

Glycyl-L-proline hemihydrate at 298 K

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Key indicators

Single-crystal X-ray study

T = 293 K

Mean $\sigma(\text{C}-\text{C}) = 0.007 \text{ \AA}$

R factor = 0.058

wR factor = 0.143

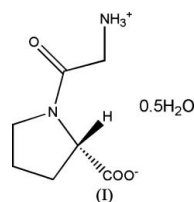
Data-to-parameter ratio = 8.2

 For 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

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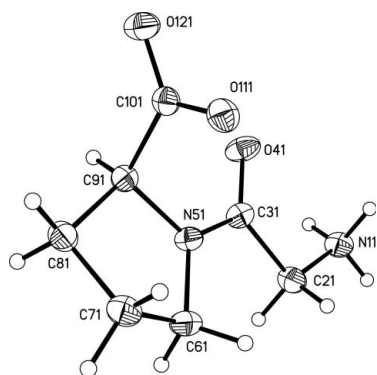


Figure 1
The structure of GLY-PRO in (I) in its *trans* configuration. The ellipsoids enclose 30% probability surfaces.

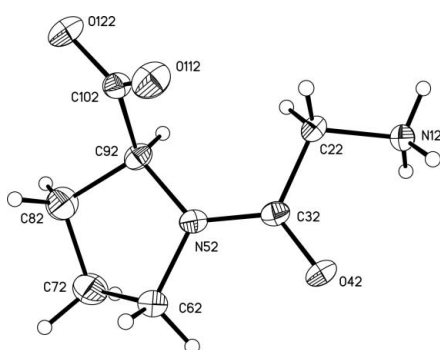


Figure 2
Structure of GLY-PRO in (I) in its *cis* configuration. The ellipsoids enclose 30% probability surfaces.

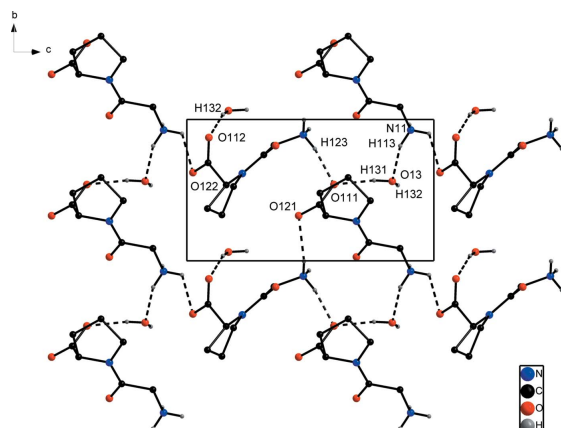


Figure 3
Hydrogen bonding (dashed lines) in layers formed in the structure of (I), viewed along [100].

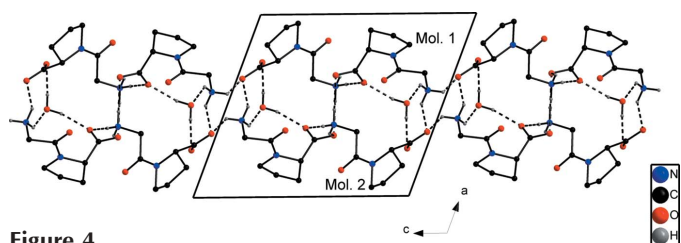


Figure 4
Pairs of layers depicted in Fig. 3 are connected through further hydrogen bonds (dashed lines). The double layers so formed stack along the *a* direction. This view is along [010]; Mol. 1 and Mol. 2 contain atoms N11, C21 etc. and N12, C22 etc., respectively.

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*.

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supporting information

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$F(000) = 388$
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 Cell parameters from 685 reflections
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 $\theta_{\max} = 26.4^\circ$, $\theta_{\min} = 2.0^\circ$
 $h = -13 \rightarrow 12$
 $k = -8 \rightarrow 8$
 $l = -15 \rightarrow 15$

Refinement

Refinement on F^2
 Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.058$
 $wR(F^2) = 0.143$
 $S = 0.98$
 1908 reflections
 233 parameters
 4 restraints
 Primary atom site location: structure-invariant
 direct methods

Secondary atom site location: difference Fourier
 map
 Hydrogen site location: calc + difmap
 H atoms treated by a mixture of independent
 and constrained refinement
 $w = 1/[\sigma^2(F^2) + (0.05P)^2 + 0.49P]$
 where $P = [\max(F_o^2, 0) + 2F_c^2]/3$
 $(\Delta/\sigma)_{\max} = 0.000089$
 $\Delta\rho_{\max} = 0.24$ e Å⁻³
 $\Delta\rho_{\min} = -0.24$ e Å⁻³

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
N11	0.4213 (3)	-0.0745 (6)	0.9062 (3)	0.0365
C21	0.3273 (4)	0.0884 (7)	0.8627 (4)	0.0372
C31	0.3095 (4)	0.1297 (6)	0.7365 (4)	0.0309

O41	0.3646 (3)	0.0276 (5)	0.6866 (3)	0.0443
N51	0.2299 (3)	0.2803 (6)	0.6865 (3)	0.0307
C61	0.1708 (4)	0.4258 (7)	0.7427 (4)	0.0373
C71	0.1209 (4)	0.5894 (7)	0.6527 (4)	0.0413
C81	0.0901 (4)	0.4790 (7)	0.5387 (4)	0.0372
C91	0.1968 (4)	0.3201 (7)	0.5622 (3)	0.0296
C101	0.3126 (4)	0.3972 (7)	0.5360 (4)	0.0305
O111	0.3764 (3)	0.5397 (5)	0.5957 (3)	0.0397
O121	0.3350 (3)	0.3195 (6)	0.4528 (3)	0.0450
N12	0.3938 (3)	0.8920 (6)	0.4713 (3)	0.0340
C22	0.3539 (4)	0.8173 (8)	0.3525 (4)	0.0365
C32	0.2154 (4)	0.7497 (6)	0.3115 (4)	0.0306
O42	0.1453 (3)	0.8150 (6)	0.3594 (3)	0.0457
N52	0.1772 (3)	0.6175 (6)	0.2245 (3)	0.0319
C62	0.0492 (4)	0.5256 (9)	0.1888 (4)	0.0462
C72	0.0702 (5)	0.3248 (10)	0.1418 (5)	0.0621
C82	0.1663 (5)	0.3697 (8)	0.0833 (5)	0.0513
C92	0.2534 (4)	0.5365 (7)	0.1593 (4)	0.0324
C102	0.2890 (4)	0.6934 (7)	0.0858 (4)	0.0342
O112	0.2605 (3)	0.8723 (5)	0.0893 (3)	0.0483
O122	0.3500 (3)	0.6245 (6)	0.0247 (3)	0.0492
O13	0.4923 (4)	0.5626 (8)	0.8312 (3)	0.0655
H111	0.4325	-0.0999	0.9806	0.0574*
H112	0.4964	-0.0368	0.9008	0.0574*
H113	0.3927	-0.1867	0.8637	0.0574*
H211	0.3586	0.2121	0.9091	0.0458*
H212	0.2446	0.0472	0.8683	0.0458*
H611	0.2350	0.4805	0.8144	0.0474*
H612	0.1001	0.3622	0.7610	0.0474*
H711	0.0430	0.6528	0.6584	0.0509*
H712	0.1869	0.6943	0.6616	0.0509*
H811	0.0051	0.4133	0.5160	0.0446*
H812	0.0914	0.5732	0.4770	0.0446*
H91	0.1623	0.1947	0.5167	0.0359*
H121	0.4761	0.9317	0.4946	0.0526*
H122	0.3443	0.9974	0.4744	0.0526*
H123	0.3855	0.7928	0.5179	0.0526*
H221	0.3634	0.9267	0.3015	0.0458*
H222	0.4087	0.7016	0.3493	0.0458*
H621	0.0208	0.5085	0.2554	0.0570*
H622	-0.0145	0.6075	0.1285	0.0570*
H721	0.1056	0.2255	0.2049	0.0770*
H722	-0.0108	0.2724	0.0851	0.0770*
H821	0.1222	0.4189	0.0033	0.0636*
H822	0.2169	0.2477	0.0817	0.0636*
H92	0.3332	0.4734	0.2142	0.0401*
H131	0.468 (4)	0.569 (11)	0.7577 (10)	0.063 (12)*
H132	0.5720 (17)	0.535 (10)	0.854 (3)	0.063 (12)*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N11	0.042 (2)	0.034 (2)	0.039 (2)	-0.0020 (17)	0.0208 (18)	0.0087 (17)
C21	0.037 (2)	0.040 (3)	0.038 (2)	0.008 (2)	0.017 (2)	0.011 (2)
C31	0.039 (2)	0.024 (2)	0.031 (2)	-0.0047 (19)	0.0155 (19)	0.0002 (19)
O41	0.066 (2)	0.0355 (18)	0.0388 (17)	0.0153 (17)	0.0277 (17)	0.0031 (16)
N51	0.0358 (18)	0.0305 (19)	0.0295 (18)	0.0023 (16)	0.0160 (15)	0.0013 (16)
C61	0.041 (2)	0.038 (3)	0.039 (2)	-0.001 (2)	0.022 (2)	-0.006 (2)
C71	0.041 (2)	0.038 (3)	0.048 (3)	0.006 (2)	0.020 (2)	0.000 (2)
C81	0.032 (2)	0.040 (3)	0.039 (3)	0.003 (2)	0.013 (2)	0.004 (2)
C91	0.030 (2)	0.028 (2)	0.031 (2)	-0.0039 (18)	0.0117 (17)	0.000 (2)
C101	0.031 (2)	0.028 (2)	0.032 (2)	0.0063 (19)	0.0102 (18)	0.006 (2)
O111	0.0356 (16)	0.0392 (18)	0.0446 (17)	-0.0080 (15)	0.0146 (14)	-0.0018 (17)
O121	0.0510 (19)	0.050 (2)	0.0417 (17)	0.0031 (17)	0.0258 (15)	0.0027 (18)
N12	0.0358 (19)	0.0326 (19)	0.037 (2)	-0.0046 (17)	0.0165 (17)	-0.0076 (17)
C22	0.036 (2)	0.047 (3)	0.031 (2)	-0.004 (2)	0.0179 (18)	-0.007 (2)
C32	0.030 (2)	0.033 (3)	0.032 (2)	0.0012 (19)	0.0146 (18)	0.005 (2)
O42	0.0383 (17)	0.061 (2)	0.0488 (18)	-0.0016 (17)	0.0287 (15)	-0.0135 (19)
N52	0.0283 (18)	0.035 (2)	0.0357 (19)	-0.0008 (16)	0.0154 (16)	0.0006 (18)
C62	0.037 (2)	0.061 (3)	0.045 (3)	-0.011 (2)	0.019 (2)	-0.010 (3)
C72	0.064 (3)	0.056 (4)	0.072 (4)	-0.024 (3)	0.032 (3)	-0.011 (3)
C82	0.064 (3)	0.036 (3)	0.058 (3)	-0.008 (2)	0.028 (3)	-0.007 (3)
C92	0.034 (2)	0.034 (2)	0.032 (2)	0.007 (2)	0.0154 (18)	0.005 (2)
C102	0.032 (2)	0.040 (3)	0.031 (2)	-0.004 (2)	0.0124 (19)	0.002 (2)
O112	0.063 (2)	0.037 (2)	0.052 (2)	0.0063 (17)	0.0292 (18)	0.0093 (17)
O122	0.055 (2)	0.057 (2)	0.0492 (19)	0.0046 (19)	0.0356 (18)	0.0030 (19)
O13	0.069 (3)	0.080 (3)	0.047 (2)	0.023 (3)	0.0198 (19)	-0.016 (2)

Geometric parameters (\AA , $^\circ$)

N11—C21	1.467 (6)	N12—H121	0.900
N11—H111	0.900	N12—H122	0.900
N11—H112	0.900	N12—H123	0.900
N11—H113	0.900	C22—C32	1.515 (6)
C21—C31	1.526 (6)	C22—H221	0.990
C21—H211	0.990	C22—H222	0.990
C21—H212	0.990	C32—O42	1.217 (5)
C31—O41	1.219 (5)	C32—N52	1.334 (5)
C31—N51	1.332 (5)	N52—C62	1.470 (6)
N51—C61	1.474 (5)	N52—C92	1.467 (5)
N51—C91	1.471 (5)	C62—C72	1.503 (9)
C61—C71	1.511 (7)	C62—H621	0.990
C61—H611	0.990	C62—H622	0.990
C61—H612	0.990	C72—C82	1.521 (7)
C71—C81	1.515 (7)	C72—H721	0.989
C71—H711	0.990	C72—H722	0.990
C71—H712	0.990	C82—C92	1.549 (7)

C81—C91	1.538 (6)	C82—H821	0.990
C81—H811	0.990	C82—H822	0.990
C81—H812	0.990	C92—C102	1.524 (6)
C91—C101	1.529 (6)	C92—H92	1.000
C91—H91	1.000	C102—O112	1.231 (6)
C101—O111	1.253 (6)	C102—O122	1.268 (5)
C101—O121	1.253 (5)	O13—H131	0.852 (10)
N12—C22	1.461 (5)	O13—H132	0.853 (10)
C21—N11—H111	109.5	C22—N12—H122	109.5
C21—N11—H112	109.5	H121—N12—H122	109.5
H111—N11—H112	109.5	C22—N12—H123	109.5
C21—N11—H113	109.5	H121—N12—H123	109.5
H111—N11—H113	109.5	H122—N12—H123	109.5
H112—N11—H113	109.5	N12—C22—C32	110.3 (3)
N11—C21—C31	108.8 (4)	N12—C22—H221	109.3
N11—C21—H211	109.6	C32—C22—H221	109.3
C31—C21—H211	109.6	N12—C22—H222	109.3
N11—C21—H212	109.6	C32—C22—H222	109.3
C31—C21—H212	109.6	H221—C22—H222	109.5
H211—C21—H212	109.5	C22—C32—O42	119.3 (4)
C21—C31—O41	120.8 (4)	C22—C32—N52	117.4 (4)
C21—C31—N51	115.6 (4)	O42—C32—N52	123.3 (4)
O41—C31—N51	123.6 (4)	C32—N52—C62	120.8 (4)
C31—N51—C61	127.3 (3)	C32—N52—C92	127.0 (3)
C31—N51—C91	119.9 (3)	C62—N52—C92	112.1 (4)
C61—N51—C91	112.8 (3)	N52—C62—C72	102.3 (4)
N51—C61—C71	103.3 (3)	N52—C62—H621	111.2
N51—C61—H611	111.0	C72—C62—H621	111.2
C71—C61—H611	111.0	N52—C62—H622	111.2
N51—C61—H612	111.0	C72—C62—H622	111.2
C71—C61—H612	111.0	H621—C62—H622	109.5
H611—C61—H612	109.5	C62—C72—C82	104.2 (4)
C61—C71—C81	104.0 (4)	C62—C72—H721	110.8
C61—C71—H711	110.8	C82—C72—H721	110.8
C81—C71—H711	110.8	C62—C72—H722	110.8
C61—C71—H712	110.8	C82—C72—H722	110.7
C81—C71—H712	110.8	H721—C72—H722	109.5
H711—C71—H712	109.5	C72—C82—C92	104.3 (4)
C71—C81—C91	104.5 (4)	C72—C82—H821	110.8
C71—C81—H811	110.7	C92—C82—H821	110.7
C91—C81—H811	110.7	C72—C82—H822	110.7
C71—C81—H812	110.7	C92—C82—H822	110.8
C91—C81—H812	110.7	H821—C82—H822	109.4
H811—C81—H812	109.5	C82—C92—N52	103.5 (3)
C81—C91—N51	102.1 (3)	C82—C92—C102	111.4 (4)
C81—C91—C101	112.9 (3)	N52—C92—C102	113.9 (4)
N51—C91—C101	111.3 (3)	C82—C92—H92	109.3

C81—C91—H91	110.1	N52—C92—H92	109.3
N51—C91—H91	110.1	C102—C92—H92	109.3
C101—C91—H91	110.1	C92—C102—O112	120.6 (4)
C91—C101—O111	118.3 (4)	C92—C102—O122	114.8 (4)
C91—C101—O121	117.9 (4)	O112—C102—O122	124.6 (4)
O111—C101—O121	123.7 (4)	H131—O13—H132	105.1 (10)
C22—N12—H121	109.5		

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) $-x+1, y-1/2, -z+1$; (ii) $x, y-1, z$; (iii) $-x+1, y+1/2, -z+1$; (iv) $x, y+1, z$.