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(4*S*,5*S*)-4-[(1*R*)-1,2-Dihydroxyethyl]-5-tridecyl-1,3-oxazolidin-2-one

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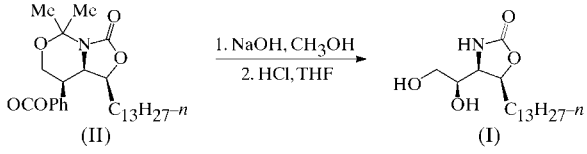
The title compound, $C_{18}H_{35}NO_4$, is a new bioactive amphiphilic lipid with a *cis*-substituted 1,3-oxazolidin-2-one head group. In the crystal structure, the molecules form intercalating bilayers in which the oxazolidinone head groups are joined together by hydrogen bonds into chains.

Comment

In the course of the synthesis of conformationally restricted sphingolipid analogues (Brodesser *et al.*, 2003; Kolter, 2003), the precursor (II) of the title compound, (I), was prepared from Garner's aldehyde (Garner *et al.*, 1988), according to Sawatzki (2003). Compound (I) was shown to be an inhibitor of sphinganine hydroxylation and a potent mitogen in *S. cerevisiae* (Sawatzki, 2003). Removal of the benzoate and isopropylidene protecting groups in (II) afforded (I).



(II) (I)

The structure of (I) with the atom-numbering is shown in Fig. 1. Selected geometrical parameters are listed in Table 1. The 1,3-oxazolidin-2-one ring adopts an open envelope conformation, with atom C2 out of the plane. The intra-ring bond lengths C5—N1 and C4—O3, which are opposite each other, are similar; also the lengths of the adjacent bonds N1—C2 and O3—C2 within the ring show comparable similarity, with a maximum deviation of 0.03 Å. The intra-ring bond angles, however, are different and range from 98.57 (13) to 113.34 (12)°. The pseudo-axially arranged dihydroxyethyl and alkyl substituents at the 4- and 5-positions of the oxazolidinone ring are in a *cisoid* configuration. Both substituents show a distorted synperiplanar conformation, with a C8—C4—C5—C6 torsion angle of 21.9 (2)°, whereas within the dihydroxyethyl moiety, the OH groups are in a fully staggered relationship, with an O6—C6—C7—O7 torsion angle of −179.55 (13)°. The conformation of the tridecyl chain is as most often found for larger alkanes, *i.e.* staggered with the largest substituents at any C—C bond antiperiplanar with respect to each other. The average C—C bond length within the chain is 1.527 (2) Å [range 1.524 (2)–1.530 (2) Å] and the average angle is 113 (2)° [range 112.6 (1)–113.9 (2)°]. These values are similar to those found in related amphiphilic lipids (Ramos Silva *et al.*, 2000; Matos Beja *et al.*, 2001). The zigzag tridecyl backbone shows a significant deviation from planarity, being bent towards atom C9; the deviation from the ideal torsion angle of 180° for C8—C9—C10—C11 is 4.10 (14)°. Also, the bond lengths C8—C9 and C9—C10 appear to diverge slightly from the average bond length found in the alkyl chain. A weaker second bend can be found at C16—

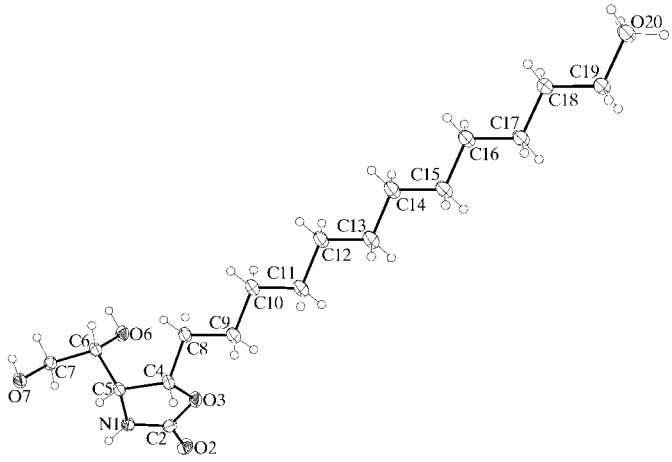


Figure 1
The structure of (I), showing the atom-numbering scheme and displacement ellipsoids at the 50% probability level for non-H atoms.

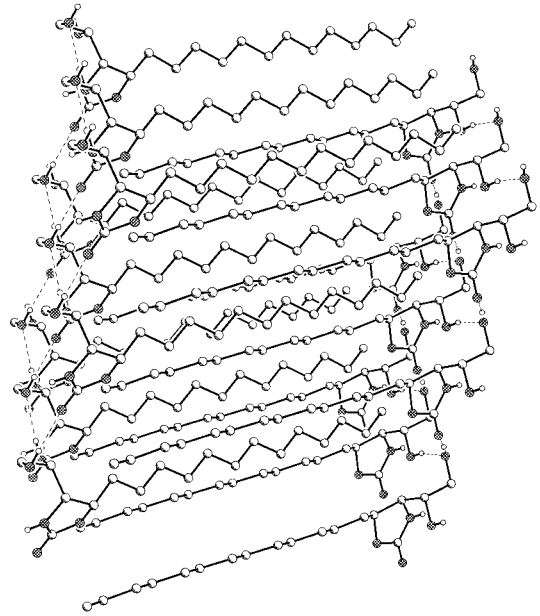


Figure 2
The packing of the hydrocarbon chains in the crystal structure, with alternating layers of carbon tails and oxazolidin-2-one head groups.

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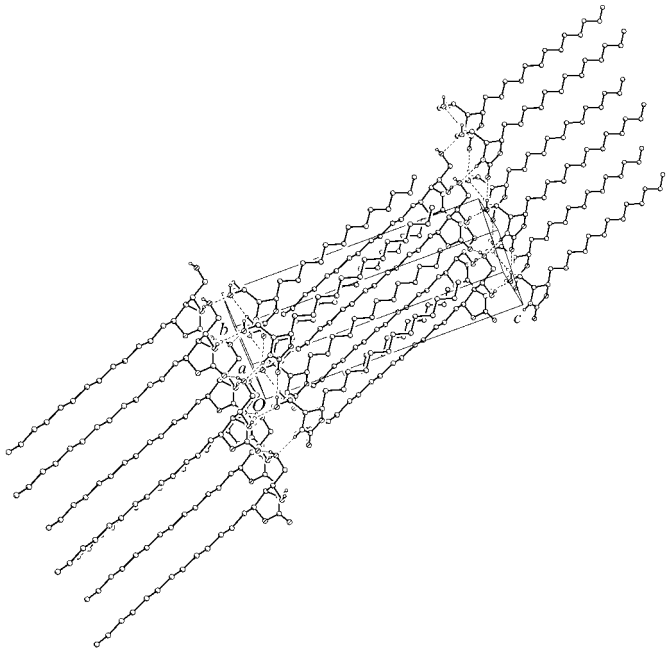

Figure 3
View of the unit-cell packing, showing the network of hydrogen bonds as dashed lines.

C17—C18—C19 of the hydrocarbon chain [deviation 2.41 (14)°].

Three intermolecular hydrogen bonds of normal strength (Steiner, 2002) are present (Table 2), forming a nearly linear arrangement in the crystal. The greatest deviation from the ideal angle of 180° is of 19.0 (2)° for the strongest hydrogen bond, *viz*. O7—H7O···O2. In the crystal structure, the molecule forms an intercalating bilayer generated by the 2_1 axis, with a lipophilic core and a hydrophilic surface (Fig. 2). The molecular packing is such that the hydrocarbon chains lie side by side, thereby forming alternating layers of carbon tails and oxazolidin-2-one heads. The hydrophilic heads are connected by a network of hydrogen bonds involving the two hydroxyl groups, the carbonyl group and an amide group, *viz*. O6—H6O···O7^{ii}, O7—H7O···O2^{iii} and N1—H1N···O7^{i} (see Table 2 for symmetry codes and geometry details). The O7—H7O hydroxy group is involved in three hydrogen bonds. It acts as a hydrogen-bond acceptor and donor in the network, connecting the hydrophilic heads of the bilayer. The 2_1 axis further relates each bilayer to its neighbours. Each bilayer is connected to the next *via* a hydrogen bond between the N1 amino group as donor and the O7 hydroxy group as acceptor. These hydrogen bonds join the oxazolidinone moieties of the molecules head-to-head within and also between the layers (Fig. 3).

Experimental

The starting material (1*S*,8*R*,8a*S*)-5,5-dimethyl-1-tridecyl-3-oxotetrahydro[1,3]oxazolo[3,4-*c*][1,3]oxazin-8-yl benzoate, (II), was prepared from Garners aldehyde (Garner *et al.*, 1988; Campbell *et al.*, 1998). In brief, Garner's aldehyde was elongated by a Wittig reaction with a long-chain phosphorous ylide followed by an intramolecular iodolactonization (Ageno *et al.*, 1995) of the (*Z*)-olefin. Molecular rearrangement induced by silver acetate in acetic acid followed by exchange of benzoyl for acetyl protection with inversion of configuration at C8 afforded (II) (Sawatzki, 2003). Glassware was flame dried under an argon atmosphere and allowed to cool. Compound (II) (207.1 mg, 437.3 µmol) was dissolved in methanol and a catalytic amount of sodium hydroxide in methanol (1 *M*) added. Stirring was continued for 18 h and the solvent evaporated under reduced pressure. The residue was dissolved in THF/0.5 *M* HCl (1:1) and stirred at 353 K for 18 h under reflux. After cooling to ambient temperature, the solution was neutralized with saturated sodium hydrogencarbonate solution and concentrated under reduced pressure. The residue was extracted with chloroform and the organic phase dried over sodium sulfate. After evaporation of the solvent, the resulting residue was purified by column chromatography on silica gel using chloroform/methanol (10:1) as eluant (yield: 122.9 mg, 85.3%). The purification afforded a few colourless crystals suitable for X-ray analysis. Thin-layer chromatography: 10:1 chloroform–methanol, R_F = 0.41; m.p.: 365 K (sharp); $[\alpha]_D = -16.1°$ (c = 0.26 in MeOH/$CHCl_3$, 1:1); ^{1}H NMR (500 MHz, $CD_3OD/CDCl_3$, 1:1): δ 0.86 (*t*, J = 7 Hz, 3H; CH_3), 1.25 (*m*, 16H; CH_2), 1.36 (*m*, 4H; CH_2), 1.56 (*m*, 2H; CH_2), 1.69 (*m*, 1H; CH_2), 1.97 (*m*, 1H; CH_2), 3.50 (*td*, J = 5.7 Hz, J = 11.5 Hz, 1H; CH_2OH), 3.54 (*td*, J = 5.7 Hz, J = 11.5 Hz, 1H; CH_2OH), 3.72 (*dt*, J = 2.2 Hz, J = 5.7 Hz, 1H; H-5), 3.81 (*dd*, J = 2.2 Hz, J = 7.8 Hz, 1H; H-4), 4.63 (*ddd*, J = 3.8 Hz, J = 7.8 Hz, J = 10.1 Hz, 1H; H-1′); ^{13}C NMR (100 MHz, $CD_3OD/CDCl_3$, 1:1): δ 14.9 (CH_3), 23.9–33.2 (CH_2), 58.1 (C-5), 65.1 (CH_2OH), 70.1 (C-4), 81.9 (C-1′), 162.8 (C-2); FAB–MS (3-nitrobenzoic acid): m/z = 330 $(M + H)^+$; IR: 1697.7 cm^{-1}.

Crystal data

$C_{18}H_{35}NO_4$	D_x = 1.203 Mg m^{-3}
M_r = 329.47	Mo $K\alpha$ radiation
Monoclinic, $P2_1$	Cell parameters from 9695 reflections
a = 5.4040 (2) Å	θ = 2–28.3°
b = 7.6062 (4) Å	μ = 0.08 mm^{-1}
c = 22.1898 (11) Å	T = 123 (2) K
β = 94.208 (3)°	Plate, colourless
V = 909.63 (7) Å^3	0.50 × 0.40 × 0.02 mm
Z = 2	

Data collection

Nonius KappaCCD diffractometer	R_{int} = 0.043
Rotation φ and ω (1°) scans	θ_{max} = 28.3°
10 314 measured reflections	$h = -7 \rightarrow 7$
2337 independent reflections	$k = -10 \rightarrow 10$
2037 reflections with $I > 2\sigma(I)$	$l = -28 \rightarrow 29$

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.330 (2)	C4—C8	1.519 (2)
N1—C5	1.454 (2)	C4—C5	1.549 (2)
C2—O3	1.3575 (19)	C5—C6	1.522 (2)
O3—C4	1.456 (2)		
C2—N1—C5	113.21 (13)	C8—C4—C5	119.62 (14)
N1—C2—O3	109.94 (14)	N1—C5—C6	113.34 (12)
C2—O3—C4	108.28 (12)	N1—C5—C4	98.57 (13)
O3—C4—C8	108.67 (13)	C6—C5—C4	118.13 (12)
O3—C4—C5	104.48 (11)	C4—C8—C9	111.28 (14)
C5—N1—C2—O3	9.64 (18)	N1—C5—C6—O6	−58.29 (15)
N1—C2—O3—C4	6.88 (17)	C4—C5—C6—C7	177.14 (14)
C2—O3—C4—C5	−19.08 (15)	O6—C6—C7—O7	−179.55 (13)
C2—N1—C5—C4	−20.13 (16)	C5—C6—C7—O7	59.78 (17)
O3—C4—C5—N1	22.39 (14)	C5—C4—C8—C9	173.19 (13)
C8—C4—C5—C6	21.9 (2)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···O7^{i}	0.85 (2)	2.07 (2)	2.9005 (17)	167.2 (18)
O6—H6O···O7^{ii}	0.88 (2)	2.25 (2)	3.1025 (17)	165 (2)
O7—H7O···O2^{iii}	0.77 (3)	1.95 (3)	2.6997 (17)	161 (2)

Symmetry codes: (i) $3-x, y-\frac{1}{2}, 2-z$; (ii) $x-1, y, z$; (iii) $x, 1+y, z$.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.084$
$S = 1.01$
2337 reflections
217 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0547P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.22$ e Å^{-3}
$\Delta\rho_{min} = -0.21$ e Å^{-3}

Friedel pairs (2076) were merged prior to the final refinement due to an inconclusive Flack (1983) parameter of −0.6 (10). The absolute configuration of (I) was assigned to agree with the chirality established by the synthesis. The positions of the amide and hydroxy H atoms were determined from a difference Fourier map and the coordinates were refined freely, with isotropic displacement parameters constrained to $U_{iso}(H) = 1.2U_{eq}(N)$ and $1.5U_{eq}(O)$. All remaining H atoms were treated as riding, with C—H = 0.98–1.00 Å and $U_{iso}(H) = 1.2U_{eq}(CH, CH_2)$ and $1.5U_{eq}(CH_3)$.

Data collection: *COLLECT* (Nonius, 1997–2000); cell refinement: *DENZO–SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN*; program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL* (Sheldrick, 2001); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA1009). Services for accessing these data are described at the back of the journal.

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