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Supramolecular hydrogen-bonded networks in cytosinium nicotinate monohydrate and cytosinium isonicotinate cytosine dihydrate

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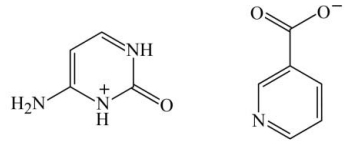
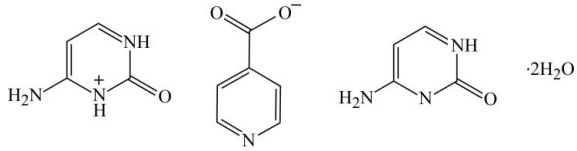
The title compounds are proton-transfer compounds of cytosine with nicotinic acid [systematic name: 4-amino-2-oxo-2,3-dihydropyrimidin-1-ium nicotinate monohydrate (cytosinium nicotinate hydrate), $C_4H_6N_3O^+\cdot C_6H_4NO_2^-\cdot H_2O$, (I)] and isonicotinic acid [systematic name: 4-amino-2-oxo-2,3-dihydropyrimidin-1-ium isonicotinate–4-aminopyrimidin-2(1*H*)-one–water (1/1/2) (cytosinium isonicotinate cytosine dihydrate), $C_4H_6N_3O^+\cdot C_6H_4NO_2^-\cdot C_4H_5N_3O\cdot 2H_2O$, (II)]. In (I), the cation and anion are interlinked by N—H···O hydrogen bonding to form a one-dimensional tape. These tapes are linked through water molecules to form discrete double sheets. In (II), the cytosinium–cytosine base pairs are connected by triple hydrogen bonds, leading to one-dimensional polymeric ribbons. These ribbons are further interconnected *via* nicotinate–water and water–water hydrogen bonding, resulting in an overall three-dimensional network.

Comment

Hydrogen-bonding interactions involving DNA nucleobases play an important role in DNA replication, gene expression and DNA repair. For example, enzymes that replicate or repair DNA often rely on hydrogen-bonding interactions between protein amino acid residues and DNA nucleobases. Understanding hydrogen-bonding interactions between DNA components and other molecules is vital to understanding the properties of DNA polymers and the mechanisms of biological processes. Cytosine is well known for its hydrogen-bonding capabilities in DNA and RNA, and several cytosine derivatives have been reported for use in biological applications (Blackburn & Gait, 1996; Kumar & Leonard, 1988) and in self-assembling triply hydrogen-bonded systems (Sessler & Jayawickramarajah, 2005). Isonicotinic and nicotinic acids play an important role in the metabolism of all living cells and they are structural isomers of pyridinecarboxylic acids. Nicotinic acid, also known as pyridine-3-carboxylic acid, is a member of the B-vitamin family. It is required by human cells for the synthesis of coenzymes and is involved in a wide range of biochemical processes. Nicotinic acid in pharmacological doses is used as an antihyperlipidaemic agent and reduces the level of cholesterol in the blood (Brutts & Lundholm, 1971). Continuing our studies of hydrogen-bond interactions and molecular recognition in the solid state (Sridhar & Ravikumar, 2007*a*,*b*, 2008, 2010; Sridhar *et al.*, 2009), we present here the solid-state structures of two salts, namely cytosinium nicotinate hydrate, (I), and cytosinium isonicotinate cytosine dihydrate, (II).



(I)



(II)

Views of (I) and (II) are shown in Figs. 1 and 2, respectively. In (I), the asymmetric unit contains one cytosinium cation, one nicotinate anion and one water molecule. In (II), one cytosine molecule (suffix *A*), one cytosinium cation (suffix *B*), one isonicotinate anion and two water molecules constitute the asymmetric unit. In both structures, the cytosinium cations are

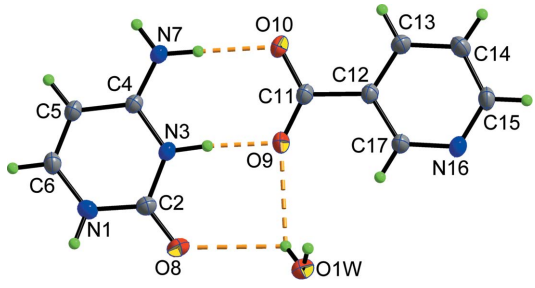


Figure 1
A view of the asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. Hydrogen bonds are shown as dashed lines.

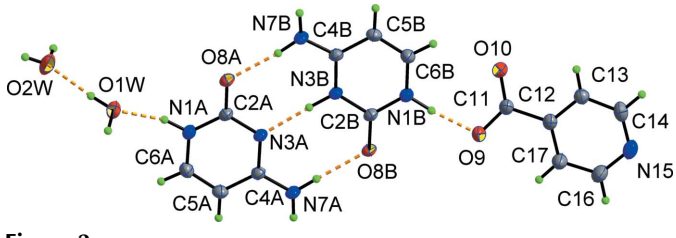


Figure 2
A view of the asymmetric unit of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. Hydrogen bonds are shown as dashed lines.

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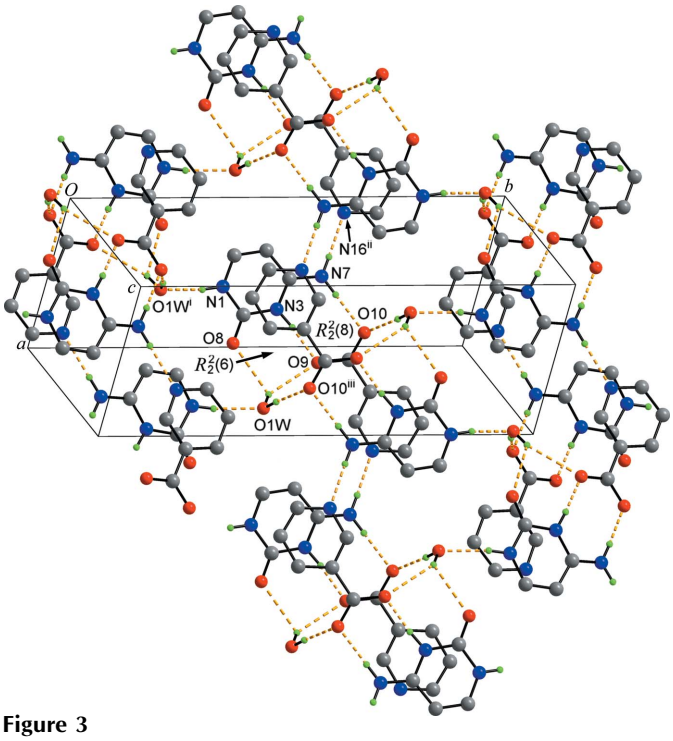

Figure 3
A partial packing diagram for (I), depicting the hydrogen-bonded tapes generated by N—H···O, N—H···N and O—H···O hydrogen bonds. Hydrogen bonds are shown as dashed lines and H atoms not involved in hydrogen bonding have been omitted for clarity. Only atoms involved in hydrogen bonding are labelled. [Symmetry codes: (i) $x-\frac{1}{2}, -y+\frac{1}{2}, z-\frac{1}{2}$; (ii) $x-1, y, z-1$; (iii) $-x+1, -y+1, -z+2$.]

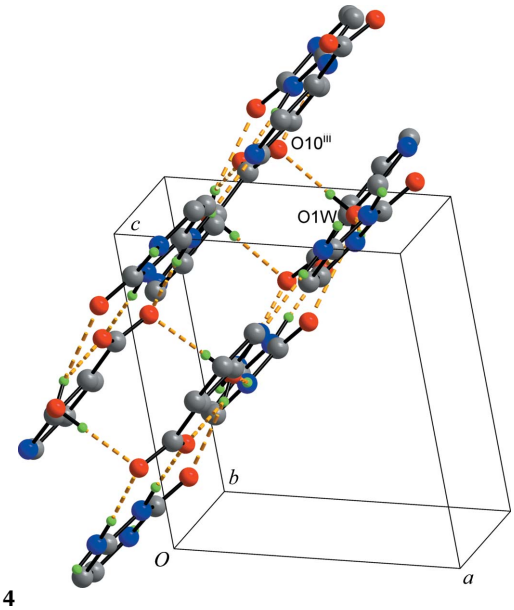

Figure 4
The crystal packing of (I), showing the pairs of tapes hydrogen bonded together to form discrete double sheets parallel to the $(10\bar{1})$ plane. H atoms not involved in hydrogen bonding have been omitted for clarity. Only atoms connecting the pairs of planes are labelled. [Symmetry code: (iii) $-x+1, -y+1, -z+2$.]

protonated at N3, leading to an increase in the internal angles (see angles C2—N3—C4 in Tables 1 and 3) compared with the neutral cytosine molecule [C—N—C = 119.4 (2)°; McClure & Craven, 1973].

The C—O bond lengths (Tables 1 and 3) of the carboxylic acid groups of both nicotinic and isonicotinic acids are closer to carboxylate bond lengths, where both C—O bond lengths are expected to be 1.255 (10) Å (Allen *et al.*, 1995). In both structures, the carboxylate groups are twisted out of the plane of the benzene ring. Least-squares planes were calculated for the benzene rings and the planes of the respective COO fragments. The dihedral angles are 9.6 (1)° for (I) and 11.8 (1)° for (II).

In the crystal structure of (I), N—H···O, N—H···N and O—H···O (Table 2) hydrogen bonds are observed. The water molecule plays a dual role as both donor and acceptor in the hydrogen-bonding interactions. It is involved in four hydrogen bonds, *via* water–cytosinium and water–anion interactions. The cytosinium cation and nicotinate anion are interlinked by two N—H···O hydrogen bonds and form an $R_2^2(8)$ motif (Etter, 1990; Etter *et al.*, 1990; Bernstein *et al.*, 1995). These cation–anion dimers are further connected by N—H···N hydrogen bonds, thereby generating a one-dimensional tape in the $(10\bar{1})$ plane (Fig. 3). One of the H atoms (H2*W*) of the water molecule further links each cation–anion dimer through a three-centred hydrogen bond (Jeffrey & Saenger, 1991) and forms an $R_2^2(6)$-type motif, while the other H atom (H1*W*) of the water molecule links to the inversion-related cation–anion dimer, thereby forming a centrosymmetric hexamer. The hexamers are further linked by the water molecules through N1—H1N···O1*W*^{i} (symmetry code given in Table 2) hydrogen bonds along the *b* axis. Thus, the combination of N—H···O, N—H···N and O—H···O hydrogen bonds leads to the formation of a supramolecular two-dimensional hydrogen-bonded network.

The cation–anion tapes of (I) are linked in pairs to form discrete double sheets. These ribbons lie in the $(10\bar{1})$ plane but are not hydrogen bonded together. Pairs of these planes are hydrogen bonded together to form discrete double planes (Fig. 4), within which aromatic π stacking occurs [centroid–centroid separation = 3.6353 (7) Å; symmetry code: $1-x, 1-y, 2-z$]. There are no significant interactions between adjacent double planes.

In the crystal structure of (II), N—H···O, N—H···N, O—H···O and O—H···N hydrogen bonds (Table 4) are observed. Cytosinium cations are connected to neutral cytosine molecules *via* triple intramolecular N—H···O and N—H···N hydrogen bonds, to give rings with an $R_2^2(8)$ graph-set motif. This is a reversed Watson–Crick base pairing which occurs *via* triple hydrogen bonds between the cation protonated at N3 and the neutral cytosine molecule (Fig. 5). Adjacent cytosinium–cytosine base pairs are held together by two N—H···O hydrogen bonds between NH_2 and carbonyl groups, leading to one-dimensional supramolecular polymeric ribbons along the crystallographic *b* axis. Similar triple hydrogen-bonded Watson–Crick base pairs are observed in cytosinium 4-nitrobenzoate cytosine monohydrate (Sridhar & Ravikumar, 2008), cytosine salicylic acid hydrate (2/3/2) complex (Sridhar & Ravikumar, 2010) and cytosine complexes with benzoic and phthalic acids (Perumalla *et al.*, 2005).

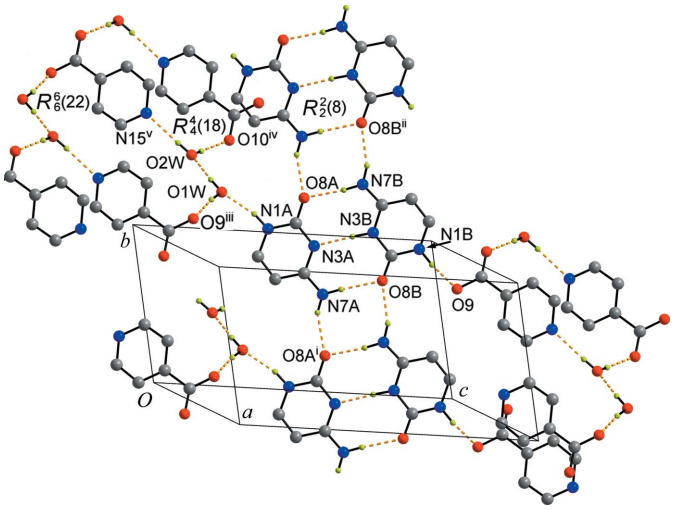

Figure 5
A partial packing diagram for (II), showing the one-dimensional polymeric ribbons. Dashed lines indicate N—H···O, N—H···N, O—H···O and O—H···N hydrogen bonds. H atoms not involved in hydrogen bonding have been omitted for clarity. Only atoms involved in the hydrogen bonding are labelled. [Symmetry codes: (i) $x, y-1, z$; (ii) $x, y+1, z$; (iii) $-x+1, -y+2, -z+1$; (iv) $-x+2, -y+3, -z+1$; (v) $x-1, y+1, z-1$.]

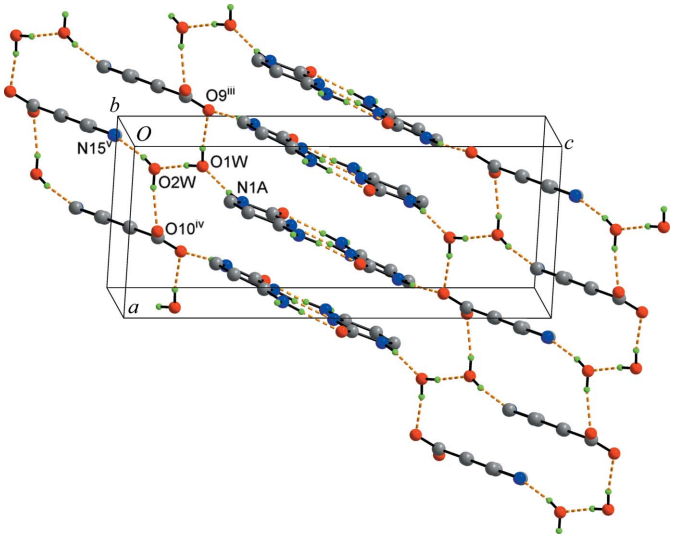

Figure 6
The crystal packing of (II), depicting the cytosinium–cytosine base pairs and their connection to adjacent nicotinate anions and water molecules *via* hydrogen-bonded linkages. H atoms not involved in hydrogen bonding have been omitted for clarity. Only atoms connecting the planes are labelled. [Symmetry codes: (iii) $-x+1, -y+2, -z+1$; (iv) $-x+2, -y+3, -z+1$; (v) $x-1, y+1, z-1$.]

In (II), atom N1*A* of the cytosine molecule forms an N—H···O hydrogen bond with water atom O1*W*, which in turn links to the second water molecule O2*W*, while atom N1*B* of the cytosinium cation links to the anion through an N—H···O hydrogen bond. The two water molecules are involved in five hydrogen bonds *via* water–cytosine, water–anion and water–water interactions. The water–water (O1*W*···O2*W*) chain links the anions into cyclic tetramer and hexamer hydrogen-bonded networks. First, the water molecules O2*W* form a cyclic tetramer containing an $R_4^4(18)$ motif, which is further linked by the O1*W* water molecules to form another hexameric $[R_6^6(22)]$ hydrogen-bonded network. Thus, the two water molecules and the anions form alternate hexamers $[R_6^6(22)]$ and tetramers $[R_4^4(18)]$ (Fig. 5).

In (II), the cytosine–cytosinium base pair ribbons along the *b* axis are connected to adjacent ribbons *via* a nicotinate–water hydrogen bonded linkage to form a plane which is tilted by about 20° from the *bc* plane (Fig. 6). Adjacent layers are hydrogen-bonded to each other to form a three-dimensional arrangement. This structure exhibits segregation of its molecular components.

By correlating the hydrogen-bonding pattern observed in the 2:1 structure of the present study with two of our previous structures (Sridhar & Ravikumar, 2008, 2010), as well as with structures reported in the literature (Perumalla *et al.*, 2005), the existence of cytosine base-pair self-assembly with triple hydrogen-bonding patterns is predominant.

Experimental

For the preparation of crystals of (I) suitable for X-ray study, cytosine (0.111 g, 1 mmol) and nicotinic acid (0.123 g, 1 mmol) were dissolved in water (10 ml) and the solvent was allowed to evaporate slowly. Crystals of (II) were obtained by slow evaporation from an equimolar solution of cytosine (0.111 g, 1 mmol) and isonicotinic acid (0.123 g, 1 mmol) in water (25 ml).

Compound (I)

Crystal data

$C_4H_6N_3O^+\cdot C_6H_4NO_2^-\cdot H_2O$
$M_r = 252.24$
Monoclinic, $P2_1/n$
$a = 7.5314$ (5) Å
$b = 18.2710$ (12) Å
$c = 8.4249$ (6) Å
$\beta = 104.374$ (1)°
$V = 1123.03$ (13) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.12$ mm^{-1}
$T = 294$ K
0.15 × 0.11 × 0.07 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
10476 measured reflections
1969 independent reflections
1794 reflections with $I > 2\sigma(I)$
$R_{int} = 0.022$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.037$
$wR(F^2) = 0.107$
$S = 1.06$
1969 reflections
187 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max} = 0.23$ e Å^{-3}
$\Delta\rho_{min} = -0.21$ e Å^{-3}

Compound (II)

Crystal data

$C_4H_6N_3O^+\cdot C_6H_4NO_2^-\cdot C_4H_5N_3O\cdot 2H_2O$
$M_r = 381.36$
Triclinic, $P\overline{1}$
$a = 7.1852$ (8) Å
$b = 7.3627$ (8) Å
$c = 17.7387$ (18) Å
$\alpha = 99.831$ (2)°
$\beta = 92.928$ (2)°
$\gamma = 107.862$ (2)°
$V = 874.70$ (16) Å^3
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 0.12$ mm^{-1}
$T = 294$ K
0.18 × 0.15 × 0.12 mm

Table 1
Selected geometric parameters (Å, °) for (I).

C11—O9	1.2481 (15)	C11—O10	1.2578 (14)
C2—N3—C4	124.46 (10)	O9—C11—C12	116.92 (10)
O9—C11—O10	125.56 (10)	O10—C11—C12	117.51 (10)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1N···O1*W*^{i}	0.89 (2)	1.98 (2)	2.854 (2)	167 (1)
N3—H3N···O9	0.94 (2)	1.71 (2)	2.651 (1)	175 (2)
N7—H7N···O10	0.91 (2)	1.91 (2)	2.816 (1)	176 (1)
N7—H8N···N16^{ii}	0.89 (2)	2.03 (2)	2.921 (1)	178 (1)
O1*W*—H1*W*···O10^{iii}	0.88 (2)	1.96 (2)	2.837 (2)	172 (2)
O1*W*—H2*W*···O9	0.81 (3)	2.51 (2)	3.207 (1)	144 (2)
O1*W*—H2*W*···O8	0.81 (3)	2.54 (2)	3.078 (2)	125 (2)

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

Table 3
Selected geometric parameters (Å, °) for (II).

C11—O10	1.2340 (18)	C11—O9	1.2645 (18)
C2*A*—N3*A*—C4*A*	120.33 (12)	O10—C11—C12	118.49 (13)
C4*B*—N3*B*—C2*B*	122.94 (12)	O9—C11—C12	116.82 (13)
O9—C11—O10	124.69 (14)		

Table 4
Hydrogen-bond geometry (Å, °) for (II).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*A*—H1*A*···O1*W*	0.94 (2)	1.81 (2)	2.730 (2)	164 (2)
N7*A*—H7*A*···O8*A*^{i}	0.87 (2)	2.02 (2)	2.835 (2)	154 (2)
N7*A*—H8*A*···O8*B*	0.91 (2)	1.98 (2)	2.883 (2)	175 (2)
N1*B*—H1*B*···O9	0.96 (2)	1.74 (2)	2.695 (2)	171 (2)
N3*B*—H3*B*···N3*A*	0.99 (2)	1.86 (2)	2.846 (2)	176 (2)
N7*B*—H7*B*···O8*B*^{ii}	0.89 (2)	2.00 (2)	2.845 (2)	159 (2)
N7*B*—H8*B*···O8*A*	0.92 (2)	1.90 (2)	2.816 (2)	174 (2)
O1*W*—H1*W*···O9^{iii}	0.86 (3)	1.94 (3)	2.792 (2)	172 (2)
O1*W*—H2*W*···O2*W*	0.88 (3)	1.82 (3)	2.691 (2)	173 (2)
O2*W*—H3*W*···O10^{iv}	0.81 (3)	1.96 (3)	2.772 (2)	171 (2)
O2*W*—H4*W*···N15^{v}	0.83 (3)	2.03 (3)	2.852 (2)	171 (3)

Symmetry codes: (i) $x, y-1, z$; (ii) $x, y+1, z$; (iii) $-x+1, -y+2, -z+1$; (iv) $-x+2, -y+3, -z+1$; (v) $x-1, y+1, z-1$.

Data collection

Bruker SMART APEX CCD area-detector diffractometer
8483 measured reflections
3083 independent reflections
2751 reflections with $I > 2\sigma(I)$
$R_{int} = 0.017$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.130$
$S = 1.10$
3083 reflections
288 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max} = 0.24$ e Å^{-3}
$\Delta\rho_{min} = -0.35$ e Å^{-3}

All N- and O-bound H atoms were located in a difference Fourier map and their positions and isotropic displacement parameters were refined. All other H atoms were located in a difference electron-density map but were positioned geometrically and included as riding atoms, with C—H = 0.93 Å and $U_{iso}(H) = 1.2U_{eq}(C)$.

For both compounds, data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *DIAMOND* (Brandenburg & Putz, 2005); software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SF3134). Services for accessing these data are described at the back of the journal.

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