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Anhydrous guanine: a synchrotron study

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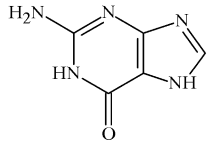
Very small crystals of anhydrous guanine (systematic name: 2-amino-1,7-dihydro-6*H*-purin-6-one), $C_5H_5N_5O$, were obtained from an attempted solvothermal synthesis of a potassium complex. Data were collected at 120 K using a synchrotron radiation source. There is one essentially planar molecule in the asymmetric unit. Molecules are linked to each other by N—H···N and N—H···O hydrogen bonds to form sheets, between which there are π–π stacking interactions. This crystal structure determination demonstrates conclusively that, in the absence of any solvent or other molecules, guanine exists as the amino–keto tautomer in the solid state, with H atoms attached to N1 and N7 (purine numbering), unlike its monohydrate, which has H atoms on N1 and N9.

Comment

In view of the importance of the nucleobases adenine, cytosine, guanine, thymine and uracil as components of the nucleic acids DNA and RNA (Blackburn & Gait, 1996), and the structural characterization of many of their derivatives, it is surprising that the crystal structures of anhydrous adenine and guanine have not yet been reported, although the structures of hydrates are known for both (Tret'yak *et al.*, 1987; Thewalt *et al.*, 1971). By contrast, the structures of anhydrous cytosine (Barker & Marsh, 1964; McClure & Craven, 1973), thymine (Ozeki *et al.*, 1969; Portalone *et al.*, 1999) and uracil (Stewart & Jensen, 1967) have been known for some time, together with hydrates of cytosine (Jeffrey & Kinoshita, 1963; Neidle *et al.*, 1976; Eisenstein, 1988; McClure & Craven, 1973) and thymine (Gerdil, 1961), but not of uracil.

For some time, an area of our research has concentrated on the synthesis and characterization of *s*-block metal complexes with pyridones and related compounds. As an extension of this work, we are studying the structural chemistry of complexes of nucleobases. Their structural chemistry with transition metals is well known and many complexes have been synthesized and characterized. In contrast, the literature does not contain many structures of *s*-block metal nucleobase complexes and little information is available on the subject (Gibson *et al.*, 2002), despite their use as reagents (often as sodium or potassium derivatives) to permit further reactions with transition metals.



(I)

The crystal structure of guanine is of great importance, as this purine is present in both DNA and RNA (Lippert *et al.*, 2000). Guanine nucleotides are involved in intermediary metabolism and can also be found in animal tissues. Guanine, like other related bases, can exist in a tautomeric keto–enol

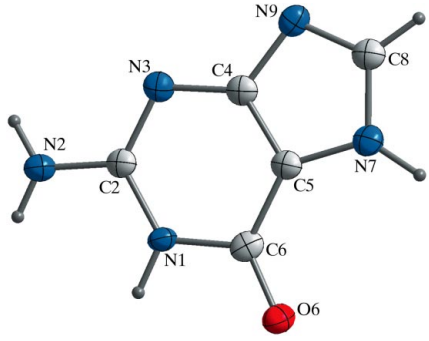


Figure 1
The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

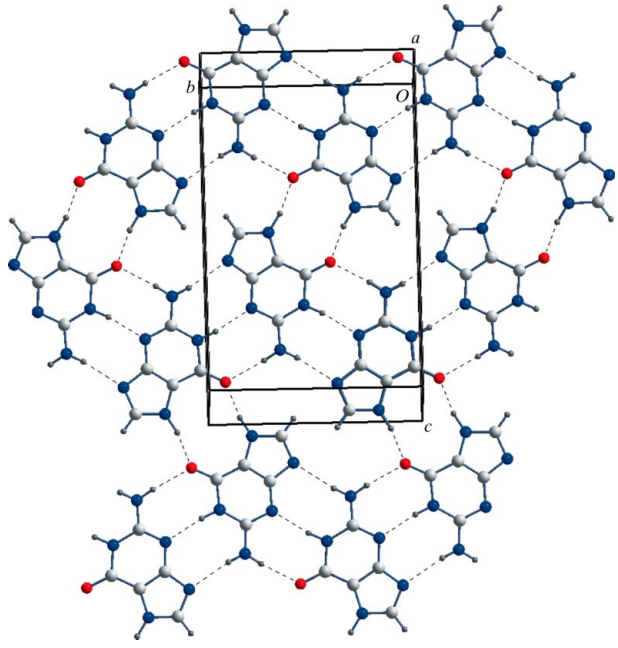


Figure 2
The hydrogen bonding (dashed lines) in the crystal structure of (I), viewed perpendicular to the sheet of molecules.

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equilibrium. It is known that the predominant form of guanine, thymine and uracil is the keto form, and the predominant form for cytosine and adenine is the amino form (Saenger, 1984). A particular interest in the crystal structure of anhydrous guanine is to see which tautomeric form occurs and which two of the four ring N atoms are protonated. In the literature, the favoured positions of these two H atoms have often been found to be at N1 and N9, as for guanine monohydrate (Thewalt *et al.*, 1971).

As part of our work, we obtained very small crystals of anhydrous guanine, (I), in an attempted solvothermal synthesis with potassium metal in ethanol. Because of the weak diffraction, data collection was carried out at Station 9.8 of the Synchrotron Radiation Source (SRS) at Daresbury Laboratory, England, through the EPSRC National Crystallography Service.

The asymmetric unit of (I) is shown in Fig. 1 and consists of one molecule of guanine. The molecule is essentially planar (r.m.s. deviation of 0.009 Å for all non-H atoms) and, in contrast with guanine monohydrate, the two protonated ring N atoms are found to be N1 and N7. Table 1 gives selected bond lengths and angles for the anhydrous structure. The most significant differences from the monohydrate (Thewalt *et al.*, 1971) are the reversal of the N7—C8 and N9—C8 bond lengths and a shortening of C5—C7 in the anhydrous structure: N7—C8 = 1.342 (5) Å in the anhydrate (*cf.* 1.319 Å in the hydrate), N9—C8 = 1.328 (6) Å (*cf.* 1.369 Å) and C5—N7 = 1.373 (5) Å (1.405 Å). These differences clearly reflect the different sites of protonation, N7 *versus* N9. Other bond lengths are very similar in the two structures.

The difference in tautomeric form between the two structures is presumably a consequence of hydrogen bonding in the crystal structures. Fig. 2 shows the hydrogen bonding in the crystal structure of anhydrous guanine. Along the *b* axis, the molecules are linked together to create infinite chains and show a triple hydrogen-bonding motif, *ADD*···*DAA* (Burrows *et al.*, 1995), where the donors are N—H and the acceptor atoms are N3, N9 and O6. Geometric details of the hydrogen bonds are given in Table 2. Hydrogen bonds in which atom N7 is the donor and atom O6 the acceptor link these chains together into sheets parallel to (102) (Fig. 3). The spacing between the sheets is 3.263 Å, typical of nucleobase stacking and indicating π–π interactions involving offset parallel rings. Guanine monohydrate also forms sheets, but the water molecules are incorporated in the hydrogen bonding and promote the transfer of an H atom from N7 to N9 in order to give favourable hydrogen-bonding interactions.

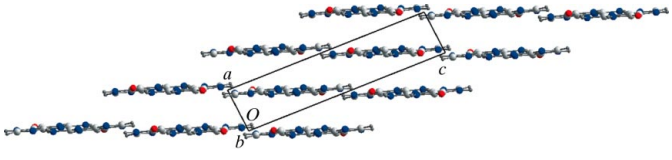

Figure 3
An edge-on view, along the *b* axis, of the stacked planar (102) sheets of hydrogen-bonded molecules.

Experimental

Very small crystals of guanine were obtained from an attempted solvothermal synthesis, using guanine (150 mg) and solid potassium (40 mg) in dry ethanol (10 ml). The mixture was stirred for 1 h and then heated in an autoclave at 523 K for 7 d.

Crystal data

$C_5H_5N_5O$
M_r = 151.14
Monoclinic, $P2_1/c$
a = 3.5530 (16) Å
b = 9.693 (4) Å
c = 16.345 (7) Å
β = 95.748 (6)°
V = 560.1 (4) Å^3
Z = 4
D_x = 1.792 Mg m^{-3}
Synchrotron radiation
λ = 0.6712 Å
μ = 0.14 mm^{-1}
T = 120 (2) K
Block, colourless
0.01 × 0.01 × 0.01 mm

Data collection

Bruker APEX2 CCD area-detector diffractometer
Thin-slice ω scans
3444 measured reflections
795 independent reflections
624 reflections with $I > 2\sigma(I)$
R_{int} = 0.054
θ_{max} = 21.9°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.059
$wR(F^2)$ = 0.183
S = 1.15
795 reflections
116 parameters
Only H-atom coordinates refined
$w = 1/[\sigma^2(F_o^2) + (0.1065P)^2 + 0.537P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.34 e Å^{-3}
Extinction correction: *SHELXTL* (Sheldrick, 2001)
Extinction coefficient: 0.12 (5)

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.372 (5)	C4—N9	1.364 (5)
N1—C6	1.387 (5)	C5—C6	1.412 (6)
N2—C2	1.330 (6)	C5—N7	1.373 (5)
C2—N3	1.330 (5)	O6—C6	1.249 (5)
N3—C4	1.356 (5)	N7—C8	1.342 (5)
C4—C5	1.378 (6)	C8—N9	1.328 (6)
C2—N1—C6	124.6 (3)	C4—C5—N7	106.7 (3)
N1—C2—N2	117.0 (4)	C6—C5—N7	132.3 (4)
N1—C2—N3	123.3 (4)	N1—C6—C5	111.8 (3)
N2—C2—N3	119.7 (4)	N1—C6—O6	120.0 (4)
C2—N3—C4	114.1 (3)	C5—C6—O6	128.3 (4)
N3—C4—C5	125.2 (4)	C5—N7—C8	105.2 (4)
N3—C4—N9	124.6 (4)	N7—C8—N9	114.1 (4)
C5—C4—N9	110.2 (4)	C4—N9—C8	103.9 (3)
C4—C5—C6	121.0 (4)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···N3^{i}	0.91 (5)	1.97 (5)	2.862 (5)	167 (4)
N2—H2A···N9^{i}	0.85 (5)	2.17 (5)	3.006 (5)	173 (4)
N2—H2B···O6^{ii}	0.88 (5)	2.03 (5)	2.902 (5)	174 (4)
N7—H7···O6^{iii}	1.00 (5)	1.76 (5)	2.742 (5)	165 (4)

Symmetry codes: (i) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$; (ii) $-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$; (iii) $-x, -y, -z+2$.

Diffraction from the very small crystals was weak, and even with synchrotron radiation significant intensities were not observed

beyond a resolution of 0.9 Å. Nevertheless, these data gave an excellent structural result, albeit with a lower data/parameter ratio than usual. *SADABS* (Sheldrick, 2003) was used to correct for the synchrotron beam decay. All H atoms were found in a difference map and their positions were freely refined [C8—H8 = 0.97 (5) Å; N—H distances are given in Table 2], with $U_{iso}(H) = 1.2U_{eq}(C,N)$.

Data collection: *APEX2* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT*; program(s) used to solve structure: *SIR2002* (Burla *et al.*, 2003); program(s) used to refine structure: *SHELXTL* (Sheldrick, 2001); molecular graphics: *SHELXTL* and *DIAMOND* (Brandenburg & Putz, 2004); software used to prepare material for publication: *SHELXTL* and local programs.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD3036). Services for accessing these data are described at the back of the journal.

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