Isomorphic Crystal Structures of Two Cholesterol Ethers

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A series of crystal structures of the ethers, esters and carbonates of cholesterol[1-13] were examined to obtain the structural information relevant to the liquid crystalline phases and the possible modes of association between the cholesterol derivatives and themselves as well as with other substances in biological systems.[14]

An examination of the unit cell parameters of the cholesterol derivatives suggests that the majority of the derivatives might have one of three common crystal packing arrangements,[15] so called monolayer type I, type II and bilayer. The crystal data of cholesteryl ethylether and isopropylether obtained in this study indicate that those ethers belong to monolayer type II. Therefore, the primary aim of this study is to obtain the structural information on the conformation and the mode of the molecular interactions.

The bond lengths and angles of cholesteryl ethylether and isopropylether are in good agreement, within experimental error, with those found in other cholesterol derivatives (see Table 1). The bond lengths in the C17 tails and ether chains show the apparent shortening which is characteristic of cholesterol derivatives, and is caused by the high thermal vibrations in these regions. In this case, it is especially pronounced in the C25-C27, C28-C29 and C28-C30 bond distances. The values of the atomic thermal parameters are unusually large, particularly in the ether groups and the terminal isopropyl group, C25, C26 and C27.

The atoms, C3, O3, C28 and C29 lie in the same plane, with the torsion angle about O3-C28 being 176.0 (5)° for ethylether and 175.6(9)° for isopropylether, respectively. The isoprenoid chain at C17 is almost fully extended. The seven atoms of C17, C20, C22-C26 are in a zigzag planar chain and C21 and C27 are out of the plane.

The crystal structures of cholesteryl ethylether and cholesteryl isopropyl ether (Fig. 2) consists of antiparallel molecules arranged to form monolayers which are parallel to the crystal (001) planes. Such monolayers are called type II. The monolayers are regions of closely packed semi-rigid cholesteryl ring systems that are separated by interface regions where the ether group atoms are more loosely packed. This packing type is similar to those of cholesteryl hexanoate,[6] heptanoate,[5] octanoate,[16] pentyl carbonate,[11] hexyl carbonate,[7] oleate[17] and chloroformate.[18] The difference in the monolayer thickness (11.10-18.76 Å) is associated primarily with structural differences in the interface region. The atoms in this region consist of the ester, carbonate or ether attached to O3 of cholesterol molecules.

Most of the layered structures show liquid crystalline states,[19] but these were not observed in the crystals of cholesteryl isopropylether. Crystals of cholesteryl isopropylether melt to give an isotropic liquid at a high temperature, 131.4 °C. On cooling the crystals, freezing occurs at a temperature (117.1 °C) which is considerably lower than the melting point. In cholesteryl ethylether, melting occurs at 87.7 °C. The cholesteric phase forms only on cooling (73.3 °C). The freezing point of the cholesteryl ethylether is

Table 1. Selected geometric parameters (Å, °)

	Cholesteryl ethylether	Cholesteryl isopropylether
C17-C20	1.527(4)	1.537(7)
C20-C21	1.526(5)	1.515(8)
C20-C22	1.530(5)	1.515(7)
C22-C23	1.508(5)	1.515(8)
C23-C24	1.507(5)	1.518(7)
C24-C25	1.513(4)	1.505(8)
C25-C26	1.531(5)	1.535(9)
C25-C27	1.476(5)	1.421(11)
C3-O3	1.449(4)	1.440(7)
O3-C28	1.321(5)	1.201(8)
C28-C29	1.483(6)	1.516(11)
C28-C30		1.396(13)
C2-C3-O3	106.7(3)	107.0(5)
C3-O3-C28	115.7(4)	126.4(6)
O3-C28-C29	111.8(5)	111.9(9)
O3-C28-C30		132.9(9)
C13-C17-C20-C22	179.2(3)	179.2(5)
C17-C20-C22-C23	−164.2(3)	−167.2(5)
C20-C22-C23-C24	−179.5(3)	177.6(5)
C22-C23-C24-C25	175.7(3)	174.2(6)
C23-C24-C25-C26	−170.5(4)	−173.8(7)
C23-C24-C25-C27	63.7(5)	55.1(9)
C1-C2-C3-O3	177.7(3)	175.6(6)
C2-C3-O3-C28	157.6(6)	139.4(11)
C3-O3-C28-C29	176.0(5)	175.6(9)
C3-O3-C28-C30		−20(2)

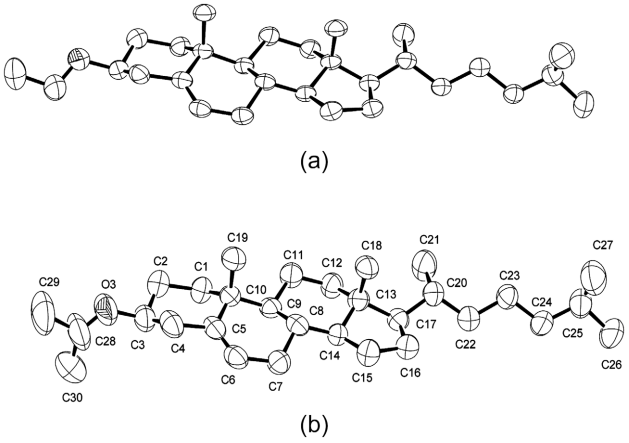

Figure 1. View of the molecules of (a) cholesteryl ethylether and (b) cholesteryl isopropylether showing the atomic numbering. Displacement ellipsoids are drawn at the 50% probablity level and H atoms have been omitted for the sake of clarity.

68.9 °C.

We have solved the crystal structures of three cholesteryl ethers. Those are methylether,[9] ethylether and isopropylether. Though the crystal structures of ethyl and isopropylethers are isomorphous each other, cholesteryl methylether ($P2_1$, a = 11.740(8), b = 7.576(5), c = 15.492(10) Å, β =

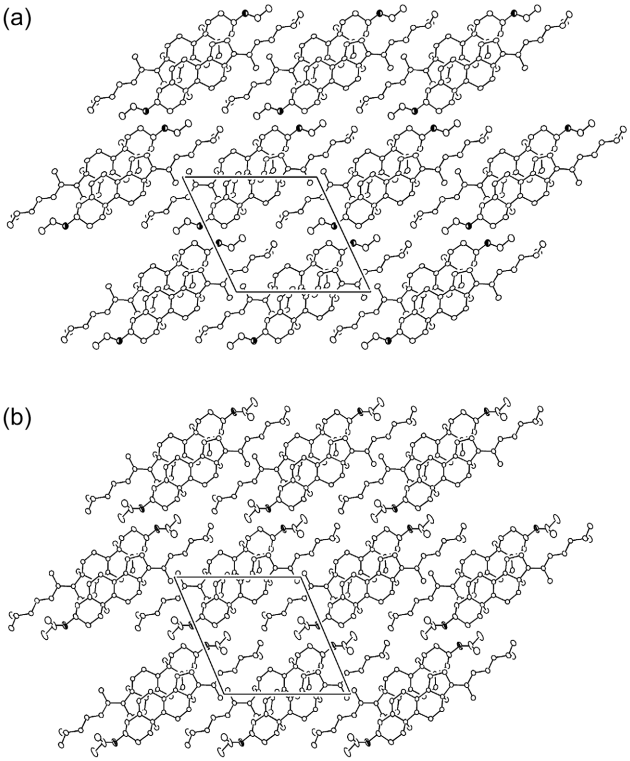

Figure 2. The crystal packing viewed down the b axis for (a) cholesteryl ethylether and (b) cholesteryl isopropylether. The a axis is horizontal.

Table 2. Crystal data and structure refinements

Cholesteryl ethylether	
Crystal data	
$C_{29}H_{50}O$	Mo Kα radiation
M_r = 414.69	Cell parameters from 2385 reflections
Monoclinic, $P2_1$	θ = 2.78-20.41°
a = 12.9594 (10) Å	μ = 0.059 mm^{-1}
b = 9.3407 (8) Å	T = 232 (2) K
c = 12.2652 (11) Å	Prism, colorless
β = 115.118 (2)°	0.35 × 0.34 × 0.16 mm
V = 1344.3 (2) Å^3	
Z = 2	
D_x = 1.025 Mg m^{-3}	m.p = 87.7 °C
Data collection	
Bruker SMART 1000 CCD area-detector diffractometer	6565 independent reflections 2799 reflections with I > 2σ(I)
ω scans	R_{int} = 0.0304
Absorption correction: integration[27]	θ_{max} = 28.3°
T_{min} = 0.973, T_{max} = 1.000	$h = -16 \rightarrow 16$
	$k = -12 \rightarrow 12$
13975 measured refletions	$l = -17 \rightarrow 17$
Refinement	
Refinement on F^2	w = 1/[σ^2(F^2_o)+(0.0000P)^2 +0.4045P]
R[F^2>2σ(F^2)] = 0.055	where P = (F^2_o+2F^2_c)/3
wR(F^2) = 0.122	$(\Delta/\sigma)_{max}$ = 0.008
S = 1.05	$\Delta\rho_{max}$ = 0.26 eÅ^{-3}
6565 reflections	$\Delta\rho_{min}$ = −0.16 eÅ^{-3}
271 parameters	
H-atom parameters constrained	

Cholesteryl isopropylether	
Crystal data	
$C_{30}H_{52}O$	MoKα radiation
M_r = 428.72	Cell parameters from 25 reflections
Monoclinic, $P2_1$	θ = 8.68-13.24°
a = 12.5786 (16) Å	μ = 0.060 mm^{-1}
b = 9.3966 (5) Å	T = 293 (2) K
c = 12.665 (2) Å	Prism, colorless
β = 113.006 (11)°	0.50 × 0.35 × 0.25 mm
V = 1377.9 (3) Å^3	
Z = 2	
D_x = 1.033 Mg m^{-3}	m.p = 131.4 °C
Data collection	
Enraf-Nonius CAD-4 diffractometer	Mo Kα radiation
θ/2θ scans	R_{int} = 0.058
Absorption correction = psi-scan[28]	θ_{max} = 26.97°
T_{min} = 0.973, T_{max} = 1.000	$h = 0 \rightarrow 16$
	$k = -11 \rightarrow 11$
	$l = -16 \rightarrow 14$
5972 measured reflections	3 standard reflections every 1 hour
5832 independent reflctions	intensity decay: negligible
Refinement	
Refinement on F^2	w = 1/[σ^2(F^2_o)+(0.1697P)^2 +0.00P]
R[F^2>2σ(F^2)] = 0.080	where P = (F^2_o+2F^2_c)/3
wR(F^2) = 0.221	$(\Delta/\sigma)_{max}$ = 0.000
S = 0.970	$\Delta\rho_{max}$ = 0.21 eÅ^{-3}
5832 reflections	$\Delta\rho_{min}$ = −0.32 eÅ^{-3}
280 parameters	
H-atom parameters constrained	

110.39(5)°, z = 2) has a different crystal structure which is isomorphous with those of cholesteryl chloride[20] and bromide.[20]

Experimental Section

The compounds of two cholesteryl ethers was obtained from Sigma Chemical Co. Ltd. The crystals were obtained by recrystallization from acetone solution. X-ray data were collected using a Brucker SMART 1000 CCD for cholesteryl ethylether and Nonius CAD-4 diffractometer with MoKα graphite monochromated radiation for cholesteryl isopropylether.

Refinement was done by full-matrix least-squares methods. All H atoms were located in geometrically calculated positions and refined isotropically. Because of the lack of significant anomalous scattering, Friedel equivalents could not be used to determine the absolute configuration.[21] The absolute configuration was assigned on the basis of known cholesteryl haxanoate molecule. The following programs are used: Data collection and cell refinement: SMART,[22] Data reduction: SAINT-Plus[22] for cholesteryl ethylether; Data collection: CAD-4-PC software,[23] Cell refinement: SET4[23] and CELDIM,[23] Data reduction: WinGX[24] for cholesteryl isopropylether. Program(s) used to solve structure: SHELXS-97,[25] Program(s) used to refine structure: SHELXL-97,[25] Molecular graphics: ORTEP3.[26] The crystal data and refinements were summarized in Table 2.

The thermal measurements were made by using Differential Scanning Calorimeter (DSC 2910, TA Instruments).

Crystallographic data for the structures reported here have been deposited with CCDC (Deposition No. CCDC 274792 (cholesteryl ethylether) and 274793 (cholesteryl isopropylether)). These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html or from CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, email: deposit@ccdc.cam.ac.kr.

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