(81% yield) of *trans*-1-(*p*-bromobenzenesulfonyl)-2-phenylcyclopropane, mp 106–107.5°.

***trans*-1-(*o*-Nitrobenzenesulfonyl)-2-phenylcyclopropane (X).**—*trans*-1-Phenyl-2-(*o*-nitrobenzenesulfonyl)ethene (2.89 g, 0.01 mol) gave, after dilution with 250 ml of water and stirring for 10 days, a finely divided, light tan solid. The solid was too finely divided to be filtered, so the water was carefully decanted leaving the light tan solid. The solid was dissolved in hot 95% ethanol, and the resulting solution was cooled giving 1.25 g of crude cyclopropyl sulfone. The crude sulfone was recrystallized from 95% ethanol to give 0.65 g (21% yield) of *trans*-(*o*-nitrobenzenesulfonyl)-2-phenylcyclopropane, mp 91.5–92.5°.

***trans*-1-(Benzenesulfonyl)-2-(*p*-tolyl)cyclopropane (XI).**—*trans*-1-(*p*-Tolyl)-2-(benzenesulfonyl)ethene (2.58 g, 0.01 mol) afforded, after one recrystallization from 95% ethanol, 1.85 g (68% yield) of *trans*-1-(benzenesulfonyl)-2-(*p*-tolyl)cyclopropane, mp 98.5–100°. The sulfone was yellow in color and was recrystallized five times from 95% ethanol to give 0.65 g, mp 102–103.5°.

***trans*-1-(Benzenesulfonyl)-2-(4-biphenyl)cyclopropane (XII).**—*trans*-1-(4-Biphenyl)-2-(benzenesulfonyl)ethene (3.20 g, 0.01 mol) gave 3.25 g of crude cyclopropyl sulfone. The crude sulfone was decolorized and recrystallized twice from 95% ethanol to give 2.10 g (63% yield) of *trans*-1-(benzenesulfonyl)-2-(4-biphenyl)-cyclopropane, mp 133–134°.

***trans*-1-(Benzenesulfonyl)-2-(2,6-dimethylphenyl)cyclopropane (XIII).**—*trans*-1-(2,6-Dimethylphenyl)-2-(benzenesulfonyl)ethene (2.72 g, 0.01 mol) afforded 2.40 g of crude cyclopropyl sulfone. The crude sulfone was recrystallized from 95% ethanol to give 2.25 g (79% yield) of *trans*-1-(benzenesulfonyl)-2-(2,6-dimethylphenyl)cyclopropane, mp 93–95°.

***trans*-1-(Benzenesulfonyl)-2-(*p*-chlorophenyl)cyclopropane (XIV).**—*trans*-1-(*p*-Chlorophenyl)-2-(benzenesulfonyl)ethene (2.78 g, 0.01 mol) gave 2.60 g of crude cyclopropyl sulfone. The crude sulfone was recrystallized from 95% ethanol to give 2.15 g (74% yield) of *trans*-1-(benzenesulfonyl)-2-(*p*-chlorophenyl)cyclopropane as light yellow crystals, mp 101–103°. In a similar experiment, the yellow sulfone was decolorized and recrystallized three times from 95% ethanol to give 1.00 g of *trans*-1-(benzenesulfonyl)-2-(*p*-chlorophenyl)cyclopropane as colorless crystals, mp 101–102°.

Attempted Preparation of *trans*-1-(Benzenesulfonyl)-2-(*m*-nitrophenyl)cyclopropane (XV).—*trans*-1-(*m*-Nitrophenyl)-2-(benzenesulfonyl)ethene (2.89 g, 0.01 mol) gave a small amount of brown tar and 0.16 g of a pale yellow solid. The infrared spectrum of the solid indicated that it was mainly starting vinyl sulfone.

Registry No.—Cyclopropanesulfonic acid, 21297-68-7; II, 21309-02-4; IV, 21309-03-5; V, 21309-04-6; VI, 21309-05-7; VII, 21309-06-8; VIII, 21309-07-9; IX, 21309-09-1; X, 21309-10-4; XI, 21309-11-5; XII, 21309-12-6; XIII, 21309-13-7; XIV, 21309-14-8; **3**, 21297-81-4; **4** (*trans*), 21309-15-9; **5**, 21297-82-5; **6**, 21297-83-6; **9**, 21297-84-7; **10**, 21297-80-3; **11** (*trans*), 17299-25-1; **12**, 21297-85-8; **13**, 21297-86-9; phenyl 3-chloropropanesulfonate, 21297-87-0.

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Liquid Crystals. II.[1] Cholesteric Properties of Some 9,19-Cyclopropane Triterpene Fatty Acid Esters[2]

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In an attempt to relate structure and the ability of certain steryl esters to form a cholesteric mesophase, nine even-chain esters of 24-methylene cycloartanol were synthesized. The esters varied in chain length from acetate to stearate. None of these esters was cholesteric, while four exhibited a smectic mesophase. This substantiates an earlier observation that the C-24 (31) double bond in esters of this triterpene interferes with formation of a cholesteric mesophase. Each of the esters was reduced by catalytic hydrogenation. Four of the dihydro esters were smectic, while three were cholesteric. To investigate the effect of modifications of the steroid nucleus, the palmitate ester of cycloeucalenol was prepared and found not to be mesomorphic, while the dihydro ester exhibited a cholesteric transition state, again demonstrating the influence of the 24-methylene group. The effect of double-bond position in the side chain was further explored by the synthesis of cycloartenol palmitate. In this case, the unsaturated ester exhibited a cholesteric mesophase. With this type of nucleus, therefore, a C-24 (25) double bond is compatible with the formation of a cholesteric transition state, at least when there is no substitution at C-24. These data strongly suggest a very critical steric requirement for cholesteric mesomorphism, and are discussed in detail.

Liquid crystals are compounds which do not pass directly from the crystalline to the isotropic liquid state when melted. The intermediate phase has properties generally associated with crystalline substances even though the material is a liquid. The seemingly contradictory term "liquid crystal" is thus used to describe these interesting substances.[4] Such compounds are anisotropic and transmit light with varying velocity in different directions.[5] They are thus birefringent (doubly refractive). The reason for this crystal-like behavior of mesomorphic liquids is the parallel alignment of the relatively rigid, rod-shaped molecules, due in part to mutual attractive forces. Liquid crystals are subdivided into three categories—nematic,

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(1) For the first paper in this series, see F. F. Knapp and H. J. Nicholas, *J. Org. Chem.*, **33**, 3995 (1968).

(2) F. F. Knapp and H. J. Nicholas, presented in part at the 6th International Symposium on the Chemistry of Natural Products (Steroids and Terpenes), Mexico City, April 1969.

(3) NASA Predoctoral Fellow. This work represents part of the research partially fulfilling the requirements for the degree of Doctor of Philosophy at St. Louis University.

(4) O. Lehmann, *Z. Phys. Chem.*, **4**, 468 (1889).

(5) G. H. Brown, *Chemistry*, **40**, 10 (1967).

smectic, and cholesteric—depending upon the particular type of molecular orientation in the mesophase. One book[6] and several excellent reviews[7,8] are available describing in detail the molecular orientation and properties of each class of these substances.

As more compounds become available, studies of structure and the ability of a given series of compounds to exhibit liquid crystallinity become an ultimate aim. Steric effects have been correlated with nematic behavior[9] and recent studies of the effect of terminal group substitution on the nematic properties of some benzylideneanilines have been reported.[10] Until our recent report of the cholesteric properties of 24-ξ-methyl-9,19-cyclolanostan-3β-yl palmitate,[1] cholesterol and closely related steryl esters were the only steroid forms known to exhibit cholesteric mesomorphism. For this reason very little is known about the relationship between structure and this phenomenon. We have therefore directed our efforts at preparing other esters of 24-ξ-methyl-9,19-cyclolanostan-3β-ol and related triterpenes in an attempt to study structural effects in this series of compounds.

Experimental Section

General.—Melting points were determined in capillary tubes using a Thomas–Hoover Uni-Melt apparatus. Phase transitions were detected using a Nalge–Axelrod hot-stage polarizing microscope. All solvents were analytical grade and were distilled before use. Mass spectra were determined using an LKB model 9000 instrument under the conditions previously described.[11]

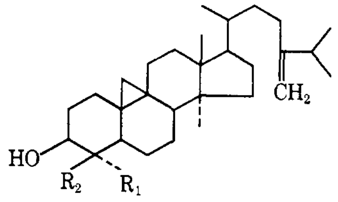
Isolation and Purification of Triterpenes.—24-Methylene cycloartanol (I) and cycloeucalenol (II) were isolated from the nonsaponifiable material from banana peel as previously described.[11] Cycloartenol (V) was isolated from the dried seeds of *Strychnos nux-vomica* in an analogous manner to that described by Bentley, *et al.*[12] The triterpene was purified by the usual procedures and melted at 106–109° (lit. mp 99°, solvent; 115°, anhydrous). It had the same chromatographic behavior (tlc, glpc) and mass spectral fragmentation[13] as that described for cycloartenol.

Chromatography.—Thin layer chromatography (tlc) was performed using silica gel G spread 250 μ thick on glass plates. With the solvent system trimethylpentane–ethyl acetate–acetic acid, 40:20:0.4 (v/v/v), esterified material ran with the solvent front while the 4α-methyl and 4,4-dimethyl triterpenes were considerably more polar (R_f = 0.54 and 0.62, respectively). Chromatograms were visualized by heating after being sprayed with anisaldehyde reagent. As a function of chain length, esters have different mobilities using the solvent system hexane–ether, 93:7 (v/v) (I acetate, R_f = 0.57; I palmitate, R_f = 0.84). Reduced counterparts were separated from the C-24 unsaturated parent compounds by using the hexane–ether solvent system and silica gel G plates impregnated with 12% silver nitrate (w/w) (I acetate, R_f = 0.26; III acetate, R_f = 0.42; I palmitate, R_f = 0.54; III palmitate, R_f = 0.87). Gas–liquid partition chromatography (glpc) was performed using a Barber-Colman model 5000 instrument. The triterpene esters were analyzed by modifications of the method of Kuksis.[14,15] Glass columns (600 × 4 mm) were packed with Gas Chrom Q (100/120 mesh) coated with 3% SE-30. The column was conditioned before use for 72 hr at 320° with the carrier gas (N_2) flowing at 100 cm^3/min. The column was routinely operated, however, at this flow rate at 290°. Palmitic acid esters had the following absolute retention times: cycloeucalenol palmitate, 7.0 min; cycloartenol palmitate, 7.5 min; 24-methylene cycloartanol palmitate, 8.0 min.

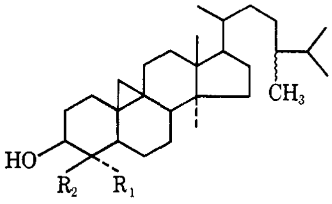
Synthesis of Triterpene Esters.—The esters were prepared essentially in the same manner as described previously.[1] The triterpene (50–100 mg) was refluxed with a 1.5 *M* excess of the acyl chloride in benzene containing a small amount of pyridine under anhydrous conditions. After 1 hr, an aliquot of the reaction mixture was analyzed by tlc to insure complete esterification. The reaction mixture was diluted with ether and washed successively with 5% hydrochloric acid and water. The solution was dried over anhydrous sodium sulfate and the solvent was removed by distillation. The residue was added in benzene to a short alumina column, the esterified material being eluted with this solvent. The esters were crystallized to constant melting point from either acetone or methanol–ether. In general, long-chain esters crystallized best from the latter solvent. Esters were reduced with hydrogen (40 psi) by shaking for 1 hr in the presence of Adams' catalyst (PtO_2) in ethyl acetate solution. The product was isolated in the usual manner and crystallized as indicated above. The purity of each preparation was carefully checked by both tlc and glpc.

Results

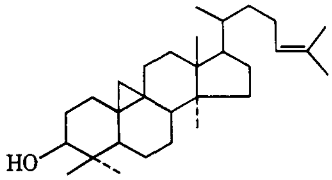
The properties of the synthetic esters are summarized in Table I. In all cases, the esters were highly purified, since we have found the formation of a mesophase to be extremely sensitive to impurities. Eight new smectic liquid crystals have been prepared. Of particular interest are the six new cholesteric compounds.



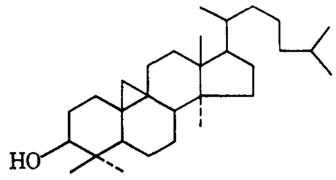
I, $R_1 = R_2 = CH_3$
II, $R_1 = CH_3, R_2 = H$



III[16], $R_1 = R_2 = CH_3$
IV[16], $R_1 = CH_3, R_2 = H$



V



VI

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[15] A. Kuksis, *Can. J. Biochem.*, **42**, 407 (1964); 419 (1964).

[16] The configuration of the C-24 methyl group has not been determined.

TABLE I

PHASE TRANSITION TEMPERATURES OF VARIOUS TRITERPENE ESTERS

Ester[a]	Mp, °C	Phase transition temp, °C	Associated color[b]
I Acetate	111–112	. . .	. . .
Reduced[c]	110–111.5	. . .	. . .
I Butyrate	72–73	sm[d] → iso[e] 110.5	. . .
Reduced	77.5–78	sm → iso 114.5	. . .
I Hexanoate	106–107	sm → iso 112	. . .
Reduced	107–108	sm → iso 122	. . .
I Octanoate	74–75	sm → iso 101.5	. . .
Reduced	63–64	sm → iso 83.5	Faint blue
I Decanoate	65–67	sm → iso 55	. . .
Reduced	82.5–84	sm → iso 83.5	. . .
I Laurate	54–57	. . .	. . .
Reduced	58–60	ch[f] → iso 65.5	Green or violet
I Myristate	61–62	. . .	. . .
Reduced	65–66	ch → iso 67.5	Green or violet
I Palmitate[g]	57–59	. . .	. . .
Reduced	64–65	iso → ch 64	Violet
HCl adduct[h]	79–80	. . .	. . .
I Stearate	55–63	. . .	. . .
Reduced	65–68	. . .	. . .
II Palmitate	60–62	. . .	. . .
Reduced	62–64	iso → ch 52	Green or violet
V Palmitate	52–54	iso → ch 51	Green or violet
Reduced	52	iso → ch 72	Green or violet

[a] I = 24-methylene cycloartanol, II = cycloeucalenol, V = cycloartenol. [b] The color sometimes varied dependent upon the light source. [c] Reduced refers to the product obtained upon catalytic reduction of the double bond. [d] Smectic. [e] Isotropic. [f] Chloesteric. [g] F. F. Knapp and H. J. Nicholas, *J. Org. Chem.*, **33**, 3995 (1968). [h] Presumably a Markovnikov addition product at the C-24 olefinic bond (patent now pending on these mesomorphic substances.)

Discussion

Cholesteric liquid crystals have a layer structure with the long axes of the parallel molecules lying within the strata. Furthermore, the direction of the axes is believed to be displaced slightly and regularly from layer to adjacent layer so that the progressive change in orientation can be considered to describe a helix. This arrangment of molecules has been deduced from the extremely high optical rotatory power of such compounds and the unusual optical interference effects.[6] This alignment results in the phenomenon of circular dichroism, and most cholesteric liquid crystals display brilliant colors. With cholesteryl esters as a model system, it has been suggested that the projection of the side chain on the D ring out of the layer plane interferes with a strictly parallel molecular orientation in adjoining layers and produces the regular layer-to-layer displacement mentioned above.[17] If this is the case, alterations of either the size or the configuration of the side chain should enhance or perhaps destroy the ability of a given steryl ester to form the cholesteric mesophase. Similarly, alterations of the steroid nucleus should affect this phenomenon. Our finding that 24-methylene cycloartanol (I) palmitate is not mesomorphic, while the 24-dihydro form, 24-ξ-methyl-9,19-cyclolanostan-3β-yl palmitate (III palmitate), exhibits a brilliant blue cholesteric mesophase[1] gave us a new model with which to study these structural effects. We have found it very difficult to differentiate between a smectic and a cholesteric mesophase using the polarizing microscope. This is because they are both turbid, birefringent phases. We therefore assign the cholesteric mesophase to those substances which form a turbid mesophase and also give a color which can be detected with the naked eye. Likewise, turbid, colorless mesophases are designated as smectic.

By the synthesis of a homologous series of esters, we have now found (Table I) that the octanoate, laurate, and myristate esters of 24-ξ-methyl-9,19-cyclolanostan-3β-ol form cholesteric mesophases which display definite colors. For the octanoate, only a faint, fugitive blue was observed as the isotropic melt underwent transition to a smectic mesophase. The colors were much brighter and more peristent in the other compounds. In analogy with the palmitate ester, the corresponding esters of 24-methylene cycloartenol are not liquid crystals. With both triterpenes, the butyrate, hexanoate, and decanoate esters are also mesomorphic, but their mesophases proved to be colorless. This lack of color, the texture observed in the polarizing microscope, and the high viscosities indicate that these esters are smectic. Although we have designated turbid, colorless mesophases as being smectic, it seems likely that the decanoate of the saturated ester also forms a cholesteric mesophase which does not exhibit the color phenomenon. A colorless cholesteric mesophase, that of cholesteryl stearate, has been observed before.[6] There is no apparent reason for a discontinuity in the octanoate through the palmitate series with regard to cholesteric liquid crystallinity. These considerations suggest that the decanoate may form a transient cholesteric mesophase which did not display any color in our experiments. The important point of these results is of course that while several esters of 24-ξ-methyl-9,19-cyclolanostan-3β-ol are cholesteric liquid crystals, none of the esters of 24-methylene cycloartanol exhibits this mesophase. This dramatically illustrates the disruptive effect the C-24 double bond has on the alignment of molecules in the cholesteric mesophase. It will also be noted from Table I that a hydrogen chloride adduct at the double bond of 24-methylene cycloartanol yielded

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(17) J. L. Fergason, *Sci. Amer.*, **211**, 77 (1964).

a compound which was not mesomorphic. In this case, the inability to form a mesophase may be due to the bulky chlorine atom or its associated dipole moment.

The disruptive effect of the 24-methylene group was further substantiated by the synthesis of cycloeucalenol palmitate (II palmitate). This triterpene differs from 24-methylene cycloartanol in that it has only one methyl group at C-4 (4α-methyl). From a structural standpoint, it therefore seemed of interest to see what effect this minor nuclear change would have on the formation of a mesophase. As is indicated in Table I, the palmitate ester of this triterpene is not mesomorphic. Catalytic reduction of the double bond, however, gave a dihydro ester (4α,14α,24ξ-trimethyl-9,19-cyclocholestan-3β-yl palmitate) which exhibited a beautiful green cholesteric transition state. These data further illustrate the effect of the 24-methylene side chain in these types of compounds.

Another variation which was studied was the effect the double bond in a different position of the side chain would have. Cycloartenol (V) resembles 24-methylene cycloartanol by having the same nucleus but with no substitution in the side chain and a C-24(25) double bond. The palmitate ester of this triterpene is cholesteric, as is indicated in Table I. The corresponding cycloartanol palmitate (VI palmitate) is also mesomorphic. This illustrates that the disruptive effect of a double bond is dependent upon its position in the side chain. This is obviously a steric effect and is important to any future studies of molecular structure and cholesteric mesomorphism.

Other than the work of Wiegand,[18] there have essentially been no reported studies on structural effects of this phenomenon with steryl esters. Wiegand's studies illustrated that while cholesterol, cholestanol, and various di- and triunsaturated derivatives of cholesterol were cholesteric, epicholesterol (3α-ol), coprosterol, and any unsaturated forms of cholesterol with a C-14(15) double bond were not. Epicholesterol and coprostanol are spatially "kinked," and this can be shown by the construction of appropriate models. It is therefore easily understood why esters of these sterols are not mesomorphic. We have constructed models of various unsaturated forms of cholesterol (cholest-5-en-3β-ol, cholest-5,8-dien-3β-ol, cholest-14-en-3β-ol, etc.) with interesting results. The side chain projects from the molecular plane at approximately the same angle, regardless of the position or the number of double bonds. However, when the double bond is between carbon atoms C-14 and C-15, the side chain projects quite differently. This is the only major difference in the three-dimensional representations of these molecules and must therefore be responsible for the inability of compounds with a C-14(15) bond to be cholesteric.

The spacial differences of the triterpene esters described in this paper are more subtle. The orientation of the side chain must be very important, and the presence of the 24-methylene group has now been shown to be responsible for the inability of these esters to form a cholesteric mesophase. Models have indicated that the side chains of those triterpenes whose esters are cholesteric (III, IV, V, and VI) can assume several configurations that the side chains of I and II cannot. Since it has not yet been shown exactly how the side chain projects in the cholesteric mesophase, we cannot predict what the critical conformation is. It is obvious, however, that the formation of a cholesteric mesophase requires maximal interaction of molecules and that rather small changes in configuration can result in disruption of the mesophase. Although these data give some insight into the subtle structural requirements of the cholesteric mesophase, their accurate interpretation must await further physical measurements.

Registry No.—I acetate, 1259-94-5; I acetate, reduced, 21562-75-4; I butyrate, 21562-76-5; I butyrate, reduced, 21562-77-6; I hexanoate, 21562-78-7; I hexanoate, reduced, 21562-79-8; I octanoate, 21562-80-1; I octanoate, reduced, 21562-81-2; I decanoate, 21562-82-3; I decanoate, reduced, 21562-83-4; I laurate, 21562-84-5; I laurate, reduced, 21562-85-6; I myristate, 21562-86-7; I myristate, reduced, 21562-87-8; I palmitate, 17478-48-7; I palmitate, reduced, 17478-39-6; I stearate, 21562-90-3; I stearate, reduced, 21562-91-4; II palmitate, 17344-72-8; II palmitate, reduced, 21562-93-6; V palmitate, 21562-94-7; V palmitate, reduced, 21562-95-8.

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[18] C. Wiegand. *Z. Naturforsch.*, **4b**, 249 (1949).