Acta Cryst E STRUCTURE REPORTS

ISSN 1600-5368

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

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Received 3 November 2014
Accepted 17 November 2014

Edited by G. Smith, Queensland University of Technology, Australia

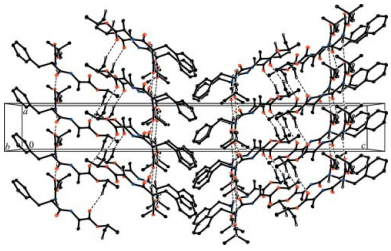
**Keywords**: crystal structure; dehydro peptides; α,β-dehydroamino acids; dehydroalanine; herringbone packing

**CCDC reference**: 1034604
**Supporting information**: this article has supporting information at journals.iucr.org/e

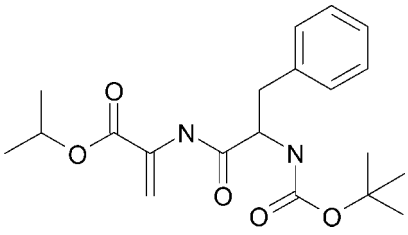
In the title compound, the dehydrodipeptide (Boc–Phe–ΔAla–OiPr, $C_{20}H_{28}N_2O_5$), the molecule has a *trans* conformation of the *N*-methylamide group. The geometry of the dehydroalanine moiety is to some extent different from those usually found in simple peptides, indicating conjugation between 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···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···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 dehydropeptides and the coupling of $\pi$-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–ΔAla–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*-acetylodehydrodimethylamide (Rzeszotarska *et al.*, 2002) and seems to be typical for $\alpha$, $\beta$-unsaturated peptide systems (Jain & Chauhan, 1996). This indicates conjugation between the $H_2C{=}C$ group 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 $\omega$, $\varphi$ and $\psi$ 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 phenylaniline and the protecting groups are normal. There are four intramolecular C—H···O close contacts but three of them have a $D$—H···$A$ angle of less than 120°.

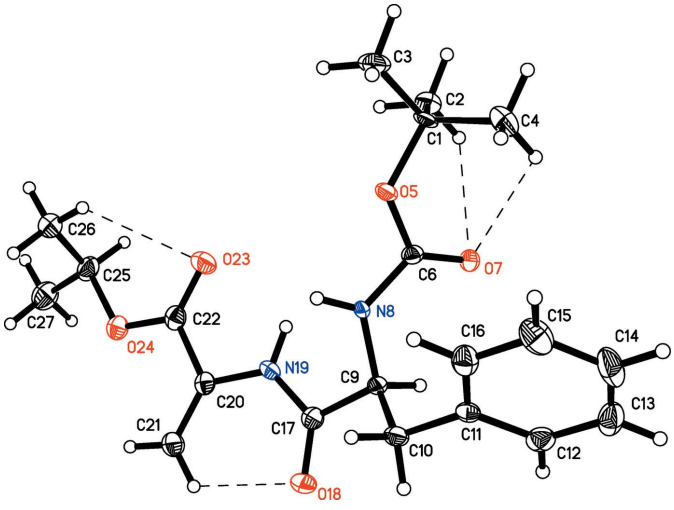



**Figure 1**
The molecular structure of *N*-(*tert*-butoxycarbonyl)phenylalanyldehydroalanine isopropyl ester (Boc–Phe–ΔAla–OiPr) showing 50% displacement ellipsoids. Intramolecular C—H···O interactions are shown as dashed lines.

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N8—H8$A$···O7$^{i}$ | 0.88 | 2.21 | 2.952 (2) | 141 |
| C3—H3$C$···O18$^{ii}$ | 0.98 | 2.51 | 3.423 (3) | 155 |
| C21—H21$A$···O18 | 0.95 | 2.27 | 2.869 (3) | 120 |
| C26—H26$B$···O23$^{i}$ | 0.98 | 2.52 | 3.462 (3) | 162 |

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

## 3. Supramolecular features

In the crystal, strong intermolecular N8—H···O7$^{i}$ 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 dehydrodipeptide was obtained by condensation of *N*-protected phenylalanylamide with pyruvic acid in the presence of *p*-toluenesulfonic acid (Makowski *et al.*, 1985). The esterification of the dehydrodipeptide was performed using the methodology described by Cossec *et al.* (2008). For this

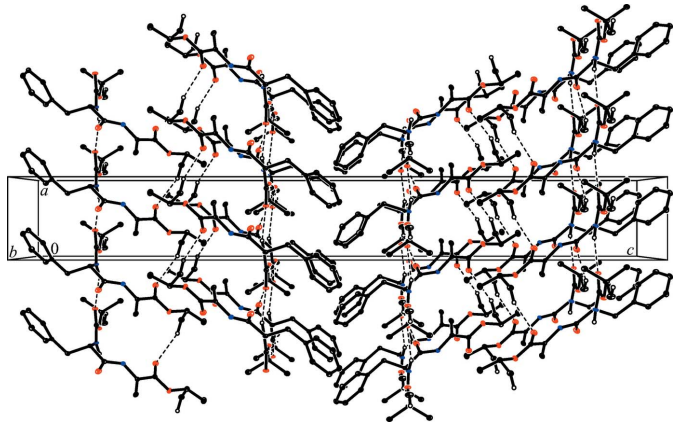



**Figure 2**
The packing diagram of the title compound, viewed along the *b* axis, showing the intermolecular hydrogen-bonding scheme (dashed lines).

purpose 0.669 g (2 m*M*) of Boc–Phe–ΔAla was dissolved in 5 ml of methanol and calcium carbonate 0.329 g (1 m*M*) 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 m*M*) 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* $Na_2S_2O_3$ 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.

$^1$H NMR (400 MHz, DMSO) $\delta$ 1.26 (*d*, *J* = 6.2 Hz, 6H, 2 × $CH_{3Pr^i}$), 1.30 (*s*, 9H, $CH_{3\ t\text{-Boc}}$), 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, $CH_{Pr^i}$), 5.70 (*s*, 1H, C═$CH_AH_B$), 6.23 (*s*, 1H, C═$CH_AH_B$), 7.15–7.36 (*m*, 6H, $ArH_{Phe}$ overlapped with $NH_{Phe}$), $\delta$ 9.30 (*s*, 1H, $NH_{\Delta Ala}$). $^{13}$C NMR (101 MHz, DMSO) $\delta$ 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 (C═$O_{ester}$), 1700 (C═$O_{urethane}$), 1690 IAB (C═$O_{amide}$), 1632 (C═C), 1526 IIAB (C–N and N–H), 1317 (CO–N–C═and N–(C═C)–CO), 1196 and 1166 (C–O–C), 896 (═$CH_2$).

## 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 N—H = 0.88 Å and $U_{iso}$ (H) = 1.2$U_{eq}$(N), C—$H_{aromatic}$ = 0.95 Å and $U_{iso}$ (H) = 1.2$U_{eq}$(C), C—$H_{methyl}$ = 0.98 Å and $U_{iso}$ (H) = 1.5$U_{eq}$(C); C—$H_{methylene}$ = 0.99 Å or C—$H_{methine}$ = 0.95 Å and $U_{iso}$ (H) = 1.2$U_{eq}$(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.

**Table 2**
Experimental details.

| | |
|---|---|
| Crystal data | |
| Chemical formula | $C_{20}H_{28}N_2O_5$ |
| $M_r$ | 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 *Kα* |
| $\mu$ (mm$^{-1}$) | 0.09 |
| Crystal size (mm) | 0.33 × 0.18 × 0.14 |
| Data collection | |
| Diffractometer | Oxford Diffraction Xcalibur CCD |
| No. of measured, independent and observed [$I > 2\sigma(I)$] reflections | 14003, 4025, 3235 |
| $R_{int}$ | 0.046 |
| (sin $\theta/\lambda)_{max}$ (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 |
| $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.22, −0.22 |
| Absolute structure | Flack *x* determined using 1095 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013) |
| Absolute structure parameter | −0.1 (6) |

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

## Acknowledgements

These studies were supported by Wroclaw Research Centre EIT+ under the project 'Biotechnologies and advanced medical technologies' – BioMed (POIG.01.01.02–02-003/08) financed from the European Regional Development Fund (Operational Programme Innovative Economy, 1.1.2). PL is the recipient of a PhD fellowship from a project funded by the European Social Foundation. MSc Błażej Dziuk is thanked for help with editing the manuscript.

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# supporting information

*Acta Cryst.* (2014). E**70**, 599-602 [doi:10.1107/S1600536814025197]

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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*

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

*Data collection*

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

*Refinement*

Refinement on $F^2$
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.079
$S$ = 0.98
4025 reflections
244 parameters
0 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0354P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.22 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.22 e Å$^{-3}$
Absolute structure: Flack $x$ determined using 1095 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
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 (Å²)*

| | *x* | *y* | *z* | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| 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, º)*

| | | | |
|---|---|---|---|
| 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, º)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N8—H8*A*···O7$^{i}$ | 0.88 | 2.21 | 2.952 (2) | 141 |
| C2—H2*A*···O7 | 0.98 | 2.48 | 3.049 (3) | 117 |
| C3—H3*C*···O18$^{ii}$ | 0.98 | 2.51 | 3.423 (3) | 155 |
| C4—H4*A*···O7 | 0.98 | 2.47 | 3.040 (3) | 116 |
| C21—H21*A*···O18 | 0.95 | 2.27 | 2.869 (3) | 120 |
| C26—H26*A*···O23 | 0.98 | 2.58 | 3.104 (3) | 114 |
| C26—H26*B*···O23$^{i}$ | 0.98 | 2.52 | 3.462 (3) | 162 |

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