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Adenosinium 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) = 0.005 Å
R factor = 0.036
wR factor = 0.122
Data-to-parameter ratio = 7.6

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

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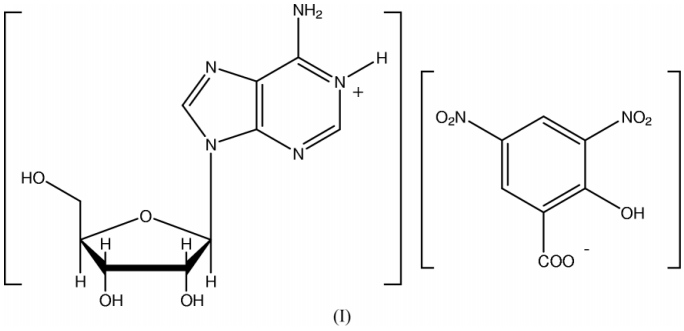
The crystal structure of adenosinium 3,5-dinitrosalicylicate, $C_{10}H_{14}N_5O_4^+\cdot C_7H_3N_2O_7^-$, shows the presence of a primary chain structure formed through homomeric head-to-tail cyclic $R_2^2(10)$ hydrogen-bonding interactions between hydroxy O- and both purine and amine *N*-donor and acceptor groups of the furanose and purine moieties of the adenosinium species. These chain structures are related by crystallographic 2_1 symmetry. Secondary hetero-ionic hydrogen bonding, involving the 3,5-dinitrosalicylate anion, including a cyclic $R_2^2(8)$ interaction between the carboxylate group and the protonated purine and amine groups of the adenosinium cation are also present, together with heteromolecular π–π interactions giving a three-dimensional hydrogen-bonded polymer structure.

Comment

The nucleoside adenosine (6-amino-9β-D-ribofuranosyl-9*H*-purine) is an essential biological molecule, which in its 5′-di- and triphosphorolated forms (ADP, ATP) is associated with energy-transfer processes in muscle tissue (Wilson *et al.*, 1991), where the ATP levels in mammals are commonly 350–400 mg per 100 g (Stecher, 1968). Also as its 3′,5′-cyclic monophosphate ester (cAMP) it is associated with G proteins in second messenger systems for a number of hormones (Wilson *et al.*, 1991). Adenosine is also involved in a number of other biological processes involving RNA where it is present with high frequency among the structural motifs (Portmann *et al.*, 1996; Ortoleva-Donnelly *et al.*, 1998), while it has also been a targeted molecule for derivatization for enzyme pro-drug therapy (Vogt *et al.*, 2000; Bressi *et al.*, 2000; Qiu *et al.*, 2002; Costanzi *et al.*, 2003). The structures of many simple neutral adenosine analogues have been reported, including the parent [Lai & Marsh, 1972 (X-ray); Klooster *et al.*, 1991 (neutron, 123 K)], adenosine-5′-phosphate (Kraut & Jensen, 1963), adenosine-3′-phosphate dihydrate (adenylic acid b) (Brown *et al.*, 1953; Sundaralingam, 1966), deoxyadenosine monohydrate (Watson *et al.*, 1965), adenosine-5′-*O*-methylphosphate (Hoogendorp *et al.*, 1978), 3′-*O*-acetyladenosine (Rao & Sundaralingam, 1970), and α-D-2′-deoxyadenosine monohydrate (Rohrer & Sundaralingam, 1970). The stereochemistry of 3′-*N*-substituted 3′-deoxyadenosines has also been reviewed (Sheldrick & Morr, 1980) and the structure of the Na salt of deoxyadenosine-5′-phosphate hexahydrate has been determined (Reddy & Viswamitra, 1975). The di- and trinucleoside phosphate esters β-adenosine-2′-β-uridine-5′-phosphate (Shefter *et al.*, 1969) and adenylyl-(3′,5′)-adenylyl-(3′,5′)-adenosine (Suck *et al.*, 1976) are also known. The structures of neutral adducts of adenosine with 5-bromouridine (Haschemeyer & Sobell, 1965), 5-bromouracil (Aiba *et*

al., 1978) and proflavine (Swaminathan *et al.*, 1982) have been reported, and in this 1:2 proflavine structure, stability is enhanced by the presence of heteromolecular π–π ring interactions, as well as the expected conventional hydrogen-bonding interactions.



(I)

As a base, adenosine will react with the stronger carboxylic acids, resulting in protonation at the N1 position of the purine ring, giving salts with enhanced crystallinity due to hydrogen-bonding interactions, such as in the adenosinium chloride structure (Shikata *et al.*, 1973) and the structural aspects of protonated and complexed adenosine have also been reviewed (Hauser & Keese, 2002). One such compound, adenosinium picrate has been known for some time (Stecher, 1968), but its crystal structure has only recently been reported (Goto *et al.*, 2004).

We report here the crystal structure of a proton-transfer compound formed from the reaction of adenosine with an acid similar to picric acid, 3,5-dinitrosalicylic acid (DNSA)–adenosinium 3,5-dinitrosalicylate, (I). We have previously completed the structures of more than 40 charge-transfer compounds of DNSA with both aliphatic and aromatic Lewis bases (Smith *et al.*, 2002; Smith *et al.*, 2003, 2004). In these,

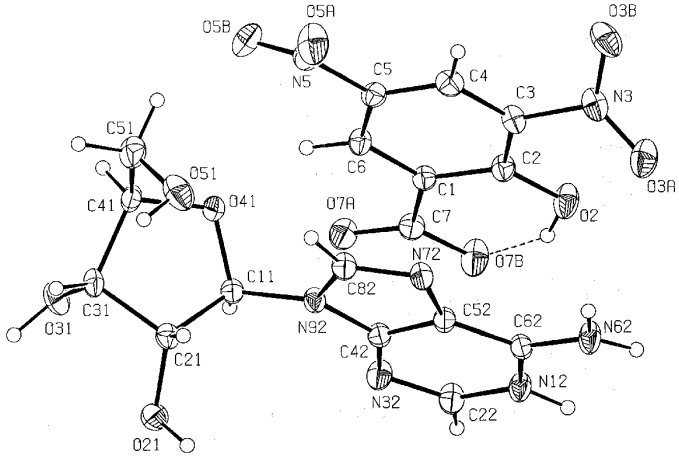


Figure 1
The molecular configuration and atom-numbering scheme for the adeninium cation and the DNSA anion in (I), with displacement ellipsoids drawn at the 30% probability level and H atoms represented by spheres of arbitrary radius. The intramolecular hydrogen bond is shown as a dashed line.

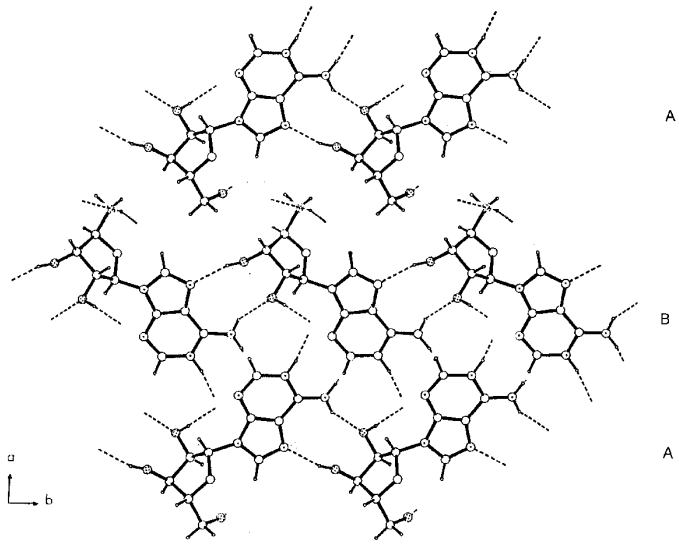


Figure 2
Head-to-tail homomeric adenosinium cation–chain associations along the *b*-cell direction, with *A* and *B* chains related by a 2_1 screw operation. Hydrogen bonds are shown as dashed lines.

conventional hydrogen bonding is the most significant intermolecular interaction in determining the crystal packing, 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.*, 2004).

In the structure of (I) (Fig. 1), proton transfer to N12 of the purine ring occurs with subsequent formation of both homo- and heteromolecular hydrogen-bonding associations (Table 1), resulting in a three-dimensional polymer structure. The primary structure involves the adenosinium cations in homomeric cyclic $R_2^2(10)$ head-to-tail associations involving two of the nitrogen groups of the purine residue and two hydroxy groups of the ribose residue [O31—H31*A*$\cdots$N72^{iii}: 2.785 (4) Å; N62—H62*A*$\cdots$O21^{v}: 2.886 (4) Å; symmetry codes: (iii) $x, y+1, z$; (v) $x, y-1, z$]. These 2_1 screw-related chains extend along the *b*-cell direction (Fig. 2). The DNSA anions are primarily associated with the adenosinium cations peripherally through $R_2^2(8)$ cyclic hydrogen-bonded dimers involving the two carboxylate O-atom acceptors and two purine donors, the protonated hetero N atom and the substituent amine N atom [N12—H12$\cdots$O7*A*^{i}: 2.763 (4) Å; N62—H62*B*$\cdots$O7*B*^{i}: 2.785 (5) Å; symmetry code: (i) $1-x, y-\frac{1}{2}, 1-z$] (Fig. 3). This type of association is similar to the common symmetric carboxylate 2-aminopyrimidine interaction found in the DNSA-2-aminopyrimidine structure (Smith *et al.*, 2003) and in other similar structures (Lynch *et al.*, 1994, 1997; Smith *et al.*, 1995). The O21 ribose hydroxy group is also strongly linked to a DNSA carboxyl O atom (O7*A*^{ii}) down the *c*-cell direction [2.782 (4) Å: symmetry code: (ii) $x, y, 1+z$]. Other weaker ribose-O$\cdots$DNSA 5-nitro-O associations also link the polymer strands while the 3-nitro group is unassociated, as are O41 of the ribose and N32 of the purine residues of the adenosinium cation. There are also significant heteromolecular π–π stacking interactions between the six-

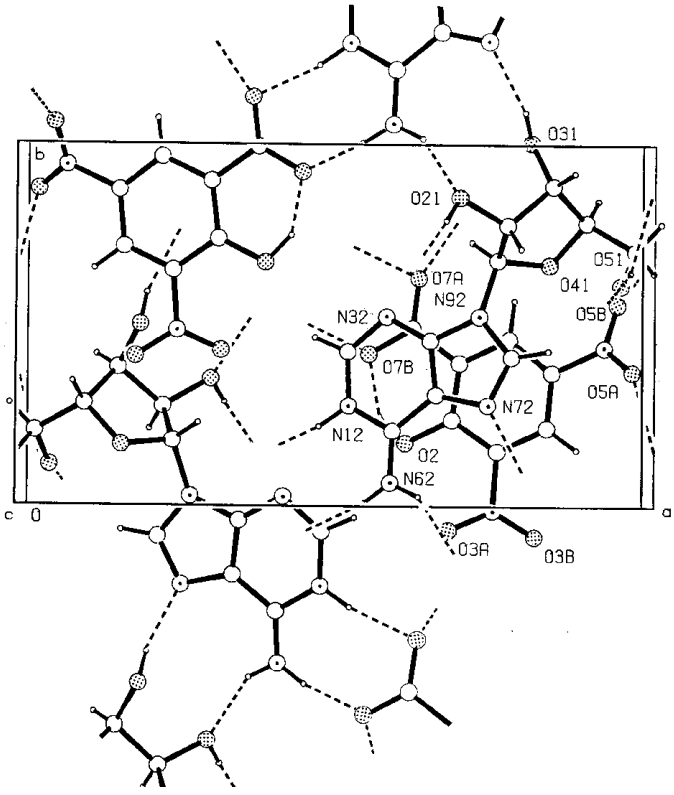


Figure 3
The crystal packing of (I), viewed down the *c* axis, showing cation–anion hydrogen-bonding associations and partial inter-species ring superimposition with π–π stacking.

membered DNSA anion benzene rings with the five-membered (N72–C82) portions of the adenosinium cation rings down the *c* axis [minimum ring centroid separation = 3.61 (1) Å]. The overall result is a three-dimensional polymer structure.

The conformation of the adenosinium cation appears to be influenced in (I) by the presence of an intramolecular C—H···O interaction between H82 and the O51 hydroxy group [3.278 (5) Å]. However, the resultant torsion angle C82—N92—C11—C21 [−71.4 (4)°] is a value which is extremely variable among the adenosine analogues.

Within the DNSA anion, the structural features vary from those of the majority of the proton-transfer compounds (Smith *et al.*, 2002, 2003) mainly in the conformation of the nitro substituent groups. The proximal nitro group at C3 is more commonly involved in hydrogen bonding and therefore shows a greater rotation out of the plane of the ring than the C5 group. However, in (I), where both O5*A* and O5*B* are associated, C5 rotation is greater than usual but C3 rotation is also significant, despite being unassociated [torsion angles: C4—C5—N5—O5*B* = 152.6 (4) Å and C2—C3—N3—O5*B* = 146.8 (4)°]. By comparison, the torsion angle C2—C1—C7—O7*A*, associated with the intramolecularly hydrogen-bonded carboxylate group, is −177.7 (4)°. This hydrogen bond [O2···O7*B* = 2.438 (5) Å] has the proton located on the phenol O atom rather than the carboxyl group, such as is found in *ca* 70% of the proton-transfer compounds of DNSA (Smith *et al.*, 2002, 2003).

Experimental

The title compound was synthesized by heating under reflux for 10 min, 1 mmol quantities of adenosine and 3,5-dinitrosalicylic acid (DNSA) in 50 ml of 50% ethanol/water. After concentration to *ca* 30 ml, partial room temperature evaporation of the hot-filtered solution gave thin pale-yellow crystal plates (m.p. 487.2–488.5 K).

Crystal data

$C_{10}H_{14}N_5O_4^+\cdot C_7H_3N_2O_7^-$
M_r = 495.38
Monoclinic, $P2_1$
a = 15.297 (2) Å
b = 8.8543 (14) Å
c = 7.2805 (8) Å
β = 92.32 (1)°
V = 985.3 (2) Å^3
Z = 2
D_x = 1.670 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 12.5–16.9°
μ = 0.14 mm^{-1}
T = 298 (2) K
Plate, pale yellow
0.40 × 0.35 × 0.03 mm

Data collection

Rigaku AFC-7*R* diffractometer
ω–2θ scans
Absorption correction: ψ scan (*TEXSAN for Windows*; Molecular Structure Corporation, 1999)
T_{min} = 0.945, T_{max} = 0.995
2690 measured reflections
2406 independent reflections
1873 reflections with $I > 2\sigma(I)$
R_{int} = 0.018
θ_{max} = 27.5°
$h = -8 \rightarrow 19$
$k = 0 \rightarrow 11$
$l = -9 \rightarrow 9$
3 standard reflections
frequency: 150 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.122
S = 0.88
2406 reflections
317 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2 + 2.5029P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.013 (3)

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2···O7*B*	0.92	1.61	2.438 (5)	147
N12—H12···O7*A*^{i}	0.90	1.87	2.763 (4)	170
N62—H62*B*···O7*B*^{i}	0.88	1.92	2.785 (5)	167
O21—H21*A*···O7*A*^{ii}	0.91	1.90	2.782 (4)	163
O51—H51*C*···O5*B*^{ii}	0.80	2.42	2.955 (5)	125
O31—H31*A*···N72^{iii}	0.93	1.93	2.785 (4)	152
O51—H51*C*···O5*A*^{iv}	0.80	2.45	3.164 (5)	149
N62—H62*A*···O21^{v}	0.84	2.12	2.886 (4)	152
C22—H22···O2^{vi}	0.96	2.22	3.041 (5)	142
C82—H82···O51	0.97	2.42	3.278 (5)	148

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

H atoms potentially involved in hydrogen-bonding interactions were located by difference methods, while others were included in the refinement at calculated positions (C—H = 0.96 Å). All were treated as riding, with U_{iso}(H) fixed at 1.2U_{eq}(attached atom). The absolute configuration was not determined but was assumed from that known for the parent adenosine [C1′(*R*), C2′(*R*), C3′(*S*) and C4′(*R*)]. Friedel pairs were merged before refinement.

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: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON for Windows* (Spek, 1999); software used to prepare material for publication: *PLATON for Windows*.

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References

Aiba, K., Hata, T., Sato, S. & Tamura, C. (1978). *Acta Cryst.* B**34**, 1259–1263.

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.

Bressi, J. C., Choe, J., Hough, M. T., Buckner, F. S., Van Voorhis, W. C., Verlinde, C. L. M. J., Hol, W. G. J. & Gelb, M. H. (2000). *J. Med. Chem.* **43**, 4135–4150.

Brown, D. M., Fasman, G. D., Magrath, D. I., Todd, A. R., Cochran, W. & Woolfson, M. M. (1953). *Nature (London)*, **172**, 1184–1185.

Costanzi, S., Lambertucci, C., Vittori, S., Volpini, R. & Cristalli, G. (2003). *J. Mol. Graph. Modelling*, **21**, 253–262.

Goto, M., Kanno, H., Sugaya, E., Osa, Y. & Takayanagi, H. (2004). *Anal. Sci.* **20**, *x*39–*x*40.

Haschemeyer, A. E. V. & Sobell, H. M. (1965). *Acta Cryst.* **18**, 525–532.

Hauser, J. & Keese, R. (2002). *Helv. Chim. Acta*, **85**, 2481–2488.

Hoogendorp, J. D., Verschoor, G. C. & Romers, C. (1978). *Acta Cryst.* B**34**, 3662–3666.

Klooster, W. T., Ruble, J. R., Craven, B. M. & McMullan, R. K. (1991). *Acta Cryst.* B**47**, 376–383.

Kraut, J. & Jensen, L. H. (1963). *Acta Cryst.* **16**, 79–88.

Lai, T. F. & Marsh, R. E. (1972). *Acta Cryst.* B**28**, 1982–1989.

Lynch, D. E., Latif, T., Smith, G., Byriel, K. A. & Kennard, C. H. L. (1997). *J. Chem. Crystallogr.* **27**, 567–575.

Lynch, D. E., Smith, G., Freney, D., Byriel, K. A. & Kennard, C. H. L. (1994). *Aust. J. Chem.* **47**, 1097–1115.

Molecular Structure Corporation (1999). *MSC/AFC Diffractometer Control Software* and *TEXSAN for Windows* (Version 1.06). MSC, 9009 New Trails Drive, The Woodlands, TX 77381, USA.

Ortoleva-Donnelly, L., Szewczak, A. A., Gutell, R. R. & Strobel, S. A. (1998). *RNA*, **4**, 498–519.

Portmann, S., Grimm, S., Workman, C., Usman, N. & Egli, M. (1996). *Chem. Biol.* **3**, 173–184.

Qiu, W., Campbell, R. L., Gangloff, A., Dupuis, P., Boivin, R. P., Tremblay, M. R., Poirier, D. & Lin, S.-X. (2002). *FASEB J.* **16**, 1829–1831.

Rao, S. T. & Sundaralingam, M. (1970). *J. Am. Chem. Soc.* **92**, 4963–4970.

Reddy, B. S. & Viswamitra, M. A. (1975). *Acta Cryst.* B**31**, 19–26.

Rohrer, D. C. & Sundaralingam, M. (1970). *J. Am. Chem. Soc.* **92**, 4956–4962.

Shefter, E., Barlow, M., Sparkes, R. A. & Trueblood, K. N. (1969). *Acta Cryst.* B**25**, 895–909.

Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.

Sheldrick, W. S. & Morr, M. (1980). *Acta Cryst.* B**36**, 2328–2333.

Shikata, K., Ueki, T. & Mitsui, T. (1973). *Acta Cryst.* B**29**, 31–38.

Smith, G., Gentner, J. M., Lynch, D. E., Byriel, K. A. & Kennard, C. H. L. (1995). *Aust. J. Chem.* **48**, 1151–1166.

Smith, G., Wermuth, U. D., Bott, R. C., Healy, P. C. & White, J. M. (2002). *Aust. J. Chem.* **55**, 349–356.

Smith, G., Wermuth, U. D., Healy, P. C. & White, J. M. (2003). *Aust. J. Chem.* **56**, 707–713.

Smith, G., Wermuth, U. D., Healy, P. C. & White, J. M. (2004). *J. Chem. Crystallogr.* Accepted.

Spek, A. L. (1999). *PLATON for Windows*. September 1999 Version. University of Utrecht, The Netherlands.

Stecher, P. G. (1968). Editor. *The Merck Index*, 8th ed., p. 20. Rahway, NJ: Merck and Co.

Suck, D., Mauor, P. C. & Saenger, W. (1976). *Acta Cryst.* B**32**, 1727–1737.

Sundaralingam, M. (1966). *Acta Cryst.* **21**, 495–506.

Swaminathan, P., Westhof, E. & Sundaralingam, M. (1982). *Acta Cryst.* B**38**, 515–522.

Vogt, J., Perozzo, R., Pautsch, A., Prota, A., Schelling, P., Pilger, B., Folkers, G., Scapozza, L. & Schulz, G. E. (2000). *Proteins*: *Struct. Funct. Genet.* **41**, 545–553.

Watson, D. G., Sutor, D. J. & Tollin, P. (1965). *Acta Cryst.* **19**, 111–124.

Wilson, J. D., Braunwald, E., Isselbacher, J., Petersdorf, R. G., Martin, J. B., Fauci, A. S. & Root, R. K. (1991). Editors. *Harrison's Principles of Internal Medicine*, 12th ed., pp. 72, 1517, 2091. New York: McGraw-Hill.