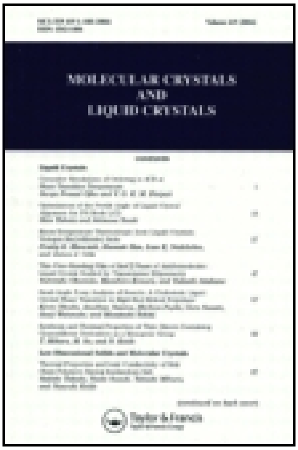

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The Crystal Structure of Cholesteryl δ-Monohydrofluoropentanoate

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The Crystal Structure of Cholesteryl δ-Monohydrofluoropentanoate

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Crystals of cholesteryl δ-monohydrofluoropentanoate (CδHFP), $C_{32}H_{46}O_2F_8$, are orthorhombic, space group $P2_12_12_1$ with cell dimensions a = 11.278(1), b = 46.511(4), c = 6.207(2)A, and Z = 4. The C(17) cholesterol side chains have in almost fully extended conformation, but the δ-monohydrofluoropentanoate chain bends out of the lath-like cholesterol skeleton by a gauche conformation about C(31)-C(34) bond. Molecular packing in the crystal structure is a unique bilayer structure which may be caused by the bend. The non-existence of a mesophase in CδHFP is explained by the bend of the δ-monohydrofluoropentanoate chain out of the cholesterol skeleton.

INTRODUCTION

Crystal structure determinations of cholesteryl esters have been undertaken by many workers,[1–11] as the structures prefigure the mesogenicity and the molecular arrangement in the mesomorphic state. Actually, the recent X-ray structural works on cholesteryl *n*-alkanoates show that the structure and molecular conformation in the crystals are closely relevant to the appearance of mesophases and to the molecular packings.

In the previous work on phase transitions in a series of cholesteryl fluoroalkanoates,[12,13] we found that the mesogenicities of these compounds are much more decreased than those of the corresponding cholesteryl *n*-alkanoates; the title compound, cholesteryl δ-monohydrofluoropentanoate[$C_{27}H_{45}OCO(CF_2)_3CF_2H$](CδHFP), has no mesophase, while cholesteryl *n*-pentanoate shows a cholesteric liquid crystalline phase between 361 and 369 K.[14]

This work is undertaken to determine the structure of CδHFP crystals and gives one answer as to why CδHFP shows no mesophase.

EXPERIMENTAL

CδHFP was synthesized by an esterification of cholesterol and δ-monohydrofluoropentanoic acid. Details of the synthesis are described in the previous paper.[13] Single crystals of CδHFP were grown by a very slow evaporation method from acetone solution at 298.2 K.

A crystal of 0.25 × 0.30 × 0.35 mm was used for the X-ray data collection on a Rigaku AFC-5 diffractometer equipped with graphite-monochromated Cu-Kα radiation. Lattice parameters were refined by a least-squares fit of 24 centered reflections ($40 < \theta < 50°$, $\lambda = 1.5418$ A).

Crystal data: $C_{32}H_{46}O_2F_8$, M = 614.7, orthorhombic, space group $P2_12_12_1$, a = 11.278(1), b = 46.511(4), c = 6.207(1)A, V = 3256.0(6)A^3, Z = 4, D_x = 1.25 gcm^{-3}, μ(Cu-Kα) = 0.95 mm^{-1}, colorless needle.

X-ray intensities were measured by $\omega/2\theta$ scan up to $2\theta = 100°$, beyond which there were few significant intensities. 1878 independent reflections were recorded. No absorption correction was applied. The structure was solved by direct methods.[15] An *E*-map gave the position of the cholesterol ring and the missing non-hydrogen atoms were located from subsequent weighted Fourier syntheses. The positions of hydrogen atoms were calculated assuming standard geometries. The structure was refined by a block-diagonal least-squares method with anisotropic temperature factors for non-hydrogen atoms. The parameters of the hydrogens were not refined. The weighting scheme employed was $w = 1/\sigma^2(F_0)$ for $|F_c| > 2\sigma(F_0)$ and $w = 0$ for $|F_c| \leqq 2\sigma(F_0)$ or $|\Delta F| > 3\sigma(F_0)$. $\sigma(F_0)$ was estimated by the relation $\sigma(F_0) = [\sigma_1^2(F_0) + 0.01165|F_0|^2]^{1/2}$, where $\sigma_1(F_0)$ is the e. s. d. based on counting errors.[16] The final *R*-value was 0.085 (R_w = 0.110) for 1569 reflections ($w \neq 0$). The atomic parameters are given in Table I. A perspective view of the molecule is shown in Figure 1.

TABLE I

Fractional atomic coordinates and isotropic thermal parameters

	x	y	z	B_{eq}
C(1)	0.1501(7)	0.3552(2)	0.4874(12)	6.9(2)
C(2)	0.1829(8)	0.3236(1)	0.4687(11)	6.8(2)
C(3)	0.3044(7)	0.3187(1)	0.5598(13)	6.7(2)
C(4)	0.3034(7)	0.3252(1)	0.7988(13)	6.6(2)
C(5)	0.2659(6)	0.3562(1)	0.8346(11)	5.3(2)
C(6)	0.3334(6)	0.3742(1)	0.9495(15)	6.4(2)
C(7)	0.3066(5)	0.4046(1)	1.0030(13)	6.1(2)
C(8)	0.1786(5)	0.4121(1)	0.9526(9)	4.4(1)
C(9)	0.1423(5)	0.3992(1)	0.7377(11)	5.5(2)
C(10)	0.1506(6)	0.3659(1)	0.7312(10)	4.9(2)
C(11)	0.0180(6)	0.4103(1)	0.6619(10)	5.9(2)
C(12)	0.0037(5)	0.4426(1)	0.6690(12)	5.4(2)
C(13)	0.0339(4)	0.4552(1)	0.8891(9)	3.8(1)
C(14)	0.1604(5)	0.4446(1)	0.9400(9)	4.1(1)
C(15)	0.1979(5)	0.4630(1)	1.1325(12)	5.7(2)
C(16)	0.1359(5)	0.4916(1)	1.0994(11)	5.4(2)
C(17)	0.0528(4)	0.4882(1)	0.9040(10)	4.6(2)
C(18)	-0.0543(5)	0.4451(1)	1.0627(11)	5.1(2)
C(19)	0.0458(6)	0.3526(1)	0.8506(11)	6.2(2)
C(20)	-0.0578(5)	0.5076(1)	0.9169(13)	6.2(2)
C(21)	-0.1471(8)	0.5033(2)	0.7331(17)	8.8(3)
C(22)	-0.0177(6)	0.5389(1)	0.9287(21)	8.1(3)
C(23)	-0.1162(7)	0.5603(2)	0.9828(19)	8.5(3)
C(24)	-0.0763(9)	0.5911(2)	0.9673(24)	10.6(4)
C(25)	-0.1681(11)	0.6129(2)	0.9892(27)	12.1(4)

TABLE I (*Continued*)

Fractional atomic coordinates and isotropic thermal parameters

	x	y	z	B_{eq}
C(26)	-0.1864(18)	0.6143(4)	1.2444(38)	18.1(8)
C(27)	-0.1262(19)	0.6387(5)	0.9494(66)	23.8(13)
O(28)	0.3308(4)	0.2878(1)	0.5493(9)	6.9(4)
C(29)	0.4053(7)	0.2800(2)	0.3916(13)	7.1(2)
O(30)	0.4543(6)	0.2946(1)	0.2722(10)	8.8(2)
C(31)	0.4195(7)	0.2458(2)	0.3992(14)	7.4(2)
F(32)	0.4538(5)	0.2387(1)	0.5993(11)	10.5(2)
F(33)	0.5119(4)	0.2395(1)	0.2805(10)	8.5(2)
C(34)	0.3194(8)	0.2262(2)	0.3446(14)	7.5(2)
F(35)	0.3510(4)	0.1985(1)	0.3560(12)	10.2(2)
F(36)	0.2338(5)	0.2309(1)	0.4979(11)	10.9(2)
C(37)	0.2700(11)	0.2334(2)	0.1623(21)	12.3(4)
F(38)	0.2173(9)	0.2579(1)	0.1302(15)	15.3(3)
F(39)	0.3512(8)	0.2374(2)	-0.0103(18)	20.8(5)
C(40)	0.1685(10)	0.2107(2)	0.0410(28)	12.7(5)
F(41)	0.0967(7)	0.2038(2)	0.2070(20)	16.8(4)
F(42)	0.2182(15)	0.1864(2)	-0.0037(22)	22.6(6)

RESULTS AND DISCUSSION

Molecular structure and molecular packing

Bond lengths and angles are listed in Table II. Some of the bond lengths, in particular, of the C(25)—C(27), C(34)—C(37) and C(37)—C(40) bonds, appear to be significantly different from the expected values. This effect could arise from large thermal librations of the two side chains.

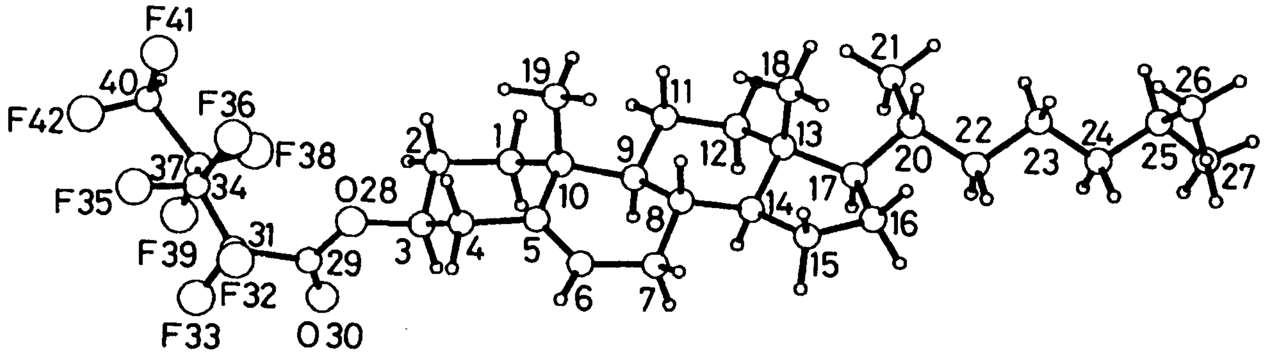

FIGURE 1 A prospective view of the molecule, showing the atom numbering.

The conformation of the cholesterol ring seems normal, although the torsion angle C(19)—C(10)—C(13)—C(18) of 14° may indicate a slight twist of the ring. The angle ranges between 8 and 12° in other related structures.[1] The C(17) side chain is fully extended as usual, whereas the fluoropentanoate chain assumes a gauche conformation about the C(31)—C(34) bond, the torsion angle C(29)—C(31)—C(34)—C(37) being 50°. Therefore, the fluoroalkanoate chain bends out of the director of the cholesteryl group, and this bend may be responsible for a unique crystal packing of the molecule which is shown in Figure 2. The CδHFP molecules are packed in a kind of bilayer structure which is quite different from that of cholesteryl *n*-alkanoates. In a plane, the molecules are packed in a zig-zag pattern. From the molecular packings, the intermolecular interaction seems to be weak.

TABLE II

Molecular dimensions
Bond distances (A)

C(1)-C(2)	1.520(13)	C(17)-C(20)	1.542(10)
C(1)-C(10)	1.593(12)	C(20)-C(21)	1.535(13)
C(2)-C(3)	1.500(12)	C(20)-C(22)	1.526(15)
C(3)-C(4)	1.514(11)	C(22)-C(23)	1.529(18)
C(3)-O(28)	1.469(10)	C(23)-C(24)	1.505(19)
C(4)-C(5)	1.519(11)	C(24)-C(25)	1.455(22)
C(5)-C(6)	1.338(12)	C(25)-C(26)	1.599(29)
C(5)-C(10)	1.519(10)	C(25)-C(27)	1.313(44)
C(6)-C(7)	1.484(12)	O(28)-C(29)	1.340(11)
C(7)-C(8)	1.518(10)	C(29)-O(30)	1.147(12)
C(8)-C(9)	1.519(9)	C(29)-C(31)	1.599(13)
C(8)-C(14)	1.527(8)	C(31)-F(32)	1.342(12)
C(9)-C(10)	1.552(10)	C(31)-F(33)	1.309(11)
C(9)-C(11)	1.566(10)	C(31)-C(34)	1.490(13)
C(10)-C(19)	1.526(10)	C(34)-F(35)	1.339(12)
C(11)-C(12)	1.512(10)	C(34)-F(36)	1.373(12)

TABLE II (*Continued*)

Molecular dimensions
Bond distances (A)

C(12)-C(13)	1.525(9)	C(34)-C(37)	1.305(16)
C(13)-C(14)	1.542(8)	C(37)-F(38)	1.301(17)
C(13)-C(17)	1.552(8)	C(37)-F(39)	1.422(17)
C(13)-C(18)	1.540(9)	C(37)-C(40)	1.730(22)
C(14)-C(15)	1.529(9)	C(40)-F(41)	1.349(21)
C(15)-C(16)	1.517(10)	C(40)-F(42)	1.292(24)
C(16)-C(17)	1.541(9)		

Bond angles (°)

C(2)-C(1)-C(10)	111,9(7)	C(13)-C(17)-C(20)	118.1(5)
C(1)-C(2)-C(3)	109,9(7)	C(16)-C(17)-C(20)	113,0(6)
C(2)-C(3)-C(4)	109,4(7)	C(17)-C(20)-C(21)	114.6(7)
C(2)-C(3)-O(28)	108,5(6)	C(17)-C(20)-C(22)	108.7(7)
C(4)-C(3)-O(28)	103,9(6)	C(21)-C(20)-C(22)	110.8(8)
C(3)-C(4)-C(5)	109.6(6)	C(20)-C(22)-C(23)	114.6(10)
C(4)-C(5)-C(6)	120.9(7)	C(22)-C(23)-C(24)	112.9(11)
C(4)-C(5)-C(10)	117.3(6)	C(23)-C(24)-C(25)	116.4(13)
C(6)-C(5)-C(10)	121.8(7)	C(24)-C(25)-C(26)	102.3(14)
C(5)-C(6)-C(7)	126.9(8)	C(24)-C(25)-C(27)	111.3(22)
C(6)-C(7)-C(8)	111.5(7)	C(26)-C(25)-C(27)	101.3(22)
C(7)-C(8)-C(9)	110.3(5)	C(3)-O(28)-C(29)	115.1(6)
C(7)-C(8)-C(14)	111.5(5)	O(28)-C(29)-O(30)	127.9(9)
C(9)-C(8)-C(14)	108.0(5)	O(28)-C(29)-C(31)	108.1(7)
C(8)-C(9)-C(10)	113.6(5)	O(30)-C(29)-C(31)	124,0(9)
C(8)-C(9)-C(11)	112.0(5)	C(29)-C(31)-F(32)	107.5(7)
C(10)-C(9)-C(11)	112.0(5)	C(29)-C(31)-F(33)	106.6(7)
C(1)-C(10)-C(5)	108.2(6)	C(29)-C(31)-C(34)	121.7(8)

TABLE II (*Continued*)

C(1)-C(10)-C(9)	109.6(6)	F(32)-C(31)-F(33)	103.7(7)
C(1)-C(10)-C(19)	109.4(6)	F(32)-C(31)-C(34)	106.2(8)
C(5)-C(10)-C(9)	109.7(5)	F(33)-C(31)-C(34)	109.8(8)
C(5)-C(10)-C(19)	109.7(6)	C(31)-C(34)-F(35)	112.0(8)
C(9)-C(10)-C(19)	110.2(5)	C(31)-C(34)-F(36)	106.1(8)
C(9)-C(11)-C(12)	114.5(6)	C(31)-C(34)-C(37)	111.3(9)
C(11)-C(12)-C(13)	112.6(6)	F(35)-C(34)-F(36)	107.7(8)
C(12)-C(13)-C(14)	105.5(5)	F(35)-C(34)-C(37)	114.0(9)
C(12)-C(13)-C(17)	117.6(5)	F(36)-C(34)-C(37)	105.1(9)
C(12)-C(13)-C(18)	111.4(5)	C(34)-C(37)-F(38)	123.6(12)
C(14)-C(13)-C(17)	100.2(4)	C(34)-C(37)-F(39)	114.3(11)
C(14)-C(13)-C(18)	110.9(5)	C(34)-C(37)-C(40)	120.2(11)
C(17)-C(13)-C(18)	110.4(5)	F(38)-C(37)-F(39)	93.7(10)
C(8)-C(14)-C(13)	116.8(5)	F(38)-C(37)-C(40)	99.5(11)
C(8)-C(14)-C(15)	118.5(5)	F(39)-C(37)-C(40)	100.3(10)
C(13)-C(14)-C(15)	103.7(5)	C(37)-C(40)-F(41)	102.1(12)
C(14)-C(15)-C(16)	104.9(6)	C(37)-C(40)-F(42)	102.5(15)
C(15)-C(16)-C(17)	107.3(5)	F(41)-C(40)-F(42)	102.5(15)
C(13)-C(17)-C(16)	103.4(5)		

Relationships in structure and mesomorphism between the alkanoate and the fluoroalkanoate

The crystal structures of cholesteryl *n*-alkanoates reported up to date were mainly classified into three types. A monolayer structure named Type II is found in the shorter esters with 6 to 8 carbon atoms, in which cholesteryl groups are closely packed antiparallel.[1–4] The medium chain length alkanoates with 9 to 12 carbon atoms form a different monolayer structure named Type I.[5–9] In the Type I, there are two molecules A and B which are mainly different in the molecular conformation of the alkanoate groups. Two molecules of each type pair in an antiparallel fashion, but the mean planes of the cholesteryl

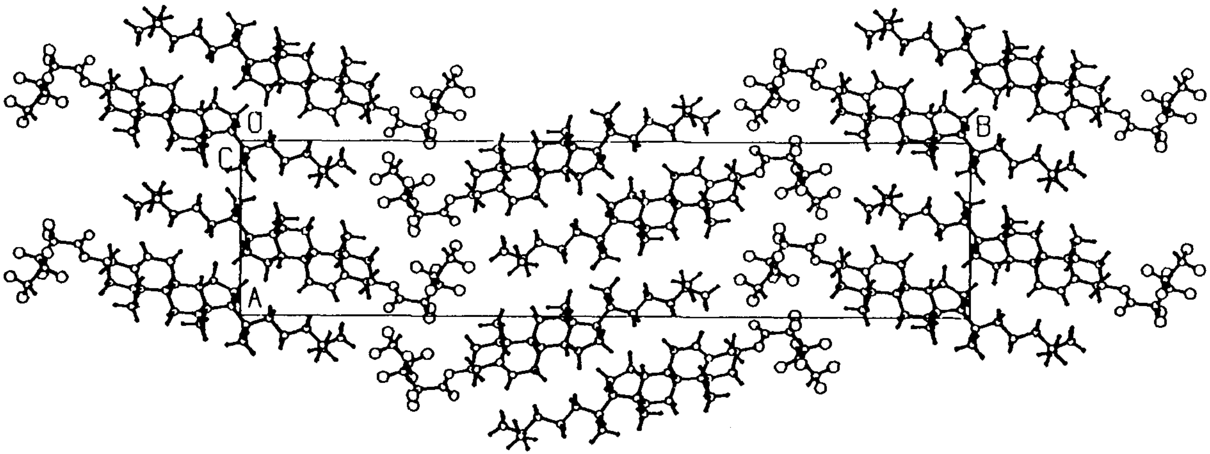

FIGURE 2 A projection of the structure viewed along the *c*-axis.

rings formed by a couple of A molecules are packed perpendicular to those formed by a couple of B molecules. In longer esters with 13 to 18 carbon atoms, the crystals show a bilayer structure, in which the interaction between alkanoate chains is predominant.[10,11] In all cholesteryl *n*-alkanoates, the alkanoate groups are almost fully extended in the direction of the cholesteryl skeleton. It has been reported that the crystal structures reflect faithfully the thermal stability of the liquid crystalline state for the cholesteryl *n*-alkanoates.

One of the most characteristic points in the molecular structure of CδHFP crystals is that the pentanoate chain bends out of the director of the cholesteryl skeleton by the gauche-trans conformation of C(31)—C(34)—C(37) moiety (Figure 1). This bend must cause the decrease of mesogenicity in the fluoralkanoates, because the bent fluoropentanoate group make CδHFP molecule non-linear shaped, and in connection with the bend, CδHFP crystals show the unique bilayer structures, in which the intermolecular interaction may be weaker than that of cholesteryl *n*-alkanoates. The above interpretation must be true for CδHFP, but that for the other cholesteryl fluoroalkanoates must of course wait the crystal structure determination, because the lattice parameters are very different for the different chain lengths of the fluoroalkanoates (for example, in the homologous series of cholesteryl ω-monohydrofluoroalkanoates [$C_{27}H_{45}OCO(CF_2)_nCF_2H$], the $n = 1$, 5 and 7 crystals are monoclinic: the $n = 1$: a = 9.33 A, b = 13.3 A, c = 12.5 A, β = 106.6°, the $n = 5$: a = 9.39 A, b = 15.0 A, c = 12.6 A, β = 91.3° and the $n = 7$: a = 11.1 A, b = 27.7 A, c = 6.37A, β = 91.0°).[13,17] However, in the $n = 1$ crystals and cholesteryl perfluoropropionate ($C_{27}H_{45}OCOCF_2CF_3$) crystals, which are nonmesogenic compounds, the fluoropropionate groups have been also found to bend out of the director of cholesteryl skeleton,[18] similar to the bend of the CδHFP crystals. Further work for the crystal structure of various cholesteryl fluoroalkanoates is in progress to clarify the relation of the crystal structure to the mesogenicity.

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