The Crystal Structure of 2-DL-Hydroxytetradecanoic Acid

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2-DL-Hydroxytetradecanoic acid is triclinic ($P\bar{1}$) with $a = 5\cdot170$, $b = 5\cdot385$, $c = 32\cdot307$ Å, $\alpha = 79\cdot97$, $\beta = 101\cdot14$ and $\gamma = 121\cdot92°$. The molecules are linked together as hydrogen-bonded dimers in which the chain axes are tilted 53° to the end group contact planes. The α-OH group is close to the plane of the carboxyl group which leads to a short intramolecular contact of 2·68 Å. The shortest intermolecular oxygen–oxygen distance involving the hydroxyl group is 2·95 Å. The hydroxyl group is thus considered to be a hydrogen donor to two weak hydrogen bonds. The carbon chain has a sharp bend at carbon C(2) and the plane through the carboxyl group is perpendicular to the carbon chain plane.

Introduction

Long-chain 2-hydroxy fatty acids (HFA) are found as components in complex lipids of animals, plants, yeasts, moulds and bacteria, as reviewed by Downing (1961). More recently a number of reports have appeared on their occurrence, either bound in different lipids of microorganisms (Kawanami, Kimura, Nakagawa & Otsuka, 1969; Yano, Furukawa & Kusunose, 1970) or free as secretion products (Karlsson, Samuelsson & Steen, 1967; Kurtzman, Vesonder & Smiley, 1973). Their stereochemistry has been discussed by Karlsson & Pascher (1974) and Tatsumi, Kishimoto & Hignite (1974).

HFA have attracted our particular attention as components of sphingolipids. In these important lipids the HFA occur along with normal fatty acids in amide linkage to long-chain bases (sphingosines) and together with these constitute the lipophilic ceramide part (Karlsson & Pascher, 1971) which anchors the lipids in the membrane.

In membranes which are exposed to a pronounced physical stress, as in renal or intestinal membranes, the sphingolipids show a very high proportion of hydroxyl groups, both in the fatty acids and the sphingosine component (Karlsson, Samuelsson & Steen, 1973; Breimer, Karlsson & Samuelsson, 1974; Smith, McKibbin, Karlsson, Pascher & Samuelsson, 1975). This suggests an engagement of these hydroxyl groups in hydrogen bonds which might improve the stability of the membrane. In fact, experimental data from monolayer studies on model sphingolipids indicate the formation of such lateral hydrogen bonds (Larsson, Löfgren & Pascher, 1976). With regard to the implications of such a lateral binding of sphingolipids on the stability and permeability of the membranes it appeared important to analyse the capability of intermolecular hydrogen bond formation both for the intact lipids and for their individual components.

The present single-crystal analysis was performed within the scope of an investigation of phase behaviour, molecular arrangement, conformation and hydrogen bonding of HFA (Dahlén & Pascher, 1976).

Experimental

2-DL-Hydroxytetradecanoic acid was synthesized according to the procedure described by Karlsson & Pascher (1974). Crystals were obtained by slow crystallization from hexane. On heating they underwent a phase transition at 67° and melted at 81·5–81·7°C.

Crystal data

Molecular formula	$C_{14}H_{28}O_3$
Unit cell: triclinic	Space group $P\bar{1}$
$a = 5\cdot170$ (9), $b = 5\cdot385$ (11),	$c = 32\cdot307$ (67) Å
$\alpha = 79\cdot97$ (15), $\beta = 101\cdot14$ (14),	$\gamma = 121\cdot92$ (12)°
V	$746\cdot1$ Å³
Molecular weight	$244\cdot38$
Z	2
D_c	$1\cdot088$ g cm^{-3}
D_m	$1\cdot087$
λ	$1\cdot54051$ Å
μ	$5\cdot95$ cm^{-1}
Crystal dimensions	$0\cdot5 \times 0\cdot47 \times 0\cdot02$ mm
Number of independent reflexions	1429.

The crystal used for the data collection was mounted along the *b* axis. Data were recorded on a Picker FACS1 automatic diffractometer with the Vanderbilt disc-oriented program system of Dr P. G. Lenhert. Graphite-monochromated Cu *K*α radiation was used to measure all reflexions up to $2\theta = 100°$. The reflexions were scanned ($\theta/2\theta$) in 15 steps of 2 s with a total scan width of 2·6°. 4 s background counts were taken on both sides of the peak.

1429 independent reflexions were recorded, of which

1199 were greater than $2\sigma(I)$ and considered as observed. The Lorentz and polarization factor corrections were applied. Scattering factors for carbon and oxygen atoms were those in *International Tables for X-ray Crystallography* (1962) and for hydrogen atoms those of Stewart, Davidson & Simpson (1965).

The calculations were at first performed on a Datasaab D21 computer using a program system developed at this department and later on a System DEC10 using *MULTAN* by Germain, Main & Woolfson (1971) and the X-RAY system of crystallographic programs (Stewart, Kruger, Ammon, Dickinson & Hall, 1972).

Table 1. *Fractional atomic parameters and thermal parameters with their estimated standard deviations for the non-hydrogen atoms*

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

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

|	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	7795 (9)	4207 (9)	403 (1)	287 (25)	297 (25)	355 (25)	133 (22)	91 (19)	−40 (21)
C(2)	9954 (8)	3475 (8)	712 (1)	273 (22)	291 (23)	418 (26)	133 (20)	−8 (19)	−21 (19)
C(3)	9007 (9)	2570 (8)	1157 (1)	396 (24)	364 (24)	410 (27)	201 (20)	−14 (20)	28 (20)
C(4)	8798 (9)	4802 (9)	1353 (1)	498 (25)	381 (25)	450 (28)	245 (22)	−12 (21)	−96 (21)
C(5)	7715 (10)	3660 (9)	1788 (1)	661 (30)	452 (26)	450 (28)	327 (24)	103 (23)	2 (22)
C(6)	7384 (10)	5769 (10)	1992 (1)	567 (28)	500 (28)	489 (30)	287 (24)	71 (23)	1 (23)
C(7)	6217 (10)	4565 (10)	2424 (1)	692 (31)	498 (28)	528 (31)	333 (25)	129 (25)	−29 (24)
C(8)	5833 (11)	6623 (10)	2637 (1)	698 (32)	533 (30)	557 (32)	339 (26)	48 (26)	−131 (25)
C(9)	4681 (12)	5385 (10)	3065 (1)	913 (36)	539 (30)	478 (31)	424 (28)	216 (27)	−2 (24)
C(10)	4309 (11)	7422 (11)	3280 (2)	796 (35)	628 (32)	547 (32)	414 (28)	121 (27)	−67 (26)
C(11)	3169 (12)	6163 (11)	3707 (2)	925 (38)	612 (32)	566 (33)	435 (29)	194 (29)	−57 (26)
C(12)	2800 (13)	8187 (11)	3927 (2)	989 (40)	682 (33)	579 (34)	537 (31)	188 (29)	−39 (27)
C(13)	1711 (15)	6912 (13)	4358 (2)	1303 (52)	895 (42)	732 (42)	639 (40)	396 (38)	−14 (33)
C(14)	1313 (19)	8942 (16)	4581 (2)	1985 (80)	1340 (61)	865 (48)	1143 (61)	648 (50)	108 (42)
O(1)	8617 (6)	6661 (6)	223 (1)	284 (15)	272 (17)	452 (18)	102 (12)	27 (13)	29 (14)
O(2)	4985 (5)	1966 (5)	344 (1)	259 (16)	249 (15)	527 (19)	53 (15)	10 (13)	16 (13)
O(3)	13009 (6)	5902 (6)	713 (1)	285 (17)	380 (16)	669 (21)	125 (14)	14 (14)	15 (15)
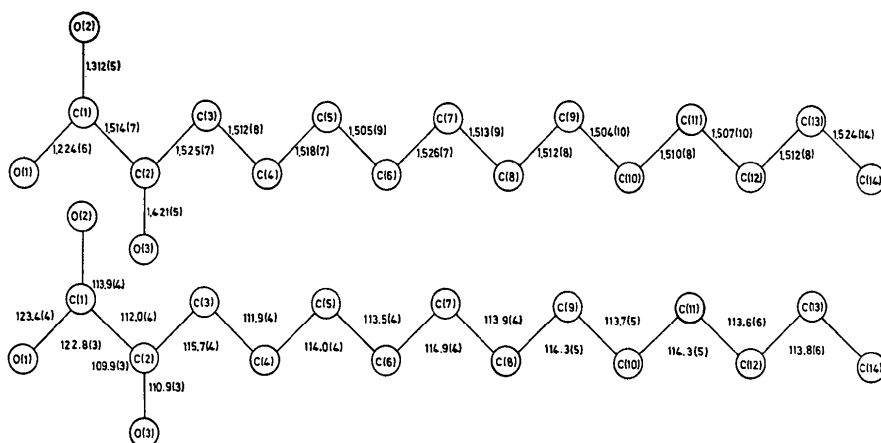
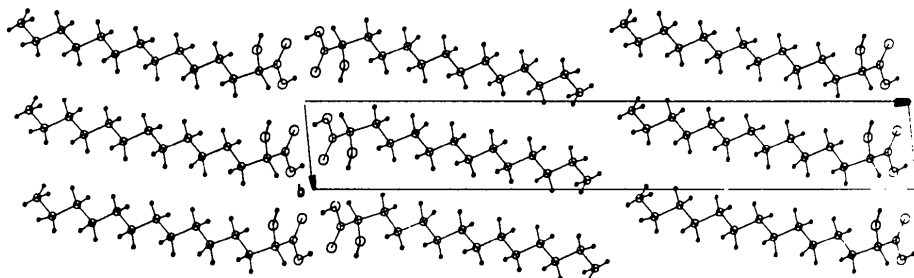Fig. 1. Bond distances and angles in 2-DL-hydroxytetradecanoic acid.

Fig. 2. Molecular packing of 2-DL-hydroxytetradecanoic acid viewed along the a axis.

X-RAY72 modifications for the DEC10 were made by Dr Steve Ernst at Pittsburgh University and by Dr Robert Pearson at this department.

Structure determination and refinement

The structure solution was started with a crystal which only gave 624 reflexions greater than 2σ. As the compound was a racemate the space group was assumed to be $P\bar{1}$. 170 reflexions with $E \geq 1\cdot4$ were used to run *MULTAN*. 12 atoms in a chain were selected from the E map with the highest figure of merit which all showed up as reasonably large peaks in the following Fourier map. This, however, was not the correct solution but after a shift of half a subcell period in the chain direction the rest of the non-hydrogen atoms could be located.

The structure was then refined with full-matrix least-squares methods. All positional parameters and isotropic temperature factors were varied and the structure refined to an R of $0\cdot17$. However, at this stage a better crystal became available which gave twice as many observed reflexions. The refinement was continued varying all positional and anisotropic temperature parameters. A difference Fourier revealed all the hydrogen atoms. They were included in the calculations with the same isotropic temperature factors as those of the corresponding parent atoms. Only the two hydroxyl hydrogens were refined.

Further refinement lowered R to $0\cdot06$. An R 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 3σ (thereby removing 445 observations). Using the 984 reflexions above this limit the structure refined to a final R of $0\cdot048$.* The weighting scheme used during the final stages of the refinement was $w = 1/[1 + \{(F_o - 7\cdot0)/10\cdot0\}^2]$.

Description of the structure

The final atomic parameters are given for the non-hydrogen atoms in Table 1 and for hydrogen atoms in Table 2. Interatomic distances and angles and atomic numbering are given in Fig. 1.

The molecules are arranged head to head as shown in Fig. 2 and in a stereoscopic drawing in Fig. 3. Hydrogen bonds between carboxyl groups hold the double layer together whereas only weak methyl end-group interactions exist between the double layers. The packing arrangement in the methyl-contact plane is normal with closest C(14)–C(14) distances of $3\cdot82$ and $3\cdot96$ Å.

The hydrocarbon chains pack laterally according to the monoclinic chain packing $M\|$. The subcell is somewhat distorted with the dimensions: $a_s = 4\cdot74$, $b_s = 4\cdot30$, $c_s = 2\cdot54$ Å; $\alpha_s = 94\cdot7$, $\beta_s = 89\cdot2$, $\gamma_s = 110\cdot9°$.

The monoclinic subcell was first observed in 3-thia-dodecanoic acid (Abrahamsson & Westerdahl, 1963), where the subcell was also slightly deformed. It has also been found in racemic 1-monoglycerides (Larsson, 1964). These compounds with monoclinic chain packing have almost the same angle of tilt of the chain axis

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* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31606 (5 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.
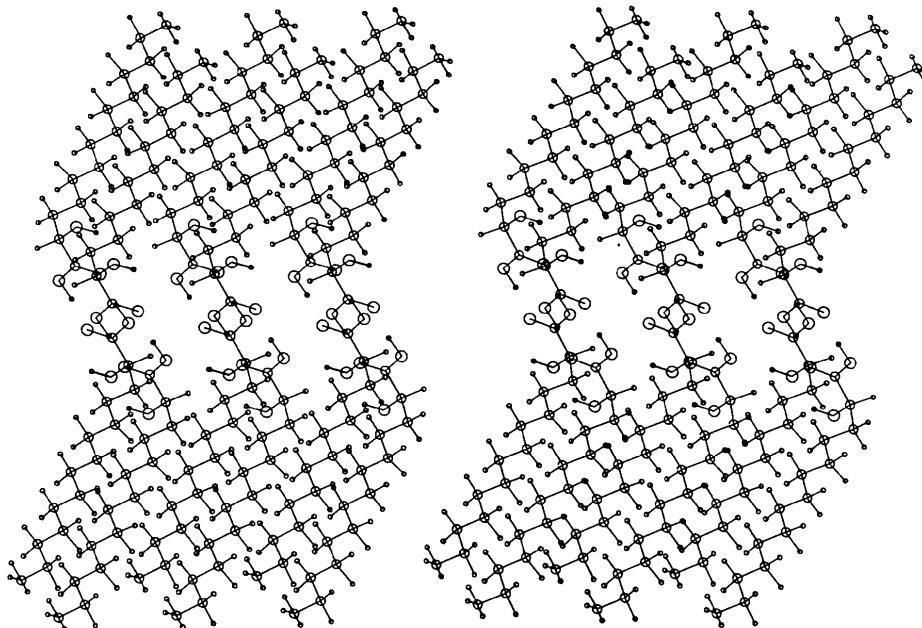

Fig. 3. Stereoscopic drawing of 2-DL-hydroxytetradecanoic acid slightly rotated as compared to Fig. 2 to improve the stereo image.

Table 2. *Fractional atomic parameters and isotropic temperature factors for the hydrogen atoms*

The first appended numbers refer to the parent atom.

	x	y	z	B
H(21)	0·977	0·156	0·0584	2·61
H(31)	0·708	0·066	0·1150	3·20
H(32)	1·035	0·199	0·1341	3·20
H(41)	1·086	0·666	0·1399	3·73
H(42)	0·746	0·536	0·1158	3·73
H(51)	0·539	0·162	0·1769	4·23
H(52)	0·875	0·260	0·1981	4·23
H(61)	0·933	0·767	0·2028	4·28
H(62)	0·577	0·635	0·1780	4·28
H(71)	0·421	0·254	0·2412	4·76
H(72)	0·766	0·392	0·2591	4·76
H(81)	0·769	0·837	0·2695	4·79
H(82)	0·432	0·707	0·2433	4·79
H(91)	0·302	0·339	0·3058	5·23
H(92)	0·622	0·460	0·3268	5·23
H(101)	0·631	0·911	0·3313	5·38
H(102)	0·277	0·797	0·3097	5·38
H(111)	0·114	0·424	0·3677	5·83
H(112)	0·485	0·529	0·3911	5·83
H(121)	0·510	1·011	0·3980	6·07
H(122)	0·166	0·900	0·3733	6·07
H(131)	−0·048	0·527	0·4349	8·00
H(132)	0·342	0·650	0·4585	8·00
H(141)	0·258	1·033	0·4454	10·24
H(142)	0·000	0·941	0·4389	10·24
H(143)	0·075	0·820	0·4791	10·24
H(24)*	0·370 (11)	0·260 (10)	0·0130 (16)	9·81 (1·44)
H(34)*	1·294 (9)	0·751 (9)	0·0624 (12)	6·70 (1·05)

* Refers to the hydroxyl hydrogens.

towards the end-group contact planes. The tilt is 57° in 3-thiadodecanoic acid, 55° in 1-monoglyceride and 53° in the title compound. This may, however, be an effect of the molecular conformation adopted.

The hydrocarbon chain between C(4) and C(14) is almost undistorted and has a mean C–C bond length of 1·514 (7) Å and a mean C–C–C angle of 114·0° (4). The average C–H bond is 1·07 Å and the mean angle involving hydrogen atoms is 109°. The deviations from these mean values are quite large for the hydrogen atoms, as they were located from the difference Fourier and have not been refined.

The carbon chain has a sharp bend at carbon atom C(2) due to a *gauche–gauche* conformation about the C(1)–C(2) and C(2)–C(3) bonds. The hydrogen H(21)

Table 3. *The equation of the best least-squares plane through C(4) to C(14)*

The equation expressed in orthogonalized space is
$$0·79176I + 0·39099J + 0·46931K = 4·81799 .$$

Atom	Deviation	Atom	Deviation
C(1)	−1·348 Å	C(10)	−0·010 Å
C(2)	−0·137	C(11)	−0·016
C(3)	−0·055	C(12)	−0·007
C(4)	−0·011	C(13)	0·012
C(5)	0·011	C(14)	0·012
C(6)	0·018	O(1)	−1·261
C(7)	0·004	O(2)	−2·492
C(8)	−0·002	O(3)	1·044
C(9)	−0·012	H(21)	−0·282

thereby continues in the carbon chain direction. The carbon chain least-squares plane together with the out of plane deviations are given in Table 3. The chain is planar between C(4) and C(14) within 0·02 Å while C(2) and C(3) are somewhat out of the plane due to distortions in the polar region. A similar bend at carbon C(2) of a fatty acid chain has also been observed in *N*-(2-hydroxyethyl)octadecanamide (Dahlén, Pascher & Sundell, 1976), where the molecule is bent to allow a close amide plane packing.

In 2-hydroxytetradecanoic acid the molecule is bent to give what seems to be a preferred conformation to the hydroxyl oxygen O(3). The carboxyl group [C(1), C(2), O(1), O(2)] is planar within 0·004 Å and perpendicular to the carbon chain plane (89·8°). The arrangement of the polar groups with contact distances is shown in Fig. 4.

As usual the carboxyl groups form hydrogen bonds over centres of symmetry. The hydrogen-bonded oxygen–oxygen distance is 2·653 (6) Å. The hydrogen atom H(24) bound to O(2) (1·01 Å) has a contact to O(1) of 1·65 Å. The O–H···O angle is 175°. The carboxyl groups linked together in dimers are almost coplanar, with a plane separation of only 0·014 Å. These values
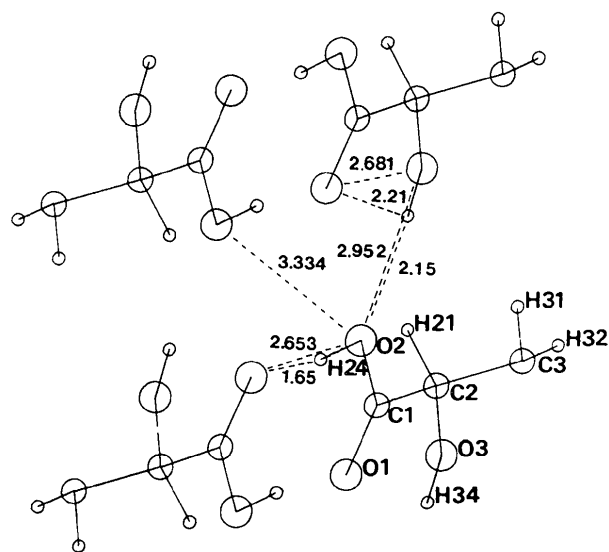

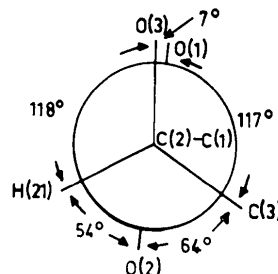Fig. 4. The polar region with the shorter interatomic distances indicated.

Fig. 5. Torsion angles around the C(2)–C(1) bond

are in good agreement with those found in 13-oxoiso-stearic acid (Dahlén, 1972).

The α-OH group is nearly in the plane of the carboxyl group. O(3) and H(34) deviate from the carboxyl group plane by only 0·14 and 0·08 Å, respectively. They thereby adopt an eclipsed synplanar position with the closest contact towards the carbonyl oxygen O(1). The conformation about the C(1)–C(2) bond is shown in Fig. 5 and is in good agreement with the conformation reported for other α-hydroxycarboxylic acids by Kanters, Kroon, Peerdeman & Schoone (1967). The mean value for the dihedral angle reported by these authors is 10° and in the title compound the angle is 7°. The intramolecular close contact between O(1) and O(3) thus becomes 2·681 Å. The corresponding mean value given by Kanters et al. (1967) is 2·69 Å. However, according to their results the hydrogen atom is pointing away from the carbonyl oxygen and the α-hydroxy group is not considered to participate in a hydrogen bond. In 2-hydroxytetradecanoic acid the hydroxyl hydrogen is pointing towards the carbonyl oxygen with an H(34)···O(1) distance of 2·21 (4) Å. This is shorter than the sum of the van der Waals radii which is about 2·6 Å (Hamilton & Ibers, 1968) and indicates a participation of the α-hydroxyl group in an intramolecular hydrogen bond by forming a five-membered ring. There is also a short intermolecular contact of 2·952 Å between O(3) and O(2) in a molecule translated one unit cell in the **a** and **b** directions. The corresponding H(34)···O(2) distance is 2·15 (4) Å which is not significantly different from the intramolecular H···O contact.

The α-hydroxyl group has thus to be considered as a hydrogen donor in a weak intra- and intermolecular hydrogen bond, which is consistent with the results from infrared spectroscopy. A more detailed discussion on phase behaviour, molecular arrangement, conformation and hydrogen bonding of long-chain HFA in different polymorphic phases, based on a comparison of this single-crystal analysis with powder diffraction and infrared data will be given in a subsequent paper (Dahlén & Pascher, 1976).

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