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Conformation and structure of bis(glycyl-L-aspartic acid) oxalate 0.4-hydrate

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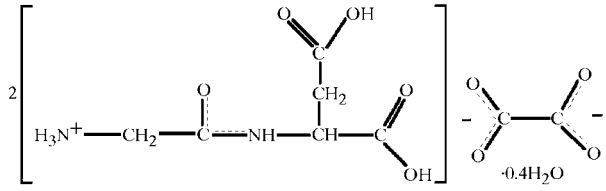
The title bis(glycyl-L-aspartic acid) oxalate complex {systematic name: bis[2-(2-ammonioacetamido)butanedioic acid] oxalate 0.4-hydrate}, $2C_6H_{11}N_2O_5^+\cdot C_2O_4^{2-}\cdot 4H_2O$, crystallizes in a triclinic space group with the planar peptide unit in a *trans* conformation. The asymmetric unit consists of two glycyl-L-aspartic acid molecules with positively charged amino groups and neutral carboxyl groups, and an oxalate dianion. The twist around the C—Cα bond indicates that both the peptide molecules adopt extended conformations, while the twist around the N—Cα bond shows that one has a folded and the other a semi-extended state. The present complex can be described as an inclusion compound with the dipeptide molecule as the host and the oxalate anion as the guest. The usual head-to-tail sequence of aggregation is not observed in this complex, as is also the case with the glycyl-L-aspartic acid dihydrate molecule. The study of aggregation and interaction patterns in binary systems is the first step towards understanding more complex phenomena. This further leads to results that are of general interest in bimolecular aggregation.

Comment

The X-ray analysis of complexes of amino acids and peptides formed among themselves as well as with relevant molecules helps in understanding the geometrical features of elementary patterns of these complexes (Vijayan, 1988). The aggregation patterns of biological molecules largely depend on the non-covalent interactions. In these complexes, there is always an extensive network of hydrogen bonds. The aggregation pattern can divulge information relating to chemical evolution and the origin of life. In addition, structural and conformational studies of peptides that contain acidic residues have shown that these compounds are implicated in the binding of calcium and similar metals to proteins (Wasserman *et al.*, 1977). It has been observed that these residues are involved in the complexation of calcium in all calcium proteins of known structure (Kretsinger & Nelson, 1976). Most of the calcium-specific site sequences contain glycine adjacent to one or more of the coordinating acid peptide residues (Potter *et al.*, 1977). The acidic side chain of these peptides offers unique possibilities of hydrogen bonding, which may result in unusual conformational properties. The crystal structure of the peptide glycyl-L-aspartic acid has been determined using single-crystal X-ray diffraction (Eggleston & Hodgson, 1982; Pichon-Pesme *et al.*, 2000). Oxalic acid is the simplest dicarboxylic acid and it can, in principle, exist in three ionization states, *viz.* singly charged (semi-oxalate), doubly charged (oxalate) and neutral (oxalic acid). Oxalic acid has also been complexed with the peptides glycylglycine (Ejsmont *et al.*, 2003), glycyl-L-histidine and L-histidyl-L-alanine (Manoj & Vijayan, 2000). We present here the crystal structure of a bis(glycyl-L-aspartic acid) oxalate complex, (I), solved using single-crystal X-ray diffraction. Using the Cambridge Structural Database (CSD; Version 5.26 of November 2004; Allen, 2002), an analysis of the geometry in the salts of the peptide and oxalic acid has been carried out.



(I)

A displacement ellipsoid representation of the complex is shown in Fig. 1. The asymmetric unit consists of two glycyl-L-aspartic acid molecules with positively charged amino groups and neutral carboxyl groups, and an oxalate ion, which is doubly negatively charged. A comparison of the bond parameters of the peptide unit in the complex and in the pure structure shows that only the bond parameters involving the main-chain COOH group differ, as a result of the zwitterionic nature of the pure glycyl-L-aspartic acid. The peptide plane is defined by atoms C2, C3, O4, N5, C6 and H6 for the first molecule and C15, C16, O17, N18, C19 and H18 for the second molecule of the peptide. The maximum deviations from the least-squares plane through these atoms occur for C6 [−0.023 (3) Å] and C15 [0.022 (4) Å].

The torsion angles of the two molecules of (I) and that of glycyl-L-aspartic acid dihydrate are compared in Table 2. The planarity of the peptide unit is defined by the torsion angle ω, which characterizes the rotation around the C—N peptide bond. An ω value of 180° corresponds to a planar peptide unit (*trans* conformation). In the present complex, the deviation of ω (C2—C3—N4—C5 and C15—C16—N18—C19) for both the peptide residues is about 3°, and hence they adopt *trans* conformations. The full conformation of a peptide chain is described by two additional torsion angles, ψ and φ, which characterize the twist around the C—Cα and N—Cα bonds, respectively (Suresh & Vijayan, 1985; Vijayan, 1988). The ψ angle around C—Cα is extended in the present structure, which is also true for the pure glycyl-L-aspartic acid molecule.

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As a rough guide, the conformation may be considered as extended if the magnitude of φ is between 60 and 180°; otherwise it may be considered folded. According to this guide, one of the peptide molecules (molecule 2) is in a folded state and the other (molecule 1) is in a semi-extended state in the complex, unlike the molecule of pure glycyl-L-aspartic acid, which is extended, having a value of −133.3°. The aspartic acid residue has ψ1 of around 60° with the side chain *trans* to the carboxyl group in both the peptide molecules, unlike the case in pure glycyl-L-aspartic acid, which has a side chain having a *cis* conformation to the carboxyl group.

Comparison of the oxalate bond parameters for the three above-mentioned peptide–oxalate complexes shows that in all cases, with the exception of glycyl-L-histidine oxalate, the oxalate unit exists as a doubly ionized oxalate anion. The stoichiometry in the case of the present complex and bis(glycyl glycinium) oxalate is 2:1. The other two have 1:1 stochiometry. In all the complexes, the oxalate ion is essentially planar, the O—C—C—O torsion angle deviating by around 6° from planarity. Table 1 gives the hydrogen-bonding parameters in the present complex. The peptide molecule has a number of potential H-atom donors and acceptors in the structures. As observed previously (Eggleston & Hodgson, 1982) and in the present complex, intramolecular hydrogen bonding is absent. An arrangement in which the terminal amino group and the carboxylate group are brought into periodic hydrogen-bonded proximity is called a head-to-tail sequence. In the present complex, the terminal amino groups (*i.e.* N14—H14*A* and N1—H1*A*) are hydrogen bonded to atoms O8 and O21, respectively, which are the main-chain α carboxyl O atoms. However, the arrangement is not the usual head-to-tail arrangement. Rather, the two molecules are related by a pseudo-inversion center. It is also seen that the amino N atoms of each peptide molecule (N14—H14*C* and N1—H1*C*) are hydrogen bonded to atoms O12 and O25, respectively, which are the side-chain carboxyl O atoms. Amino atoms H1*B* and H14*B* also form bifurcated hydrogen bonds to the oxalate O atoms (O29/O28 and O30/O27, respectively). The O-bound H atoms of the carboxyl groups of the main chain and the side chain act as hydrogen-bond donors to the oxalate O atom. Each oxalate O atom, in turn, acts as an acceptor of two hydrogen bonds (one to the amino N atom and the other to the OH group of the carboxyl group). Another interesting observation is that the peptide N atom forms a hydrogen bond to the peptide carbonyl group (*i.e.* N5—H5···O4^{iii} and N18—H18···O4^{ii}; Table 1) of a symmetry-related molecule of the same type, resulting in an *S*5-4 (Vijayan, 1988) sequence. Adjacent molecules are parallel. A hydrogen bond between the peptide N atom and the peptide carbonyl group is also observed in the pure glycyl-L-aspartic acid, bis(glycyl-L-histidine) oxalate and glycyl-L-histidine–oxalic acid complexes, but the same is not true for the L-histidyl-L-alanine complex. Hence, the formation of this type of hydrogen bond might be possible because the glycyl residue occupying the amino terminal position does not cause steric hindrance. Of course, a systematic study of complexes of oxalic acid with peptides involving a glycyl residue at the amino terminal position is required to prove this point. In terms of graph-set notation (Bernstein *et al.*, 1995), the largest motif has the first-level graph set $N1 = DDD$, the binary level being $R_4^2(22)$. The next level graph set is $N1 = DD$, the binary level being $R_1^2(5)$ and $C4$. The dipeptide and oxalate molecules are arranged parallel to the *ab* plane. Fig. 2 shows the packing as viewed down the crystallographic *a* axis. It is observed that the dipeptide molecules are stacked in such a way that the oxalate molecules are enclosed in the voids created during stacking. The present complex can be described as an inclusion compound with the dipeptide molecule as the host and the oxalate ion as the guest.

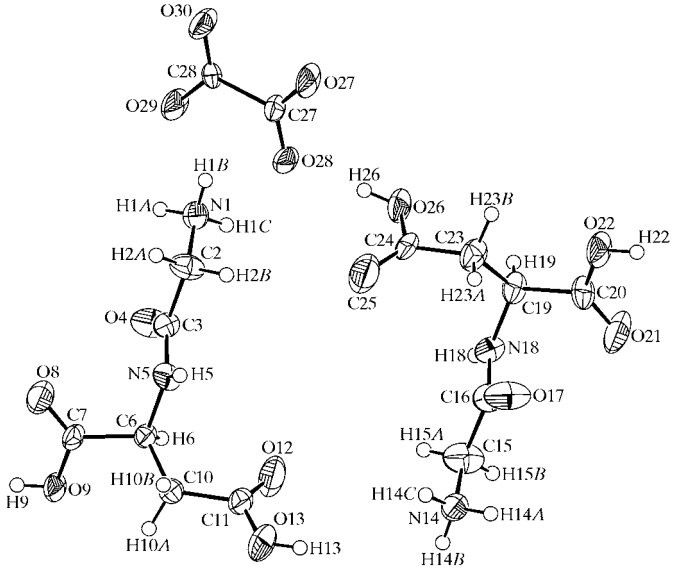

Figure 1
An ellipsoid plot of bis(glycyl-L-aspartic acid) oxalate, showing the atom-numbering scheme and 50% probability displacement ellipsoids.

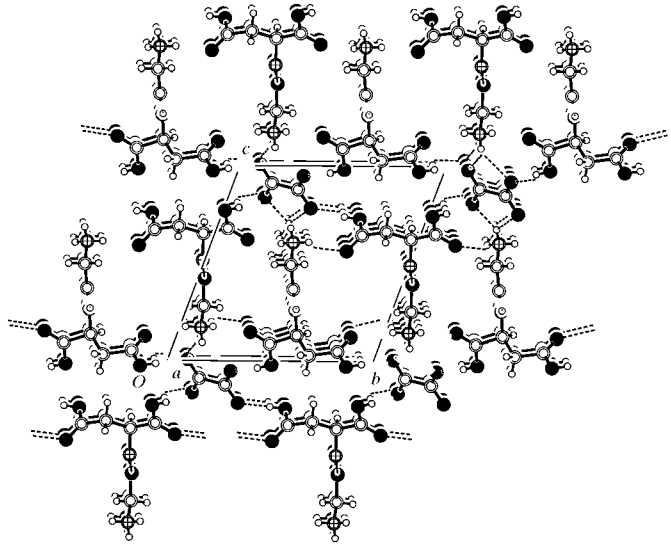

Figure 2
The packing of the title salt, viewed down the *a* axis.

Experimental

Crystals of bis(glycyl-L-aspartic acid) oxalate were grown by slow evaporation from a saturated aqueous solution containing stoichiometric quantities of glycyl-L-aspartic acid and oxalic acid.

Crystal data

$2C_6H_{11}N_2O_5^+\cdot C_2O_4^{2-}\cdot 0.4H_2O$
M_r = 477.56
Triclinic, $P\overline{1}$
a = 4.8100 (8) Å
b = 10.7760 (18) Å
c = 10.8756 (18) Å
α = 69.325 (3)°
β = 85.792 (3)°
γ = 81.946 (3)°
V = 522.03 (15) Å^3
Z = 1
D_x = 1.519 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.14 mm^{-1}
T = 300 K
Irregular, colorless
0.24 × 0.19 × 0.13 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
5499 measured reflections
2081 independent reflections
1732 reflections with $I > 2\sigma(I)$
R_{int} = 0.028
θ_{max} = 26.4°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.059
$wR(F^2)$ = 0.133
S = 1.11
2081 reflections
297 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0749P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O21^{i}	0.89	1.95	2.793 (7)	158
N1—H1B···O28	0.89	2.25	2.902 (6)	130
N1—H1B···O29	0.89	1.94	2.727 (6)	147
N1—H1C···O25^{ii}	0.89	1.90	2.741 (7)	157
N5—H5···O4^{iii}	0.86	2.170	2.991 (5)	160
O9—H9···O27^{iv}	0.82	1.72	2.531 (6)	167
O13—H13···O30^{v}	0.82	1.76	2.571 (6)	170
N14—H14A···O8^{vi}	0.89	2.11	2.947 (6)	156
N14—H14B···O27^{v}	0.89	2.15	2.882 (6)	139
N14—H14B···O30^{v}	0.89	2.06	2.793 (6)	139
N14—H14C···O12^{iii}	0.89	2.20	3.035 (7)	157
N18—H18···O17^{ii}	0.86	2.02	2.870 (6)	171
O22—H22···O29^{vi}	0.82	1.81	2.622 (6)	170
O26—H26···O28	0.82	1.81	2.618 (6)	170
C2—H2A···O21^{vii}	0.97	2.59	3.432 (8)	145
C10—H10B···O9^{iii}	0.97	2.47	3.388 (7)	158

Symmetry codes: (i) $x-1, y-1, z$; (ii) $x-1, y, z$; (iii) $x+1, y, z$; (iv) $x-1, y, z-1$; (v) $x, y+1, z-1$; (vi) $x+1, y+1, z$; (vii) $x, y-1, z$.

All H atoms were positioned using geometrical constraints and were considered as riding on the atoms to which they are attached, with C—H, N—H and O—H distances of 0.97–0.98, 0.86–0.89 and 0.82 Å, respectively. At this stage, the maximum difference density of 0.60 e Å^{-3} indicated the presence of a possible atom site. In addition, a check for solvent-accessible volume using *PLATON* (Spek, 2003) showed a void of 128 Å^3. An attempt to refine this peak as a water O atom with full occupancy resulted in a high U_{iso} value. An alternative strategy, employing the SQUEEZE function of *PLATON* (van der Sluis & Spek, 1990; Spek, 2003), was used to eliminate the contribution of the electron density in the solvent region from the intensity data. *PLATON* estimated a total potential solvent area volume of 29.4 Å^3, with a total electron count of 4, which is equivalent to one partially occupied solvent water molecule. The *PLATON* suite was used to generate the reflection file and the refinement was carried out using this file.

Table 2
Comparison of the torsion angles (°) of bis(glycyl-L-aspartic acid) oxalate and glycyl-L-aspartic acid dihydrate.

	Bis(glycyl-L-aspartic acid) oxalate		Glycyl-L-aspartic acid
	Molecule 1	Molecule 2	
N1—C1—C3—N5 (ψ)	170.1 (5)	−171.4 (6)	−164.40
C2—C3—N5—C6 (ω)	177.6 (5)	−177.5 (6)	−175.90
C3—N5—C6—C7 (φ)	−76.3 (6)	57.7 (7)	−133.24
N5—C6—C10—C11 (ψ1)	−71.0 (5)	−57.5 (6)	56.43
N5—C6—C7—O8 (ψ_2')	−5.9 (7)	31.6 (7)	1.04
N5—C6—C7—O9(ψ_2'')	173.0 (4)	−151.3 (5)	−179.46
C7—C6—C10—C11 (ψ2)	164.7 (4)	177.4 (5)	−68.02

Data collection: *SMART* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: HJ3023). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Bruker (2004). *SMART* and *SAINT*. Bruker AXS Inc., Madison, Wisconsin, USA.
Eggleston, D. S. & Hodgson, D. J. (1982). *Int. J. Pept. Protein Res.* **19**, 206–211.
Ejsmont, K., Zaleski, J., Joe, I. H. & Jayakumar, V. S. (2003). *Acta Cryst.* C**59**, o553–o555.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Kretsinger, R. H. & Nelson, D. J. (1976). *Coord. Chem. Rev.* **18**, 29–124.
Manoj, N. & Vijayan, M. (2000). *J. Pept. Res.* **56**, 210–217.
Pichon-Pesme, V., Lachekar, H., Souhassou, M. & Lecomte, C. (2000). *Acta Cryst.* B**56**, 728–737.
Potter, J. D., Johnson, J. D., Dedman, J. R., Schreiber, W. E., Mandel, F., Jackson, R. L. & Means, A. R. (1977). *Calcium Binding Proteins and Calcium Functions*, edited by R. H. Wasserman, R. A. Corrandino, E. Carafoli, R. H. Kretsinger, D. H. MacLennan & F. L. Siegel. Amsterdam: Elsevier–North Holland.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Sluis, P. van der & Spek, A. L. (1990). *Acta Cryst.* A**46**, 194–201.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Suresh, C. G. & Vijayan, M. (1985). *Int. J. Pept. Protein Res.* **26**, 311–328.
Vijayan, M. (1988). *Prog. Biophys. Mol. Biol.* **52**, 71–99.
Wasserman, R. H., Corrandino, R. A., Carafoli, E., Kretsinger, R. H., MacLennan, D. H. & Siegel, F. L. (1977). Editors. *Calcium Binding Proteins and Calcium Functions.* Amsterdam: Elsevier–North Holland.