Crystal structure of cholesteryl decanoate[1]
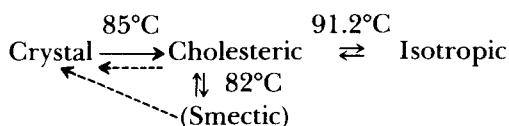
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Abstract Cholesteryl decanoate ($C_{37}H_{64}O_2$) is monoclinic, space group $P2_1$, with cell dimensions $a = 12.931$ (6), $b = 9.066$ (2), $c = 30.22$ (1) Å, $\beta = 91.14$ (4)°, and $Z = 4$. The atomic coordinates from cholesteryl laurate were used in an initial trial structure which was refined by block diagonal least-squares methods with 1846 observed X-ray reflections ($R = 0.129$). Molecules A and B have almost fully extended conformations, except at the ester bonds and towards the end of the decanoate B chain. The molecules are arranged in antiparallel array forming monolayers of thickness $d_{001} = 30.22$ Å, with the molecular long axis making an angle of about 67° with the layer interface. The crystal structure is very similar to that of cholesteryl nonanoate and cholesteryl laurate.—**Pattabhi, V., and B. M. Craven.** Crystal structure of cholesteryl decanoate. *J. Lipid Res.* 1979. **20:** 753–759.

Supplementary key words cholesteryl nonanoate · cholesteryl laurate · phospholipids

The crystal structure determination of cholesteryl decanoate was undertaken as part of a series involving cholesteryl esters of fatty acids. The crystal structures of the homologous cholesteryl *n*-alkanoates are of interest because of the differences in cholesteryl–cholesteryl, alkyl–alkyl, and cholesteryl–alkyl interactions as a function of chain length. The crystalline and liquid crystalline phases of cholesteryl decanoate undergo phase transformations which are similar to those of the nonanoate ester and have been summarized (1) as

$$\text{Crystal} \xrightarrow{85°C} \text{Cholesteric} \xrightarrow{91.2°C} \rightleftarrows \text{Isotropic}$$
$$\updownarrow 82°C$$
$$\text{(Smectic)}$$

(---- indicates the transformation takes place on super cooling).

Cholesteryl decanoate appears to have only one crystalline phase, as in the case of cholesteryl nonanoate.

The crystals are isostructural with those of cholesteryl nonanoate (2) and cholesteryl laurate (3).[3]

EXPERIMENTAL

Cholesteryl decanoate, obtained from Supelco Chemical Co., Bellefonte, PA, was crystallized by Patricia Sawzik of this laboratory as thick needles by slow evaporation (2 months) from *n*-pentanol. These crystals melt at 83.8°C to a cloudy liquid which on further heating is transformed to clear isotropic liquid at ~91°C. On cooling, the transition from a clear to a cloudy liquid (91°C) is followed by rapid color changes and crystallization over a narrow temperature range near 81°C. Preliminary crystal data obtained from X-ray Weissenberg photographs were in agreement with those reported by Barnard and Lydon (4). Subsequent X-ray data collection was carried out at room temperature using a Nonius CAD-4 diffractometer and graphite–monochromated Mo$K\alpha$ radiation ($\lambda = 0.7107$ Å). A crystal of dimensions $0.4 \times 1.0 \times 0.2$ mm along the a, b, and c directions was mounted with its b^* axis making an angle of 1.2° with the diffractometer Φ-axis. The crystal lattice parameters (**Table 1**) were obtained by a least-squares fit of 46 reflections with $9 \leq \theta < 17°$. X-ray intensities of 2492 non-symmetry-related reflections with $\sin\theta/\lambda < 0.48$ Å^{-1} were collected by $\omega/2\theta$ scan, out of which 1846 reflections with $I > 2\sigma(I)$ were used in structure refinement. The variance in the intensity was assumed to be $\sigma^2(I) = \sigma^2 + (0.02\ I)^2$ where σ^2 is the variance due to counting statistics.

Since the cell dimensions and X-ray intensity data

TABLE 1. Crystal data

Crystal system	monoclinic
Space group	$P2_1$
Z	4
Molecular weight	540
Cell dimensions	$a = 12.931(6)$ Å
	$b = 9.066(2)$
	$c = 30.22(1)$
	$\beta = 91.14(4)°$
Volume	$3542(3)$ Å^3
D_c	1.012 gcm^{-3}
D_m	1.010 gcm^{-3}
$\mu(MoK\alpha)$	0.646 cm^{-1}
Molecular formula	$C_{37}H_{64}O_2$

for cholesteryl decanoate were similar to those of cholesteryl laurate (except a difference of 2.2 Å in the c-axis length), the atomic positional parameters of the latter were used as a starting model in Fourier refinement. The initial R-factor for the model obtained from the Fourier map was 0.38, where $R = \Sigma|\Delta|/\Sigma|F_{obs}|$ and $\Delta = |F_{obs}| - |F_{calc}|$. After five cycles of block diagonal least-squares refinement, the R-factor dropped to 0.24. The function minimized was $\Sigma w\Delta^2$, where $w = 1/\sigma^2$ (F_{obs}). The X-ray scattering factors were those of Cromer and Waber (5) for carbon and oxygen and of Stewart, Davidson, and Simpson (6) for hydrogen.

The refinement did not progress satisfactorily due to some of the chain atoms having thermal parameters that increased to very large values. A Fourier map leaving out atoms C(24) through C(27) in molecule A and C(34) through C(37) in molecule B indicated revised configurations for atoms C(25) through C(27) in molecule A and for C(36) and C(37) in molecule B. Further refinement with damping factors 0.2 in the changes of both positional and thermal parameters reduced the R-value to 0.20. A difference map computed at this stage revealed all the hydrogen atoms except those bonded to the terminal carbon atoms C(27) and C(37). Hydrogen atoms were included in the refinement with fixed parameter values. For convenience, hydrogen atomic positions were calculated from the carbon framework assuming standard geometry (C–H distances 1.0 Å) with isotropic temperature factors corresponding to the bonded carbon atom. In the final cycles, anisotropic thermal parameters were refined only for the tetracyclic ring atoms. Final positional parameters for the non-hydrogen atoms are listed in **Table 2**.[4] The final R-value was 0.129.

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[4] Observed and calculated structure amplitudes, thermal parameters of the non-hydrogen atoms, and the assumed hydrogen atom parameters can be obtained as described in footnote 1.

TABLE 2. Positional parameters for non-hydrogen atoms ($\times 10^4$)

Atom	x/a	y/b	z/c
Molecule A			
C 1A	-4894 (17)[a]	2201 (28)	1653 (7)
C 2A	-5433 (20)	1852 (28)	1209 (6)
C 3A	-5228 (15)	249 (27)	1083 (6)
C 4A	-5436 (19)	-843 (23)	1471 (8)
C 5A	-4895 (15)	-420 (24)	1873 (6)
C 6A	-4346 (21)	-1308 (28)	2103 (7)
C 7A	-3895 (20)	-1073 (27)	2552 (7)
C 8A	-4126 (16)	385 (26)	2763 (7)
C 9A	-4187 (16)	1593 (24)	2406 (6)
C10A	-5038 (15)	1218 (25)	2043 (7)
C11A	-4412 (21)	3145 (27)	2605 (7)
C12A	-3589 (20)	3515 (28)	2941 (8)
C13A	-3584 (16)	2518 (31)	3300 (7)
C14A	-3389 (19)	919 (27)	3126 (6)
C15A	-3100 (22)	-128 (30)	3454 (9)
C16A	-2514 (23)	691 (38)	3848 (8)
C17A	-2727 (23)	2305 (33)	3676 (9)
C18A	-4565 (20)	2392 (34)	3590 (9)
C19A	-6185 (19)	1407 (26)	2180 (9)
C20A	-2730 (22)	3513 (37)	4006 (9)
C21A	-2733 (21)	5109 (35)	3883 (9)
C22A	-1759 (36)	3375 (67)	4310 (14)
C23A	-1693 (27)	3834 (46)	4676 (11)
C24A	-1025 (44)	4149 (76)	5164 (18)
C25A	-454 (26)	2930 (42)	5261 (10)
C26A	303 (57)	3145 (108)	5610 (21)
C27A	-1382 (43)	2067 (77)	5458 (16)
C28A	-5571 (15)	241 (26)	289 (6)
C29A	-6240 (19)	-267 (30)	-62 (8)
C30A	-6152 (16)	437 (25)	-496 (6)
C31A	-6939 (18)	-109 (29)	-841 (7)
C32A	-6910 (15)	568 (24)	-1276 (6)
C33A	-7718 (22)	116 (34)	-1609 (9)
C34A	-7867 (19)	986 (31)	-2015 (8)
C35A	-8787 (21)	637 (35)	-2293 (8)
C36A	-8903 (24)	1592 (37)	-2703 (9)
C37A	-9851 (25)	1470 (40)	-2963 (10)
O 3A	-5800 (11)	-182 (17)	712 (4)
O28A	-4858 (11)	1088 (18)	261 (4)
Molecule B			
C 1B	-2838 (15)	946 (24)	-499 (6)
C 2B	-3222 (17)	744 (25)	-985 (7)
C 3B	-2416 (18)	714 (26)	-1292 (7)
C 4B	-1543 (18)	-311 (26)	-1181 (7)
C 5B	-1189 (16)	-239 (22)	-714 (7)
C 6B	-166 (17)	-199 (24)	-629 (8)
C 7B	349 (16)	-97 (27)	-224 (7)
C 8B	-385 (15)	-307 (24)	180 (6)
C 9B	-1458 (15)	382 (22)	71 (7)
C10B	-1977 (16)	-86 (24)	-359 (7)
C11B	-2122 (15)	427 (25)	441 (7)
C12B	-1641 (17)	956 (25)	904 (6)
C13B	-693 (16)	167 (23)	1007 (7)
C14B	18 (18)	230 (25)	577 (8)
C15B	1055 (19)	-391 (27)	775 (9)
C16B	1132 (18)	149 (29)	1233 (8)
C17B	99 (17)	755 (24)	1369 (7)
C18B	-881 (18)	-1554 (29)	1111 (7)
C19B	-2475 (17)	-1722 (26)	-342 (6)
C20B	-166 (17)	494 (28)	1824 (7)
C21B	-1298 (19)	911 (31)	1958 (8)
C22B	542 (20)	1253 (33)	2159 (8)

TABLE 2. (*Continued*)

Atom	x/a	y/b	z/c
C23B	584 (23)	996 (39)	2609 (9)
C24B	1268 (25)	1974 (42)	2864 (10)
C25B	1343 (36)	1818 (63)	3380 (14)
C26B	563 (50)	2063 (84)	3562 (19)
C27B	2145 (43)	2183 (74)	3583 (17)
C28B	−2652 (22)	1375 (35)	−2071 (9)
C29B	−3172 (20)	979 (34)	−2448 (8)
C30B	−3130 (23)	2078 (39)	−2847 (9)
C31B	−3811 (21)	1610 (33)	−3214 (8)
C32B	−3694 (31)	2501 (52)	−3557 (12)
C33B	−4277 (28)	2450 (45)	−3955 (11)
C34B	−4501 (34)	3412 (60)	−4336 (13)
C35B	−4931 (40)	3175 (65)	−4774 (13)
C36B	−5795 (30)	3242 (55)	−4857 (12)
C37B	−6474 (27)	3166 (48)	−5301 (10)
O 3B	−2847 (11)	484 (18)	−1737 (5)
O28B	−1989 (16)	2266 (26)	−2035 (6)

a Estimated standard deviations are given in parentheses.

RESULTS AND DISCUSSION

Molecular structure

The average bond distances and angles for the crystallographically independent molecules A and B (**Fig. 1**) are in agreement, within experimental error, with those found in cholesteryl acetate (7) and other related structures (2, 3). The level of accuracy is considered to be consistent with the large atomic thermal vibrations in the crystal structure. The C–C distances range from 1.43 to 1.58 Å within the tetracyclic system. The average e.s.d. is 0.03 Å in bond lengths and 2° in bond angles. However, e.s.d.'s in lengths and angles involving terminal carbon atoms C(26) and C(27) are larger (0.08 Å and 4.5°).

The tetracyclic systems in molecules A and B have very similar conformations, but there are differences in the ester chains and in the C(17) substituents (Fig. 1). The r.m.s. displacement between the corresponding atoms, when atoms C(1) to C(19) were superimposed and a best least-squares fit was obtained (8), was 0.11 Å. The torsion angle C(19)–C(10)–C(13)–C(18), which is a measure of the twist within the tetracyclic system, is 15° for molecule A and 10° for molecule B. This angle ranges between 7.9° and 12.0° in other related structures (7). The intramolecular distance C(3)···C(16), which is useful for comparing the length of the tetracyclic system, has values 9.0 Å and 8.8 Å in molecules A and B, respectively, which are close to the limits of the range (8.86–9.01 Å) observed in other related molecules (7).

The torsion angle C(2)–C(3)–O(3)–C(28) is 75° in A and 126° in B. The major conformational difference in molecules A and B comes from this difference of 51° in the rotation at the ester bond. The corresponding
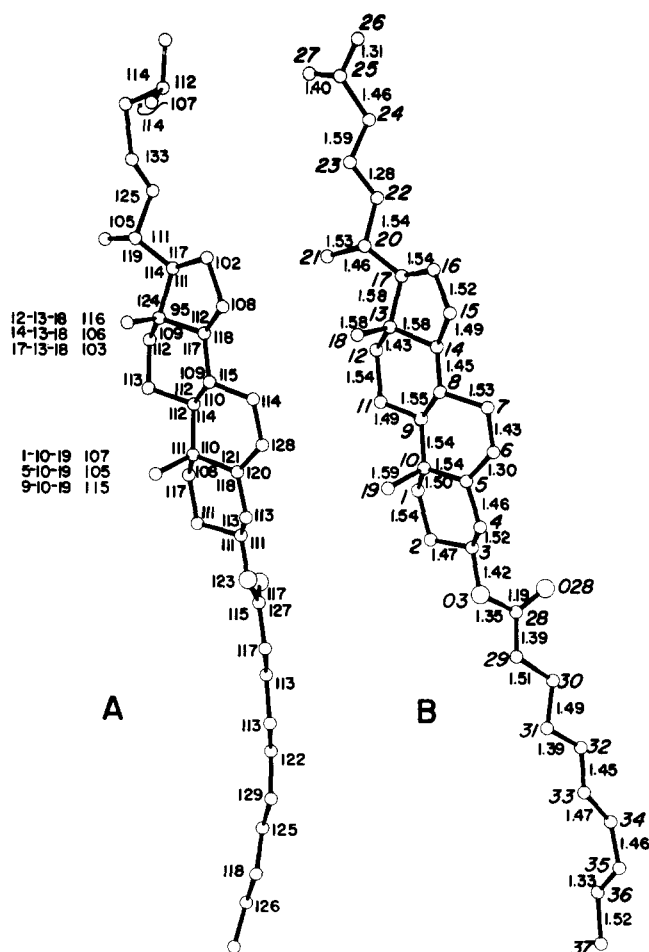

Fig. 1. Cholesteryl decanoate. Atomic numbering, averaged bond lengths (Å) and bond angles (°). The tetracyclic systems of molecules A and B are shown in the same orientation. The molecules have the observed conformations.

torsion angles are 82° and 136° in cholesteryl nonanoate and 79° and 127° in cholesteryl laurate (see also Fig. 3 in ref. 9).

The C(17) side chain is almost fully extended (**Table 3**) in both the molecules except at the bonds involving the last four atoms, C(24) through C(27). However, the electron density distribution is diffuse in this re-

TABLE 3. Selected torsion angles in cholesteryl decanoate

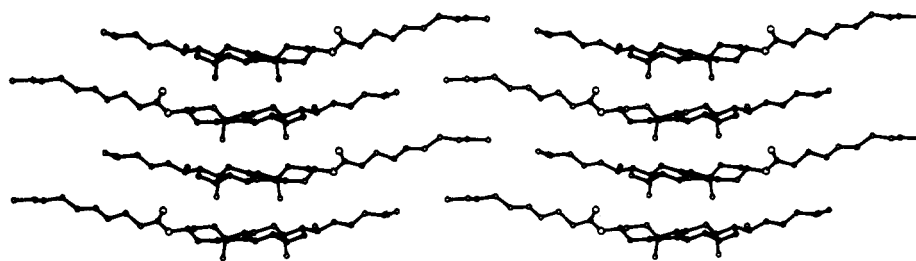|	Molecule A	Molecule B
C(13)–C(17)–C(20)–C(21)	−49°	−48°
C(13)–C(17)–C(20)–C(22)	−170	−172
C(17)–C(20)–C(22)–C(23)	−154	−168
C(20)–C(22)–C(23)–C(24)	−178	−175
C(22)–C(23)–C(24)–C(25)	−41	178
C(23)–C(24)–C(25)–C(26)	168	−63
C(23)–C(24)–C(25)–C(27)	−80	152
C(2)–C(3)–O(3)–C(28)	75	126
C(3)–O(3)–C(28)–C(29)	−179	−177
O(3)–C(28)–C(29)–C(30)	166	171
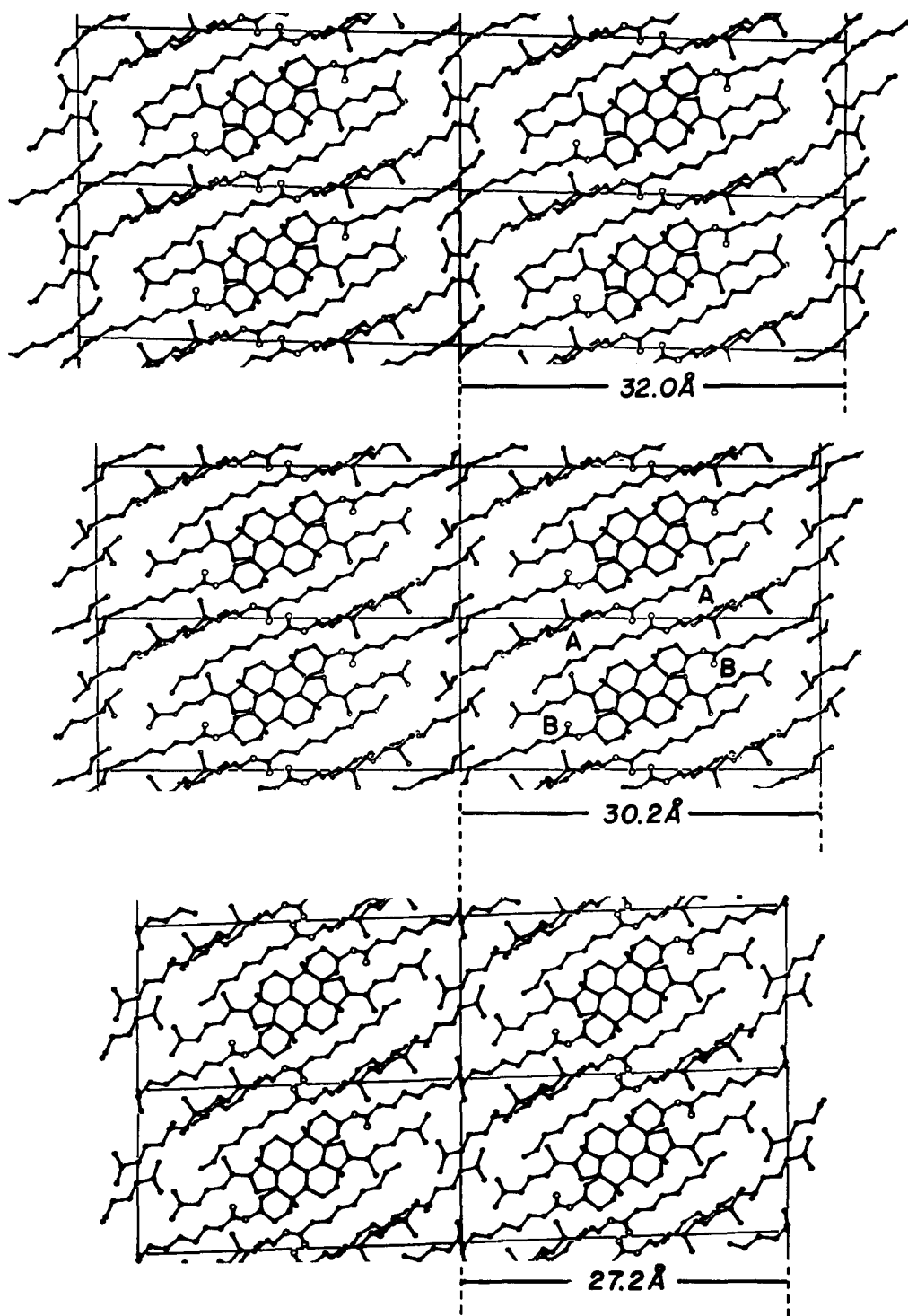
Fig. 2. Molecular packing arrangement in monolayer type 1 structures. Top, cholesteryl laurate, (3); middle, cholesteryl decanoate; bottom, cholesteryl nonanoate (2); The two molecules not related by crystal symmetry are A (ring system viewed on edge) and B. For each structure, adjacent monolayers extend vertically with the interface region occurring in vertical strips at the center and each edge of the figure.

gion and atomic positions are poorly defined because of the thermal motion.

The decanoate chains are almost fully extended, except for a twist near the free end of the B chain

(Fig. 1). Along the chains, the torsion angles about the bonds from C(28)–C(29) through C(35)–C(36) are 166, −176, 178, −176, 167, −170, 179, and −172° for molecule A and 171, −174, −175, −175,

Fig. 3. A partial crystal structure consisting of B-molecules in adjacent monolayers. The *b*-axis direction is from the bottom to the top of the page with the two-fold screw axis passing through the center of each monolayer. This projection is orthogonal to the molecular long axes and to the view shown in Fig. 2.

163, 164, 90, and 174° for molecule B. From C(28) to C(34) the chains have conformations similar to those in cholesteryl nonanoate (2) and laurate (3). Relative to the ester linkage, the twist in the decanoate B-chain occurs at the same bond, C(34)–C(35), as in the nonanoate B-chain.

Molecular packing

In the crystal structure of cholesteryl decanoate (**Fig. 2**) the molecules are packed to form layers which are parallel to the crystal planes (001) with a thickness of one unit cell (d_{001} = 30.22 Å). The cholesteryl groups lie within the layers while the ends of the molecules make up the layer interface region. The molecular long axes are approximately parallel to the crystal [101] direction, which makes an angle of 67° with the (001) plane. Normals to the best least-squares planes through atoms of the tetracyclic system in molecules A and B make angles of 93° and 165°, respectively, with the crystal *b*-axis.

A projection of the partial structure (**Fig. 3**) shows the packing of B molecules with one another. There is a stacking of antiparallel nearest neighbor molecules along the *b*-direction so that there is close association between the B-cholesteryl groups. The twist at the C(34)–C(35) bond in the decanoate chain leads to an end-to-end molecular alignment. The B-molecules are then bent to form a wave pattern which runs along the [101] direction.

The nearest neighbor A-molecules are shown in **Fig. 4.** There are 14 C···C intermolecular distances

less than 4.5 Å between A-decanoate chains and A-cholesteryl atoms. The nearest neighbor A- and B-molecules are shown in **Fig. 5.** There are 20 C···C intermolecular distances less than 4.5 Å between A-decanoate chains and B-cholesteryl atoms and 17 between B-decanoate chains and A-cholesteryl atoms. The shortest intermolecular C···C distances C(6)A··· C(34)A and C(28)A···C(19)B, are 3.78 Å and 3.74 Å, respectively. The decanoate chains do not pack with one another. Although the ends of the B-decanoate chains appear to overlap in Fig. 2, the closest C···C intermolecular distance is C(34)···C(37), 4.6 Å.

The cholesteryl-chain packing interactions in this crystal structure are important because similar arrangements may occur when cholesterol becomes incorporated within phospholipid bilayers (10).

Relationships within the isostructural series

The crystal structures of cholesteryl laurate, decanoate, and nonanoate contain closely related monolayer arrangements (Fig. 2)[5] called type I (2) because they are different from the monolayers of type II found in the crystal structures of shorter chain esters, such as cholesteryl octanoate (9).

In the three crystal structures (Fig. 2), the arrangement within the central region of the type I monolayers is very similar. The decrease in monolayer thick-

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[5] The crystal structure of cholesteryl undecanoate also belongs to this series. The crystals are monoclinic, space group P2₁, with a = 12.99 Å, b = 9.00 Å, c = 31.03 Å, β = 90.6°. (Patricia Sawzik, unpublished data.)
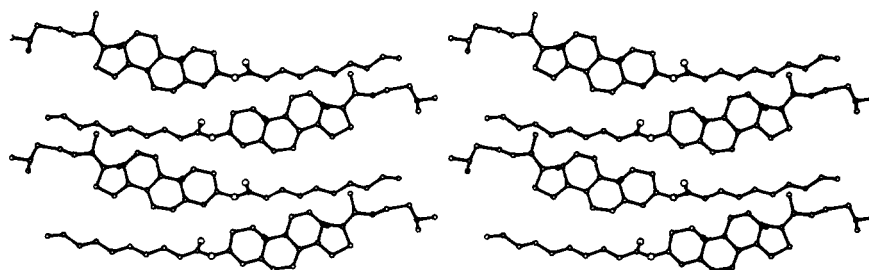
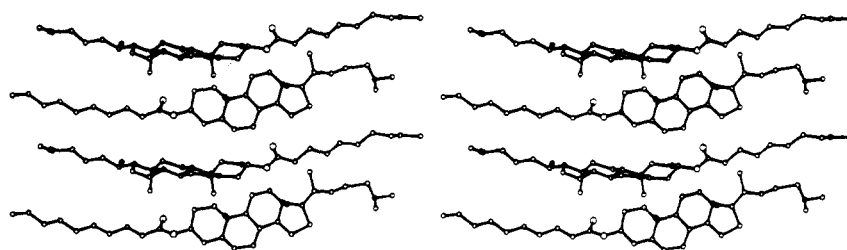**Fig. 4.** A partial structure consisting of A-molecules, other specifications as in Fig. 3.

Fig. 5. A partial structure consisting of A and B molecules, other specifications as in Fig. 3.

ness (32.02 Å, 30.22 Å, 27.24 Å) in the sequence laurate, decanoate, nonanoate is associated primarily with structural differences in the interlayer region. The atoms in this region consist of the C(17) tails of the A-molecules and the ends of the alkanoate chains of the B-molecules.

In each structure, Fig. 2 shows that the B-alkanoate chains from opposing monolayers overlap from about the C(34)–C(35) bond to the free end. The C(34)–C(35) bond is the seventh C–C bond counting from the ester group. Thus the change in monolayer thickness is not directly related to the number of carbon atoms in the alkanoate chain. The monolayer thickness and the space that is available for the ends of the B-alk-
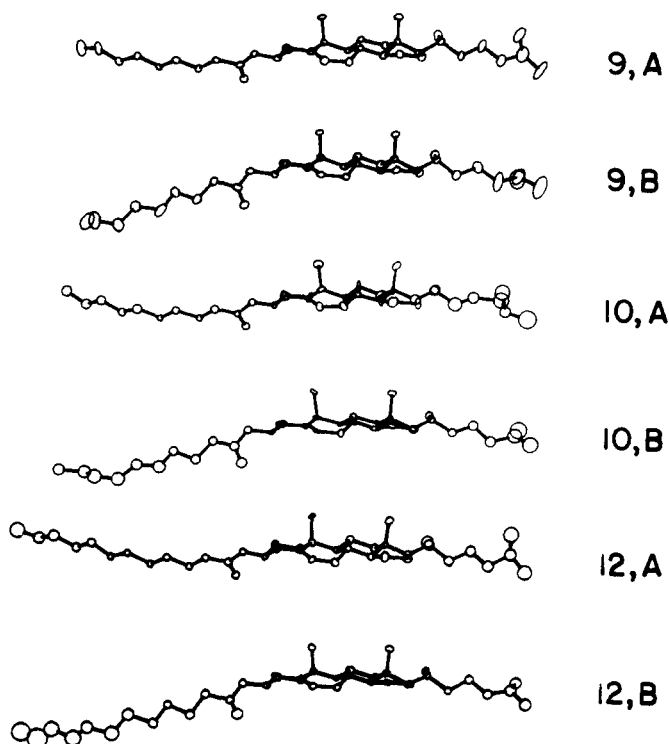

Fig. 6. Thermal ellipsoids of A and B molecules as seen in cholesteryl nonanoate, decanoate, and laurate structures. Thermal ellipsoids have 10% probability of enclosing atoms during vibration about mean positions.

anoate chains seem to be determined primarily by the conformation and packing arrangement of the C(17) tails of the A-molecules.

In the laurate structure, these A-tails are almost fully extended. In the decanoate structure, the tails are twisted so as to permit a closer monolayer separation. In the nonanoate structure, the tails are again extended, but there is deeper penetration of the A-tails from opposing monolayers, which allows a further contraction in the monolayer separation.

It is of interest to correlate the nature of the molecular packing with the degree of thermal motion in the series of crystal structures. The thermal ellipsoids (**Fig. 6**) are generally greater for the alkanoate B-chains than for the A-chains, and they are also greater for the A-tails than for the B-tails. There is greater freedom of motion in those parts of the molecules that project into the interlayer regions. The restricted motion for the A-chains, which are surrounded by A- and B-cholesteryl groups for most of their length, may be similar to the stiffening effect that cholesterol confers on phospholipid chains within membranes (11).

Relationships with other structure types

Outside the sequence C_9 to C_{12}, the most stable crystalline form of the cholesteryl n-alkanoate esters has a different structure. For longer chains, the preferred structure is the bilayer arrangement, as in cholesteryl myristate (12). In the bilayer structure, the most striking feature is the regular packing of alkanoate chains with each other. For shorter chains, a different monolayer structure is formed (type II), which is dominated by the antiparallel packing of the cholesteryl groups with one another as in cholesteryl octanoate (9). The extensive packing of alkanoate chains with cholesteryl groups provides the most stable structure only within the range of medium length chains that is considered here (Fig. 2).

puter programs that were used, including the ORTEP program by Dr. C. K. Johnson.

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