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Cytosinium 3,5-dinitrosalicylate

Graham Smith,[a]* Urs D. Wermuth[a] and Peter C. Healy[b]

[a]School of Physical and Chemical Sciences, Queensland University of Technology, GPO Box 2434, Brisbane 4001, Australia, and [b]School of Science, Griffith University, Nathan 4111, Australia

Correspondence e-mail: g.smith@qut.edu.au

Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.004 Å
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.

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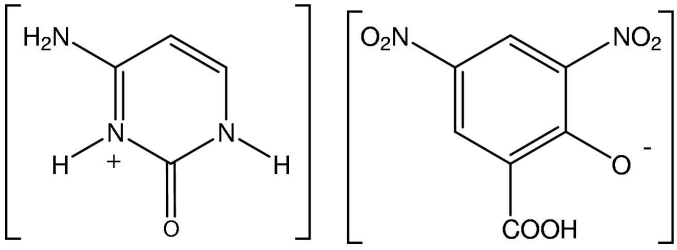
The crystal structure of cytosinium 3,5-dinitrosalicylicate (systematic name: 6-amino-2-oxo-2,3-dihydropyrimidinium 3,5-dinitrosalicylate), $C_4H_6N_3O^+\cdot C_7H_3N_2O_7^-$, shows the presence of a primary heteroionic cyclic $R_2^2(8)$ interaction between the H-atom donors of the protonated cytosinium 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 (Cytarbine) 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 (pK_{a2} = 12.2 and pK_{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), pentaiodide (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*-

phthaloylglutamate (Takenaka *et al.*, 1980), trichloroacetate (Gdaniec *et al.*, 1989), resorcylate (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).



(I)

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-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···O71^{iii} = 2.839 (3) Å and N41—H41*B*···O72^{iii} = 2.892 (3) Å; 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 aceptors 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).

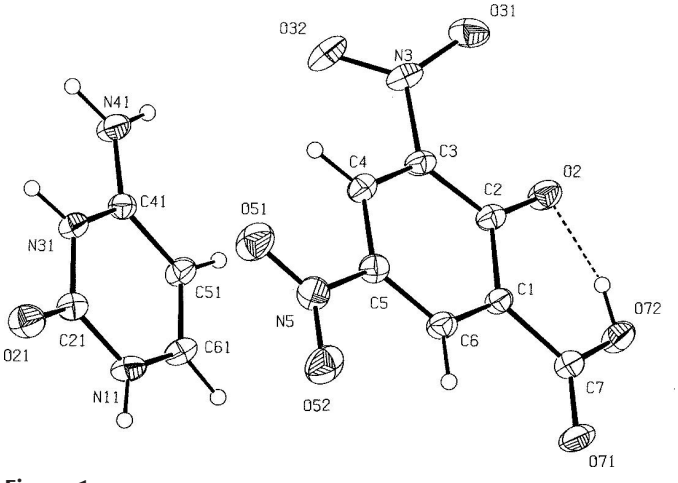


Figure 1
The molecular configuration and atom-numbering scheme for the cytosinium cation and the DNSA anion in (I). Non-H atoms are shown as 30% probability displacement ellipsoids. The dashed line indicates a hydrogen bond.

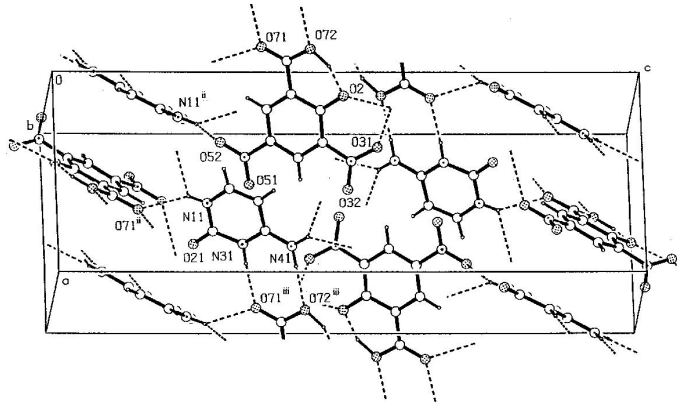


Figure 2
Perspective view of the packing of (I) in the unit cell, viewed approximately down the *b* axis, showing cation–anion hydrogen-bonding associations as dashed lines.

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)°] than the less associative C5 nitro group [torsion angle C4—C5—N5—O52 = 178.9 (2)°]. As expected for the intramolecularly associated carboxyl group, coplanarity with the parent ring is maintained [torsion angle C2—C1—C7—O71 = −178.6 (2)°]. The proton is located on the carboxyl O atom [O72—H72···O2 = 2.425 (3) Å], 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
β = 90.07 (3)°
V = 1328.0 (9) Å^3
Z = 4
D_x = 1.697 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 12.7–17.3°
μ = 0.15 mm^{-1}
T = 298 (2) K
Prism, yellow
0.55 × 0.30 × 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
θ_{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*.

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