

The Crystal Structure of 12-D-Hydroxyoctadecanoic Acid Methyl Ester

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12-D-Hydroxyoctadecanoic acid methyl ester is monoclinic ($P2_1$) with $a=8.380$, $b=4.861$, $c=25.59$ Å and $\beta=102.18^\circ$. The molecules are arranged 'head-to-tail' in single layers in which the chain axes are tilted 69.5° to the end-group contact planes. The hydrocarbon chains pack according to the orthorhombic subcell $O\perp$ with $a_s=4.86$, $b_s=7.87$ and $c_s=2.54$ Å. The hydroxyl groups are accommodated into the chain matrix without any major local distortion but by a general expansion of the chain packing. The b_s axis is thus 0.46 Å longer than in hydrocarbons. The hydroxyl groups link the molecules by hydrogen bonds along the twofold screw axis.

Introduction

Long-chain hydroxy fatty acids in which the hydroxyl group is attached in the middle of the hydrocarbon chain are frequently found in nature. Such acids have been isolated from beeswax and bee mandibular gland, from the bark, roots and seeds of a variety of plant species and also from human faecal lipids (for a review see Downing, 1961).

The research programme at this department concerns compounds which can provide information on the conformation and molecular arrangement of membrane lipids. A series of substituted lipids have been studied to explore how different functional groups can be accommodated in a lipophilic layer. It is of special interest to determine whether hydroxyl groups located in a hydrocarbon chain matrix disturb the chain packing or if they instead promote a close packing and rigidity of the chain layers by forming intermolecular hydrogen bonds. This is of importance for the understanding of the functional significance of hydroxyl groups in the lipophilic ceramide part of sphingolipids. In these membrane lipids, which are rather abundant in the surface layer of plasma membranes, the number of hydroxyl groups varies characteristically in different tissues and is considered to effect the stability of the membrane (Pascher, 1976).

Experimental

The methyl ester of 12-D-hydroxyoctadecanoic acid was prepared from 12-D-hydroxy-*cis*-8-octadecenoic acid (ricinoleic acid) of castor oil by hydrogenation and esterification. Crystals grew from ethyl acetate as thin plates, which melt at 57.1°C .

Crystal data

$\text{C}_{19}\text{H}_{38}\text{O}_3$, 12-D-hydroxyoctadecanoic acid methyl ester, M.W. 314.30; unit cell: monoclinic, $a=8.380$ (6), $b=4.861$ (4), $c=25.59$ (2) Å, $\beta=102.18$ (8)°, $V=$

1019.12 Å³, $Z=2$; $D_c=1.02$, $D_m=1.02$ g cm⁻³; $\lambda=1.54051$ Å (Cu $K\alpha_1$ radiation), $\mu=5.27$ cm⁻¹; systematic absences: $0k0$, $k=2n+1$; space group $P2_1$.

Reflexion data were collected on a Picker FACS-1 diffractometer using graphite-monochromated Cu $K\alpha$ radiation. The $\theta/2\theta$ scanning mode was used with a scan speed of 1° min⁻¹. The scan width was 2.2° . The background level was determined by 10 s counts on each side of the reflexion. In all, 1619 reflexions were measured with $2\theta < 120^\circ$ and, of these, 1157 were considered observed ($I > 2\sigma$).

The intensities were corrected for Lorentz and polarization effects and for extinction but not for absorption. Scattering factors for C and O were those in *International Tables for X-ray Crystallography* (1962) and for H those of Stewart, Davidson & Simpson (1965). The calculations were performed on a System DEC 10 using *MULTAN* by Germain, Main & Woolfson (1971) and the X-RAY system (Stewart, Kruger, Ammon, Dickinson & Hall, 1972). X-RAY 72 modifications for the DEC 10 were made by Dr Steve Ernst at Pittsburgh University and by Dr Robert Pearson at this Department.

Structure determination and refinement

The crystal structure solution was started with a crystal which only gave 624 reflexions greater than 2σ . 180 reflexions with $E > 1.3$ were used in *MULTAN*. 17 atoms in a chain were selected from the E map with the highest figure of merit. They all showed up as reasonably large peaks in the following Fourier map. However, a ghost chain also appeared with weak peaks parallel to the input atoms. The whole chain was now moved half the distance towards the ghost peaks and after a few rounds of structure factor and Fourier calculations all atoms in the molecule could be located. However, there were two additional peaks at the ester end of the molecule which formed a continuation of the chain. The molecule was therefore shifted one sub-

cell period in the chain direction which led to a decrease in the R value from 0.45 to 0.35.

The structure was then refined by full-matrix least-squares methods. All positional parameters and isotropic temperature factors were varied and the structure refined to an R of 0.18. However, at this stage new intensity data became available with twice as many observed reflexions. The refinement was continued varying all positional and anisotropic temperature parameters for the non-H atoms. A difference Fourier later revealed all the H atoms. They were included in the calculations with isotropic temperature factors corresponding to those of the parent atoms.

When R was 0.05, all H atom parameters were refined. An R value analysis showed poor agreement for the smallest reflexions. As most of them were calculated too low, the threshold value for observed reflexions was increased to $F = 3.0$. With the 868 reflex-

ions above this limit the structure refined to a final R of 0.044.*

The weighting scheme used during the final stages of the refinement was $W = 1/\{1 + [(F_o - 10.0)/9.0]^2\}$.

Description of the structure

The final atomic parameters are given for the non-H atoms in Table 1 and for the H atoms in Table 2. Interatomic distances and angles are given in Fig. 1, where the atomic numbering is also shown.

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31881 (11 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1. Fractional atomic and thermal parameters with their *e.s.d.*'s for the non-hydrogen atoms

All values have been multiplied by 10^4 . The anisotropic temperature factors are in the form:

$$\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2hka^*b^*U_{12} + 2hla^*c^*U_{13} + 2klb^*c^*U_{23})].$$

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	7688 (8)	987 (26)	9500 (3)	1462 (58)	4207 (159)	1280 (52)	1551 (85)	-516 (43)	-925 (74)
O(2)	7083 (5)	3468 (18)	107 (2)	1007 (31)	1761 (61)	635 (25)	-33 (49)	-257 (23)	-67 (43)
O(3)	5132 (3)	3029 (11)	4766 (1)	449 (16)	522 (18)	593 (18)	-6 (23)	87 (14)	8 (24)
C(1)	6776 (8)	2367 (24)	9634 (3)	742 (48)	1642 (103)	579 (40)	119 (61)	-78 (34)	-104 (58)
C(2)	5204 (7)	3359 (22)	9299 (2)	924 (42)	1089 (57)	620 (33)	156 (57)	-114 (30)	27 (51)
C(3)	4781 (7)	2012 (16)	8758 (2)	928 (42)	899 (61)	554 (31)	43 (44)	-84 (31)	48 (40)
C(4)	3237 (7)	3083 (22)	8400 (2)	853 (38)	760 (43)	583 (30)	-39 (60)	-72 (28)	-7 (53)
C(5)	2908 (7)	1855 (15)	7848 (2)	797 (40)	709 (47)	566 (32)	83 (40)	-93 (29)	52 (35)
C(6)	1440 (6)	3017 (22)	7458 (2)	689 (33)	726 (39)	523 (27)	3 (55)	-29 (24)	75 (50)
C(7)	1208 (7)	1844 (15)	6898 (2)	736 (37)	649 (43)	499 (31)	9 (35)	-7 (27)	61 (33)
C(8)	9803 (6)	3060 (20)	6496 (2)	592 (30)	656 (37)	462 (26)	8 (49)	-6 (22)	-41 (46)
C(9)	9620 (6)	1929 (14)	5939 (2)	549 (31)	572 (42)	542 (30)	18 (30)	-27 (24)	2 (30)
C(10)	8237 (5)	3229 (18)	5532 (2)	494 (26)	541 (35)	484 (26)	22 (41)	31 (21)	-74 (38)
C(11)	8020 (5)	2009 (15)	4974 (2)	426 (28)	528 (37)	464 (26)	17 (26)	62 (22)	23 (26)
C(12)	6615 (5)	3272 (18)	4572 (2)	428 (25)	388 (30)	495 (26)	20 (37)	93 (20)	-30 (37)
C(13)	6306 (6)	1933 (14)	4029 (2)	567 (31)	441 (34)	479 (28)	28 (29)	55 (23)	17 (27)
C(14)	4888 (6)	3148 (19)	3625 (2)	630 (30)	511 (33)	515 (27)	-10 (46)	-39 (23)	-23 (44)
C(15)	4598 (6)	1840 (15)	3081 (2)	753 (37)	656 (45)	459 (30)	20 (36)	-56 (26)	31 (32)
C(16)	3157 (6)	2942 (20)	2681 (2)	745 (34)	755 (42)	534 (29)	83 (55)	-29 (25)	58 (51)
C(17)	2887 (8)	1684 (19)	2141 (2)	996 (49)	1111 (67)	621 (39)	-73 (51)	-110 (34)	-18 (46)
C(18)	1438 (8)	2737 (25)	1737 (2)	1031 (45)	1220 (75)	671 (35)	-80 (67)	-244 (33)	53 (58)
C(19)	8610 (8)	2890 (34)	463 (2)	970 (47)	2378 (120)	834 (43)	48 (100)	-356 (36)	150 (90)

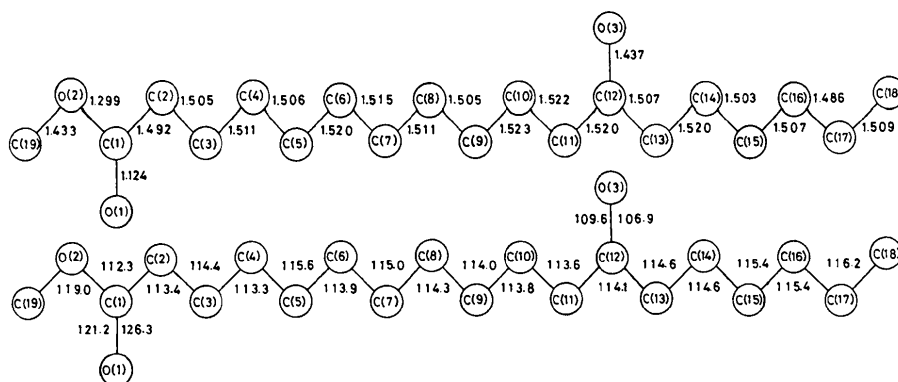


Fig. 1. Bond distances and angles in 12-D-hydroxyoctadecanoic acid methyl ester.

The molecules are arranged 'head-to-tail' as shown in Fig. 2. Hydrogen bonds in a zigzag pattern between the hydroxyl groups in the middle of the chains hold the molecules together in the **b** direction (Fig. 3). The O—H...O angle is 164.6°. The packing arrangement in the methyl-contact plane is normal with a closest C—C distance of 3.60 Å between C(18) and C(19). The carbonyl O has a rather unsymmetrical environment with the closest contacts to C(19) (3.43 Å) and C(18) (3.75 Å). Details of the packing arrangements in the end-group region are shown in Fig. 4.

The hydrocarbon chains pack according to the orthorhombic chain packing $O\perp$. The subcell dimensions are $a_s=4.86$, $b_s=7.87$, $c_s=2.54$ Å. The b_s axis is considerably longer than is found in an undisturbed chain environment (Abrahamsson, Stållberg-Stenhagen & Stenhagen, 1963) where the axis is about 7.40 Å. In 14-haptacosanol (Welsh, 1956) the dimensions of the distorted orthorhombic subcell are: $a_s=4.95$, $b_s=7.8$,

$c_s=2.58$ Å and $\beta=92^\circ$ and thus show the same expansion of the b_s axis.

As is usual in the chain packing $O\perp$, the extra space for the hydroxyl groups is provided by expanding the b_s axis. At the same time a_s contracts slightly and the chain axes approach a hexagonal pattern (Fig. 3). This expansion of the chain packing together with the unsymmetrical environment of the O atom on the carbonyl C explains the rather large anisotropic temperature factors of this O atom (Fig. 5).

An oxo group (Dahlén, 1972; O'Connell, 1968) will, on the other hand, fit well into the chain packing and give normal subcell dimensions. The only disturbance is a slight chain bend or twist due to the incorporation in the chain packing of the sp^2 -hybridized carbonyl C. However, even in this case the chain axis is somewhat bent in a direction perpendicular to the zigzag plane. Thus, C(12) in the middle of the chain is out of the chain plane by 0.116 Å on one side and C(18) at the

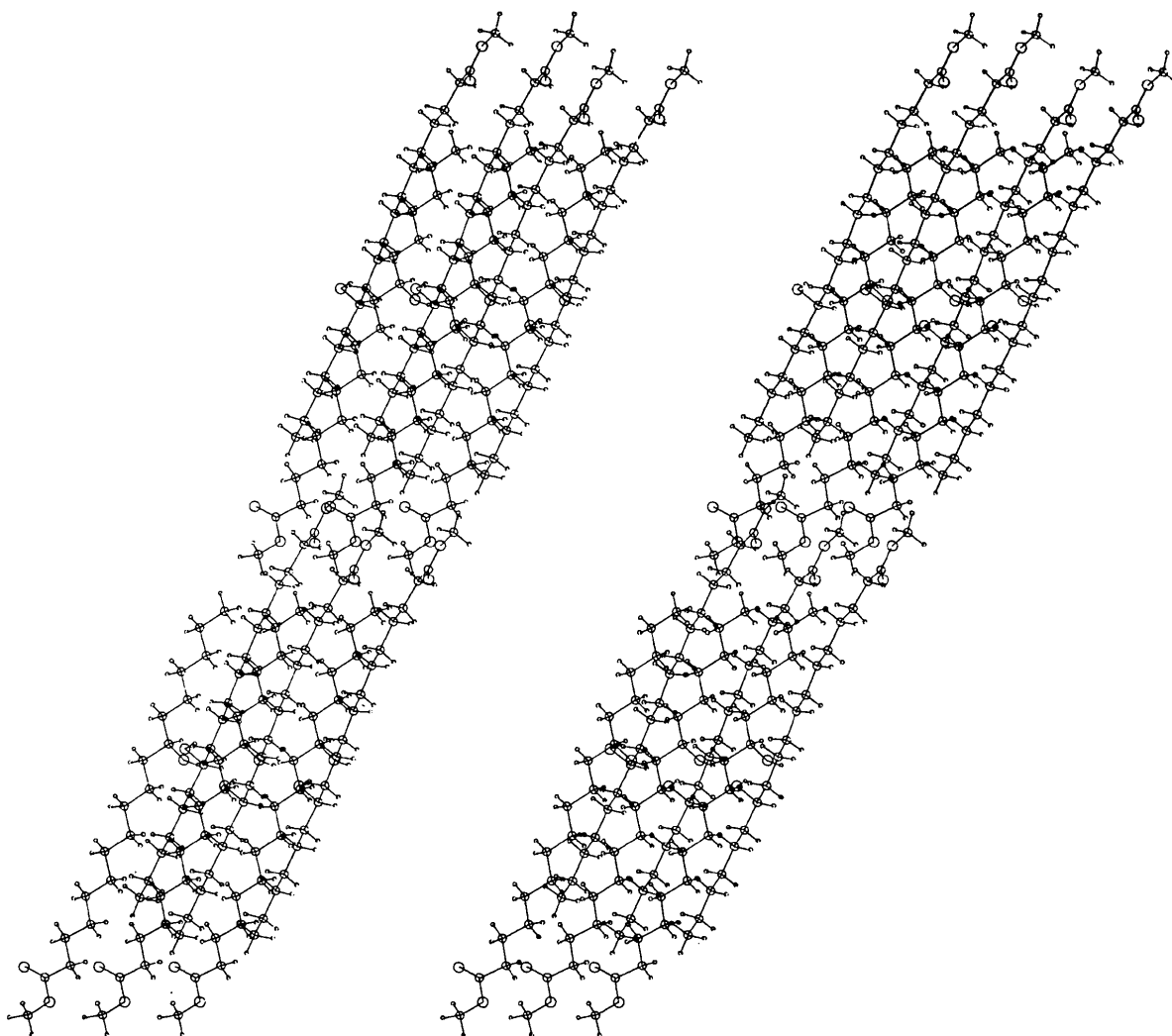


Fig. 2. Stereoscopic drawing of 12-D-hydroxyoctadecanoic acid methyl ester.

Table 2. Fractional atomic parameters and isotropic temperature factors with their *e.s.d.*'s for the hydrogen atoms

The first appended number refers to that of the parent atom. The fractional atomic coordinates are multiplied by 10^3 .

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i>
H(21)	1439 (7)	314 (21)	947 (2)	12.9 (2.2)
H(22)	1530 (7)	544 (19)	923 (3)	15.0 (2.5)
H(31)	1566 (6)	219 (15)	857 (2)	10.1 (2.0)
H(32)	1458 (6)	1 (13)	881 (2)	9.7 (2.0)
H(41)	1228 (5)	266 (15)	855 (2)	8.1 (1.7)
H(42)	1331 (6)	518 (14)	837 (2)	8.5 (1.8)
H(51)	1387 (6)	218 (15)	769 (2)	9.8 (2.0)
H(52)	1275 (7)	2 (15)	788 (2)	10.9 (2.2)
H(61)	1041 (5)	265 (14)	759 (2)	6.9 (1.5)
H(62)	1155 (6)	487 (13)	744 (2)	7.8 (1.7)
H(71)	1220 (5)	211 (14)	677 (2)	8.5 (1.8)
H(72)	1103 (6)	-14 (14)	692 (2)	10.7 (2.0)
H(81)	878 (5)	283 (15)	663 (2)	6.3 (1.4)
H(82)	998 (6)	506 (14)	649 (2)	9.0 (1.8)
H(91)	1063 (6)	227 (14)	583 (2)	8.2 (1.7)
H(92)	946 (6)	-10 (13)	594 (2)	7.8 (1.7)
H(101)	721 (5)	292 (16)	566 (2)	6.5 (1.3)
H(102)	847 (5)	512 (14)	551 (2)	7.6 (1.6)
H(111)	903 (4)	224 (11)	483 (1)	5.4 (1.4)
H(112)	783 (5)	-7 (12)	500 (2)	6.8 (1.5)
H(121)	683 (4)	524 (11)	452 (2)	4.7 (1.3)
H(131)	731 (5)	213 (12)	390 (2)	7.5 (1.6)
H(132)	609 (5)	6 (13)	407 (2)	7.1 (1.6)
H(141)	388 (5)	287 (18)	376 (2)	8.4 (1.5)
H(142)	519 (6)	503 (13)	358 (2)	8.1 (1.7)
H(151)	557 (6)	201 (15)	295 (2)	9.7 (1.8)
H(152)	448 (6)	-22 (13)	312 (2)	8.2 (1.8)
H(161)	218 (6)	262 (16)	284 (2)	9.3 (1.8)
H(162)	332 (6)	487 (15)	262 (2)	10.5 (2.0)
H(171)	389 (6)	195 (15)	202 (2)	10.5 (2.1)
H(172)	270 (8)	-38 (16)	221 (2)	14.8 (2.8)
H(181)	40 (7)	230 (17)	187 (2)	12.3 (2.2)
H(182)	160 (7)	490 (16)	169 (2)	11.9 (2.4)
H(183)	130 (6)	191 (15)	139 (2)	10.5 (2.2)
H(191)	1876 (7)	69 (20)	1052 (2)	12.2 (2.5)
H(192)	1952 (7)	358 (20)	1030 (2)	13.7 (2.5)
H(193)	1860 (8)	347 (23)	1082 (3)	17.4 (3.0)
H(123)*	493 (7)	462 (12)	485 (2)	9.0 (1.9)

* Refers to the hydroxyl H.

Table 3. The equation of the best least-squares plane through C(4) to C(17)

The equation expressed in orthogonalized space is $-0.69189J - 0.67515J + 0.25587K = -0.15848$.

Atom deviations from the plane (Å)

C(4)	-0.012	C(9)	-0.031	C(14)	-0.034
C(5)	0.021	C(10)	-0.069	C(15)	0.013
C(6)	0.096	C(11)	-0.108	C(16)	0.081
C(7)	0.048	C(12)	-0.116	C(17)	0.103
C(8)	0.056	C(13)	-0.048		

end of the chain is out by 0.103 Å on the other side (Table 3). The group C(19), O(1), O(2), C(1), C(2) is planar within 0.03 Å and the angle between this plane and the chain plane is 9.8°.

The cross-sectional area per chain is 19.1 Å² and the angle the zigzag plane makes with the $a_s c_s$ face is 45.8°. This means that the chain planes of adjacent chains intersect at 88.4°. As expected, the IR spectrum shows

the double (722 and 728 cm⁻¹) CH₂-rocking absorption bands which are characteristic for chains with mutually perpendicular zigzag planes.

The hydrocarbon chain has a mean C-C bond length of 1.510 (8) Å and a mean C-C angle of 114.5 (5)°. They compare well with the values found in other long-chain structures, *e.g.* 1.514 Å and 114.0° for 2-DL-hydroxytetradecanoic acid (Dahlén, Lundén & Pascher, 1976), 1.515 Å and 113.3° for isostearic acid (Abrahamsson & Lundén, 1972). The average C-H bond distance is 0.99 (6) Å, the average H-C-H angle

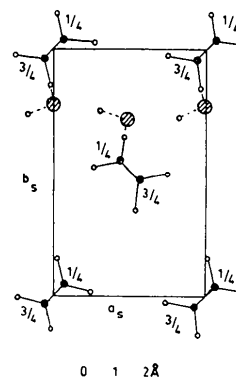


Fig. 3. The O_{\perp} subcell in 12-D-hydroxyoctadecanoic acid methyl ester viewed along the c_s axis. The hydroxyl group is shown by dashed lines.

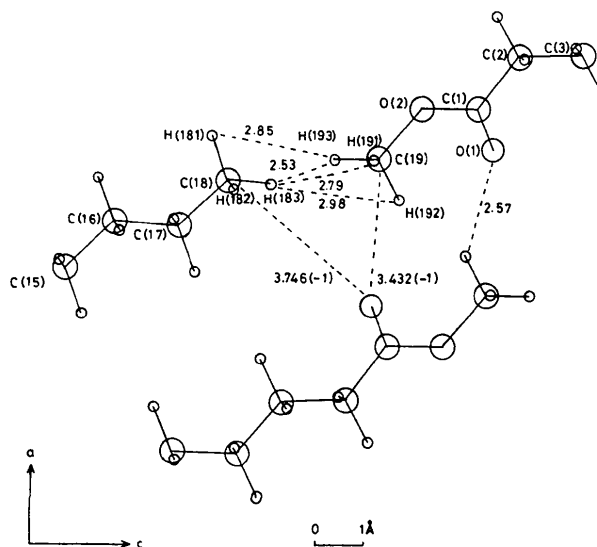


Fig. 4. Some packing contacts in the methyl ester region.

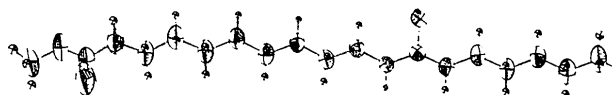


Fig. 5. Drawing of 12-D-hydroxyoctadecanoic acid methyl ester showing the thermal ellipsoids as viewed along the b axis.

