Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

N-[*tert*-Butoxycarbonylglycyl-(*Z*)-α,β-dehydrophenylalanylglycyl-(*Z*)-α,β-dehydrophenylalanyl]glycine methyl ester

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Received 17 January 2007
Accepted 19 January 2007

In the crystal structure of the pentapeptide Boc^0—Gly^1–Δ^ZPhe^2—Gly^3–Δ^ZPhe^4—Gly^5—OMe, $C_{30}H_{35}N_5O_8$, the values of torsion angles Φ and Ψ show the presence of two type III′ β-turns, at the Δ^ZPhe^2 and Gly^3 residues, and Gly^3 and Δ^ZPhe^4 residues. All amino acids in the peptide are linked *trans* to each other. Two intramolecular N—H···O hydrogen bonds, between CO and NH groups, stabilize β-turns present in the peptide.

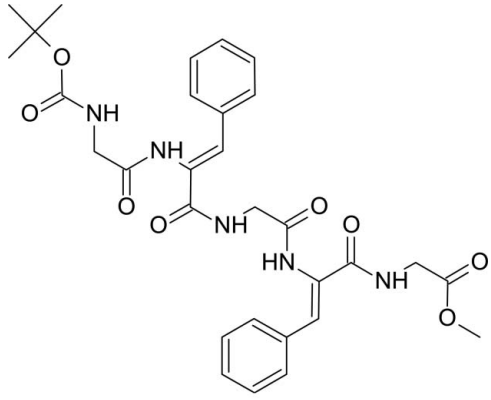
Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.004 Å
R factor = 0.038
wR factor = 0.102
Data-to-parameter ratio = 7.7

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

Comment

Continuing our studies (Makowski *et al.*, 2005, 2006, 2007) on dehydropeptides containing the ΔPhe residue, in this paper we present the crystal structure of pentapeptide Boc^0—Gly^1–Δ^ZPhe^2—Gly^3–Δ^ZPhe^4—Gly^5—OMe. The peptide contains two dehydrophenylalanyl residues of the *Z* configuration (their phenyl rings are *cis* to the N atom), each situated between two flexible glycine residues. There is one molecule in the asymmetric unit (Fig. 1). Selected bond lengths, bond angles and torsion angles are shown in Table 1.



(I)

An α,β-dehydrophenylalanyl residue contains the double bond between the Cα and Cβ atoms. The Cα—Cβ distances (C8═C9 and C19═C20) are very similar to those found in other structures containing two ΔPhe residues (Tuzi *et al.*, 1997; Makowski *et al.*, 2005, 2006). A shortening of the Cα═Cβ distance because of the double bond causes unfavorable steric contacts between the side-chain and the main-chain atoms of the dehydro residues. Those disadvantages are partially relaxed by rearrangement of bond angles, namely N—Cα—C′, which is decreased from the ideal value of 120°, and N—Cα—Cβ and Cα—Cβ—Cγ are larger than this value. Similar effects have been noticed in other dehydropeptides,

e.g. Boc-L-Val–ΔPhe–ΔPhe–ΔPhe–L-Val–OMe (Jain *et al.*, 1997), Boc–Gly–Δ^{Z}Phe–Gly Phe–*p*-NA (Ejsmont *et al.*, 2001) or Boc–Gly–Δ^{Z}Phe–Gly–Δ^{E}Phe–Gly–OMe dihydrate (Makowski *et al.*, 2006).

The torsion angles χ^2 [1.2 (5)°], $\chi^{2,1}$ [14.6 (5)°], $\chi^{2,2}$ [−164.4 (3)°] of the first ΔPhe residue and χ^4 [4.0 (4)°], $\chi^{4,1}$ [23.7 (4)°], $\chi^{4,2}$ [−155.4 (3)°] of the second one suggest a synperiplanar conformation of the side chains. The pentapeptide forms two overlapping type III′ β-turns (Venkatachalam, 1968) at the Δ^{Z}Phe^2–Gly^3 residues with Φ^2, Ψ^2 and Φ^3, Ψ^3 torsion angles of 56.8 (3), 23.5 (3)° and 65.6 (3), 9.9 (3)°, respectively, and at the Gly^3–Δ^{Z}Phe^4 residues with Φ^3, Ψ^3 and Φ^4, Ψ^4 torsion angles of 65.6 (3), 9.9 (3)° and 54.2 (3), 25.1 (3)°, respectively. This shows that the Δ^{Z}Phe^2–Gly^3—Δ^{Z}Phe^4 fragment forms a left-handed 3_{10}-helix. In a very similar peptide, Boc–Ala–ΔPhe–Gly–ΔPhe–Ala–OMe, the same central fragment flanked by two chiral alanine residues adopts a right-handed 3_{10}-helical conformation (Ciajolo *et al.*, 1990). All the amino acids in the title peptide are linked *trans* to each other. The deviations from the standard values are not larger than 7° with the exception of ω^3 [14.6 (2)°]. The Boc (*tert*-butoxycarbonyl) group, characterized by ω^0 and Φ^0 torsion angles, adopts a *trans–trans* conformation (Benedetti *et al.*, 1980).

Two intramolecular 4→1 hydrogen bonds, N4—H4···O3 and N5—H5···O4, shown in Fig. 1, stabilize the described β-turns. The N4—H4···O3 hydrogen bond is similar to the hydrogen bond formed in Boc–Gly–Δ^{Z}Phe–Gly–Δ^{E}Phe–Gly–OMe dihydrate (Makowski *et al.*, 2006). The second one, N5—H5···O4, does not occur in the dihydrate structure because of the bridging water molecule which takes part in two different intermolecular hydrogen bonds, N5—H5···O9 and O9—H9*A*···O4, where atoms O9 and H9*A* belong to a water molecule. For this reason there is no possibility of formation of the second β-turn in the dihydrate peptide. In addition to the N—H···O hydrogen bond, there are intra- and intermolecular hydrogen bonds, namely C—H···O, C—H···N and N—H···N, which stabilize the structure of the title pentapeptide. All data concerning the hydrogen bonds are presented in Table 2.

Experimental

Triethylamine (TEA, 0.057 ml, 0.41 mmol) was added to a solution of Boc–Gly–Δ^{Z}Phe–OH (0.064 g, 0.2 mmol) and Gly–Δ^{Z}Phe–Gly OMe·TFA (TFA is trifluoroacetic acid; 0.082 g, 0.2 mmol) in acetonitrile (2 ml). After 5 min 2-(1*H*-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (0.068 g, 0.21 mmol) was added with stirring and the reaction was carried out for 24 h at room temperature. MeCN was then evaporated until a dense oil was obtained. The oil was dissolved in EtOAc (40 ml) and washed with 1 *M* HCl (4 × 2 ml), a saturated solution of $KHCO_3$ (4 × 2 ml) and brine (3 ml). The organic layer was dried with $MgSO_4$ and EtOAc was evaporated *in vacuo*. The product was crystallized by precipitation with hexane from EtOAc–diethyl ether (4:1 *v*/*v*) solution [yield 0.083 g, 70%, m.p. 454–456 K]. Elemental analysis calculated for $C_{30}H_{35}N_5O_8$ (593.63): C 60.70, H 5.94, N 11.80%; found: C 60.45, H 5.99, N 11.63%.

Crystal data

$C_{30}H_{35}N_5O_8$
M_r = 593.63
Monoclinic, $P2_1$
a = 10.127 (3) Å
b = 10.036 (3) Å
c = 14.700 (4) Å
β = 90.23 (3)°
V = 1494.0 (7) Å^3
Z = 2
D_x = 1.320 Mg m^{-3}
Cu $K\alpha$ radiation
μ = 0.81 mm^{-1}
T = 100 (2) K
Needle, colourless
0.29 × 0.11 × 0.04 mm

Data collection

Oxford Diffraction Excalibur PX κ-geometry diffractometer with CCD detector
ω and φ scans
Absorption correction: numerical (*CrysAlis RED*; Oxford Diffraction, 2003)
T_{min} = 0.842, T_{max} = 0.966
8750 measured reflections
3011 independent reflections
2792 reflections with $I > 2\sigma(I)$
R_{int} = 0.028
θ_{max} = 75.3°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.102
S = 1.12
3011 reflections
389 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0714P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.008
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0065 (8)

Table 1
Selected geometric parameters (Å, °).

N2—C8	1.425 (3)	N4—C19	1.420 (3)
C8—C9	1.343 (4)	C19—C20	1.344 (3)
C9—C8—N2	124.1 (2)	C20—C19—N4	124.4 (2)
C9—C8—C16	119.1 (2)	C20—C19—C27	118.5 (2)
N2—C8—C16	116.7 (2)	N4—C19—C27	116.4 (2)
C8—C9—C10	131.6 (3)	C19—C20—C21	129.7 (2)
C6—N1—C5—O1	−176.7 (2)	N3—C17—C18—N4	9.9 (3)
N1—C5—O1—C1	173.6 (2)	C17—C18—N4—C19	−165.4 (2)
C5—N1—C6—C7	88.3 (3)	C18—N4—C19—C27	54.2 (3)
N1—C6—C7—N2	−112.9 (2)	N4—C19—C20—C21	4.0 (4)
C6—C7—N2—C8	−179.6 (2)	C19—C20—C21—C22	23.7 (4)
C7—N2—C8—C16	56.8 (3)	C19—C20—C21—C26	−155.4 (3)
N2—C8—C9—C10	1.2 (5)	C20—C19—C27—O6	30.7 (4)
C8—C9—C10—C15	−164.4 (3)	N4—C19—C27—N5	25.1 (3)
C8—C9—C10—C11	14.6 (5)	C19—C27—N5—C28	174.4 (2)
C9—C8—C16—O4	25.5 (4)	C27—N5—C28—C29	68.2 (3)
N2—C8—C16—N3	23.5 (3)	N5—C28—C29—O8	−165.5 (2)
C8—C16—N3—C17	−174.2 (2)	C28—C29—O8—C30	178.3 (2)
C16—N3—C17—C18	65.6 (3)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4—H4···O3	0.88	1.99	2.836 (3)	162
N5—H5···O4	0.88	2.18	3.047 (3)	170
N2—H2···O6^{i}	0.88	1.89	2.738 (3)	160
N3—H3···O5^{ii}	0.88	2.04	2.857 (3)	155
C4—H4*C*···O3^{iii}	0.98	2.50	3.422 (4)	156
C30—H30*B*···O4^{iv}	0.98	2.48	3.419 (4)	160
N3—H3···N2	0.88	2.43	2.771 (3)	103
N4—H4···N3	0.88	2.39	2.742 (3)	104

D—H···A	D—H	H···A	D···A	D—H···A
N5—H5···N4	0.88	2.45	2.795 (3)	104
C11—H11A···N2	0.95	2.51	3.100 (4)	120
C22—H22A···N4	0.95	2.58	3.105 (3)	115
C2—H2A···O2	0.98	2.36	2.955 (5)	118
C4—H4A···O2	0.98	2.53	3.089 (4)	116
C9—H9A···O4	0.95	2.48	2.848 (3)	103
C11—H11A···O2	0.95	2.58	3.412 (4)	146
C20—H20A···O6	0.95	2.48	2.839 (3)	102

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

All H atoms were positioned geometrically with the C—H distances in the range 0.95–0.99 Å, N—H = 0.88 Å, and refined with U_{iso}(H) = 1.5U_{eq}(methyl C) and U_{iso}(H) = 1.2U_{eq}(non-methyl C, N). In the absence of significant anomalous dispersion effects, the 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*.

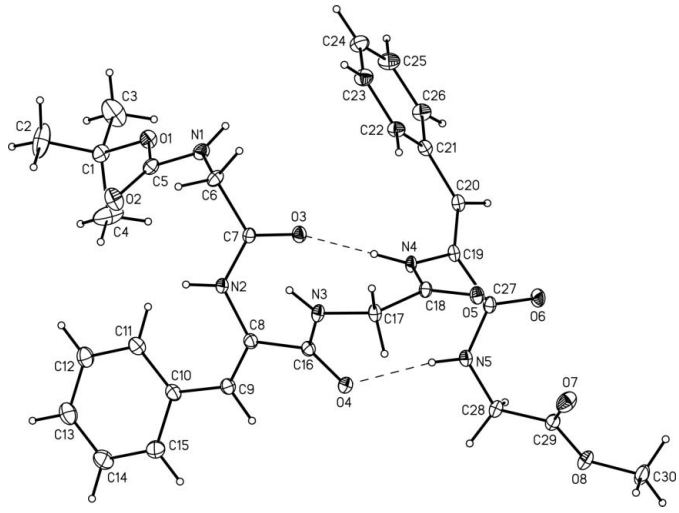


Figure 1
Molecular structure of Boc^0–Gly^1–Δ^ZPhe^2–Gly^3–Δ^ZPhe^4–Gly^5–OMe and the numbering of atoms. Displacement ellipsoids are drawn at the 30% probability level. Intramolecular hydrogen bonds are marked as dashed lines.

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