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Redetermined crystal structure of N-(β-carboxyethyl)-α-isoleucine

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Redetermination of the crystal structure of N-(β-carboxyethyl)-α-isoleucine, $C_9H_{18}N_2O_3$, reported earlier by Nehls et al. [Acta Cryst. (2013), E**69**, o172–o173], was undertaken in which the ionization state assigned to the molecule as unionized has been modified as zwitterionic in the present work. Single-crystal X-ray intensity data obtained from freshly grown crystals and freely refining the amino H atoms provide enhanced refinement and structural parameters, particularly the hydrogen-bonding scheme. N—H···O hydrogen bonds dominate the intermolecular interactions along with a C—H···O hydrogen bond. The intermolecular interaction pattern is a three-dimensional network. The structure was refined as a two-component perfect inversion twin.

1. Related literature

For earlier work on the crystal structure of N-(β-carboxyethyl)-α-isoleucine, see: Nehls et al. (2013). For the crystal structure of L-isoleucine and its indolylacetyl derivative, respectively, see Görbitz & Dalhus (1996); Kojić-Prodić et al. (1991). For the importance of freely refining the positions of amino-group H atoms, see: Görbitz (2014). For absolute configuration and structure parameters, see Flack (1983); Flack & Bernardinelli (2000); Hooft et al. (2008); Spek (2009); Parsons et al. (2013). For chiral and achiral crystal structures, see Flack (2003).
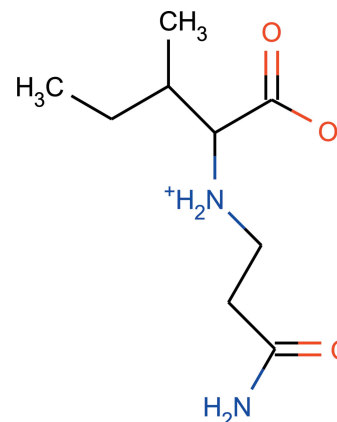
2. Experimental

2.1. Crystal data

$C_9H_{18}N_2O_3$	$V = 1107.75\ (17)$ Å³
$M_r = 202.25$	$Z = 4$
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation
$a = 5.2996\ (5)$ Å	$\mu = 0.09$ mm⁻¹
$b = 9.0053\ (7)$ Å	$T = 293$ K
$c = 23.211\ (2)$ Å	$0.26 \times 0.18 \times 0.10$ mm

2.2. Data collection

Bruker APEXII CCD diffractometer	22904 measured reflections
Absorption correction: multi-scan (SADABS; Bruker, 2009)	3127 independent reflections
$T_{min} = 0.97$, $T_{max} = 0.99$	2538 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.036$

2.3. Refinement

$R[F^2 > 2\sigma(F^2)] = 0.042$	$\Delta\rho_{max} = 0.30$ e Å⁻³
$wR(F^2) = 0.102$	$\Delta\rho_{min} = -0.19$ e Å⁻³
$S = 1.08$	Absolute structure: refined as a perfect inversion twin.
3127 reflections	
146 parameters	Absolute structure parameter: fixed at 0.5 and not refined
H atoms treated by a mixture of independent and constrained refinement	

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N1···O2ⁱ	0.89 (2)	1.96 (2)	2.7772 (19)	152 (2)
N1—H2N1···O1ⁱⁱ	0.88 (2)	1.83 (2)	2.7047 (19)	174 (2)
N2—H1N2···O3ⁱⁱⁱ	0.90 (3)	2.11 (3)	2.970 (3)	161 (3)
N2—H2N2···O3ⁱⁱ	0.84 (3)	2.34 (3)	3.092 (3)	149 (2)
C2—H2···O1ⁱᵛ	0.98	2.53	3.469 (2)	160

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

Data collection: APEX2 (Bruker, 2009); cell refinement: SAINT (Bruker, 2009); data reduction: SAINT; program(s) used to solve structure: SHELXS2013 (Sheldrick, 2008); program(s) used to refine structure: SHELXL2014 (Sheldrick, 2015); molecular graphics: PLATON (Spek, 2009); software used to prepare material for publication: SHELXL2014.

data reports

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supporting information

Redetermined crystal structure of *N*-(*β*-carboxyethyl)-*α*-isoleucine

M. Chandrarekha, N. Srinivasan and R. V. Krishnakumar

S1. Introduction

Amino acids in their free form exist as 'zwitterions' in their crystals with a deprotonated carboxyl group (COO–) and a protonated NH_3^+ group (NH_2^+ in proline). Any deviation from this general preferences of amino acids is worth careful considerations. The motivation for the present work is the unionized state reported by Nehls *et al.*, 2013, for the title compound in contrast to the usually preferred 'zwitterionic' state. In this context, redetermination of the crystal structure of the title compouned was undertaken.

S2. Experimental

S2.1. Synthesis and crystallization

For crystallization details, see Nehls *et al.* (2013).

S2.2. Refinement

Coordinates were refined for amino H atoms; other H atoms were positioned with idealized geometry, with fixed C— H = 0.98 (methyl), 0.99 (methylene) or 1.00 Å (methine). $U_{iso}(H)$ values were set at $1.2U_{eq}$ of the carrier atom or at $1.5U_{eq}$ for methyl and amino groups. The absolute configuration could not be determined by anomalous-dispersion effects in the X-ray diffraction measurements of the crystal, but assigned as L- based on an unchanged chiral centre in the synthetic procedure. The absolute structure was refined as a perfect inversion twin.

S3. Results and discussion

Nehls *et al.*, (2013) seem to have presumed an unionized state for the title compound with an undissociated carboxyl (COOH) and a deprotonated amino (NH) group. A scrutiny of the work by Nehls *et al.* revealed that all the H-atoms, including the donor group H atoms were assigned an idealized geometry and refined as riding on their respective non-H atoms to which they are attached. Redetermination of the crystal structure carried out by measuring X-ray intensity data from freshly grown crystals and freely refining the amino-H atoms clearly indicate that the title compound indeed exist as a zwitterion. The correct assignment of the ionized state provided enhanced refinement and structural parameters. Thus, the present redtermination demonstrates the importance of freely refining donor group hydrogens. The S,S (equivalently L-) absolute configuration is deduced from the synthetic pathway as the starting material involved L-isoleucine. The absolute structure was refined as a perfect inversion twin in order that the Flack x (Flack, 1983; Flack & Bernardinelli, 2000; Parsons *et al.*, 2013) and Hooft y parameters (Spek, 2009) showed good agreement.

The correct assignment of the ionization state to the title compound as 'zwitterion' presents an acceptable description of the intermolecular interaction patterns with all the amino-H atoms participating in them. The carboxylate O1 atom of the amino acid derivative participates in a strong head-to-tail N—H···O hydrogen bond characteristic of amino acids, in addition to a C—H···O hydrogen-bond as acceptor. This has consequently resulted in the lengthening of the C6—

O1[1.253 (2)Å] bond compared to its counterpart C6—O2[1.234 (2)Å]. The carbamoyl group N2 and O3 form N—H···O hydrogen-bonds within themselves leading to $C^3_2(8)$ chains linking screw related molecules along the shortest a-axis. The respective amino and carboxylate group N and O atoms form characteristic head-to-tail hydrogen-bonds leading to a layers parallel to the ab-plane. The intermolecular interaction pattern is a three-dimensional network dominated by N—H···O hydrogen bonds, in addition to a C—H···O hydrogen-bond involving the α-carbon atom (C2) as donor and the carboxylate O1 as acceptor.
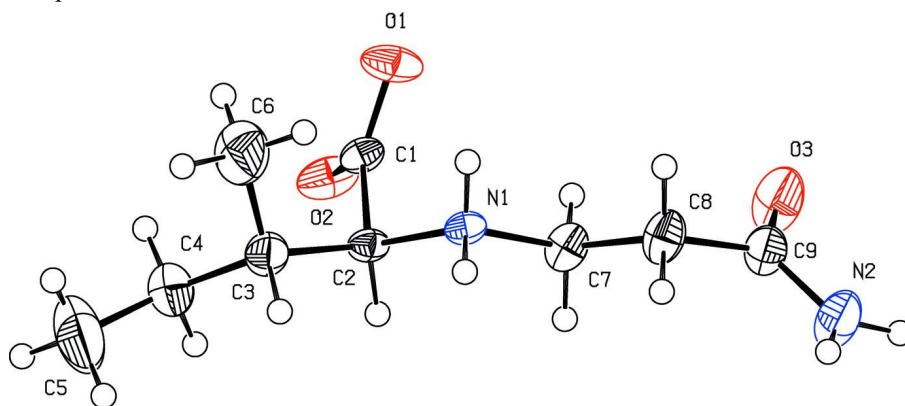

Figure 1

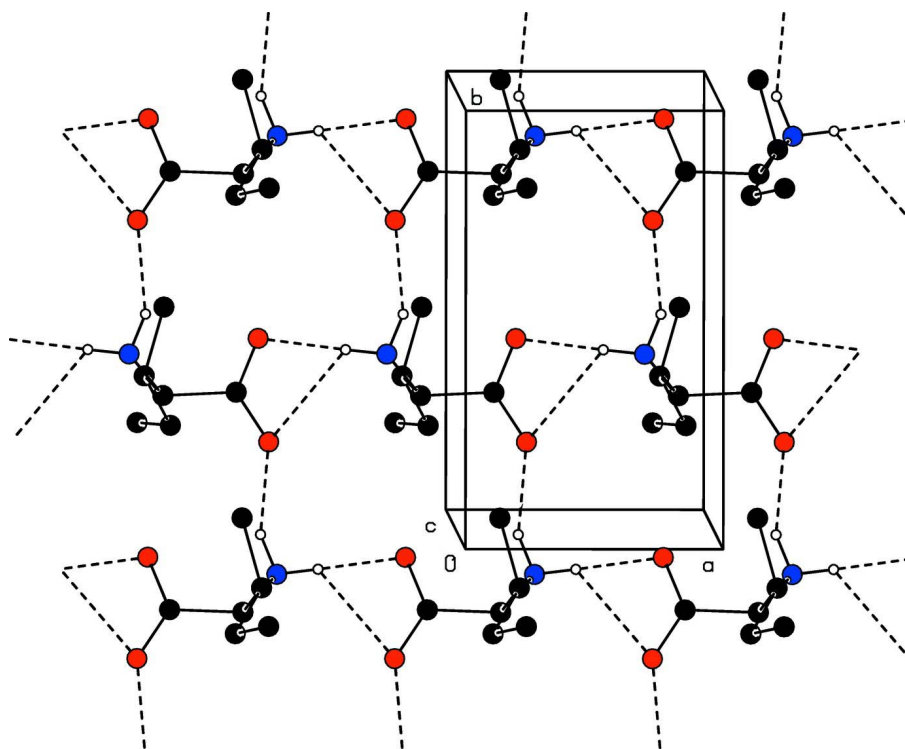Thermal ellipsoid plot of the title compound, showing the atom numbering scheme.

Figure 2

The characteristic head-to-tail N—H···O hydrogen bonds involving the carboxylate and the amino groups. Non pariticipating *N*-carboxyethl group atoms have been omitted for clarity.
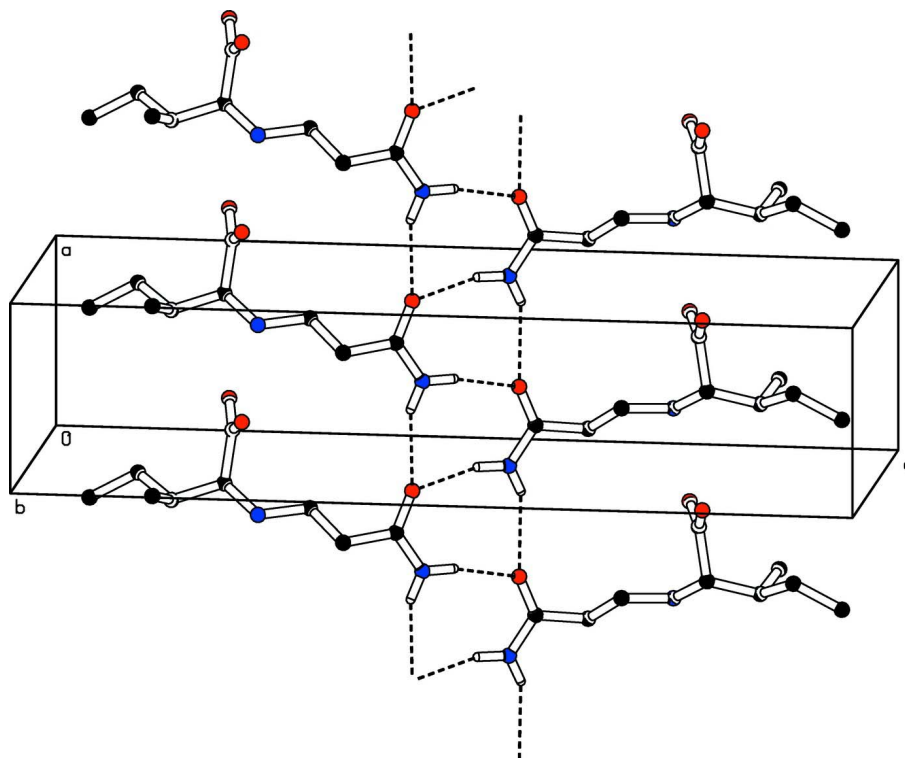
Figure 3

Carbamoyl group N2 and O3 forming N—H···O hydrogen-bonds within themselves leading to C32(8) chains linking screw related molecules along the *a* axis.

(2*S*,3*S*)-2-[(2-Carbamoylethyl)azaniumyl]-3-methylpentanoate

Crystal data

$C_9H_{18}N_2O_3$	$D_x = 1.213$ Mg m^{-3}
$M_r = 202.25$	$D_m = 1.21$ Mg m^{-3}
Orthorhombic, $P2_12_12_1$	D_m measured by floatation method
$a = 5.2996$ (5) Å	Mo *Kα* radiation, $λ = 0.71073$ Å
$b = 9.0053$ (7) Å	$μ = 0.09$ mm^{-1}
$c = 23.211$ (2) Å	$T = 293$ K
$V = 1107.75$ (17) Å^3	Needle, colourless
$Z = 4$	$0.26 × 0.18 × 0.10$ mm
$F(000) = 440$	

Data collection

Bruker APEXII CCD diffractometer	3127 independent reflections
ω and *φ* scans	2538 reflections with $I > 2σ(I)$
Absorption correction: multi-scan (*SADABS*; Bruker, 2009)	$R_{int} = 0.036$
	$θ_{max} = 29.9°$, $θ_{min} = 2.4°$
$T_{min} = 0.97$, $T_{max} = 0.99$	$h = -7→7$
22904 measured reflections	$k = -12→11$
	$l = -31→32$

Refinement

Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement	
Least-squares matrix: full		
$R[F^2 > 2\sigma(F^2)] = 0.042$	$w = 1/[\sigma^2(F_o^2) + (0.0479P)^2 + 0.1014P]$	
$wR(F^2) = 0.102$	where $P = (F_o^2 + 2F_c^2)/3$	
$S = 1.08$	$(\Delta/\sigma)_{max} < 0.001$	
3127 reflections	$\Delta\rho_{max} = 0.30$ e Å⁻³	
146 parameters	$\Delta\rho_{min} = -0.19$ e Å⁻³	
0 restraints	Absolute structure: Refined as a perfect inversion twin.	
Hydrogen site location: mixed	Absolute structure parameter: 0.5	

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. Refined as a 2-component perfect inversion twin.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.2868 (2)	0.54162 (13)	0.74549 (7)	0.0379 (4)
O2	0.2473 (3)	0.77532 (13)	0.71778 (7)	0.0383 (4)
O3	0.6665 (3)	0.6614 (2)	0.94137 (7)	0.0550 (5)
N1	0.7861 (3)	0.57896 (16)	0.76272 (6)	0.0213 (3)
N2	1.0857 (4)	0.6555 (3)	0.95384 (9)	0.0475 (5)
C5	0.7705 (8)	0.7167 (5)	0.55526 (12)	0.0942 (12)
H5A	0.9472	0.7357	0.5606	0.141*
H5B	0.7017	0.7884	0.5290	0.141*
H5C	0.7479	0.6188	0.5398	0.141*
C4	0.6370 (5)	0.7281 (3)	0.61215 (10)	0.0506 (6)
H4A	0.4584	0.7101	0.6062	0.061*
H4B	0.6555	0.8285	0.6267	0.061*
C3	0.7352 (4)	0.6194 (2)	0.65736 (8)	0.0329 (4)
H3	0.9199	0.6235	0.6558	0.040*
C6	0.6603 (6)	0.4612 (3)	0.64363 (10)	0.0571 (7)
H6A	0.7232	0.3961	0.6731	0.086*
H6B	0.7304	0.4330	0.6071	0.086*
H6C	0.4797	0.4540	0.6420	0.086*
C2	0.6583 (3)	0.66957 (19)	0.71782 (7)	0.0224 (4)
H2	0.7123	0.7729	0.7227	0.027*
C1	0.3732 (3)	0.66295 (19)	0.72788 (8)	0.0244 (4)
C7	0.7684 (4)	0.6481 (2)	0.82050 (8)	0.0297 (4)
H7A	0.5926	0.6536	0.8319	0.036*
H7B	0.8340	0.7485	0.8187	0.036*
C8	0.9134 (4)	0.5614 (2)	0.86493 (8)	0.0354 (5)
H8A	1.0912	0.5611	0.8551	0.042*
H8B	0.8547	0.4594	0.8655	0.042*

C9	0.8776 (4)	0.6301 (2)	0.92372 (8)	0.0348 (4)
H1N1	0.723 (4)	0.488 (2)	0.7648 (9)	0.029 (5)*
H2N1	0.947 (4)	0.568 (2)	0.7544 (9)	0.027 (5)*
H2N2	1.228 (6)	0.631 (3)	0.9411 (11)	0.051 (7)*
H1N2	1.082 (6)	0.697 (3)	0.9890 (13)	0.064 (9)*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0150 (6)	0.0337 (7)	0.0651 (10)	−0.0005 (5)	0.0039 (6)	0.0146 (6)
O2	0.0213 (7)	0.0261 (6)	0.0675 (10)	0.0044 (6)	−0.0089 (7)	−0.0012 (6)
O3	0.0324 (8)	0.0925 (14)	0.0400 (9)	0.0071 (9)	0.0034 (7)	−0.0200 (8)
N1	0.0129 (6)	0.0224 (7)	0.0287 (8)	−0.0001 (5)	0.0007 (5)	−0.0012 (6)
N2	0.0339 (11)	0.0737 (15)	0.0348 (10)	−0.0011 (10)	−0.0030 (8)	−0.0149 (10)
C5	0.101 (3)	0.142 (3)	0.0405 (15)	−0.019 (3)	0.0009 (16)	0.0249 (17)
C4	0.0549 (15)	0.0597 (14)	0.0371 (11)	−0.0110 (12)	−0.0076 (11)	0.0114 (11)
C3	0.0225 (9)	0.0464 (11)	0.0299 (9)	−0.0034 (9)	0.0010 (8)	−0.0003 (8)
C6	0.080 (2)	0.0488 (14)	0.0423 (13)	0.0016 (14)	0.0050 (13)	−0.0135 (11)
C2	0.0141 (7)	0.0235 (8)	0.0296 (8)	−0.0012 (6)	−0.0007 (6)	0.0019 (7)
C1	0.0142 (7)	0.0270 (8)	0.0319 (9)	−0.0006 (7)	−0.0014 (7)	−0.0027 (7)
C7	0.0266 (9)	0.0320 (9)	0.0305 (9)	0.0073 (8)	−0.0013 (7)	−0.0079 (7)
C8	0.0320 (11)	0.0428 (11)	0.0313 (10)	0.0088 (9)	−0.0057 (8)	−0.0070 (9)
C9	0.0319 (10)	0.0430 (11)	0.0295 (9)	0.0018 (9)	−0.0019 (9)	−0.0027 (8)

Geometric parameters (Å, º)

O1—C1	1.253 (2)	C4—H4B	0.9700
O2—C1	1.234 (2)	C3—C6	1.513 (3)
O3—C9	1.224 (3)	C3—C2	1.530 (2)
N1—C7	1.481 (2)	C3—H3	0.9800
N1—C2	1.487 (2)	C6—H6A	0.9600
N1—H1N1	0.89 (2)	C6—H6B	0.9600
N1—H2N1	0.88 (2)	C6—H6C	0.9600
N2—C9	1.326 (3)	C2—C1	1.530 (2)
N2—H2N2	0.84 (3)	C2—H2	0.9800
N2—H1N2	0.90 (3)	C7—C8	1.504 (3)
C5—C4	1.502 (4)	C7—H7A	0.9700
C5—H5A	0.9600	C7—H7B	0.9700
C5—H5B	0.9600	C8—C9	1.510 (3)
C5—H5C	0.9600	C8—H8A	0.9700
C4—C3	1.527 (3)	C8—H8B	0.9700
C4—H4A	0.9700		
C7—N1—C2	112.03 (13)	H6A—C6—H6B	109.5
C7—N1—H1N1	108.3 (13)	C3—C6—H6C	109.5
C2—N1—H1N1	111.9 (14)	H6A—C6—H6C	109.5
C7—N1—H2N1	107.9 (14)	H6B—C6—H6C	109.5
C2—N1—H2N1	110.4 (14)	N1—C2—C3	111.07 (14)

H1N1—N1—H2N1	106.1 (19)	N1—C2—C1	108.74 (14)
C9—N2—H2N2	121.0 (18)	C3—C2—C1	113.06 (15)
C9—N2—H1N2	122 (2)	N1—C2—H2	107.9
H2N2—N2—H1N2	117 (3)	C3—C2—H2	107.9
C4—C5—H5A	109.5	C1—C2—H2	107.9
C4—C5—H5B	109.5	O2—C1—O1	125.42 (16)
H5A—C5—H5B	109.5	O2—C1—C2	118.20 (15)
C4—C5—H5C	109.5	O1—C1—C2	116.38 (15)
H5A—C5—H5C	109.5	N1—C7—C8	111.73 (14)
H5B—C5—H5C	109.5	N1—C7—H7A	109.3
C5—C4—C3	113.6 (2)	C8—C7—H7A	109.3
C5—C4—H4A	108.9	N1—C7—H7B	109.3
C3—C4—H4A	108.9	C8—C7—H7B	109.3
C5—C4—H4B	108.9	H7A—C7—H7B	107.9
C3—C4—H4B	108.9	C7—C8—C9	110.04 (16)
H4A—C4—H4B	107.7	C7—C8—H8A	109.7
C6—C3—C4	111.70 (19)	C9—C8—H8A	109.7
C6—C3—C2	113.68 (17)	C7—C8—H8B	109.7
C4—C3—C2	110.48 (17)	C9—C8—H8B	109.7
C6—C3—H3	106.9	H8A—C8—H8B	108.2
C4—C3—H3	106.9	O3—C9—N2	122.98 (19)
C2—C3—H3	106.9	O3—C9—C8	120.75 (18)
C3—C6—H6A	109.5	N2—C9—C8	116.27 (19)
C3—C6—H6B	109.5		

C5—C4—C3—C6	−71.2 (3)	N1—C2—C1—O2	144.24 (16)
C5—C4—C3—C2	161.2 (2)	C3—C2—C1—O2	−91.9 (2)
C7—N1—C2—C3	165.30 (14)	N1—C2—C1—O1	−36.3 (2)
C7—N1—C2—C1	−69.67 (18)	C3—C2—C1—O1	87.5 (2)
C6—C3—C2—N1	62.6 (2)	C2—N1—C7—C8	−176.01 (15)
C4—C3—C2—N1	−170.95 (17)	N1—C7—C8—C9	−176.58 (17)
C6—C3—C2—C1	−60.0 (2)	C7—C8—C9—O3	48.8 (3)
C4—C3—C2—C1	66.5 (2)	C7—C8—C9—N2	−130.4 (2)

Hydrogen-bond geometry (Å, º)

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1*N*1···O2^i	0.89 (2)	1.96 (2)	2.7772 (19)	152 (2)
N1—H2*N*1···O1^{ii}	0.88 (2)	1.83 (2)	2.7047 (19)	174 (2)
N2—H1*N*2···O3^{iii}	0.90 (3)	2.11 (3)	2.970 (3)	161 (3)
N2—H2*N*2···O3^{ii}	0.84 (3)	2.34 (3)	3.092 (3)	149 (2)
C2—H2···O1^{iv}	0.98	2.53	3.469 (2)	160

Symmetry codes: (i) −*x*+1, *y*−1/2, −*z*+3/2; (ii) *x*+1, *y*, *z*; (iii) *x*+1/2, −*y*+3/2, −*z*+2; (iv) −*x*+1, *y*+1/2, −*z*+3/2.