Acta Crystallographica Section E
Structure Reports
Online
ISSN 1600-5368

N-[*tert*-Butoxycarbonylglycyl-(*E*)-α,β-dehydrophenylalanylglycylglycyl-(*E*)-α,β-dehydrophenylalanyl]glycine

Maciej Makowski,[a] Marek Lisowski,[b] Iwona Mikołajczyk[b]* and Tadeusz Lis[b]

[a]Institute of Chemistry, University of Opole, 48 Oleska St, 45-052 Opole, Poland, and [b]Faculty of Chemistry, University of Wrocław, 14 F. Joliot-Curie St, 50-383 Wrocław, Poland

Correspondence e-mail:
poor.twisted.me@wp.pl

Received 25 October 2006
Accepted 20 November 2006

In the molecule of the title hexapeptide, Boc^0–Gly^1–Δ^EPhe^2–Gly^3–Gly^4–Δ^EPhe^5–Gly^6–OH, $C_{31}H_{36}N_6O_9$, there are two overlapping β-turns, one of type II on the Δ^EPhe^2 (Δ^EPhe is isomer *E* of the α,β-dehydrophenylalanine residue) and Gly^3 residues and the second of type III′ on the Gly^3 and Gly^4 residues. All amino acids in the peptide are linked *trans* to each other. Three relatively strong intramolecular N—H···O hydrogen bonds stabilize the crystal structure. Two of them, of the 4→1 type, are responsible for two β-turns in the peptide.

Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.006 Å
R factor = 0.057
wR factor = 0.153
Data-to-parameter ratio = 8.5

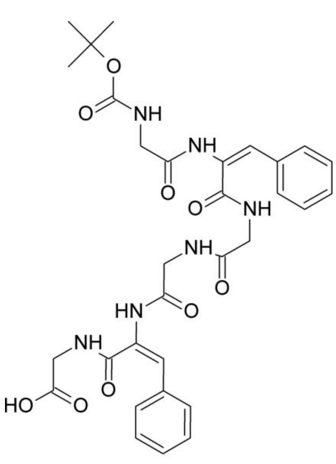
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

α,β-Dehydroamino acid residues contain a double bond between the Cα and Cβ atoms. They have been found in several microbial peptides and antibiotics (Noda *et al.*, 1983; Spatola, 1983). Their presence in a peptide chain results in an increased resistance of dehydropeptides (peptides containing dehydroamino acid residues) to enzymatic degradation (Shimohigashi *et al.*, 1987) and an increased binding ability of dehydropeptides to metal ions (Brasuń *et al.*, 2004). Dehydroamino acid residues decrease the conformational flexibility of peptides. It has been found that they are strong inducers of the β-turn conformation in short peptides (Główka *et al.*, 1987; Główka, 1988; Aubry *et al.*, 1991) and the 3_{10} helical conformation in longer sequences (Rajashankar *et al.*, 1992; Padmanabhan & Singh, 1993; Rajashankar, Ramakumar, Jain & Chauhan, 1995; Rajashankar, Ramakumar, Mal *et al.*, 1995; Jain *et al.*, 1997). The dehydroamino acid residue which has been the most studied so far is dehydrophenylalanine, ΔPhe, of the *Z* configuration (Vijayaraghavan *et al.*, 1998, and references therein; Siddiqui, 1999; Kubica *et al.*, 2000). This residue usually adopts one of the three conformations with average Φ and Ψ torsion angles of 80 and 0°, −60 and 140°, or −60 and −30°, or their enantiomeric values. It has also been found that ΔPhe residues at the (i + 2) position in a three-peptide unit sequence induce a type II β-turn conformation with Φ and Ψ torsion angles close to 80 and 0°, respectively (Singh *et al.*, 1987; Główka, 1988; Patel *et al.*, 1990; Busseti *et al.*, 1992). Studies on peptides containing more than one ΔPhe residue, or one ΔPhe and another dehydroamino acid residue, separated by one or more saturated residue(s), have shown that these peptides adopt a 3_{10} helical conformation with Φ and Ψ torsion angles of about −60 and −30°, respectively (Singh & Kaur, 1996; Padyana *et al.*, 2003; Goel *et al.*, 2005).

The present paper reports the crystal structure of peptide Boc^0–Gly^1–Δ^EPhe^2–Gly^3–Gly^4–Δ^EPhe^5–Gly^6–OH, (I). The peptide contains two dehydrophenylalanyl residues of the *E* configuration, *i.e.* their phenyl rings are *trans* to the N atom. There is one molecule in the asymmetric unit (Fig. 1). In Table 1 important bond lengths and angles are presented.

doi:10.1107/S1600536806049841



(I)

The $C\alpha - C\beta$ distances (C8=C9 and C21=C22) agree with the standard double-bond distances observed in molecules containing α,β-dehydroamino acid residues (Makowski *et al.*, 2006). The lengths of the $N - C\alpha$ and $C\alpha - C'$ bonds in both Δ^{E}Phe residues suggest that the carbonyl group and the N atom are conjugated with the styrene unit. A shortening of the $C\alpha - C\beta$ distance in relation to a single bond causes the side-chain atoms of the ΔPhe residues to be situated closer to the main chain than in saturated peptides. This has an influence on some values of the bond angles. For example, the N2—C8—C16 bond angle is smaller than 120° and the C8—C9—C10 bond angle in the same Δ^{E}Phe^{2} residue is larger than this value. The same is observed for the Δ^{E}Phe^{5} residue. These effects are consistent with the structures of other similar dehydropeptides, Boc^{0}–Gly^{1}–Δ^{Z}Phe^{2}–Gly^{3}–Δ^{E}Phe^{4}–Gly^{5}–OMe (Makowski *et al.*, 2006), Boc^{0}–Gly^{1}–Δ^{Z}Phe^{2}–Gly^{3}–Phe^{4}–*p*-NA (Ejsmont *et al.*, 2001) or Boc^{0}–Gly^{1}–Δ^{Z}Phe^{2}–Gly^{3}–Δ^{E}Phe^{4}–L-Phe^{5}–*p*-NA ethanol solvate (Makowski *et al.*, 2005).

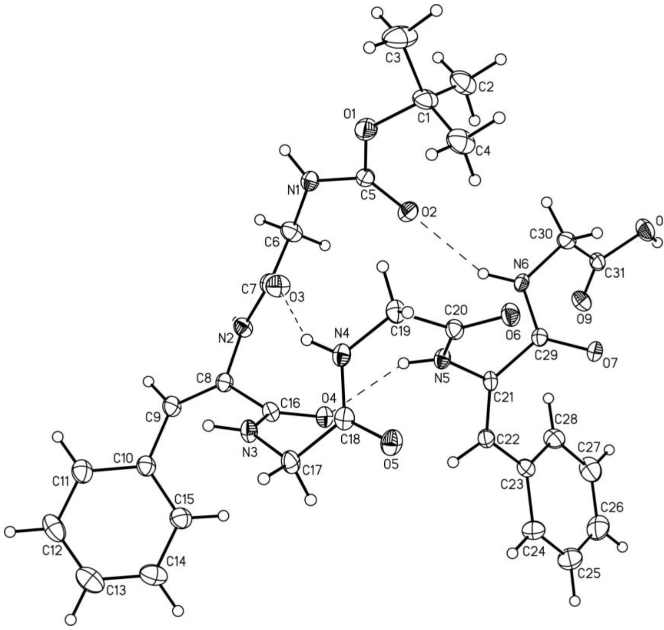


Figure 1

The molecular structure of (I). Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. Intramolecular hydrogen bonds are shown as dashed lines.

All the amino acids in the title hexapeptide are linked *trans* to each other. The deviations from the ideal values are not larger than 7° except for ω^{0} [18.3 (4)°]. The torsion angles χ^{2} [173.1 (4)°], $\chi^{2,1}$ [146.5 (5)°], $\chi^{2,2}$ [−33.5 (7)°] of the first ΔPhe residue and χ^{4} [176.4 (4)°], $\chi^{4,1}$ [149.1 (5)°], $\chi^{4,2}$ [−31.3 (7)°] of the second show antiperiplanar conformations of the side chains. The values of dihedral angles between the C=C and C=O bonds of ΔPhe^{2} and ΔPhe^{5} are 127.5 (4) and −46.7 (6)°, respectively. The structure of the peptide shows the presence of two overlapping β-turns. The torsion angles of Δ^{E}Phe^{2} [$\Phi^{2} = -45.1$ (5)°, $\Psi^{2} = 129.1$ (4)°] and Gly^{3} [$\Phi^{3} = 65.0$ (5)°, $\Psi^{3} = 9.9$ (5)°] correspond with the values typical of the type II β-turn (−60, 120° and 80, 0°). Another β-turn is present at the Gly^{3} and Gly^{4} residues. The torsion angles of the two glycyl residues are $\Phi^{3} = 65.0$ (5)°, $\Psi^{3} = 9.9$ (5)° and $\Phi^{4} = 65.5$ (5)°, $\Psi^{4} = 28.1$ (5)°. These angles are the closest to the values typical of a type III′ β-turn. Ideal values of torsion angles for this type of β-turn are 60 and 30° for both residues. Although the angles present in the Gly^{3} and Gly^{4} residues differ from these values, especially Ψ^{3}, the β-turn at these residues can be considered as type III'. The torsion angles of the Boc (*tert*-butoxycarbonyl) group correspond to a *trans*–*trans* conformation although the values of the ω^{0} and Φ^{0} angles are somewhat different from 180°.

Three intramolecular hydrogen bonds, N4—H4···O3, N5—H5···O4 and N6—H6···O2, are shown in Fig. 1. In the crystal structure, there are intermolecular hydrogen bonds where *D* (donor atom) = N, O or C , and *A* (acceptor atom) = O; all details are presented in Table 2. Two intramolecular hydrogen bonds of the 4→1 type (N4—H4···O3 and N5—H5···O4) stabilize two β-turns present in the peptide.

Experimental

The synthesis of the peptide has been described by Brasuń *et al.*, (2005). The crystals were obtained by precipitation with hexane from EtOAc–MeOH (4:1 *v*/*v*).

Crystal data

$C_{31}H_{36}N_{6}O_{9}$
$M_r = 636.66$
Orthorhombic, $P2_{1}2_{1}2_{1}$
$a = 9.552$ (2) Å
$b = 14.008$ (3) Å
$c = 24.214$ (5) Å
$V = 3239.9$ (12) Å^{3}
$Z = 4$
$D_x = 1.305$ Mg m^{-3}
Cu $K\alpha$ radiation
$\mu = 0.81$ mm^{-1}
$T = 100$ (2) K
Block, colourless
0.15 × 0.10 × 0.10 mm

Data collection

Oxford Diffraction Xcalibur PX κ-geometry CCD detector diffractometer
ω and φ scans
Absorption correction: numerical (*CrysAlis RED*; Oxford Diffraction, 2003)
$T_{\min} = 0.900$, $T_{\max} = 0.948$
25776 measured reflections
3590 independent reflections
3139 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.066$
$\theta_{\max} = 76.7°$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.057$
$wR(F^2) = 0.153$
$S = 1.07$
3590 reflections
420 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.088P)^2 + 1.68P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.42$ e Å^{-3}
$\Delta\rho_{min} = -0.30$ e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0031 (4)

Table 1
Selected geometric parameters (Å, °).

N2—C8	1.411 (5)	N5—C21	1.425 (4)
C8—C9	1.341 (6)	C21—C22	1.347 (5)
C9—C8—N2	120.2 (4)	C22—C21—N5	117.9 (3)
C9—C8—C16	126.2 (4)	C22—C21—C29	125.7 (3)
N2—C8—C16	113.5 (3)	N5—C21—C29	116.5 (3)
C8—C9—C10	129.0 (4)	C21—C22—C23	127.9 (4)
C5—N1—C6—C7	80.1 (5)	C18—N4—C19—C20	65.5 (5)
N1—C6—C7—N2	169.8 (4)	N4—C19—C20—N5	28.1 (5)
C6—C7—N2—C8	174.2 (4)	C19—C20—N5—C21	−174.4 (4)
C7—N2—C8—C16	−45.1 (5)	C20—N5—C21—C29	−51.4 (5)
N2—C8—C9—C10	173.1 (4)	N5—C21—C22—C23	176.4 (4)
C8—C9—C10—C15	−33.5 (7)	C21—C22—C23—C28	−31.3 (7)
C8—C9—C10—C11	146.5 (5)	C21—C22—C23—C24	149.1 (5)
C9—C8—C16—O4	127.5 (4)	C22—C21—C29—O7	−46.7 (6)
N2—C8—C16—N3	129.1 (4)	N5—C21—C29—N6	−48.9 (5)
C8—C16—N3—C17	−179.2 (4)	C21—C29—N6—C30	−178.2 (3)
C16—N3—C17—C18	65.0 (5)	C6—N1—C5—O1	−166.0 (4)
N3—C17—C18—N4	9.9 (5)	N1—C5—O1—C1	−161.7 (4)
C17—C18—N4—C19	−173.0 (3)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4—H4···O3	0.88	1.96	2.728 (4)	145
N5—H5···O4	0.88	2.20	3.013 (4)	154
N6—H6···O2	0.88	2.22	3.007 (4)	148
N1—H1···O9^{i}	0.88	2.18	2.848 (5)	133
N2—H2···O7^{ii}	0.88	2.03	2.852 (4)	155
N3—H3···O5^{iii}	0.88	1.98	2.740 (5)	144
O8—H8···O6^{iv}	0.84	1.87	2.695 (4)	166
C2—H2*B*···O2	0.98	2.52	3.064 (6)	115
C4—H4*A*···O2	0.98	2.56	3.130 (6)	117
C28—H28*A*···O9	0.95	2.46	3.339 (5)	154
C6—H6*B*···O7^{ii}	0.99	2.51	3.222 (5)	128
C11—H11*A*···O5^{ii}	0.95	2.32	3.234 (6)	163

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

All H atoms were placed in calculated positions, with C—H distances in the range 0.95–0.99 Å, N—H = 0.88 Å and O—H = 0.84 Å, and refined with U_{iso}(H) = 1.5U_{eq}(methyl C, O) and U_{iso}(H) = 1.2U_{eq}(other C, N). In the absence of significant anomalous dispersion effects, Friedel pairs were merged and the absolute configuration was not determined.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2003); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2003); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXL97*.

References

Aubry, A., Pietrzyński, G., Rzeszotarska, B., Boussard, G. & Marraud, M. (1991). *Int. J. Pept. Protein Res.* **37**, 39–45.

Brasuń, J., Makowski, M., Janicka, A. & Świątek-Kozłowska, J. (2005). *Polyhedron*, **24**, 1929–1936.

Brasuń, J., Makowski, M., Kołodziej, S. & Świątek-Kozłowska, J. (2004). *J. Inorg. Biochem.* **98**, 1391–1398.

Bruker (1997). *SHELXTL*. Version 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.

Busseti, V., Crisma, M., Toniolo, C., Salvadari, S. & Balboni, G. (1992). *Int. J. Biol. Macromol.* **14**, 23–28.

Ejsmont, K., Makowski, M. & Zaleski, J. (2001). *Acta Cryst.* C**57**, 205–207.

Główka, M. L. (1988). *Acta Cryst.* C**44**, 1639–1641.

Główka, M. L., Gilli, G., Bertolasi, V. & Makowski, M. (1987). *Acta Cryst.* C**43**, 1403–1406.

Goel, V. K., Somvanshi, R. K., Dey, S. & Singh, T. P. (2005). *J. Pept. Res.* **66**, 68–74.

Jain, R. M., Rajashankar, K. R., Ramakumar, S. & Chauhan, V. S. (1997). *J. Am. Chem. Soc.* **119**, 3205–3211.

Kubica, Z., Koźlecki, T. & Rzeszotarska, B. (2000). *Chem. Pharm. Bull.* **48**, 296–297.

Makowski, M., Brzuszkiewicz, A., Lisowski, M. & Lis, T. (2005). *Acta Cryst.* C**61**, o424–o426.

Makowski, M., Lisowski, M., Maciąg, A. & Lis, T. (2006). *Acta Cryst.* E**62**, o807–o810.

Noda, K., Shimohigashi, Y. & Izumiya, N. (1983). *Peptides: Analysis, Synthesis, Biology*, Vol. 5, edited by E. Gross & J. Meienhofer, pp. 285–339. New York: Academic Press.

Oxford Diffraction (2003). *CrysAlis CCD* and *CrysAlis RED*. Version 1.171. Oxford Diffraction Poland, Wrocław, Poland.

Padmanabhan, B. & Singh, T. P. (1993). *Biopolymers*, **33**, 613–619.

Padyana, A. K., Ramakumar, S., Mathur, P., Jagannathan, N. R. & Chauhan, V. S. (2003). *J. Pept. Sci.* **9**, 54–63.

Patel, H. C., Singh, T. P., Chauhan, V. S. & Kaur, P. (1990). *Biopolymers*, **29**, 509–515.

Rajashankar, K. R., Ramakumar, S. & Chauhan, V. S. (1992). *J. Am. Chem. Soc.* **114**, 9225–9226.

Rajashankar, K. R., Ramakumar, S., Jain, R. M. & Chauhan, V. S. (1995). *J. Am. Chem. Soc.* **1174**, 11773–11779.

Rajashankar, K. R., Ramakumar, S., Mal, T. K., Jain, R. M. & Chauhan, V. S. (1995). *Biopolymers*, **35**, 141–147.

Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.

Shimohigashi, Y., Kodama, H., Imazu, S., Horimoto, H., Sagakuchi, K., Waki, M., Uchida, H., Kondo, M., Kato, T. & Izumiya, N. (1987). *FEBS Lett.* **222**, 251–255.

Siddiqui, M. Z. (1999). *Int. J. Biol. Macromol.* **26**, 17–21.

Singh, T. P., Haridas, M., Chauhan, V. S., Kumar, A. & Witerbo, D. (1987). *Biopolymers*, **26**, 819–829.

Singh, T. P. & Kaur, P. (1996). *Prog. Biophys. Mol. Biol.* **66**, 141–165.

Spatola, A. F. (1983). *Chemistry and Biochemistry of Amino Acids, Peptides and Proteins*, Vol. VII, edited by B. Weinstein, pp. 267–357. New York: Marcel Dekker.

Vijayaraghavan, R., Kumar, P., Dey, S. & Singh, T. P. (1998). *Pept. Res.* **52**, 89–94.