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Crystal structure of a new polymorph of (2*S*,3*S*)-2-amino-3-methylpentanoic acid

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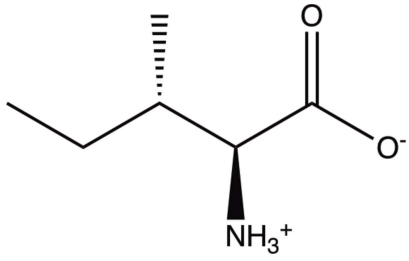
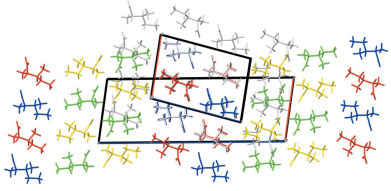
A new polymorph of (2*S*,3*S*)-2-amino-3-methylpentanoic acid, L-isoleucine $C_6H_{13}NO_2$, crystallizes in the monoclinic space group $P2_1$ with four independent molecules in the asymmetric unit. The molecules are *zwitterions*. In the crystal, N—H···O hydrogen bonds link two pairs of independent molecules and their symmetry-related counterparts to form two types of layers stacked in an *anti-parallel* manner parallel to (001). The hydrophobic aliphatic isopropyl groups protrude from these layers.

1. Chemical context

(2*S*,3*S*)-2-Amino-3-methylpentanoic acid, known as L-isoleucine (L-Ile), is one of the 20 amino acids common in animal proteins and required for normal functioning in humans. L-Ile is classified as a hydrophobic amino acid and is one of the two common amino acids that has a chiral side chain. L-Ile is essential for human muscle tissue recovery after exercise, along with Valine and Leucine.



The structure of L-Ile was first determined by Torii & Iitaka (1971). The crystal was found to belong to the monoclinic space group $P2_1$, with four molecules in the unit cell, $Z = 4$. The asymmetric unit contains two independent molecules, with the side chain of the L-Ile molecules exhibiting two different conformations (Görbitz & Dalhus, 1996; Torii & Iitaka, 1971). Another polymorph in the orthorhombic space group $P222_1$ with the unit cell containing eight molecules was reported by Khawas (1970). The presence of an additional L-Ile polymorph is supported by X-ray powder diffraction measurements by Anuar *et al.* (2009), who suggested that L-Ile is prone to polymorphism as a result of the structural thermal motion of the aliphatic side chain.



2. Structural commentary

In the structure of the title compound there are four L-Ile molecules in the asymmetric unit (Fig. 1). The molecules are

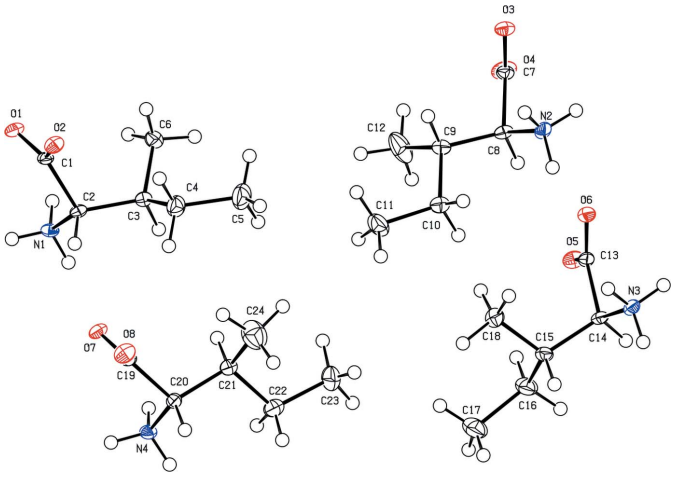


Figure 1
The asymmetric unit of the title compound with atomic numbering. Displacement ellipsoids are shown at the 50% probability level.

zwitterions and organized in pairs. The hydrophilic parts of the molecules are facing each other and generate intermolecular N—H···O hydrogen bonds (Table 1), within the pair and with symmetry-related pairs. The aliphatic parts of the molecules are exposed, pointing away from the hydrogen-bonded network, creating a hydrophobic layer (Fig. 2). A similar network pattern was described previously (Görbitz & Dalhus, 1996; Torii & Iitaka, 1971).

The existence of another chiral center in the side chain allows for conformational differences. Each L-Ile pair consists of two types of conformers. This is presented in the values of the following torsion angles. The two molecules of conformer type I have torsion angles N1—C2—C3—C6 = 80.1 (4)°, N1—C2—C3—C4 = −155.4 (3)° and N3—C14—C15—C18 = 78.1 (4)°, N3—C14—C15—C16 = −155.8 (3)°. The other two molecules are of conformer type II with the torsion angles N2—C8—C9—C12 = 178.6 (4)°, N2—C8—C9—C10 = −56.9 (5)° and N4—C20—C21—C24 = 179.1 (4)°, N4—C20—C21—C22 = −56.8 (5)°. Furthermore, there is a minor conformational variance between all the four independent molecules, as illustrated by the torsion angles of the *iso*-propyl side chains: C6—C3—C4—C5 = −56.6 (5)°, C12—C9—C10—C11 = −51.6 (6)°, C18—C15—C16—C17 = −58.9 (5)° and C24—C21—C22—C23 = −53.2 (6)°.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*A*···O2^{i}	0.91	1.96	2.853 (5)	165
N3—H3*A*···O5^{ii}	0.91	1.93	2.820 (5)	165
N3—H3*B*···O3^{iii}	0.91	2.01	2.818 (5)	147
N3—H3*C*···O3^{iv}	0.91	1.87	2.773 (4)	172
N4—H4*D*···O8^{i}	0.91	1.97	2.843 (5)	162
N2—H2*A*···O5	0.91	2.19	3.055 (5)	159
N2—H2*A*···O6	0.91	2.20	2.953 (5)	139
N2—H2*C*···O6^{v}	0.91	1.85	2.762 (5)	174
N2—H2*B*···O4^{ii}	0.91	1.94	2.826 (5)	163

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

3. Supramolecular features

In the crystal, N—H···O hydrogen bonds (Table 1) connect the molecules, forming layers parallel to (001). The polar side of L-Ile is embedded inside the layers while the side chains are oriented away, creating a hydrophobic surface. However, this hydrogen-bonding network has directionality along the polar *b* axis and specifically parallel to (001) (see Figs. 2 and 3). The adjacent layer is slightly rotated and grows in the opposite direction to the first one, an *anti-parallel* layer. The structure is composed of alternating layers with the hydrophilic side generating a hydrogen-bonding network growing in the opposite direction and the hydrophobic side chains are

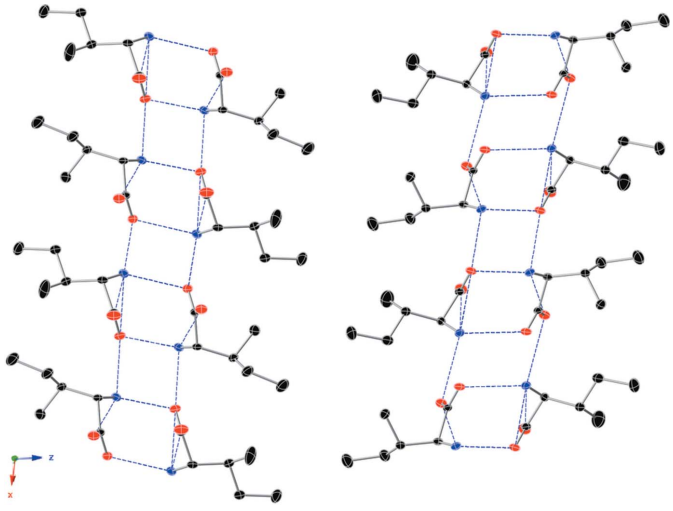


Figure 2
Part of the crystal structure viewed perpendicular to the *ac* plane showing adjacent *anti-parallel* layers formed by hydrogen-bonded pairs and symmetry-related molecules. The hydrophobic side chains protrude away and stack together. Displacement ellipsoids are shown at the 50% probability level (C atoms black, O red, N blue). H atoms are omitted for clarity. Blue dashed lines denote hydrogen bonds.

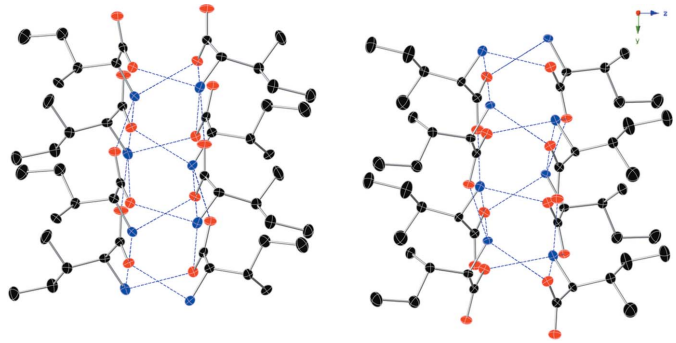


Figure 3
Part of the crystal structure viewed perpendicular to the *bc* plane showing adjacent *anti-parallel* layers formed by the hydrogen-bonded molecule pairs and symmetry-related molecules. The hydrophobic side chains protrude away and are stacked together. Displacement ellipsoids are shown at the 50% probability level (C atoms black, O red, N blue). H atoms are omitted for clarity. Blue dashed lines denote hydrogen bonds.

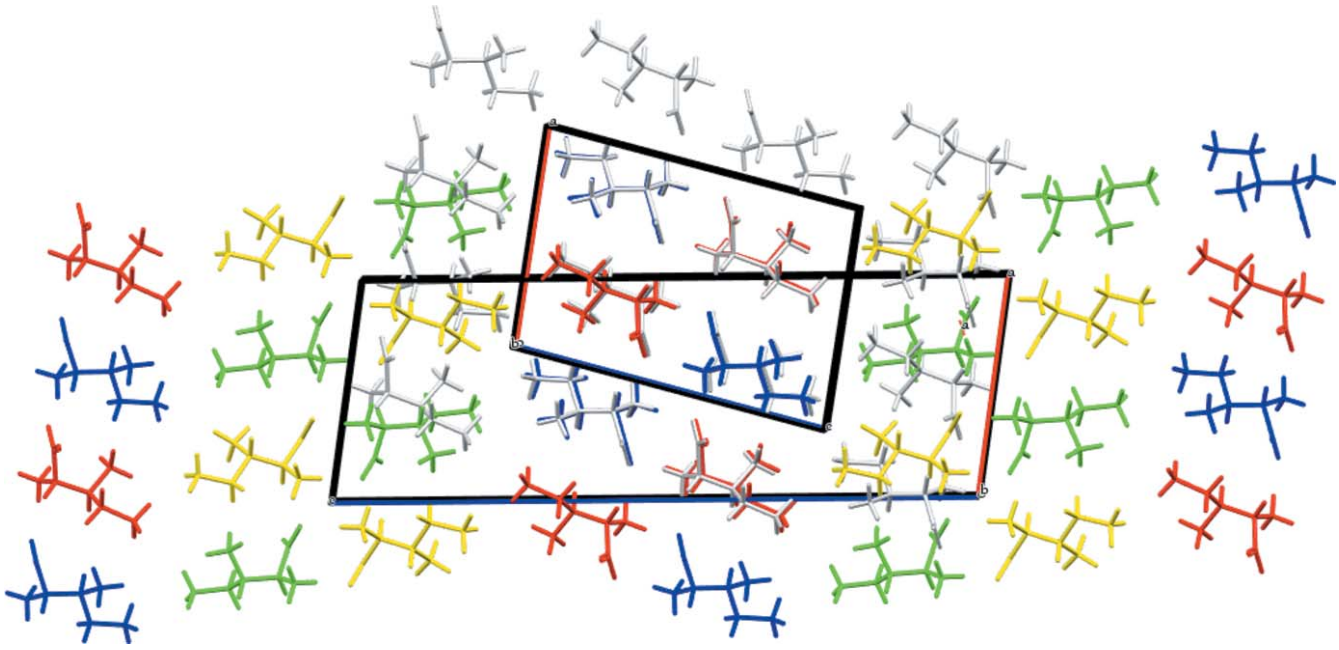


Figure 4
Overlay of two structures with molecules presented as capped sticks along the *b* axis. The previous monoclinic $P2_1$ polymorph with two molecules in the asymmetric unit is the small unit cell with all molecules colored in gray and ordered in a *parallel* layer arrangement. The new monoclinic $P2_1$ polymorph has four molecules in the asymmetric unit (colored red, blue, yellow and green). The colors are according to symmetry equivalence. While the blue and red pairs form exactly the same network layer as the polymorph reported by Görbitz & Dalhus (1996), it is evident that the green and yellow pairs have a different orientation, with an *anti-parallel* layer arrangement.

directed outside. There is a slight offset between the layers to allow the hydrophobic side chains to fit the gaps in the adjacent layer surface.

4. Database survey

A comparison between the polymorph presented in this paper and the one reported by Görbitz & Dalhus (1996) is presented in Fig. 4. Both structures have the same monoclinic crystallographic $P2_1$ symmetry; however, one has four molecules in the unit cell and the other has only two. As described above, the layers show growth directionality and a pair of L-Ile molecules manage the layer organization. The new polymorph has alternating layers in opposite direction, *anti-parallel*, unlike the polymorph reported by Görbitz & Dalhus (1996), that has only *parallel* layers.

5. Synthesis and crystallization

Single crystals of L-Ile were grown from supersaturated aqueous solutions, *via* slow evaporation at 323 K in a clean-room environment. The L-Ile powder (Holand–Moran 99%) was dissolved in water (Ultra-pure Millipore water, 18.2 MΩ cm at 298 K, Millipore Synergy UV, Type 1 water) by heating to 353 K, with constant stirring until total dissolution. The hot solution was then filtered through cotton wool into glass crystallization dishes, which were covered with filter paper in order to allow slow evaporation, placed in a heating bath. Colorless crystal chunks, suitable for X-ray crystallographic

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_6H_{13}NO_2$
M_r	131.17
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	100
a, b, c (Å)	9.6757 (5), 5.2885 (3), 28.0136 (15)
β (°)	98.300 (3)
V (Å^3)	1418.44 (13)
Z	8
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.09
Crystal size (mm)	0.50 × 0.20 × 0.15
Data collection	
Diffractometer	Bruker APEXII KappaCCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2015)
T_{min}, T_{max}	0.956, 0.987
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	44938, 7935, 7188
R_{int}	0.060
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.694
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.077, 0.211, 1.15
No. of reflections	7935
No. of parameters	338
No. of restraints	7
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.58, −0.42
Absolute structure	Flack x determined using 2758 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	−0.2 (4)

Computer programs: *APEX2* and *SAINT* (Bruker, 2015), *SHELXT* (Sheldrick, 2015*a*), *SHELXL2014* (Sheldrick, 2015*b*), *PLATON* (Spek, 2009), *CrystalMaker* (*CrystalMaker*, 2013) and *Mercury* (Macrae *et al.*, 2008).

analysis were obtained. The absolute configuration of the title compound is already known.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. H atoms were placed in calculated positions with C—H = 0.98–1.00 Å, N—H = 0.91 Å and included in the refinement in a riding-model approximation with U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(N, C_{methyl}).

Acknowledgements

The authors thank Professor Leslie Leiserowitz, Dr Isabelle Weissbuch and Dr David Ehre (Weizmann Institute) for helpful discussions.

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supporting information

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Crystal structure of a new polymorph of (2*S*,3*S*)-2-amino-3-methylpentanoic acid

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Computing details

Data collection: *APEX2* (Bruker, 2015); cell refinement: *SAINT* (Bruker, 2015); data reduction: *SAINT* (Bruker, 2015); program(s) used to solve structure: SHELXT (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015b); molecular graphics: *PLATON* (Spek, 2009), *CrystalMaker* (*CrystalMaker*, 2013) and *Mercury* (Macrae *et al.*, 2008); software used to prepare material for publication: *SHELXL2014* (Sheldrick, 2015b).

(2*S*,3*S*)-2-Amino-3-methylpentanoic acid

Crystal data

$C_6H_{13}NO_2$
M_r = 131.17
Monoclinic, $P2_1$
a = 9.6757 (5) Å
b = 5.2885 (3) Å
c = 28.0136 (15) Å
β = 98.300 (3)°
V = 1418.44 (13) Å^3
Z = 8
$F(000)$ = 576
D_x = 1.228 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 47498 reflections
θ = 0.7–30.6°
μ = 0.09 mm^{-1}
T = 100 K
Prism, colorless
0.50 × 0.20 × 0.15 mm

Data collection

Bruker APEXII KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (SADABS; Bruker, 2015)
T_{min} = 0.956, T_{max} = 0.987
44938 measured reflections
7935 independent reflections
7188 reflections with $I > 2\sigma(I)$
R_{int} = 0.060
θ_{max} = 29.6°, θ_{min} = 2.8°
h = −13→13
k = −7→7
l = −38→38

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.077
$wR(F^2)$ = 0.211
S = 1.15
7935 reflections
338 parameters
7 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0831P)^2 + 2.4061P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.005
$\Delta\rho_{max}$ = 0.58 e Å^{-3}
$\Delta\rho_{min}$ = −0.42 e Å^{-3}
Extinction correction: SHELXL2014 (Sheldrick, 2015b), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.043 (6)

Absolute structure: Flack *x* determined using 2758 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter: −0.2 (4)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.8884 (3)	0.5064 (6)	0.04413 (11)	0.0166 (6)
O2	0.8218 (3)	0.8831 (6)	0.06814 (11)	0.0162 (6)
C1	0.8005 (4)	0.6525 (8)	0.05824 (14)	0.0125 (7)
C2	0.6598 (4)	0.5418 (8)	0.06684 (14)	0.0126 (7)
H2	0.5843	0.6615	0.0531	0.015*
N1	0.6375 (3)	0.2952 (7)	0.04012 (12)	0.0128 (6)
H1A	0.7063	0.1847	0.0518	0.019*
H1B	0.6396	0.3219	0.0081	0.019*
H1C	0.5531	0.2297	0.0443	0.019*
C3	0.6498 (4)	0.5036 (8)	0.12085 (15)	0.0155 (8)
H3	0.5734	0.3791	0.1234	0.019*
C4	0.6086 (5)	0.7558 (10)	0.14216 (16)	0.0223 (9)
H4A	0.6805	0.8837	0.1379	0.027*
H4B	0.5192	0.8135	0.1237	0.027*
C5	0.5922 (6)	0.7431 (12)	0.19564 (18)	0.0311 (11)
H5A	0.6832	0.7080	0.2148	0.047*
H5B	0.5265	0.6080	0.2007	0.047*
H5C	0.5566	0.9051	0.2057	0.047*
C6	0.7850 (4)	0.3964 (9)	0.14852 (15)	0.0194 (8)
H6A	0.7685	0.3426	0.1807	0.029*
H6B	0.8576	0.5269	0.1516	0.029*
H6C	0.8153	0.2510	0.1310	0.029*
O3	0.8415 (3)	0.0087 (6)	0.45421 (11)	0.0164 (6)
O4	0.7533 (3)	−0.3784 (6)	0.44210 (13)	0.0219 (7)
C7	0.7422 (4)	−0.1469 (8)	0.44123 (14)	0.0142 (7)
C8	0.6019 (4)	−0.0244 (8)	0.42024 (15)	0.0146 (8)
H8	0.5250	−0.1492	0.4218	0.018*
N2	0.5777 (4)	0.2014 (8)	0.44997 (13)	0.0172 (7)
H2A	0.4852	0.2410	0.4452	0.026*
H2B	0.6278	0.3345	0.4411	0.026*
H2C	0.6053	0.1661	0.4817	0.026*
C9	0.6022 (4)	0.0536 (9)	0.36746 (15)	0.0178 (8)
H9	0.6802	0.1769	0.3666	0.021*
C10	0.4661 (5)	0.1855 (10)	0.34710 (17)	0.0229 (9)
H10A	0.4579	0.3436	0.3654	0.027*

H10B	0.3868	0.0751	0.3521	0.027*
C11	0.4548 (6)	0.2498 (11)	0.29339 (17)	0.0286 (11)
H11A	0.4369	0.0949	0.2743	0.043*
H11B	0.5424	0.3263	0.2869	0.043*
H11C	0.3779	0.3692	0.2846	0.043*
C12	0.6304 (8)	−0.1739 (12)	0.3372 (2)	0.0400 (15)
H12A	0.6393	−0.1183	0.3044	0.060*
H12B	0.5527	−0.2938	0.3360	0.060*
H12C	0.7172	−0.2562	0.3516	0.060*
O5	0.2587 (3)	0.1881 (6)	0.43174 (12)	0.0184 (6)
O6	0.3479 (3)	0.5641 (6)	0.45466 (11)	0.0165 (6)
C13	0.2467 (4)	0.4193 (8)	0.44065 (14)	0.0144 (8)
C14	0.0998 (4)	0.5344 (8)	0.43171 (15)	0.0138 (7)
H14	0.0340	0.4158	0.4448	0.017*
N3	0.1002 (3)	0.7776 (7)	0.45836 (12)	0.0145 (7)
H3A	0.1555	0.8911	0.4457	0.022*
H3B	0.1338	0.7515	0.4900	0.022*
H3C	0.0116	0.8390	0.4557	0.022*
C15	0.0477 (4)	0.5754 (9)	0.37737 (15)	0.0162 (8)
H15	−0.0310	0.6995	0.3749	0.019*
C16	−0.0116 (5)	0.3277 (10)	0.35459 (17)	0.0241 (10)
H16A	−0.0829	0.2629	0.3736	0.029*
H16B	0.0645	0.2014	0.3567	0.029*
C17	−0.0782 (6)	0.3523 (12)	0.30162 (19)	0.0325 (12)
H17A	−0.0061	0.3961	0.2818	0.049*
H17B	−0.1495	0.4853	0.2987	0.049*
H17C	−0.1216	0.1912	0.2905	0.049*
C18	0.1600 (5)	0.6889 (9)	0.35062 (16)	0.0192 (8)
H18A	0.1184	0.7351	0.3178	0.029*
H18B	0.2343	0.5644	0.3492	0.029*
H18C	0.1993	0.8401	0.3677	0.029*
O7	0.3780 (3)	0.0868 (6)	0.04550 (11)	0.0161 (6)
O8	0.3022 (3)	0.4780 (6)	0.05701 (12)	0.0201 (7)
C19	0.2915 (4)	0.2440 (8)	0.05879 (14)	0.0141 (7)
C20	0.1698 (4)	0.1267 (8)	0.08112 (14)	0.0134 (7)
H20	0.0926	0.2535	0.0795	0.016*
N4	0.1169 (4)	−0.1027 (7)	0.05243 (13)	0.0156 (7)
H4C	0.0295	−0.1410	0.0585	0.023*
H4D	0.1749	−0.2357	0.0610	0.023*
H4E	0.1143	−0.0702	0.0204	0.023*
C21	0.2165 (4)	0.0562 (9)	0.13404 (15)	0.0169 (8)
H21	0.2944	−0.0688	0.1352	0.020*
C22	0.0973 (5)	−0.0696 (12)	0.15609 (18)	0.0301 (12)
H22A	0.0153	0.0445	0.1517	0.036*
H22B	0.0702	−0.2275	0.1382	0.036*
C23	0.1336 (6)	−0.1325 (13)	0.20962 (18)	0.0325 (12)
H23A	0.1303	0.0220	0.2287	0.049*
H23B	0.2278	−0.2048	0.2157	0.049*

H23C	0.0662	−0.2552	0.2188	0.049*
C24	0.2721 (7)	0.2875 (13)	0.1629 (2)	0.0404 (14)
H24A	0.1940	0.3971	0.1681	0.061*
H24B	0.3357	0.3806	0.1450	0.061*
H24C	0.3225	0.2338	0.1941	0.061*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0092 (12)	0.0188 (16)	0.0221 (15)	−0.0007 (11)	0.0029 (10)	−0.0017 (12)
O2	0.0148 (13)	0.0118 (14)	0.0225 (15)	−0.0048 (11)	0.0043 (11)	−0.0015 (12)
C1	0.0086 (16)	0.0147 (18)	0.0139 (16)	−0.0025 (13)	0.0001 (12)	0.0019 (14)
C2	0.0090 (15)	0.0120 (18)	0.0170 (17)	−0.0032 (14)	0.0020 (13)	−0.0007 (14)
N1	0.0104 (14)	0.0107 (15)	0.0165 (15)	−0.0019 (11)	−0.0011 (12)	0.0008 (12)
C3	0.0121 (16)	0.018 (2)	0.0159 (17)	−0.0024 (14)	0.0017 (13)	−0.0004 (15)
C4	0.024 (2)	0.024 (2)	0.021 (2)	0.0029 (18)	0.0066 (16)	−0.0020 (17)
C5	0.035 (3)	0.036 (3)	0.025 (2)	0.001 (2)	0.012 (2)	−0.006 (2)
C6	0.0179 (19)	0.023 (2)	0.0168 (18)	0.0006 (16)	0.0000 (15)	0.0030 (16)
O3	0.0109 (12)	0.0159 (15)	0.0218 (14)	0.0014 (11)	−0.0001 (10)	−0.0033 (11)
O4	0.0164 (15)	0.0124 (15)	0.0365 (19)	0.0049 (11)	0.0030 (13)	−0.0001 (13)
C7	0.0112 (17)	0.0148 (19)	0.0160 (18)	0.0024 (14)	−0.0001 (13)	−0.0005 (14)
C8	0.0094 (16)	0.0138 (18)	0.0205 (19)	−0.0011 (13)	0.0019 (14)	−0.0010 (15)
N2	0.0128 (15)	0.0223 (19)	0.0172 (16)	0.0095 (14)	0.0045 (12)	0.0038 (14)
C9	0.0129 (17)	0.021 (2)	0.0187 (19)	0.0011 (15)	−0.0004 (14)	0.0004 (16)
C10	0.0144 (19)	0.033 (3)	0.021 (2)	0.0019 (18)	0.0013 (15)	0.0027 (18)
C11	0.031 (2)	0.034 (3)	0.019 (2)	0.009 (2)	−0.0027 (17)	0.0027 (19)
C12	0.060 (4)	0.036 (3)	0.021 (2)	0.017 (3)	−0.003 (2)	−0.011 (2)
O5	0.0156 (14)	0.0139 (15)	0.0257 (15)	0.0046 (11)	0.0028 (11)	−0.0002 (12)
O6	0.0122 (13)	0.0194 (16)	0.0177 (14)	0.0013 (11)	0.0015 (10)	−0.0007 (12)
C13	0.0107 (16)	0.018 (2)	0.0139 (17)	0.0063 (14)	0.0017 (13)	0.0034 (14)
C14	0.0080 (15)	0.0159 (19)	0.0176 (18)	0.0008 (14)	0.0016 (13)	0.0012 (15)
N3	0.0118 (15)	0.0158 (17)	0.0166 (16)	0.0020 (13)	0.0043 (12)	0.0028 (13)
C15	0.0119 (17)	0.020 (2)	0.0162 (18)	0.0027 (15)	−0.0004 (14)	−0.0009 (15)
C16	0.020 (2)	0.027 (2)	0.023 (2)	−0.0042 (18)	−0.0031 (16)	−0.0015 (18)
C17	0.028 (2)	0.040 (3)	0.027 (2)	−0.003 (2)	−0.0058 (19)	−0.007 (2)
C18	0.0201 (19)	0.017 (2)	0.0203 (19)	0.0000 (16)	0.0041 (15)	0.0056 (16)
O7	0.0101 (12)	0.0177 (15)	0.0214 (14)	−0.0005 (11)	0.0048 (10)	−0.0034 (11)
O8	0.0194 (15)	0.0144 (15)	0.0273 (16)	−0.0022 (12)	0.0060 (12)	0.0006 (12)
C19	0.0097 (16)	0.0160 (19)	0.0161 (17)	−0.0004 (14)	0.0007 (13)	0.0008 (14)
C20	0.0122 (17)	0.0145 (18)	0.0135 (17)	0.0011 (13)	0.0023 (13)	0.0024 (14)
N4	0.0114 (15)	0.0192 (18)	0.0155 (15)	−0.0044 (13)	0.0001 (12)	0.0018 (13)
C21	0.0134 (17)	0.020 (2)	0.0171 (18)	−0.0005 (15)	0.0022 (14)	0.0010 (15)
C22	0.016 (2)	0.051 (3)	0.024 (2)	0.000 (2)	0.0035 (17)	0.010 (2)
C23	0.034 (3)	0.045 (3)	0.020 (2)	−0.005 (2)	0.0069 (19)	0.006 (2)
C24	0.051 (2)	0.037 (2)	0.032 (2)	−0.010 (2)	0.0032 (19)	−0.0004 (18)

Geometric parameters (Å, º)

O1—C1	1.255 (5)	O5—C13	1.256 (5)
O2—C1	1.261 (5)	O6—C13	1.260 (5)
C1—C2	1.532 (5)	C13—C14	1.534 (5)
C2—N1	1.504 (5)	C14—N3	1.487 (5)
C2—C3	1.543 (6)	C14—C15	1.548 (6)
C2—H2	1.0000	C14—H14	1.0000
N1—H1A	0.9100	N3—H3A	0.9100
N1—H1B	0.9100	N3—H3B	0.9100
N1—H1C	0.9100	N3—H3C	0.9100
C3—C6	1.530 (6)	C15—C18	1.529 (6)
C3—C4	1.537 (6)	C15—C16	1.532 (6)
C3—H3	1.0000	C15—H15	1.0000
C4—C5	1.530 (7)	C16—C17	1.535 (7)
C4—H4A	0.9900	C16—H16A	0.9900
C4—H4B	0.9900	C16—H16B	0.9900
C5—H5A	0.9800	C17—H17A	0.9800
C5—H5B	0.9800	C17—H17B	0.9800
C5—H5C	0.9800	C17—H17C	0.9800
C6—H6A	0.9800	C18—H18A	0.9800
C6—H6B	0.9800	C18—H18B	0.9800
C6—H6C	0.9800	C18—H18C	0.9800
O3—C7	1.277 (5)	O7—C19	1.273 (5)
O4—C7	1.229 (5)	O8—C19	1.243 (5)
C7—C8	1.542 (5)	C19—C20	1.541 (5)
C8—N2	1.493 (6)	C20—N4	1.504 (5)
C8—C9	1.536 (6)	C20—C21	1.532 (6)
C8—H8	1.0000	C20—H20	1.0000
N2—H2A	0.9100	N4—H4C	0.9100
N2—H2B	0.9100	N4—H4D	0.9100
N2—H2C	0.9100	N4—H4E	0.9100
C9—C12	1.519 (7)	C21—C24	1.521 (8)
C9—C10	1.526 (6)	C21—C22	1.536 (6)
C9—H9	1.0000	C21—H21	1.0000
C10—C11	1.531 (6)	C22—C23	1.526 (7)
C10—H10A	0.9900	C22—H22A	0.9900
C10—H10B	0.9900	C22—H22B	0.9900
C11—H11A	0.9800	C23—H23A	0.9800
C11—H11B	0.9800	C23—H23B	0.9800
C11—H11C	0.9800	C23—H23C	0.9800
C12—H12A	0.9800	C24—H24A	0.9800
C12—H12B	0.9800	C24—H24B	0.9800
C12—H12C	0.9800	C24—H24C	0.9800
O1—C1—O2	124.6 (4)	O5—C13—O6	124.2 (4)
O1—C1—C2	118.2 (4)	O5—C13—C14	117.7 (4)
O2—C1—C2	117.1 (4)	O6—C13—C14	118.0 (4)

N1—C2—C1	108.7 (3)	N3—C14—C13	109.0 (3)
N1—C2—C3	110.5 (3)	N3—C14—C15	110.5 (3)
C1—C2—C3	112.8 (3)	C13—C14—C15	112.2 (3)
N1—C2—H2	108.3	N3—C14—H14	108.3
C1—C2—H2	108.3	C13—C14—H14	108.3
C3—C2—H2	108.3	C15—C14—H14	108.3
C2—N1—H1A	109.5	C14—N3—H3A	109.5
C2—N1—H1B	109.5	C14—N3—H3B	109.5
H1A—N1—H1B	109.5	H3A—N3—H3B	109.5
C2—N1—H1C	109.5	C14—N3—H3C	109.5
H1A—N1—H1C	109.5	H3A—N3—H3C	109.5
H1B—N1—H1C	109.5	H3B—N3—H3C	109.5
C6—C3—C4	112.1 (4)	C18—C15—C16	112.4 (4)
C6—C3—C2	112.0 (3)	C18—C15—C14	112.6 (3)
C4—C3—C2	108.9 (3)	C16—C15—C14	109.8 (4)
C6—C3—H3	107.9	C18—C15—H15	107.2
C4—C3—H3	107.9	C16—C15—H15	107.2
C2—C3—H3	107.9	C14—C15—H15	107.2
C5—C4—C3	114.3 (4)	C15—C16—C17	114.2 (4)
C5—C4—H4A	108.7	C15—C16—H16A	108.7
C3—C4—H4A	108.7	C17—C16—H16A	108.7
C5—C4—H4B	108.7	C15—C16—H16B	108.7
C3—C4—H4B	108.7	C17—C16—H16B	108.7
H4A—C4—H4B	107.6	H16A—C16—H16B	107.6
C4—C5—H5A	109.5	C16—C17—H17A	109.5
C4—C5—H5B	109.5	C16—C17—H17B	109.5
H5A—C5—H5B	109.5	H17A—C17—H17B	109.5
C4—C5—H5C	109.5	C16—C17—H17C	109.5
H5A—C5—H5C	109.5	H17A—C17—H17C	109.5
H5B—C5—H5C	109.5	H17B—C17—H17C	109.5
C3—C6—H6A	109.5	C15—C18—H18A	109.5
C3—C6—H6B	109.5	C15—C18—H18B	109.5
H6A—C6—H6B	109.5	H18A—C18—H18B	109.5
C3—C6—H6C	109.5	C15—C18—H18C	109.5
H6A—C6—H6C	109.5	H18A—C18—H18C	109.5
H6B—C6—H6C	109.5	H18B—C18—H18C	109.5
O4—C7—O3	125.2 (4)	O8—C19—O7	125.2 (4)
O4—C7—C8	119.7 (4)	O8—C19—C20	119.3 (4)
O3—C7—C8	115.0 (4)	O7—C19—C20	115.4 (4)
N2—C8—C9	110.2 (3)	N4—C20—C21	110.5 (3)
N2—C8—C7	108.9 (3)	N4—C20—C19	109.2 (3)
C9—C8—C7	110.9 (3)	C21—C20—C19	110.8 (3)
N2—C8—H8	109.0	N4—C20—H20	108.8
C9—C8—H8	109.0	C21—C20—H20	108.8
C7—C8—H8	109.0	C19—C20—H20	108.8
C8—N2—H2A	109.5	C20—N4—H4C	109.5
C8—N2—H2B	109.5	C20—N4—H4D	109.5
H2A—N2—H2B	109.5	H4C—N4—H4D	109.5

C8—N2—H2C	109.5	C20—N4—H4E	109.5
H2A—N2—H2C	109.5	H4C—N4—H4E	109.5
H2B—N2—H2C	109.5	H4D—N4—H4E	109.5
C12—C9—C10	111.6 (4)	C24—C21—C20	110.5 (4)
C12—C9—C8	110.5 (4)	C24—C21—C22	111.3 (4)
C10—C9—C8	111.2 (3)	C20—C21—C22	111.2 (3)
C12—C9—H9	107.8	C24—C21—H21	107.9
C10—C9—H9	107.8	C20—C21—H21	107.9
C8—C9—H9	107.8	C22—C21—H21	107.9
C9—C10—C11	113.8 (4)	C23—C22—C21	114.2 (4)
C9—C10—H10A	108.8	C23—C22—H22A	108.7
C11—C10—H10A	108.8	C21—C22—H22A	108.7
C9—C10—H10B	108.8	C23—C22—H22B	108.7
C11—C10—H10B	108.8	C21—C22—H22B	108.7
H10A—C10—H10B	107.7	H22A—C22—H22B	107.6
C10—C11—H11A	109.5	C22—C23—H23A	109.5
C10—C11—H11B	109.5	C22—C23—H23B	109.5
H11A—C11—H11B	109.5	H23A—C23—H23B	109.5
C10—C11—H11C	109.5	C22—C23—H23C	109.5
H11A—C11—H11C	109.5	H23A—C23—H23C	109.5
H11B—C11—H11C	109.5	H23B—C23—H23C	109.5
C9—C12—H12A	109.5	C21—C24—H24A	109.5
C9—C12—H12B	109.5	C21—C24—H24B	109.5
H12A—C12—H12B	109.5	H24A—C24—H24B	109.5
C9—C12—H12C	109.5	C21—C24—H24C	109.5
H12A—C12—H12C	109.5	H24A—C24—H24C	109.5
H12B—C12—H12C	109.5	H24B—C24—H24C	109.5

O1—C1—C2—N1	−19.5 (5)	O5—C13—C14—N3	162.0 (4)
O2—C1—C2—N1	163.7 (3)	O6—C13—C14—N3	−20.6 (5)
O1—C1—C2—C3	103.3 (4)	O5—C13—C14—C15	−75.3 (5)
O2—C1—C2—C3	−73.5 (5)	O6—C13—C14—C15	102.1 (4)
N1—C2—C3—C6	80.1 (4)	N3—C14—C15—C18	78.1 (4)
C1—C2—C3—C6	−41.7 (5)	C13—C14—C15—C18	−43.8 (5)
N1—C2—C3—C4	−155.4 (3)	N3—C14—C15—C16	−155.8 (3)
C1—C2—C3—C4	82.8 (4)	C13—C14—C15—C16	82.3 (4)
C6—C3—C4—C5	−56.6 (5)	C18—C15—C16—C17	−58.9 (5)
C2—C3—C4—C5	178.9 (4)	C14—C15—C16—C17	174.9 (4)
O4—C7—C8—N2	141.7 (4)	O8—C19—C20—N4	141.5 (4)
O3—C7—C8—N2	−41.9 (5)	O7—C19—C20—N4	−41.7 (5)
O4—C7—C8—C9	−96.9 (5)	O8—C19—C20—C21	−96.5 (5)
O3—C7—C8—C9	79.4 (5)	O7—C19—C20—C21	80.3 (4)
N2—C8—C9—C12	178.6 (4)	N4—C20—C21—C24	179.1 (4)
C7—C8—C9—C12	58.0 (5)	C19—C20—C21—C24	57.9 (5)
N2—C8—C9—C10	−56.9 (5)	N4—C20—C21—C22	−56.8 (5)
C7—C8—C9—C10	−177.5 (4)	C19—C20—C21—C22	−178.0 (4)
C12—C9—C10—C11	−51.6 (6)	C24—C21—C22—C23	−53.2 (6)
C8—C9—C10—C11	−175.4 (4)	C20—C21—C22—C23	−176.9 (5)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*A*···O2^{i}	0.91	1.96	2.853 (5)	165
N3—H3*A*···O5^{ii}	0.91	1.93	2.820 (5)	165
N3—H3*B*···O3^{iii}	0.91	2.01	2.818 (5)	147
N3—H3*C*···O3^{iv}	0.91	1.87	2.773 (4)	172
N4—H4*D*···O8^{i}	0.91	1.97	2.843 (5)	162
N2—H2*A*···O5	0.91	2.19	3.055 (5)	159
N2—H2*A*···O6	0.91	2.20	2.953 (5)	139
N2—H2*C*···O6^{v}	0.91	1.85	2.762 (5)	174
N2—H2*B*···O4^{ii}	0.91	1.94	2.826 (5)	163

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