



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Glycyl-L-proline hemihydrate at 298 K

Citation for published version:

Moggach, SA, Parsons, S & Sawyer, L 2006, 'Glycyl-L-proline hemihydrate at 298 K', *Acta Crystallographica Section E: Structure Reports Online*, vol. 62, no. Part 3, pp. o1046-o1048.
<https://doi.org/10.1107/S1600536806004922>

Digital Object Identifier (DOI):

[10.1107/S1600536806004922](https://doi.org/10.1107/S1600536806004922)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Publisher's PDF, also known as Version of record

Published In:

Acta Crystallographica Section E: Structure Reports Online

Publisher Rights Statement:

Open Access

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Glycyl-L-proline hemihydrate at 298 K

Stephen A. Moggach,^a Simon Parsons^{a*} and Lindsay Sawyer^b^aSchool of Chemistry, The University of Edinburgh, King's Buildings, West Mains Road, Edinburgh EH9 3JJ, Scotland, and ^bInstitute for Cell and Molecular Biology, The University of Edinburgh, King's Buildings, West Mains Road, Edinburgh EH9 3JR, Scotland

Correspondence e-mail: s.parsons@ed.ac.uk

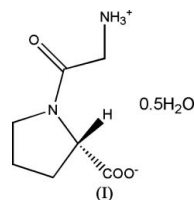
Key indicators

Single-crystal X-ray study
 $T = 293\text{ K}$
Mean $\sigma(\text{C}-\text{C}) = 0.007\text{ \AA}$
 R factor = 0.058
 wR factor = 0.143
Data-to-parameter ratio = 8.2For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

The crystal structure of glycyl-L-proline (GLY-PRO) hemihydrate, $\text{C}_7\text{H}_{12}\text{N}_2\text{O}_3 \cdot 0.5\text{H}_2\text{O}$, has two molecules of GLY-PRO in the asymmetric unit; one molecule adopts the *cis* configuration at the peptide bond and the other adopts the *trans* configuration.

Comment

The *trans* form of the peptide bond is generally favoured over the *cis* form by a ratio of around 1000 to 1 (*ca* 7.5 kJ mol^{-1} at 300 K) as the result of more favourable steric interactions between side chains (Glusker *et al.*, 1994). In the case of proline, however, this ratio drops to 4 to 1 (see, for example, Creighton, 1993).



Glycyl-L-proline (GLY-PRO), a dipeptide consisting of a glycine (GLY) residue at the N-terminus and a proline (PRO) residue at the carboxy terminus, provides an excellent example of a simple structure relevant to protein folding. *cis-trans* Isomerization of the prolyl peptide bond has been implicated in the slow refolding of proteins (*e.g.* Brandts *et al.*, 1975) and nature has overcome this potential restriction by providing a prolyl isomerase.

Recrystallization of GLY-PRO by slow diffusion of ethanol into an aqueous solution yielded crystals of the hemihydrate, (I). The structure of (I) contains two GLY-PRO molecules in the asymmetric unit, *viz.* one (based on N11) in the *trans* form and the other in the *cis* form (Figs. 1 and 2, respectively). The relevant ω torsion angles are, in the *trans* form, $\tau(\text{C21}-\text{C31}-\text{N51}-\text{C91}) = -174.3(4)^\circ$ and, in the *cis* form, $\tau(\text{C22}-\text{C32}-\text{N52}-\text{C92}) = -3.3(7)^\circ$.

The two molecules interact with each other *via* hydrogen bonds between the carboxylate and ammonium groups. The water molecules are double hydrogen-bond donors, linking *cis* to *trans* isomers *via* their carboxylate groups. Overall, the hydrogen bonds form double layers which stack along the *a* direction (Figs. 3 and 4).

Experimental

A sample of glycyl-L-proline was obtained from Sigma-Aldrich. Crystals were grown at room temperature by slow diffusion of

Received 3 February 2006

Accepted 9 February 2006

Online 15 February 2006

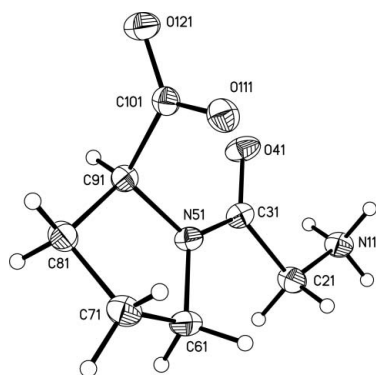


Figure 1
The structure of GLY-PRO in (I) in its *trans* configuration. The ellipsoids enclose 30% probability surfaces.

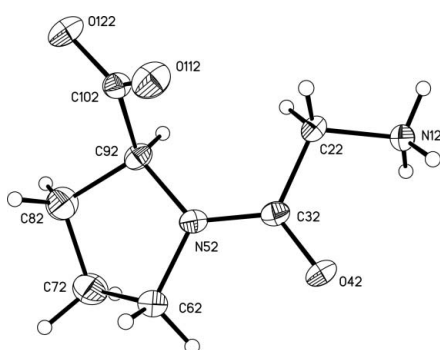


Figure 2
Structure of GLY-PRO in (I) in its *cis* configuration. The ellipsoids enclose 30% probability surfaces.

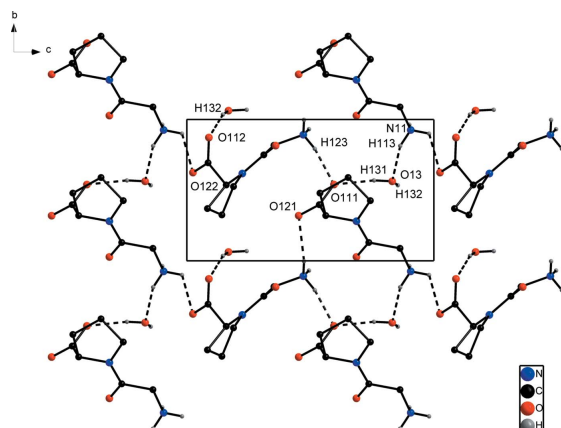


Figure 3
Hydrogen bonding (dashed lines) in layers formed in the structure of (I), viewed along [100].

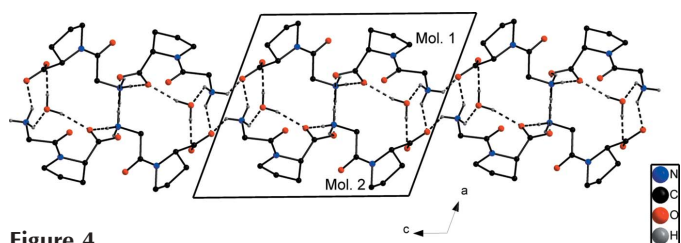


Figure 4
Pairs of layers depicted in Fig. 3 are connected through further hydrogen bonds (dashed lines). The double layers so formed stack along the *a* direction. This view is along [010]; Mol. 1 and Mol. 2 contain atoms N11, C21 *etc.* and N12, C22 *etc.*, respectively.

ethanol into an aqueous solution over a period of 7 d. Data were collected at room temperature, rather than low temperature, as a preliminary to a high-pressure study, which was also to have been carried out at room temperature. In the event, the crystals proved too weakly diffracting for the high-pressure study.

Crystal data

$C_7H_{12}N_2O_3 \cdot 0.5H_2O$
 $M_r = 181.19$
 Monoclinic, $P2_1$
 $a = 11.171$ (4) Å
 $b = 6.619$ (3) Å
 $c = 12.371$ (5) Å
 $\beta = 110.818$ (7)°
 $V = 855.0$ (6) Å³
 $Z = 4$

$D_x = 1.408$ Mg m⁻³
 Mo $K\alpha$ radiation
 Cell parameters from 685 reflections
 $\theta = 4$ –20°
 $\mu = 0.11$ mm⁻¹
 $T = 293$ K
 Block, colourless
 $0.12 \times 0.11 \times 0.09$ mm

Data collection

Bruker SMART diffractometer
 ω scans
 Absorption correction: multi-scan (SADABS; Siemens, 1996)
 $T_{min} = 0.73$, $T_{max} = 0.99$
 5465 measured reflections
 1909 independent reflections

1487 reflections with $I > 2\sigma(I)$
 $R_{int} = 0.063$
 $\theta_{max} = 26.4^\circ$
 $h = -13 \rightarrow 12$
 $k = -8 \rightarrow 8$
 $l = -15 \rightarrow 15$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.058$
 $wR(F^2) = 0.143$
 $S = 0.98$
 1908 reflections
 233 parameters

H atoms treated by a mixture of independent and constrained refinement
 $w = 1/[\sigma^2(F^2) + (0.05P)^2 + 0.49P]$
 where $P = [\max(F_o^2, 0) + 2F_c^2]/3$
 $(\Delta/\sigma)_{max} < 0.001$
 $\Delta\rho_{max} = 0.24$ e Å⁻³
 $\Delta\rho_{min} = -0.24$ e Å⁻³

Table 1

Selected geometric parameters (Å, °).

| | | | |
|----------------|-----------|----------------|-----------|
| N11—C21 | 1.467 (6) | N12—C22 | 1.461 (5) |
| C21—C31 | 1.526 (6) | C22—C32 | 1.515 (6) |
| C31—O41 | 1.219 (5) | C32—O42 | 1.217 (5) |
| C31—N51 | 1.332 (5) | C32—N52 | 1.334 (5) |
| N51—C61 | 1.474 (5) | N52—C62 | 1.470 (6) |
| N51—C91 | 1.471 (5) | N52—C92 | 1.467 (5) |
| C61—C71 | 1.511 (7) | C62—C72 | 1.503 (9) |
| C71—C81 | 1.515 (7) | C72—C82 | 1.521 (7) |
| C81—C91 | 1.538 (6) | C82—C92 | 1.549 (7) |
| C91—C101 | 1.529 (6) | C92—C102 | 1.524 (6) |
| C101—O111 | 1.253 (6) | C102—O112 | 1.231 (6) |
| C101—O121 | 1.253 (5) | C102—O122 | 1.268 (5) |
| | | | |
| N11—C21—C31 | 108.8 (4) | N12—C22—C32 | 110.3 (3) |
| C21—C31—O41 | 120.8 (4) | C22—C32—O42 | 119.3 (4) |
| C21—C31—N51 | 115.6 (4) | C22—C32—N52 | 117.4 (4) |
| O41—C31—N51 | 123.6 (4) | O42—C32—N52 | 123.3 (4) |
| C31—N51—C61 | 127.3 (3) | C32—N52—C62 | 120.8 (4) |
| C31—N51—C91 | 119.9 (3) | C32—N52—C92 | 127.0 (3) |
| C61—N51—C91 | 112.8 (3) | C62—N52—C92 | 112.1 (4) |
| N51—C61—C71 | 103.3 (3) | N52—C62—C72 | 102.3 (4) |
| C61—C71—C81 | 104.0 (4) | C62—C72—C82 | 104.2 (4) |
| C71—C81—C91 | 104.5 (4) | C72—C82—C92 | 104.3 (4) |
| C81—C91—N51 | 102.1 (3) | C82—C92—N52 | 103.5 (3) |
| C81—C91—C101 | 112.9 (3) | C82—C92—C102 | 111.4 (4) |
| N51—C91—C101 | 111.3 (3) | N52—C92—C102 | 113.9 (4) |
| C91—C101—O111 | 118.3 (4) | C92—C102—O112 | 120.6 (4) |
| C91—C101—O121 | 117.9 (4) | C92—C102—O122 | 114.8 (4) |
| O111—C101—O121 | 123.7 (4) | O112—C102—O122 | 124.6 (4) |

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

| <i>D</i> —H··· <i>A</i> | <i>D</i> —H | H··· <i>A</i> | <i>D</i> ··· <i>A</i> | <i>D</i> —H··· <i>A</i> |
|--------------------------------|-------------|---------------|-----------------------|-------------------------|
| N11—H112···O122 ⁱ | 0.90 | 1.95 | 2.728 (5) | 143 |
| N11—H113···O13 ⁱⁱ | 0.90 | 2.11 | 2.789 (6) | 131 |
| N12—H121···O121 ⁱⁱⁱ | 0.90 | 2.11 | 2.876 (5) | 142 |
| N12—H122···O121 ^{iv} | 0.90 | 2.15 | 2.896 (6) | 140 |
| N12—H123···O111 | 0.90 | 1.95 | 2.839 (5) | 168 |
| O13—H131···O111 | 0.85 (1) | 1.91 (2) | 2.739 (5) | 164 (5) |
| O13—H132···O112 ⁱ | 0.85 (1) | 2.06 (3) | 2.872 (5) | 160 (6) |

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

H atoms in the GLY-PRO molecules were all placed in calculated positions, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C}, \text{N})$, C—H = 0.99 and 1.00 Å, and N—H = 0.90 Å. The H atoms of the water of crystallization (O13) were located in a difference map and refined, subject to the restraints O—H = 0.85 (1) Å and H—O—H = 105 (1)°. A common isotropic displacement parameter was also refined. The 102 reflection was omitted from the refinement since it seemed to suffer from the effects of extinction. In the absence of significant anomalous dispersion effects, Friedel pairs were averaged. The absolute configuration of the model reported here is based on the known configuration of the sample.

Data collection: *SMART* (Siemens, 1993); cell refinement: *SAINTE* (Siemens, 1995); data reduction: *SAINTE*; program(s) used to solve

structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *XP* (Sheldrick, 1997) and *DIAMOND* (Crystal Impact, 2004); software used to prepare material for publication: *CRYSTALS*.

We thank the EPSRC for funding.

References

- Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.
- Betteridge, P. W., Carruthers, J. R., Cooper, R. I., Prout, K. & Watkin, D. J. (2003). *J. Appl. Cryst.* **36**, 1487.
- Brandts, J. F., Halvorson, H. R. & Brennan, M. (1975). *Biochemistry*, **14**, 4953–4963.
- Creighton, T. E. (1993). *Proteins: Structure and Molecular Properties*, 2nd ed., p. 174. New York: W. H. Freeman.
- Crystal Impact (2004). *DIAMOND*. Version 3.0. Crystal Impact GbR, Postfach 1251, 53002 Bonn, Germany. (<http://www.crystalimpact.com/diamond>.)
- Glusker, J. P., Lewis, M. & Rossi, M. (1994). *Crystal Structure Analysis for Chemists and Biologists*, p. 483. New York: VCH.
- Sheldrick, G. M. (1997). *XP*. University of Göttingen, Germany.
- Siemens (1993). *SMART*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
- Siemens (1995). *SAINTE*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
- Siemens (1996). *SADABS*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.