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7-Amino-2,5-dimethylpyrazolo[1,5-*a*]-pyrimidine hemihydrate redetermined at 120 K: a three-dimensional hydrogen-bonded framework

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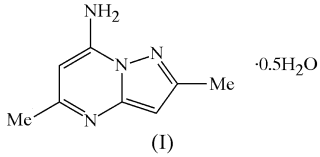
In the title compound, $C_8H_{10}N_4\cdot0.5H_2O$, where the water molecules lie on twofold rotation axes in the space group *C*2, the components are linked by three hydrogen bonds, one each of O—H···N, N—H···N and N—H···O types, into a complex three-dimensional framework structure.

Comment

Pyrazolo[1,5-*a*]pyrimidines are purine analogues which exhibit a number of useful properties as antimetabolites in purine biochemical reactions; they are of particular interest because of their antitrypanosomal (Novinson *et al.*, 1976) and antischistosomal activities (Senga *et al.*, 1981). Such interesting biological properties have prompted the development of new and efficient general procedures for the synthesis of pyrazolo[1,5-*a*]pyrimidine derivatives (Al-Shiekh *et al.*, 2004; Makarov *et al.*, 2005). We present here the structure of 7-amino-2,5-dimethylpyrazolo[1,5-*a*]pyrimidine, (I), prepared by the solvent-free cyclocondensation reaction between 5-amino-3-methyl-1*H*-pyrazole and 3-aminocrotononitrile induced by microwave irradiation, and crystallized from ethanol as the hemihydrate.



(I)

The structure of (I) was determined many years ago using diffraction data collected at ambient temperature (Mornon *et al.*, 1975). The coordinates and displacement parameters for the H atoms bonded to C and O atoms were all refined and the refinement converged to $R = 0.058$ with a data/parameter ratio of only 5.94, giving typical s.u. values on the distances and angles of 0.01 Å and 1.5°, respectively. Although three intermolecular hydrogen bonds were identified, the authors gave no analysis or discussion of their structural consequences.

We have now taken the opportunity to redetermine this structure using diffraction data collected at 120 K, and the resulting refinement, which converged to $R = 0.037$ for a data/parameter ratio of 9.62, gives much greater geometric precision, with typical s.u. values on distances and angles of 0.002 Å and 0.15°, respectively. We report here this redetermination, with a detailed description of the supramolecular structure.

Within the heterocyclic component, the bond distances (Table 1) show a number of deviations from the pattern expected if the bond-localized form (I) (see scheme) is the correct representation. In particular, the C3*A*—N4 bond, which is formally a single bond, is not very much longer than the N1—C2 and N4—C5 bonds, both of which are formally double bonds; similarly, the lengths of the C2—C3 and C5—C6 bonds, which are formally single bonds, differ very little from those of the C3—C3*A* and C6—C7 bonds, which are formally double bonds. This pattern points to a considerable degree of aromatic type 10-π electron delocalization. Also noteworthy is the difference between the two exocyclic angles at atom C7, a difference which has no obvious explanation. All these metrical observations closely mimic those obtained, at much lower precision, from the ambient-temperature determination (Mornon *et al.*, 1975), although some of the geometric and displacement parameters involving H atoms in that report are clearly unreliable.

As reported previously, the water molecules lie on twofold rotation axes in space group *C*2, with the heterocyclic component in a general position. For the sake of convenience, the reference water molecule has been selected as that lying across the rotation axis along ($\frac{1}{2}$, *y*, $\frac{1}{2}$), with the two independent molecular components linked by an O—H···N hydrogen

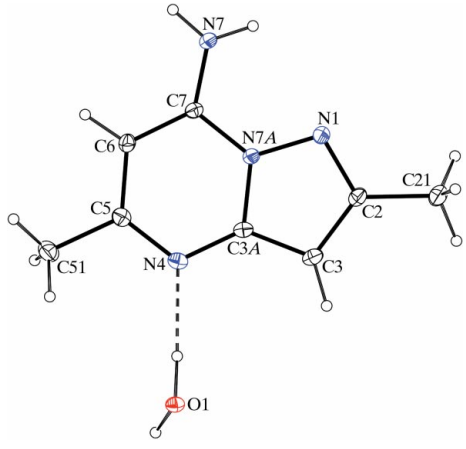


Figure 1
The independent molecular components of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. Atom O1 lies on a twofold rotation axis (see *Comment*).

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bond (Fig. 1 and Table 1). Three independent hydrogen bonds (Table 2), one each of O—H···N, N—H···N and N—H···O types, link the molecular components into a three-dimensional framework of some complexity. However, descriptive analysis of the formation of this framework is markedly simplified by the identification of a number of simple substructures in zero, one and two dimensions, whose combination generates the overall framework structure.

A basic building block in the supramolecular structure is a cyclic dimer containing only the heterocyclic component. Amine atom N7 in the bicyclic molecule at (x, y, z) acts as a

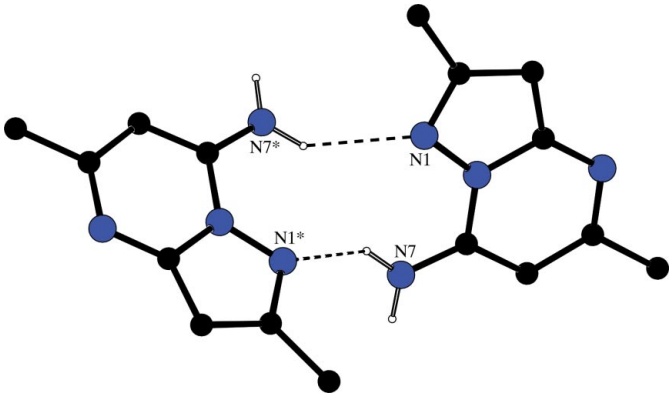

Figure 2
Part of the crystal structure of (I), showing the formation of an $R_2^2(10)$ dimer. For the sake of clarity, the unit-cell outline, the water molecule and H atoms bonded to C atoms have all been omitted. Atoms marked with an asterisk are at the symmetry position $(2 - x, y, 2 - z)$.

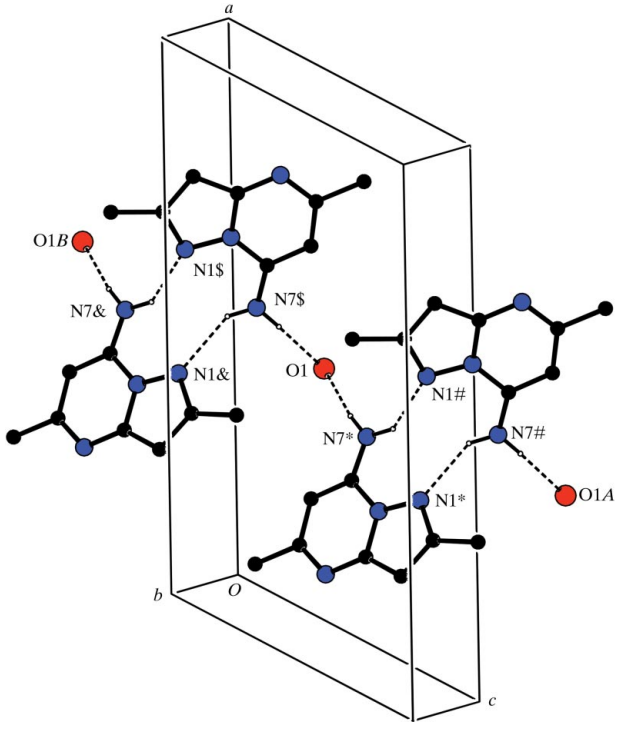

Figure 3
Part of the crystal structure of (I), showing the formation of a [001] chain of linked $R_2^2(10)$ dimers. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*), a hash (#), a dollar sign ($) or an ampersand (&) are at the symmetry positions $(-\frac{1}{2}+x, \frac{1}{2}+y, z)$, $(\frac{3}{2}-x, \frac{1}{2}+y, 2-z)$, $(\frac{3}{2}-x, \frac{1}{2}+y, 1-z)$ and $(-\frac{1}{2}+x, -\frac{1}{2}+x, \frac{1}{2}+y, -1+z)$, respectively. Atoms O1*A* and O1*B* are at $(\frac{1}{2}, y, \frac{3}{2})$ and $(\frac{1}{2}, y, -\frac{1}{2})$, respectively.

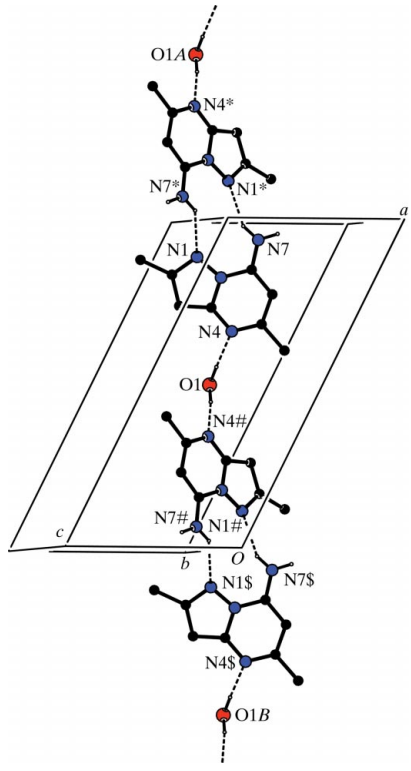

Figure 4
Part of the crystal structure of (I), showing the formation of a [101] chain of linked $R_2^2(10)$ dimers. For the sake of clarity, H atoms bonded to C atoms have been omitted. Atoms marked with an asterisk (*), a hash (#) or a dollar sign ($) are at the symmetry positions $(2 - x, y, 2 - z)$, $(1 - x, y, 1 - z)$ and $(-1 + x, y, -1 + z)$, respectively.

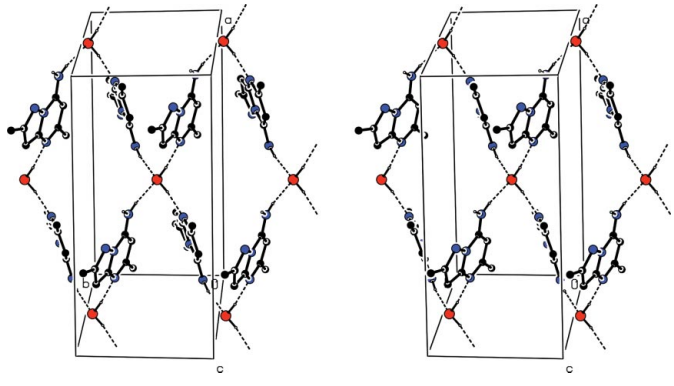

Figure 5
A stereoview of a part of the crystal structure of (I), showing the formation of a (001) sheet of $R_8^8(32)$ rings. For the sake of clarity, H atoms bonded to C atoms have been omitted.

hydrogen-bond donor, *via* H7*A*, to ring atom N1 at ($2 - x$, y, $2 - z$), so forming a cyclic $R_2^2(10)$ (Bernstein *et al.*, 1995) dimer (Fig. 2). The water molecules act as twofold donors in O—H···N hydrogen bonds and as twofold acceptors in N—H···O hydrogen bonds (Table 2), and the resulting linking of the water molecules and the heterocycles generates three independent chains, whose combination leads to the formation of the three-dimensional framework.

The water O atom at ($\frac{1}{2}$, y, $\frac{1}{2}$) accepts hydrogen bonds from amine atoms N7 in the two heterocyclic molecules at ($-\frac{1}{2} + x$, $\frac{1}{2} + y$, z) and ($\frac{3}{2} - x$, $\frac{1}{2} + y$, $1 - z$). These molecules are components of the $R_2^2(10)$ dimers lying across the twofold rotation axes along ($\frac{1}{2}$, y, 1) and ($\frac{1}{2}$, y, 0), and these dimers in turn also act as hydrogen-bond donors to the O atoms at ($\frac{1}{2}$, y, $\frac{3}{2}$) and ($\frac{1}{2}$, y, $-\frac{3}{2}$), respectively. In this manner, a chain of linked dimers running parallel to the [001] direction is generated by successive twofold rotations (Fig. 3).

The same water O atom at ($\frac{1}{2}$, y, $\frac{1}{2}$) acts as a hydrogen-bond donor to pyridine atoms N4 in the molecules at (x, y, z) and ($1 - x$, y, $1 - z$), respectively, which are themselves components of the $R_2^2(10)$ dimers lying across the rotation axes along (1, y, 1) and (0, y, 0). Propagation of these hydrogen bonds by successive rotations then generates a second chain of linked dimers, this time running parallel to the [101] direction (Fig. 4). The combination of the [001] and [101] chains (Figs. 3 and 4) generates the first of the two-dimensional substructures in the form of a (010) sheet.

In the final substructure, which is also two-dimensional, the reference water O atom at ($\frac{1}{2}$, y, $\frac{1}{2}$) acts as a hydrogen-bond donor to the heterocyclic molecules at (x, y, z) and ($1 - x$, y, $1 - z$), and as a hydrogen-bond acceptor from the corresponding molecules at ($-\frac{1}{2} + x$, $\frac{1}{2} + y$, z) and ($\frac{3}{2} - x$, $\frac{1}{2} + y$, $1 - z$), and propagation of these two hydrogen bonds in combination generates a (001) sheet built from a single type of $R_8^8(32)$ ring (Fig. 5). The combination of (010) and (001) sheets is sufficient to generate a single three-dimensional framework structure.

Experimental

An intimate mixture of 5-amino-3-methyl-1*H*-pyrazole (194 mg, 2 mmol) and 3-aminocrotononitrile (328 mg, 4 mmol) was placed in an open Pyrex glass vessel and irradiated in a domestic microwave oven for 2.5 min (at 600 W). The reaction mixture was then extracted with ethanol and, after removal of the solvent, the product was crystallized from ethanol as white crystals suitable for single-crystal X-ray diffraction (yield 92%, m.p. 470–472 K). MS: (30 eV) *m*/*z* (%) = 162 (100, M^+), 161 (24), 147 (5), 134 (11), 122 (26).

Crystal data

$C_8H_{10}N_4{\cdot}0.5H_2O$
M_r = 171.21
Monoclinic, *C*2
a = 16.0851 (5) Å
b = 7.9458 (3) Å
c = 8.0003 (3) Å
β = 117.309 (2)°
V = 908.55 (6) Å^3
Z = 4
D_x = 1.252 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1116 reflections
θ = 4.5–27.5°
μ = 0.09 mm^{-1}
T = 120 (2) K
Block, colourless
0.54 × 0.36 × 0.20 mm

Data collection

Nonius KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.967, T_{max} = 0.983
6163 measured reflections
1116 independent reflections
1032 reflections with $I > 2\sigma(I)$
R_{int} = 0.024
θ_{max} = 27.5°
$h = -20 \rightarrow 20$
$k = -10 \rightarrow 10$
$l = -9 \rightarrow 10$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.090
S = 1.06
1116 reflections
116 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0579P)^2 + 0.2034P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.342 (2)	C6—C7	1.390 (2)
C2—C3	1.401 (3)	C7—N7*A*	1.371 (2)
C3—C3*A*	1.392 (3)	N7*A*—N1	1.368 (2)
C3*A*—N4	1.355 (2)	C3*A*—N7*A*	1.384 (2)
N4—C5	1.332 (2)	C7—N7	1.333 (2)
C5—C6	1.393 (3)		
N7—C7—N7*A*	117.38 (15)	N7—C7—C6	127.60 (16)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···N4	0.96	1.81	2.763 (2)	172
N7—H7*A*···N1^{i}	0.88	2.21	2.971 (2)	144
N7—H7*B*···O1^{ii}	0.88	2.01	2.877 (2)	168

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

The systematic absences permitted *C*2, *Cm* and *C*2/*m* as possible space groups; *C*2 was selected and then confirmed by the successful structure analysis. All H atoms were located from difference maps and then treated as riding atoms, with C—H distances of 0.95 (aromatic) or 0.98 Å (methyl), N—H distances of 0.88 Å, and U_{iso}(H) values of $1.2U_{eq}$(C,N), $1.5U_{eq}$(O) or $1.5U_{eq}$(methyl C). In the absence of significant anomalous scattering, the Flack (1983) parameter was indeterminate (Flack & Bernardinelli, 2000), and the Friedel equivalent reflections were merged prior to the final refinement. Accordingly, it was not possible to establish the absolute configuration of the asymmetric unit (Jones, 1986).

Data collection: *COLLECT* (Hooft, 1999); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *OSCAIL* (McArdle, 2003) and *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *OSCAIL* and *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PRPKAPPA* (Ferguson, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3006). Services for accessing these data are described at the back of the journal.

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