

Cytosinium 3,5-dinitrosalicylate

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Key indicators

Single-crystal X-ray study

T = 298 K

Mean $\sigma(\text{C}-\text{C}) = 0.004 \text{ \AA}$

R factor = 0.044

wR factor = 0.160

Data-to-parameter ratio = 13.1

For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.

The crystal structure of cytosinium 3,5-dinitrosalicylate (systematic name: 6-amino-2-oxo-2,3-dihydropyrimidinium 3,5-dinitrosalicylate), $\text{C}_4\text{H}_6\text{N}_3\text{O}^+ \cdot \text{C}_7\text{H}_3\text{N}_2\text{O}_7^-$, shows the presence of a primary heteroionic cyclic $R_2^2(8)$ interaction between the H-atom donors of the protonated cytosinium cation and the carboxylate O-atom acceptors of the 3,5-dinitrosalicylate anion. Additional peripheral hydrogen-bonding interactions involving all available cytosinium H-atom donors and both phenol and nitro O-atom acceptors of the anion species give a three-dimensional polymeric structure.

Comment

Cytosine [4-aminopyrimidin-2(1*H*)-one] is one of the three pyrimidine bases (together with thymine and uracil) which are essential biological molecules in the DNA replication process (Wilson *et al.*, 1991). Cytosine complements the nucleic acid guanine; it leads to the nucleoside cytidine and the corresponding nucleotide and may also be found in very small quantities as a post-modified form, 5-methylcytosine, in certain nucleic acids (Devlin, 1986) such as in tuberculinic acid (Johnson & Coghill, 1925). A derivative compound, cytosine arabinoside, is a commercial drug (Cytarabine) which is used for the treatment of acute leukaemia and malignant lymphoma, acting through DNA polymerase inhibition (Wilson *et al.*, 1991; Berkow, 1992). More recently, 5-fluorocytosine (5-FC) has been used as a prodrug in suicide gene therapy of cancer with the crystal structure of bacterial cytosine deaminase (bCD) also being reported (Mahan *et al.*, 2004). The crystal structures of cytosine (Barker & Marsh, 1964) and cytosine monohydrate (Jeffrey & Kinoshita, 1963) were determined many years ago and have been reinvestigated [McClure & Craven, 1973; Eisenstein, 1988 (97 K)], while those of the neutral adducts with other organic bases are also known: with acridine (1:1 monohydrate; Shefter, 1968), 5-fluorouracil (1:1; Voet & Rich, 1969) and ninhydrin (1:1; Guin, 1970).

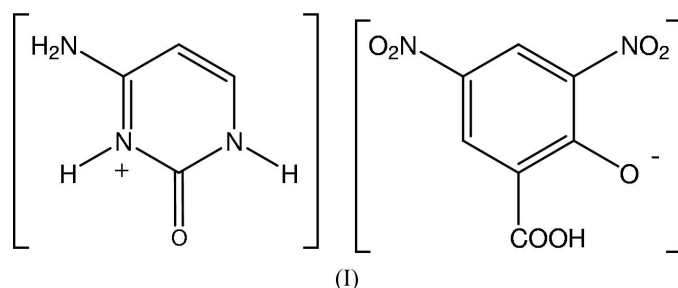
As a base, cytosine is quite strong ($\text{p}K_{a2} = 12.2$ and $\text{p}K_{a1} = 4.6$; Stecher, 1968) and, in the presence of acids, is readily protonated at the N3 ring position. The crystal structures of a number of inorganic cytosinium salts are known [chloride (Mandel, 1977), nitrate (Cherouana *et al.*, 2003), dihydrogenphosphate (Jaskólski, 1989; Bagieu-Beucher, 1990), penta iodide (Wang *et al.*, 2001) and the cyclophosphate (Swamy *et al.*, 2001)]. Cytosinium salts of organic acids are also common, the structures of a number of these, including some with *N*-protected amino acids, having been reported [*N*-formylglycinate (Ohki *et al.*, 1975), *N*-benzoylglycinate (Tamura *et al.*, 1972; Görbitz & Sagstuen, 2004) (105 K), *N,N*-

Received 8 February 2005

Accepted 14 February 2005

Online 26 February 2005

phthaloylglutamate (Takenaka *et al.*, 1980), trichloroacetate (Gdaniec *et al.*, 1989), resorcyate (Tamura *et al.*, 1973) and hydrogen maleate (Balasubramanian *et al.*, 1996)]. An unusual proton-transfer compound with the dye orange G [disodium 7-hydroxy-8-(phenylazo)-1,3-naphthalenedisulfonate] is also known (Ojala *et al.*, 1994)], as well as the nucleoside 1-(β -D-arabinofuranosyl)cytosine (Sherfinski & Marsh, 1973). Among these, the carboxylate salts feature stabilization through strong hydrogen-bonding interactions which commonly involve, among other types, a primary cyclic $R_2^2(8)$ association between the protonated N3 and adjacent C4 amine donors and the two carboxylate O-atom acceptors. This is similar to those found in the proton-transfer compounds of 2-aminopyrimidine with carboxylic acids (Lynch *et al.*, 1994; Smith *et al.*, 1995; Lynch *et al.*, 1997; Lynch & Jones, 2004).



We report here the crystal structure of a proton-transfer compound formed from the reaction of cytosine with 3,5-dinitrosalicylic acid (DNSA), namely cytosinium 3,5-dinitrosalicylate, (I). We have previously determined the structures of more than 40 charge-transfer compounds of DNSA with both aliphatic and aromatic Lewis bases (Smith *et al.*, 2002, 2003, 2004, 2005). In these, conventional hydrogen bonding is most significant in the structural assembly, with inter-species π - π interactions limited to those examples with the polycyclic heteroaromatic bases, quinoline, 2,2'-bipyridine and 1,10-

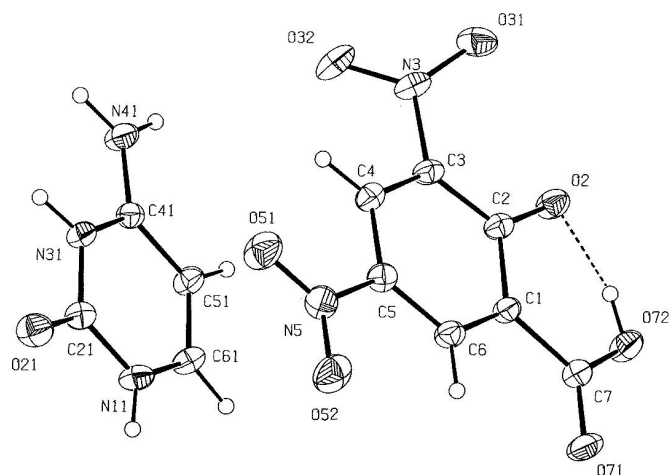


Figure 1
The molecular configuration and atom-numbering scheme for the cytosinium cation and the DNSA anion in (I). Non-H atoms are shown as 30% probability displacement ellipsoids. The dashed line indicates a hydrogen bond.

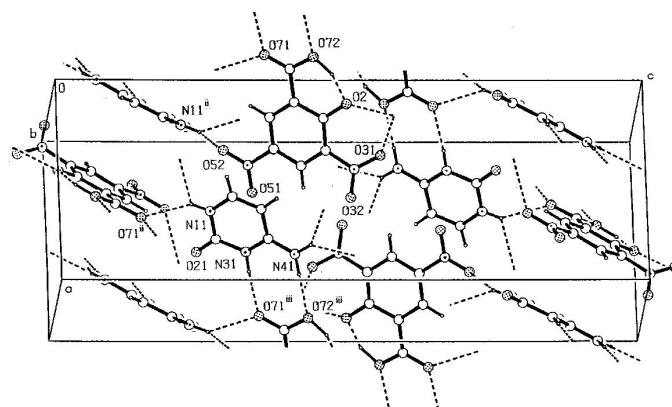


Figure 2
Perspective view of the packing of (I) in the unit cell, viewed approximately down the *b* axis, showing cation-anion hydrogen-bonding associations as dashed lines.

phenanthroline (Smith *et al.*, 2005) and adenosine (Smith *et al.*, 2004). In the structure of (I) (Fig. 1), a single proton transfer to N3 of the pyrimidine ring occurs, with the two cytosinium cation donors then giving the previously mentioned cyclic $R_2^2(8)$ hydrogen-bonding association with the DNSA carboxylate O-atom acceptors [$N31-H31 \cdots O71^{iii} = 2.839(3) \text{ \AA}$ and $N41-H41B \cdots O72^{iii} = 2.892(3) \text{ \AA}$; symmetry code: (iii) $1 + x, 1 + y, z$]. Peripheral associations involving all other proton donors of the cytosinium species and both phenol and nitro O-atom acceptors of the DNSA anions (Table 1) give a three-dimensional polymeric structure (Fig. 2). Neither the cytosinium carbonyl O atom (O21) nor nitro atoms O32 and O51 are involved in hydrogen bonding. Although the layers of associated cations and anions form stacks, there is no molecular superposition within the stacks to suggest any π - π interaction in this structure, such as is present in the cytosinium-orange G structure (Ojala *et al.*, 1994).

The structural features of the DNSA anion in (I) are similar to those found in the majority of the DNSA proton-transfer compounds (Smith *et al.*, 2002, 2003), with the more associative proximal nitro group at C3 showing greater rotation out of the plane of the benzene ring [torsion angle $C2-C3-N3-O32 = 143.6(2)^\circ$] than the less associative C5 nitro group [torsion angle $C4-C5-N5-O52 = 178.9(2)^\circ$]. As expected for the intramolecularly associated carboxyl group, coplanarity with the parent ring is maintained [torsion angle $C2-C1-C7-O71 = -178.6(2)^\circ$]. The proton is located on the carboxyl O atom [$O72-H72 \cdots O2 = 2.425(3) \text{ \AA}$], which is also the case in *ca* 70% of the known proton-transfer compounds of DNSA (Smith *et al.*, 2002, 2003, 2005).

Experimental

The title compound was synthesized by heating cytosine (1 mmol) and 3,5-dinitrosalicylic acid (DNSA) in 80% ethanol/water (50 ml) under reflux for 10 min. After concentration to *ca* 30 ml, partial room-temperature evaporation of the hot-filtered solution gave yellow prisms (m.p. 527.3–529.6 K).

Crystal data

$C_7H_3N_2O_7^+ \cdot C_4H_6N_3O^-$
 $M_r = 339.23$
 Monoclinic, $P2_1/n$
 $a = 9.339$ (3) Å
 $b = 5.766$ (3) Å
 $c = 24.662$ (9) Å
 $\beta = 90.07$ (3)°
 $V = 1328.0$ (9) Å³
 $Z = 4$

$D_x = 1.697$ Mg m⁻³
 Mo $K\alpha$ radiation
 Cell parameters from 25 reflections
 $\theta = 12.7$ – 17.3 °
 $\mu = 0.15$ mm⁻¹
 $T = 298$ (2) K
 Prism, yellow
 $0.55 \times 0.30 \times 0.15$ mm

Data collection

Rigaku AFC-7R diffractometer
 ω - 2θ scans
 Absorption correction: none
 3572 measured reflections
 3059 independent reflections
 1728 reflections with $F^2 > 2\sigma(F^2)$
 $R_{int} = 0.025$

$\theta_{max} = 27.5$ °
 $h = -5 \rightarrow 12$
 $k = -7 \rightarrow 3$
 $l = -32 \rightarrow 32$
 3 standard reflections
 frequency: 150 min
 intensity decay: 1.0%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.044$
 $wR(F^2) = 0.160$
 $S = 0.93$
 3059 reflections
 233 parameters
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.1P)^2 + 0.9288P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} = 0.002$
 $\Delta\rho_{max} = 0.24$ e Å⁻³
 $\Delta\rho_{min} = -0.29$ e Å⁻³

Table 1

Hydrogen-bonding geometry (Å, °).

D—H...A	D—H	H...A	D...A	D—H...A
O72—H72...O2	1.07	1.40	2.425 (3)	156
N11—H11...O52 ⁱ	0.85 (3)	2.60 (3)	3.113 (4)	121 (2)
N11—H11...O71 ⁱⁱ	0.85 (3)	2.26 (3)	2.953 (3)	139 (2)
N31—H31...O71 ⁱⁱⁱ	0.89 (4)	1.95 (4)	2.839 (3)	173 (3)
N41—H41A...O2 ^{iv}	0.93 (3)	2.16 (3)	2.921 (3)	137 (2)
N41—H41A...O31 ^{iv}	0.93 (3)	2.32 (3)	3.150 (4)	148 (2)
N41—H41B...O72 ⁱⁱⁱ	0.93 (3)	1.96 (3)	2.892 (3)	176 (3)

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

H atoms potentially involved in hydrogen-bonding interactions were located by difference methods and, with the exception of H72 which was constrained, their positional and isotropic displacement parameters were refined. Other H atoms were included in the refinement at calculated positions (C—H = 0.95 Å). Using the riding-model approximation, $U_{eq}(H)$ values were fixed at $1.2U_{eq}(C)$.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1999); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN for Windows* (Molecular Structure Corporation, 1999); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *PLATON*.

The authors acknowledge financial support from the School of Physical and Chemical Sciences (Queensland University of Technology) and the School of Science, Griffith University.

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