

Structure of the 3_{10} -Helical Pentapeptide Boc-Aib-L-Ala-Aib-L-Ala-Aib-OMe Dihydrate, $C_{24}H_{43}N_5O_8 \cdot 2H_2O$

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Abstract. $M_r = 565.67$, orthorhombic, $P2_12_12_1$, $a = 8.960$ (2), $b = 16.534$ (2), $c = 21.398$ (3) Å, $V = 3170.0$ (9) Å³, $Z = 4$, $D_x = 1.185$ (1) Mg m⁻³, Mo $K\alpha$, $\lambda = 0.71069$ Å, $\mu = 0.051$ mm⁻¹, room temperature, $F(000) = 1224$. The structure was solved by direct methods and refined by the full-matrix least-squares method. The final R value was 0.068 for 2193 unique reflexions. The pentapeptide adopts a 3_{10} -helical secondary structure consisting of three β -turns (type III) in accordance with three intramolecular hydrogen bonds. By participation of the two hydrate molecules, 3_{10} -helices are connected head to tail with intermolecular hydrogen bonds. This leads to a left-handed 'superhelical' arrangement along [001] with parallel helix axes.

Introduction. The conformational analysis of α -aminoisobutyric acid (Aib)-containing oligopeptides is a matter of considerable interest, since this unusual amino acid was found to occur in several peptide antibiotics (Brückner & Jung, 1982). The crystallographic investigation of the title compound was undertaken in order to obtain information about the secondary structure of short linear Aib-containing peptides. Recent experiments on lipid bilayers revealed that at micromolar concentrations Boc-Aib-Ala-Aib-Ala-Aib-OMe and Boc-(Ala-Aib-Ala-Aib-Ala) $_n$ -OMe ($n = 1-4$) induce voltage-dependent ion-conducting pores (Jung, Katz, Schmitt, Voges, Menestrina & Boheim, 1982). Boc-Aib-Ala-Aib-Ala-Aib-OMe was prepared according to published procedures (Oekonomopulos & Jung, 1979).

Experimental. A single crystal for X-ray studies with approximate dimensions $0.4 \times 0.3 \times 0.25$ mm was obtained by crystallization from a methanol/water solution. Intensity measurement: Enraf-Nonius CAD-4, Mo $K\alpha$ radiation (graphite monochromator), 3178 reflexions (ω/θ scan mode, $\theta = 3-25^\circ$, hkl up to 10 19 25), 2195 unique reflexions ($|F| > 0$). Structure solution: direct methods; refinement: nonhydrogen atoms with anisotropic temperature factors, methyl and tertiary C-H as rigid groups with fixed C-H distance

(0.96 Å), final R values: $R = 0.068$ and $R_G = 0.064$ (unit weights).† Final difference map no electron density > 0.1 e Å⁻³, flat analysis of variance (with respect to hkl , $|F_o|$ and $\sin \theta/\lambda$). Scattering factors from Cromer & Mann (1968), Cromer & Liberman (1970). Programs: *SHELX76* (Sheldrick, 1976), *MULTAN80* (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980), *XANADU* (Roberts & Sheldrick) and *PLUTO* (Motherwell).

Discussion. Final atomic coordinates are listed in Table 1, geometrical parameters in Table 2. Fig. 1 shows the numbering of the pentapeptide.

† Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38401 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Atomic coordinates and equivalent isotropic thermal parameters with e.s.d.'s in parentheses

	$[U_{eq} = (U_{11} \times U_{22} \times U_{33})^{1/3} \times 10^3 \text{ \AA}^2]$			
	x	y	z	U_{eq}
O(1)	0.4153 (6)	1.2365 (3)	0.2934 (2)	6.1 (3)
O(2)	0.3842 (5)	1.1859 (3)	0.3914 (2)	4.7 (3)
O(3)	0.2432 (5)	0.9840 (3)	0.4251 (2)	5.1 (3)
O(4)	0.5948 (6)	0.9319 (3)	0.4900 (2)	5.8 (3)
O(5)	0.4855 (6)	1.0427 (3)	0.6344 (2)	6.0 (3)
O(6)	0.2316 (6)	0.8451 (3)	0.6628 (2)	5.4 (3)
O(7)	0.5386 (6)	0.8039 (3)	0.7109 (2)	5.8 (3)
O(8)	0.4263 (6)	0.6863 (3)	0.6920 (2)	5.1 (3)
N(1)	0.2539 (7)	1.1390 (3)	0.3086 (2)	4.6 (3)
N(2)	0.4189 (6)	1.0116 (3)	0.3536 (2)	3.7 (3)
N(3)	0.5306 (7)	1.0615 (3)	0.4687 (2)	4.7 (3)
N(4)	0.3312 (6)	1.0058 (3)	0.5568 (2)	4.1 (3)
N(5)	0.4197 (6)	0.8527 (3)	0.5930 (2)	4.1 (3)
C(1)	0.5563 (9)	1.2784 (4)	0.3063 (4)	5.9 (5)
C(2)	0.6729 (9)	1.2182 (5)	0.3262 (4)	7.3 (6)
C(3)	0.5317 (14)	1.3444 (6)	0.3544 (6)	10.6 (9)
C(4)	0.5938 (12)	1.3127 (6)	0.2426 (5)	10.7 (8)
C(5)	0.3546 (7)	1.1879 (4)	0.3364 (3)	4.1 (4)
C(6)	0.1757 (7)	1.0748 (4)	0.3419 (3)	4.2 (4)
C(7)	0.0957 (10)	1.0226 (5)	0.2935 (4)	7.0 (6)
C(8)	0.0597 (9)	1.1101 (5)	0.3874 (4)	6.3 (5)
C(9)	0.2831 (7)	1.0193 (4)	0.3780 (3)	3.8 (4)
C(10)	0.5322 (7)	0.9613 (4)	0.3843 (3)	4.4 (4)
C(11)	0.6799 (8)	0.9694 (5)	0.3496 (4)	5.8 (5)
C(12)	0.5541 (8)	0.9849 (4)	0.4521 (3)	4.8 (4)
C(13)	0.5486 (10)	1.0921 (5)	0.5325 (3)	5.7 (5)
C(14)	0.7120 (11)	1.0882 (8)	0.5512 (5)	9.7 (8)
C(15)	0.4867 (15)	1.1783 (5)	0.5335 (4)	7.7 (7)
C(16)	0.4544 (8)	1.0439 (4)	0.5788 (3)	4.3 (4)
C(17)	0.2319 (8)	0.9603 (4)	0.5967 (3)	4.5 (4)
C(18)	0.0856 (8)	0.9450 (5)	0.5624 (4)	6.4 (5)

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Table 1 (cont.)

C(19)	0.2967 (7)	0.8812 (4)	0.6204 (3)	4.3 (4)
C(20)	0.4751 (8)	0.7704 (4)	0.6048 (3)	4.6 (4)
C(21)	0.6347 (9)	0.7664 (5)	0.5807 (4)	6.3 (5)
C(22)	0.3773 (11)	0.7093 (5)	0.5707 (3)	6.0 (5)
C(23)	0.4824 (8)	0.7576 (4)	0.6747 (3)	4.1 (4)
C(24)	0.4310 (10)	0.6675 (5)	0.7579 (3)	5.5 (5)
O(9)	0.0027 (7)	0.9439 (3)	0.7263 (3)	6.1 (1)
O(10)	0.7112 (8)	0.9442 (4)	0.6875 (3)	8.2 (2)

Table 2. Bond lengths (Å), bond angles (°) and torsion angles (°) with e.s.d.'s in parentheses

C(1)—C(2)	1.504 (12)	N(3)—C(13)	1.465 (9)
C(1)—C(3)	1.516 (13)	C(13)—C(14)	1.520 (13)
C(1)—C(4)	1.513 (14)	C(13)—C(15)	1.528 (12)
C(1)—O(1)	1.466 (9)	C(13)—C(16)	1.525 (10)
O(1)—C(5)	1.338 (8)	C(16)—O(5)	1.223 (8)
C(5)—O(2)	1.207 (8)	C(16)—N(4)	1.355 (9)
C(5)—N(1)	1.350 (9)	N(4)—C(17)	1.445 (8)
N(1)—C(6)	1.458 (8)	C(17)—C(18)	1.523 (10)
C(6)—C(7)	1.527 (11)	C(17)—C(19)	1.518 (9)
C(6)—C(8)	1.538 (11)	C(19)—O(6)	1.234 (8)
C(6)—C(9)	1.538 (9)	C(19)—N(5)	1.334 (9)
C(9)—O(3)	1.217 (8)	N(5)—C(20)	1.471 (8)
C(9)—N(2)	1.331 (8)	C(20)—C(21)	1.521 (11)
N(2)—C(10)	1.466 (8)	C(20)—C(22)	1.524 (11)
C(10)—C(11)	1.524 (10)	C(20)—C(23)	1.512 (9)
C(10)—C(12)	1.516 (9)	C(23)—O(7)	1.199 (8)
C(12)—O(4)	1.249 (8)	C(23)—O(8)	1.333 (8)
C(12)—N(3)	1.332 (9)	O(8)—C(24)	1.445 (8)
C(4)—C(1)—O(1)	101.4 (7)	N(3)—C(13)—C(14)	109.6 (7)
C(2)—C(1)—C(3)	112.7 (8)	N(3)—C(13)—C(15)	107.1 (6)
C(2)—C(1)—C(4)	110.4 (7)	C(14)—C(13)—C(15)	112.7 (9)
C(2)—C(1)—O(1)	109.8 (6)	N(3)—C(13)—C(16)	111.3 (6)
C(1)—O(1)—C(5)	120.3 (6)	C(13)—C(16)—O(5)	121.0 (6)
O(1)—C(5)—O(2)	126.7 (6)	C(13)—C(16)—N(4)	117.9 (6)
O(1)—C(5)—N(1)	109.2 (6)	C(16)—N(4)—C(17)	122.6 (5)
C(5)—N(1)—C(6)	122.9 (5)	N(4)—C(17)—C(18)	109.4 (5)
N(1)—C(6)—C(7)	107.8 (6)	N(4)—C(17)—C(19)	114.2 (6)
N(1)—C(6)—C(8)	111.0 (5)	C(18)—C(17)—C(19)	110.3 (6)
C(7)—C(6)—C(8)	109.1 (6)	C(17)—C(19)—O(6)	118.8 (6)
N(1)—C(6)—C(9)	112.3 (5)	C(17)—C(19)—N(5)	118.3 (6)
C(6)—C(9)—O(3)	121.2 (6)	C(19)—N(5)—C(20)	122.0 (5)
C(6)—C(9)—N(2)	115.6 (5)	N(5)—C(20)—C(21)	107.4 (6)
C(9)—N(2)—C(10)	120.7 (5)	N(5)—C(20)—C(22)	109.8 (6)
N(2)—C(10)—C(11)	109.5 (5)	C(21)—C(20)—C(22)	110.5 (6)
N(2)—C(10)—C(12)	111.9 (5)	N(5)—C(20)—C(23)	108.3 (5)
C(11)—C(10)—C(12)	109.4 (6)	C(20)—C(23)—O(7)	124.6 (6)
C(10)—C(12)—O(4)	118.6 (6)	C(20)—C(23)—O(8)	112.4 (5)
C(10)—C(12)—N(3)	118.6 (6)	C(23)—O(8)—C(24)	116.7 (5)
C(12)—N(3)—C(13)	124.1 (6)		

Torsion angles as defined by IUPAC (1970) (e.s.d.'s ~0.8–0.9°)

Aib(1)	φ -51.1	ψ -29.6	ω 179.0
Ala(2)	-53.6	-29.8	180.0
Aib(3)	-55.3	-25.4	-178.3
Ala(4)	-71.2	-14.1	-168.9
Aib(5)	-50.2	-48.7	—
Theoretical values			
3_{10} -helix	-60	-30	180
α_R -helix	-57	-47	180

Table 3. Average bond angles (°) at an Aib residue compared with the values observed in the title compound (e.s.d.'s about 0.6°)

	α	β	γ	δ	ε	η	ζ	ρ	σ	ω
Aib(1)	122.9	107.8	109.1	107.3	109.3	111.0	112.3	115.6	123.2	121.2
Aib(2)	124.1	107.1	112.7	106.2	109.9	109.6	111.3	117.9	121.0	121.0
Aib(3)	122.0	107.4	110.5	106.7	113.9	109.8	108.3	112.4	122.9	124.6
Literature values (see text)	122.2	106.8	110.6	106.8	110.6	110.6	111.1	116.8	122.6	120.4

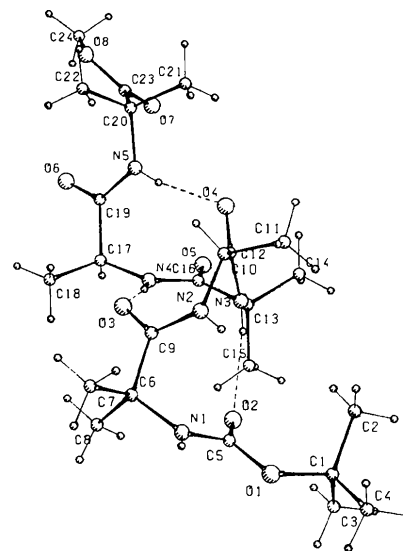


Fig. 1. Perspective view of the title compound with the atomic numbering.

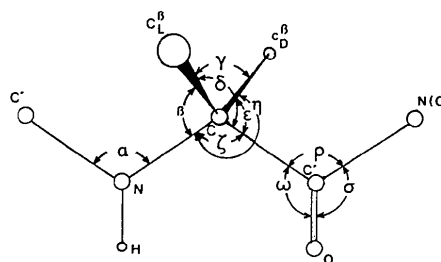


Fig. 2. Notation of bond angles at an Aib residue (see also Table 3).

The pentapeptide adopts a 3_{10} -helical conformation consisting of type III β -turns (Venkatachalam, 1968; Chou & Fasman, 1977) and three intramolecular $4 \rightarrow 1$ hydrogen bonds. The (φ/ψ) values (Table 2) agree with the angle combinations so far found in other Aib peptides (Benedetti, Bavoso, Di Blasio, Pavone, Pedone, Crisma, Bonora & Toniolo, 1982; Nagaraj, Shamala & Balaran, 1979; Shamala, Nagaraj & Balaran, 1978; Prasad, Shamala, Nagaraj & Balaran, 1980; Smith, Pletnev, Duax, Balasubramanian, Bossard, Czerwinski, Kendrick, Mathews & Marshall, 1981; Bosch, Winter & Jung, 1982; Bosch, Voges, Jung & Winter, 1983). Recently it was found that a tetrahedral, symmetrical geometry at C_α favours the α -helical conformation, whereas asymmetric geometry at C_α gives the 3_{10} conformation as the preferred structure (Paterson, Rumsey, Benedetti, Némethy & Scheraga, 1981). The angles around C_α of about 20 observations in well refined ($R \leq 0.08$) structures were averaged, and the results compared with the values we found in the title compound are shown in Table 3 (for the notation of the angles see Fig. 2).

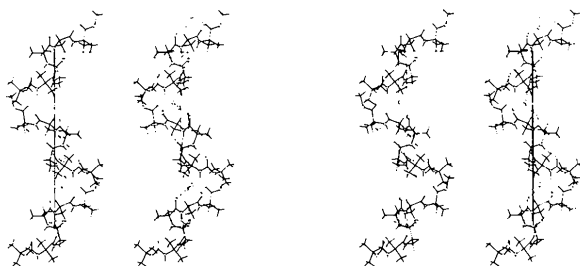


Fig. 3. Stereoscopic view of the molecular packing. Hydrogen bonds are indicated as dashed lines.

Indeed, the bond angles β and δ of the title compound are significantly less whereas ϵ and η tend to be greater than the tetrahedral value. The bond lengths do not show significant deviations from ideal peptide geometry.

Three intramolecular hydrogen bonds in accordance with type III β -turns (right-handed helical conformation) are observed: N(3)···O(2) 2.95 (1) Å, N(4)···O(3) 2.95 (1) Å and N(5)···O(4) 3.01 (1) Å.

The pentapeptide molecules are connected head-to-tail along [001] by a system of intermolecular hydrogen bonds: One hydrogen bond connects directly two peptide molecules [N(1)···O(6') 3.13 (1) Å; symmetry code: $\frac{1}{2}-x, 2-y, -\frac{1}{2}+z$]. The two water molecules [O(9) and O(10)], which fill the space between the head-to-tail connexion, are used for a 'long-range' bridge between N(2) and O(5') [N(2)···O(9') 2.91 (1) Å; symmetry code: $\frac{1}{2}-x, 2-y, -\frac{1}{2}+z$; O(9)···O(10') 2.74 (1) Å; symmetry code: $-1+x, y, z$; and O(10)···O(5) 2.83 (1) Å]. Finally there is a hydrogen bond between O(9) and O(6), which is bifurcated at the carbonyl O atom [O(9)···O(6) 2.95 (1) Å]. Fig. 3 shows that the head-to-tail connexion of the 3_{10} -helices leads to left-handed 'superhelices' along [001]. The latter are held together by hydrophobic interactions. It is of particular interest that these superhelices have a parallel packing in contrast to the antiparallel packing of the α -helices of the undecapeptide Boc-L-Ala-Aib-Ala-Aib-Ala-Glu(OBzl)-Ala-Aib-Ala-Aib-Ala-OMe (Butters, Hütter, Jung, Pauls, Schmitt, Sheldrick & Winter, 1981; Schmitt, Winter, Bosch & Jung, 1982).

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Structure of the Monoclinic Form of 2,6-Di-*tert*-butyl-4-methylphenol (DBMP), C₁₅H₂₄O

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Abstract. $M_r = 220.34$, monoclinic, $C2/c$, $a = 1.050$ Mg m⁻³, $\lambda(\text{Mo } K\alpha) = 0.71073$ Å, $\mu(\text{Mo } K\alpha) = 25.810$ (9), $b = 8.488$ (1), $c = 16.481$ (7) Å, $\beta = 0.059$ mm⁻¹, $T = 288\text{K}$, $F(000) = 976$, final $R = 0.041$ 129.45 (2)°, $U = 2788$ (1) Å³, $Z = 8$, $D_x =$ for 1164 unique reflections. Some of the bond angles