

Benzyl *tert*-butoxycarbonyl- $\alpha$ -amino-  
isobutyrate

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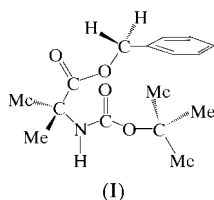
Received 7 November 2000

Accepted 15 January 2001

The small synthetic peptide, benzyl 2-(*tert*-butoxycarbonyl-amino)isobutyrate,  $C_{16}H_{23}NO_4$ , has the  $\alpha$ -helical conformation [ $|\varphi| = 55.8(2)^\circ$  and  $|\psi| = 37.9(2)^\circ$ ] observed in peptide fragments of peptaibols containing the  $\alpha$ -aminoisobutyric acid (Aib) residue. The structure shows no intramolecular hydrogen bonding, which would disrupt the limited conformational freedom associated with this amino acid. Two weak intermolecular hydrogen contacts are observed.

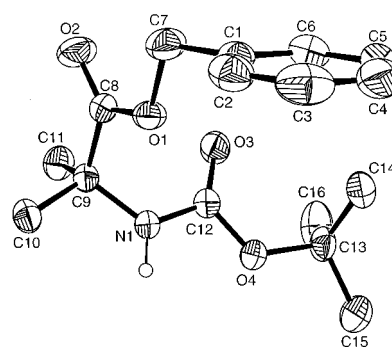
## Comment

The  $\alpha$ -amino acid  $\alpha$ -aminoisobutyric acid (Aib) is a major constituent of several natural products, including peptaibols, a class of antibiotic peptides isolated from the Trichoderma species (Mueller & Rudin, 1968). The presence of a methyl group in place of an H atom at  $C_\alpha$  has been shown to create severe restrictions in the conformational space of Aib (Paterson *et al.*, 1981). The  $\varphi$  and  $\psi$  values [ $(\varphi, \psi) = (-55^\circ; -45^\circ)$  and  $(\varphi, \psi) = (-60^\circ; -30^\circ)$ ] for the torsional angles of the Aib residue are characteristic of  $\alpha$ - or  $3_{10}$ -helices, respectively, with the preferred secondary structure dependent on chain length, peptide composition, and the positions of the Aib residues (Toniolo & Benedetti, 1991; Van Roey *et al.*, 1983).



Toniolo has previously reported the X-ray crystal structure of the simple Aib derivative Cbz-Aib-OtBu (Crisma *et al.*, 1995). In this work, we describe the structure of an isomer of this compound, *i.e.* Boc-Aib-OBzl, (I), in which the aliphatic and aromatic moieties are interchanged. There is no intramolecular hydrogen bonding in either compound and as a result, the folding in both structures shows similar  $\alpha$ -helical

conformations. In comparison, the torsion angles are  $(\varphi, \psi) = [-55.8(2)^\circ; -37.9(2)^\circ]$  for the title compound and  $(-50.8^\circ; -39.3^\circ)$  for the Cbz derivative. Intermolecular contacts of different types are, however, observed between Boc-Aib-OBzl and Cbz-Aib-OtBu. The Cbz derivative forms one intermolecular hydrogen bond between the NH and the carbonyl oxygen, O3, of the amide. The overall result is an extended hydrogen-bonding network. In contrast for the title compound, N1 donates one H atom to the ether oxygen, O1, of an adjacent molecule in the unit cell to form a weak hydrogen bond [H1n...O1 2.60(3) Å]. There are two of these intermolecular hydrogen-bond contacts between two molecules in the cell, resulting in a structure that resembles a cyclic dimer.



**Figure 1**  
ORTEP-3 (Farrugia, 1997) diagram of (I) showing 45% displacement ellipsoids. H atoms, except for the amide NH atom, have been omitted for clarity.

## Experimental

The title compound was synthesized by esterification of Boc-Aib-OH (1.0 equivalents) with dicyclohexylcarbodiimide (1.1 equivalents), benzyl alcohol (1.1 equivalents) and a catalytic amount (0.1 equivalents) of 4-dimethylaminopyridine in dichloromethane (Hassner & Alexanian, 1978). Crystallization was from an ethanol solution to which had been added a very small amount of water (3 drops) until turbid. The mixture was allowed to stand overnight at 281 K.

## Crystal data

$C_{16}H_{23}NO_4$   
 $M_r = 293.35$   
Triclinic,  $P\bar{1}$   
 $a = 9.273(3) \text{ \AA}$   
 $b = 9.333(3) \text{ \AA}$   
 $c = 10.372(4) \text{ \AA}$   
 $\alpha = 94.16(2)^\circ$   
 $\beta = 112.17(2)^\circ$   
 $\gamma = 93.09(2)^\circ$   
 $V = 825.9(4) \text{ \AA}^3$

$Z = 2$   
 $D_x = 1.180 \text{ Mg m}^{-3}$   
Mo  $K\alpha$  radiation  
Cell parameters from 25 reflections  
 $\theta = 15.0\text{--}18.0^\circ$   
 $\mu = 0.084 \text{ mm}^{-1}$   
 $T = 293(2) \text{ K}$   
Plate, colorless  
 $0.49 \times 0.33 \times 0.17 \text{ mm}$

## Data collection

CAD-4 diffractometer  
Data from  $\omega/2\theta$  scans  
Absorption correction: empirical  
via  $\psi$  scan (North *et al.*, 1968)  
 $T_{\min} = 0.94, T_{\max} = 0.99$   
3043 measured reflections  
2846 independent reflections  
2312 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.007$   
 $\theta_{\text{max}} = 25^\circ$   
 $h = 0 \rightarrow 11$   
 $k = -11 \rightarrow 11$   
 $l = -12 \rightarrow 12$   
3 standard reflections  
frequency: 60 min  
intensity decay: <0.5%

## Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F_o^2) + (0.0340P)^2 + 0.4831P]$
$R[F^2 > 2\sigma(F^2)] = 0.048$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.116$	$(\Delta/\sigma)_{\max} < 0.001$
$S = 1.011$	$\Delta\rho_{\max} = 0.22 \text{ e } \text{\AA}^{-3}$
2846 reflections	$\Delta\rho_{\min} = -0.19 \text{ e } \text{\AA}^{-3}$
195 parameters	Extinction correction: <i>SHELXL97</i>
H atoms treated by a mixture of independent and constrained refinement	(Sheldrick, 1997)
	Extinction coefficient: 0.249 (9)

**Table 1**

Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ ).

N1—C12	1.346 (2)	O2—C8	1.194 (2)
N1—C9	1.454 (2)	O3—C12	1.202 (2)
O1—C8	1.338 (2)	O4—C12	1.341 (2)
O1—C7	1.459 (3)	O4—C13	1.477 (2)
C1—C7	1.489 (3)	C8—C9	1.521 (3)
C12—N1—C9	122.40 (17)	O1—C8—C9	113.11 (16)
C9—N1—H1N	119.4 (17)	N1—C9—C8	111.10 (15)
C8—O1—C7	115.00 (16)	N1—C9—C11	111.53 (17)
C12—O4—C13	121.49 (16)	N1—C9—C10	107.66 (16)
O1—C7—C1	108.56 (17)	O3—C12—O4	126.05 (18)
O2—C8—O1	123.5 (2)	O3—C12—N1	123.80 (19)
O2—C8—C9	123.25 (19)		

The H atom bonded to N1 was located on a difference map and was refined isotropically with  $U_{\text{iso}} = 1.3U_{\text{eq}}(\text{attached N atom})$ . H-atom positions were calculated using a riding model with  $U(\text{H}) = 1.2U_{\text{eq}}(\text{attached atom})$  for the phenyl and methylene H atoms and  $U(\text{H}) = 1.5U_{\text{eq}}(\text{attached C atom})$  for the methyl groups.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1988); cell refinement: *CAD-4 Software*; data reduction: *SHELXTL* (Bruker, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

The X-ray equipment was purchased with assistance from the National Science Foundation (CHE-9016978).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BK1584). Services for accessing these data are described at the back of the journal.

## References

- Bruker (1997). *SHELXTL*. Version 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.
- Crisma, M., Valle, G., Formaggio, F. & Toniolo, C. (1995). *Z. Kristallogr.* **210**, 636–637.
- Enraf–Nonius (1988). *CAD-4 Software*. Enraf–Nonius, Delft, The Netherlands.
- Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
- Hassner, A. & Alexanian, V. (1978). *Tetrahedron Lett.* **46**, 4475–4478.
- Mueller, P. & Rudin, D. O. (1968). *J. Am. Chem. Soc.* **217**, 713–719.
- North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* **A24**, 351–359.
- Paterson, Y., Runsey, S., Benedetti, E., Nemethy, G. & Scheraga, H. A. (1981). *J. Am. Chem. Soc.* **103**, 2947–2955.
- Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
- Toniolo, C. & Benedetti, E. (1991). *Macromolecules*, **24**, 4004–4009.
- Van Roey, P., Smith, G. D., Balasubramanian, T. M. & Marshall, G. R. (1983). *Acta Cryst.* **C39**, 894–896.