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# The Crystal Structure of Cholesteryl Acetate at 123 K

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## Abstract

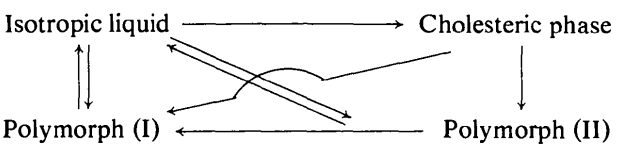
Cholesteryl acetate ($C_{29}H_{48}O_2$) at 123 K is monoclinic, space group $P2_1$ with $a$ = 16·537 (6), $b$ = 9·289 (3), $c$ = 17·640 (5) Å, $\beta$ = 106·95 (3)°, and $Z$ = 4. Integrated intensities for 3799 reflections with $I > 2\sigma(I)$ were measured at 123 K, using an automatic diffractometer and graphite-monochromated Mo $K\alpha$ radiation. The structure was solved using Patterson rotation and translation methods. Refinement by block-diagonal least-squares methods gave a final $R$ factor of 0·033. In contrast to the room-temperature studies of related molecules, atoms of the eight-carbon chains at C(17) are clearly resolved, with all H atoms experimentally located. In the two symmetry-independent molecules, these chains are almost fully extended. The greatest conformational differences are in the steroid $A$ and $B$ rings and in the twist at the ester linkages. Comparison with cholesterol conformations in other crystal structures gives an estimate of the rigidity of the ring system. The crystal structure consists of molecules stacked along screw axes so that they are antiparallel, with steroid $\alpha$ and $\beta$ faces in contact. The two distinct molecules form separate stacks with almost the same orientation, but with differing degrees of steroid overlap.

## Introduction

We have undertaken a series of crystal-structure determinations of fatty acid esters of cholesterol. From the observed molecular conformations and modes of packing, we seek aspects of structural behavior which may be relevant to more complex systems, such as the liquid-crystalline phases and fatty arterial deposits involving these lipids.

Other crystal structure determinations in this series have been carried out at room temperature (Craven, 1976; Craven & DeTitta, 1976; Guerina & Craven, 1977*a*,*b*). Because of the weak intermolecular forces in nonpolar lipid structures, atomic details tend to be obscured by large apparent thermal-vibrational averaging. These effects are particularly severe in the chain at C(17) and sometimes also in the fatty acid chain. In several crystal structures, there appeared to be conformational disorder at the ends of the molecule. Generally, room-temperature studies of these lipids represent a convenient and desirable compromise, in that the crystal is near a phase transition, yet the number of available X-ray intensity data is still adequate for a structure determination. The crystal structure of cholesteryl acetate, which we now report, was determined at low temperature in order to minimize thermal-motion effects and hence obtain greater detail and accuracy.

The thermographic behavior of cholesteryl acetate is rather complex, involving at least two (Usol'tseva & Chistyakov, 1963) and possibly three solid phases (Kunihisa & Gotoh, 1977). The acetate ester melts around 387–388 K to give an isotropic liquid and forms a monotropic cholesteric phase around 367–368 K on cooling (Barrall & Johnson, 1974). The phase transformations of cholesteryl acetate have been summarized by Usol'tseva & Chistyakov (1963) as follows:




Polymorph (I) is reported to crystallize from solution.

## Experimental

Cholesteryl acetate was obtained from Supelco Chemical Company. Crystallization was carried out by slow evaporation from *n*-pentanol at room temperature, resulting in monoclinic needle-like crystals which melted at 387–388 K. This is consistent with the behavior of polymorph (I). The space group and preliminary cell dimensions, determined from room-temperature Weissenberg and precession photographs, agreed with those of Barnard & Lydon (1974).

X-ray data were collected at 123 K using a Nonius CAD-4 diffractometer equipped with the Enraf–Nonius Universal Low-Temperature Device (liquid nitrogen as the coolant) and Mo $K\alpha$ graphite-monochromated radiation. Icing on the crystal was prevented by

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Table 1. *Crystal data for cholesteryl acetate*

| | |
|---|---|
| $C_{29}H_{48}O_2$ | $M_r = 428{\cdot}7$ |
| Space group: $P2_1$ | $Z = 4$ (2 molecules per asymmetric unit) |
| $a = 16{\cdot}537\ (6)$ Å | $\beta = 106{\cdot}95\ (3)°$ |
| $b = 9{\cdot}289\ (3)$ | $V = 2592\ (2)$ Å$^3$ } 123 K |
| $c = 17{\cdot}640\ (5)$ | |
| $D_c = 1{\cdot}099$ Mg m$^{-3}$ (123 K) | $D_m = 1{\cdot}068$ Mg m$^{-3}$ (296 K) |
| Mo $K\alpha$, $\lambda = 0{\cdot}7093$ Å, $\mu = 0{\cdot}065$ mm$^{-1}$ | |
| Crystal dimensions: $0{\cdot}42 \times 0{\cdot}43 \times 0{\cdot}40$ mm | |
| M.p. = 387–388 K | |

enclosing the diffractometer in a plastic bag together with containers of phosphorus pentoxide. Unit-cell parameters (Table 1) were determined by a least-squares fit of $\sin^2\theta$ values for 64 reflections with $30 \leq 2\theta \leq 40°$. Intensity data were collected from a crystal mounted with the $b$ axis 4·4° from the diffractometer $\varphi$ axis. An $\omega$ scan of 0·33° s$^{-1}$ was used to collect 5352 reflections. Three standard reflections, which were collected every 50 reflections, showed fluctuations of ±2·5% and were used to put the intensity data on a uniform scale. In the range $\sin\theta/\lambda < 0{\cdot}59$ Å$^{-1}$, 4877 non-symmetry-related reflections were measured, of which there were 3799 with $I > 2\sigma(I)$. The variance in an integrated intensity was assumed to be $\sigma^2(I) = \sigma^2 + (0{\cdot}02I)^2$ where $\sigma^2$ is the variance due to counting statistics.

## Structure determination

The phase problem was solved using Patterson rotation and translation methods (Crowther, 1973; Langs, 1975). The atomic coordinates of the cholesterol ring system used as the search model were derived from the crystal structure of 3$\beta$-chloro-5-androsten-17$\beta$-ol (Weeks, Cooper & Norton, 1971). This cholesterol fragment was arranged to form an artificial crystal structure with space group $P1$. The rotation function was used to match the Patterson function of the cholesteryl acetate structure (calculated from the 1932 largest quasi-normalized $E^2$ coefficients) with the Patterson of the search structure (calculated from 1864 generated $E^2$ coefficients). Only the first of the six largest rotation-map peaks gave feasible molecular packing. Thus both molecules ($A$) and ($B$) in the asymmetric unit of cholesteryl acetate were assumed to have the same or very similar orientations. The translation searches could be interpreted on this basis. One molecule (hereafter $A$) appeared to stack with itself close to the screw axis which was chosen to pass through the crystallographic origin. The other molecule (hereafter $B$), demonstrating a different packing mode, was then required to stack close to the screw axis through the center of the unit cell (Fig. 1). Intermolecular distances for this scheme yielded no contacts less than the appropriate sum of the van der Waals radii. A structure factor calculation with 40 of the 62 non-hydrogen atoms gave an $R$ of 0·53. To reduce computing time, reflections with $I < 2\sigma(I)$ were not included here or in any subsequent calculations.

The remaining 22 C and O atoms of the C(17) side chain and acetate group were located from Fourier maps calculated after each of six cycles of full-matrix least-squares refinement of positional and isotropic thermal parameters for atoms whose positions had been located. The $R$ factor with all non-hydrogen atoms was 0·18. After three additional cycles of full-matrix refinement of positional and thermal parameters, the $R$ factor dropped to 0·112.

The 96 H atoms were located near their expected positions in a difference Fourier synthesis. Two cycles of block-diagonal least-squares refinement of H atom positions yielded $R = 0{\cdot}072$. A total of 12 cycles of block-diagonal least-squares refinement followed. Positional and anisotropic thermal parameters for non-hydrogen atoms (damping factors 0·75 and 0·2 respectively) were refined in the first six and last two cycles. H atom positional and isotropic thermal parameters (damping factors 0·4, 0·2) were refined in the other four cycles. In the least-squares refinement, the function $\sum_H w_H \Delta_H^2$ was minimized, where $\Delta_H = |F_o| - |F_c|$ and $w_H = 1/\sigma^2(F_o)$.* The X-ray scattering factors used were those of Cromer & Waber (1965) for C and O and Stewart, Davidson & Simpson (1965) for H. The final $R$ factor was 0·033 with all shifts in parameter values less than $0{\cdot}5\sigma$. The final atomic parameters are listed in Table 2.

## Discussion

### *Intermolecular geometry*

The crystal structure of cholesteryl acetate consists of molecules stacked around $2_1$ axes so that they are antiparallel with steroid $\alpha$ and $\beta$ faces in contact. The two distinct molecules form separate stacks which have similar orientations but with differing degrees of steroid overlap (Fig. 1). The cholesteryl packing of symmetry-related ($A$) molecules, which is characterized by extensive overlap of steroid rings along the $2_1$ axis, is isostructural with cholesteryl iodide polymorph $B$ (Carlisle & Crowfoot, 1945). In stacks of acetate ($B$) molecules, only steroid $A$ and $B$ rings† overlap one

* Lists of structure factors, thermal parameters and ring-puckering coordinates for various cholesteryl ester and cholesterol monohydrate molecules have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34082 (57 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

† The standard chemical ring nomenclature ($A$,$B$,$C$,$D$) for steroids is used, but with an effort always to distinguish $A$ and $B$ rings from ($A$) and ($B$) molecules in the text.

Table 2. *Atomic parameters as fractional coordinates*

E.s.d.'s are given in parentheses.

(*a*) Non-hydrogen atoms (× $10^5$)

| | *x* | *y* | *z* | | *x* | *y* | *z* |
|---|---|---|---|---|---|---|---|
| Molecule (*A*) | | | | Molecule (*B*) | | | |
| C(1) | −22471 (14) | 43812 (30) | 4546 (14) | C(1) | 37406 (14) | −526 (29) | 39865 (13) |
| C(2) | −25350 (15) | 45225 (30) | 12039 (14) | C(2) | 33802 (15) | 3273 (32) | 46710 (14) |
| C(3) | −17765 (14) | 43307 (31) | 19175 (14) | C(3) | 40813 (14) | 4247 (30) | 54420 (13) |
| C(4) | −11361 (15) | 55134 (31) | 19440 (13) | C(4) | 47923 (15) | 14206 (30) | 53807 (14) |
| C(5) | −8504 (14) | 54824 (27) | 12013 (13) | C(5) | 50967 (14) | 10965 (28) | 46754 (13) |
| C(6) | −317 (14) | 54710 (29) | 12652 (13) | C(6) | 59057 (15) | 8744 (31) | 47574 (14) |
| C(7) | 3382 (14) | 54477 (29) | 5886 (13) | C(7) | 62701 (14) | 6190 (32) | 40807 (13) |
| C(8) | −3173 (13) | 56870 (27) | −2192 (13) | C(8) | 56616 (14) | 10690 (30) | 32886 (13) |
| C(9) | −11510 (13) | 49233 (28) | −2502 (13) | C(9) | 47722 (14) | 4740 (28) | 32124 (13) |
| C(10) | −15388 (14) | 54577 (28) | 4085 (13) | C(10) | 44088 (14) | 10350 (29) | 38814 (13) |
| C(11) | −17766 (14) | 49968 (31) | −10929 (14) | C(11) | 41653 (14) | 7060 (30) | 23771 (14) |
| C(12) | −14001 (14) | 44416 (31) | −17353 (14) | C(12) | 45131 (14) | 2135 (31) | 17034 (13) |
| C(13) | −5846 (14) | 52519 (29) | −17249 (13) | C(13) | 53779 (14) | 9050 (28) | 17682 (13) |
| C(14) | 177 (13) | 51120 (28) | −8790 (13) | C(14) | 59588 (14) | 5116 (28) | 25990 (13) |
| C(15) | 8561 (14) | 56858 (29) | −9449 (14) | C(15) | 68402 (15) | 9226 (34) | 25721 (14) |
| C(16) | 8779 (14) | 51376 (30) | −17661 (13) | C(16) | 68327 (15) | 5066 (33) | 17211 (14) |
| C(17) | −261 (14) | 45675 (28) | −22013 (14) | C(17) | 58873 (14) | 2530 (29) | 12336 (13) |
| C(18) | −7734 (14) | 68254 (30) | −19705 (14) | C(18) | 52845 (15) | 25381 (29) | 16445 (14) |
| C(19) | −19260 (15) | 69705 (30) | 2352 (15) | C(19) | 40071 (16) | 25287 (31) | 36756 (15) |
| C(20) | −2585 (14) | 48202 (29) | −31042 (13) | C(20) | 57029 (14) | 8069 (29) | 3731 (13) |
| C(21) | −11489 (15) | 42838 (35) | −35366 (14) | C(21) | 47765 (14) | 5510 (33) | −1090 (14) |
| C(22) | 4017 (15) | 40847 (30) | −34336 (14) | C(22) | 62990 (15) | 1008 (31) | −383 (14) |
| C(23) | 3145 (15) | 44138 (32) | −43028 (14) | C(23) | 62352 (15) | 6907 (30) | −8669 (14) |
| C(24) | 10664 (15) | 38402 (31) | −45537 (15) | C(24) | 69542 (16) | 1781 (34) | −11761 (15) |
| C(25) | 9762 (16) | 39555 (33) | −54357 (15) | C(25) | 68287 (15) | 3772 (33) | −20575 (15) |
| C(26) | 8877 (24) | 54726 (45) | −57288 (19) | C(26) | 66186 (18) | 19177 (34) | −23309 (16) |
| C(27) | 17185 (19) | 32148 (42) | −56238 (17) | C(27) | 76034 (16) | −1380 (37) | −22821 (16) |
| C(28) | −16044 (15) | 36579 (30) | 32617 (14) | C(28) | 41173 (15) | 7693 (30) | 67943 (14) |
| C(29) | −19270 (17) | 38918 (36) | 39595 (15) | C(29) | 36685 (17) | 14152 (32) | 73365 (16) |
| O(3) | −20582 (10) | 44045 (21) | 26254 (9) | O(3) | 36947 (10) | 9948 (21) | 60263 (9) |
| O(28) | −10090 (11) | 29138 (24) | 32635 (10) | O(28) | 47701 (11) | 1141 (24) | 70128 (10) |

(*b*) Hydrogen atoms (× $10^4$)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Molecule (*A*) | | | | Molecule (*B*) | | | |
| H1(1) | −2014 (14) | 3299 (29) | 424 (13) | H1(1) | 4005 (12) | −1051 (25) | 4104 (12) |
| H1(2) | −2730 (12) | 4507 (25) | −15 (12) | H1(2) | 3234 (13) | −102 (26) | 3484 (12) |
| H2(1) | −2772 (12) | 5446 (26) | 1197 (11) | H2(1) | 3149 (14) | 1295 (29) | 4581 (13) |
| H2(2) | −2999 (13) | 3709 (26) | 1173 (12) | H2(2) | 2964 (14) | −463 (29) | 4747 (13) |
| H3(1) | −1537 (13) | 3388 (25) | 1923 (12) | H3(1) | 4299 (13) | −583 (28) | 5580 (13) |
| H4(1) | −650 (13) | 5411 (27) | 2432 (12) | H4(1) | 5258 (13) | 1356 (26) | 5868 (12) |
| H4(2) | −1392 (13) | 6518 (26) | 2009 (13) | H4(2) | 4587 (13) | 2427 (25) | 5368 (12) |
| H6(1) | 394 (13) | 5470 (27) | 1812 (12) | H6(1) | 6332 (14) | 875 (28) | 5298 (13) |
| H7(1) | 635 (13) | 4530 (25) | 587 (12) | H7(1) | 6414 (13) | −420 (26) | 4048 (12) |
| H7(2) | 792 (13) | 6209 (27) | 660 (13) | H7(2) | 6833 (14) | 1090 (28) | 4171 (13) |
| H8(1) | −406 (12) | 6759 (24) | −289 (11) | H8(1) | 5629 (14) | 2197 (27) | 3237 (13) |
| H9(1) | −1033 (12) | 3856 (24) | −132 (12) | H9(1) | 4839 (12) | −554 (26) | 3296 (12) |
| H11(1) | −1944 (14) | 6002 (28) | −1202 (13) | H11(1) | 4065 (13) | 1732 (27) | 2314 (13) |
| H11(2) | −2295 (13) | 4403 (29) | −1116 (13) | H11(2) | 3598 (12) | 159 (26) | 2316 (12) |
| H12(1) | −1855 (12) | 4538 (25) | −2273 (12) | H12(1) | 4102 (12) | 411 (26) | 1176 (12) |
| H12(2) | −1258 (14) | 3420 (27) | −1632 (13) | H12(2) | 4603 (13) | −861 (27) | 1716 (13) |
| H14(1) | 85 (12) | 4044 (25) | −745 (12) | H14(1) | 5939 (12) | −574 (26) | 2646 (12) |
| H15(1) | 1382 (13) | 5372 (29) | −482 (13) | H15(1) | 7289 (13) | 423 (27) | 2976 (12) |
| H15(2) | 850 (13) | 6742 (26) | −967 (12) | H15(2) | 6954 (14) | 2029 (29) | 2652 (13) |
| H16(1) | 1303 (13) | 4326 (27) | −1728 (12) | H16(1) | 7166 (14) | −371 (28) | 1724 (14) |
| H16(2) | 1056 (13) | 5883 (26) | −2093 (12) | H16(2) | 7091 (13) | 1328 (26) | 1474 (12) |
| H17(1) | −33 (12) | 3475 (24) | −2118 (11) | H17(1) | 5798 (12) | −840 (27) | 1197 (12) |
| H18(1) | −1227 (14) | 6933 (30) | −2467 (13) | H18(1) | 4863 (13) | 2726 (26) | 1119 (12) |
| H18(2) | −981 (14) | 7357 (27) | −1593 (13) | H18(2) | 5057 (13) | 2999 (28) | 2048 (12) |
| H18(3) | −242 (13) | 7374 (25) | −2019 (12) | H18(3) | 5799 (14) | 2979 (30) | 1676 (13) |
| H19(1) | −2412 (13) | 6949 (27) | −222 (12) | H19(1) | 3446 (14) | 2470 (27) | 3259 (13) |

Table 2 (*cont.*)

| Molecule (*A*) | *x* | *y* | *z* |
|---|---|---|---|
| H19(2) | −2084 (14) | 7366 (27) | 699 (13) |
| H19(3) | −1550 (14) | 7640 (26) | 121 (13) |
| H20(1) | −213 (13) | 5974 (26) | −3209 (12) |
| H21(1) | −1242 (14) | 3268 (30) | −3420 (14) |
| H21(2) | −1589 (14) | 4890 (28) | −3418 (13) |
| H21(3) | −1271 (13) | 4327 (29) | −4107 (13) |
| H22(1) | 358 (14) | 3034 (30) | −3365 (13) |
| H22(2) | 987 (13) | 4364 (27) | −3106 (12) |
| H23(1) | 324 (14) | 5469 (31) | −4363 (13) |
| H23(2) | −209 (13) | 3923 (27) | −4650 (13) |
| H24(1) | 1127 (15) | 2851 (30) | −4434 (14) |
| H24(2) | 1599 (13) | 4343 (29) | −4264 (13) |
| H25(1) | 434 (14) | 3385 (30) | −5723 (14) |
| H26(1) | 2218 (16) | 3780 (33) | −5388 (15) |
| H26(2) | 1740 (17) | 2159 (36) | −5465 (16) |
| H26(3) | 1645 (16) | 3304 (34) | −6196 (15) |
| H27(1) | 414 (19) | 5933 (39) | −5614 (17) |
| H27(2) | 849 (17) | 5568 (37) | −6289 (16) |
| H27(3) | 1423 (18) | 6012 (37) | −5429 (17) |
| H29(1) | −2500 (15) | 3682 (30) | 3819 (14) |
| H29(2) | −1597 (17) | 3397 (36) | 4401 (16) |
| H29(3) | −1876 (17) | 4867 (33) | 4086 (15) |

| Molecule (*B*) | *x* | *y* | *z* |
|---|---|---|---|
| H19(2) | 3889 (14) | 2983 (30) | 4147 (14) |
| H19(3) | 4440 (14) | 3158 (30) | 3528 (14) |
| H20(1) | 5802 (13) | 1992 (27) | 399 (12) |
| H21(1) | 4651 (12) | −571 (28) | −76 (13) |
| H21(2) | 4377 (14) | 1160 (28) | 88 (13) |
| H21(3) | 4656 (14) | 873 (28) | −673 (13) |
| H22(1) | 6210 (13) | −952 (26) | −69 (12) |
| H22(2) | 6886 (13) | 200 (29) | 266 (13) |
| H23(1) | 6250 (14) | 1763 (30) | −831 (14) |
| H23(2) | 5686 (13) | 327 (27) | −1257 (12) |
| H24(1) | 7076 (14) | −859 (31) | −1048 (14) |
| H24(2) | 7522 (15) | 694 (31) | −877 (14) |
| H25(1) | 6320 (14) | −277 (28) | −2379 (13) |
| H26(1) | 8094 (15) | 369 (32) | −2013 (13) |
| H26(2) | 7708 (15) | −1202 (31) | −2110 (14) |
| H26(3) | 7481 (14) | −122 (29) | −2851 (13) |
| H27(1) | 6058 (15) | 2288 (29) | −2252 (14) |
| H27(2) | 6543 (15) | 2082 (32) | −2930 (15) |
| H27(3) | 7072 (15) | 2519 (30) | −2025 (15) |
| H29(1) | 3364 (15) | 710 (32) | 7507 (14) |
| H29(2) | 4130 (15) | 1834 (34) | 7771 (15) |
| H29(3) | 3269 (14) | 2065 (30) | 7071 (14) |

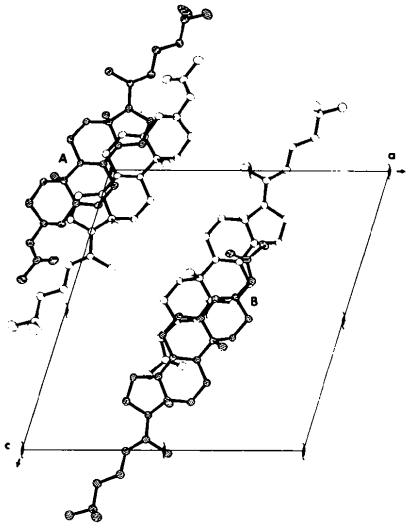


Fig. 1. Projection of the cholesteryl acetate crystal structure down the *b* axis. Shaded molecules lie at about the same height in the unit cell. The molecular origin [defined as the center of the C(8)–C(9) bond] of (*A*) is translated from the $2_1$ axis at the origin of the cell by $x = -0{\cdot}074$, $z = -0{\cdot}024$, while that of (*B*) is translated from the $2_1$ axis at the center of the cell by $x = 0{\cdot}012$, $z = -0{\cdot}175$. Atoms are represented as 50% probability thermal ellipsoids.

Table 3. *Best least-squares planes calculated for selected groups of atoms*

The planes are: (1) tetracyclic ring system, C(1)–C(17); (2) ethylenic group, C(5), C(6), C(10), C(4), C(7); (3) ester group, O(3), C(28), C(29), O(28). Equations are of the form $ax + by + cz = d$, referred to the crystallographic axes. The plane constants are in Å. Values for molecule (*A*) are above those for (*B*).

(*a*) Plane constants

| Plane | *a* | *b* | *c* | *d* |
|---|---|---|---|---|
| (1) | −3·267 | 9·010 | −1·374 | 4·850 |
| | 1·695 | −9·182 | 1·348 | 0·719 |
| (2) | 0·109 | 9·287 | −0·354 | 5·039 |
| | 2·483 | 9·114 | −2·819 | 0·951 |
| (3) | 9·183 | 7·270 | 1·890 | 1·807 |
| | 8·649 | 7·915 | −2·366 | 2·559 |

(*b*) Distances (Å) of atoms from the plane

| Plane | | | | | |
|---|---|---|---|---|---|
| (2) | C(5) | C(6) | C(10) | C(4) | C(7) |
| | 0·001 (4) | −0·004 (4) | −0·001 (4) | 0·001 (5) | 0·002 (4) |
| | −0·004 (5) | −0·031 (6) | −0·005 (5) | 0·016 (5) | 0·022 (5) |
| (3) | O(3) | C(28) | C(29) | O(28) | |
| | 0·001 (4) | −0·004 (4) | 0·001 (4) | 0·002 (5) | |
| | −0·001 (4) | +0·004 (5) | −0·001 (4) | −0·002 (4) | |

another, while *B*, *C* and *D* rings pack with the acetate side group. The best least-squares planes through the tetracyclic ring system of molecules (*A*) and (*B*) are nearly parallel, with a dihedral angle of 174° (Table 3). The normals to these planes form angles of 14° (*A*) and 171° (*B*) with the *b* axis. Both independent molecules have about the same *y* coordinate in the unit cell, forming a layered structure. Each layer is made up of rows of (*A*) and (*B*) molecules packed tail to tail within each row, and with all molecular long axes parallel to the [201] direction (Fig. 2). Close intermolecular contacts for non-hydrogen atoms are given in Table 4.

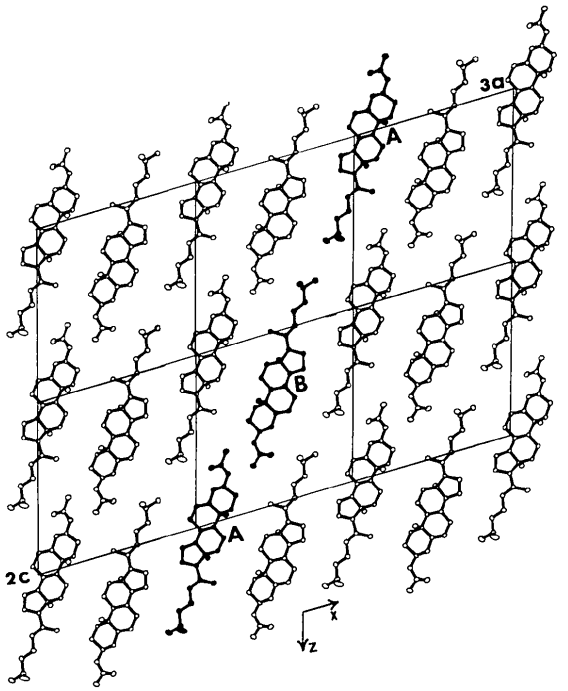


Fig. 2. A single layer of molecules in the cholesteryl acetate crystal structure. Within each layer are rows of antiparallel (*A*) and (*B*) molecules with long axes parallel to the [201] direction.

Table 4. *Intermolecular distances less than* 3·8 Å *for* C···C *and less than* 3·4 Å *for* C···O

| | | |
|---|---|---|
| Molecule (*A*)–Molecule (*A*) | | |
| C(6)–C(18) | 2/0$\bar{1}$0* | 3·7178 (35) |
| Molecule (*B*)–Molecule (*B*) | | |
| C(11)–C(27) | 2/1$\bar{1}$0 | 3·7428 (29) |
| C(19)–C(26) | 2/$\bar{1}$00 | 3·7437 (40) |
| C(25)–O(28) | 1/00$\bar{1}$ | 3·2910 (34) |
| Molecule (*A*)–Molecule (*B*) | | |
| C(2)–C(21) | 2/000 | 3·7693 (37) |
| C(16)–C(16) | 2/$\bar{1}$00 | 3·7792 (37) |
| C(26)–C(2) | 1/00$\bar{1}$ | 3·7661 (43) |
| C(28)–C(15) | 1/$\bar{1}$00 | 3·5675 (38) |
| O(3)–C(29) | 2/001 | 3·2694 (34) |
| C(21)–C(2) | 2/000 | 3·7753 (38) |

* Distance is between C(6) at symmetry position 1 ($x,y,z$) and C(18) at symmetry position 2 ($-x, \frac{1}{2}+y, -z$) and translated 0 unit cells along **a**, −1 unit cell along **b**, 0 unit cells along **c**.

### *Intramolecular geometry*

Mean values of bond distances and angles (Fig. 3) for the independent molecules (*A*) and (*B*) are consistent with those found in other structure determinations (Craven & DeTitta, 1976; Guerina & Craven, 1977*a*,*b*; Abrahamsson & Dahlén, 1977). For the two cholesteryl acetate molecules, the r.m.s. difference between observed and mean values is 0·0038 Å for distances and 0·54° for angles, while the average least-squares estimated standard deviations for these values are 0·0036 Å and 0·20° respectively. The only significant differences are in the bond angles within the steroid *A* rings. These rings are also slightly different in their conformation (see below).

Atomic thermal vibrations in molecules (*A*) and (*B*) (Fig. 4) have root-mean-square amplitudes which range from 0·12–0·23 Å for the cholesteryl ring atoms and 0·12–0·35 Å for the chains at C(17) and for the acetate groups.* Thermal parameters for the C atoms of the C(1)–C(19) fragment in each molecule are nearly consistent with those of a rigid body (Table 5) (Schomaker & Trueblood, 1968). The rigid-body translation motion is almost isotropic with an average r.m.s. amplitude of 0·14 Å. The largest r.m.s. principal value for librational motion is about the long axes of the molecules and is 2·7° for (*A*) and 3·8° for (*B*). Librational corrections to bond distances and angles (ranging from 0·0005–0·0035 Å and 0·003–0·098° respectively) were negligibly small.

* See deposition footnote.

Table 5. *Rigid-body parameters for the* C(1)–C(19) *fragment of molecules* (*A*) *and* (*B*)

Tensor components for **T** and **ω** are referred to the orthogonal axial system (**a**, **b**, **c***). E.s.d.'s are in parentheses.

| | Molecule (*A*) | | | Molecule (*B*) | | |
|---|---|---|---|---|---|---|
| **T** (Å² × 10⁴) | 191 (6) | −1 (6) | −29 (5) | 196 (7) | −18 (7) | −11 (6) |
| | | 194 (9) | −7 (6) | | 215 (10) | 6 (6) |
| | | | 191 (6) | | | 194 (6) |
| **ω** (degree²) | 3·9 (6) | 0·3 (3) | −3·1 (5) | 4·2 (6) | 0·4 (3) | −5·8 (5) |
| | | 1·2 (2) | −1·0 (3) | | 0·7 (3) | −0·8 (3) |
| | | | 4·2 (7) | | | 10·9 (8) |
| R.m.s. magnitudes of principal axes | | | | | | |
| *T* (Å) | 0·15 | 0·14 | 0·13 | 0·15 | 0·14 | 0·13 |
| *ω* (°) | 2·72 | 1·24 | 0·77 | 3·79 | 0·95 | 0·82 |
| R.m.s. $(U_o - U_c)$ (Å) | | 0·0019 | | | 0·0021 | |

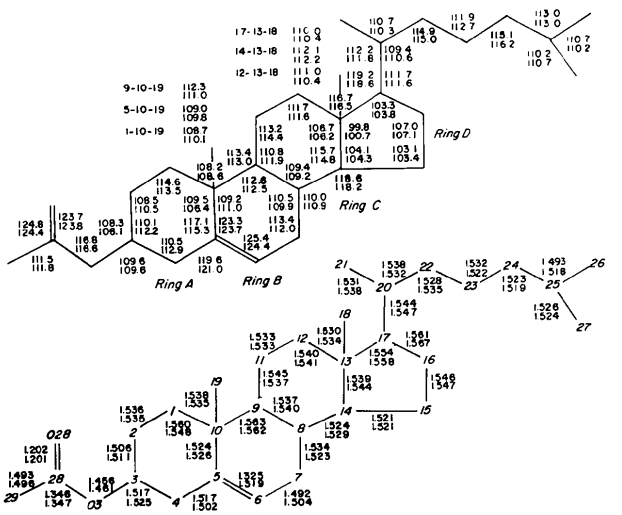


Fig. 3. Atomic-numbering system and interatomic distances (Å) and angles (°). The values are not corrected for libration. Values for molecule (*A*) are above those for (*B*).

The C(17) side chain of both molecules (*A*) and (*B*) is almost fully extended, as is the case in most of the cholesteryl ester structures (Fig. 4). There is an apparent shortening of bond lengths near the end of the chains, but the effect of thermal vibration is much less pronounced here than in structures determined using the room-temperature data (Craven, 1976; Craven & DeTitta, 1976; Guerina & Craven, 1977*a*,*b*; Abrahamsson & Dahlén, 1977). The conformation at the ester linkage is slightly different in the two molecules. The C(2)–C(3)–O(3)–C(28) torsion angle has a value of 151·1 (2)° in (*A*) and 160·2 (2)° in (*B*), the C(4)–C(3)–O(3)–C(28) angle is −88·8 (3) and −78·4 (3)° respectively. The atoms within the ester and ethylenic groups of each cholesteryl acetate molecule are nearly coplanar (Table 3).

A best least-squares fit (Nyburg, 1974) for the superposition of the C(1)–C(19) fragment from (*A*) and (*B*) molecules resulted in an r.m.s. displacement for corresponding atoms of 0·175 Å. The significant differences in steroid conformations of these two molecules are in the *A* and *B* rings. Ring-puckering coordinates (Cremer & Pople, 1975) are in Table 6. Ring *A* of molecule (*A*) is distorted from the chair conformation with considerable magnitude ($\theta = 13{\cdot}1°$), toward a 2$\beta$,3$\alpha$-half-chair. In molecule (*B*) this ring has a much smaller distortion toward a 1$\alpha$-envelope. The *B* rings of both molecules are distorted from an 8$\beta$,9$\alpha$-half-chair in different directions. For molecule (*A*) the distortion is toward a 9$\alpha$-envelope and in (*B*) toward an 8$\beta$-envelope. The result is a twisting of the *A* and *B* rings of molecule (*B*) relative to (*A*). This swings the C(19) methyl group of (*B*) away from the region of steroid overlap avoiding unfavorable intermolecular contacts with the *A* ring of the next molecule in the $+b$ direction. This twisting accounts for the differences in the C(19)–C(10)–C(13)–C(18) torsion angle which has a value of 8·8 (5)° for molecule (*A*) and 18·0 (5)° for (*B*).*

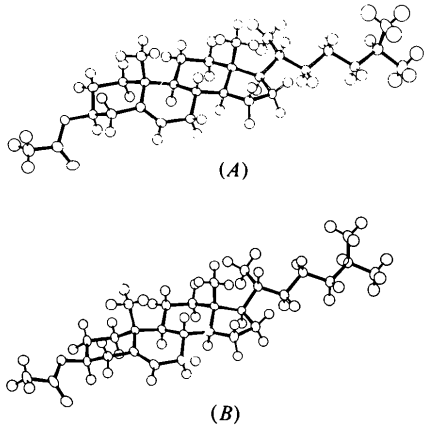


Fig. 4. Molecules (*A*) and (*B*) shown in their observed configuration with their tetracyclic ring systems in the same orientation. Atoms, including hydrogens, are represented as 50% probability thermal ellipsoids.

The *C* and *D* rings of both cholesteryl acetate molecules are very similar in conformation. A best least-squares fit for the superposition of the *C* and *D* rings gave an r.m.s. displacement for corresponding atoms of 0·034 Å. Both *C* rings are distorted slightly from a chair and the *D* rings are in a 13$\beta$,14$\alpha$-twist conformation. The steroid nucleus of molecule (*A*) is slightly bowed (the $\beta$ face is on the upper side of the bow), a feature observed in several steroid structures (Duax & Norton, 1975). In (*B*), the twisting of the *A* and *B* rings tends to flatten this bow. The effective steroid length, taken as the C(3)–C(16) distance, is thus longer for (*B*), 9·016 Å, compared to 8·872 Å for (*A*).

The ring-puckering analysis was carried out for other cholesteryl moieties, as observed in crystal structures at

* This torsion angle ranges from 7·9–12·1° in six other cholesteryl ester molecules, myristate (*A* and *B*) (Craven & DeTitta, 1976); nonanoate (*A* and *B*) (Guerina & Craven, 1977*b*); octanoate, oleate (Guerina & Craven, 1977*a*); and four cholesterol monohydrate molecules (ACEG) (Craven, 1976).

Table 6. *Ring-puckering coordinates*

Values for six-membered rings are transformed to a spherical polar set of puckering coordinates ($Q$, $\theta$, $\varphi$) where $Q$ is the total puckering amplitude and $\theta$ is an angle ($0 \le \theta \le \pi$) such that $q_2 = Q \sin\theta$, $q_3 = Q\cos\theta$. For a given $Q$ these coordinates can be mapped on the surface of a sphere. The chair conformation results in $\theta = 0, 180°$. Values of $\theta = 90°$ and $\varphi = (0, 60, 120° \ldots)$ give six boat conformations and $\theta = 90°$, $\varphi = (30, 90, 150° \ldots)$ give six twist-boat conformations (Cremer & Pople, 1975). Values for molecule (*A*) are above those for (*B*).

| | $Q$ (Å) | $\theta$ (°) | $\varphi$ (°) |
|---|---|---|---|
| Ring *A* | 0·555 | 13·06 | 97·82 |
| | 0·549 | 5·96 | 347·85 |
| Ring *B* | 0·473 | 50·46 | 220·69 |
| | 0·486 | 52·71 | 201·56 |
| Ring *C* | 0·569 | 3·07 | 241·76 |
| | 0·568 | 7·42 | 260·29 |
| Ring *D* | 0·468 | | 194·34 |
| | 0·447 | | 198·14 |

A unique mean plane is defined where $\sum_{j=1}^{N} Z_j = 0$. $Z_j$ is the distance of the $j$th atom from the plane and is related to the puckering coordinates for the ring by the expressions:

$$(N \text{ odd})\ Z_j = (2/N)^{1/2} \sum_{m=2}^{\frac{1}{2}(N-1)} q_m \cos[\varphi_m + 2\pi m(j-1)/N]$$

$$(N \text{ even})\ Z_j = (2/N)^{1/2} \sum_{m=1}^{N/2-1} q_m \cos[\varphi_m + 2\pi m(j-1)/N] + N^{-1/2} q_{N/2}(-1)^{j-1}.$$

For $N = 5$ there is one amplitude–phase pair ($q$, $\varphi$), with values of $\varphi = (0, 36, 72° \ldots)$ corresponding to 10 envelope conformations and $\varphi = (18, 54, 90° \ldots)$ corresponding to 10 twist conformations. For $N = 6$ there is one amplitude–phase pair ($q_2$, $\varphi_2$) and a puckering coordinate $q_3$.

Table 7. *Best least-squares fit for superposability of the* C(1)–C(19) *steroid fragment of various cholesteryl esters and cholesterol monohydrate molecules*

Values are average r.m.s. displacements for corresponding atoms (Å).

| Ester chain length | 18:1 | 14 | 14 | 9 | 9 | 8 | 2 | 2 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Oleate | Myristate *A* | Myristate *B* | Non-anoate *A* | Non-anoate *B* | Octanoate | Acetate *A* | Acetate *B* | Mono-hydrate *A* | Mono-hydrate *C* | Mono-hydrate *E* |
| Myristate *A* | 0·104 | 0 | | | | | | | | | |
| Myristate *B* | 0·090 | 0·055 | 0 | | | | | | | | |
| Nonanoate *A* | 0·095 | 0·097 | 0·070 | 0 | | | | | | | |
| Nonanoate *B* | 0·096 | 0·091 | 0·075 | 0·061 | 0 | | | | | | |
| Octanoate | 0·086 | 0·075 | 0·054 | 0·060 | 0·067 | 0 | | | | | |
| Acetate *A* | 0·131 | 0·140 | 0·126 | 0·100 | 0·087 | 0·097 | 0 | | | | |
| Acetate *B* | 0·134 | 0·132 | 0·101 | 0·098 | 0·120 | 0·111 | 0·175 | 0 | | | |
| Monohydrate *A* | 0·156 | 0·153 | 0·148 | 0·147 | 0·126 | 0·133 | 0·101 | 0·204 | 0 | | |
| Monohydrate *C* | 0·136 | 0·121 | 0·102 | 0·094 | 0·093 | 0·088 | 0·096 | 0·138 | 0·121 | 0 | |
| Monohydrate *E* | 0·123 | 0·102 | 0·098 | 0·102 | 0·097 | 0·103 | 0·129 | 0·134 | 0·152 | 0·108 | 0 |
| Monohydrate *G* | 0·132 | 0·126 | 0·112 | 0·105 | 0·089 | 0·107 | 0·095 | 0·163 | 0·112 | 0·111 | 0·117 |

room temperature. These consisted of cholesteryl myristate (*A* and *B*) (Craven & DeTitta, 1976), cholesteryl nonanoate (*A* and *B*) (Guerina & Craven, 1977*b*), cholesteryl oleate and cholesteryl octanoate (Guerina & Craven, 1977*a*), and the four molecules of cholesterol monohydrate (Craven, 1976). In general, the magnitudes of distortion in the six-membered rings of these molecules lie in a relatively narrow range, $\Delta\theta \sim 10°$. The only exceptions are the *A* rings of cholesterol monohydrate, where $\Delta\theta \sim 20°$. The *D* rings of the esters are slightly distorted from a $13\beta,14\alpha$-twist, while those of the monohydrate molecules are near a $13\beta$-envelope conformation.*

The overall conformation of the steroid ring system includes the manner in which the rings are fused as well as individual ring geometry. A best least-squares fit for superposition was used for pair-wise comparison of the overall conformation of the C(1)–C(19) fragments in the cholesteryl ester and cholesterol monohydrate molecules enumerated above (Table 7). With the exception of cholesteryl acetate, the steroid rings of the cholesteryl esters are very similar. The average r.m.s. displacement of corresponding atoms for pairs of ester molecules ranges from 0·055–0·104 Å. It is the ester groups and fatty acid conformations which are irregular in these structures. The conformations of the ring systems in the cholesterol monohydrate and cholesteryl acetate crystal structures are more diverse than in the other esters. However, the average r.m.s. displacement of corresponding atoms is still ≤0·2 Å in all cases, indicating that the fused rings of the cholesterol monohydrate and cholesteryl ester molecules behave as an almost rigid system.

* See deposition footnote.

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