

1,3-Dimethylisoguanine

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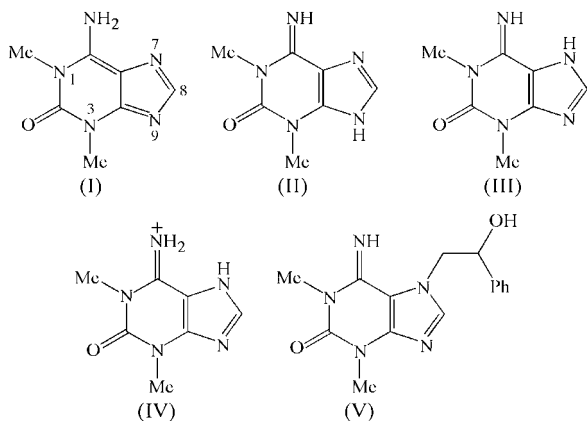
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The structure of 1,3-dimethylisoguanine [or 6-amino-1,3-dimethyl-1*H*-purin-2(3*H*)-one], C₇H₉N₅O, has been redetermined and the correct assignment of H atoms on the heterocycle is now reported. Intermolecular hydrogen-bonding interactions confirm that this form is the correct molecular structure; this form is also in agreement with an earlier reported structure of the trihydrate form.

Comment

Methylated purine bases are frequently isolated from marine sponges and ascidians, and their presence is often associated with pronounced biological activity. Rapid dereplication of these compounds in polar extracts of sponges is complicated by difficulties in their characterization. One such example is 1,3-dimethylisoguanine, (I), which has been described by three different groups but with differences in the ¹³C NMR and MS data published in each report (Chehade *et al.*, 1997; Mitchell *et al.*, 1997; Jeong *et al.*, 2003). In addition to the form shown as (I), other tautomers, namely (II) and (III), are also possible.



Consequently, compound (I) has been subjected to two X-ray crystallographic studies. The crystal structure of the trihydrate of (I) has been reported (Do Prado Gambardella *et al.*, 1999), where tautomeric form (I) was identified. Hydrogen-bonding (H—O—H···N) interactions between the

water molecules and ring atoms N7 and N9 were identified, in addition to N—H···O hydrogen bonds from the exocyclic —NH₂ group to the water O atoms. In a more recent report (Jeong *et al.*, 2003), the crystal structure of the putative 1,3-dimethylisoguaninium cation, (IV), was reported but without any counter-ion. We have redetermined the structure of this compound and have found that it is actually (I) in an anhydrous form.

A view of (I) is shown in Fig. 1. We have adopted the same atom-numbering scheme as was used in the reported structure of the trihydrate form of (I) (Do Prado Gambardella *et al.*, 1999). As shown in Fig. 1, both H atoms reside on atom N13 (the primary amine group), while the two N atoms in the five-membered ring (atoms N7 and N9) are not protonated. The bond lengths (Table 1) and angles in (I) do not differ significantly from those reported for the trihydrate form of (I) (Do Prado Gambardella *et al.*, 1999).

This protonation scheme was confirmed by examination of intermolecular hydrogen bonding within the structure. A view of the unit cell is shown in Fig. 2. Both of the N-bound H atoms participate in hydrogen bonds, one with each of the five-membered-ring N atoms (Table 2). Thus, atoms N7 and N9 cannot be protonated while accepting hydrogen bonds from an —NH₂ group.

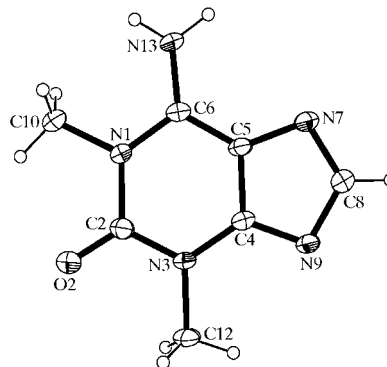


Figure 1
An ORTEP-3 plot (Farrugia, 1997) of (I) (30% probability displacement ellipsoids).

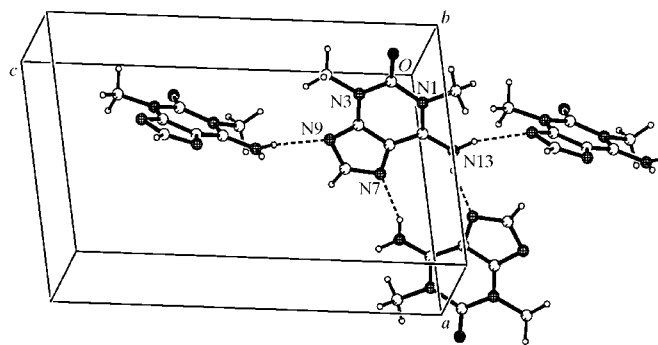


Figure 2
A PLATON plot (Spek, 2003) of the hydrogen bonding (dashed lines) in (I). See Table 2 for symmetry codes and bond lengths for hydrogen bonds.

Structure (IV) was proposed (Jeong *et al.*, 2003) for an isomorphous compound (which is evidently the same as that reported here). The presence of a H atom on N7 demands an anion to balance the charge, but none was reported (Jeong *et al.*, 2003). The origin of this error became apparent to us during refinement. At convergence, there is a small peak ($0.23 \text{ e } \text{\AA}^{-3}$) *ca* 1.07 \AA from atom N7. However, this peak is not coplanar with the purine ring (the H8—C8—N7—peak pseudo-torsion angle is 40.8°) as it should be for a typical NH group within a heterocyclic ring. Jeong *et al.* (2003) have evidently assigned this peak to a H atom, despite the fact that doing so introduces an unbalanced positive charge, a fact unfortunately overlooked. If atom N7 was indeed protonated then a H atom would have to be removed from atom N13 to give the neutral tautomer (III). In refinement, both H atoms appeared quite clearly on atom N13 and could be refined without restraints. The $-\text{NH}_2$ bond lengths, angles and displacement parameters are sensible, and the group is close to being coplanar with the purine ring. Deviations of the $-\text{NH}_2$ group from this plane may be attributed to a slight twisting of the C6—N13 bond to accommodate intermolecular hydrogen bonding.

One way of enforcing the exocyclic C=NH tautomeric form shown in (III) is by alkylation of atom N7. The structure of (V) (Kozai *et al.*, 2000) is an example of this. The exocyclic C=NH bond length in (V) is 1.275 \AA , while the adjacent C—C bond length is 1.429 \AA . These may be compared with the corresponding bonds C6—N13 [$1.322(4) \text{ \AA}$] and C5—C6 [$1.384(5) \text{ \AA}$] in (I), which indicate that electron delocalization across the N13—C6—C5 group in (I) is significantly greater than that seen in the alternative analogous tautomeric form (V).

Our NMR data for (I) differ from those provided by Chehade *et al.* (1997) but match very closely the spectroscopic data reported by Mitchell *et al.* (1997) and Jeong *et al.* (2003). However, Mitchell *et al.* (1997) did not provide a chemical shift for C8, possibly as a consequence of a deuterium exchange experiment conducted on the sample. Facile deuterium exchange has been reported at atom C8 of 7,9-dimethylguaniam salts (Yagi *et al.*, 1994). Despite the differences in spectroscopic data, the solid-state molecular structure of (I) is the same as that described for the trihydrate (Do Prado Gambardella *et al.*, 1999). Hydrogen-bonding interactions in the present structure of (I), involving the $-\text{NH}_2$ group as donor and atoms N7 and N9 as acceptors, are replaced by comparable hydrogen bonds with water molecules in the trihydrate form (Do Prado Gambardella *et al.*, 1999).

Experimental

Compound (I) was obtained from a butanol extract of the sponge *Xestospongia exigua* collected at Lizard Island on the northern Great Barrier Reef. The compound was isolated by flash chromatography on silica using CHCl_3 —MeOH (5:1). ^1H NMR (d_4 -MeOH + CDCl_3 , p.p.m.): δ 3.54 (N1—Me), 3.59 (N3—Me) and 7.58 (H-8); ^{13}C NMR (d_4 -MeOH + CDCl_3 , p.p.m.): δ 150.3 (C-2), 152.1 (C-4), 110.7 (C-5), 151.4 (C-6), 151.1 (C-8), 31.0 (N1—Me) and 31.4 (N3—Me). After

NMR analysis, slow recrystallization of the sample from MeOH— CHCl_3 provided crystals suitable for X-ray crystallographic analysis (m.p. 593–595 K).

Crystal data

$\text{C}_7\text{H}_9\text{N}_5\text{O}$
 $M_r = 179.19$
 Monoclinic, $P2_1/c$
 $a = 8.9352(9) \text{ \AA}$
 $b = 6.1050(6) \text{ \AA}$
 $c = 14.678(2) \text{ \AA}$
 $\beta = 96.37(1)^\circ$
 $V = 795.73(16) \text{ \AA}^3$
 $Z = 4$
 $D_x = 1.496 \text{ Mg m}^{-3}$

Mo $K\alpha$ radiation
 Cell parameters from 25 reflections
 $\theta = 8.3\text{--}15.5^\circ$
 $\mu = 0.11 \text{ mm}^{-1}$
 $T = 293(2) \text{ K}$
 Prism, colourless
 $0.33 \times 0.3 \times 0.3 \text{ mm}$

Data collection

Enraf-Nonius CAD-4 diffractometer
 Non-profiled $\omega/2\theta$ scans
 1473 measured reflections
 1380 independent reflections
 771 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.143$

$\theta_{\text{max}} = 25.0^\circ$
 $h = 0 \rightarrow 10$
 $k = 0 \rightarrow 7$
 $l = -17 \rightarrow 17$
 3 standard reflections
 frequency: 120 min
 intensity decay: -3%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.054$
 $wR(F^2) = 0.166$
 $S = 1.00$
 1380 reflections
 128 parameters

H atoms treated by a mixture of independent and constrained refinement
 $w = 1/[\sigma^2(F_o^2) + (0.0895P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.23 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.22 \text{ e } \text{\AA}^{-3}$

Table 1
 Selected bond lengths (\AA).

C2—O2	1.218 (4)	C5—C6	1.384 (5)
C2—N3	1.368 (5)	C6—N13	1.322 (4)
C2—N1	1.413 (4)	C6—N1	1.372 (4)
C4—N9	1.339 (4)	C8—N7	1.329 (4)
C4—N3	1.375 (4)	C8—N9	1.363 (4)
C4—C5	1.386 (4)	C10—N1	1.458 (4)
C5—N7	1.383 (4)	C12—N3	1.459 (4)

Table 2
 Hydrogen-bond geometry (\AA , $^\circ$).

$D\text{---}H\cdots A$	$D\text{---}H$	$H\cdots A$	$D\cdots A$	$D\text{---}H\cdots A$
N13—H3A \cdots N9 ⁱ	0.85 (5)	2.20 (5)	2.992 (4)	156 (4)
N13—H3B \cdots N7 ⁱⁱ	0.88 (4)	2.01 (4)	2.846 (5)	158 (3)

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

The H-atom positions on all C atoms were first identified from difference maps and subsequently constrained using a riding model during refinement. In contrast, the N-bound H atoms were located from difference maps, and their positional and displacement parameters were refined without restraints so as to avoid introducing any bias into our model.

Data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD-4 EXPRESS*; data reduction: *XCAD4* (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Version 1.70; Farrugia, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ1243). Services for accessing these data are described at the back of the journal.

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