Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

(2*S*)-1-Carbamoylpyrrolidine-2-carboxylic acid

Luis E. Seijas,[a] Gerzon E. Delgado,[a]* Asiloé J. Mora,[a] Ali Bahsas[b] and Alexander Briceño[c]

[a]Laboratorio de Cristalografía, Facultad de Ciencias, Departamento de Química, Universidad de Los Andes, Mérida 5101, Venezuela, [b]Laboratorio de Resonancia Magnética Nuclear, Facultad de Ciencias, Departamento de Química, Universidad de Los Andes, Mérida 5101, Venezuela, and [c]Laboratorio de Síntesis y Caracterización de Nuevos Materiales, IVIC, Venezuela
Correspondence e-mail: gerzon@ula.ve

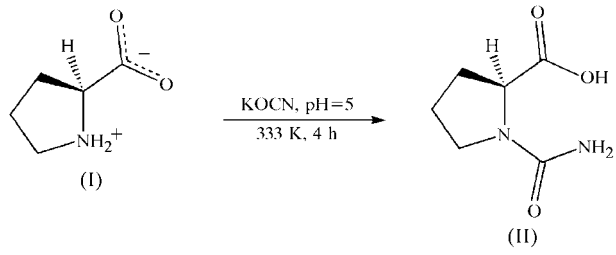
Received 12 March 2007
Accepted 23 March 2007
Online 21 April 2007

In the title compound, also known as *N*-carbamoyl-L-proline, $C_6H_{10}N_2O_3$, the pyrrolidine ring adopts a half-chair conformation, whereas the carboxyl group and the mean plane of the ureide group form an angle of 80.1 (2)°. Molecules are joined by N—H···O and O—H···O hydrogen bonds into cyclic structures with graph-set $R_2^2(8)$, forming chains in the *b*-axis direction that are further connected *via* N—H···O hydrogen bonds into a three-dimensional network.

Comment

N-Carbamoyl derivatives of α-amino acids are compounds closely related to biochemical processes of great importance, for example, the biosynthesis of pyrimidine nucleotides (van Kuilenburg *et al.*, 2004), which are essential in a number of biochemical processes, such as the synthesis of RNA, DNA and phospholipids and glycosylation of proteins (Huang & Graves, 2003). In addition, in recent years there has been an increasing interest in the industrial use of *N*-carbamoyl compounds, since natural and non-natural amino acids can be obtained through an enantioselective enzymatic reaction (Chen *et al.*, 2003; Altenbuchner *et al.*, 2001; Burton & Dorrington, 2004). Wang *et al.* (2001) modeled the enzyme–substrate interaction in the complex DNCAase-*N*-carbamoyl-D-*p*-hydroxyphenylglycine; they concluded that the substrate specificity in the enzyme–substrate complex is essentially due to hydrogen bonds formed between the carboxyl and ureide groups of the *N*-carbamoyl and the side groups of the amino acid units in the active site of the enzyme, acting as anchors to fix and orient the substrate and facilitating the amido-hydrolytic reaction. We present here the crystal structure of a new compound, namely *N*-carbamoyl-L-proline, (II).

Fig. 1 shows the molecular structure and the atom-labelling scheme. *N*-Carbamoyl-L-proline crystallizes in a neutral form [unlike L-proline, (I) (Kayushina & Vainshtein, 1965), which crystallizes in a zwitterionic form]; this is the result of a resonance effect in the ureide unit, which causes a diminution in the nucleophilic character of the N atoms, and makes it impossible for this atom to withdraw the acidic H atom of the



carboxyl group. The neutral character of the compound is confirmed by the clear difference of the values for the O1—C5 and O2—C5 bond distances (Table 1). The carboxyl group is axial to the pyrrolidine ring, forming an angle of 82.9 (2)°. This value matches that observed in (I) (Kayushina & Vainshtein, 1965). However, this group adopts a different orientation in (II), with an O2—C5—C4—N1 torsion angle of −33.8 (3)° compared with −6.9 (5)° in (I). The ureide group is equatorial and almost coplanar with atoms C1, N1 and C4, forming an angle of 5.4 (2)° with the average plane of the pyrrolidine ring. The intercepting angle between the average planes of the two functional groups is 80.1 (2)°. This value differs from that observed in two *N*-carbamoyl derivatives of α-amino acids reported in the Cambridge Structural Database (CSD; Allen, 2002), *viz.* *N*-carbamoyl-L-asparagine (CSD refcode GEMZED; Yennawar & Viswamitra, 1988) and *N*-carbamoyl-DL-aspartic acid (BERBOP01; Zvargulis & Hambley, 1994), which have intercepting angles of 155.0 (3) and 164.2 (5)°, respectively. This difference with compound (II) is due to the fact that here the Cα atom belongs to a pyrrolidine ring, forcing the two substituent groups (carboxyl and ureide) to form a more acute intercepting angle. The asymmetry parameters ΔC_2 [maximum = +41.5 (4)°, minimum = +0.5 (4)°], ΔC_s [maximum = +33.4 (4)°, minimum = +27.2 (4)°], ΔC_2(N1) = 0.5 (4)° and ΔC_2(C2—C3) = 0.5 (4)° reveal the presence of a twofold axis through N1 and bisecting the C2—C3 bond,

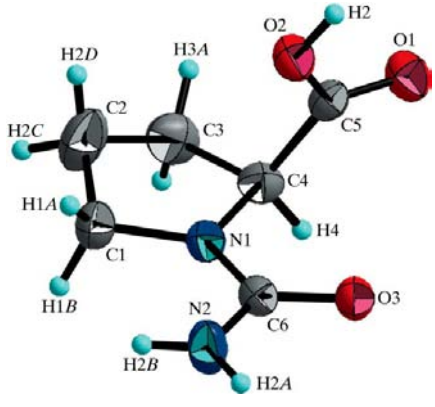


Figure 1
View of *N*-carbamoyl-L-proline with the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown with an arbitrary radius.

 DOI: 10.1107/S0108270107014102 © 2007 International Union of Crystallography

which indicates that the pyrrolidine ring adopts a half-chair conformation (Griffin *et al.*, 1984; Cremer & Pople, 1975). This conformation is also observed in the structures of L-proline (PROLIN; Kayushina & Vainshtein, 1965), DL-proline (QANRUT; Myung *et al.*, 2005), L-proline monohydrate (RUWGEV; Janczak & Luger, 1997) and DL-proline monohydrate (DLPROM02; Flaig *et al.*, 2002).

The crystalline structure is stabilized by three hydrogen bonds, which involve the carboxyl and ureide groups in the molecule, serving as both acceptors and donors in a set of head-to-tail interactions, as depicted in Fig. 2. The geometrical parameters of these hydrogen bonds are summarized in Table 2. The O2—H2···O3($-x$, $y-\frac{1}{2}$, $-z+\frac{3}{2}$) and N2—H2*A*···O1($-x$, $y+\frac{1}{2}$, $-z+\frac{3}{2}$) hydrogen bonds form rings with graph set $R_2^2(8)$ (Bernstein *et al.*, 1995). In these interactions, the O2···O3 distance is markedly different from N2···O1. The presence of the two N atoms in the ureide group affords a better hydrogen-bond acceptor capacity to the carbonyl group O3. Atom O1 acts as a bifurcated acceptor for two N—H···O hydrogen bonds originating from two different molecules, with graph set $C_2^1(4)$. The $R_2^2(8)$ sets join into zigzag molecular chains running along the *b* axis with graph set $R_2^2(8)C(7)$ (Fig. 3). This graph set is also observed in the *N*-carbamoyl α-amino acids GEMZED (Yennawar & Viswamitra, 1988) and BERBOP01 (Zvargulis & Hambley, 1994). The zigzag chains are connected laterally by N2—H2*B*···O1($-x+\frac{1}{2}$, $-y$, $z+\frac{1}{2}$) hydrogen bonds, which generates a three-dimensional network.

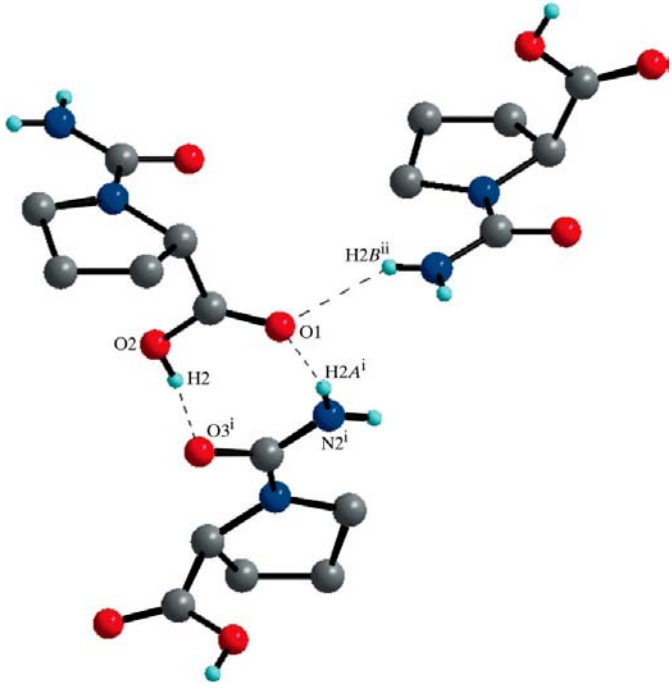


Figure 2
Intermolecular hydrogen bonds in *N*-carbamoyl-L-proline. Broken lines indicate hydrogen bonds. H atoms not involved in hydrogen bonding have been omitted for clarity. [Symmetry codes: (i) $-x$, $y-\frac{1}{2}$, $-z+\frac{3}{2}$; (ii) $-x+\frac{1}{2}$, $-y$, $z-\frac{1}{2}$.]

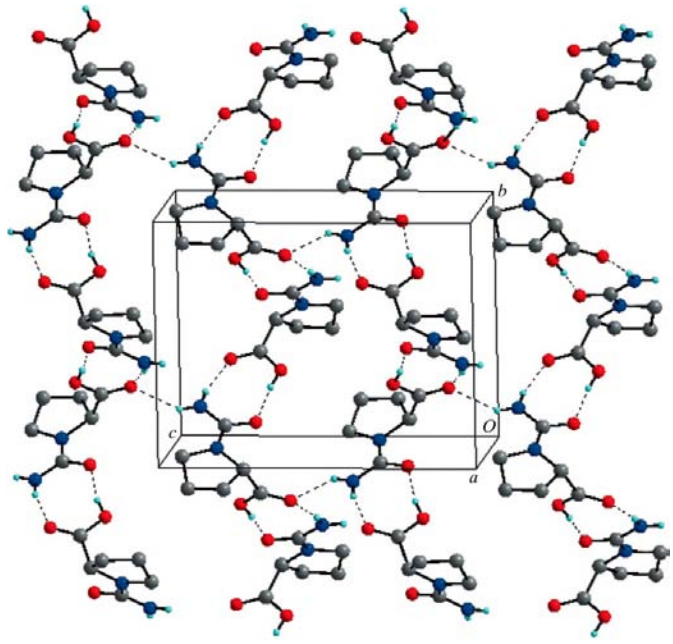


Figure 3
A partial packing view of (II). Broken lines indicate hydrogen bonds. H atoms not involved in hydrogen bonding have been omitted for clarity.

Experimental

L-Proline (500 mg, 4.3 mmol) was dissolved in 20 ml of water and the solution was acidified with concentrated HCl (37% *v*/*v*) to pH 5. KOCN (1050 mg, 12.9 mmol) was then added to this solution. The mixture was warmed, with agitation, to 333 K over a period of 4 h. The resulting solution was cooled to room temperature and acidified with concentrated HCl (37% *v*/*v*) to pH 4, at which point a white solid precipitated. The solid was filtered off and washed with cool water (yield 421 mg, 62%; m.p. 476–477 K). The solid was recrystallized from a mixture of methanol and water (2:1), producing colourless crystals with a rectangular form. FT–IR (cm^{-1}): 1695.5 [*t*, C═O (acid group)], 1660.8 [*t*, C═O (ureide group)]. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.45 (H2, *bs*), 5.88 (H2*A* = H2*B*, *s*), 4.14 (H4, *dd*), 3.32 (H1*B*, *m*), 3.23 (H1*A*, *m*), 1.84 (H3*A*, *m*), 2.06 (H3*B*, *m*), 1.84 (H2*C*, H2*D*, *m*); ^{13}C NMR (100.6 MHz, DMSO-d_6): δ 174.7 (C5), 157.2 (C6), 58.4 (C4), 46.4 (C1), 29.6 (C3), 24.4 (C2).

Crystal data

$C_6H_{10}N_2O_3$
M_r = 158.16
Orthorhombic, $P2_12_12_1$
a = 6.4711 (13) Å
b = 9.781 (2) Å
c = 12.524 (3) Å
V = 792.7 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.11 mm^{-1}
T = 298 (2) K
0.50 × 0.20 × 0.10 mm

Data collection

Rigaku AFC-7S Mercury diffractometer
Absorption correction: multi-scan (Jacobson, 1998)
T_{min} = 0.978, T_{max} = 0.988
9201 measured reflections
952 independent reflections
815 reflections with $I > 2\sigma(I)$
R_{int} = 0.031

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.132
S = 1.05
952 reflections
100 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C5	1.215 (3)	N2—C6	1.327 (4)
O2—C5	1.300 (3)	C1—C2	1.503 (5)
O3—C6	1.265 (3)	C2—C3	1.452 (6)
N1—C6	1.337 (4)	C3—C4	1.542 (5)
N1—C4	1.455 (4)	C4—C5	1.513 (4)
N1—C1	1.462 (4)		
C6—N1—C4	119.6 (2)	C5—C4—C3	112.5 (3)
C6—N1—C1	126.4 (3)	O3—C6—N2	121.4 (3)
C4—N1—C1	113.9 (3)	O3—C6—N1	119.4 (3)
N1—C1—C2	102.6 (3)	N2—C6—N1	119.3 (3)
C3—C2—C1	108.0 (3)	O1—C5—O2	124.0 (3)
C2—C3—C4	105.9 (3)	O1—C5—C4	121.0 (3)
N1—C4—C5	113.2 (2)	O2—C5—C4	115.0 (2)
N1—C4—C3	102.3 (3)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O3^{i}	0.82	1.73	2.536 (3)	167
N2—H2*A*···O1^{iii}	0.86	2.08	2.914 (4)	165
N2—H2*B*···O1^{ii}	0.86	2.13	2.901 (3)	149

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

H atoms of the pyrrolidine ring were positioned geometrically and allowed to ride on their respective parent atoms [C—H = 0.97–0.98 Å and U_{iso}(H) = 1.2U_{eq}(parent)]. The H atoms of the ureide group were positioned geometrically in the plane of the nearest substituent on the N atom and allowed to ride on their respective parent atoms, with N—H bond lengths of 0.86 Å and isotropic displacement parameters equal to 1.2U_{eq}(parent). The H atom in the carboxyl group was positioned geometrically as an idealized OH group, with an O—H bond length of 0.82 Å and an isotropic displacement parameter equal to 1.5U_{eq}(O2). The absolute structure was assigned from the known configuration of L-proline.

Data collection: *CrystalClear* (Rigaku, 2000); cell refinement: *CrystalClear*; data reduction: *CrystalStructure* (Rigaku/MSC, 2004); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *DIAMOND* (Brandenburg, 2001); software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2003).

This work was supported by CDCHT–ULA (grants Nos. C-1416-06-08-B and C-1417-06-08-F) and FONACIT (grant No. LAB-97000821).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3108). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Altenbuchner, J., Siemann-Herzberg, M. & Syldatk, C. (2001). *Chem. Biotechnol.* **12**, 559–563.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Brandenburg, K. (2001). *DIAMOND*. Version 2.1e. Crystal Impact GbR, Bonn, Germany.
Burton, S. & Dorrington, R. A. (2004). *Tetrahedron Asymmetry*, **15**, 2737–2741.
Chen, H., Ho, C., Liu, J., Lin, K., Wang, Y., Lu, Ch. & Liu, H. (2003). *Biotechnol. Prog.* **19**, 864–873.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Flaig, R., Koritsanszky, T., Dittrich, B., Wagner, A. & Luger, P. (2002). *J. Am. Chem. Soc.* **124**, 3407–3417.
Griffin, J. F., Duax, W. & Weeks, M. (1984). *Atlas of Steriod Structure*. New York: Plenum Publishing Corporation.
Huang, M. & Graves, L. M. (2003). *Cell. Mol. Life Sci.* **60**, 321–336.
Jacobson, R. (1998). Private communication to the Rigaku Corporation, Tokyo, Japan.
Janczak, J. & Luger, P. (1997). *Acta Cryst.* C**53**, 1954–1956.
Kayushina, R. L. & Vainshtein, B. K. (1965). *Kristallografiya*, **10**, 833–835. (In Russian.)
Kuilenburg, A. B. P. van, van Lenthe, H., Loffler, M. & van Gennip, A. H. (2004). *Clin. Chem.* **50**, 2117–2124.
Myung, S., Pink, M., Baik, M.-H. & Clemmer, D. E. (2005). *Acta Cryst.* C**61**, o506–o508.
Rigaku (2000). *CrystalClear*. Version 1.3.6. Rigaku Corporation, Tokyo, Japan.
Rigaku/MSC (2004). *CrystalStructure*. Version 3.6.0. Rigaku/MSC, The Woodlands, Texas, USA.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Wang, W., Hsu, W., Chien, F. & Chen, C. (2001). *J. Mol. Biol.* **306**, 251–261.
Yennawar, H. P. & Viswamitra, M. A. (1988). *Acta Cryst.* C**44**, 718–720.
Zvargulis, E. S. & Hambley, T. W. (1994). *Acta Cryst.* C**50**, 2058–2060.