

Crystal Structure and Liquid Crystalline State of Cholesteryl Butylcarbonate

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The crystal structures of a series of esters and carbonates of cholesterol was examined, in order to obtain structural information relevant to their liquid crystalline phases and the possible modes of association of the cholesterol derivatives, as well as of other substances in biological systems.¹ An examination of the unit-cell parameters of the cholesterol derivatives suggests that the majority of them might have one of the four common crystal packing arrangements.²⁻⁵ However, the crystal data of the cholesteryl butylcarbonate obtained in this study indicate that this carbonate belongs to none of these four crystal structure types.

Cholesteryl butylcarbonate crystallized into two polymorphic forms, both of which exhibited liquid crystalline states. By carrying out the crystal structure determination of cholesteryl butylcarbonate, we have provided information on which to base extrapolations concerning the structures of the liquid phases of cholesteryl butylcarbonate.

Experimental Section

The title compound was obtained from Tokyo Kasei Kogyo Co. Ltd. The compound crystallized into two polymorphic forms, viz. platelike and blocklike, from an acetone solution at room temperature, as shown in Figure 1. The platelike crystals can be obtained from a DMF-chloroform mixed solution and a hexane solution.

The x-ray diffraction data of both crystals mounted on a loop were measured at 100 K with synchrotron radiation ($\lambda = 0.7000 \text{ \AA}$) on a 4A MXW ADSC Quantum-210 detector with a silicon double crystal monochromator at the Pohang Accelerator Laboratory, Korea. The raw data were processed and scaled using the program HKL2000.⁶ The structure of platelike form was solved by direct methods and the refinements were carried out with full-matrix least-squares on F^2

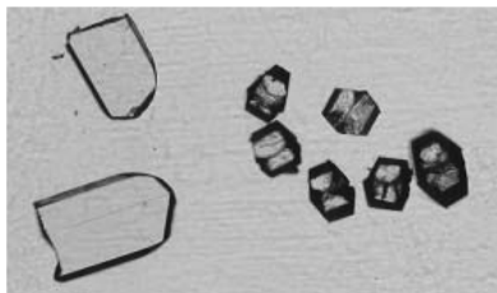


Figure 1. Photograph of single crystals of cholesteryl butylcarbonate, which exhibits a plate and block morphology.

Table 1. Summary of crystal data of cholesteryl butylcarbonate

Platelike crystal	
Crystal data	
$C_{32}H_{54}O_3$	$D_x = 1.100$ (calc.) $g\ cm^{-3}$
$M_w = 486.78$	Synchrotron radiation
Monoclinic, $P2_1$	($\lambda = 0.7000 \text{ \AA}$)
$a = 13.983(6) \text{ \AA}$	$\mu = 0.068\ mm^{-1}$
$b = 7.5350(15) \text{ \AA}$	$T = 100(2) \text{ K}$
$c = 28.526(6) \text{ \AA}$	Plate, Colorless
$\beta = 101.95(3)^\circ$	$0.40 \times 0.27 \times 0.15\ mm$
$V = 2940.4(10) \text{ \AA}^3$	
$Z = 4$	
Data collection	
ADSC Quantum 210 CCD	
Diffractometer	$\theta_{max} = 30.4^\circ$
ω scan type	$h = -20 \rightarrow 20$
Absorption correction: none	$k = -10 \rightarrow 0$
16617 measured reflections	$l = -40 \rightarrow 41$
9337 reflections with $I > 2\sigma(I)$	$R_{int} = 0.035$
Refinement	
Refinement on F^2	$w = 1/[s^2(F_o^2) + (0.0731P)^2 + 0.226P]$
$R[F^2 > 2\sigma(F^2)] = 0.0393$	where $P = (F_o^2 + F_c^2)/3$
$wR(F^2) = 0.1063$	
$S = 1.050$	$(\Delta/\sigma)_{mean} = 0.000$
9337 reflections	$\Delta\rho_{max} = 0.266\ e\text{\AA}^{-3}$
631 parameters	$\Delta\rho_{min} = -0.272\ e\text{\AA}^{-3}$
Blocklike crystal	
Crystal data	
$D_x = 1.102$ (calc.) $g\ cm^{-3}$	Synchrotron radiation
Monoclinic, $P2_1$	($\lambda = 0.7000 \text{ \AA}$)
$a = 8.878(2) \text{ \AA}$	$\mu = 0.068\ mm^{-1}$
$b = 23.796(5) \text{ \AA}$	$T = 100(2) \text{ K}$
$c = 27.815(6) \text{ \AA}$	Block, Colorless
$\beta = 95.45(3)^\circ$	$0.50 \times 0.35 \times 0.15\ mm$
$V = 5866(2) \text{ \AA}^3$	
$Z = 8$	
Data collection	
$\theta_{max} = 22.82^\circ$	$h = 0 \rightarrow 9$
Absorption correction: none	$k = -25 \rightarrow 25$
12911 measured reflections	$l = -29 \rightarrow 29$
9750 reflections with $I > 2\sigma(I)$	$R_{int} = 0.047$

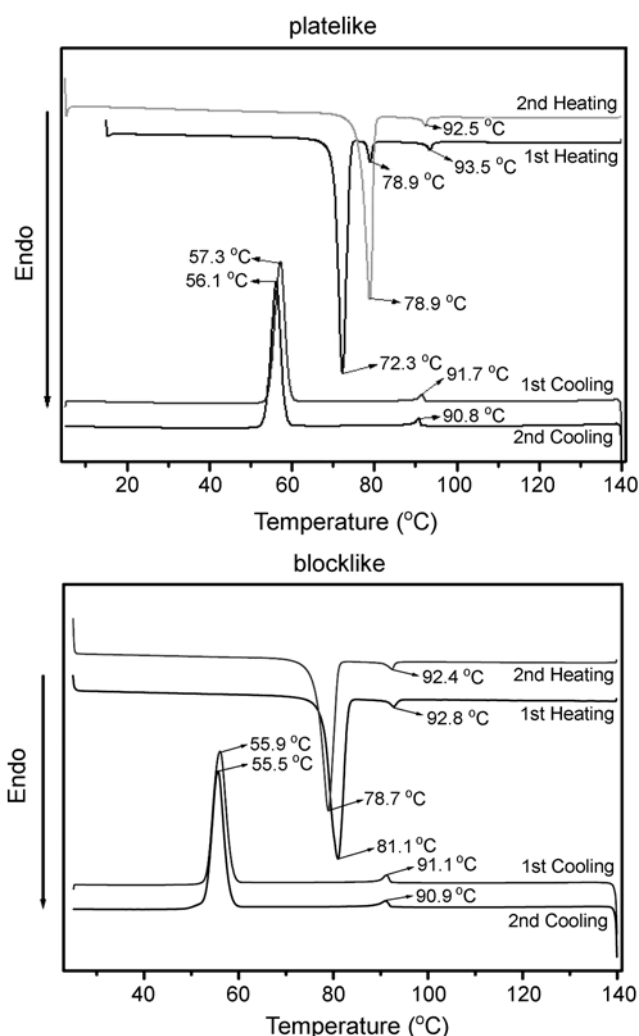


Figure 2. DSC diagram (5 °C/min.) of two crystal forms of cholesteryl butylcarbonate.

using the SHELXL-97 program.⁷ All of the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were positioned geometrically. As a result of the lack of significant anomalous scattering, the Friedel pairs were merged before the final refinement. The absolute configuration was assigned on the basis of the known cholesterol molecule. The structure determination of the blocklike form is in progress. The crystal data are listed in Table 1.

The thermal measurements were made using a Differential Scanning Calorimeter (Mettler Toledo DSC 821^e) with heating and cooling rates are of 5 °C/min. An Olympus BH-2 optical polarized microscope equipped with a Mettler FP-82HT hot stage and a Mettler FP-90 central processor was used to observe the thermal transitions and liquid crystalline states. Figure 2 shows the DSC diagrams for the two crystal forms. The liquid crystalline states are presented in Figure 3.

Results and Discussion

Cholesteryl butylcarbonate contains two molecules (A and B) in an asymmetric unit. The molecular structures of these

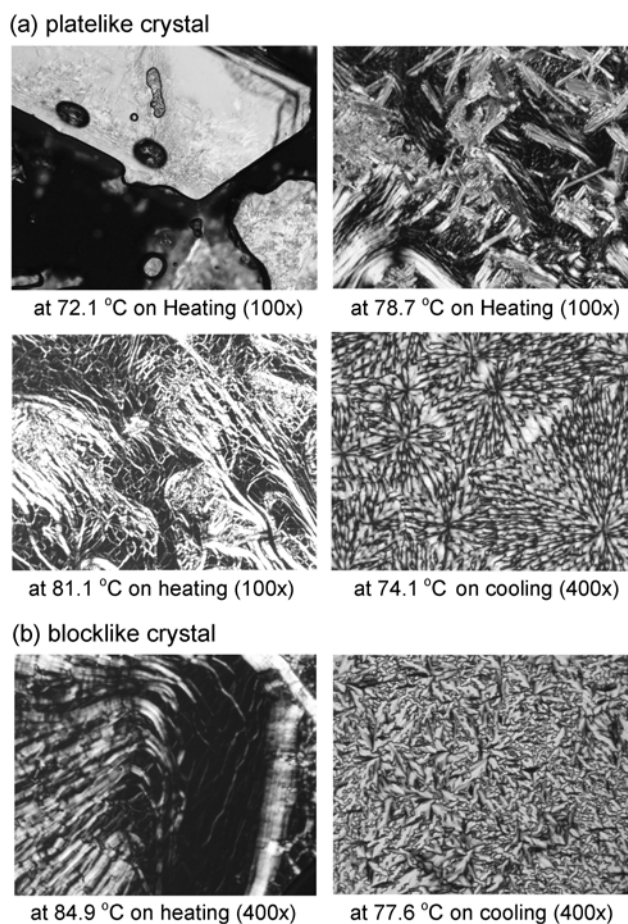


Figure 3. Optical polarized micrographs of cholesteryl butylcarbonate: (a) platelike crystal (b) blocklike crystal

two molecules are shown in Figure 4. The bond lengths and angles agree well with those of other cholesterol derivatives.⁸⁻¹¹ The conformations of the tetracyclic ring systems in molecules A and B are quite similar. The selected torsion angles in Table 2 are for the cholesteryl tails and carbonate chains, where the major differences in conformation occur. The C17-C26 tail of the two molecules is almost fully extended, as in most cholesterol derivatives. 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. The torsion angle of C2-C3-O3-C28 are 151.27(12) and 80.76(16)° in molecule A and B, respectively. The carbonate chains of both molecules are fully extended.

In the crystal structure (Figure 5) of cholesteryl butylcarbonate, the molecules are arranged in bilayers, in each of which there is a parallel arrangement of the two crystallographically independent molecules, A and B, and an anti-parallel arrangement of molecules related by a screw axis. The molecules in bilayer are partly interdigitated and tilted with respect to the layer planes. The best least-squares planes through the atoms of the cholesterol rings in molecules A and B are almost parallel with an interplanar angle of 4.34(3)°. At the center of the bilayers, there is a close packing involving the cholesteryl-cholesteryl, cholesteryl-C17 tails and

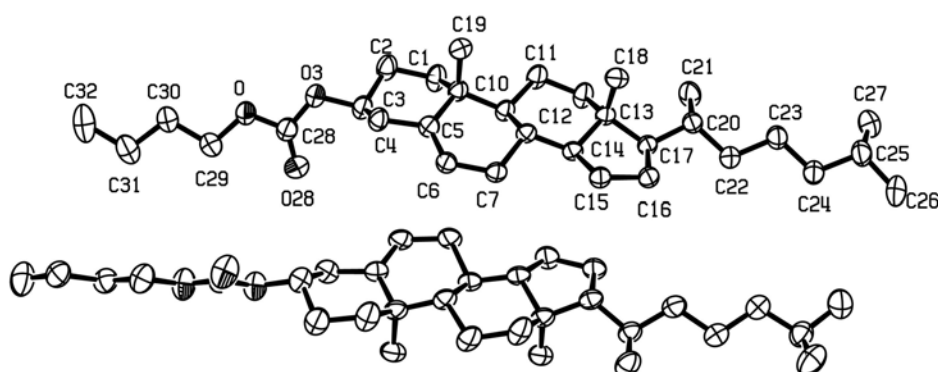


Figure 4. Best view of the asymmetric unit, with the atomic numbering shown only for molecule A. Displacement ellipsoids are drawn at the 80% probability level and the H atoms have been omitted for the sake of clarity.

Table 2. Comparison of selected torsion angles ($^{\circ}$) The e.s.d.'s are in parentheses

	Molecule A	Molecule B
Butylcarbonate chain		
C1-C2-C3-O3	179.61(11)	171.89(11)
C2-C3-O3-C28	151.27(12)	80.76(16)
C4-C3-O3-C28	-89.16(14)	-158.82(13)
C3-O3-C28-O28	-3.6(2)	-4.3(2)
C3-O3-C28-O	176.45(11)	175.86(13)
O28-C28-O-C29	-4.7(2)	0.2(3)
O3-C28-O-C29	175.19(12)	-179.93(13)
C28-O-C29-C30	-173.02(12)	175.13(13)
O-C29-C30-C31	-177.15(12)	-178.74(13)
C29-C30-C31-C32	-178.11(14)	-177.10(13)
C17 side tail		
C13-C17-C20-C21	-61.03(14)	-59.41(16)
C13-C17-C20-C22	175.71(10)	176.69(11)
C16-C17-C20-C21	177.54(11)	179.76(12)
C16-C17-C20-C22	54.28(14)	55.86(14)
C17-C20-C22-C23	-170.24(11)	-177.54(12)
C21-C20-C22-C23	65.54(14)	57.56(16)
C20-C22-C23-C24	176.65(11)	172.80(12)
C22-C23-C24-C25	-175.88(12)	-179.50(12)
C23-C24-C25-C26	173.74(14)	176.39(14)
C23-C24-C25-C27	-62.81(16)	-60.41(17)

cholesteryl-butylcarbonate chains. Within each layer, there are three different packing regions. Regions of packed cholesteryl ring systems alternate with regions of packed C17 tails, and with butylcarbonate packing regions (See Figure 5).

As expected, the crystal structure does not belong to any of the four main crystal structure types, but is similar to that of cholesteryl myristate.⁵ Both of these crystal structures form bilayers. The main crystal structural differences are the packing mode involving the cholesteryl ring systems and the longer myristate chain packing in the cholesteryl myristate.

As shown in Figure 3, the platelike crystals melt to give an isotropic liquid (at 93.5 $^{\circ}$ C) with two intermediate liquid crystalline phases (at 72.3 and 78.9 $^{\circ}$ C). The blocklike crystals

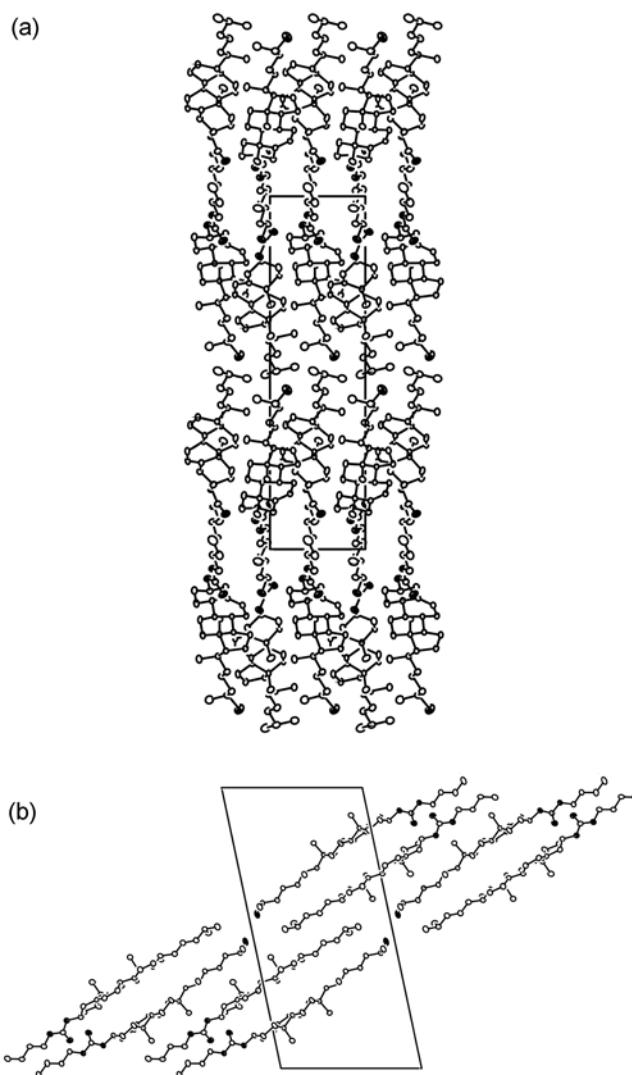


Figure 5. (a) The crystal packing viewed down the *a* axis. The *b* axis is horizontal. (b) Part of the crystal structure showing the parallel and antiparallel molecular arrangement viewed down the *b* axis. Octant shading indicates oxygen atoms and C26 atoms of molecule A.

melt at 92.8 with an intermediate cholesteric phase (at 81.1 $^{\circ}$ C). The following thermal transition path is suggested:

72 °C 78 °C 93 °C
Platelike crystal → mesophase → cholesteric ↔ isotropic liquid
53 °C ↓ ↑ 78 °C
blocklike crystal

The cholesteric liquid crystalline phases are confirmed by representative oily streak textures exhibited on heating at 81 °C and on cooling at 74 °C. The first mesophase observed in the platelike crystal can be considered as a mixture of crystal and cholesteric liquid crystal or smectic phases, but more data are needed to confirm this inference. Small angle x-ray diffraction data may be necessary to confirm the smectic phase. Cholesteryl myristate also shows smectic and cholesteric phases.

In the smectic mesophase, the molecules are arranged side by side in a series of stratified layers. The molecules in the layers may be arranged in a regular or random side by side spacing arrangement. The long axes of the molecules are parallel to one another, and each layer can be one or more molecules thick. The cholesteric mesophase resembles the smectic mesophase in that the molecules are arranged in layers.¹² The crystal structures of cholesteryl butylcarbonate as well as that of cholesteryl myristate exhibit the parallel arrangement of the molecules within bilayers, which may be retained in corresponding smectic or cholesteric mesophases. The liquid crystalline behavior of cholesteryl butylcarbonate seems to be consistent with the nature of the layer packing arrangement.

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Supporting Information Materials. The crystallographic data for cholesteryl butylcarbonate have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 632244. That data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/per1/catreq.cgi>

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