water to yield *XVIIb* (460 mg), m.p. 103–105°C, $[\alpha]_D^{20}$ −29° (*c* 1·8). IR spectrum: 852, 1235, 1250, 1282, 1640, 1722, 1745, 3480, 3595 cm^{-1}. ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·24 (3 H, s, 19-H), 5·29 (2 H, m, 2α-H and 3α-H), 4·91 (1 H, 6α-H). For $C_{31}H_{51}NO_8$ (565·8) calculated: 65·81% C, 9·09% H; found: 65·76% C, 9·09% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-2β,3β,6β-triol 2,3-Diacetate 6-Nitrate (*XVIIIa*)

Powdered potassium hydrogen sulfate (200 mg) was added to a stirred solution of the nitrate *XVIIb* (700 mg) in acetic anhydride (5 ml) at 90°C. The mixture was stirred at the same temperature for an additional 5 min, poured onto ice and pyridine, the product taken up in ether and worked up as usual. The residue was crystallized from aqueous ethanol to afford *XVIIIa* (500 mg), m.p. 141–142°C, $[\alpha]_D^{20}$ +21° (*c* 2·1). IR spectrum: 858, 1228, 1246, 1278, 1633, 1749 cm^{-1}. ^{1}H-NMR spectrum: 0·82 (3 H, s, 18-H), 1·27 (3 H, s, 5β-methyl), 4·96 (1 H, dd, $J_{6\alpha,7\alpha}$ = = 5 Hz, $J_{6\alpha,7\beta}$ = 10·5 Hz). For $C_{31}H_{49}NO_7$ (547·7) calculated: 67·98% C, 9·02% H; found: 67·85% C, 9·03% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-2β,3β,6β-triol 2,3-Diacetate (*XVIIIb*)

Zinc powder (2 g) was added to a stirred solution of the nitrate *XVIIIa* (400 mg) in acetic acid (25 ml) and the mixture was stirred at room temperature for an additional 15 min. The inorganic material was separated by filtration, washed with methanol, the filtrate evaporated under reduced pressure, the residue dissolved in ether, the solution washed with 5% aqueous potassium hydrogen carbonate, water, dried and evaporated. The residue was crystallized from a mixture of ethyl-acetate and n-heptane to afford *XVIIIb*, (290 mg), m.p. 120–121°C and 141–142°C $[\alpha]_D^{20}$ + 54° (*c* 2·1). IR spectrum: 1250, 1747, 3530, 3630 cm^{-1}. ^{1}H-NMR spectrum: 0·82 (3 H, s, 18-H), 1·18 (3 H, s, 5β-methyl), 3·51 (1 H, dd, $J_{6\alpha,7\alpha}$ = 4 Hz, $J_{6\alpha,7\beta}$ = 11 Hz). For $C_{31}H_{50}O_5$ (502·7) calculated: 74·06% C, 10·02% H; found: 73·99% C, 9·96% H.

2β,3β-Diacetoxycholest-4-en-6-one (*XIXa*)

The alcohol[8] *XVIa* (50 mg) was dissolved in pyridine (1 ml) and treated with thionyl chloride (0·05 ml) at 0°C for 5 min. The mixture was worked up as in the case of *VI*. The residue was crystallized from aqueous ethanol to afford *XIXa* (21 mg), m.p. 129–130°C, $[\alpha]_D^{20}$ −72° (*c* 1·9). IR spectrum: 1232, 1248, 1647, 1703, 1748 cm^{-1}. ^{1}H-NMR spectrum: 0·71 (3 H, s, 18-H), 1·14 (3 H, s, 19-H), 5·89 (1 H, 4-H). CD spectrum: Δε −2·32, 315 nm; Δε −5·81, 240 nm. UV spectrum: log ε = 4·32, 220 nm. For $C_{31}H_{48}O_5$ (500·7) calculated: 74·36% C, 9·66% H; found: 74·42% C, 9·61% H.

2β,3β-Dibenzoyloxycholest-4-en-6-one (*XIXb*)

The alcohol *XVIb* (100 mg) was dissolved in pyridine (2 ml) and treated with thionyl chloride (0·2 ml) at 0°C for 20 min. The mixture was worked up as in *VI* and the residue was crystallized from a mixture of acetone, methanol and water to yield *XIXb* (60 mg), m.p. 173–175°C, $[\alpha]_D^{20}$ −53° (*c* 1·8). IR spectrum: 1278, 1645, 1705, 1727 cm^{-1}. ^{1}H-NMR spectrum: 0·72 (3 H, s, 18-H), 1·22 (3 H, s, 19-H), 6·13 (1 H, 4-H). CD spectrum: $\Delta\varepsilon$ −1·59, 315 nm; $\Delta\varepsilon$ −10·17, 240 nm. UV spectrum: $\log\varepsilon \approx 4{\cdot}31$, 231 nm. For $C_{41}H_{52}O_5$ (624·9) calculated: 78·81% C, 8·39% H; found: 78·96% C, 8·30% H.

2β,3β-Diacetoxy-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (*XXIa*)

The alcohol *XVIIIb* (430 mg) was dissolved in acetone (10 ml) and treated with Jones' reagent for 10 min. at room temperature. The excess reagent was destroyed with methanol, ether was added, and the mixture was washed with water, aqueous 5% potassium hydrogen carbonate solution, water, dried and evaporated to afford the oily ketone *XXIa* (390 mg), $[\alpha]_D^{20}$ −36° (*c* 3·6). IR spectrum: 1228, 1247, 1716, 1750 cm^{-1}. ^{1}H-NMR spectrum: 0·79 (3 H, s, 18-H), 1·39 (3 H, s, 5β-methyl). For $C_{31}H_{48}O_5$ (500·7) calculated: 74·36% C, 9·96% H; found: 74·32% C, 9·78% H.

2β,3β-Dihydroxy-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (*XXIb*)

A solution of the diacetate *XXIa* (300 mg) in methanol (30 ml) was treated with a solution of potassium hydrogen carbonate (300 mg) in water (5 ml) at reflux temperature for 3 h. Methanol was distilled off under reduced pressure, the residue was dissolved in ethyl acetate, the organic layer was washed with water, dried and evaporated to afford the amorphous diol XXIb (265 mg), $[\alpha]_D^{20}$ −42° (*c* 2·1). IR spectrum: 1707, 3585, 3631 cm^{-1}. ^{1}H-NMR spectrum: 0·87 (3 H, s, 18-H), 1·43 (3 H, s, 5β-methyl), 3·55 (1 H, m, 2α-H), 4·07 (1 H, m, 3α-H). For $C_{27}H_{44}O_3$ (416·6) calculated: 77·84% C, 10·64% H; found: 77·81% C, 10·60% H.

2β,3β-Dibenzoyloxy-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (*XXIc*)

The diol *XXIb* (50 mg) was dissolved in pyridine (2 ml) and benzoylated with benzoyl chloride (0·5 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 oily dibenzoate *XXIc* (49 mg), $[\alpha]_D^{20}$ −40° (*c* 2·7). ^{1}H-NMR spectrum: 0·77 (3 H, s, 18-H), 1·40 (3 H, s, 5β-methyl), 5·82 (1 H, m, 2α-H), 5·30 (1 H, broad m, 3α-H). CD spectrum: $\Delta\varepsilon$ −0·98, 297 nm, $\Delta\varepsilon$ −11·23, 235 nm. For $C_{41}H_{52}O_5$ (624·9) calculated: 78·81% C, 8·39% H; found: 78·73% C, 8·45% H.

3β-Acetoxy-cholest-4-en-6-one (*XXIIIa*)

The alcohol *XXII* (400 mg) was dissolved in pyridine (3 ml), and treated with thionyl chloride (0·4 ml) at 0°C for 10 min. The mixture was worked up as in the case of *XIXa*. The residue was crystallized from a mixture of acetone, methanol and water to yield *XXIIIa* (280 mg), m.p. 108–109°C, $[\alpha]_D^{20}$ −57° (*c* 1·6) in accordance with the literature[12]. ^{1}H-NMR spectrum: 0·69 (3 H, s, 18-H), 1·01 (3 H, s, 19-H), 2·05 (3 H, s, CH_3COO—), 5·30 (1 H, brd m, 3α-H), 6·08 (1 H, m, $W_{1/2} = 4{\cdot}2$ Hz, 4-H).

3β-Hydroxycholest-4-en-6-one (*XXIIIb*)

A solution of the acetate *XXIIIa* (200 mg) in methanol (10 ml) was treated with a solution of potassium hydrogen carbonate (200 mg) in water (2 ml) at reflux temperature for 1 h. The solvent was distilled off under reduced pressure, the residue was treated with ether and water, the ethereal phase was dried and the ether evaporated. The residue was crystallized from aqueous methanol to afford *XXIIIb* (130 mg), m.p. 152–154°C, $[\alpha]_D^{20}$ −13° (*c* 2·0) in accordance with the literature[22]. ^{1}H-NMR spectrum: 0·70 (3 H, s, 18-H), 1·01 (3 H, s, 19-H), 4·25 (1 H, m, 3α-H), 6·61 (1 H, m, $W_{1/2}$ = 4·7 Hz, 4-H).

3β,5-Diacetoxy-5α-cholestan-6-one (*XXIV*)

The hydroxy ketone *XXII* (70 mg) in acetic acid (2 ml) was acetylated with acetic anhydride (0·5 ml) in the presence of *p*-toluenesulfonic acid (20 mg) at room temperature overnight. The mixture was worked up as in the case of *III*. The residue was crystallized from a mixture of acetone, methanol and water to yield *XXIV* (32 mg), m.p. 174–175°C, $[\alpha]_D^{20}$ −11° (*c* 1·8) in accordance with the literature[13]. ^{1}H-NMR spectrum: 0·64 (3 H; s, 18-H), 0·86 (3 H, s, 19-H), 2·00 (3 H, s, CH_3COO—$C_{(3)}$), 2·16 (3 H, s, CH_3COO—$C_{(5)}$).

3β-Acetoxy-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (*XXVa*)

A solution of the benzoate[10] *XXVb* (300 mg) and potassium hydroxide (200 mg) in methanol (20 ml) was refluxed for 1·5 h. Methanol was distilled off under reduced pressure, the residue was treated with ether and water, the organic layer was washed with water, dried and evaporated. The crude alcohol *XXVc* was dissolved in pyridine (3 ml) and acetylated with acetic anhydride (1 ml) at room temperature overnight. The mixture was decomposed with ice, the product taken up in ether and worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to yield the acetate *XXVa* (160 mg), m.p. 94–96°C, $[\alpha]_D^{20}$ −48° (*c* 2·0) in accordance with the literature[23]. ^{1}H-NMR spectrum: 0·74 (3 H, s, 18-H), 1·36 (3 H, s, 5β-methyl), 2·04 (3 H, s, CH_3COO—), 5·10 (1 H, 3α-H).

Cholest-5-ene-2β,3β-diol 2,3-Diacetate (*XXVIIa*)

Powdered potassium hydrogen sulfate (100 mg) was added to a stirred solution of 5α-hydroxy compound[8] *XXVI* (80 mg) in acetic anhydride (5 ml) at 90°C, the mixture was stirred at 90°C for 45 min, poured onto ice and pyridine, the product was taken up in ether and the ethereal solution was worked up as usual. The residue was crystallized from aqueous ethanol to afford *XXVIIa* (47 mg), m.p. 192–193°C, $[\alpha]_D^{20}$ −7° (*c* 1·9) in accordance with the literature[9]. ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·13 (3 H, s, 19-H), 5·28 (1 H, m, 2α-H), 4·74 (1 H, m, 3α-H), 5·44 (1 H, d, *J* = 5 Hz, 6-H).

Cholest-5-ene-2β,3β-diol 2,3-Dibenzoate (*XXVIIc*)

The diacetate *XXVIIa* (180 mg) was dissolved in ether (10 ml) and reduced with lithium aluminum hydride (100 mg) at room temperature for 2 h, the mixture was decomposed with saturated aqueous sodium sulfate solution and worked up as usual. The residue (crude alcohol *XXVIIb*) was dried azeotropically with benzene, dissolved in pyridine (3 ml) and benzoylated with benzoyl chloride (1 ml) at room temperature for 3 h. The mixture was decomposed with ice, the product was taken up in ether and the ethereal solution was worked up as usual. The residue

was crystallized from a mixture of chloroform and methanol to yield *XXVIIc* (154 mg), m.p. 228–229°C, $[\alpha]_D^{20}$ +20° (*c* 1·7). IR spectrum: 1282, 1721 cm^{-1}. CD spectrum: $\Delta\varepsilon$ +24·3, 238 nm. ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·26 (3 H, s, 19-H), 5·73 (1 H, m, 2α-H), 5·11 (1 H, m, 3α-H), 5·55 (1 H, d, *J* = 4·5 Hz, 6-H). For $C_{41}H_{54}O_4$ (610·9) calculated: 80·61% C, 8·91% H; found: 80·53% C, 9·02% H.

4β,5-Epoxy-5β-cholestan-2α-ol (*XXIX*)

The olefin[9] *XXVIII* (3 g) in chloroform (30 ml) was treated with *m*-chloroperoxybenzoic acid (2 g) for 30 min. at room temperature. The excess peracid was extracted into 5% aqueous potassium hydrogen carbonate solution, the organic layer was washed with water, dried and the solvent removed. The residue was chromatographed on a silica gel column (130 g) in a mixture of light petroleum and ether (9 : 1). The lipophilic fractions were collected and evaporated to yield the amorphous epoxide *XXIX* (0·9 g), $[\alpha]_D^{20}$ +36° (*c* 1·6). IR spectrum: 3460, 3630 cm^{-1}. ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·04 (3 H, s, 19-H), 3·97 (1 H, broad m, 2β-H), 3·06 (1 H, m, 4α-H). For $C_{27}H_{46}O_2$ (402·7) calculated: 80·54% C, 11·51% H; found: 80·56% C, 11·47% H.

4α,5-Epoxy-5α-cholestan-2α-ol (*XXX*)

After isolation of the epoxide *XXIX* elution was continued using the same solvent mixture to afford fractions with a polar component. Combination and evaporation of the solvent gave the amorphous epoxide *XXX* (2·0 g), $[\alpha]_D^{20}$ +72° (*c* 1·8). IR spectrum: 3420, 3610, 3628 cm^{-1}. ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·09 (3 H, s, 19-H), 3·80 (1 H, broad m, 2β-H), 2·91 (1 H, d, *J* = 4·5 Hz, 4β-H). For $C_{27}H_{46}O_2$ (402·7) calculated: 80·54% C, 11·51% H; found: 80·62% C, 11·53% H.

5α-Cholestane-2α,5-diol (*XXXI*)

a) *From 4α,5-epoxy-5α-cholestan-2α-ol* (XXX): The epoxide *XXX* (400 mg) was dissolved in ether (20 ml) and refluxed with lithium aluminum hydride (200 mg) for 30 min. The mixture was decomposed with saturated aqueous sodium sulfate solution, the product was extracted with ether and the ethereal solution worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to give *XXXI* (160 mg), m.p. 155–156°C, $[\alpha]_D^{20}$ +19° (*c* 2·0) in accordance with the literature[24,25].

b) *From 5-hydroxy-5α-cholestan-2-one* (XXXII): Elution of the chromatography after isolation of the diol *XXXIIIa* with the same solvent mixture afforded fractions with a polar component. Combination and evaporation of the solvents gave the diol *XXXI* (82 mg, 39%), identical with the compound described under *a*); m.p. 155–156°C.

5-Hydroxy-5α-cholestan-2-one (*XXXII*)

The alcohol *XXXI* (100 mg) was dissolved in acetone (15 ml) and treated with excess Jones' reagent at room temperature for 10 min. The excess oxidizing agent was decomposed with methanol, ether was added, and the mixture was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and the solvent evaporated. The residue was crystallized from aqueous ethanol to yield *XXXII* (57 mg), m.p. 186–187°C in accordance with the literature[24].

5α-Cholestane-2β,5-diol (*XXXIIIa*)

The ketone *XXXII* (300 mg) was dissolved in ethanol (50 ml) and reduced with sodium borohydride (200 mg) at room temperature for 2 h. The excess of reagent was decomposed with 5% aqueous hydrochloric acid solution, the product was extracted with ether and the ethereal solution was worked up as usual. The residue was chromatographed on a silica gel column (30 g) in a mixture of light petroleum and ether (9 : 1). The lipophilic fractions were collected and evaporated to yield *XXXIIIa* (128 mg, 61%), m.p. 173—175°C (aqueous ethanol), (literature reports[26] 168—170°C), $[\alpha]_D^{20}$ +25° (*c* 1·9), (literature reports[26] $[\alpha]_D^{20}$ +19·7°). IR spectrum: 3627 cm^{-1}. ^{1}H-NMR spectrum: 0·67 (3 H, s, 18-H), 1·20 (3 H, s, 19-H), 4·16 (1 H, p, J = 4 Hz, 2α-H). ^{1}H-NMR spectrum after trichloroacetyl isocyanate treatment: 0·67 (18-H), 1·22 (19-H), 5·28 (2α-H).

5α-Cholestane-2β,5-diol 2-Monopivalate (*XXXIIIc*)

The diol *XXXIIIa* (60 mg) was dissolved in pyridine (2 ml) and treated with pivaloyl chloride (0·3 ml) for 20 h at 35°C. The mixture was decomposed with ice, the product was taken up in ether and the ethereal solution worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to afford *XXXIIIc* (55 mg), m.p. 179—180°C. For $C_{32}H_{56}O_3$ (488·8) calculated: 78·63% C, 11·55% H; found: 78·75% C, 11·54% H.

Cholest-4-en-2β-ol (*XXXIVa*)

a: Elution of the corresponding zone after isolation of the compound *XXXVa* obtained from reduction of the mixture of acetates *XXXIVb* and *XXXVb* gave the alcohol *XXXIVa* (17·6 mg, 41%), m.p. 104—105°C (methanol) in accordance with the literature[19]. IR spectrum: 3360, 3652 cm^{-1}. ^{1}H-NMR spectrum: 0·69 (3 H, s, 19-H), 1·12 (3 H, s, 19-H), 3·95 (1 H, m, 2α-H), 5·18 (1 H, m, 4-H).

b) Elution of the corresponding zone after isolation of the compound *XXXVa* obtained from reduction of the mixture of pivalates *XXXIVc* and *XXXVc* gave the alcohol *XXXIVa* (14·2 mg, 53%), m.p. 104—105°C, identical with the compound described under *a*).

Cholest-5-en-2β-ol (*XXXVa*)

a) *From* 5α-*cholestane*-2β,5-*diol* XXXIIIa: the diol *XXXIIIa* (50 mg) was refluxed with acetic anhydride (6 ml) for 30 min. Powdered potassium hydrogen sulfate (100 mg) was added to the stirred solution at 90°C and the mixture was stirred for an additional 45 min at 90°C. The solution was poured onto ice and pyridine, the product was extracted with ether, the ethereal solution was worked up as usual to yield the inseparable mixture of two acetates *XXXIVb* and *XXXVb*. This mixture was dissolved in ether (10 ml) and reduced with lithium aluminum hydride (50 mg) at room temperature for 2 h. The mixture was decomposed with saturated aqueous sodium sulfate solution and the organic layer was worked up as usual. The residue was chromatographed on one preparative plate of silica gel (20 × 20 cm) using double development with a mixture of benzene and ether (97 : 3) as eluent. Zones containing the lipophilic component were collected, eluted, and the solvent evaporated to afford the alcohol *XXXVa* (25·3 mg, 59%), m.p. 151—153°C (aqueous ethanol) in accordance with the literature[19]. IR spectrum: 3630 cm^{-1}. ^{1}H-NMR spectrum: 0·69 (3 H, s, 18-H), 1·22 (3 H, s, 19-H), 4·18 (1 H, m, 2α-H), 5·35 (1 H, 6-H).

b) *From* 5α-*cholestane*-2β,5-*diol* 2-*monopivalate* XXXIIIc: Powedered potassium hydrogen sulfate (100 mg) was added to a stirred solution of the pivalate *XXXIIIc* (40 mg) in acetic an-

hydride (5 ml) at 90°C, the mixture was stirred for 45 min at 90°C and worked up as given under *a*). The residue was reduced with lithium aluminum hydride (20 mg) in ether (5 ml) and the products chromatographed as given under *a*) to yield the alcohol *XXXVa* (12·6 mg, 48%) as a more lipophilic fraction, m.p. 151—153°C.

2β-Benzoyloxy-3α-bromo-5-hydroxy-5α-cholestan-6-one (*XXXVIb*)

The alcohol[14] *XXXVIa* (500 mg) was dissolved in pyridine (10 ml) and benzoylated with benzoyl chloride (1 ml) at room temperature overnight. The mixture was decomposed with ice, the product was taken up in ether and the ethereal solution worked up as usual to yield the oily benzoate *XXXVIb* (490 mg), $[\alpha]_D^{20}$ +4° (*c* 3·8). ^{1}H-NMR spectrum: 0·65 (3 H, s, 18-H), 1·05 (3 H, s, 19-H), 5·60 (1 H, m, 2α-H), 4·54 (1 H, m, 3β-H), 2·91 (1 H, dd, $J_{4\alpha,5\beta}$ = 17 Hz, $J_{3\beta,4\xi}$ = 5 Hz). For $C_{34}H_{49}BrO_4$ (601·7) calculated: 67·87% C, 8·21% H, 13·28% Br; found: 67·75% C, 8·25% H, 13·42% Br.

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

The hydroxy ketone *XXXVIb* (450 mg) was dissolved in dimethylformamide (15 ml) and treated with sodium borohydride (200 mg) for 2 h at room temperature. The mixture was diluted with ether, excess hydride was decomposed with 5% aqueous hydrochloric acid, the organic layer was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and evaporated to give the amorphous 6β-alcohol *XXXVII* (435 mg), $[\alpha]_D^{20}$ −21° (*c* 2·0). IR spectrum (chloroform): 1274, 1715, 3580, 3625 cm^{-1}. ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·35 (3 H, s, 19-H). For $C_{34}H_{51}BrO_4$ (603·7) calculated: 67·65% C, 8·52% H; found: 67·79% C, 8·36% H.

5α-Cholestane-2β,5,6β-diol 2-Monobenzoate (*XXXVIII*)

The bromo compound *XXXVII* (200 mg) was dissolved in methanol (10 ml) and hydrogenated for 20 h on 5% palladium calcium carbonate (100 mg). The inorganic material was filtered off, the solvent evaporated and the residue was chromatographed on three preparative plates of silica gel (20 × 20 cm) using a mixture of benzene and ether (4 : 1) as eluent. Corresponding zones were eluted with ether and evaporated. The residue was crystallized from aqueous ethanol to afford *XXXVIII* (111 mg), m.p. 202—203°C, $[\alpha]_D^{20}$ −48° (*c* 1·6). IR spectrum (chloroform): 1281, 1709, 3510, 3625 cm^{-1}. ^{1}H-NMR spectrum: 0·68 (3 H, s, 18-H), 1·42 (3 H, s, 19-H). For $C_{34}H_{52}O_4$ (524·8) calculated: 77·82% C, 9·99% H; 77·83% C, 10·06% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-2β,6β-diol 2-Benzoate 6-Acetate (*XXXIXa*)

The diol *XXXVIII* (90 mg) was refluxed with acetic anhydride (5 ml) for 15 min. Powdered potassium hydrogen sulfate (100 mg) was added to a stirred reaction mixture at 90°C and stirring was continued at 90°C for 15 min. The solution was poured onto ice and pyridine, the product was taken up in ether and the ethereal solution was worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to yield *XXXIXa* (46 mg), m.p. 145—146°C, $[\alpha]_D^{20}$ −24° (*c* 1·5). IR spectrum: 1247, 1275, 1720, 1738 cm^{-1}. ^{1}H-NMR spectrum: 0·81 (3 H, s, 18-H), 1·18 (3 H, s, 5β-methyl). For $C_{36}H_{52}O_4$ (548·8) calculated: 78·79% C, 9·55% H; found: 78·75% C, 9·44% H.

5-Methyl-19-nor-5β-cholest-9(10)-ene-2β,6β-diol 2-Monobenzoate (*XXXIXb*)

The diester *XXXIXa* (27 mg) dissolved in chloroform (0·5 ml) and methanol (2 ml) was treated with concentrated hydrochloric acid (0·1 ml) and allowed to stand for 30 h at 35°C. About one half of the solvents was distilled off under reduced pressure, the residue was treated with ether and water, the organic layer was washed with 5% aqueous potassium hydrogen carbonate solution, water, dried and evaporated. The residue was crystallized from a mixture of methanol, acetone and water to afford *XXXIXb* (16 mg), m.p. 187—189°C, $[\alpha]_D^{20}$ −10° (*c* 1·3). IR spectrum (chloroform): 1280, 1711, 3500, 3615 cm^{-1}. ^{1}H-NMR spectrum: 0·82 (3 H, s, 18-H), 1·14 (3 H, s, 5β-methyl), 4·78 (1 H, m, 2α-H), 3·56 (1 H, dd, $J_{6\alpha,7\alpha}$ = 4 Hz, $J_{6\alpha,7\beta}$ = 10·6 Hz, 6α-H). For $C_{34}H_{50}O_3$ (506·8) calculated: 80·58% C, 9·94% H; found: 80·72% C, 10·02% H.

2β-Benzoyloxy-5-methyl-19-nor-5β-cholest-9(10)-en-6-one (*XL*)

The alcohol *XXXIXa* (150 mg) was dissolved in a mixture of acetone (5 ml) and benzene (3 ml) and treated with Jones' reagent at room temperature for 5 min. The excess oxidizing agent was destroyed with methanol, ether was added, the mixture was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and evaporated to yield the oily ketone *XL* (132 mg), $[\alpha]_D^{20}$ −92° (*c* 0·9). IR spectrum: 1275, 1715 sh, 1720 cm^{-1}. CD spectrum: Δε −0·72, 302 nm, Δε −2·31, 232 nm. ^{1}H-NMR spectrum: 0·78 (3 H, s, 18-H), 1·32 (3 H, s, 5β-methyl). For $C_{34}H_{48}O_3$ (504·8) calculated: 80·91% C, 9·59% H; found: 80·84% C, 9·67% H.

5-Methyl-19-nor-5β-cholest-9(10)-en-2β-ol (*XLI*)

The solution of ketone *XL* (65 mg) in triethylene glycol (4 ml) was treated with 98% hydrazine hydrate (0·2 ml) and solid potassium hydroxide (100 mg) and heated at 140°C for 1 h at 200°C for 2 h. After cooling off, the mixture was diluted with water, neutralized with 10% aqueous hydrochloric acid, the product was taken up in ether, the ethereal solution was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and evaporated to afford *XLI* (27 mg), m.p. 129—130°C (ether), $[\alpha]_D^{20}$ +30° (*c* 1·2). IR spectrum: 3420, 3625 cm^{-1}. ^{1}H-NMR spectrum: 0·79 (3 H, s, 18-H), 1·07 (3 H, s, 5β-methyl). For $C_{27}H_{46}O$ (386·7) calculated: 83·87% C, 11·99% H; found: 83·91% C, 12·03% H.

The analyses were carried out in the Analytical Laboratory of this Institute (under the direction of Dr J. Horáček). The IR *and* CD *spectra were recorded by Mrs K. Matoušková and Mr P. Formánek and interpreted by Dr S. Vašíčková.* ^{1}H-NMR *spectra were recorded by Dr M. Synáčková.*

REFERENCES

1. Kirk D. N., Hartshorn M. P.: *Steroid Reaction Mechanisms*. Elsevier, Amsterdam 1968.
2. Westphalen T.: Ber. Deut. Chem. Ges. *48*, 1064 (1915).
3. Blunt J. W., Fischer A., Hartshorn M. P., Jones F. W., Kirk D. N., Yoong S. W.: Tetrahedron *21*, 1567 (1965).
4. Davis M., Petrow V.: J. Chem. Soc. *1949*, 2973.
5. Ll. Jones J. G., Marples B. A.: J. Chem. Soc. (C) *1970*, 2273.
6. Ll. Jones J. G., Marples B. A.: J. Chem. Soc. (C) *1971*, 572.
7. Fischer A., Hardman M. J., Hartshorn M. P., Kirk D. N., Thawley A. R.: Tetrahedron *23*, 159 (1967).
8. Kočovský P., Černý V.: This Journal *42*, 163 (1977).
9. Černý V., Kasal A., Šorm F.: This Journal *35*, 1235 (1970).

10. Kočovský P., Černý V.: This Journal *41*, 2620 (1976).
11. Dauben W. G., Boswell G. A., Templeton W.: J. Org. Chem. *25*, 1853 (1960).
12. Heilborn I. M., Jones E. R. H.: J. Chem. Soc. *1937*, 801.
13. Norymberski J. K.: J. Chem. Soc. *1954*, 762.
14. Kočovský P., Černý V.: This Journal *42*, 353 (1977).
15. Burstein S. H., Ringold H. J.: J. Amer. Chem. Soc. *86*, 4952 (1964).
16. Kuriyama K., Kondo E., Tori K.: Tetrahedron Lett. *1963*, 1485.
17. Patashnik S. L., Kimball H. L., Bernstein S.: Steroids *2*, 19 (1963).
18. Douax W. L., Eger Ch., Pokrywiecki S., Osawa Y.: J. Med. Chem. *1971*, 4.
19. Černý V., Buděšínský M., Šorm F.: This Journal *38*, 565 (1973).
20. Harada N., Nakanishi K.: J. Amer. Chem. Soc. *91*, 3989 (1969).
21. Milburn A. H., Truter E. V., Woodford F. P.: J. Chem. Soc. *1956*, 1740.
22. Fieser L. F., Yuan C., Goto T.: J. Amer. Chem. Soc. *82*, 1996 (1960).
23. Snatzke G., Fehlhaber H. W.: Justus Liebigs Ann. Chem. *676*, 188 (1964).
24. Conca R. J., Bergmann W.: J. Org. Chem. *18*, 1104 (1953).
25. Ambles A., Jacquesy R.: Bull. Chim. France *1972*, 804.
26. Komeno T., Itani H., Iwakura H., Nabeyama K.: Chem. Pharm. Bull. *18*, 1145 (1970).

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