Two Polymorphic Crystal Structures of Cholesteryl 2,4-Dichlorobenzoate

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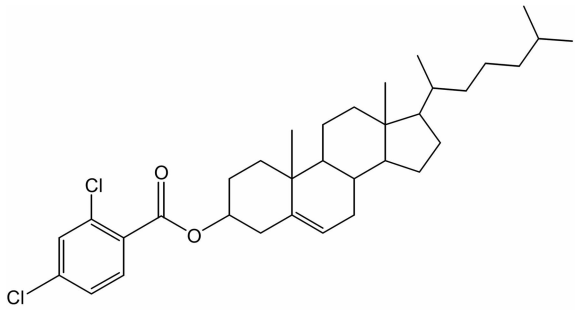
Cholesterol derivatives are important constituents of pathological conditions such as atherosclerosis, the formation of thick deposits on the inner surfaces of blood vessels.[1] The crystal structures of cholesteryl 2,4-dichlorobenzoate are of interest because their mode of crystallization and packing might be useful in understanding their deposition in arteries.



The cholesteryl 2,4-dichlorobenzoate ($C_{34}H_{48}O_2Cl_2$), has been crystallized in two polymorphic forms. Both forms are orthorhombic, space group $P2_12_12_1$, with form (**1a**) crystallizing from dichloromethane and form (**1b**) from hexane solution.

The molecular conformation is depicted in Figure 1 . The bond distances and angles of two molecules are constistent with those found in other other cholesterol derivatives.[2-10] There are considerable differences in the conformations of molecules **1a** and **1b** but not in the tetracyclic system. The major difference in the overall shape of the molecules can be attributed to the twist of the ester chains about the C3-O3 bond and C28-C29 bond. The torsion angles of C2-C3-O3-C28 and O3-C28-C29-C30 are 88.2(7) and 160.8(6)° in molecule **1a** and 156.7(7) and -10.7(11)° in molecule **1b**, respectively. (See Table 1)

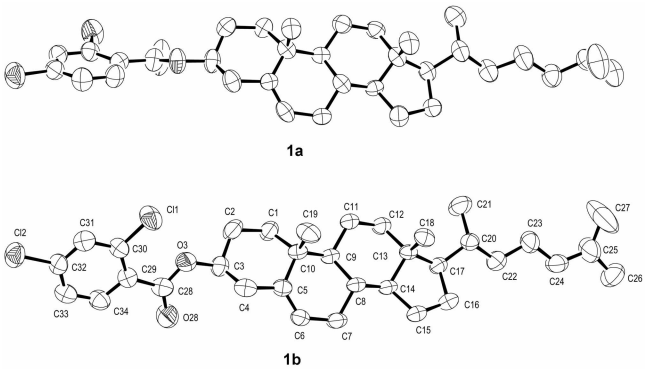


Figure 1. View of the molecules of polymorph (**1a**) and polymorph (**1b**) showing the atomic numbering. Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted for the sake of clarity.

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The packing diagrams for the two polymorphs are shown in Figure 2. The crystal structures are quite different each other although both forms crystallize in $P2_12_12_1$, and their corresponding unit cell distances are in good agreement within the 1 Å. The polymorphism could modify molecular geometries,[11,12] **1a** and **1b**, which are the conformational isomers each other. These lead to different molecular packings. No solvent molecules of crystallization are observed in both crystals.

The crystal structure of **1a** is remarkable in forming layer structures in which the central region of the layers, composed largely of semi-rigid cholesteryl groups is closely packed, and the packing of dichlorobenzoate and the isoprenoid tail of the cholesterol form the interface region between layers. The molecules are aligned antiparellel to form layers alternately. These layers are piled up in a herring-bone arrangements.

Crystals of **1a** melt to give an isotropic liquid (at 132.5 °C) with an intermediate cholesteric phase (at 130.8 °C). Such behavior seems consistent with the nature of the layer packing arrangement, which is dominated by the strong cholesteryl-cholesteryl interactions.

$$\text{solid} \xrightarrow{130.8\ ^\circ\text{C}} \text{cholesteric phase} \xrightarrow{132.5\ ^\circ\text{C}} \text{isotropic liquid}$$

The molecules of **1b** adopt extended conformations along

Table 1. Comparison of selected torsion angles (°)

	1a	**1b**
C1-C2-C3-O3	178.0 (6)	178.6 (7)
C5-C4-C3-O3	-179.0 (5)	-171.0 (5)
C2-C3-O3-C28	88.2 (7)	156.7 (7)
C4-C3-O3-C28	-149.8 (6)	-82.5 (8)
C3-O3-C28-O28	-3.0 (12)	7.7 (12)
C3-O3-C28-C29	177.1 (6)	-172.0 (6)
O3-C28-C29-C30	160.8 (6)	-10.7 (11)
O3-C28-C29-C34	-23.2 (9)	165.6 (7)
O28-C28-C29-C30	-19.1 (12)	169.6 (7)
O28-C28-C29-C34	157.0 (9)	-14.1 (11)

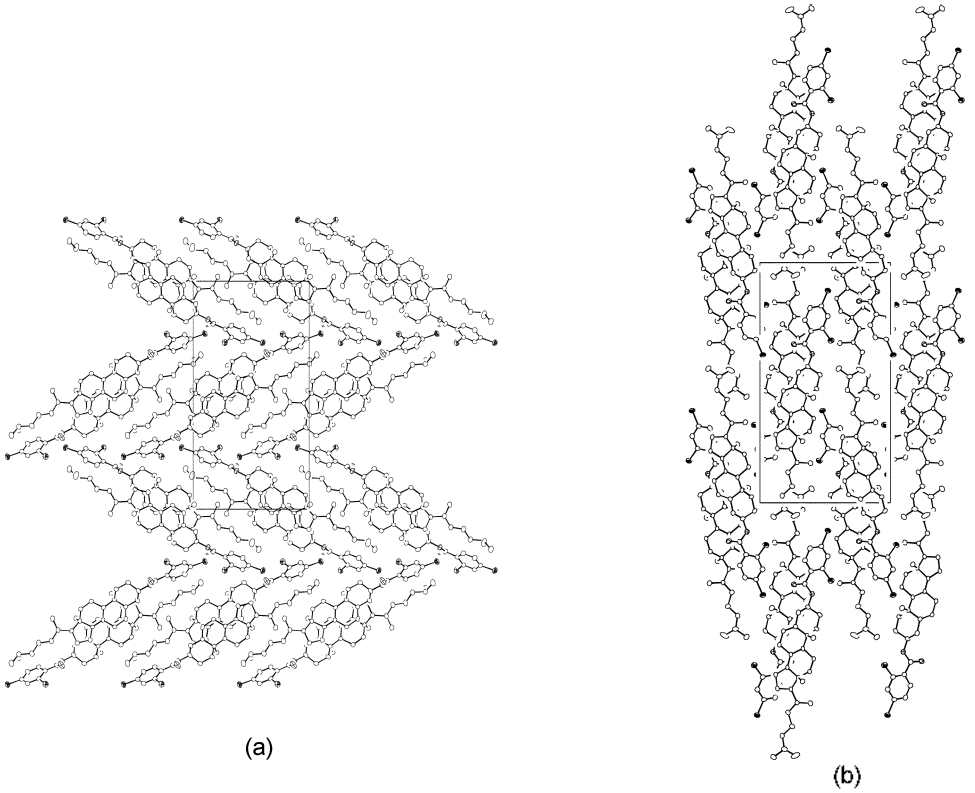

Figure 2. The crystal packing viewed down the *a* axis for (a) polymorph (**1a**) and (b) polymorph (**1b**). The *b* axis is horizontal.

the *c* axis and are orientated antiparallel, as shown in Figure 2(b). The plane of the tetracyclic rings and benzoate is parallel to *bc* plane. There are the close-stacking of cholesteryl and benzoate rings, with the terminal isoprenoid tails overlapping partially. The molecules form no distinct layer structures.

Crystals of **1b** melt at 133.7 °C without any liquid crystalline state.

Experimental Section

The crystal of title compound was obtained from Tokyo Kasei Kogyo Co., LTD. The crystals **1a** were obtained by recrystallization from dichloromethane and **1b** from hexane at room temperature.

Crystals of **1a** melt to give an isotropic liquid (at 132.5 °C) with an intermediate cholesteric phase (at 130.8 °C). Crystals of **1b** melt at 133.7 °C. The measurements were made by using Differential Scanning Calorimeter (DSC 2910, TA Instruments).

X-ray data were collected using a Nonius CAD-4 diffractometer with MoKα graphite monochromated radiation up to θ_{max} of 25°. Space Group of both crystals is orthorhombic, $P2_12_12_1$. The $\omega/2\theta$ scan width was $(1.10 + 0.35\tan\theta)°$.

Refinement was by full-matrix least-squares methods. All H atoms were located in geometrically calculated positions and refined isotropically. The following programs are used: Data collection: CAD-4-PC software,[13] Cell refinement: SET4[13] and CELDIM,[13] Data reduction: WinGX,[14] Program(s) used to solve structure: SHELXS-97,[15] Program(s) used to refine structure: SHELXL-97,[15] Molecular graphics: ORTEP3.[16] The crystal data and refinements were summarized in Table 2.

Table 2. Crystal data and structure refinements of cholesteryl 2,4-dichlorobenzoate

	1a	**1b**
a	9.6209 (15) A	9.2944 (9)
b	12.8168 (12) A	13.4570 (13)
c	25.198 (3) A	24.7277 (17)
Absorption coefficent	0.238 mm^{-1}	0.238
Absorption correction by psi-scans[17] T_{min}/T_{max}	0.913/0.999	0.872/0.998
Number of measured reflections	3097	3441
Number of observed reflections [I>2σ(I)]	2190	2461
Number of refined parameters	344	344
R(F^2)	0.056	0.068
Goodness-of-fit on F^2	1.056	1.168
$\Delta\rho$max	0.26 eÅ ^{3}	0.35
$\Delta\rho$min	-0.23 eÅ ^{3}	-0.41

Supporting Information Materials. Crystallographic data for cholesteryl 2,4-dichlorobenzoate have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC 230251 for **1a** and 230252 for **1b**.

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