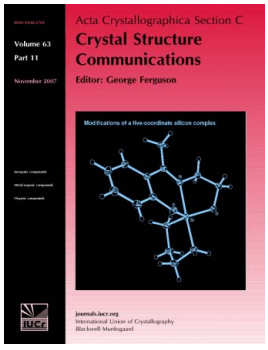
Acta Crystallographica Section C
Structural Chemistry
ISSN 2053-2296

The peptide *Z*-Aib-Aib-Aib-L-Ala-OtBu

Renate Gessmann, Hans Brückner and Kyriacos Petratos

Acta Cryst. (2014). C**70**, 405–407



Acta Crystallographica Section C
Structural Chemistry
ISSN 2053-2296

The peptide *Z*-Aib-Aib-Aib-L-Ala-OtBu

Renate Gessmann,[a]* Hans Brückner[b] and Kyriacos Petratos[a]

[a]IMBB/FORTH, 70013 Iraklion Crete, Greece, and [b]Department of Food Sciences, Interdisciplinary Research Center, Justus Liebig University of Giessen, 35392 Giessen, Germany
Correspondence e-mail: reges777@gmail.com

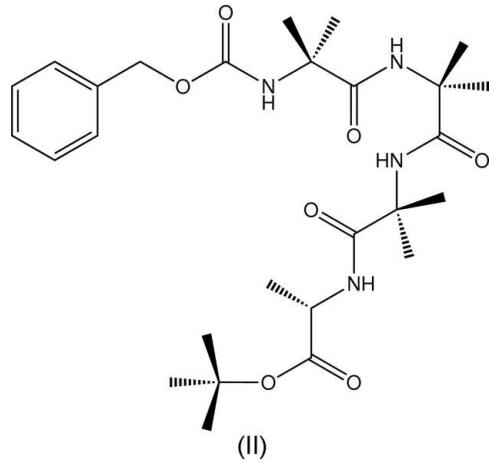
Received 24 January 2014
Accepted 11 March 2014

The title peptide, *N*-benzyloxycarbonyl-α-aminoisobutyryl-α-aminoisobutyryl-α-aminoisobutyryl-L-alanine *tert*-butyl ester or *Z*-Aib-Aib-Aib-L-Ala-OtBu (Aib is α-aminoisobutyric acid, *Z* is benzyloxycarbonyl and OtBu indicates the *tert*-butyl ester), $C_{27}H_{42}N_4O_7$, is a left-handed helix with a right-handed conformation in the fourth residue, which is the only chiral residue. There are two 4→1 intramolecular hydrogen bonds in the structure. In the lattice, molecules are hydrogen bonded to form columns along the *c* axis.

Keywords: crystal structure; peptide; left-handed helix; hydrogen bonding; α-aminoisobutyric acid; peptaibol antibiotic peptides; Aib-Aib-Aib-Ala.

1. Introduction

The sequence Aib-Aib-Aib-Ala represents a segment of the naturally occurring peptaibol antibiotic peptides containing α-aminoisobutyric acid (Aib) and a C-terminal β-amino alcohol (Brückner & Graf, 1983; Benedetti *et al.*, 1982) such as



(II)

trichotoxin (Brückner *et al.*, 1985). We present here the crystal structure of *Z*-Aib$_3$-L-Ala-OtBu containing this tetrapeptide.

2. Experimental

2.1. Synthesis and crystallization

For the synthesis of *Z*-Aib-Aib-Aib-Ala-OtBu, the protected tripeptide acid *Z*-Aib-Aib-Aib-OH was reacted with acetic anhydride to provide the oxazolone *Z*-Aib-Aib-AibOx, (I) (AibOx is the oxazolone of C-terminal Aib; Leplawy *et al.* 1960; Brückner & Jung, 1982; Toniolo *et al.*, 1983). To a solution of (I) (6.51 mmol) in propionitrile (30 ml), L-Ala-OtBu·HCl (7.81 mmol, 1.20 equivalents) and *N*-methylmorpholine (0.87 ml, 1.20 equivalents) were added and the mixture was heated for 17 h at 373 K. This was followed by evaporation to dryness *in vacuo* using a rotary evaporator. To the remaining residue, *n*-butanol–ethyl acetate (1:1 *v*/*v*, 750 ml) was added, and the organic phase was washed successively with 5% aqueous $KHSO_4$, 5% aqueous $NaHCO_3$ and water. On evaporation of the organic phase, the protected tetrapeptide *Z*-Aib$_3$-L-Ala-OtBu, (II) (see Scheme), started to crystallize. Crystallization was completed by addition of ethyl acetate and petroleum ether (b.p. 313–333 K), until the beginning of turbidity, providing white needles (yield 2.01 g, 57.8%), pure by thin-layer chromatography. A further quantity of *Z*-Aib$_3$-L-Ala-OtBu could be obtained from the mother liquor. Crystals suitable for X-ray crystallography were obtained by cooling a hot methanol–water mixture (70:30 *v*/*v*) in which the peptide had been dissolved. Block-shaped crystals of *Z*-Aib$_3$-L-Ala-OtBu were observed after a few days at room temperature.

2.2. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1. In view of the crystal size, a spherical absorption correction was applied in addition to the correction based on symmetry-related measurements (Bruker, 2008). The four N-bound H atoms were located in a difference Fourier synthesis. Their positional parameters were refined with N—H distance restraints of 0.86 (2) Å and their isotropic displacement parameters were refined freely, except that of the N2—H02 group which was fixed at $1.2U_{eq}$(N). C-bound H atoms were placed in calculated positions, with C—H = 0.93 (aryl), 0.96 (methyl), 0.97 (methylene) and 0.98 Å (methine H atoms), and refined as riding, with U_{iso}(H) = $1.5U_{eq}$(C) for methyl H atoms and $1.2U_{eq}$(C) otherwise.

3. Results and discussion

The backbone of the tetrapeptide of *Z*-Aib$_3$-L-Ala-OtBu adopts quite an unusual conformation, namely an incipient left-handed 3_{10}-helix with a reversal of the helical sense in the Ala residue (Fig. 1 and Table 2). The helix is stabilized by two 4→1 hydrogen bonds (Table 3). All residues, including the N-terminal protecting group, are involved in intramolecular hydrogen bonding.

The peptide adopts the usual *trans*-planar conformation, with significant deviations from planarity (ω = 180°; Table 2). The valence geometry around the C$^\alpha$ atom is asymmetric for the Aib residues (Table 3). If one designates as C*L* and C*R* the

 doi:10.1107/S2053229614005567

Table 1
Experimental details.

Crystal data	
Chemical formula	$C_{27}H_{42}N_4O_7$
M_r	534.65
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	293
a, b, c (Å)	9.3730 (19), 17.032 (3), 19.032 (4)
V (Å^3)	3038.3 (11)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.69
Crystal size (mm)	1.4 × 1.1 × 0.9
Data collection	
Diffractometer	Bruker D8 Venture diffractometer
Absorption correction	Multi-scan (*SADABS*; Bruker, 2008) (see *Refinement*)
T_{min}, T_{max}	0.423, 0.754
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	5835, 5541, 5018
R_{int}	0.034
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.618
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.044, 0.142, 1.16
No. of reflections	5541
No. of parameters	358
No. of restraints	4
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.18, −0.23
Absolute structure	Flack (1983), with 2503 Friedel pairs
Absolute structure parameter	0.05 (18)

Computer programs: *PROTEUM2* (Bruker, 2008), *SAINT* (Bruker, 2008), *SHELXS86* (Sheldrick, 2008), *SHELXL97* (Sheldrick, 2008), *XTALVIEW* (McRee 1999), *SwissPDBViewer* (Guex & Peitsch, 1997), *CHEMDRAW* (Mills, 2006) and *ORTEP-3 for Windows* (Farrugia, 2012).

atoms which occupy the same position as C$^\beta$ and the α-hydrogen in the L-amino acids, respectively, the bond angles N—C$^\alpha$—C*L* and C—C$^\alpha$—C*L* are significantly greater than N—C$^\alpha$—C*R* and C—C$^\alpha$—C*R*. This observation is in excellent agreement with theoretical calculations and with the bond angles of other left-handed 3_{10}-helical Aib peptides (Gessmann *et al.*, 1997).

In the crystal structure, one molecule of *Z*-Aib$_3$-L-Ala-OtBu is hydrogen bonded in a head-to-tail manner to a symmetry-related molecule *via* two hydrogen bonds (Table 4 and Fig. 2), thus building infinite columns in the [001] direction. These columns pack parallel to the same columns translated in the [100] direction along the small *a* axis in the next unit cell, and these hydrogen-bonded columns pack in an

Table 2
Backbone torsion angles (°).

$\omega(z)$	O00—C80—N1—C*A*1	173.8 (2)
$\varphi(1)$	C80—N1—C*A*1—C1	54.8 (3)
$\psi(1)$	N1—C*A*1—C1—N2	36.3 (2)
$\omega(1)$	C*A*1—C1—N2—C*A*2	173.2 (2)
$\varphi(2)$	C1—N2—C*A*2—C2	54.2 (2)
$\psi(2)$	N2—C*A*2—C2—N3	39.4 (2)
$\omega(2)$	C*A*2—C2—N3—C*A*3	172.5 (2)
$\varphi(3)$	C2—N3—C*A*3—C3	75.7 (2)
$\psi(3)$	N3—C*A*3—C3—N4	15.5 (3)
$\omega(3)$	C*A*3—C3—N4—C*A*4	165.9 (2)
$\varphi(4)$	C3—N4—C*A*4—C4	−69.2 (2)
$\psi(4)$	N4—C*A*4—C4—O5	−38.3 (2)
$\omega(4)$	C4A—C4—O5—C15	−176.0 (2)

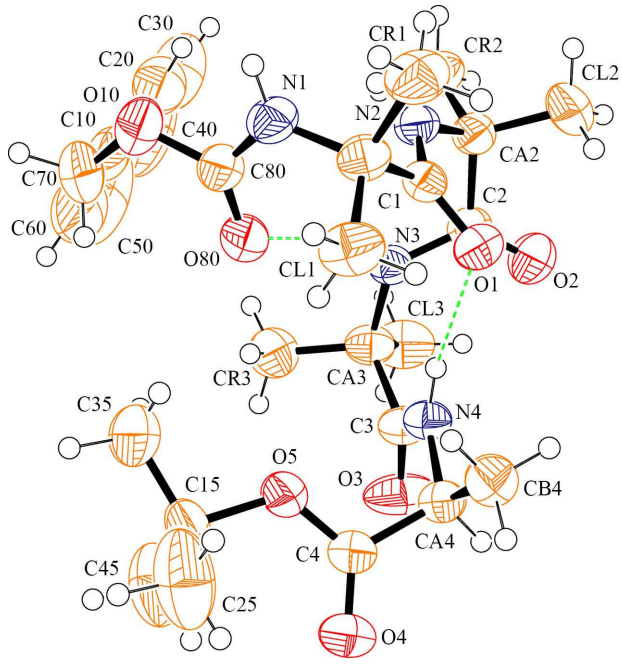


Figure 1
The molecular structure of *Z*-Aib$_3$-L-Ala-OtBu, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. The two intramolecular hydrogen bonds are shown as green dashed lines.

Table 3
Selected bond angles (°).

N1—C*A*1—C*R*1	107.73 (16)	N1—C*A*1—C*L*1	111.44 (18)
C1—C*A*1—C*R*1	107.06 (17)	C1—C*A*1—C*L*1	109.61 (14)
N2—C*A*2—C*R*2	107.58 (14)	N2—C*A*2—C*L*2	109.97 (17)
C2—C*A*2—C*R*2	107.19 (16)	C2—C*A*2—C*L*2	110.12 (17)
N3—C*A*3—C*R*3	107.07 (17)	N3—C*A*3—C*L*3	111.98 (17)
C3—C*A*3—C*R*3	105.60 (17)	C3—C*A*3—C*L*3	109.77 (16)

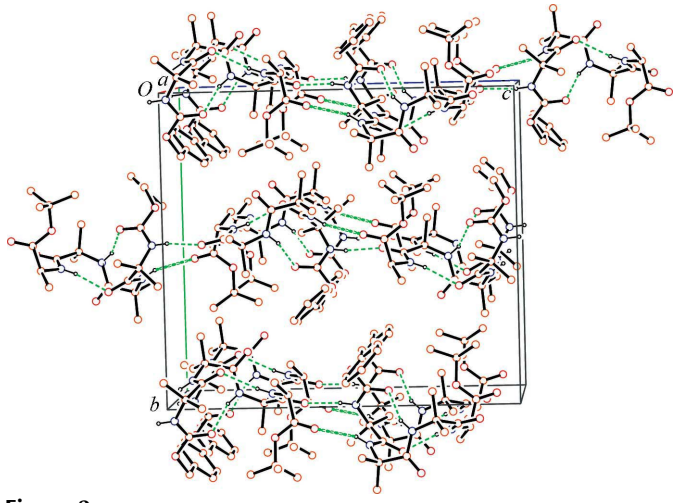


Figure 2
The crystal packing of *Z*-Aib$_3$-L-Ala-OtBu, viewed approximately along the *a* axis. The four molecules in the unit cell and, by translation along the unit-cell axes, symmetry-related molecules are shown when they possess atoms inside the unit cell. Hydrogen bonds are indicated as dashed lines and H atoms not involved in hydrogen bonding have been omitted for clarity.

Table 4
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N3—H03···O80	0.86 (2)	2.31 (2)	3.117 (2)	156 (2)
N4—H04···O1	0.85 (2)	2.22 (2)	3.059 (2)	169 (2)
N1—H01···O3^{i}	0.89 (2)	2.05 (2)	2.929 (2)	171 (3)
N2—H02···O4^{i}	0.87 (2)	2.27 (2)	3.121 (2)	165 (2)

Symmetry code: (i) $-x+\frac{3}{2}, -y+1, z+\frac{1}{2}$.

antiparallel manner to the space group symmetry-related columns in the [010] direction. The only polar group not involved in hydrogen bonding is the C═O group of Aib2, with a closest apolar contact of 3.44 Å to a C atom of the benzyloxycarbonyl protecting group.

The structure of the related peptide *Z*-Aib-Aib-Aib-L-Val-OtBu has been solved previously (Gessmann *et al.*, 1997). The overall folding of the two molecules in the asymmetric unit is essentially the same as for the structure described herein, with an incipient left-handed 3_{10}-helix with reversal of the helical sense in the last residue. The r.m.s. deviation of the backbone and the common side-chain atoms in residues 1 to 4 of molecule *A* of the Val-substituted tetrapeptide and *Z*-Aib$_3$-L-Ala-OtBu is 0.69 Å, while the corresponding value for molecule *B* and *Z*-Aib$_3$-L-Ala-OtBu is 0.42 Å.

The diffractometer used in this work was acquired by the EU Programme FP7-REGPOT-2012 INNOVCRETE (grant Agreement No. 316223). This work was partly performed in the framework of the BIOSYS research project, Action KRIPIS, project No. MIS-448301 (grant No. 2013SE01380036), which was funded by the General Secretariat for Research and Technology, Ministry of Education, Greece, and by the European Regional Development Fund (Sectoral Operational Programme: Competitiveness and Entrepreneurship, NSRF 2007–2013)/European Commission.

Supporting information for this paper is available from the IUCr electronic archives (Reference: EG3150). The coordinates and structure factors have been deposited with the Cambridge Structural Database (Allen, 2002) under the accession code CCDC 973278.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Benedetti, E., Bavoso, A., Di Blasio, B., Pavone, V., Toniolo, C. & Bonora, G. M. (1982). *Proc. Natl Acad. Sci. USA*, **79**, 7951–7954.
Brückner, H. & Graf, H. (1983). *Experientia*, **39**, 528–530.
Brückner, H. & Jung, G. (1982). *Liebigs Ann. Chem.* pp. 1677–1699.
Brückner, H., König, W. A., Aydin, M. & Jung, G. (1985). *Biochim. Biophys. Acta*, **827**, 51–62.
Bruker (2008). *PROTEUM2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Gessmann, R., Brückner, H. & Kokkinidis, M. (1997). *Z. Kristallogr.* **212**, 819–825.
Guex, N. & Peitsch, M. C. (1997). *Electrophoresis*, **18**, 2714–2723.
Leplawy, M. T., Jones, D. S., Kenner, G. W. & Sheppard, R. C. (1960). *Tetrahedron*, **11**, 39–51.
McRee, D. E. (1999). *J. Struct. Biol.* **125**, 156–165.
Mills, N. (2006). *J. Am. Chem. Soc.* **128**, 13649–13650.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Toniolo, C., Bonora, G. M., Crisma, M., Benedetti, E., Bavoso, A., Di Blasio, B., Pavone, V. & Pedone, C. (1983). *Int. J. Pept. Protein Res.* **22**, 603–610.

supplementary materials

Acta Cryst. (2014). C**70**, 405-407 [doi:10.1107/S2053229614005567]

The peptide *Z*-Aib-Aib-Aib-L-Ala-OtBu

Renate Gessmann, Hans Brückner and Kyriacos Petratos

Computing details

Data collection: PROTEUM2 (Bruker, 2008); cell refinement: *SAINT* (Bruker, 2008); data reduction: *SAINT* (Bruker, 2008); program(s) used to solve structure: *SHELXS86* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: XTALVIEW (McRee 1999) and SwissPDBViewer (Guex & Peitsch, 1997); software used to prepare material for publication: *CHEMDRAW* (Mills, 2006) and *ORTEP-3 for Windows* (Farrugia, 2012).

N-benzyloxycarbonyl-*α*-aminoisobutyryl-*α*-aminoisobutyryl-*α*-aminoisobutyryl-*L*-alanine *tert*-butyl ester

Crystal data

$C_{27}H_{42}N_4O_7$
$M_r = 534.65$
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a = 9.3730$ (19) Å
$b = 17.032$ (3) Å
$c = 19.032$ (4) Å
$V = 3038.3$ (11) Å^3
$Z = 4$
$F(000) = 1152$
$D_x = 1.169$ Mg m^{-3}
Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å
$\mu = 0.69$ mm^{-1}
$T = 293$ K
Block, colourless
1.4 × 1.1 × 0.9 mm

Data collection

Bruker D8 Venture diffractometer
Radiation source: microfocus tube IμS
Multilayer optics monochromator
ω and ψ scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2008)
$T_{min} = 0.423$, $T_{max} = 0.754$
5835 measured reflections
5541 independent reflections
5018 reflections with $I > 2\sigma(I)$
$R_{int} = 0.034$
$\theta_{max} = 72.4°$, $\theta_{min} = 3.5°$
$h = -11 \rightarrow 11$
$k = -20 \rightarrow 21$
$l = -22 \rightarrow 22$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.044$
$wR(F^2) = 0.142$
$S = 1.16$
5541 reflections
358 parameters
4 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.18$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}
Absolute structure: Flack (1983), **with how many Friedel pairs?**
Absolute structure parameter: 0.05 (18)

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}
C10	0.5062 (4)	0.31972 (14)	0.92733 (13)	0.0807 (8)
C20	0.4369 (4)	0.37358 (17)	0.96801 (16)	0.0857 (8)
H20	0.4895	0.4042	0.9991	0.103*
C30	0.2917 (5)	0.3838 (2)	0.9643 (2)	0.1199 (13)
H30	0.2469	0.4203	0.9933	0.144*
C40	0.2136 (6)	0.3407 (3)	0.9183 (4)	0.166 (3)
H40	0.1154	0.3475	0.9151	0.199*
C50	0.2831 (9)	0.2862 (4)	0.8760 (4)	0.198 (4)
H50	0.2300	0.2561	0.8447	0.237*
C60	0.4284 (6)	0.2756 (2)	0.8794 (2)	0.1279 (17)
H60	0.4737	0.2397	0.8501	0.153*
C70	0.6653 (5)	0.30493 (15)	0.93185 (17)	0.0986 (10)
H7A0	0.6816	0.2568	0.9579	0.118*
H7B0	0.7027	0.2975	0.8848	0.118*
O00	0.7426 (2)	0.36826 (10)	0.96550 (9)	0.0749 (5)
C80	0.7712 (2)	0.43054 (12)	0.92446 (10)	0.0541 (4)
O80	0.73385 (19)	0.43571 (8)	0.86297 (7)	0.0628 (4)
N1	0.84362 (18)	0.48500 (10)	0.95943 (8)	0.0531 (4)
H01	0.869 (3)	0.4784 (17)	1.0040 (10)	0.096 (9)*
CA1	0.8991 (2)	0.55453 (12)	0.92371 (9)	0.0502 (4)
CL1	1.0180 (2)	0.53321 (15)	0.87215 (12)	0.0658 (6)
HL11	0.9815	0.4977	0.8374	0.099*
HL21	1.0949	0.5086	0.8971	0.099*
HL31	1.0521	0.5800	0.8496	0.099*
CR1	0.9568 (3)	0.61072 (15)	0.98015 (12)	0.0701 (6)
HR11	1.0319	0.5853	1.0058	0.105*
HR21	0.8812	0.6247	1.0118	0.105*
HR31	0.9933	0.6572	0.9581	0.105*
C1	0.77989 (19)	0.59811 (10)	0.88472 (9)	0.0428 (4)
O1	0.80434 (14)	0.63206 (8)	0.82935 (7)	0.0517 (3)
N2	0.65117 (16)	0.59936 (9)	0.91577 (7)	0.0444 (3)
H02	0.643 (3)	0.5779 (12)	0.9571 (8)	0.053*
CA2	0.5316 (2)	0.64628 (11)	0.88785 (10)	0.0471 (4)
CL2	0.5637 (3)	0.73332 (13)	0.89584 (13)	0.0681 (6)
HL12	0.6483	0.7461	0.8698	0.102*
HL22	0.5782	0.7454	0.9446	0.102*
HL32	0.4849	0.7634	0.8782	0.102*

CR2	0.3978 (2)	0.62341 (14)	0.92878 (11)	0.0626 (5)
HR12	0.3803	0.5682	0.9232	0.094*
HR22	0.3176	0.6525	0.9112	0.094*
HR32	0.4113	0.6351	0.9777	0.094*
C2	0.50370 (19)	0.62624 (11)	0.80957 (9)	0.0481 (4)
O2	0.4652 (2)	0.67669 (10)	0.76925 (8)	0.0721 (5)
N3	0.51572 (15)	0.54954 (9)	0.79299 (8)	0.0443 (3)
H03	0.557 (2)	0.5194 (11)	0.8230 (10)	0.050 (5)*
CA3	0.47843 (19)	0.51504 (12)	0.72466 (9)	0.0498 (4)
CL3	0.3308 (2)	0.54203 (18)	0.69914 (12)	0.0726 (7)
HL13	0.2609	0.5309	0.7346	0.109*
HL23	0.3066	0.5146	0.6567	0.109*
HL33	0.3328	0.5975	0.6902	0.109*
CR3	0.4804 (3)	0.42615 (14)	0.73379 (13)	0.0677 (6)
HR13	0.5731	0.4099	0.7495	0.102*
HR23	0.4592	0.4014	0.6897	0.102*
HR33	0.4101	0.4111	0.7679	0.102*
C3	0.59109 (19)	0.53298 (11)	0.66821 (9)	0.0489 (4)
O3	0.56553 (18)	0.51739 (14)	0.60668 (8)	0.0823 (6)
N4	0.71787 (15)	0.55887 (9)	0.68888 (7)	0.0441 (3)
H04	0.741 (3)	0.5730 (14)	0.7301 (9)	0.059 (6)*
CA4	0.83797 (19)	0.55982 (11)	0.64070 (9)	0.0451 (4)
HA4	0.8076	0.5855	0.5971	0.054*
CL4	0.9623 (2)	0.60637 (13)	0.67140 (12)	0.0568 (5)
HL14	0.9309	0.6585	0.6829	0.085*
HL24	1.0380	0.6092	0.6375	0.085*
HL34	0.9962	0.5807	0.7131	0.085*
C4	0.88906 (19)	0.47719 (11)	0.62274 (9)	0.0470 (4)
O4	0.93292 (19)	0.45995 (10)	0.56531 (8)	0.0723 (4)
O5	0.88386 (18)	0.43023 (8)	0.67759 (7)	0.0631 (4)
C15	0.9361 (2)	0.34770 (12)	0.67624 (12)	0.0609 (5)
C25	1.0925 (3)	0.34759 (19)	0.6623 (3)	0.1191 (14)
H2A5	1.1101	0.3666	0.6156	0.179*
H2B5	1.1287	0.2951	0.6667	0.179*
H2C5	1.1396	0.3810	0.6956	0.179*
C35	0.8974 (6)	0.3175 (2)	0.74756 (17)	0.1367 (19)
H3A5	0.7957	0.3189	0.7532	0.205*
H3B5	0.9412	0.3498	0.7828	0.205*
H3C5	0.9305	0.2645	0.7525	0.205*
C45	0.8569 (4)	0.30347 (18)	0.6201 (2)	0.1093 (11)
H4A5	0.8820	0.3241	0.5748	0.164*
H4B5	0.7560	0.3092	0.6273	0.164*
H4C5	0.8819	0.2489	0.6223	0.164*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C10	0.136 (2)	0.0469 (12)	0.0593 (13)	−0.0278 (15)	−0.0160 (14)	0.0080 (10)
C20	0.109 (2)	0.0717 (16)	0.0765 (16)	−0.0142 (15)	−0.0238 (15)	0.0014 (13)
C30	0.123 (3)	0.099 (2)	0.137 (3)	−0.014 (2)	−0.024 (3)	0.038 (2)

C40	0.142 (4)	0.117 (4)	0.239 (7)	−0.058 (4)	−0.082 (5)	0.082 (4)
C50	0.236 (8)	0.122 (4)	0.234 (7)	−0.112 (5)	−0.138 (6)	0.057 (4)
C60	0.217 (5)	0.0707 (19)	0.095 (2)	−0.055 (3)	−0.035 (3)	0.0001 (17)
C70	0.165 (3)	0.0422 (12)	0.0889 (19)	−0.0050 (15)	0.008 (2)	−0.0008 (12)
O00	0.1035 (12)	0.0553 (8)	0.0660 (9)	0.0009 (8)	−0.0050 (8)	0.0133 (7)
C80	0.0628 (11)	0.0519 (10)	0.0475 (10)	0.0096 (9)	−0.0007 (9)	0.0028 (8)
O80	0.0881 (10)	0.0515 (8)	0.0487 (7)	−0.0016 (7)	−0.0046 (7)	−0.0041 (6)
N1	0.0583 (9)	0.0590 (9)	0.0418 (8)	0.0058 (7)	−0.0078 (7)	0.0050 (7)
CA1	0.0468 (9)	0.0610 (11)	0.0429 (9)	−0.0013 (8)	−0.0020 (7)	0.0001 (8)
CL1	0.0484 (10)	0.0894 (16)	0.0596 (12)	0.0119 (11)	0.0025 (9)	0.0035 (11)
CR1	0.0752 (14)	0.0852 (15)	0.0498 (11)	−0.0208 (12)	−0.0142 (10)	−0.0013 (10)
C1	0.0478 (9)	0.0419 (9)	0.0386 (8)	−0.0022 (7)	−0.0011 (7)	−0.0053 (7)
O1	0.0546 (7)	0.0562 (7)	0.0443 (6)	−0.0024 (6)	0.0027 (5)	0.0044 (6)
N2	0.0472 (7)	0.0488 (8)	0.0371 (7)	0.0032 (6)	0.0030 (6)	−0.0001 (6)
CA2	0.0499 (9)	0.0462 (9)	0.0451 (9)	0.0077 (7)	0.0046 (7)	0.0010 (7)
CL2	0.0834 (15)	0.0475 (11)	0.0733 (14)	0.0123 (10)	0.0044 (12)	−0.0111 (10)
CR2	0.0522 (10)	0.0807 (14)	0.0548 (11)	0.0133 (11)	0.0095 (9)	0.0110 (10)
C2	0.0495 (9)	0.0513 (10)	0.0435 (9)	0.0044 (8)	0.0033 (7)	0.0032 (7)
O2	0.0969 (12)	0.0620 (9)	0.0573 (9)	0.0175 (8)	−0.0084 (8)	0.0147 (7)
N3	0.0448 (7)	0.0502 (8)	0.0379 (7)	0.0033 (6)	−0.0026 (6)	0.0000 (6)
CA3	0.0421 (9)	0.0649 (11)	0.0425 (9)	−0.0024 (8)	−0.0018 (7)	−0.0061 (8)
CL3	0.0454 (10)	0.109 (2)	0.0632 (12)	0.0041 (11)	−0.0092 (9)	−0.0072 (13)
CR3	0.0762 (14)	0.0627 (13)	0.0642 (12)	−0.0178 (11)	−0.0037 (11)	−0.0073 (10)
C3	0.0494 (9)	0.0602 (10)	0.0371 (8)	0.0002 (8)	−0.0018 (7)	−0.0039 (7)
O3	0.0675 (9)	0.1385 (17)	0.0408 (7)	−0.0235 (10)	0.0002 (7)	−0.0187 (9)
N4	0.0421 (7)	0.0550 (9)	0.0353 (7)	0.0037 (6)	−0.0016 (6)	−0.0029 (6)
CA4	0.0432 (8)	0.0524 (10)	0.0397 (8)	0.0058 (7)	0.0010 (7)	0.0012 (7)
CL4	0.0499 (9)	0.0596 (11)	0.0609 (11)	−0.0012 (8)	0.0025 (9)	−0.0020 (9)
C4	0.0451 (8)	0.0534 (10)	0.0426 (9)	0.0017 (8)	0.0016 (7)	−0.0031 (7)
O4	0.0936 (11)	0.0714 (10)	0.0519 (8)	0.0141 (8)	0.0192 (8)	−0.0052 (7)
O5	0.0907 (10)	0.0507 (7)	0.0479 (7)	0.0204 (7)	0.0081 (7)	0.0014 (6)
C15	0.0717 (13)	0.0451 (10)	0.0659 (12)	0.0141 (9)	0.0015 (11)	−0.0056 (9)
C25	0.0610 (15)	0.0785 (18)	0.218 (4)	0.0135 (14)	−0.015 (2)	0.014 (2)
C35	0.240 (5)	0.0813 (19)	0.089 (2)	0.078 (3)	0.040 (3)	0.0299 (17)
C45	0.125 (3)	0.0600 (15)	0.143 (3)	−0.0191 (16)	−0.033 (2)	−0.0080 (17)

Geometric parameters (Å, º)

C10—C60	1.389 (4)	CR2—HR22	0.9600
C10—C20	1.365 (5)	CR2—HR32	0.9600
C10—C70	1.515 (5)	C2—O2	1.207 (2)
C20—C30	1.375 (5)	C2—N3	1.349 (3)
C20—H20	0.9300	N3—CA3	1.469 (2)
C30—C40	1.358 (7)	N3—H03	0.861 (16)
C30—H30	0.9300	CA3—CL3	1.537 (3)
C40—C50	1.390 (11)	CA3—CR3	1.524 (3)
C40—H40	0.9300	CA3—C3	1.537 (3)
C50—C60	1.376 (9)	CL3—HL13	0.9600
C50—H50	0.9300	CL3—HL23	0.9600
C60—H60	0.9300	CL3—HL33	0.9600

C70—O00	1.449 (4)	CG3—HR13	0.9600
C70—H7A0	0.9700	CG3—HR23	0.9600
C70—H7B0	0.9700	CG3—HR33	0.9600
O00—C80	1.344 (3)	C3—O3	1.224 (2)
C80—O80	1.225 (2)	C3—N4	1.327 (2)
C80—N1	1.328 (3)	N4—CA4	1.452 (2)
N1—CA1	1.461 (3)	N4—H04	0.849 (16)
N1—H01	0.888 (18)	CA4—CL4	1.526 (3)
CA1—CL1	1.528 (3)	CA4—C4	1.525 (3)
CA1—CR1	1.537 (3)	CA4—HA4	0.9800
CA1—C1	1.533 (3)	CL4—HL14	0.9600
CL1—HL11	0.9600	CL4—HL24	0.9600
CL1—HL21	0.9600	CL4—HL34	0.9600
CL1—HL31	0.9600	C4—O4	1.204 (2)
CR1—HR11	0.9600	C4—O5	1.316 (2)
CR1—HR21	0.9600	O5—C15	1.489 (2)
CR1—HR31	0.9600	C15—C35	1.496 (4)
C1—O1	1.224 (2)	C15—C25	1.490 (4)
C1—N2	1.344 (2)	C15—C45	1.503 (4)
N2—CA2	1.475 (2)	C25—H2A5	0.9600
N2—H02	0.871 (15)	C25—H2B5	0.9600
CA2—CL2	1.521 (3)	C25—H2C5	0.9600
CA2—CR2	1.527 (3)	C35—H3A5	0.9600
CA2—C2	1.551 (3)	C35—H3B5	0.9600
CG2—HL12	0.9600	C35—H3C5	0.9600
CG2—HL22	0.9600	C45—H4A5	0.9600
CG2—HL32	0.9600	C45—H4B5	0.9600
CR2—HR12	0.9600	C45—H4C5	0.9600

C60—C10—C20	119.1 (4)	CA2—CL2—HL32	109.5
C60—C10—C70	117.7 (4)	HL12—CL2—HL32	109.5
C20—C10—C70	123.2 (3)	HL22—CL2—HL32	109.5
C30—C20—C10	121.9 (3)	O2—C2—N3	124.44 (18)
C30—C20—H20	119.1	O2—C2—CA2	120.30 (17)
C10—C20—H20	119.1	N3—C2—CA2	115.08 (15)
C20—C30—C40	119.9 (5)	C2—N3—CA3	125.08 (16)
C20—C30—H30	120.1	C2—N3—H03	117.5 (14)
C40—C30—H30	120.1	CA3—N3—H03	117.1 (14)
C30—C40—C50	118.8 (6)	N3—CA3—CL3	111.98 (17)
C30—C40—H40	120.6	N3—CA3—C3	112.07 (14)
C50—C40—H40	120.6	C3—CA3—CL3	109.77 (16)
C60—C50—C40	121.6 (5)	CL3—CA3—CR3	110.13 (19)
C60—C50—H50	119.2	CA3—CR3—HR13	109.5
C40—C50—H50	119.2	CA3—CR3—HR23	109.5
C50—C60—C10	118.7 (5)	HR13—CR3—HR23	109.5
C50—C60—H60	120.7	CA3—CR3—HR33	109.5
C10—C60—H60	120.7	HR13—CR3—HR33	109.5
O00—C70—C10	113.2 (2)	HR23—CR3—HR33	109.5
O00—C70—H7A0	108.9	CA3—CL3—HL13	109.5

C10—C70—H7A0	108.9	CA3—CL3—HL23	109.5
O00—C70—H7B0	108.9	HL13—CL3—HL23	109.5
C10—C70—H7B0	108.9	CA3—CL3—HL33	109.5
H7A0—C70—H7B0	107.8	HL13—CL3—HL33	109.5
C80—O00—C70	115.51 (19)	HL23—CL3—HL33	109.5
O80—C80—N1	125.1 (2)	O3—C3—N4	122.05 (17)
O80—C80—O00	123.7 (2)	O3—C3—CA3	119.40 (17)
N1—C80—O00	111.22 (17)	N4—C3—CA3	118.30 (15)
C80—N1—CA1	120.98 (16)	C3—N4—CA4	120.71 (14)
C80—N1—H01	122 (2)	C3—N4—H04	126.8 (16)
CA1—N1—H01	117 (2)	CA4—N4—H04	112.4 (17)
N1—CA1—CR1	107.73 (16)	N4—CA4—CL4	110.86 (14)
N1—CA1—C1	110.98 (15)	N4—CA4—C4	112.00 (15)
C1—CA1—CR1	107.06 (17)	CL4—CA4—C4	108.99 (15)
N2—CA2—CR2	107.58 (14)	N4—CA4—HA4	108.3
C2—CA2—CR2	107.19 (16)	CL4—CA4—HA4	108.3
N3—CA3—CR3	107.07 (17)	C4—CA4—HA4	108.3
C3—CA3—CR3	105.60 (17)	CL4—CL4—HL14	109.5
N1—CA1—CL1	111.44 (18)	CL4—CL4—HL24	109.5
CR1—CA1—CL1	109.90 (18)	HL14—CL4—HL24	109.5
C1—CA1—CL1	109.61 (14)	CA4—CL4—HL34	109.5
CA1—CL1—HL11	109.5	HL14—CL4—HL34	109.5
CA1—CL1—HL21	109.5	HL24—CL4—HL34	109.5
HL11—CL1—HL21	109.5	O4—C4—O5	125.77 (17)
CA1—CL1—HL31	109.5	O4—C4—CA4	122.39 (17)
HL11—CL1—HL31	109.5	O5—C4—CA4	111.79 (14)
HL21—CL1—HL31	109.5	C4—O5—C15	123.23 (16)
CA1—CR1—HR11	109.5	O5—C15—C35	103.25 (18)
CA1—CR1—HR21	109.5	O5—C15—C25	109.1 (2)
HR11—CR1—HR21	109.5	C35—C15—C25	113.5 (3)
CA1—CR1—HR31	109.5	O5—C15—C45	108.9 (2)
HR11—CR1—HR31	109.5	C35—C15—C45	110.7 (3)
HR21—CR1—HR31	109.5	C25—C15—C45	111.0 (3)
O1—C1—N2	122.64 (17)	C15—C25—H2A5	109.5
O1—C1—CA1	120.60 (16)	C15—C25—H2B5	109.5
N2—C1—CA1	116.71 (14)	H2A5—C25—H2B5	109.5
C1—N2—CA2	122.16 (14)	C15—C25—H2C5	109.5
C1—N2—H02	118.2 (16)	H2A5—C25—H2C5	109.5
CA2—N2—H02	118.9 (16)	H2B5—C25—H2C5	109.5
N2—CA2—CL2	109.97 (17)	C15—C35—H3A5	109.5
CR2—CA2—CL2	111.13 (17)	C15—C35—H3B5	109.5
N2—CA2—C2	110.79 (14)	H3A5—C35—H3B5	109.5
C2—CA2—CL2	110.12 (17)	C15—C35—H3C5	109.5
CA2—CR2—HR12	109.5	H3A5—C35—H3C5	109.5
CA2—CR2—HR22	109.5	H3B5—C35—H3C5	109.5
HR12—CR2—HR22	109.5	C15—C45—H4A5	109.5
CA2—CR2—HR32	109.5	C15—C45—H4B5	109.5
HR12—CR2—HR32	109.5	H4A5—C45—H4B5	109.5
HR22—CR2—HR32	109.5	C15—C45—H4C5	109.5

CA2—CL2—HL12	109.5	H4A5—C45—H4C5	109.5
CA2—CL2—HL22	109.5	H4B5—C45—H4C5	109.5
HL12—CL2—HL22	109.5		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H03···O80	0.86 (2)	2.31 (2)	3.117 (2)	156 (2)
N4—H04···O1	0.85 (2)	2.22 (2)	3.059 (2)	169 (2)
N1—H01···O3^{i}	0.89 (2)	2.05 (2)	2.929 (2)	171 (3)
N2—H02···O4^{i}	0.87 (2)	2.27 (2)	3.121 (2)	165 (2)

Symmetry code: (i) −*x*+3/2, −*y*+1, *z*+1/2.

Backbone torsion angles (°)

ω(z)	O00—C80—N1—CA1	173.8 (2)
φ(1)	C80—N1—CA1—C1	54.8 (3)
ψ(1)	N1—CA1—C1—N2	36.3 (2)
ω(1)	CA1—C1—N2—CA2	173.2 (2)
φ(2)	C1—N2—CA2—C2	54.2 (2)
ψ(2)	N2—CA2—C2—N3	39.4 (2)
ω(2)	CA2—C2—N3—CA3	172.5 (2)
φ(3)	C2—N3—CA3—C3	75.7 (2)
ψ(3)	N3—CA3—C3—N4	15.5 (3)
ω(3)	CA3—C3—N4—CA4	165.9 (2)
φ(4)	C3—N4—CA4—C4	-69.2 (2)
ψ(4)	N4—CA4—C4—O5	-38.3 (2)
ω(4)	C4A—C4—O5—C15	-176.0 (2)