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Structure Dependence of Cholesteric Mesophases III.(1)†
Minor Changes within the 17β-side Chain of Cholesterol

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Abstract—Several modifications were made within the 17β-side chain of cholesterol to determine the influence of minor structural changes on the mesomorphic behavior. Alkyl substitution at C-24 leads to smectic mesophases as experienced with campesteryl alkanoates. Moving the methyl group to C-25 leads to a loss of mesomorphic properties as found in 3β-acetoxy-25-methylcholest-5-ene. Replacing the 27-methyl group by an oxo group, a methylene group, or by hydrogen, alters only the stability of the cholesteric mesophases as shown with 3β-acetoxy-27-norcholest-5-en-25-one, 3β-acetoxycholesta-5, 25-diene, and 3β-acetoxy-27-norcholest-5-ene. However, the same modifications at C-20 lead to drastic changes in the mesomorphic properties. 3β-Acetoxycholest-5, 20-diene is both cholesteric and smectic, but no mesophases were observed in 3β-acetoxy-21-norcholest-5-en-20-one and 3β-acetoxy-21-norcholest-5-ene. 3β-Acetoxy-20-hydroxycholest-5-ene, 3β-octadecanoyloxy-20-azacholest-5-ene, and 3β-octadecanoyloxy-20,25-diazacholest-5-ene, were also not mesomorphic.

Introduction

The lack of sufficient experimental data precludes linking the existence and type of mesophases with structural features of the molecule. Systematic investigations were reported mainly for derivatives of cholesterol(2,3) and stigmasterol.(4,5) Only scattered data have been published for a few derivatives of other 3β-sterols with the sterane ring system of cholesterol and differing only by modifications within the 17β-side chain. Šorm(6) observed colors on melting of the

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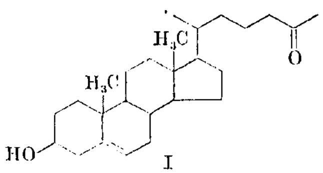
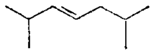
† Presented at the Third International Liquid Crystal Conference in Berlin, August 24–28, 1970.

4-nitrobenzoate of 3β-hydroxy-27-norcholest-5-en-25-one (I). Cholesteric colors were also noted for 3β-benzoyloxycholesta-5,22-diene (II)⁽⁷⁾ and for 3β-acetoxycholest-5-en-24-one (III).⁽⁸,⁹⁾ In a recent publication, Knapp and Nicholas⁽¹⁰⁾ attempted to derive the structural dependence of the cholesteric-mesophase from changes at the side chain of some sterols and tetracyclic triterpenes. However, most of the palmitates in their study contained, in addition to the modifications in the 17β-side chain, also deviations in the sterane moiety, and thereby reflect the simultaneous influence of several parameters.



I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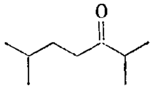
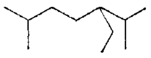


III


IV


V


VI


VII

For this study we selected 3β-sterols with a sterane nucleus identical with that of cholesterol, but with modifications in the 17β-side chain. The changes incorporated were all minor because they consisted mainly of the addition or elimination of methyl groups, introduction of double bonds or keto groups and the replacement of carbon by nitrogen. The results are summarized in Tables 1–4 and details of preparations are discussed in the experimental part.

Discussion

The following modifications at the 17β-side chain were performed:

(1) Alkyl substitution at C-24 and C-25
(2) Modifications at C-25
(3) Modifications at C-20
(4) Substitution by hetero atoms

Each change will be compared with the corresponding cholesteryl alkanoate in order to assess its influence on the mesomorphic behavior. Phase transitions were determined under the microscope. Cholesteric mesophases were determined by the optical sign and the sign of elongation whenever cholesteric colors were not observed.

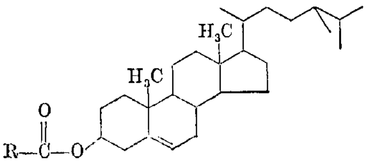
1. Alkyl Substitution at the 17β-side Chain

The thoroughly investigated alkanoates of cholesterol exhibit both cholesteric and smectic mesophases depending on the length of the ester chain.(2) A 24R-ethyl group in the 17β-side chain prevents the occurrence of cholesteric mesophases, but retains the smectic character, as observed in alkanoates of stigmasterol (IV)(5) and of β-sitosterol (V).(11) In order to investigate the influence of the smaller 24*R*-methyl group on the mesomorphic behavior we synthesized some *alkanoates of campesterol* (VI).(12)

In campesteryl heptanoate (Table I) we observed a monotropic cholesteric mesophase in addition to a monotropic smectic mesophase. To our surprise, the higher members octanoate, nonanoate, and octadecanoate were only smectic, with the nonanoate being enantiotropic smectic. This rather unusual behavior of a lower member being cholesteric and smectic, and the higher members being only smectic, differs from the mesomorphic behavior observed in other homologous series.

A possible explanation might be an impurity effect. The employed

Table 1



Campesteryl Alkanoate	mp	S–I	S–Ch	Ch–I
heptanoate	98.2	—	74.8	75.8
octanoate	84.2	78.9	—	—
nonanoate	69.4	79.5	—	—
octadecanoate	94.0	70.0	—	—

S–I: Smectic-isotropic transition, °C; S–Ch: Smectic-cholesteric transition, °C; Ch–I: Cholesteric-isotropic transition, °C campesterol(13) had a purity of 97.6%, with β-sitosterol (2.3%) and cholesterol (0.1%) as the contaminants, as determined by gas chromatography (3% XE-61); the employed alkanoic acids had a purity of 99 + %. The synthesized campesteryl alkanoates were purified by column chromatography, followed by recrystallization, and were uniform on thin-layer chromatographic analysis. But the R_F-values of campesteryl, β-sitosteryl, and cholesteryl acetates are approximately the same on silica gel. Therefore, we cannot rule out that the prepared campesteryl alkanoates still contained impurities. These contaminants might be responsible for the colors and the cholesteric mesophase in campesteryl heptanoate. This problem could be solved with a campesterol of 99 + % purity; unfortunately this is very difficult to obtain.

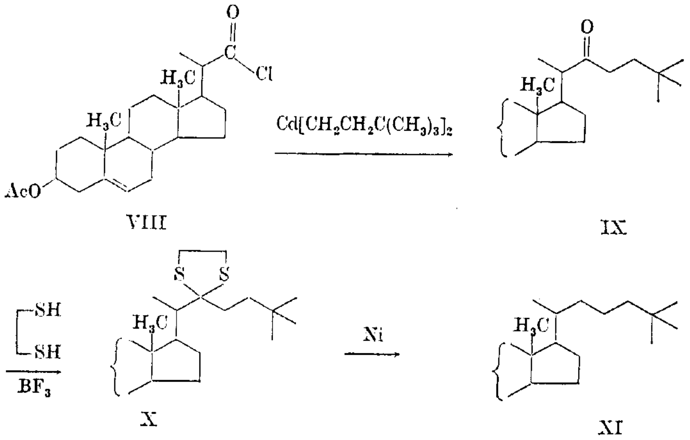
Steric crowding, caused by the 24R-alkyl substituent, might also be responsible for the suppression of a cholesteric mesophase in derivatives of stigmasterol, β-sitosterol, and campesterol, but the absolute configuration of the C-24 substituent apparently is unimportant since the higher alkanoates of ergosterol(10) with a 24S-methyl group exhibit only smectic mesophases. However, this comparison of campesterol and ergosterol is of limited value only, since ergosterol (the trivial name for (24S)-24-methylcholesta-5, 7, 22-trien-3β-ol) has an additional double bond each in ring *B* and in the 17β-side chain. The sterol of choice for a proper comparison would be 22,23-dihydrobrassicasterol (VII),(11) the 24-epimer of campesterol.

Another consideration is the flexibility of the 17β-side chain. The mesomorphic properties are completely lost if the flexibility is restricted by a C-24 alkylidene substitution. This was recently observed with fucosteryl hexadecanoate(10) which has a 24-ethylidene group.

Another possibility would be the analogy to the nematic–smectic case. In many systems of this type the nematic mesophase is eventually displaced by a smectic mesophase with increasing chain length. If we assume that the impurity content is the same in all the campesteryl alkanoates investigated, the impurity effect also should be the same. If this is so, the campesteryl alkanoates would be the first case where the cholesteric mesophase is displaced by the smectic mesophase.

But, with the few data presently available, it is too early to speculate about the cholesteric mesophase observed in campesteryl heptanoate. Further studies with a complete homologous series of alkanoates of a 99+% campesterol are necessary in order to clearly establish the mesomorphic behavior of campesteryl alkanoates.

We prepared 25-*methylcholesteryl acetate*, where the terminal isopropyl group is replaced by the bulkier *tert.*-butyl group, in order to determine whether methyl substitution at C-25 has an influence on the mesomorphic properties. It was synthesized from 3β-acetoxypregn-5-en-20β-carbonyl chloride (VIII) and di(3, 3-dimethylbutyl)cadmium. The intermediate 3β-acetoxy-25-methylcholest-5-en-22-one (IX) yields 3β-acetoxy-25-methylcholest-5-ene (25-methylcholesteryl acetate) (XI) in a two step reaction.



Neither of the two compounds IX and XI exhibited a mesophase although the keto compound IX could be undercooled by more than 100°. Although the acetates might not have been suitable representatives for the study of the mesomorphic properties, Stuart–Briegleb models of these two esters indicated a restriction of the flexibility of the 17β-side chain of cholesterol by the bulky *tert.*-butyl group.

2. *Modifications at C–25*

The effects of changes made at the C-25 position of the 17β-side chain of cholesteryl acetate on the mesomorphic behavior were studied with the following three compounds (Table 2):

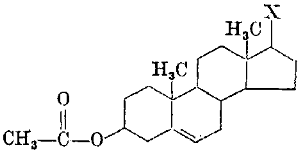
3β-*Acetoxy*-27-*norcholest*-5-*en*-25-*one* (XII)(14) was purified by column chromatography on silica gel. In agreement with an earlier report(6) for the corresponding 4-nitrobenzoate of I, it exhibited a monotropic cholesteric mesophase and cholesteric colors.

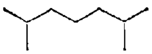
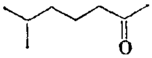
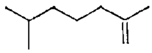
3β-*Acetoxycholesta*-5, 25-*diene* (XIII)(15) was obtained from XII by a modified Wittig reaction.(16) It exhibited a monotropic cholesteric mesophase, but no cholesteric colors.

By another procedure, we also prepared 3β-*acetoxy*-27-*norcholest*-5-*ene* (XIV), where the original 25-keto group has been removed, and found an enantiotropic cholesteric mesophase.

Table 2 summarizes the results obtained for alterations at C-25 in comparision with data for cholesteryl acetate. As long as extreme steric crowding by alkyl substituents is avoided, the mesomorphic transition temperatures do not change much due to alterations in the C-25 position; the cholesteric mesophase is retained and no additional smectic mesophases occur for the 25-keto (XII) or the 25-dehydro (XIII) derivatives. However, if the 27-methyl group is omitted, (XIV), then an enantiotropic cholesteric mesophase is experienced.

TABLE 2



X	Nr	mp	Ch–I
	—	114.2	95.4
	XII	141.0	119.0
	XIII	112.3	86.2
	XIV	112.7	118.8

3. *Modifications at C-20*

The influence of alterations at C-20 on the mesomorphic behavior was studied with the following three compounds (Table 3):

3β-Acetoxy-21-norcholest-5-en-20-one (XV)(17) was prepared and had, after repeated chromatographic purifications, the reported(18) physical properties. Although the isotropic liquid of this compound could be undercooled to about 80° where crystallization occurs, we could not detect any mesophase.

3β-Acetoxycholesta-5, 20-diene (XVI) was obtained from the 20-ketone XV by a normal Wittig reaction,(19) because the modified version(20) did not yield the desired product. It was purified by column chromatography and exhibited a monotropic cholesteric mesophase and a monotropic smectic mesophase.

3β-Acetoxy-21-norcholest-5-ene (XVII) was obtained from the ketone XV by Wolff-Kishner reduction, followed by re-acetylation. The isotropic melt could be cooled below room temperature by chilling the sample with ice water, whereby a bluish tint could be observed briefly before crystallization. It was not possible to observe any mesophase under the polarizing microscope because crystallization interfered. Therefore, it could not be determined whether this blue tint was caused by a mesophase or by light scattering due to small crystallites.

A comparison of these compounds with cholesteryl acetate shows the following differences (see Table 3).

Replacing the 21-methyl group by an oxo group (XV) destroys the mesomorphic character, while replacing it with a methylene group (XVI) reduces the cholesteric-isotropic transition temperature and enhances the mesomorphic properties to a degree that a monotropic smectic phase in addition to a monotropic cholesteric mesophase can be obtained upon cooling. Removing the 21-methyl group (XVII) leads to the loss of a stable cholesteric mesophase.

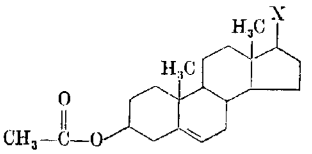
The most surprising fact of this investigation is the comparison between XV and XVI for the following reasons:

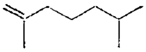
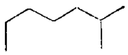
1. Stuart–Briegleb models show very little deviation of the 17β-side chain from that of cholesterol;
2. the rotation of the 17β-side chains about the 17β-bond is restricted to approximately the same degree;

3. the bond polarizabilities of the keto group and the double bond both perpendicular and parallel to the bond differ by only about 30%,†

and yet XVI exhibits a smectic mesophase indicating an increased lateral attraction. This indicates that slight distortions of the electron cloud at the oxygen atom are responsible for the difference in mesomorphic behavior, unless there is a severe impurity effect, which we think we can rule out (both XV and XVI were uniform on thin-layer chromatography on silica gel and silver nitrate-impregnated silica gel).

TABLE 3



X	Nr	mp	Ch–I	S–Ch
	—	114.2	95.4	—
	XV	141.1	—	—
	XVI	99.5	86.6	66.4
	XVII	89.3	—	—

The Stuart–Briegleb model of XVII demonstrates that the 17β-side chain can be freely rotated about the 17β-bond. This unrestricted rotation might deny the molecule the anisotropy of polarizability and asymmetry of sterical arrangement,(21) and thereby apparently prevents the occurrence of mesophases.

† Bond polarizabilities $\alpha \times 10^{25}$ cm^3

	Parallel	Perpendicular
C=O	19.9	7.5
C=C	28.6	10.5

Denbigh, K.G., *Trans. Faraday Soc.* **36**, 936 (1940).

4. *Substitution by Hetero Atoms*

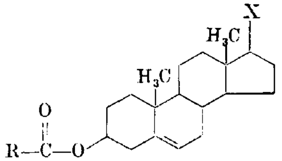
In this last group of compounds we investigated the effects of hetero atoms in the 17β-side chain of cholesteryl alkanoates on the mesomorphic behavior (Table 4).

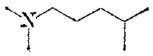
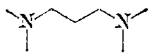
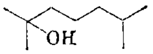
3β-Octadecanoyloxy-20-azacholest-5-ene (XVIII) was obtained by the esterification of 20-azacholest-5-en-3β-ol⁽²²⁾ *via* the imidazolide; it was not mesomorphic. A monotropic mesophase might not be obtainable since the isotropic liquid crystallized already 7° below the melting point.

Similar results were obtained for *3β-octadecanoyloxy-20, 25-diaza-cholest-5-ene* (XIX), which was prepared by esterification of 20, 25-diazacholest-5-en-3β-ol.⁽²³⁾ The isotropic liquid could only be undercooled by about 3°, and no mesophase could be observed.

Although *3β-acetoxy-20-hydroxycholest-5-ene* (XX) could be undercooled from the isotropic liquid by over 80°, it did not reveal any mesomorphic behavior.

TABLE 4



X	Nr	R	mp	Ch–I
	—	acetate	114.2	95.4
	XVIII	octadecanoate	71.7	—
	XIX	octadecanoate	70.1	—
	XX	acetate	156.4	—

In this last group of compounds (see Table 4) all alterations at the 17β-side chain of cholesteryl alkanoates result in a loss of mesomorphic properties. Neither Dreiding stereo models nor Stuart–Briegleb models show any significant difference in the sterical arrangement for the azacholesterols, and the 20-hydroxy group can easily be incorporated without distorting the side chain. Therefore, we conclude that the forces exercised by the free electron pairs of nitrogen and oxygen prevent the materials from arranging in the order which is necessary for mesophases of the cholesteric or smectic type.

Summary and Conclusion

The results of this investigation indicate that the mesomorphic characteristics of 3β-sterol derivatives are very susceptible to structural modifications in the 17β-side chain of cholesteryl alkanoates. Both substitution and changes in the configuration drastically influence the mesomorphic properties.

Alkyl substituents at C-24 retain smectic mesophases but apparently suppress cholesteric properties, while an additional methyl group at C-25 leads to the complete loss of all mesomorphic characteristics.

Variations of the substituents at C-25 only alter the stability of the cholesteric mesophase without causing the loss of mesomorphic properties or increasing the number of mesophases observed.

Modifications at C-20 greatly affect the mesomorphic properties. Increased polarizability as a result of a C-20 double bond leads to the appearance of a monotropic smectic mesophase in addition to a monotropic cholesteric mesophase. If the 21-methyl group is replaced by hydrogen, the 17β-side chain obtains a high degree of rotation about the 17β-bond which might explain why no mesophases are observed. Forces associated with the electron pairs of oxygen might be responsible for the fact that a 20-keto group prevents the occurrence of mesophases. The same forces might account for the observation that a 20-hydroxyl group, or nitrogen in place of C-25 and/or C-20, lead to a complete loss of the mesomorphic properties.

The results presented here once more demonstrate that a very precarious interplay of many factors is responsible for the existence of mesomorphism and the type of mesophase exhibited.

Experimental Part

General: All reactions were carried out in standard glassware and purified nitrogen was used as an inert gas. The purity of starting materials and derivatives was checked by thin-layer chromatography on silica gel and silver nitrate-impregnated silica gel. Transition points were determined with a microscopic Mettler FP-II hot stage; the temperature values are corrected. Combustion analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y. For analogous preparations only one experiment will be given in detail.

Campesteryl alkanoates (VI). A solution of 4.01 g (10 mmol) of campesterol in 100 ml of absolute benzene was distilled azeotropically until about 25 ml remained. This was added to a benzene solution in which 1.58 g (10 mmol) of nonanoic acid had been reacted with 1.78 g (11 mmol) of 1, 1′-carbonyldiimidazole. The progress of the reaction was monitored by thin-layer chromatography. Without catalysis with sodium methoxide hardly any reaction took place at either room temperature or under reflux, therefore, about 50 mg were added. After 4 hr of reflux the benzene was distilled off and replaced with *n*-hexane. The precipitated imidazole was filtered off. Purification was achieved by column chromatography on silica gel using benzene/*n*-hexane 3/7 (v/v) as eluent. The fractions were checked by thin-layer chromatography, and the ones containing campesteryl nonanoate were combined, the solvent distilled off *in vacuo*, and the residue recrystallized twice from ethanol. Its physical properties, as well as those of the other alkanoates, are listed in Tables 1 and 5.

3β-Acetoxy-25-methylcholest-5-en-22-one (IX). To a Grignard solution, prepared from 33.02 g (0.2 mol) of 1-bromo-3, 3-dimethylbutane and 5.35 g (0.22 g-atom) of magnesium in 200 ml of absolute ether, 20.16 g (0.11 mol) of dry cadmium chloride was added. The mixture was refluxed for 30 min and the solvent removed *in vacuo*. Absolute benzene (250 ml) was added, the mixture boiled under reflux for 1 hr and about 100 ml of benzene distilled off to carry over the last traces of ether. A solution of crude 3β-acetoxy-pregn-5-en-20β-carbonyl chloride(24) (from 38.86 g (0.1 mol) of the acid) in 350 ml of absolute benzene was added during 1 hr of vigorous stirring. After 3 hr of reflux the reaction mixture was cooled and decomposed by the addition of 10 ml of water and 150 ml of 2N hydrochloric acid. The crude material was collected and recrystal-

TABLE 5

Campesteryl alkanoate	Yield %	Mp, °C	Formula	Mol. Wt.	Analyses					
					calc'd			found		
					C	H	O	C	H	O
heptanoate	72	98.2	$C_{35}H_{60}O_2$	512.9	81.97	11.79	6.24	81.78	11.70	6.14
octanoate	79	84.2	$C_{36}H_{62}O_2$	526.9	82.07	11.86	6.07	81.90	11.87	5.99
nonanoate	63	69.4	$C_{37}H_{64}O_2$	540.9	82.16	11.93	5.92	82.20	12.00	5.95
octadecanoate	68	94.0	$C_{46}H_{82}O_2$	667.1	82.86	12.39	4.80	82.96	12.53	4.74

lized from acetone and from ethanol. Yield: 30.0 g (65%); mp 188.5°. Not mesomorphic.

Calc'd for $C_{30}H_{48}O_3$ (456.7)	C, 78.90;	H, 10.59;	O, 10.51
Found	C, 78.96;	H, 10.56;	O, 10.45

3β-Acetoxy-25-methylcholest-5-en-22-one ethylenethioketal (X). 25 ml of 1, 2-ethanedithiol and 25 ml of borontrifluoride etherate were added to a solution of 18.3 g (40 mmol) of IX in 100 ml of hot glacial acetic acid. The oil, which had separated after 24 hr, was extracted into chloroform; the solution washed with water, 2N sodium carbonate, dried, and concentrated. The oil did not solidify and therefore was used immediately in the following desulfurization.

3β-Acetoxy-25-methylcholest-5-ene (XI). Exploiting a well-established desulfurization method,(25) the solution of the crude ethylenethioketal X in 100 ml of warm absolute dioxan was added slowly to a vigorously stirred slurry of Raney nickel, which had been freshly prepared from 150 g of the alloy, in 100 ml of absolute ethanol. Progress of the desulfurization was monitored by thin-layer chromatography. After 1 hr the reaction was complete, the mixture was filtered, and the solid residue was washed twice with 100 ml of hot benzene. The combined filtrates were evaporated to dryness, and the residue chromatographed on silica gel, using benzene/*n*-hexane 1/1 as eluent. The material, which was obtained in a yield of about 50%, was then recrystallized from acetone and melted at 146.8°. It was not mesomorphic.

Calc'd for $C_{30}H_{50}O_2$ (442.7)	C, 81.39;	H, 11.38;	O, 7.23
Found	C, 81.51;	H, 11.33;	O, 7.02

3β-Acetoxycholesta-5, 25-diene (XIII). Methylenetriphenylphosphorane (8 mmol), prepared according to Greenwald *et al.*,(20) was obtained as an orange solution in 100 ml of dimethylsulfoxide. A solution of 2.14 g (5 mmol) of 3β-acetoxycholest-5-en-25-one (XII) was added, whereby the color of the solution immediately turned pale yellow and then almost vanished as the reaction was kept under reflux. Progress of the Wittig reaction was monitored by thin-layer chromatography.(26) After 4 hr the reaction mixture was filtered and cooled to room temperature, whereby the crude product crystallized. Purification was achieved by column chromatography using silica gel as adsorbent and a 1/1-mixture of benzene/*n*-hexane as eluent. The acetate was then recrystallized from acetonitrile/butanone. Yield: 0.8 g (37.5%). It melted at 112.3° (reported 112°(15); 113–114° (26)) and cleared at 86.2°. The monotropic cholesteric mesophase did not exhibit colors.

3β-*Acetoxy*-27-*norcholest*-5-*ene* (XIV). Because of a possible epimerization at C-20(24,27) we did not attempt a Wolff–Kishner reduction of 3β-acetoxy-27-norcholest-5-en-25-one (XII), but chose another method. This procedure is given in the following paper. The material was enantiotropic cholesteric with mp 112.7° and cp 118.8° (reported(28) mp 123–124°).

3β-*Acetoxy*-21-*norcholest*-5-*en*-20-*one*(17) (XV) was purified by chromatography on silica gel using benzene/*n*-hexane 1/1 as eluent. After recrystallization from ethanol it melted at 141.1° (reported(18) 142–143°). Not mesomorphic.

3β-*Acetoxycholesta*-5, 20-*diene* (XVI). Attempts to achieve the Wittig reaction by the method employed for XIII, as given in detail above, failed completely. Even under reflux only traces of reaction product were formed and most of the starting ketone could be recovered by extraction. Therefore, the procedure of the normal Wittig reaction(19) was followed. The crude material was purified by chromatography on silica gel with ethyl acetate/*n*-hexane 1/9 as eluent. It was uniform on thin-layer chromatography on silver nitrate-impregnated silica gel. After recrystallization from acetonitrile it melted at 99.3° (reported(19) 95–98°). However, the yield of 6% was only a fraction of that obtained by previous authors. Microscopic investigation gave the following data: mp 99.3°, Ch-I 86.6°, S-Ch 66.9°. Cholesteric colors were observed between 86.5° and 85.9°.

3β-*Acetoxy*-21-*norcholest*-5-*ene* (XVII) was prepared according to Bergmann *et al.*(17) by Wolff–Kishner reduction of 3β-acetoxy-21-norcholest-5-en-20-one (XV) followed by reacetylation. After chromatography on silica gel with benzene/*n*-hexane 1/1 as eluent, followed by recrystallization from acetonitrile, it melted at 89.3° (reported(17) 84°).

3β-*Octadecanoyloxy*-20-*azacholest*-5-*ene* (XVIII). The preferred method of esterification(29) was carried out in the same manner as for the campesteryl alkanoates from 20-azacholesterol(22) and octadecanoic acid. The crude material was purified by column chromatography using silica gel as adsorbent and a 5/95-mixture of ethyl acetate/*n*-hexane as eluent. After recrystallization from ethanol, the ester (69% yield) melted at 71.7°. Not mesomorphic.

Calc'd for $C_{44}H_{79}NO_2$ (654.1)	C, 80.79;	H, 12.17;	N, 2.14
Found	C, 80.88;	H, 12.08;	N, 2.27

3β-*Octadecanoyloxy*-20, 25-*diazacholest*-5-*ene* (XIX) was prepared as above from 20, 25-diazacholesterol.(23) It was purified on aluminum oxide (Merck, acc. to Brockmann) by elution with ethyl acetate/*n*-hexane 3/7. Recrystallization from ethanol gave a yield of 42%, mp 70.1°. Not mesomorphic.

Calc'd for $C_{43}H_{78}N_2O_2$ (655.1)	C, 78.84;	H, 12.00;	N, 4.28;	O, 4.88
Found	C, 78.73;	H, 12.14;	N, 4.14;	O, 4.81

3β-*Acetoxy*-20-*hydroxycholest*-5-*ene* (XX) was prepared according to literature.(30,31) After chromatography on silica gel with benzene/*n*-hexane 3/7 as eluent and recrystallization from acetonitrile/butanone a yield of 43% was obtained; mp 156.4° (reported 155–156°).

Microscopic investigation revealed that this compound has several solid modifications. We observed a first melting at 125°, followed by resolidification, and a second melting at 156.4°. On cooling it solidified around 50° without exhibiting any mesophase.

3β-*Acetoxycholesta*-5, 20(22)-*diene* was obtained by Bergmann *et al.*(30) by dehydration of 20-hydroxycholesteryl acetate (XX) with phosphorous oxychloride in absolute pyridine. The material obtained in our experiment had the reported properties and was uniform on thin-layer chromatography (Silica Gel, Merck, pre-coated plates, ethyl acetate/*n*-hexane 1/9). However, thin-layer chromatography on silver nitrate-impregnated silica gel HR (20% silver nitrate) with benzene, revealed three distinct spots, probably the mixture of all three possible isomers. A similar non-specificity has been reported recently(26) for the dehydration of 3β-acetoxy-25-hydroxycholest-5-one.

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