$wR = 0.086$
$S = 1.66$
2198 reflections
325 parameters
All H-atom parameters refined

$\Delta\rho_{max} = 0.14$ e Å^{-3}
$\Delta\rho_{min} = -0.10$ e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$B_{eq} = \frac{4}{3}\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
O(1)	0.1305 (3)	0.2597 (4)	0.00482 (2)	5.25
O(2)	−0.0772 (3)	0.0557 (4)	0.01777 (2)	4.96
C(1)	0.0246 (4)	0.2249 (5)	0.01663 (3)	4.16
C(2)	0.0432 (5)	0.4184 (6)	0.02851 (3)	4.75
C(3)	−0.0499 (5)	0.3674 (6)	0.04353 (3)	4.50
C(4)	0.0378 (5)	0.1714 (6)	0.05299 (3)	4.30
C(5)	−0.0415 (5)	0.1497 (6)	0.06895 (3)	4.42
C(6)	0.0401 (5)	−0.0489 (6)	0.07853 (3)	4.36
C(7)	−0.0395 (5)	−0.0651 (6)	0.09445 (3)	4.60
C(8)	0.0399 (5)	−0.2643 (6)	0.10415 (3)	4.50
C(9)	−0.0392 (5)	−0.2773 (6)	0.12021 (3)	4.59
C(10)	0.0404 (5)	−0.4751 (6)	0.12989 (3)	4.60
C(11)	−0.0382 (5)	−0.4869 (6)	0.14598 (3)	4.58
C(12)	0.0402 (5)	−0.6833 (6)	0.15582 (4)	4.70
C(13)	−0.0391 (5)	−0.6935 (6)	0.17176 (4)	4.67
C(14)	0.0387 (5)	−0.8902 (6)	0.18182 (4)	4.92
C(15)	−0.0396 (5)	−0.8982 (6)	0.19754 (4)	5.1
C(16)	0.0383 (5)	−1.0917 (6)	0.20795 (4)	5.12
C(17)	−0.0419 (6)	−1.0968 (7)	0.22360 (4)	6.1
C(18)	0.0378 (9)	−1.288 (1)	0.23382 (6)	7.8

Table 2. *Selected geometric parameters* (Å, °)

O(1)—C(1)	1.313 (3)	C(2)—C(3)	1.513 (5)
O(2)—C(1)	1.214 (3)	C(3)—C(4)	1.520 (4)
C(1)—C(2)	1.508 (4)		
O(1)—C(1)—C(2)	112.6 (3)	C(1)—C(2)—C(3)	115.1 (3)
O(2)—C(1)—C(2)	124.0 (3)	C(2)—C(3)—C(4)	114.6 (3)
O(1)—C(1)—O(2)	123.5 (3)	C(3)—C(4)—C(5)	113.3 (3)
O(1)—C(1)—C(2)—C(3)	−169.8 (3)	C(2)—C(3)—C(4)—C(5)	171.5 (3)
O(2)—C(1)—C(2)—C(3)	10.5 (4)	C(3)—C(4)—C(5)—C(6)	178.5 (3)
C(1)—C(2)—C(3)—C(4)	70.3 (4)		

A relatively small ω-scan width of 0.8° was used in order to avoid overlapping of neighboring reflections; the ω-scan rate was 4.0° min^{-1} and background counts were made for 4 s on each side of every scan. The molecular model was initially built for 18 C and two O atoms by reference to the structure of the *Mon* type of the B form of stearic acid. Refinement was by full-matrix least-squares methods. Data collection: Rigaku AFC-5 with software *AFCM* of the Research Center for Protein Engineering, Institute for Protein Research Center, Osaka University, Japan. Program(s) used to refine structure: *HBLS-V FMLS* (Ashida, 1979). Molecular graphics: *ORTEP*II (Johnson, 1971). Software used to prepare material for publication: *POTP* (Yasuoka, Kimura & Mizuma, 1979); *DAPH* (Ashida, 1979).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, least-squares-planes data and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71488 (15 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: OH1030]

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Double-Layered Polytypic Structure of the E Form of Octadecanoic Acid, $C_{18}H_{36}O_2$

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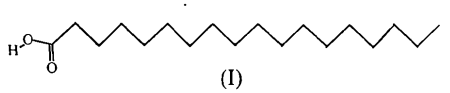
Abstract

Two bimolecular layers forming a double-layered polytypic structure exist in a repeating unit along the stacking direction. The acyl chain inclines toward the

ab plane by 27° and the direction of the inclination is turned by 180° at every stacking of bimolecular layers. One bimolecular layer has essentially the same structure as that of the ordinary single-layered type of the E form.

Comment

The E form of *n*-fatty acids was found by Holland & Nielson (1962, 1963) and the structure was determined for octadecanoic acid (I) (stearic acid) by



(I)

Kaneko, Kobayashi, Kitagawa & Matsuura (1990). Recently, we found that the E form exhibits polytypism, as in the B form of stearic acid (Kobayashi, Kobayashi, Itoh & Sato, 1984) and in even-numbered *n*-alkanes (Amelinckx, 1955, 1956; Kobayashi, Kobayashi, Itoh, Chatani & Tadokoro, 1980). Besides the ordinary monoclinic modification (*Mon*) consisting of one bimolecular layer, single crystals which exhibit IR and Raman spectra characteristic of the double-layered orthorhombic modification (referred as *Orth* II) were frequently obtained from solutions (Kaneko, Sakashita, Kobayashi & Suzuki, 1992). In order to confirm the structure of *Orth* II, we undertook the structure determination of the new modification of the E form.

One bimolecular layer in the *Orth* II type of the E form has essentially the same structure as that of the *Mon* type. The polymethylene chain takes an all-*trans* conformation constructing an orthorhombic subcell with a perpendicular arrangement of the skeletal planes (O⊥), whose average subcell parameters are $a_s = 7.36$, $b_s = 5.01$ and $c_s = 2.55$ Å [the setting of the axes is made in accordance with orthorhombic polyethylene determined by Bunn (1939)]. The setting angle of the zigzag plane to the a_sc_s plane is 45.0°. The direction of the a_s axis agrees with that of the *a* axis of the main lattice and the c_s axis tilts towards the *b* axis by about 27°. In other words, the (011) plane of the subcell is nearly parallel to the basal (*ab*) plane. This arrangement of the O⊥ subcell is a common characteristic among the polymorphic phases of long-chain compounds which exhibit the polytypism.

The stacking arrangement of the bimolecular layers is identical with that of the double-layered polytypic structure determined for the B form of stearic acid (Kaneko *et al.*, 1994), the low-melting phase of petroselinic acid (Kaneko *et al.*, 1992) and *n*-$C_{28}H_{58}$ (Boistelle, Simon & Pepé, 1976). The *c*-axis dimension [88.41 (1) Å] is twice as long as the thickness of the bimolecular layer in the *Mon* type (44.25 Å). Two bimolecular layers are related to each other by the screw axis along the *c* axis. Hence, the direction of the inclination of the acyl chain toward the *ab* plane is turned by 180° at every stacking of bimolecular layers. This herringbone structure of acyl chains results in a markedly different interface between bimolecular layers from that of the ordinary single-layered structure, as shown in Fig. 2. In addition to the orientation of the terminal methyls, there is a systematic difference between the *Orth* II and *Mon* types with respect to the distances between neighboring terminal methyls. In the *Orth* II type, a methyl C atom in one layer is located at the center of a dimple surrounded by four methyl C atoms in the adjacent layer by the requirement of its crystal symmetry. On the other hand, the methyl C atom is displaced from the center along the b_s direction in the *Mon* type.

The carboxyl plane is nearly coplanar with the C(1)—C(2)—C(3) plane. The carbonyl group C(1)=O(2) and the C(2)—C(3) bond adopt *cis* geometry about the C(1)—C(2) bond. The O···O hydrogen-bond distance in the dimer is 2.671 (3) Å.

A recent study showed that the E form is a metastable phase and transforms to the B form (the most stable polymorph below 305 K) through solid-state phase transition under certain conditions

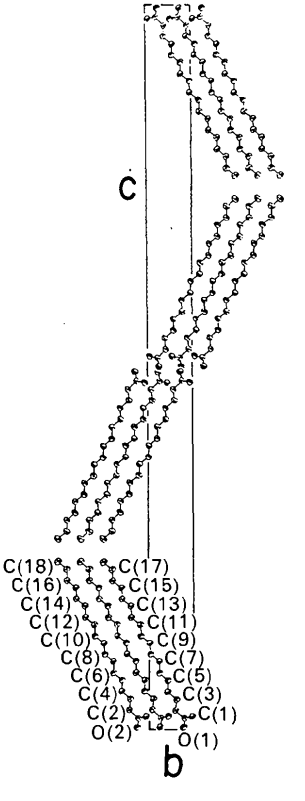


Fig. 1. *ORTEP*II view of the *Orth* II type of stearic acid E form. Thermal ellipsoids are at the 50% probability level.

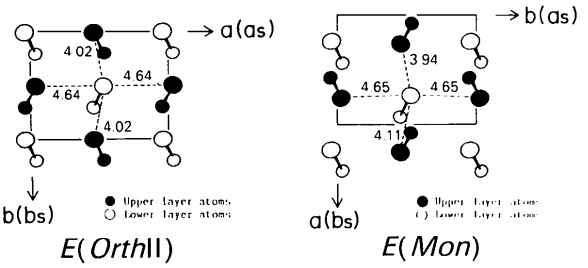


Fig. 2. Projection of terminal methyls onto the basal (*ab*) plane. The larger circles denote the methyl C atoms and the smaller circles correspond the next methylene C atoms.

(Kaneko, Simofuku, Miyamoto, Kobayashi & Suzuki, 1992). The volume per monomer is 456.1 Å^3 in the E form, being 0.55% larger compared to the B form of stearic acid (453.6 Å^3). This suggests that the cohesive energy is one of the main factors to stabilize the B form despite its larger conformational energy due to the *gauche* conformation around the carboxyl group.

Experimental

Crystal data

$C_{18}H_{36}O_2$
M_r = 284.48
Orthorhombic
Pbca
a = 7.359 (1) Å
b = 5.609 (1) Å
c = 88.41 (1) Å
V = 3649.0 (8) Å^3
Z = 8
D_x = 1.04 Mg m^{-3}
D_m = 1.02 Mg m^{-3}
Density measured by flotation

Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 25 reflections
θ = 21-50°
μ = 0.466 mm^{-1}
T = 286 K
Plate
1.00 × 0.80 × 0.05 mm
Colorless
Crystal source: grown from hexane solution

Data collection

Rigaku AFC-5 four-circle diffractometer
ω scans
Absorption correction: none
13 184 measured reflections
2934 independent reflections
2392 observed reflections [$F > 3\sigma(F)$]

R_{int} = 0.036
θ_{max} = 62.5°
$h = -9 \rightarrow 9$
$k = 0 \rightarrow 7$
$l = -102 \rightarrow 102$
3 standard reflections
frequency: 50 min
intensity variation: 3%

Refinement

Refinement on F
R = 0.064
wR = 0.095
S = 1.99
2392 reflections
325 parameters
All H-atom parameters refined

$w = 1/[\sigma^2(F) + 0.001F^2]$
$(\Delta/\sigma)_{max}$ = 0.016
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.08 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$B_{eq} = \frac{4}{3}\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
O(1)	0.1251 (3)	−0.2616 (4)	0.00354 (2)	6.22
O(2)	−0.0657 (3)	−0.0594 (4)	0.01821 (2)	5.84
C(1)	0.0335 (4)	−0.2307 (5)	0.01604 (3)	4.96
C(2)	0.0666 (5)	−0.4240 (5)	0.02748 (3)	5.62
C(3)	−0.0289 (4)	−0.3984 (5)	0.04250 (3)	5.11
C(4)	0.0347 (4)	−0.5930 (5)	0.05332 (3)	5.19
C(5)	−0.0442 (4)	−0.5854 (5)	0.06898 (3)	5.13
C(6)	0.0329 (4)	−0.7782 (5)	0.07928 (3)	5.16
C(7)	−0.0442 (4)	−0.7801 (5)	0.09522 (3)	5.22
C(8)	0.0357 (4)	−0.9731 (5)	0.10516 (3)	5.03
C(9)	−0.0405 (4)	−0.9803 (5)	0.12110 (3)	5.12
C(10)	0.0392 (4)	−1.1771 (5)	0.13091 (3)	5.04
C(11)	−0.0381 (4)	−1.1869 (5)	0.14673 (3)	5.18
C(12)	0.0406 (4)	−1.3829 (5)	0.15662 (3)	5.26
C(13)	−0.0390 (4)	−1.3938 (5)	0.17244 (3)	5.26
C(14)	0.0407 (4)	−1.5875 (5)	0.18226 (3)	5.30
C(15)	−0.0396 (4)	−1.5948 (5)	0.19818 (3)	5.46
C(16)	0.0387 (4)	−1.7901 (6)	0.20826 (3)	5.58
C(17)	−0.0413 (5)	−1.7953 (6)	0.22388 (3)	6.46
C(18)	0.0364 (7)	−1.9867 (7)	0.23402 (4)	7.87

Table 2. *Selected geometric parameters* (Å, °)

O(1)—C(1)	1.306 (3)	C(2)—C(3)	1.509 (4)
O(2)—C(1)	1.222 (3)	C(3)—C(4)	1.524 (4)
C(1)—C(2)	1.503 (4)		
O(1)—C(1)—C(2)	112.9 (2)	C(1)—C(2)—C(3)	116.6 (2)
O(2)—C(1)—C(2)	123.9 (2)	C(2)—C(3)—C(4)	109.9 (2)
O(1)—C(1)—O(2)	123.1 (2)	C(3)—C(4)—C(5)	116.1 (2)
O(1)—C(1)—C(2)—C(3)	178.0 (2)	C(2)—C(3)—C(4)—C(5)	178.0 (2)
O(2)—C(1)—C(2)—C(3)	−0.7 (4)	C(3)—C(4)—C(5)—C(6)	−177.3 (2)
C(1)—C(2)—C(3)—C(4)	−173.9 (2)		

The ω-scan width was (1.3-0.45tanθ)° in order to avoid the overlapping of neighboring reflections; the ω-scan rate was 3.0° min^{-1} and background counts were made for 4 s on each side of every scan. The molecular model was initially built for 18 C and two O atoms by reference to the structure of the *Mon* type of the E form of stearic acid. Refinement was by full-matrix least-squares methods. Data collection: Rigaku AFC-5 with software *AFCM* of the Research Center for Protein Engineering, Institute for Protein Research Center, Osaka University, Japan. Programs used to refine structure: *HBLS-V FMLS* (Ashida, 1979). Molecular graphics: *ORTEP*II (Johnson, 1971). Software used to prepare material for publication: *POTP* (Yasuoka, Kimura & Mizuma, 1979); *DAPH* (Ashida, 1979).

Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71480 (15 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: OH1038]

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Structure of the Tripeptide Amide H-L-Pro-L-Leu-L-Pro-NH_2, a Dopamine Receptor Modulating Agent

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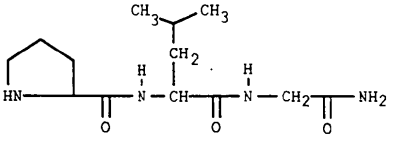
Abstract

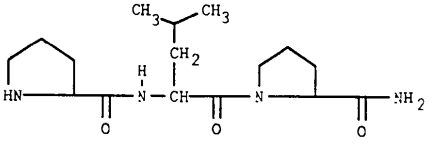
The title compound, L-Prolyl-L-leucyl-L-prolinamide, $C_{16}H_{28}N_4O_3$, is folded at the N-terminal L-Pro residue and semi-extended at the central L-Leu and C-terminal L-Pro residues. The L-Leu side chain is in the common $g^-(t,g^-)$ disposition.

Comment

Several of the hypothalamic release-inhibiting factors have effects on the central nervous system which are independent of their endocrine effects. Among these oligopeptides is H-L-Pro-L-Leu-Gly-NH_2 (1). This tripeptide amide, the hypothalamic factor that inhibits the release of melanocyte-stimulating hormone from the anterior pituitary gland, has been shown to possess a pharmacological profile typical of a dopamine-receptor modulating agent (Johnson, Rajakumar & Mishra, 1986). In an attempt to gain better understanding of the bioactive conformation of (1), we have undertaken the structural analysis of a number of conformationally restricted analogues of this tripeptide (Valle *et al.*, 1988; Valle, Crisma, Toniolo, Yu & Johnson, 1989). In this paper, we describe the structure of H-L-Pro-L-Leu-L-Pro-NH_2 (2), a bioactive analogue of (1), which possesses a



(1)



(2)

chiral cyclic amino acid residue at the C-terminal position (Johnson *et al.*, 1986). The synthesis and characterization of (2) have been reported (Johnson, Smissman & Plotnikoff, 1978).

The backbone conformation of (2) is folded at the N-terminal L-Pro residue [$\psi_1 = -5.9$ (5)°] and semi-extended at the central L-Leu [$\phi_2 = -98.8$ (5)°, $\psi_2 = 129.6$ (6)°] and at the C-terminal L-Pro [$\phi_3 = -72.5$ (5)°, $\psi_T = 154.4$ (6)°] residues (IUPAC–IUB Commission on Biochemical Nomenclature, 1970). The peptide torsion angles are in the usual *trans*-planar conformation [$\omega_1 = 175.4$ (6), $\omega_2 = 178.3$ (6)° (Benedetti, 1982)]. Interestingly, in the crystal state the prototype tripeptide amide (1) is extended at the N terminus, while folded in a type-II β-turn conformation (Venkatachalam, 1968) at the -L-Leu-Gly- sequence (Reed & Johnson, 1973).

The L-Leu side chain of (2) takes the common $g^-(t,g^-)$ conformation (Benedetti, Morelli, Némethy & Scheraga, 1983), with the χ^1, $\chi^{2,1}$ and $\chi^{2,2}$ torsion angles −66.8 (6), 167.4 (7) and −70.4 (6)°, respectively. The pyrrolidine rings of the L-Pro[1] and L-Pro[3] residues have close to C_2 (twist) symmetry, with ring-puckering parameters $q_2 = 0.353$ Å and $\phi_2 =$