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Hydrogen bonding potentiality of serine in more aquated environment : crystal and molecular structure of dihydrated DL-serine, $C_3H_7NO_3.2H_2O$

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Abstract The dihydrated DL-Serine crystal belongs to the monoclinic space group $P2_1/n$ with cell dimensions a = 4.831(2)Å, b = 9.150(4)Å, c = 10.444(4) Å and β = 99.97(2)°. Its structure has been solved by direct methods from single crystal X ray diffraction data (CuK_α 1.5418 Å) and refined to a conventional R factor of 0.045 using 855 unique reflections. The structure is stabilized by hydrogen bonds involving the water molecules with the amino, carboxyl, hydroxyl groups of the serine residue. The serine molecules are inter-connected through hydrogen-bonding forming layers along the b axis and are held by the water channels along the same direction. Superposition of this hydrated serine molecule on the dodeca hydrated Inosine 5'-monophosphate-L-serine co-complex structure solved by us earlier reveals that the serine and water molecules fit nicely on the hydrated nucleotide serine complex environment indicating conservative nature of the complexes. This crystal structure, with manifestation of coexistence and compromise of interactions of various types of hydrogen-bonds (N-H...O, O-H...O, C-H...O) for self-stabilization is a good example of biomolecular recognition and crystal engineering.

Keywords dihydrated serine, crystal structure, hydrogen bonding

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1. Introduction

The crucial role of water molecules, the coexistence/compromise of various interactions (N-H...O, O-H...O, C-H...O), maintaining the structure function activity of protein nucleic acid complexes *in vivo* [1,2] and also in crystal packing pattern are emerging as an important branch of science. The involvement of intermolecular hydrogen-bonding of the amino-acids through the water molecules are found to be very site specific (3), which thus affect the catalytic activity of proteins or enzymes with a reasonable sense. More the aquation, more will be the interaction, though it may be weak or strong, but the synergistic role of these waters may change the free energy of a system in their chemical scenario in a rational way. The detail geometries of the hydrogen-bonding networks of the amino-acid in different aquated environment may put forward some rational basis of the presence of that amino acid residue in the homologous protein endowing variable or differential activities. Accordingly, this kind of delicate interplay of the amphoteric water molecules and their variable donor acceptor capabilities towards the hydrogen-bond switching potentialities, may be followed in the structure of various amino acids in their different aquated crystals (4). In the present structural work of dihydrated DL-Serine, we are thus trying to investigate and understand the survival feature of serine in differential aquatic situation.

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2. Experimental

Single crystal of dihydrated DL-Serine ($C_3H_7NO_3.2H_2O$) was grown by controlling the humidity condition at 90% (in climatizing chamber) by slow evaporation of its aqueous solution at 290K. Two morphologically different crystals appeared in the crystallization bath and were grown in one week. The block shaped colourless forms were characterized (by TGA) as the more hydrated derivative of serine. The crystals were hygroscopic in nature, effervesced and deteriorated quickly on exposure to natural humidity. The crystal was mounted in a thin walled quartz capillary and used for X-ray data collection. The crystal parameters are given in Table 1. The structure was solved by direct methods using SHELXS-86(5) and successive Fourier methods and further refined by SHELXL-93(6) with full

matrix least square refinement Two water oxygens were indicated clearly in the successive difference electron density maps (ΔF).

Table 1. Crystal data and refinement parameters

Compound	Dihydrated DL-Serine
Colour / shape	Colourless / block shaped
Empirical formula	$C_3H_7NO_3.2H_2O$
Formula weight	141 12
Temperature	293(2)K
Radiation / wave length	CuK_α / 1 5418 Å
Crystal system	Monoclinic
Space group	$P2_1/n$
Unit cell dimensions	a = 4 831(2) Å
	b = 9 150(4) Å, β = 99 97 (2)°
	c = 10 444(4) Å
Volume	455(3) Å^3
Z	4
Density (calculated)	2 076 gm/cc
Absorption coefficient	1 734 mm^{-1}
F(000)	308
Crystal size	2 mm × 1 63 mm × 1 13 mm
Theta range for data collection	6 47 to 75 25°
Index ranges	$0 \le h \le 6, 0 < k \le 11,$
	$13 \le l \le 12$
Reflections collected	965
Independent reflections	855 [R (int) = 0 3260]
Refinement method	Full matrix least squares on F_o^2
Data / restraints / parameters	855 / 0 / 116
Goodness of fit on F_o^2	1 107
Final R indices [$I > 2\ \sigma$ (I)]	$R1$ = 0 045, $wR2$ = 0 122
R indices (all data)	$R1$ = 0 053, $wR2$ = 0 124
Extinction coefficient	0 005 (3)
Largest diff peak and hole	0 556 and 0 232 eÅ^{-3}

Finally, the least-square refinement of the positional and anisotropic temperature factors of the non-hydrogen atoms together with the hydrogen atoms keeping the temperature factors fixed at 0.05 Å^2, reduced the R and wR to 0.045 and 0.122 respectively.

3. Description and discussion

The final positional coordinates and the thermal parameters (U_{eqv}) of the structure are given in Table 2. The diagram produced by Insight II program (7) containing the numbering scheme of atom is shown in Figure 1. The intramolecular bond distances, angles and the torsion angles are given in Table 3. The bond lengths and angles involving the non-hydrogen atoms agree with the results of earlier X-ray and Neutron diffraction studies of DL-Serine (8), monohydrated L-Serine (9), free L-Serine (9) and hydrated IMP-L-Serine complex (10). The configurations around the C_α–C_β and C_α–N bonds are staggered. The crystal packing is held together by extensive hydrogen-bonding

Table 2. Positional coordinates (× 10^4 Å) and the equivalent isotropic temperature factor parameters (× 10^3 Å^2) of the non-hydrogen atoms (e.s.d.'s are given in the parenthesis)

Atom				U(eq)
NA	5925 (3)	3293 (2)	8479 (1)	23 (1)
O1	4204 (3)	- 61 (2)	6679 (1)	33 (1)
OH	2670 (2)	975 (1)	8362 (1)	31 (1)
OG	2974 (3)	3307 (2)	5683 (1)	33 (1)
C	4181 (3)	942 (2)	7505 (2)	24 (1)
CA	6228 (4)	2206 (2)	7449 (1)	23 (1)
CB	5820 (4)	2909 (2)	6113 (2)	28 (1)
W1	-2004 (5)	-135 (6)	5270 (4)	60 (3)
W2	2659 (6)	4288 (1)	7299 (3)	65 (4)

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor
$U = 1/3\Sigma\Sigma\ U\,aa,\,aa$

Table 3. Geometric parameters bond distances (in Å), angles (in°) and dihedral angles (in °)

Atomic distances (Å)				
Na	CA			1 491 (5)
O1	C			1 260 (4)
OH	C			1 249 (4)
OG	CB			1 418 (6)
C	CA			1 530 (5)
CA	CB			1 517 (5)
Angles (°)				
OH	C	O1		125 7 (2)
OH	C	CA		118 1 (2)
O1	C	CA		116 2 (2)
NA	CA	CB		111 6 (3)
NA	CA	C		109 4 (2)
CB	CA	C		111.9 (2)
OG	CB	CA		111 4 (2)
Dihedral angles (°)				
O1	C	CA	NA	179 7 (2)
OH	C	CA	NA	1.1 (1)
NA	CA	CB	OG	70 6 (1)
O1	C	CA	CB	55.5 (1)
OH	C	CA	CB	- 125.3 (2)
C	CA	CB	OG	52 4 (1)

interaction among the functional groups of serine and water molecules. The possible hydrogen bonding parameters along with the donor acceptor interactions are given in Table 4. The molecular packing is shown in Figure 2 down the a-axis. The C-O bond distances of the carboxy group (O1–C=1.260, OH–C=

1.249 Å) and C–N distance of the amino group (NA–Ca = 1.491Å) listed in Table 3 strongly suggest the zwitterionic form as were observed in their different free and hydrated crystals (11). The

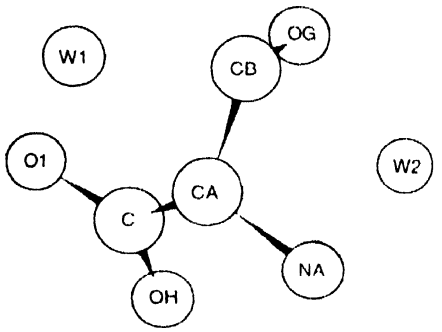

Figure 1. A diagram of the asymmetric unit with atom names

Table 4. Possible donor acceptor atoms with distances (in Å)

Donor	Acceptor	D···A (Å)
NA H2NA	W2	2.940
NA H2NA	OG$^{(iii)}$	2.762
NA H1NA	W1$^{(iv)}$	3.042
NA H1NA	O1	2.879
NA H2NA	O1$^{(iv)}$	2.822
W1 H1W1	O1	3.104
OH HOH	OG$^{(iv)}$	2.676
OH HOH	W2	3.227
CB H1CB	W2	3.472

Symmetry codes (i) 1/2-x, y-1/2, 3/2-z, (ii) 3/2-x, y-1/2, 3/2-z, (iii) x+1/2, 1/2-y, z+1/2, (iv) 1/2-x, y-1/2, z+1/2.

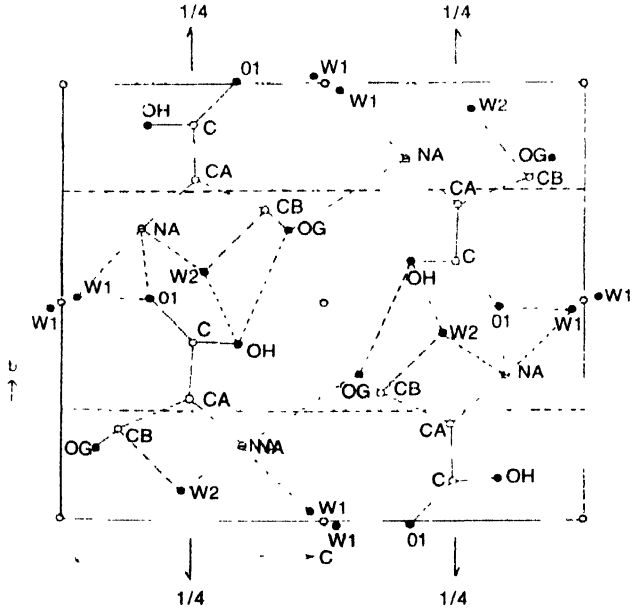

Figure 2. Molecular packing diagram viewed down the *a*-axis with possible hydrogen-bonds involving water molecules and DL-Serine (shown by dashed lines)

O = Carbon, ● = Oxygen/Water, Ø = Nitrogen

serine molecules are stabilized by hydrogen-bonds between amino and carboxyl terminals of different residues and water molecules in a cooperative fashion forming parallel layers along the *b*-axis. The water molecules have also formed hydrophilic layers parallel to the serine layers. In this structure, the amino end is acting as donor through all of its hydrogens and can interact with the waters, carboxyl and hydroxyl oxygens. Both the water molecules form hydrogen-bonds with the serine sites and also interact among themselves thus stabilizing the serine in the lattice. The U_{eq} of W1 and W2 oxygens are obviously higher than other non-hydrogen atoms of compact serine. Interestingly, the presence of water molecules in this structure, enforces the plausibility of C–H ···O interaction (C–H···O=2.472 Å) which is observed in several amino-acid peptide structures (12). Intermolecular interactions of various types co exist usually in crystals for stable packing. These C–H ···O hydrogen bonds often accompany stronger O–H···O and N–H···O bonds as are observed in this crystal structure too. Since molecular recognition and crystal engineering are very important area of research in recent times and it is interesting to note that even this highly aquated small biomolecule in its supramolecular association (packing) adequately displays the molecular recognition mechanism strategies which have wide importance in biology. It is unlikely that many of these strategies will not be exploited *in vivo*.

Acknowledgment

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