

The 1:1 cocrystals of the proton-transfer compound dilituric acid–phenylbiguanide monohydrate

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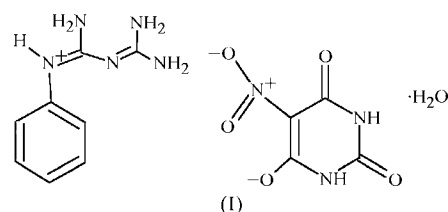
A proton-transfer compound, 1-phenylbiguanidium 5-nitro-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate monohydrate, $C_8H_{12}N_5^+ \cdot C_4H_2N_3O_5^- \cdot H_2O$, has been synthesized by a reaction between dilituric acid (5-nitro-2,4,6-trihydroxypyrimidine, Dilit) and phenylbiguanide (*N*-phenylimidocarbonimidic diamide, Big). This compound cocrystallized as a 1:1 adduct, and the asymmetric unit consists of two dilituric amino–oxo planar tautomeric anions (Dilit[−]), two monoprotonated phenylbiguanidium cations (BigH⁺) and two water molecules of crystallization ($Z' = 2$). Protonation occurs at the N atom attached to the phenyl ring of Big as a result of the proton-transfer process from the acidic hydroxy group of Dilit. In the crystal structure, the hydrated 1:1 adduct is stabilized by 25 two- and three-center hydrogen bonds.

Comment

Since Jean-Marie Lehn's famous description of supramolecular chemistry, the chemistry of molecular assemblies and the intermolecular bond, non-covalent binding interactions (*i.e.* hydrogen bonding, ionic interactions and π – π stacking) have attracted increasing attention in crystal engineering. In particular, it has been shown that hydrogen bonding plays a crucial role in the *de novo* design of self-assembled or self-associated compounds that may go by the more general title of 'supramolecule' (Desiraju, 1996). This is especially true for biological structures, and we previously demonstrated that crystalline adducts of DNA/RNA pyrimidine bases can mimic, if coupled with amino derivatives of aromatic N-heterocycles *via* multiple hydrogen bonds, the base-pairing of nucleic acids (Brunetti *et al.*, 2000, 2002; Portalone *et al.*, 1999, 2002; Portalone & Colapietro, 2004*b*, 2007).

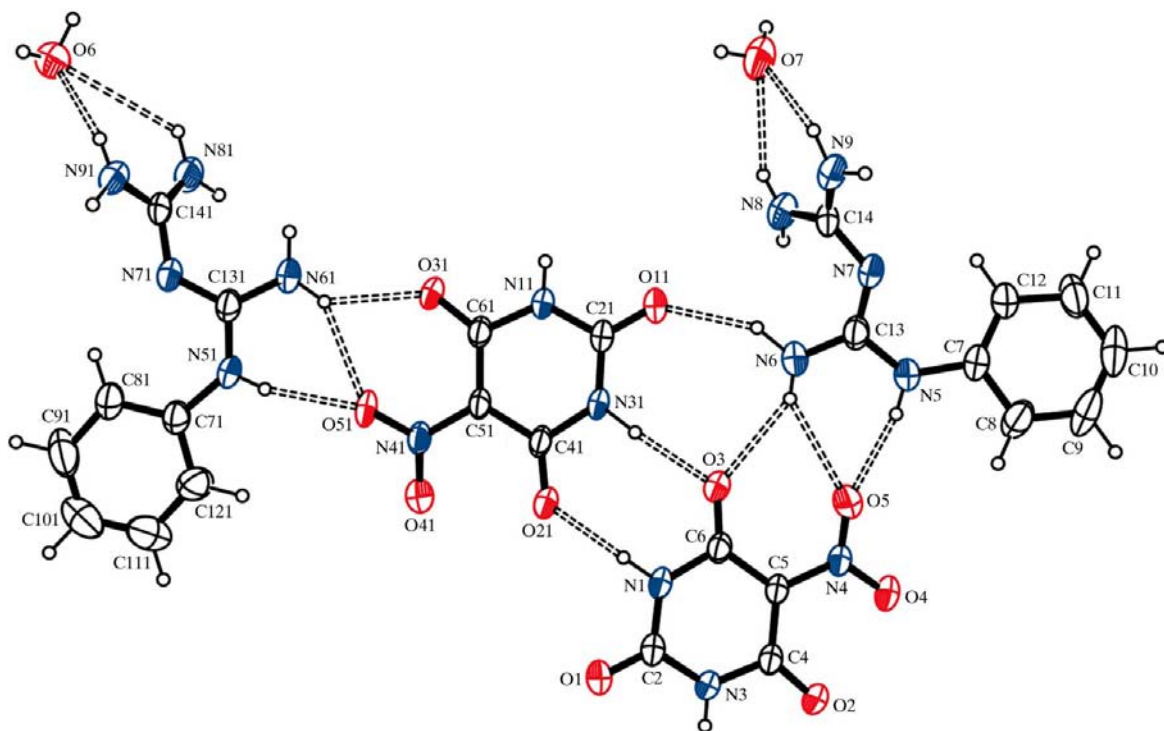
There is a very close relationship between hydrogen bonding and proton transfer; whenever the hydrogen-bonding associations result in complete proton transfer, an ionic compound is produced, and the non-covalent interactions between hydrogen-bonding groups are reinforced (Swift *et al.*,

1998). As the relevance of proton transfer in DNA/RNA systems was demonstrated many years ago (Steenken, 1989), we thought it would be interesting to analyze uracil acidic derivatives coupled with aromatic N-heterocycles to obtain proton-transfer supramolecular structures. In this paper, the title compound, (I), has been synthesized by a reaction between dilituric acid [5-nitro-2,4,6-trihydroxypyrimidine (Dilit), a quite strong acid ($pK_a = 0.77$ in dimethyl sulfoxide) structurally related to 5-nitrouracil (5-nitro-2,4-dihydroxypyrimidine)] and phenylbiguanide (*N*-phenylimidocarbonimidic diamide, Big) and can be represented as $BigH^+ \cdot Dilit^- \cdot H_2O$. Big, which has been chosen as the biguanide residue mimics the aromatic N-heterocyclic fragment of 2-amino-adenine, as a Lewis base is readily protonated at the N atom attached to the benzene ring (Portalone & Colapietro, 2004*a*).

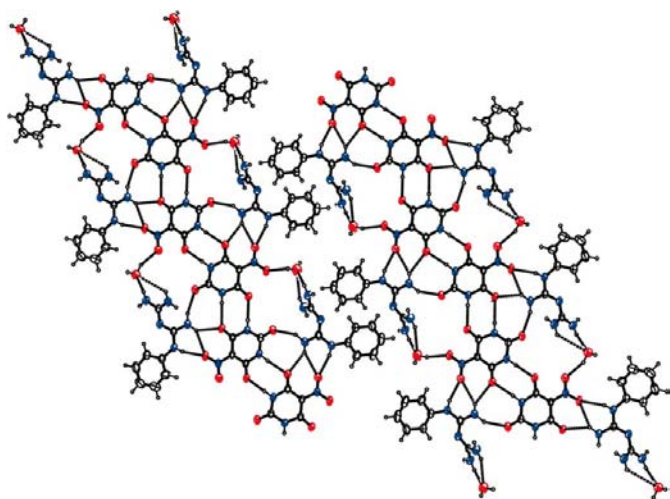


The asymmetric unit of (I) comprises two subunits, each of them consisting of a planar amino–oxo tautomeric anion (Dilit[−]), a monoprotonated phenylbiguanidium cation (BigH⁺) and a water molecule (Fig. 1). Protonation occurs as a result of the proton-transfer process from the hydroxy group of Dilit to the N atom attached to the phenyl ring of Big. The corresponding bond lengths and angles of the two independent 1:1 adducts are equal within experimental error (Table 1). In planar Dilit[−] anions, the release of a proton from O3 and O31 causes a redistribution of π -electron density so that the geometry of the anions approaches mirror symmetry through a mirror plane along the lines C2···C5 and C21···C51. In the BigH⁺ cations, the two biguanidinium groups are not planar. In each cation, the two halves of the biguanide residue are slightly pyramidal and make dihedral angles of 49.2 (1) and 53.2 (1)[°]. Nevertheless, the equivalence of the C–N bond lengths (Table 1) suggests some degree of delocalization of π -electron density through these fragments. The two biguanidinium groups are slightly rotated with respect to the phenyl rings by the angles τ_1 [21.1 (4)[°]] and τ_2 [9.7 (4)[°]] [the angle τ is defined as $\tau = |\omega_1 + \omega_2 \pm \pi|/2$, the torsion angles ω_1 and ω_2 being, respectively, C8–C7–N5–C13 and C12–C7–N5–C13 for τ_1 , and C81–C71–N51–C131 and C121–C71–N51–C131 for τ_2], at variance with that observed for the corresponding angles of 52.4 (5)[°] in phenylbiguanide hydrochloride (Portalone & Colapietro, 2004*a*) and 29.2 (2)[°] in 1-(*p*-chlorophenyl)biguanide hydrochloride (Brown & Sengier, 1984). This change in conformation is presumably a consequence of the different hydrogen-bonding configuration caused by the nature of the counter-ions, *i.e.* Dilit[−] versus Cl[−].

In the crystal structure, the hydrogen-bonding scheme is rather complex and involves all available hydrogen-bond donor/acceptor sites, apart from O41, which remains partially unsaturated, and water atom O7, which participates unex-


Figure 1

A view down c of the independent components of (I), showing the atom-labeling scheme and hydrogen bonding (dashed lines) within the selected asymmetric unit. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.


Figure 2

A part of the crystal structure of (I), viewed down c , showing the formation of a (010) two-dimensional network of hydrogen-bonded BigH⁺ cations, Dilit⁻ anions and water molecules. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Hydrogen bonding is indicated by dashed lines.

pectedly as a hydrogen-bond donor in only one intermolecular interaction. In total, the supramolecular structure of (I) is characterized by 25 two- and three-center hydrogen bonds, namely 22 N—H···O and three O_{water}—H···O bonds (Table 2). In one of the four three-center N—H···O inter-

actions, where atom N81 acts as a hydrogen-bond donor *via* H81A, there is some uncertainty as to whether this is a hydrogen bond or not. However, as is very frequently found for bifurcated hydrogen bonds, the sum of the inter-bond angles at the H atom is close to 360° and the H···O distance can be greater than the van der Waals separation (Jeffrey & Saenger, 1991; Desiraju & Steiner, 1999; Steiner, 2002).

Compound (I) crystallizes with $Z' = 2$. In the crystal structure, each independent molecular adduct is linked by multiple hydrogen bonds to form a three-dimensional framework. For descriptive purposes, it is convenient to select a 'superadduct' (Gregson *et al.*, 2000) consisting of one asymmetric unit and then analyze firstly the hydrogen bonding within this aggregate and secondly the hydrogen-bonding patterns between neighboring individual superadducts.

As mentioned previously, in the superadduct, one Big molecule forms a cation as a result of the incorporation of a H atom from one Dilit molecule (Fig. 1). Thus, the Dilit⁻ anion acts as an acceptor of bifurcated $R_2^1(6)$ and $R_2^1(6)$ hydrogen bonds (Etter, 1990; Bernstein *et al.*, 1995; Motherwell *et al.*, 1999) through the hydroxy O atom and one O atom of the nitro group. The BigH⁺ cation then links a solvent molecule through a bifurcated $R_2^1(6)$ hydrogen bond. The two subunits are interconnected *via* N—H···O triple intermolecular hydrogen bonds, forming two adjoining hydrogen-bonded rings with graph-set motifs $R_2^2(8)$ and $R_3^2(8)$.

In addition to the 13 hydrogen bonds within the asymmetric unit, there are a further five distinct interactions which link, by translation along the b axis, neighboring superadducts into

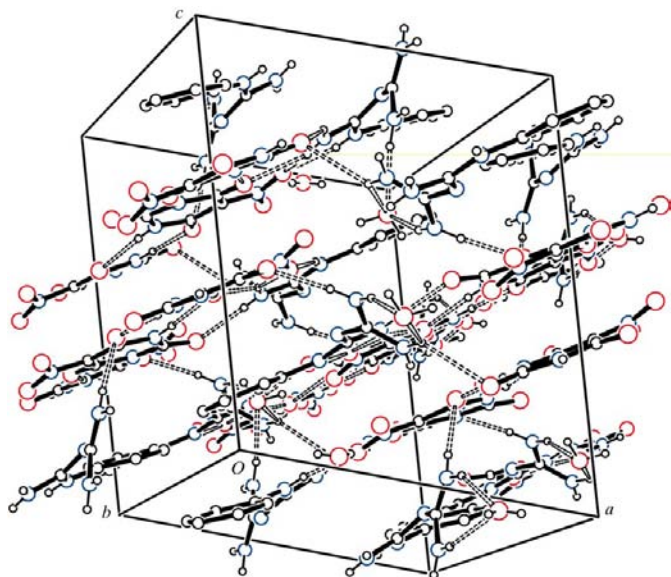


Figure 3

The packing of (I), viewed down *c*. All atoms are shown as small spheres of arbitrary radii. For the sake of clarity, only those H atoms that are involved in hydrogen bonds have been included. Hydrogen bonding is indicated by dashed lines.

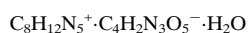
sheets parallel to the *ab* plane (Fig. 2). N—H...O triple intermolecular hydrogen bonds, forming two adjoining hydrogen-bonded rings of $R_2^2(8)$ and $R_3^2(8)$ motif, connect two Dilit[−] anions. The formation of this two-dimensional array is then reinforced by two water molecules, which act as bridges between Dilit[−] anions and BigH⁺ cations to form two $R_4^4(18)$ hydrogen-bond rings. Overall, adjacent superadducts form a two-dimensional substructure built from a combination of 18 N—H...O and O_{water}—H...O interactions, and hydrogen bonds delineate patterns in which rings are the most prominent features.

The (010)-nets thus formed are themselves linked into a three-dimensional network by means of a further series of seven hydrogen bonds, all but one (O6—H614...O1^{vi}; Table 2) of N—H...O type, generated by translation from the superadduct at (*x*, *y*, *z*) to adjacent sheets in the [001] direction (Fig. 3).

Experimental

BigH⁺·Dilit[−] was obtained as a white powder from an equimolar mixture of dilituric acid and phenylbiguanide (Sigma Aldrich, 99% purity, 1 mmol each compound) in ethanol (20 ml). The 1:1 molecular adduct was recrystallized from water by slow evaporation of the solvent.

Crystal data



$M_r = 368.33$

Triclinic, $P\bar{1}$

$a = 11.387$ (2) Å

$b = 12.135$ (3) Å

$c = 13.804$ (3) Å

$\alpha = 97.48$ (3)°

$\beta = 106.37$ (3)°

$\gamma = 116.39$ (4)°

$V = 1565.3$ (10) Å³

$Z = 4$

$D_x = 1.563$ Mg m^{−3}

Mo $K\alpha$ radiation

$\mu = 0.13$ mm^{−1}

$T = 298$ (2) K

Tablet, colorless

0.20 × 0.20 × 0.10 mm

Data collection

Huber CS four-circle diffractometer

ω scans

6392 measured reflections

6002 independent reflections

5586 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.032$

$\theta_{\text{max}} = 26.0^\circ$

3 standard reflections

every 97 reflections

intensity decay: 3%

Refinement

Refinement on F^2

$R[F^2 > 2\sigma(F^2)] = 0.064$

$wR(F^2) = 0.191$

$S = 1.07$

6002 reflections

529 parameters

H atoms treated by a mixture of independent and constrained refinement

$$w = 1/[\sigma^2(F_o^2) + (0.136P)^2 + 0.5189P]$$

$$\text{where } P = (F_o^2 + 2F_c^2)/3$$

$$(\Delta/\sigma)_{\text{max}} < 0.001$$

$$\Delta\rho_{\text{max}} = 0.31 \text{ e } \text{Å}^{-3}$$

$$\Delta\rho_{\text{min}} = -0.31 \text{ e } \text{Å}^{-3}$$

Table 1

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

	$n = \text{nil}$	$n = 1$		$n = \text{nil}$	$n = 1$
O1 <i>n</i> —C2 <i>n</i>	1.235 (3)	1.232 (3)	N5 <i>n</i> —C13 <i>n</i>	1.355 (3)	1.351 (3)
O2 <i>n</i> —C4 <i>n</i>	1.247 (3)	1.239 (3)	N6 <i>n</i> —C13 <i>n</i>	1.336 (3)	1.339 (3)
O3 <i>n</i> —C6 <i>n</i>	1.229 (3)	1.238 (2)	N7 <i>n</i> —C13 <i>n</i>	1.331 (3)	1.326 (3)
O4 <i>n</i> —N4 <i>n</i>	1.249 (2)	1.237 (3)	N7 <i>n</i> —C14 <i>n</i>	1.335 (3)	1.339 (3)
O5 <i>n</i> —N4 <i>n</i>	1.239 (3)	1.245 (2)	N8 <i>n</i> —C14 <i>n</i>	1.338 (3)	1.333 (3)
N1 <i>n</i> —C2 <i>n</i>	1.350 (3)	1.362 (3)	N9 <i>n</i> —C14 <i>n</i>	1.339 (3)	1.334 (3)
N1 <i>n</i> —C6 <i>n</i>	1.395 (3)	1.387 (3)	C7 <i>n</i> —C8 <i>n</i>	1.398 (3)	1.382 (3)
N3 <i>n</i> —C2 <i>n</i>	1.375 (3)	1.363 (3)	C7 <i>n</i> —C12 <i>n</i>	1.388 (4)	1.389 (4)
N3 <i>n</i> —C4 <i>n</i>	1.385 (3)	1.389 (3)	C8 <i>n</i> —C9 <i>n</i>	1.388 (4)	1.401 (4)
N4 <i>n</i> —C5 <i>n</i>	1.395 (3)	1.407 (3)	C9 <i>n</i> —C10 <i>n</i>	1.369 (5)	1.356 (5)
C4 <i>n</i> —C5 <i>n</i>	1.435 (3)	1.441 (3)	C10 <i>n</i> —C11 <i>n</i>	1.371 (5)	1.368 (5)
C5 <i>n</i> —C6 <i>n</i>	1.454 (3)	1.445 (3)	C11 <i>n</i> —C12 <i>n</i>	1.393 (3)	1.366 (4)
N5 <i>n</i> —C7 <i>n</i>	1.409 (3)	1.408 (3)			
C8 <i>n</i> —C7 <i>n</i> — N5 <i>n</i> —C13 <i>n</i>	160.6 (2)	−170.5 (2)	C12 <i>n</i> —C7 <i>n</i> — N5 <i>n</i> —C13 <i>n</i>	−22.8 (4)	9.6 (4)

Table 2

Hydrogen-bond geometry (Å, °).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
N1—H1...O21	0.92 (3)	1.90 (3)	2.814 (3)	171 (2)
N3—H3...O31 ⁱ	0.84 (3)	2.14 (3)	2.983 (3)	177 (3)
N11—H11...O2 ⁱⁱ	0.85 (3)	1.97 (3)	2.818 (3)	178 (3)
N31—H31...O3	0.93 (3)	2.01 (3)	2.932 (3)	171 (2)
N5—H5...O5	0.83 (3)	2.02 (3)	2.832 (3)	164 (3)
N6—H61...O11	1.00 (3)	2.09 (3)	2.989 (3)	148 (3)
N6—H62...O3	0.86 (3)	2.30 (3)	3.038 (3)	144 (3)
N6—H62...O5	0.86 (3)	2.38 (3)	3.099 (3)	142 (3)
N8—H811...O6 ⁱⁱⁱ	0.94 (3)	2.18 (3)	3.103 (3)	167 (3)
N8—H812...O7	0.83 (3)	2.38 (3)	3.137 (4)	152 (3)
N9—H911...O2 ^{iv}	0.87 (3)	2.21 (3)	3.083 (3)	175 (3)
N9—H912...O7	0.91 (3)	2.23 (3)	3.033 (4)	147 (3)
N51—H51...O51	0.79 (3)	2.07 (3)	2.834 (3)	163 (3)
N61—H611...O1 ⁱⁱ	0.89 (3)	2.12 (3)	2.973 (3)	161 (3)
N61—H612...O31	0.90 (3)	2.17 (3)	2.903 (3)	139 (3)
N61—H612...O51	0.90 (3)	2.30 (3)	3.086 (3)	146 (3)
N81—H81A...O6	0.91	2.90	3.549 (3)	129
N81—H81A...O11 ⁱⁱⁱ	0.91	2.69	3.374 (3)	133
N81—H81B...O2 ^v	0.91	2.17	2.993 (3)	151
N81—H81B...O4 ^v	0.91	2.47	3.211 (3)	138
N91—H913...O6	0.84 (3)	2.14 (3)	2.945 (3)	160 (3)
N91—H914...O21 ^{vi}	0.89 (3)	2.07 (3)	2.945 (3)	169 (3)
O6—H613...O41 ⁱⁱ	0.92 (5)	1.94 (5)	2.804 (3)	156 (4)
O6—H614...O1 ^{vi}	0.92 (4)	2.18 (4)	3.019 (3)	151 (4)
O7—H711...O4 ⁱⁱ	0.79 (7)	2.03 (7)	2.778 (4)	158 (6)

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

All H atoms were found in a difference map. Positional parameters of all H atoms, apart from those on the benzene rings and atom N81, were refined. The latter H atoms were positioned with idealized geometry and refined isotropically using a riding model (C–H = 0.98 Å and N–H = 0.91 Å). The U_{iso} values of the H atoms were kept equal to $1.2U_{\text{eq}}(\text{C,N})$, $1.6U_{\text{eq}}(\text{O6})$ and $1.3U_{\text{eq}}(\text{O7})$.

Data collection: *XCS* (Colapietro *et al.*, 1992); cell refinement: *XCS*; data reduction: *XCS*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: HJ3031). Services for accessing these data are described at the back of the journal.

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