



Hydrogen bond patterns in 3-carboxypiperidinium semi-oxalate monohydrate

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Resumen

El cristal multicomponente $C_6H_{12}NO_2^+C_2HO_4^- \cdot H_2O$, o $NIPE^+ \cdot OXAL^- \cdot HYDR$, es un ensamblaje iónico asistido por enlaces de hidrógeno. El aminoácido $NIPE^+$ es un catión, una molécula $OXAL^-$ es un ión semi-oxalato, y la molécula de agua actúa como solvente. Las moléculas están conectadas por enlaces de hidrógeno del tipo $O-H \cdots O$ y $N-H \cdots O$, formando cadenas lineales \cdots semi-oxalato \cdots semi-oxalato \cdots extendidas a lo largo de a y descritas por el grafo $C(5)$. Estas cadenas interactúan con el grupo NH_2^+ del $NIPE^+$ construyendo un empaquetamiento cristalino bidimensional descrito por los grafos $R^2_1(5)$, $R^2_4(8)$ y $R^5_5(19)$, con capas corrugadas que corren en un plano (001), y separadas por interacciones hidrofóbicas en $c/2$. Se presenta el análisis de las estructuras de los componentes individuales y de la red de enlaces de hidrógeno de la estructura cristalina.

Palabras clave: estructura cristalina por difracción de rayos-X; enlaces de hidrógeno; cristales multi-componente

Abstract

The crystal structure of compound $C_6H_{12}NO_2^+ \cdot C_2HO_4^- \cdot H_2O$, or $NIPE^+ \cdot OXAL^- \cdot HYDR$, is an ionic ensemble assisted by hydrogen bonds established between $NIPE^+$ cations, $OXAL^-$ semi-oxalate anions and water molecules. The molecules are connected by $O-H \cdots O$ and $N-H \cdots O$ hydrogen bonds, forming linear \cdots semi-oxalate \cdots semi-oxalate \cdots chains extending along the a axis and described by the graph-set motif $C(5)$. These chains interact with the NH_2^+ group of $NIPE^+$ and the water molecules building a two-dimensional crystal packing of rings described by graph-set $R^2_1(5)$, $R^2_4(8)$ and $R^5_5(19)$, with corrugated layers running parallel to the (001) plane, and separated by hydrophobic interactions at $c/2$. Analyses of the structures of the individual components and the hydrogen-bond network of the crystal structure are given.

Keywords: Single-crystal X-ray diffraction; Hydrogen bonding; multi-component crystal

Introduction

Amino acids with oxalic acid form interesting ionic ensembles assisted by hydrogen bonds^{1,2}, in which the oxalic acid exists as semi-oxalate^{3,4} or oxalate⁵, or even with both forms cohabitating in the same structure⁶. In these ensembles, mostly formed with α -amino acids, the acidic proton goes to the amino acid acting as the counter-ion⁷. In addition to the ionic interactions, there are strong hydrogen bonds making these structures very stable chemical systems. For example, in the multi-component crystal reported in the Cambridge Structural Database (CSD, Version 5.33, Aug. 2012)⁸ L-leucinium oxalate⁹, semi-oxalate ions, strongly linked with each other by hydrogen bonds of the type $O-H \cdots O$, form linear and planar chains described by graph-set motif $C(5)$. These chains link to L-leucinium by means of bifurcated

hydrogen bonds of the type $N-H \cdots O$ and $O-H \cdots O$ forming rings described by graph-set motif $R^2_1(5)$. These types of supra-molecular structures are also seen in L-lysine dioxalate¹⁰; DL-alaninium oxalate⁴; L-alaninium oxalate¹¹; L-cysteinium semioxalate¹² and β -alaninium oxalate¹³. On the other hand, glycine oxalate³ and DL-alaninium semioxalate monohydrate¹⁴ display similar motifs although with non-planar \cdots semi-oxalate \cdots semi-oxalate \cdots chains.

In recent years, we have been interested in a systematic study of cyclic amino acids directed to understanding the influence on the observed crystal packing of the position of the amino group inside the cycloalkane ring such as in 2-piperidine carboxylic acid¹⁵, 3-piperidine carboxylic acid and 4-piperidine carboxylic acid¹⁶⁻¹⁹ and outside the cycloalkane ring such as in 4-aminoclohexane carboxylic acid^{20,21}.

In this work, we used 3-carboxypiperidinic acid (nipecotic acid), NIPE, an inhibitor in the synthesis of γ -aminobutyric acid and reported as a zwitterion²²⁻²⁴, mixed with oxalic acid, OXAL, a very strong acid reported in the solid state as catamers (α -form) or dimers (β -form)²⁵, to obtain the multicomponent crystal 1:1:1 NIPE⁺:OXAL⁻:HYDR, scheme 1.

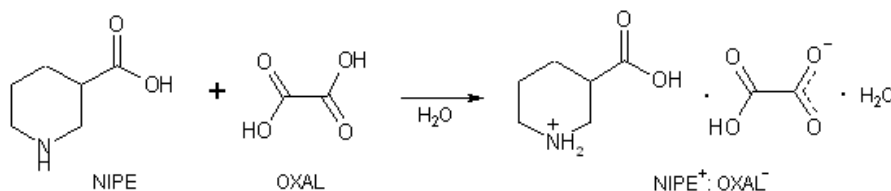
Experimental

Synthesis

The multi-component crystal NIPE⁺OXAL⁻·HYDR was prepared by mixing equimolar quantities of nipecotic acid (0.0462g, Aldrich 98%) with commercial grade oxalic acid dehydrated (0.0671 g, Aldrich 99.8%) dissolved in sufficient water (scheme 1). The mixture was placed in a reflux system for three hours at constant temperature of $\sim 343\text{K}$. Colorless crystals of suitable size for X-ray diffraction experiments were obtained by the slow evaporation during two months of the reflux solution. Melting point: 498.4-500.6K.

FT-IR analysis

FT-IR, 3420 cm^{-1} [t, OH (acid group)], 3240 cm^{-1} [t, OH (crystallization water)], 1728 cm^{-1} [t, C=O (acid group from OXAL and NIPE)], 2602 cm^{-1} [t, N-H (amino group of NIPE)].



Scheme 1: Synthesis of NIPE⁺:OXAL⁻:HYDR.

Results and Discussion

The multi-component crystal NIPE⁺OXAL⁻·HYDR crystallizes as a monohydrate. The asymmetric unit (see figure 1) consists of a NIPE⁺ ion with a positive charge resting over the nitrogen atom N1, an OXAL⁻ molecule as a semi-oxalate ion and a solvent water molecule.

In NIPE⁺, the piperidinium ring adopts the chair conformation³¹, and the COOH group has C1-O1 and C1-O2 distances of 1.292(4)Å and 1.204(4)Å, respectively. The semi-oxalate OXAL⁻ has a planar conformation, with torsion angles O3-C7-C8-O5 and O4-C7-C8-O6 of -1,7(4)° and -1,1(4), respectively. A search in the CSD⁸ (with R-factors less than 0.05) showed 94 structures with the semi-oxalate almost planar with torsion angles close to 0,0°, 55 structures in the range (2-10)°, 43 in the range (10-50)°, 13 in the range (50-90)° and only one structure in the bended conformation with torsion angle near 90°.

X-ray data collection and structure determination

A colorless rectangular crystal (0.4, 0.2, 0.1mm) was used for data collection. Diffraction data were collected at 298(2)K by ω -scan technique on a Rigaku AFC7S Mercury diffractometer²⁶ equipped with graphite-mono-chromatized MoK α radiation ($\lambda = 0.71073\text{Å}$). The data were corrected for Lorentz-polarization and absorption effects²⁷. The structure was solved by direct methods using the SIR08 program²⁸ and refined by a full-matrix least-squares calculation on F^2 using SHELXL²⁹. All hydrogen atoms were placed in calculated positions and refined using the riding model with C-H = 0.97Å, N-H = 0.90Å and O-H = 0.82Å and with their isotropic temperature factors set to 1.2 times those of their riding C, N and O atoms. The hydrogen atoms of the crystallization water molecule were localized in a difference Fourier map and refined isotropically in an independent manner. Table 1 displays the crystallographic data and the structure refinement parameters. All figures were performed using the Diamond software³⁰.

Crystallographic data for the structure reported here have been deposited with the Cambridge Crystallographic Data Centre (Deposition No. CCDC-892976). The data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/products/csd/request/> (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

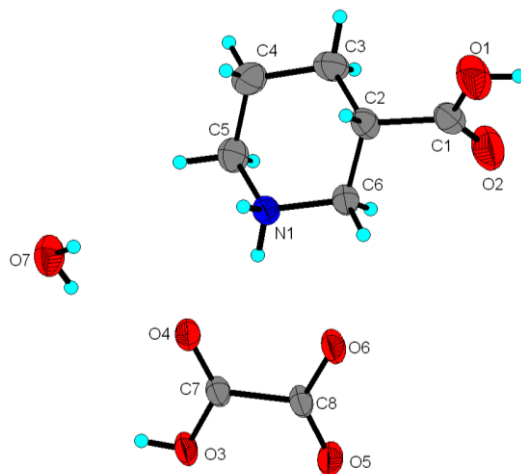


Fig. 1: Asymmetric unit of NIPE⁺:OXAL⁻·HYDR, showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 35% probability level

Table 1: Crystal data, data collection and structure refinement

Chemical formula	C ₆ H ₁₂ NO ₂ ·C ₂ HO ₄ ·H ₂ O
Formula weight	237.21
Crystal system	Orthorhombic
Space group	Pbca
<i>a</i> (Å)	11.184(4)
<i>b</i> (Å)	11.895(4)
<i>c</i> (Å)	16.781(6)
<i>V</i> (Å ³)	2232.4(1)
<i>Z</i>	8
<i>d_x</i> (g cm ⁻³)	1.412
<i>F</i> (000)	1008
<i>μ</i> (mm ⁻¹)	0.125
<i>θ</i> range (°)	2.4-27.6
<i>hkl</i> range	-13 ≤ <i>h</i> ≤ 14 -13 ≤ <i>k</i> ≤ 13 -21 ≤ <i>l</i> ≤ 21
Reflections	
Collected	23407
Unique (<i>R</i> _{int})	2318 (0.053)
With <i>I</i> > 2σ(<i>I</i>)	1634
Refinement method	Full-matrix least-squares on <i>F</i> ²
Number of parameters	153
<i>R</i> (<i>F</i> ²) [<i>I</i> > 2σ(<i>I</i>)]	0.071
<i>wR</i> (<i>F</i> ²) [<i>I</i> > 2σ(<i>I</i>)]	0.180
Goodness of fit on <i>F</i> ²	1.16
Max/min Δρ (e Å ⁻³)	0.36/-0.22

Table 2 shows the geometry of the hydrogen bonds in the multi-component crystal NIPE⁺OXAL⁻HYDR. The OXAL⁻ molecules interact with each other by means of hydrogen bonds of the type O3--H3...O6ⁱⁱⁱ, forming linear ...semi-oxalate...semi-oxalate... chains extending along the *a*

axis which can be described by the graph-set motif C(5)^{32,33} (see figure 2). The torsion angle formed by two adjacent semi-oxalate molecules and linked by the abovementioned hydrogen bond is 71.10° describing a coiled chain. A search in the CSD⁸ showed no preference in the conformation of these types of chains, with reported torsion angles varying in the range 0° (planar) to 90° (coiled).

NIPE⁺OXAL⁻HYDR packs in a two-dimensional structure, with corrugated layers running parallel to (001) plane, with the layers being separated by hydrophobic interactions at *c*/2 (see figure 3). Figure 2 also shows the various hydrogen bonds involved in the construction of one layer; the coiled OXAL⁻ chain, with the graph-set motif C(5), interacts with the NH₂⁺ group of NIPE⁺ forming two bifurcated hydrogen bonds, H1A interacting with O3 and O5, and H1B interacting with O4 and O6 of the OXAL⁻ by means of hydrogen bonds of the type N1--H1A...O3ⁱ, N1--H1A...O5ⁱ and N1--H1B...O4ⁱⁱ, N1--H1B...O6ⁱⁱ, respectively. These set of hydrogen bonds form two rings described by graph R²₁(5), also observed in compounds ammonium hydrogen oxalate³⁴ and 4-hydroxyiminomethyl-pyridine oxalate³⁵. OXAL⁻ interacts with the water molecule through O7--H7A...O4^{iv} and O7--H7B...O5ⁱⁱⁱ, forming by combination with N1--H1A...O5ⁱ and N1--H1B...O4ⁱⁱ H-bonds a R²₄(8) ring also observed in ammonium oxalate³⁶. Finally, the HOOC- group of the amino acid NIPE⁺ forms a hydrogen bond with the water molecule through O1--H1...O7. An ample view of the packing shows that along the *b* axis, a chain of edge-fused rings, R²₁(5)-R²₄(8)-R²₁(5), illustrates how the oxalate links to water and to the amino acid.

This chain and its symmetry equivalent one (by lattice translation along the *a* axis) are connected via OXAL⁻, NIPE⁺ and water molecules to form R⁵₅(19) ring.

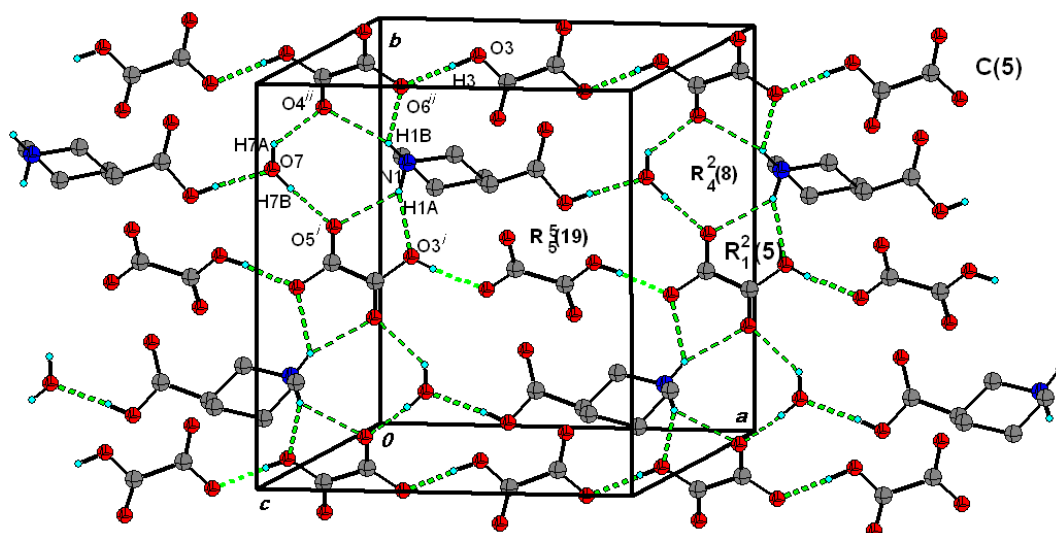
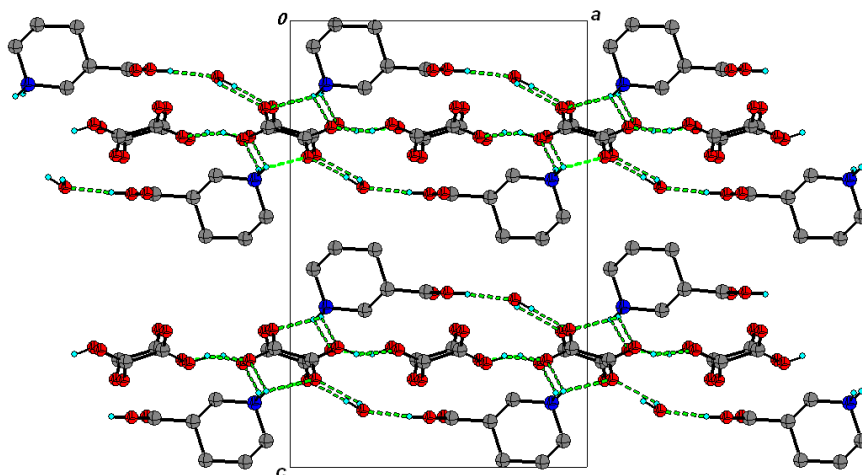


Fig. 2: Partial view of one of the corrugated layers running parallel to (001) plane. H atoms not involved in hydrogen bonding have been omitted for clarity.

Table 2:Hydrogen bonds geometry (Å, °)

D--H...A	D--H	H...A	D...A	D--H...A
O1--H1...O7	0.82	1.84	2.66(3)	175
N1--H1A...O3 ⁽ⁱ⁾	0.90	2.20	3.02(3)	151
N1--H1A...O5 ⁽ⁱ⁾	0.90	2.15	2.84(3)	133
N1--H1B...O4 ⁽ⁱⁱ⁾	0.90	2.16	2.98(3)	151
N1--H1B...O6 ⁽ⁱⁱ⁾	0.90	2.24	2.92(3)	132
O3--H3...O6 ⁽ⁱⁱⁱ⁾	0.82	1.69	2.46(3)	157
O7--H7A...O4 ^(iv)	0.82(6)	2.27(6)	2.93(4)	137(5)
O7--H7B...O5 ⁽ⁱⁱⁱ⁾	0.89(6)	1.91(6)	2.796(4)	176(6)

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

**Fig. 3:** Partial view of the two-dimensional crystal packing of NIPE⁺·OXAL⁻·HYDR in the *ac* plane, showing the corrugated layers separated by hydrophobic interactions at *c*/2. H atoms not involved in hydrogen bonding have been omitted for clarity.

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