Acta Crystallographica Section E
**Structure Reports Online**
ISSN 1600-5368

# Isovaline monohydrate

**Ray J. Butcher,[a]* Greg Brewer,[b] Aaron S. Burton[c] and Jason P. Dworkin[d]**

[a]Department of Chemistry, Howard University, 525 College Street NW, Washington, DC 20059, USA, [b]Department of Chemistry, Catholic University of America, Washington, DC 20064, USA, [c]NASA Johnson Space Center, Astromaterial and Exploration Science Directorate, Houston, TX 77058, USA, and [d]Solar System Exploration Division, NASA Goddard Space Flight Center, Greenbelt, MD 20771, USA
Correspondence e-mail: rbutcher99@yahoo.com

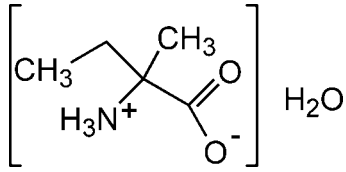
Received 23 October 2013; accepted 20 November 2013

Key indicators: single-crystal X-ray study; $T$ = 123 K; mean $\sigma$(C–C) = 0.005 Å; $R$ factor = 0.056; $wR$ factor = 0.162; data-to-parameter ratio = 13.2.

The title compound, $C_5H_{11}NO_2\cdot H_2O$, is an isomer of the $\alpha$-amino acid valine that crystallizes from water in its zwitterion form as a monohydrate. It is not one of the 20 proteinogenic amino acids that are used in living systems and differs from the natural amino acids in that it has no $\alpha$-H atom. The compound exhibits hydrogen bonding between the water molecule and the carboxylate O atoms and an amine H atom. In addition, there are intermolecular hydrogen-bonding interactions between the carboxylate O atoms and amine H atoms. In the crystal, these extensive N—H···O and O—H···O hydrogen bonds lead to the formation of a three-dimensional network.

## Related literature

The structure of the title compound or its salts have not been reported to the CCDC but there are reports of homoleptic coordination complexes of zinc(II) with isovaline, see: Strasdelt *et al.* (2001). For literature related to eighty amino acids that have been detected in meteorites or comets, see: Glavin & Dworkin (2009); Burton *et al.* (2012). For the role that crystallization plays in chiral separation, see: Blackmond & Klussmann (2007); Blackmond *et al.* (2008). For the role of the H atom on the $\alpha$-C atom in enhancing the rate of racemization, see: Yamada *et al.* (1983). For the mechanism of racemization of amino acids lacking an $\alpha$-H atom, see: Pizzarello & Groy (2011). For the role that crystallization can play in the enrichment of L-isovaline, see: Glavin & Dworkin (2009); Bada (2009); Bonner *et al.* (1979). For normal bond lengths and angles, see: Orpen (1993).




## Experimental

### Crystal data

$C_5H_{11}NO_2\cdot H_2O$
$M_r$ = 135.16
Orthorhombic, $P2_12_12_1$
$a$ = 5.9089 (5) Å
$b$ = 10.4444 (10) Å
$c$ = 11.9274 (11) Å
$V$ = 736.10 (12) Å$^3$
$Z$ = 4
Cu $K\alpha$ radiation
$\mu$ = 0.84 mm$^{-1}$
$T$ = 123 K
0.48 × 0.08 × 0.06 mm

### Data collection

Agilent Xcalibur (Ruby, Gemini) diffractometer
Absorption correction: multi-scan (*CrysAlis PRO*; Agilent, 2012)
$T_{min}$ = 0.383, $T_{max}$ = 1.000
1662 measured reflections
1204 independent reflections
1072 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.072

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.162
$S$ = 1.11
1204 reflections
91 parameters
3 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.37 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.27 e Å$^{-3}$

**Table 1**
Hydrogen-bond geometry (Å, °).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O1$W$—H1$W$1···O1$^{i}$ | 0.83 (2) | 2.05 (2) | 2.811 (3) | 152 (4) |
| O1$W$—H1$W$2···O2$^{ii}$ | 0.83 (2) | 1.96 (2) | 2.787 (3) | 171 (5) |
| N1—H1$A$···O2$^{i}$ | 0.91 | 1.84 | 2.745 (3) | 177 |
| N1—H1$C$···O1$W$ | 0.91 | 2.09 | 2.792 (4) | 133 |
| N1—H1$B$···O1$^{iii}$ | 0.91 | 1.98 | 2.832 (3) | 156 |

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

Data collection: *CrysAlis PRO* (Agilent, 2012); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

RJB wishes to acknowledge the NSF–MRI program (grant CHE-0619278) for funds to purchase the diffractometer. GB wishes to acknowledge support of this work from NASA (NNX10AK71A)

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: JJ2178).

## References


Agilent (2012). *CrysAlis PRO*. Agilent Technologies UK Ltd, Yarnton, England.

Bada, J. L. (2009). *Proc. Natl Acad. Sci.* **106**, E85.

Blackmond, D. G. & Klussmann, M. (2007). *Chem. Commun.* pp. 3990–3996.

Blackmond, D., Viedma, C., Ortiz, J., Torres, T. & Izuma, T. (2008). *J. Am. Chem. Soc.* **130**, 15274–15275.

Bonner, W. A., Blair, N. E., Lemmon, R. M., Flores, J. J. & Pollock, G. E. (1979). *Geochim. Cosmochim. Acta*, **43**, 1841–1846.

Burton, A. S., Stern, J. C., Elsila, J. E., Dworkin, J. P. & Glavin, D. P. (2012). *Chem. Soc. Rev.* **41**, 5459–5472.

Glavin, D. P. & Dworkin, J. P. (2009). *Proc. Natl Acad. Sci.* **106**, 5487–5492.

Orpen, G. A. (1993). *Chem. Soc. Rev.* **22**, 191–197.

Pizzarello, S. & Groy, T. L. (2011). *Geochim. Cosmochim. Acta*, **75**, 645–656.

Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

Strasdelt, H., Busching, I., Behrends, S., Saak, W. & Barklage, W. (2001). *Chem. Eur. J.* **7**, 1133–1137.

Yamada, S., Hongo, C., Yoshioka, R. & Chibata, I. (1983). *J. Org. Chem.* **48**, 843–846.

# supplementary materials

*Acta Cryst.* (2013). E**69**, o1829–o1830 [doi:10.1107/S1600536813031620]

## Isovaline monohydrate

**Ray J. Butcher, Greg Brewer, Aaron S. Burton and Jason P. Dworkin**

### 1. Comment

The alpha amino acids are essential for life as they are the building blocks of all proteins and enzymes. Nature uses almost exclusively the *L* form of the nineteen naturally occurring chiral amino acids. Glycine is achiral. However, it is known that there are over eighty amino acids that have been detected in meteorites or comets (Glavin & Dworkin 2009; Burton *et al.*, 2012). One of these extraterrestrial non proteinogenic amino acids is isovaline. The majority of these amino acids show little or no enrichment of one enantiomer over the other. An intriguing question is the process that lead to the separation and enrichment of the *L* enantiomer over the *D*. There are several possible explanations for this including the role that crystallization plays (Blackmond & Klussmann, 2007). Only two of the twenty amino acids used biologically crystallize in a chiral space group, which allows for spontaneous separation of enantiomers, at the level of the crystal, from a racemic solution (Blackmond *et al.*, 2008). Isovaline, a non proteinogenic amino acid also allows for this separation of enantiomers at the level of the crystal as it crystallizes in the chiral space group, $P2_12_12_1$.

Another important aspect in the prebiotic chemistry of the amino acids is the role of racemization. All of the nineteen naturally occurring chiral amino acids have a hydrogen atom on the alpha carbon atom, which enhances the rate of racemization (Yamada *et al.*, 1983). However, little is known about the mechanism of racemization of amino acids lacking an alpha hydrogen atom (Pizzarello & Groy, 2011). The structure of isovaline given here can be used to examine the role that crystallization can play in the enrichment of *L* isovaline (Glavin & Dworkin 2009; Bada, 2009), and as a starting point in mechanistic studies of racemization mechanisms of isovaline (Bonner *et al.*, 1979).

In the structure of the title compound the amino acid is in the usual zwitterionic form. While the structure of the title compound or its salts have not been reported there are reports of homoleptic coordination complexes of isovaline with zinc(II) (Strasdelt *et al.* (2001). However, there are several important differences between these structures and the title compound. The metal complexes all crystallized in non-chiral space groups and, of course, when coordinated to a metal, the isovaline will not be in a zwitterionic form but, apart from the $COO^-$ group, all the the bond lengths and angles are in the normal range for such compounds (Orpen, 1993). There is extensive N—H···O and O—H···O hydrogen bonding linking the zwitterions into a 3-D array.

### 2. Experimental

A sample of the title compound was obtained from Acros Organics. Crystals of the title compound were grown from the slow evaporation of a ***racemic*** solution of the amino acid in water.

### 3. Refinement

H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms with a C—H distances of 0.98 and 0.99 Å and an N—H distance of 0.91 \%A $U_{iso}$(H) = 1.2$U_{eq}$(C) and 0.96 Å for $NH_3$ [$U_{iso}$(H) = 1.5$U_{eq}$(C)]. The water H's were refined isotropically with O—H distances constrained to be 0.82 Å and the H—O—H

angle close to 104.5°.

### Computing details

Data collection: *CrysAlis PRO* (Agilent, 2012); cell refinement: *CrysAlis PRO* (Agilent, 2012); data reduction: *CrysAlis PRO* (Agilent, 2012); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL* (Sheldrick, 2008).

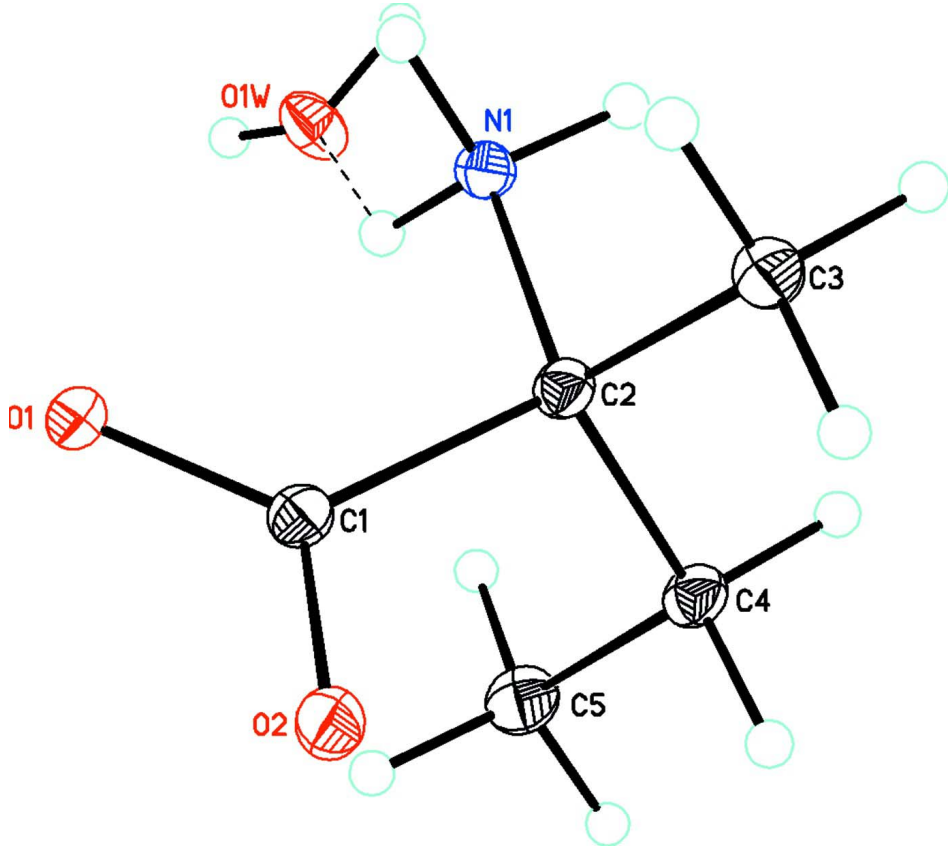



**Figure 1**

Diagram of the title compound showing atom labeling. Atomic displacement parameters are at the 30% probablity level. Hydogen bonds are shown as dashed lines.

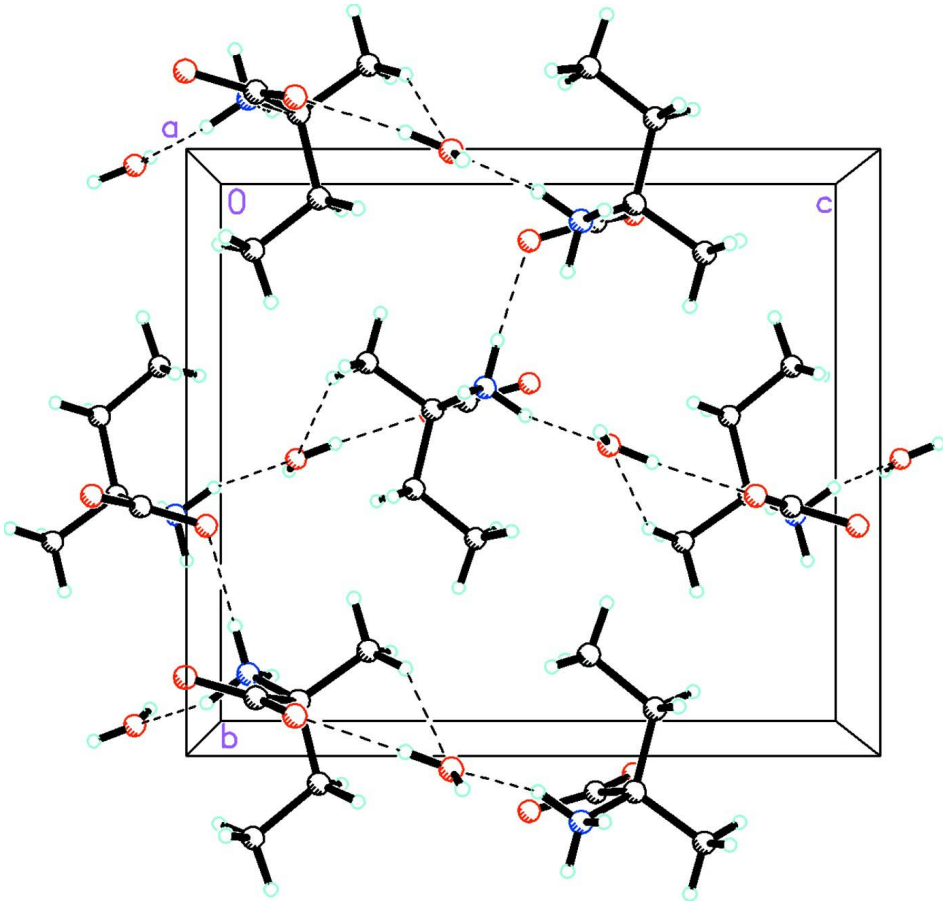



**Figure 2**

Packing diagram of the title compound viewed along the *a* axis showing tthe extensive N—H···O and O—H···O hydrogen bonds as dashed lines.

### 2-Azaniumyl-2-methylbutanoate monohydrate

*Crystal data*

$C_5H_{11}NO_2·H_2O$
$M_r$ = 135.16
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a$ = 5.9089 (5) Å
$b$ = 10.4444 (10) Å
$c$ = 11.9274 (11) Å
$V$ = 736.10 (12) Å$^3$
$Z$ = 4
$F(000)$ = 296
$D_x$ = 1.220 Mg m$^{-3}$
Cu $K\alpha$ radiation, $\lambda$ = 1.54184 Å
Cell parameters from 679 reflections
$\theta$ = 3.7–75.3°
$\mu$ = 0.84 mm$^{-1}$
$T$ = 123 K
Needle, colorless
0.48 × 0.08 × 0.06 mm

*Data collection*

Agilent Xcalibur (Ruby, Gemini) diffractometer
Radiation source: Enhance (Cu) X-ray Source
Graphite monochromator
Detector resolution: 10.5081 pixels mm$^{-1}$
$\omega$ scans
Absorption correction: multi-scan (*CrysAlis PRO*; Agilent, 2012)
$T_{min}$ = 0.383, $T_{max}$ = 1.000
1662 measured reflections
1204 independent reflections
1072 reflections with $I > 2\sigma(I)$

$R_{int}$ = 0.072
$\theta_{max}$ = 75.4°, $\theta_{min}$ = 5.6°
$h$ = −7→4
$k$ = −12→8
$l$ = −14→14

*Refinement*

Refinement on $F^2$
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.162
$S$ = 1.11
1204 reflections
91 parameters
3 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.093P)^2 + 0.2964P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.37 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.27 e Å$^{-3}$

*Special details*

**Geometry**. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.
**Refinement**. Refinement of $F^2$ against ALL reflections. The weighted $R$-factor $wR$ and goodness of fit $S$ are based on $F^2$, conventional $R$-factors $R$ are based on $F$, with $F$ set to zero for negative $F^2$. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating $R$-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. $R$-factors based on $F^2$ are statistically about twice as large as those based on $F$, and $R$- factors based on ALL data will be even larger.

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

| | $x$ | $y$ | $z$ | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| O1 | 0.0058 (4) | 0.37096 (19) | 0.50201 (18) | 0.0316 (5) |
| O2 | −0.1536 (4) | 0.4257 (3) | 0.33811 (19) | 0.0385 (6) |
| O1W | 0.6455 (4) | 0.4874 (3) | 0.6172 (2) | 0.0467 (7) |
| H1W1 | 0.776 (5) | 0.465 (5) | 0.601 (3) | 0.070* |
| H1W2 | 0.661 (8) | 0.517 (5) | 0.682 (2) | 0.070* |
| N1 | 0.4267 (4) | 0.3850 (2) | 0.4302 (2) | 0.0297 (6) |
| H1A | 0.5663 | 0.3957 | 0.3994 | 0.045* |
| H1B | 0.4074 | 0.3014 | 0.4493 | 0.045* |
| H1C | 0.4141 | 0.4348 | 0.4925 | 0.045* |
| C1 | 0.0133 (6) | 0.4049 (2) | 0.4006 (3) | 0.0302 (6) |
| C2 | 0.2504 (5) | 0.4229 (3) | 0.3472 (2) | 0.0294 (6) |
| C3 | 0.2766 (6) | 0.3382 (3) | 0.2440 (3) | 0.0367 (7) |
| H3A | 0.2503 | 0.2486 | 0.2648 | 0.055* |
| H3B | 0.4301 | 0.3474 | 0.2139 | 0.055* |
| H3C | 0.1664 | 0.3640 | 0.1869 | 0.055* |
| C4 | 0.2832 (6) | 0.5657 (3) | 0.3178 (3) | 0.0344 (7) |
| H4A | 0.4384 | 0.5779 | 0.2885 | 0.041* |
| H4B | 0.1762 | 0.5888 | 0.2572 | 0.041* |
| C5 | 0.2477 (7) | 0.6556 (3) | 0.4151 (3) | 0.0451 (9) |
| H5A | 0.2565 | 0.7442 | 0.3886 | 0.068* |
| H5B | 0.3650 | 0.6408 | 0.4716 | 0.068* |
| H5C | 0.0984 | 0.6401 | 0.4482 | 0.068* |

*Atomic displacement parameters (Å²)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| O1 | 0.0326 (11) | 0.0293 (9) | 0.0329 (10) | 0.0009 (8) | 0.0031 (9) | 0.0061 (9) |
| O2 | 0.0268 (11) | 0.0510 (13) | 0.0376 (11) | 0.0010 (11) | 0.0007 (9) | 0.0110 (11) |
| O1W | 0.0379 (13) | 0.0627 (17) | 0.0396 (13) | 0.0087 (13) | −0.0008 (11) | −0.0148 (12) |
| N1 | 0.0268 (12) | 0.0270 (11) | 0.0352 (14) | −0.0004 (9) | 0.0016 (11) | 0.0015 (11) |
| C1 | 0.0324 (15) | 0.0214 (12) | 0.0367 (15) | −0.0017 (11) | 0.0027 (12) | 0.0020 (11) |
| C2 | 0.0279 (15) | 0.0275 (13) | 0.0328 (14) | −0.0009 (12) | 0.0009 (11) | 0.0051 (13) |
| C3 | 0.0371 (18) | 0.0392 (16) | 0.0338 (16) | 0.0040 (15) | −0.0005 (13) | 0.0010 (14) |
| C4 | 0.0320 (15) | 0.0317 (15) | 0.0394 (15) | −0.0038 (13) | −0.0001 (13) | 0.0085 (14) |
| C5 | 0.055 (2) | 0.0260 (14) | 0.054 (2) | −0.0030 (14) | 0.0026 (18) | 0.0020 (15) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| O1—C1 | 1.261 (4) | C2—C4 | 1.545 (4) |
| O2—C1 | 1.255 (4) | C3—H3A | 0.9800 |
| O1W—H1W1 | 0.830 (19) | C3—H3B | 0.9800 |
| O1W—H1W2 | 0.832 (19) | C3—H3C | 0.9800 |
| N1—C2 | 1.490 (4) | C4—C5 | 1.507 (5) |
| N1—H1A | 0.9100 | C4—H4A | 0.9900 |
| N1—H1B | 0.9100 | C4—H4B | 0.9900 |
| N1—H1C | 0.9100 | C5—H5A | 0.9800 |
| C1—C2 | 1.550 (4) | C5—H5B | 0.9800 |
| C2—C3 | 1.524 (4) | C5—H5C | 0.9800 |
| | | | |
| H1W1—O1W—H1W2 | 102 (3) | C2—C3—H3B | 109.5 |
| C2—N1—H1A | 109.5 | H3A—C3—H3B | 109.5 |
| C2—N1—H1B | 109.5 | C2—C3—H3C | 109.5 |
| H1A—N1—H1B | 109.5 | H3A—C3—H3C | 109.5 |
| C2—N1—H1C | 109.5 | H3B—C3—H3C | 109.5 |
| H1A—N1—H1C | 109.5 | C5—C4—C2 | 114.2 (3) |
| H1B—N1—H1C | 109.5 | C5—C4—H4A | 108.7 |
| O2—C1—O1 | 126.2 (3) | C2—C4—H4A | 108.7 |
| O2—C1—C2 | 116.4 (3) | C5—C4—H4B | 108.7 |
| O1—C1—C2 | 117.4 (3) | C2—C4—H4B | 108.7 |
| N1—C2—C3 | 108.1 (3) | H4A—C4—H4B | 107.6 |
| N1—C2—C4 | 108.6 (3) | C4—C5—H5A | 109.5 |
| C3—C2—C4 | 111.3 (3) | C4—C5—H5B | 109.5 |
| N1—C2—C1 | 109.1 (2) | H5A—C5—H5B | 109.5 |
| C3—C2—C1 | 110.7 (3) | C4—C5—H5C | 109.5 |
| C4—C2—C1 | 108.9 (2) | H5A—C5—H5C | 109.5 |
| C2—C3—H3A | 109.5 | H5B—C5—H5C | 109.5 |
| | | | |
| O2—C1—C2—N1 | −175.8 (3) | O1—C1—C2—C4 | −114.2 (3) |
| O1—C1—C2—N1 | 4.2 (4) | N1—C2—C4—C5 | −64.0 (3) |
| O2—C1—C2—C3 | −57.0 (3) | C3—C2—C4—C5 | 177.0 (3) |
| O1—C1—C2—C3 | 123.0 (3) | C1—C2—C4—C5 | 54.7 (4) |
| O2—C1—C2—C4 | 65.8 (3) | | |

*Hydrogen-bond geometry (Å, º)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O1*W*—H1*W*1···O1$^{i}$ | 0.83 (2) | 2.05 (2) | 2.811 (3) | 152 (4) |
| O1*W*—H1*W*2···O2$^{ii}$ | 0.83 (2) | 1.96 (2) | 2.787 (3) | 171 (5) |
| N1—H1*A*···O2$^{i}$ | 0.91 | 1.84 | 2.745 (3) | 177 |
| N1—H1*C*···O1*W* | 0.91 | 2.09 | 2.792 (4) | 133 |
| N1—H1*B*···O1$^{iii}$ | 0.91 | 1.98 | 2.832 (3) | 156 |

Symmetry codes: (i) *x*+1, *y*, *z*; (ii) −*x*+1/2, −*y*+1, *z*+1/2; (iii) *x*+1/2, −*y*+1/2, −*z*+1.