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cis- and *trans*-Conformers at the urethane linkage: *tert*-butoxycarbonyl-L-alanyl-L-proline methyl ester (Boc-L-Ala-L-Pro-OMe)

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Crystals of the title compound, $C_{16}H_{28}N_2O_7$, were successfully grown from an oily product at low temperature (below 260 K). There are two independent molecules in the asymmetric unit. One molecule has a *cis* and the other a *trans* conformation at the urethane linkage, —O—CO—NH—. Independent molecules are linked into dimers, but not into chains, by N—H···O═C hydrogen bonds.

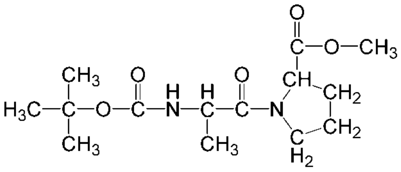
Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.015 Å
R factor = 0.089
wR factor = 0.193
Data-to-parameter ratio = 9.8

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

The title compound, (I), is a key starting material in our studies of synthetic antigens (Ishiguro *et al.*, 2001) and models of enzyme-active sites (Abe *et al.*, 2001). Similar to (I), compounds Boc-*Xaa*-Pro-OMe (where *Xaa* is any amino acid) do not often crystallize at room temperature. Therefore, in this study, the crystal structure of (I) has been determined in order to find out what makes these types of compounds exist in an oily state.



Boc-L-Ala-L-Pro-OMe

(I)

The structure of the two molecules in the asymmetric unit of (I) is shown in Fig. 1. The difference in the two independent molecules is found at the linkage between Boc and Ala. One has a *cis* and the other a *trans* conformation at the urethane linkage, —O—CO—NH—. The *cis* conformation is not common, but it is sometimes observed in short peptides (Benedetti *et al.*, 1980).

The *cis*-urethane in one independent molecule forms hydrogen bonds with a *trans*-urethane of the amide group in the other independent molecule. Thus the two independent molecules are linked into dimers by two N—H···O═C hydrogen bonds.

Intermolecular interaction networks, such as are formed with N—H···O═C hydrogen bonds, especially extended hydrogen-bonded chains, are often found in peptide compounds (Karle, 1992; Goerbitz & Etter, 1992; Clegg *et al.*, 2003). This is an important crystallizing force for peptide compounds. An intermolecular hydrogen-bonded network of molecules is, however, not found in the crystal structure of (I).

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A relatively high $U_{\rm iso}$ value [0.141 (6) Å^2] was observed for atom C134. This is probably due to the puckering motion of the five-membered ring in the Pro residue. In this case, disorder, which might be associated with this puckering, was not modelled.

The puckering motion is responsible for the short bond lengths of C135—C134 and C133—C134 [1.43 (2) and 1.37 (2) Å, respectively]. These values are unusual for sp^3—sp^3 bond lengths. These geometries represent the averaged geometries of the puckering conformers of the five-membered ring in the Pro residue.

In conclusion, from the structural analysis, we have found the *cis–trans* isomerization of the urethane linkage, the lack of an intermolecular hydrogen-bond network, and the puckering motion of a Pro side chain. These three features can weaken intermolecular association in the crystal and probably lower the melting point of (I).

Experimental

Crystals of the title compound were successfully grown from a carefully purified oil at low temperature (below 260 K). Analytical data (^{1}H NMR, ESI–MS and $[\alpha]_D$) were in accordance with the expected structure; $[\alpha]_D = -108.4°$ (*c* 0.1, MeOH).

Crystal data

$C_{14}H_{24}N_2O_5$
$M_r = 300.35$
Monoclinic, $P2_1$
$a = 10.131$ (5) Å
$b = 9.940$ (5) Å
$c = 16.784$ (8) Å
$\beta = 97.33$ (3)°
$V = 1676.4$ (14) Å^3
$Z = 4$
$D_x = 1.190$ Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 4739 reflections
$\theta = 6.3$–$62.2°$
$\mu = 0.75$ mm^{-1}
$T = 173.1$ K
Platelet, colorless
0.20 × 0.20 × 0.10 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans
Absorption correction: refined from ΔF (*DIFABS*; Walker & Stuart, 1983)
$T_{\rm min} = 0.841$, $T_{\rm max} = 0.928$
31 310 measured reflections
3190 independent reflections
2122 reflections with $F^2 > 2\sigma(F^2)$
$R_{\rm int} = 0.040$
$\theta_{\rm max} = 68.3°$
$h = -12 \rightarrow 11$
$k = -11 \rightarrow 11$
$l = -19 \rightarrow 19$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.089$
$wR(F^2) = 0.193$
$S = 1.76$
2122 reflections
217 parameters
All H-atom parameters refined
$w = 1/[0.001F_o^2 + 3\sigma(F_o^2) + 0.5]/(4F_o^2)$
$(\Delta/\sigma)_{\rm max} = 0.007$
$\Delta\rho_{\rm max} = 0.59$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.33$ e Å^{-3}

Table 1
Selected geometric parameters (°).

C111—O111—C115—N121	168.1 (6)	C221—N221—C215—O211	176.3 (7)
C141—O141—C132—C131	175.4 (7)	C215—N221—C221—*C*222	−76.3 (11)
C211—O211—C215—N221	−177.6 (7)	C231—N231—*C*222—C221	172.0 (7)
C241—O241—C232—C231	172.6 (6)	*C*222—N231—C231—C232	−61.0 (9)
C121—N121—C115—O111	−6.0 (13)	N121—C121—C122—N131	153.2 (8)
C115—N121—C121—C122	−60.4 (11)	N131—C131—C132—O141	168.7 (8)
C131—N131—C122—C121	173.0 (7)	N221—C221—*C*222—N231	140.3 (8)
C122—N131—C131—C132	−71.1 (11)	N231—C231—C232—O241	153.3 (7)

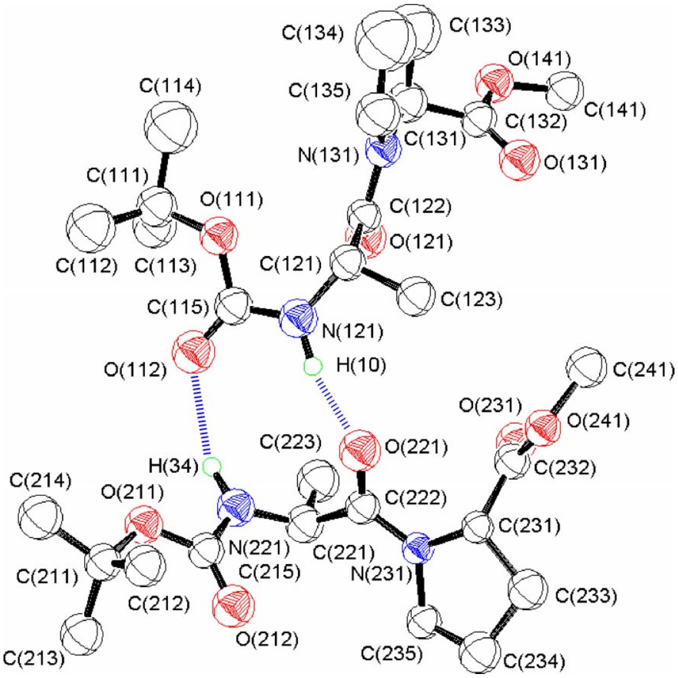

Figure 1
The asymmetric unit of (I) with the atomic numbering scheme. Displacement ellipsoids (spheres) are drawn at the 50% probability level. Hydrogen bonds are shown with dotted lines. All H atoms have been omitted, except for those involved in hydrogen bonding.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N121—H10···O221	0.95	1.86	2.794 (12)	168
N221—H34···O112	0.95	2.21	3.070 (11)	150

All non-H atoms were refined with isotropic displacement parameters due to the limited numbers of observed reflections. Even at the low-temperature condition (173 K), diffraction from the crystal of (I) was too weak to collect enough data for anisotropic refinement. H atoms were placed in calculated positions (C—H = 0.95 Å) and refined with a riding model, and with $U_{\rm iso}$ constrained to be $1.2U_{\rm iso}$ of the carrier atom. The absolute stereochemistry was not established from the diffraction experiment. Friedel pairs were averaged. The absolute configuration was confirmed from the spectroscopic data, α_D, of the compound.

Data collection: *RAPID-AUTO* (Rigaku/MSC and Rigaku, 2003); cell refinement: *RAPID-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC and Rigaku, 2003); program(s) used to solve structure: *SIR*2002 (Burla *et al.*, 2003); program(s) used to refine structure: *CRYSTALS* (Watkin *et al.*, 1996); molecular graphics: *ORTEP* (Johnson, 1965); software used to prepare material for publication: *CrystalStructure*.

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