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α-L-Glutamylglycine

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Abstract. $C_7H_{12}N_2O_5$, orthorhombic, $P2_12_12_1$, a = 5·525(5), b = 12·565(4), c = 13·211(6) Å, Z = 4, D_c = 1·48, D_m (flotation in chloroform/methylene chloride) = 1·48(1) Mg m^{-3}; R_1 = 0·039, R_2 = 0·040 for 1172 observations. The dipeptide crystallizes as a zwitterion with the main-chain carboxyl ionized and the amino terminus protonated. The conformation of the peptide group is *trans*; the glutamyl side chain is extended, but

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the carboxy terminus is held by hydrogen bonding in a non-extended conformation with a torsional angle $\varphi_{Gly} = -74\cdot1°$.

Introduction. Crystals of α-L-glutamylglycine were grown from aqueous ethanol at pH 6–7. A crystal of dimensions 0·275 × 0·475 × 0·800 mm was used in the analysis. Preliminary cell constants were obtained on an Enraf–Nonius CAD-4 diffractometer using Mo *Kα* radiation and a graphite monochromator. The crystals were assigned to the orthorhombic system, space group $P2_12_12_1$ (systematic absences: *h*00, *h* odd; 0*k*0, *k* odd; 00*l*, *l* odd). Final cell constants were determined after careful centering of 24 reflections with $35° \geq 2\theta \geq 30°$. Intensity data were collected in a θ-2θ scan mode out to $2\theta = 55°$. Intensity standards monitored at regular intervals showed no sign of crystal deterioration. The data were corrected for Lorentz–polarization effects, but not for absorption ($\mu = 0\cdot136$ mm^{-1}). Excluding 71 data with $I < 0\cdot01\sigma(I)$, 1172 reflections were measured. The programs used throughout the analysis were those provided by Enraf–Nonius with the CAD-4–SDP system.

The data were converted to *E* values and the structure was determined by *MULTAN* (Main, Woolfson & Germain, 1971) using 141 reflections for which $E \geq 1\cdot50$. An *E* map calculated from that set of phases having the highest absolute figure of merit revealed all the non-hydrogen atoms. These positions, together with their isotropic temperature factors, were refined by two cycles of least squares. In all least-squares calculations the function minimized was $\sum w(|F_o| - |F_c|)^2$ where the weights were initially assigned as unity but were eventually assigned (see below) as $4F_o^2/\sigma^2(I)$.

Following the inclusion of anisotropic thermal parameters for the non-hydrogen atoms and two cycles of least-squares refinement, a difference Fourier map was calculated; it revealed the positions of all H atoms. Three final cycles of full-matrix least-squares refinement using the weights defined above [with $\sigma(I)$ as defined by Corfield, Doedens & Ibers (1967) with $p = 0\cdot01$] converged to final values of the standard agreement factors $R_1 = 0\cdot039$ and $R_2 = 0\cdot040$ based on all of the observed reflections. The error on an observation of unit weight was 2·976. The atom positions along with their standard deviations, as estimated from the inverse matrix, are listed in Table 1.* A final difference Fourier map was featureless except for small peaks intermediate between covalently linked atoms which may be attributable to bonding electron density.

Table 1. *Positional parameters and thermal parameters for α-L-glutamylglycine*

	x	y	z	U_{eq}*/B† (Å^2)
N_1	0·9852 (3)	−0·0358 (1)	0·3279 (1)	0·0331
N_2	0·8654 (3)	0·2455 (1)	0·3712 (1)	0·0324
$O_1^{\epsilon1}$	1·2468 (3)	0·0780 (1)	0·0078 (1)	0·0511
$O_1^{\epsilon2}$	0·8951 (3)	0·1496 (1)	−0·0406 (1)	0·0458
O_1	0·6294 (3)	0·1006 (1)	0·3593 (1)	0·0462
O'	0·6053 (3)	0·3420 (1)	0·2181 (1)	0·0396
O''	0·2924 (3)	0·3660 (1)	0·3205 (1)	0·0361
C_1^α	1·0502 (4)	0·0792 (2)	0·3203 (1)	0·0361
C_1^β	1·1375 (4)	0·1068 (2)	0·2133 (2)	0·0376
C_1^γ	0·9401 (4)	0·1088 (2)	0·1325 (2)	0·0376
C_1^δ	1·0471 (4)	0·1109 (2)	0·0274 (1)	0·0376
C_1'	0·8247 (4)	0·1427 (2)	0·3523 (1)	0·0317
C_2^α	0·6640 (4)	0·3142 (2)	0·3948 (2)	0·0365
C_2'	0·5078 (4)	0·3423 (1)	0·3036 (2)	0·0313
H_1^1	0·948 (4)	−0·052 (1)	0·390 (2)	2·8 (5)
H_1^2	0·869 (4)	−0·064 (2)	0·282 (2)	4·7 (6)
H_1^3	1·120 (4)	−0·078 (2)	0·315 (2)	4·7 (6)
H_1^α	1·178 (4)	0·094 (1)	0·368 (2)	2·6 (4)
$H_1^{\beta1}$	1·226 (4)	0·177 (2)	0·218 (2)	3·3 (5)
$H_1^{\beta2}$	1·262 (4)	0·058 (1)	0·198 (1)	2·7 (4)
$H_1^{\gamma1}$	0·811 (4)	0·169 (2)	0·141 (2)	3·6 (5)
$H_1^{\gamma2}$	0·832 (5)	0·048 (2)	0·134 (2)	4·8 (6)
H_1^ϵ	0·979 (5)	0·150 (2)	−0·099 (2)	5·9 (7)
H_2	1·001 (4)	0·278 (2)	0·363 (2)	3·3 (5)
$H_2^{\alpha1}$	0·556 (3)	0·277 (1)	0·444 (1)	2·4 (4)
$H_2^{\alpha2}$	0·725 (4)	0·376 (1)	0·420 (1)	2·6 (5)

* Calculated from the principal r.m.s. amplitudes in Å, with $U_{eq}^3 = (U_1 U_2 U_3)$; e.s.d.'s are 0·0007 Å^2.

† For H atoms.

Discussion. As part of our research on the structures of peptides containing acidic amino acids (Valente, Hiskey & Hodgson, 1979; Eggleston, Valente & Hodgson, 1981) we are examining the crystal structures of peptides containing L-glutamyl residues. To our knowledge only the structures of the totally blocked dipeptide Z-(γ-ethyl)-L-glutamyl-(γ-ethyl)-L-glutamic acid ethyl ester (Benedetti, DiBlasio, Pavone, Pedone, Germain & Goodman, 1979) and of glutathione (Wright, 1958), in which the glutamyl residue is bound to the peptide chain through its γ-carboxyl group, have appeared. We find no published structural information for linear peptides containing α-glutamyl residue(s) in which the γ-carboxyl group is not blocked. We here report the structure of α-L-glutamylglycine.

An *ORTEP* drawing (Johnson, 1965) of a single molecule of the dipeptide is shown in Fig. 1; the notation used in the labeling of atoms is that adopted by the IUPAC–IUB Commission on Biochemical Nomenclature (1970). Most of the backbone bond distances are similar to the average values tabulated for peptides by Marsh & Donohue (1967). Notable exceptions, however, occur for the N–C$^\alpha$ distance,

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* Lists of structure factors, anisotropic thermal parameters, and bond angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35958 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

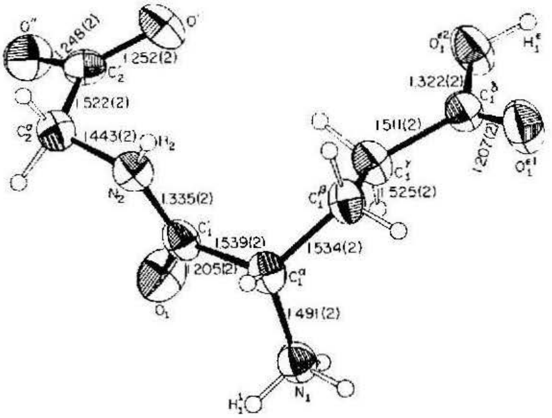

Fig. 1. View of the α-L-glutamylglycine molecule, showing the principal bond lengths (Å) with their e.s.d.'s. Thermal ellipsoids are drawn at the 50% probability level; H atoms are shown as small circles of arbitrary size.

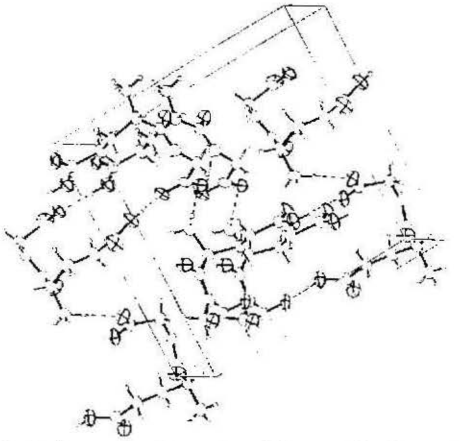

Fig. 3. The hydrogen-bonding network in crystals of α-L-glutamylglycine with the *a* axis horizontal. Oxygen atoms are shown as principal ellipses.

1.491(2) Å, of the Glu residue which is 0.04 Å longer than the tabulated average of 1.45 Å, and for the peptide carbonyl distance of 1.205(2) Å which is shorter than the reported 1.24 Å average. A progressive shortening of the C–C distances along the glutamyl side chain in proceeding to the γ-carbon atom is noted. The bond angles in the molecule have been deposited.*

The torsional angles along the peptide chain are shown in Fig. 2; the definitions of the torsional angles are those of the IUPAC–IUB Commission on Biochemical Nomenclature (1970). The values of +166.0 and +175.6° for ψ_{Glu} and $\omega_{\mathrm{Glu\text{-}Gly}}$ respectively describe an extended conformation along the peptide backbone. The χ^1 and χ^2 angles of −47.8 and −166.7° observed here in the Glu side chain are similar to those reported in other Glu structures (Benedetti *et al.*, 1979). The φ_{Gly} angle of −74.1°, however, is very different from that expected for an extended β-peptide conformation; this non-extended structural feature is presumably due to the strong hydrogen bonding involving both O′ and O″ (see below).

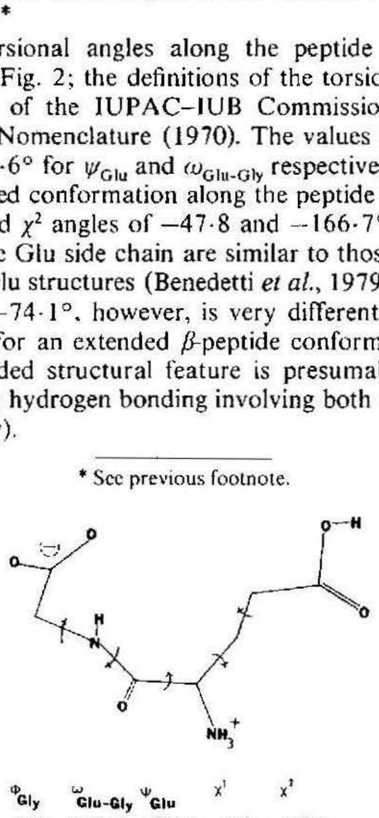

Fig. 2. Schematic showing the torsional angles (°) in the peptide backbone as defined by the IUPAC–IUB Commission on Biochemical Nomenclature (1970).

A drawing of the hydrogen-bonding network is given in Fig. 3. The molecule is held in a bent conformation with intermolecular hydrogen bonding between the ionized carboxyl O′ and the protonated $O_1^{\varepsilon 2}$ of the side-chain carboxyl of molecules related by the screw along **c** with $O'\cdots O_1^{\varepsilon 2}$ and $H_1^{\varepsilon}\cdots O'$ distances of 2.617 (1) Å and 1.73 (2) Å and $O_1^{\varepsilon 2}–H_1^{\varepsilon}\cdots O'$ angle of 172(2)°. The ionized carboxyl is also hydrogen bonded through O″ to the protonated amino group at N_1 of a screw-related molecule along **b** with $N_1\cdots O''$ and $H_1^1\cdots O''$ distances of 2.777 (2) Å and 1.85 (2) Å and $N_1–H_1^1\cdots O''$ angle of 166 (2)°. A second hydrogen bond through O″ extends to the amide N_2 of a screw-related molecule along **a** with $N_2\cdots O''$ and $H_2\cdots O''$ distances of 2.883 (2) Å and 2.03 (2) Å and $N_2–H_2\cdots O''$ angle of 170 (2)°. The peptide oxygen atom O_1 apparently does not participate in hydrogen bonding.

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* See previous footnote.

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