

Crystal structure of *N*-(*tert*-butoxycarbonyl)-phenylalanyldehydroalanine isopropyl ester (Boc–Phe– Δ Ala–OiPr)

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Keywords: crystal structure; dehydro peptides; α,β -dehydroamino acids; dehydroalanine; herringbone packing

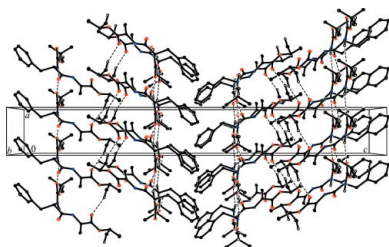
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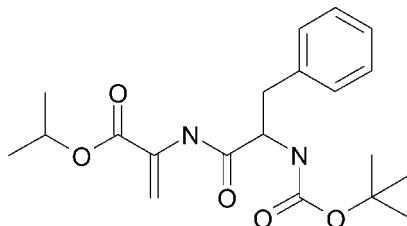
In the title compound, the dehydrodipeptide (Boc–Phe– Δ Ala–OiPr, $C_{20}H_{28}N_2O_5$), the molecule has a *trans* conformation of the *N*-methylamide group. The geometry of the dehydroalanine moiety is to some extent different from those usually found in simple peptides, indicating conjugation between the $H_2C=C$ group and the peptide bond. The bond angles around dehydroalanine have unusually high values due to the steric hindrance, the same interaction influencing the slight distortion from planarity of the dehydroalanine. The molecule is stabilized by intramolecular interactions between the isopropyl group and the N atoms of the peptide main chain. In the crystal, an $N-H\cdots O$ hydrogen bond links the molecules into ribbons, giving a herringbone head-to-head packing arrangement extending along the [100] direction. In the stacks, the molecules are linked by weak $C-H\cdots O$ hydrogen-bonding associations.

1. Chemical context

Dehydropeptides are a class of compounds containing at least one residue of an α,β -dehydroamino acid. These compounds are of interest in many fields of science because of their structural and chemical properties. Dehydroamino acids are found in natural products (Bonauer *et al.*, 2006). One of the important classes of natural bacteriocins are lantibiotics (*e.g.* nisin, subtilin), which are biosynthesized by Gram-positive bacteria. The unsaturated amino acid is introduced into the structure of these polycyclic peptides by post-translational modification of selected serine and threonine residues (Willey & van der Donk, 2007). The development of synthetic methods for dehydropeptide preparation has resulted in a search for practical applications for these compounds. The dehydroamino acids are considered to be building blocks for the synthesis of new non-proteinogenic amino acids (Ferreira *et al.*, 2010). The double bond of the dehydropeptide can be used in different types of reaction, namely: addition of nucleophiles (Ferreira *et al.*, 2001); alkylation, providing α,α -disubstituted amino acids (Miyabe *et al.*, 2005); Rh-catalysed conjugate addition of arylboronic acids providing β -aryl-alanine derivatives (Ferreira *et al.*, 2013); Cu-catalysed asymmetric hydroboration as a step in the preparation of β -hydroxy- α -amino acid derivatives being then used for the preparation of chiral drugs and bioactive molecules (He *et al.*, 2014). Compounds containing dehydroamino acid residues also are considered to be inhibitors of enzymes (Makowski *et al.*, 2001; Latajka *et al.*, 2006, 2008). They are more resistant towards proteolytic enzymes than saturated analogues



(English & Stammer, 1978). The presence of sp^2 hybridized carbon atoms in structures of dehydropolypeptides and the coupling of π -electrons between double and peptide bonds entail a number of structural consequences in the conformation of the peptides, and make them excellent subjects for conformational study (e.g. Jewgiński *et al.*, 2014, 2013; Demizu *et al.*, 2010; Lisowski *et al.*, 2008). In this paper, the preparation of the title compound, *N*-(*tert*-butoxycarbonyl)-phenylalanyldehydroalanine isopropyl ester and its structure determination by single-crystal X-ray crystallographic methods are presented.



2. Structural commentary

The molecular structure of *N*-(*tert*-butoxycarbonyl)phenylalanyldehydroalanine isopropyl ester (Boc-Phe- Δ Ala-OiPr, $C_{20}H_{28}N_2O_5$) is shown in Fig. 1. The molecule has a *trans*-conformation of the *N*-methylamide group. The geometry of the dehydroalanine is to some extent different from those usually found in simple peptides (Pauling, 1960). In particular, the N19–C20 bond length is shorter while C17–N19 is longer [1.402 (3) Å and 1.354 (3) Å, respectively]. This is in excellent agreement with the values reported for *N*-acetyldehydroalanine (Ajó *et al.*, 1979), *N*-acetylbis-(dehydrophenylalanyl)-glycine (Pieroni *et al.* 1975) and *N*-acetyldehydrodimethylamide (Rzeszotarska *et al.*, 2002) and seems to be typical for α , β -unsaturated peptide systems (Jain & Chauhan, 1996). This indicates conjugation between the $H_2C=C$ group

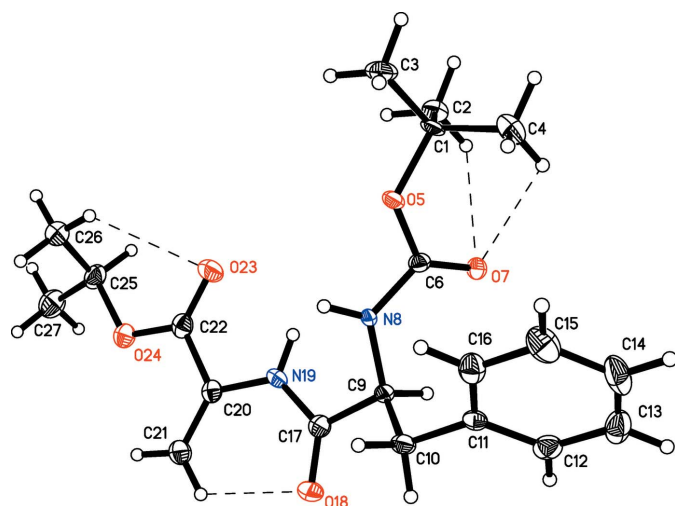


Figure 1
The molecular structure of *N*-(*tert*-butoxycarbonyl)phenylalanyldehydroalanine isopropyl ester (Boc-Phe- Δ Ala-OiPr) showing 50% displacement ellipsoids. Intramolecular C–H...O interactions are shown as dashed lines.

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N8–H8A...O7 ⁱ	0.88	2.21	2.952 (2)	141
C3–H3C...O18 ⁱⁱ	0.98	2.51	3.423 (3)	155
C21–H21A...O18	0.95	2.27	2.869 (3)	120
C26–H26B...O23 ⁱ	0.98	2.52	3.462 (3)	162

Symmetry codes: (i) $x - 1, y, z$; (ii) $x + 1, y - 1, z$.

and the peptide bond. The valance angles around dehydroalanine have unusually large values [C21–C20–N19 = 126.9 (2), C17–N19–C20 = 126.8 (2) and O18–C17–N19 = 123.5 (2)°] due to the steric hindrance between atoms C21 and O18. The same interaction influences the slight distortion from planarity of the dehydroalanine moiety. The ω , φ and ψ torsion angles (C9–C17–N19–C20, C17–N19–C20–C22 and N19–C20–C22–O24, respectively) of the dehydroalanine residue are -166.9 (2), 175.1 (2) and 178.0 (2)°. The geometries of the phenylalanine and the protecting groups are normal. There are four intramolecular C–H...O close contacts but three of them have a $D-H\cdots A$ angle of less than 120°.

3. Supramolecular features

In the crystal, strong intermolecular N8–H...O7ⁱ hydrogen bonds (Table 1) link the molecules, giving a herringbone head-to-head packing arrangement, forming ribbons which extend along [100] (Fig. 2). The ribbon structures are consolidated by weak intra-chain C–H...O hydrogen-bonding interactions.

4. Synthesis and crystallization

The dehydrideptide was obtained by condensation of *N*-protected phenylalanylamine with pyruvic acid in the presence of *p*-toluenesulfonic acid (Makowski *et al.*, 1985). The esterification of the dehydrideptide was performed using the methodology described by Cossec *et al.* (2008). For this

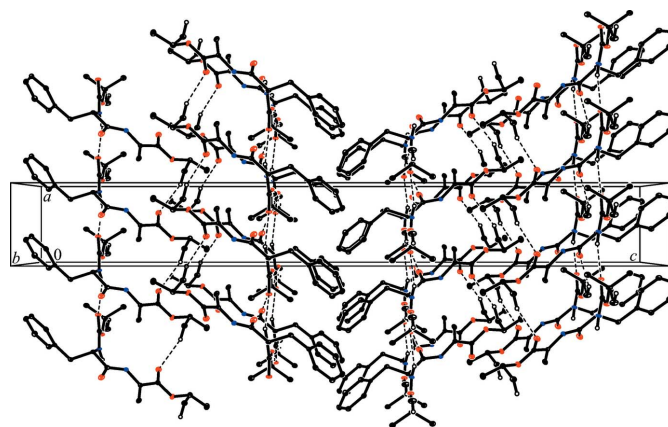


Figure 2
The packing diagram of the title compound, viewed along the b axis, showing the intermolecular hydrogen-bonding scheme (dashed lines).

purpose 0.669 g (2 mM) of Boc-Phe- Δ Ala was dissolved in 5 ml of methanol and calcium carbonate 0.329 g (1 mM) was added. The mixture was stirred for one h at room temperature, after which the solvent was evaporated. The residue was dissolved in 7 ml of DMF and isopropyl iodide (1.01 ml, 10 mM) was added in portions to the stirred mixture at room temperature during the reaction, the progress of which was monitored by thin-layer chromatography, using 5% methanol in chloroform as eluent. After completion of the reaction, the solvent was evaporated and the oily residue was dissolved in ethyl acetate and washed consecutively with: 1 M HCl, saturated KHCO_3 , 0.1 M $\text{Na}_2\text{S}_2\text{O}_3$ and brine. The organic layer was dried over anhydrous MgSO_4 and the title compound was obtained in 81% yield (m.p. = 367–369 K). Recrystallization was performed using mixture of diethyl ether and hexane.

^1H NMR (400 MHz, DMSO) δ 1.26 (*d*, $J = 6.2$ Hz, 6H, 2 \times CH_3 Pr), 1.30 (*s*, 9H, CH_3 *t*-Boc), 2.76 (*dd*, ABX system, $J = 13.6$, 10.8 Hz, 1H, CH_AH_B Phe), 3.02 (*dd*, ABX system, $J = 13.6$, 3.9 Hz, 1H, CH_AH_B Phe), 4.27–4.39 (*m*, 1H, CH Phe), 5.01 (hept, $J = 6.2$ Hz, 1H, CH Pr), 5.70 (*s*, 1H, $\text{C}=\text{CH}_A\text{H}_B$), 6.23 (*s*, 1H, $\text{C}=\text{CH}_A\text{H}_B$), 7.15–7.36 (*m*, 6H, ArH Phe overlapped with NH Phe), δ 9.30 (*s*, 1H, $\text{NH}_{\Delta\text{Ala}}$). ^{13}C NMR (101 MHz, DMSO) δ 21.43, 28.10, 36.63, 56.34, 69.40, 78.41, 108.65, 126.29, 128.07, 129.25, 132.71, 138.03, 155.53, 162.81, 171.53. IR (KBr, cm^{-1}) 3600–2800 broad (H-bonding), 1715 ($\text{C}=\text{O}_{\text{ester}}$), 1700 ($\text{C}=\text{O}_{\text{urethane}}$), 1690 IAB ($\text{C}=\text{O}_{\text{amide}}$), 1632 ($\text{C}=\text{C}$), 1526 IIAB (C–N and N–H), 1317 (CO–N–C and N–(C=C)–CO), 1196 and 1166 (C–O–C), 896 ($=\text{CH}_2$).

5. Refinement details

Crystal data, data collection and structure refinement details are summarized in Table 2. All hydrogen atoms were positioned geometrically and treated as riding on their parent atoms with $\text{N–H} = 0.88$ Å and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$, $\text{C–H}_{\text{aromatic}} = 0.95$ Å and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$, $\text{C–H}_{\text{methyl}} = 0.98$ Å and $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$; $\text{C–H}_{\text{methylene}} = 0.99$ Å or $\text{C–H}_{\text{methine}} = 0.95$ Å and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$. Although not definitive, the absolute structure factor (Parsons *et al.*, 2013) with the C9(*S*) configuration, was $-0.1(6)$ for 1095 Friedel pairs.

Acknowledgements

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References

- Ajó, D., Granozzi, G., Tondello, E., Del Pra, A. & Zanotti, G. (1979). *J. Chem. Soc. Perkin Trans. 2*, pp. 927–929.
Bonauer, C., Walenzyk, T. & König, B. (2006). *Synthesis*, pp. 1–20.

Table 2

Experimental details.

Crystal data	
Chemical formula	$\text{C}_{20}\text{H}_{28}\text{N}_2\text{O}_5$
M_r	376.44
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	100
a, b, c (Å)	5.2123 (2), 9.5031 (3), 41.3363 (17)
V (Å ³)	2047.51 (13)
Z	4
Radiation type	Mo $K\alpha$
μ (mm ⁻¹)	0.09
Crystal size (mm)	$0.33 \times 0.18 \times 0.14$
Data collection	
Diffraction	Oxford Diffraction Xcalibur CCD
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	14003, 4025, 3235
R_{int}	0.046
$(\sin \theta/\lambda)_{\text{max}}$ (Å ⁻¹)	0.617
Refinement	
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.046, 0.079, 0.98
No. of reflections	4025
No. of parameters	244
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$ (e Å ⁻³)	0.22, -0.22
Absolute structure	Flack x determined using 1095 quotients $[(I^-)-(I^+)]/[(I^-)+(I^+)]$ (Parsons <i>et al.</i> , 2013)
Absolute structure parameter	-0.1 (6)

Computer programs: *CrysAlis CCD* and *CrysAlis RED* (Oxford Diffraction, 2008), *SHELXL2014* and *SHELXTL* (Sheldrick, 2008).

- Cossec, B., Cosnier, F. & Burgart, M. (2008). *Molecules*, **13**, 2394–2407.
Demizu, Y., Yamagata, N., Sato, Y., Doi, M., Tanaka, M., Okuda, H. & Kurihara, M. (2010). *J. Pept. Sci.* **16**, 153–158.
English, M. L. & Stammer, C. H. (1978). *Biochem. Biophys. Res. Commun.* **83**, 1464–1467.
Ferreira, P. M. T., Maia, H. L. S., Monteiro, L. S. & Sacramento, J. (2001). *J. Chem. Soc. Perkin Trans. 1*, pp. 3167–3173.
Ferreira, P. M. T., Monteiro, L. S. & Pereira, G. (2010). *Amino Acids*, **39**, 499–513.
Ferreira, P. M. T., Monteiro, L. S., Pereira, G., Castanheira, E. M. S. & Frost, C. G. (2013). *Eur. J. Org. Chem.* **3**, 550–556.
He, Z. T., Zhao, Y. S., Tian, P., Wang, C. C., Dong, H. Q. & Lin, G. Q. (2014). *Org. Lett.* **16**, 1426–1429.
Jain, R. & Chauhan, V. S. (1996). *Biopolymers*, **40**, 105–119.
Jewgiński, M., Krzciuk-Gula, J., Makowski, M., Latajka, R. & Kafarski, P. (2014). *Beilstein J. Org. Chem.* **10**, 660–666.
Jewgiński, M., Latajka, R., Krezel, A., Haremza, K., Makowski, M. & Kafarski, P. (2013). *J. Mol. Struct.* **1035**, 129–139.
Latajka, R., Jewgiński, M., Makowski, M., Pawełczak, M., Huber, T., Sewald, N. & Kafarski, P. (2008). *J. Pept. Sci.* **14**, 1084–1095.
Latajka, R., Makowski, M., Jewgiński, M., Pawełczak, M., Koroniak, H. & Kafarski, P. (2006). *New J. Chem.* **30**, 1009–1018.
Lisowski, M., Latajka, R., Picur, B., Lis, T., Bryndal, I., Rospenk, M., Makowski, M. & Kafarski, P. (2008). *Biopolymers*, **89**, 220–234.
Makowski, M., Pawełczak, M., Latajka, R., Nowak, K. & Kafarski, P. (2001). *J. Pept. Sci.* **7**, 141–145.
Makowski, M., Rzeszutarska, B., Kubica, R. & Pietrzyński, G. (1985). *Liebigs Ann. Chem.* **5**, 893–900.
Miyabe, H., Asada, R. & Takemoto, Y. (2005). *Tetrahedron*, **61**, 385–393.
Oxford Diffraction (2008). *CrysAlis PRO* and *CrysAlis RED*. Oxford Diffraction Ltd., Yarnton, England.
Parsons, S., Flack, H. D. & Wagner, T. (2013). *Acta Cryst. B* **69**, 249–259.

- Pauling, L. (1960). *The Nature of the Chemical Bond*, p. 282. New York: Cornell University Press.
- Pieroni, O., Montagnoli, G., Fissi, A., Merlino, S. & Ciardelli, F. (1975). *J. Am. Chem. Soc.* **97**, 6820–6826.
- Rzeszotarska, B., Siodlak, D., Broda, M. A., Dybała, I. & Koziol, A. E. (2002). *J. Pept. Res.* **59**, 79–89.
- Sheldrick, G. M. (2008). *Acta Cryst. A* **64**, 112–122.
- Willey, J. M. & van der Donk, W. A. (2007). *Annu. Rev. Microbiol.* **61**, 477–501.

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Computing details

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2008); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2008); data reduction: *CrysAlis RED* (Oxford Diffraction, 2008); program(s) used to solve structure: *SHELXL2014* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXL2014* (Sheldrick, 2008).

N-(*tert*-Butoxycarbonyl)phenylalanyldehydroalanine isopropyl ester

Crystal data

$C_{20}H_{28}N_2O_5$	$D_x = 1.221 \text{ Mg m}^{-3}$
$M_r = 376.44$	Melting point = 367–369 K
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
$a = 5.2123 (2) \text{ \AA}$	Cell parameters from 4025 reflections
$b = 9.5031 (3) \text{ \AA}$	$\theta = 3.3\text{--}26.0^\circ$
$c = 41.3363 (17) \text{ \AA}$	$\mu = 0.09 \text{ mm}^{-1}$
$V = 2047.51 (13) \text{ \AA}^3$	$T = 100 \text{ K}$
$Z = 4$	Irregular, colourless
$F(000) = 808$	$0.33 \times 0.18 \times 0.14 \text{ mm}$

Data collection

Oxford Diffraction Xcalibur CCD diffractometer	3235 reflections with $I > 2\sigma(I)$
Radiation source: fine-focus sealed tube	$R_{\text{int}} = 0.046$
Graphite monochromator	$\theta_{\text{max}} = 26.0^\circ$, $\theta_{\text{min}} = 3.3^\circ$
ω scans	$h = -3 \rightarrow 6$
14003 measured reflections	$k = -11 \rightarrow 11$
4025 independent reflections	$l = -50 \rightarrow 50$

Refinement

Refinement on F^2	H-atom parameters constrained
Least-squares matrix: full	$w = 1/[\sigma^2(F_o^2) + (0.0354P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.046$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.079$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 0.98$	$\Delta\rho_{\text{max}} = 0.22 \text{ e \AA}^{-3}$
4025 reflections	$\Delta\rho_{\text{min}} = -0.22 \text{ e \AA}^{-3}$
244 parameters	Absolute structure: Flack x determined using
0 restraints	1095 quotients $[(I^+) - (I^-)] / [(I^+) + (I^-)]$ (Parsons <i>et al.</i> , 2013)
Hydrogen site location: inferred from neighbouring sites	Absolute structure parameter: $-0.1 (6)$

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 (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	1.2709 (4)	0.0969 (2)	0.10948 (7)	0.0184 (6)
C2	1.4195 (5)	0.1063 (3)	0.14083 (7)	0.0249 (7)
H2A	1.5204	0.1933	0.1411	0.037*
H2B	1.5348	0.0252	0.1427	0.037*
H2C	1.2995	0.1065	0.1591	0.037*
C3	1.1120 (5)	-0.0366 (3)	0.10835 (8)	0.0325 (7)
H3A	1.0176	-0.0406	0.0879	0.049*
H3B	0.9903	-0.0369	0.1264	0.049*
H3C	1.2254	-0.1185	0.1100	0.049*
C4	1.4374 (5)	0.1068 (3)	0.07954 (7)	0.0264 (7)
H4A	1.5397	0.1932	0.0804	0.040*
H4B	1.3282	0.1085	0.0602	0.040*
H4C	1.5520	0.0252	0.0786	0.040*
O5	1.0713 (3)	0.20736 (16)	0.10856 (4)	0.0194 (4)
C6	1.1322 (5)	0.3446 (2)	0.10987 (6)	0.0151 (5)
O7	1.3475 (3)	0.39442 (16)	0.10970 (4)	0.0188 (4)
N8	0.9116 (3)	0.4203 (2)	0.11214 (5)	0.0148 (5)
H8A	0.7675	0.3751	0.1160	0.018*
C9	0.9025 (4)	0.5718 (2)	0.10849 (6)	0.0150 (5)
H9A	1.0784	0.6105	0.1122	0.018*
C10	0.8141 (5)	0.6145 (3)	0.07443 (6)	0.0176 (6)
H10A	0.6402	0.5761	0.0707	0.021*
H10B	0.8020	0.7184	0.0734	0.021*
C11	0.9882 (5)	0.5648 (3)	0.04781 (6)	0.0167 (6)
C12	1.1944 (5)	0.6462 (3)	0.03752 (6)	0.0231 (6)
H12A	1.2281	0.7335	0.0479	0.028*
C13	1.3509 (5)	0.6026 (3)	0.01250 (7)	0.0312 (7)
H13A	1.4897	0.6601	0.0056	0.037*
C14	1.3057 (6)	0.4757 (3)	-0.00244 (7)	0.0338 (8)
H14A	1.4134	0.4455	-0.0196	0.041*
C15	1.1046 (5)	0.3924 (3)	0.00748 (7)	0.0317 (7)
H15A	1.0739	0.3046	-0.0028	0.038*
C16	0.9473 (5)	0.4367 (3)	0.03241 (6)	0.0244 (7)
H16A	0.8088	0.3787	0.0391	0.029*
C17	0.7185 (5)	0.6377 (3)	0.13324 (6)	0.0177 (6)
O18	0.6189 (4)	0.75177 (19)	0.12844 (4)	0.0266 (5)
N19	0.6785 (4)	0.5605 (2)	0.16029 (5)	0.0168 (5)
H19A	0.7841	0.4897	0.1636	0.020*
C20	0.4865 (4)	0.5814 (3)	0.18356 (6)	0.0163 (6)

C21	0.3165 (5)	0.6849 (3)	0.18436 (6)	0.0233 (6)
H21A	0.3171	0.7549	0.1679	0.028*
H21B	0.1940	0.6892	0.2013	0.028*
C22	0.4947 (5)	0.4660 (3)	0.20809 (6)	0.0197 (6)
O23	0.6457 (4)	0.36963 (19)	0.20637 (4)	0.0282 (5)
O24	0.3215 (3)	0.48235 (17)	0.23152 (4)	0.0232 (4)
C25	0.3210 (5)	0.3753 (3)	0.25720 (6)	0.0249 (6)
H25A	0.5018	0.3520	0.2633	0.030*
C26	0.1889 (6)	0.2446 (3)	0.24504 (6)	0.0274 (7)
H26A	0.2849	0.2060	0.2267	0.041*
H26B	0.0143	0.2682	0.2381	0.041*
H26C	0.1814	0.1746	0.2624	0.041*
C27	0.1881 (6)	0.4430 (3)	0.28559 (6)	0.0323 (7)
H27A	0.2836	0.5269	0.2923	0.049*
H27B	0.1807	0.3761	0.3036	0.049*
H27C	0.0135	0.4699	0.2793	0.049*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0114 (11)	0.0108 (13)	0.0330 (15)	0.0059 (10)	-0.0014 (12)	-0.0004 (12)
C2	0.0222 (14)	0.0209 (15)	0.0315 (16)	0.0048 (13)	0.0001 (13)	0.0041 (13)
C3	0.0235 (14)	0.0132 (13)	0.061 (2)	0.0028 (12)	-0.0025 (16)	0.0000 (14)
C4	0.0188 (14)	0.0302 (17)	0.0301 (16)	0.0049 (14)	-0.0019 (12)	-0.0077 (14)
O5	0.0107 (9)	0.0111 (9)	0.0364 (11)	0.0019 (7)	0.0009 (9)	-0.0001 (8)
C6	0.0163 (13)	0.0113 (12)	0.0177 (14)	-0.0004 (11)	-0.0003 (12)	-0.0001 (11)
O7	0.0097 (8)	0.0159 (9)	0.0308 (10)	-0.0025 (8)	0.0001 (8)	0.0022 (8)
N8	0.0084 (9)	0.0100 (10)	0.0261 (12)	0.0007 (8)	0.0041 (9)	0.0023 (10)
C9	0.0126 (11)	0.0106 (12)	0.0218 (14)	-0.0004 (10)	0.0007 (11)	0.0011 (12)
C10	0.0163 (12)	0.0147 (13)	0.0218 (14)	0.0026 (12)	-0.0026 (12)	0.0014 (11)
C11	0.0146 (12)	0.0189 (14)	0.0167 (13)	0.0044 (12)	-0.0036 (11)	0.0053 (12)
C12	0.0219 (14)	0.0228 (15)	0.0246 (15)	0.0011 (14)	-0.0054 (14)	0.0055 (12)
C13	0.0203 (14)	0.047 (2)	0.0261 (16)	0.0016 (16)	0.0003 (14)	0.0160 (15)
C14	0.0245 (15)	0.056 (2)	0.0208 (16)	0.0117 (17)	0.0058 (13)	0.0011 (15)
C15	0.0312 (16)	0.0375 (19)	0.0265 (16)	0.0061 (16)	0.0001 (14)	-0.0093 (14)
C16	0.0197 (14)	0.0281 (16)	0.0254 (16)	-0.0011 (13)	0.0002 (12)	0.0002 (13)
C17	0.0154 (13)	0.0148 (14)	0.0228 (15)	-0.0031 (12)	-0.0022 (12)	-0.0021 (12)
O18	0.0284 (11)	0.0159 (10)	0.0356 (12)	0.0083 (9)	0.0094 (9)	0.0026 (9)
N19	0.0135 (10)	0.0170 (11)	0.0198 (12)	0.0047 (10)	0.0000 (9)	0.0016 (10)
C20	0.0149 (12)	0.0171 (14)	0.0168 (13)	-0.0033 (12)	-0.0017 (11)	-0.0029 (12)
C21	0.0232 (14)	0.0245 (15)	0.0221 (15)	0.0037 (13)	0.0067 (14)	0.0011 (12)
C22	0.0165 (13)	0.0235 (16)	0.0193 (14)	-0.0037 (12)	-0.0031 (12)	0.0003 (12)
O23	0.0242 (10)	0.0282 (11)	0.0322 (11)	0.0096 (10)	0.0027 (10)	0.0085 (9)
O24	0.0231 (10)	0.0256 (11)	0.0207 (10)	0.0009 (9)	0.0058 (9)	0.0035 (8)
C25	0.0228 (14)	0.0280 (15)	0.0238 (15)	-0.0029 (15)	0.0007 (13)	0.0102 (13)
C26	0.0238 (15)	0.0253 (15)	0.0333 (16)	0.0004 (14)	0.0023 (14)	0.0057 (13)
C27	0.0368 (17)	0.0341 (18)	0.0262 (16)	-0.0036 (16)	0.0039 (14)	0.0025 (14)

Geometric parameters (Å, °)

C1—O5	1.478 (3)	C13—C14	1.375 (4)
C1—C2	1.513 (4)	C13—H13A	0.9500
C1—C4	1.514 (4)	C14—C15	1.376 (4)
C1—C3	1.516 (3)	C14—H14A	0.9500
C2—H2A	0.9800	C15—C16	1.382 (4)
C2—H2B	0.9800	C15—H15A	0.9500
C2—H2C	0.9800	C16—H16A	0.9500
C3—H3A	0.9800	C17—O18	1.218 (3)
C3—H3B	0.9800	C17—N19	1.354 (3)
C3—H3C	0.9800	N19—C20	1.402 (3)
C4—H4A	0.9800	N19—H19A	0.8800
C4—H4B	0.9800	C20—C21	1.324 (3)
C4—H4C	0.9800	C20—C22	1.494 (3)
O5—C6	1.343 (3)	C21—H21A	0.9500
C6—O7	1.218 (3)	C21—H21B	0.9500
C6—N8	1.360 (3)	C22—O23	1.209 (3)
N8—C9	1.448 (3)	C22—O24	1.333 (3)
N8—H8A	0.8800	O24—C25	1.470 (3)
C9—C10	1.536 (3)	C25—C26	1.506 (4)
C9—C17	1.536 (3)	C25—C27	1.507 (4)
C9—H9A	1.0000	C25—H25A	1.0000
C10—C11	1.503 (3)	C26—H26A	0.9800
C10—H10A	0.9900	C26—H26B	0.9800
C10—H10B	0.9900	C26—H26C	0.9800
C11—C16	1.390 (4)	C27—H27A	0.9800
C11—C12	1.391 (3)	C27—H27B	0.9800
C12—C13	1.381 (4)	C27—H27C	0.9800
C12—H12A	0.9500		
O5—C1—C2	109.9 (2)	C11—C12—H12A	119.4
O5—C1—C4	109.7 (2)	C14—C13—C12	119.9 (3)
C2—C1—C4	113.8 (2)	C14—C13—H13A	120.0
O5—C1—C3	102.06 (17)	C12—C13—H13A	120.0
C2—C1—C3	110.8 (2)	C13—C14—C15	120.1 (3)
C4—C1—C3	109.9 (2)	C13—C14—H14A	120.0
C1—C2—H2A	109.5	C15—C14—H14A	120.0
C1—C2—H2B	109.5	C14—C15—C16	119.9 (3)
H2A—C2—H2B	109.5	C14—C15—H15A	120.0
C1—C2—H2C	109.5	C16—C15—H15A	120.0
H2A—C2—H2C	109.5	C15—C16—C11	121.1 (3)
H2B—C2—H2C	109.5	C15—C16—H16A	119.4
C1—C3—H3A	109.5	C11—C16—H16A	119.4
C1—C3—H3B	109.5	O18—C17—N19	123.5 (2)
H3A—C3—H3B	109.5	O18—C17—C9	121.4 (2)
C1—C3—H3C	109.5	N19—C17—C9	115.1 (2)
H3A—C3—H3C	109.5	C17—N19—C20	126.8 (2)

H3B—C3—H3C	109.5	C17—N19—H19A	116.6
C1—C4—H4A	109.5	C20—N19—H19A	116.6
C1—C4—H4B	109.5	C21—C20—N19	126.9 (2)
H4A—C4—H4B	109.5	C21—C20—C22	123.2 (2)
C1—C4—H4C	109.5	N19—C20—C22	109.9 (2)
H4A—C4—H4C	109.5	C20—C21—H21A	120.0
H4B—C4—H4C	109.5	C20—C21—H21B	120.0
C6—O5—C1	121.48 (18)	H21A—C21—H21B	120.0
O7—C6—O5	126.5 (2)	O23—C22—O24	124.9 (2)
O7—C6—N8	125.0 (2)	O23—C22—C20	122.3 (2)
O5—C6—N8	108.46 (19)	O24—C22—C20	112.8 (2)
C6—N8—C9	123.12 (19)	C22—O24—C25	116.4 (2)
C6—N8—H8A	118.4	O24—C25—C26	109.3 (2)
C9—N8—H8A	118.4	O24—C25—C27	105.5 (2)
N8—C9—C10	111.61 (19)	C26—C25—C27	113.7 (2)
N8—C9—C17	110.89 (19)	O24—C25—H25A	109.4
C10—C9—C17	108.39 (19)	C26—C25—H25A	109.4
N8—C9—H9A	108.6	C27—C25—H25A	109.4
C10—C9—H9A	108.6	C25—C26—H26A	109.5
C17—C9—H9A	108.6	C25—C26—H26B	109.5
C11—C10—C9	114.0 (2)	H26A—C26—H26B	109.5
C11—C10—H10A	108.7	C25—C26—H26C	109.5
C9—C10—H10A	108.7	H26A—C26—H26C	109.5
C11—C10—H10B	108.7	H26B—C26—H26C	109.5
C9—C10—H10B	108.7	C25—C27—H27A	109.5
H10A—C10—H10B	107.6	C25—C27—H27B	109.5
C16—C11—C12	117.8 (2)	H27A—C27—H27B	109.5
C16—C11—C10	121.2 (2)	C25—C27—H27C	109.5
C12—C11—C10	121.0 (2)	H27A—C27—H27C	109.5
C13—C12—C11	121.2 (3)	H27B—C27—H27C	109.5
C13—C12—H12A	119.4		
C2—C1—O5—C6	60.9 (3)	C12—C11—C16—C15	-0.6 (4)
C4—C1—O5—C6	-65.0 (3)	C10—C11—C16—C15	178.7 (2)
C3—C1—O5—C6	178.5 (2)	N8—C9—C17—O18	-156.2 (2)
C1—O5—C6—O7	5.3 (4)	C10—C9—C17—O18	-33.4 (3)
C1—O5—C6—N8	-173.4 (2)	N8—C9—C17—N19	24.2 (3)
O7—C6—N8—C9	12.2 (4)	C10—C9—C17—N19	147.0 (2)
O5—C6—N8—C9	-169.1 (2)	O18—C17—N19—C20	13.5 (4)
C6—N8—C9—C10	99.5 (3)	C9—C17—N19—C20	-166.9 (2)
C6—N8—C9—C17	-139.5 (2)	C17—N19—C20—C21	-3.8 (4)
N8—C9—C10—C11	-61.4 (3)	C17—N19—C20—C22	175.1 (2)
C17—C9—C10—C11	176.2 (2)	C21—C20—C22—O23	177.4 (2)
C9—C10—C11—C16	91.7 (3)	N19—C20—C22—O23	-1.5 (3)
C9—C10—C11—C12	-89.0 (3)	C21—C20—C22—O24	-3.0 (3)
C16—C11—C12—C13	1.0 (4)	N19—C20—C22—O24	178.0 (2)
C10—C11—C12—C13	-178.3 (2)	O23—C22—O24—C25	1.1 (4)
C11—C12—C13—C14	-0.7 (4)	C20—C22—O24—C25	-178.4 (2)

C12—C13—C14—C15	0.1 (4)	C22—O24—C25—C26	-78.0 (3)
C13—C14—C15—C16	0.3 (4)	C22—O24—C25—C27	159.4 (2)
C14—C15—C16—C11	0.0 (4)		

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>
N8—H8 <i>A</i> ...O7 ⁱ	0.88	2.21	2.952 (2)	141
C2—H2 <i>A</i> ...O7	0.98	2.48	3.049 (3)	117
C3—H3 <i>C</i> ...O18 ⁱⁱ	0.98	2.51	3.423 (3)	155
C4—H4 <i>A</i> ...O7	0.98	2.47	3.040 (3)	116
C21—H21 <i>A</i> ...O18	0.95	2.27	2.869 (3)	120
C26—H26 <i>A</i> ...O23	0.98	2.58	3.104 (3)	114
C26—H26 <i>B</i> ...O23 ⁱ	0.98	2.52	3.462 (3)	162

Symmetry codes: (i) $x-1, y, z$; (ii) $x+1, y-1, z$.