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A three-dimensional hydrogen-bonded framework in 2-amino-4,6-bis[*N*-methyl-*N*-(4-methylphenyl)amino]-pyrimidine-5-carbaldehyde and hydrogen-bonded sheets in 2-amino-4-(indolin-1-yl)-6-methoxypyrimidine-5-carbaldehyde

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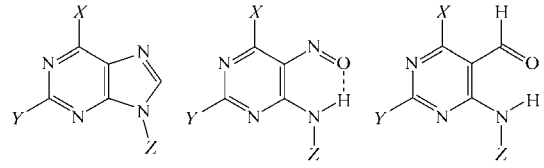
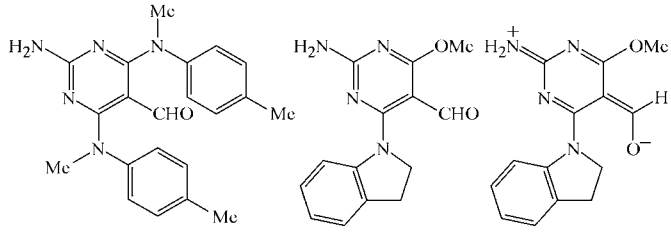
The molecules of 2-amino-4,6-bis[*N*-methyl-*N*-(4-methylphenyl)amino]pyrimidine-5-carbaldehyde, $C_{21}H_{23}N_5O$, (I), and 2-amino-4-(indolin-1-yl)-6-methoxypyrimidine-5-carbaldehyde, $C_{14}H_{14}N_4O_2$, (II), which crystallizes with $Z' = 2$ in the space group $P\overline{1}$, exhibit polarized electronic structures. Molecules of (I) are linked by a combination of N—H···O, C—H···O and C—H···π(arene) hydrogen bonds into a three-dimensional framework structure, while those of (II) are linked into sheets by a combination of two N—H···O hydrogen bonds and one N—H···π(arene) hydrogen bond.

Comment

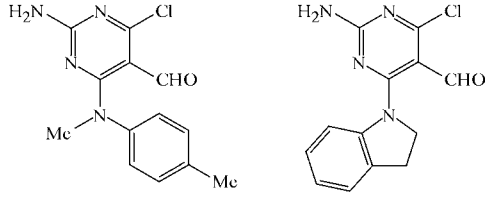
Substituted 6-amino-5-nitrosopyrimidines, *B*, often form intramolecular N—H···O hydrogen bonds and thus are interesting mimics of purines *A*. We have found that such pyrimidines often exhibit markedly polarized molecular electronic structures (Low *et al.*, 2000), leading to the formation of very strong charge-assisted intermolecular hydrogen bonds (Gilli *et al.*, 1994). Bearing in mind the close analogies between nitrosyl and formyl groups, we have recently initiated a study of the analogous formylpyrimidines, *C*. Compounds (I) and (II) (Figs. 1 and 2) were first obtained during attempts to prepare the corresponding 4-chloro analogues, (III) and (IV), respectively, by selective amino substitution at the 6-position in the precursor 2-amino-4,6-dichloro-5-formylpyrimidine (Taylor & Gillespie, 1992). In the event, we observed competition between solvolysis or aminolysis in the second substitution step, which appears to be dependent on the nucleophilic character of the reaction medium. Accordingly, we have now optimized the reaction conditions which generate compounds (I) and (II). For the formation of (I), 2-amino-4,6-dichloro-5-formylpyrimidine was reacted in ethanol with a twofold molar excess of *N*-methyltoluidine and with a twofold molar excess of triethylamine acting as a base. For the formation of (II), the same pyrimidine was reacted in methanol with an equimolar quantity of indoline in the presence of sodium hydroxide.



A *B* *C*



(I) (II) (IIa)



(III) (IV)

In both compounds, the pyrimidine rings deviate from planarity. In (I), the puckering amplitude (Cremer & Pople, 1975) is 0.167 (2) Å, with puckering angles θ = 75.7 (7)° and φ = 234.0 (8)°, so that the boat conformation [where the ideal values are θ = 90° and $\varphi = (60n)°$, where n represents zero or an integer] is the best approximate description. For the two independent molecules of (II), the puckering amplitudes for the pyrimidine rings are less than those in (I), at 0.078 (4) and 0.0108 (50) Å, respectively, for molecules of types 1 and 2 (containing atoms N11 and N31, respectively). The ring-puckering angles θ and φ are 110 (3) and 128 (3)°, respectively, in the type 1 molecule, and 74 (2) and 272 (2)°, respectively, in the type 2 molecule. These values correspond to a screw-boat conformation for the type 2 molecule, and a conformation intermediate between boat and envelope for the type 1 molecule. The five-membered rings in the two molecules of (II) both adopt envelope conformations, folded across the lines Ny1···Cy3 for y = 2 or 4. The asymmetric unit of compound (II) was selected such that the two independent molecules within it are linked by an N—H···O hydrogen bond (see below), and subject to this the two molecules in the asymmetric unit are very approximately enantiomeric.

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The bond distances in the molecules of both compounds (Tables 1 and 3) show some unusual features, consistent with a degree of polarization in their overall molecular electronic structures; this is more marked in (II) than in (I), and thus we discuss only (II) in any detail. In each molecule of compound (II), the C—O bond is long for its type (mean value 1.192 Å; Allen *et al.*, 1987), and the adjacent C5—C51 bond is short (mean value 1.488 Å). Similarly, the C—NH_2 bond length lies towards the shorter end of the range for such bonds (mean value 1.355 Å, lower quartile 1.340 Å). The data indicate a significant contribution from the polarized form, (II*a*), with a more modest contribution from the analogous form in (I).

The molecules of compound (I) are linked into a three-dimensional framework structure by a combination of N—H···O and C—H···O hydrogen bonds (Table 2), although only one N—H bond of the amino group containing atom N2 participates in the hydrogen bonding. The formation of the framework is analysed in terms of a simple chain generated by the weak N—H···O hydrogen bond, followed by the linking of different inversion-related pairs of chains to form the overall structure. Atom N2 in the molecule at (*x*, *y*, *z*) acts as hydrogen-bond donor to atom O51 in the molecule at (−1 + *x*, *y*, *z*), so generating by translation a *C*(8) (Bernstein *et al.*, 1995) chain running parallel to the [100] direction (Fig. 3). The shorter of the C—H···O hydrogen bonds links an antiparallel pair of *C*(8) chains into a chain of edge-fused $R_2^2(16)$ and $R_4^2(20)$ rings running along the line (*x*, 0, 0) (Fig. 3). The longer of the C—H···O hydrogen bonds links this chain to those along (*x*, 1, 0) and (*x*, −1, 0), while the C—H···π(arene) hydrogen bond links the chain along (*x*, 0, 0) to those along (*x*, 0, 1) and (*x*, 0, −1). Thus, all the [100] chains are linked into a single three-dimensional array.

In compound (II), the molecules are linked into sheets by a combination of two independent N—H···O hydrogen bonds and one N—H···π(arene) hydrogen bond (Table 4). Within the selected asymmetric unit, atom N12 acts as hydrogen-bond donor, *via* atom H12*A*, to atom O351. Similarly, atom N32 at

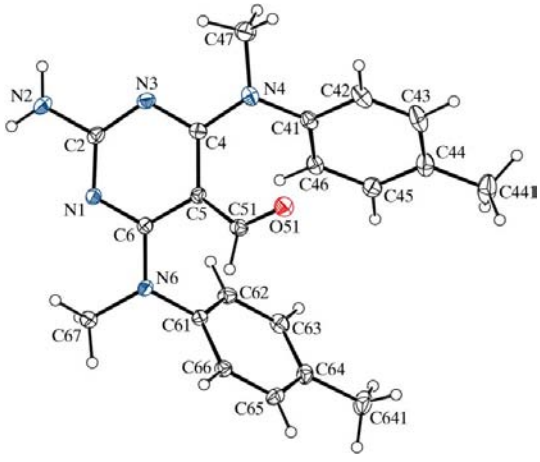

Figure 1
The molecule of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

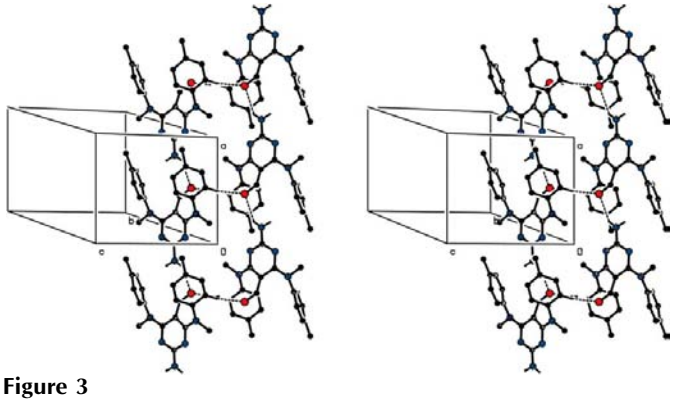

Figure 3
A stereoview of part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded chain of edge-fused $R_2^2(16)$ and $R_4^2(20)$ rings parallel to [100]. For the sake of clarity, H atoms bonded to C atoms not involved in the motif shown have been omitted.

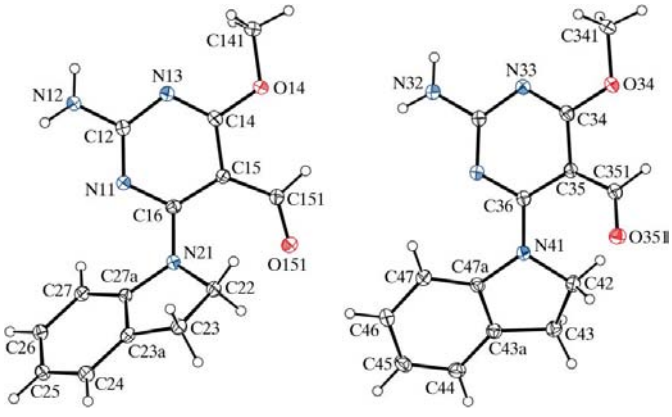

Figure 2
The two independent molecules of compound (II), showing the atom-labelling schemes for (*a*) a type 1 molecule and (*b*) a type 2 molecule. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

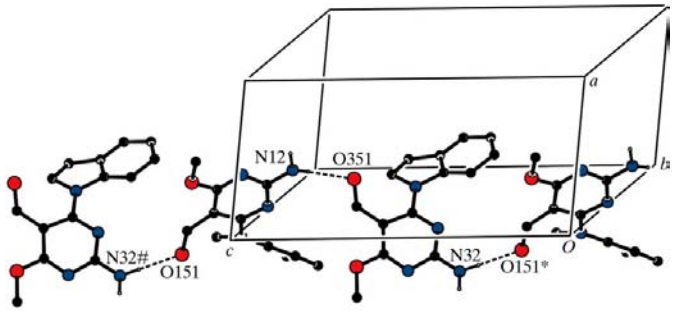

Figure 4
Part of the crystal structure of compound (II), showing the formation of a hydrogen-bonded $C_2^2(16)$ chain along [001]. For the sake of clarity, H atoms bonded to C atoms have been omitted. Atoms marked with an asterisk (*) or a hash symbol (#) are at the symmetry positions (*x*, *y*, −1 + *z*) and (*x*, *y*, 1 + *z*), respectively.

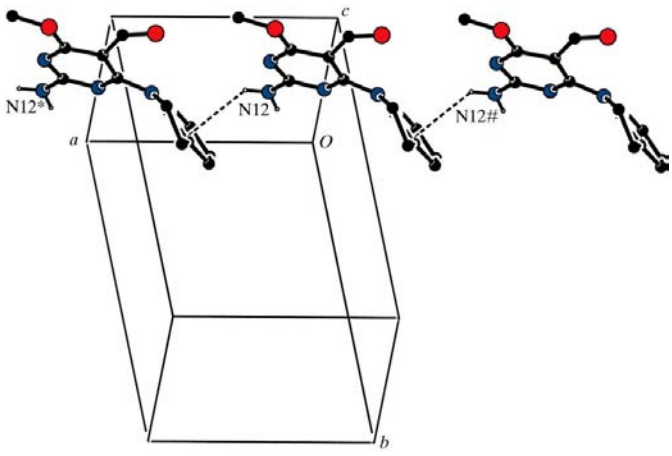

Figure 5
Part of the crystal structure of compound (II), showing the formation of a chain along [100] built from N—H···π(arene) hydrogen bonds. For the sake of clarity, H atoms bonded to C atoms have been omitted. Atoms marked with an asterisk (*) or a hash symbol (#) are at the symmetry positions $(1 + x, y, z)$ and $(-1 + x, y, z)$, respectively.

(x, y, z) acts as hydrogen-bond donor to atom O151 at $(x, y, -1 + z)$, so that the combination of these two hydrogen bonds generates by translation a $C_2^2(16)$ chain running parallel to the [001] direction (Fig. 4). Only one of the other two N—H bonds participates in the hydrogen bonding. Atom N12 in the type 1 molecule at (x, y, z) acts as hydrogen-bond donor, *via* atom H12*B*, to the fused aryl ring (C23a/C24–C27/C27a) in the type 1 molecule at $(1 + x, y, z)$, so generating by translation a chain of type 1 molecules running parallel to the [100] direction (Fig. 5). There are no potential hydrogen-bond acceptors within bonding distance of the corresponding N—H bond of the type 2 molecule. The combination of the [100] and [001] chains generates a sheet parallel to (010), but there are no direction-specific interactions between adjacent sheets.

In view of the variety of C—H···O and C—H···π(arene) hydrogen bonds evident in the structures of compounds (I) and (II), it is surprising to note that, in each compound, one of the N—H bonds plays no role in the hydrogen bonding.

Experimental

For the synthesis of (I), a solution of 2-amino-4,6-dichloropyrimidine-5-carbaldehyde (1 mmol), *N*-methyltoluidine (2 mmol) and triethylamine (2 mmol) in ethanol (5.0 ml) was heated under reflux for 3 h. The solution was cooled to ambient temperature, and the resulting solid product was collected by filtration, washed with ethanol and dried under atmospheric pressure to provide a pale-yellow crystalline solid (yield 50%, m.p. 494–495 K). For the synthesis of (II), a solution of 2-amino-4,6-dichloropyrimidine-5-carbaldehyde (1 mmol), indoline (1 mmol) and a catalytic quantity of sodium hydroxide (one pellet) in methanol (5.0 ml) was stirred at room temperature for 1 h. The resulting solid product was collected by filtration, washed with methanol and dried at atmospheric pressure to provide a colourless solid (yield 60%, m.p. 446–447 K). Crystals of (I) and (II) suitable for single-crystal X-ray diffraction were grown by slow evaporation of solutions in ethanol.

Compound (I)

Crystal data

$C_{21}H_{23}N_5O$
$M_r = 361.44$
Triclinic, $P\overline{1}$
$a = 8.6844$ (6) Å
$b = 10.7807$ (19) Å
$c = 10.8903$ (10) Å
$\alpha = 69.998$ (14)°
$\beta = 88.918$ (7)°
$\gamma = 76.822$ (13)°
$V = 930.9$ (2) Å^3
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 0.08$ mm^{-1}
$T = 120$ (2) K
0.31 × 0.24 × 0.21 mm

Data collection

Bruker Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.965$, $T_{max} = 0.983$
24528 measured reflections
4249 independent reflections
2988 reflections with $I > 2\sigma(I)$
$R_{int} = 0.046$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.060$
$wR(F^2) = 0.153$
$S = 1.08$
4249 reflections
248 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.51$ e Å^{-3}
$\Delta\rho_{min} = -0.35$ e Å^{-3}

Table 1
Selected bond lengths (Å) for (I).

N1—C2	1.347 (3)	C2—N2	1.345 (3)
C2—N3	1.345 (3)	C4—N4	1.376 (3)
N3—C4	1.336 (3)	C6—N6	1.374 (3)
C4—C5	1.426 (3)	C5—C51	1.450 (3)
C5—C6	1.427 (3)	C51—O51	1.219 (3)
C6—N1	1.330 (3)		

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

*Cg*1 is the centroid of the C41–C46 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2*B*···O51^{i}	0.86	2.53	3.038 (3)	118
C42—H42···O51^{ii}	0.95	2.29	3.203 (3)	162
C66—H66···O51^{iii}	0.95	2.52	3.228 (3)	131
C63—H63···*Cg*1^{iv}	0.95	2.87	3.736 (2)	152

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

Compound (II)

Crystal data

$C_{14}H_{14}N_4O_2$
$M_r = 270.29$
Triclinic, $P\overline{1}$
$a = 8.2846$ (4) Å
$b = 11.2710$ (4) Å
$c = 15.0024$ (7) Å
$\alpha = 108.983$ (4)°
$\beta = 95.403$ (4)°
$\gamma = 101.908$ (3)°
$V = 1276.35$ (10) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.10$ mm^{-1}
$T = 120$ (2) K
0.52 × 0.41 × 0.14 mm

Data collection

Bruker Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.967$, $T_{max} = 0.986$
31946 measured reflections
5864 independent reflections
3790 reflections with $I > 2\sigma(I)$
$R_{int} = 0.045$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.055$	363 parameters
$wR(F^2) = 0.164$	H-atom parameters constrained
$S = 1.08$	$\Delta\rho_{max} = 0.30$ e Å^{-3}
5864 reflections	$\Delta\rho_{min} = -0.38$ e Å^{-3}

Table 3
Selected bond lengths (Å) for (II).

N11—C12	1.338 (3)	N31—C32	1.334 (3)
C12—N13	1.355 (3)	C32—N33	1.355 (3)
N13—C14	1.317 (3)	N33—C34	1.317 (3)
C14—C15	1.418 (3)	C34—C35	1.417 (3)
C15—C16	1.423 (3)	C35—C36	1.425 (3)
C16—N11	1.343 (3)	C36—N31	1.345 (3)
C12—N12	1.337 (3)	C32—N32	1.343 (3)
C14—O14	1.345 (2)	C34—O34	1.344 (2)
C16—N21	1.370 (3)	C36—N41	1.359 (3)
C15—C151	1.439 (3)	C35—C351	1.440 (3)
C151—O151	1.226 (3)	C351—O351	1.233 (3)

Table 4
Hydrogen-bond geometry (Å, °) for (II).

*Cg*2 is the centroid of the C23a/C24–C27/C27a ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N12—H12*A*···O351	0.86	2.13	2.952 (2)	160
N32—H32*A*···O151^{i}	0.86	2.07	2.930 (3)	175
N12—H12*B*···*Cg*2^{ii}	0.86	2.61	3.294 (4)	136

Symmetry codes: (i) $x, y, z-1$; (ii) $x+1, y, z$.

Crystals of both (I) and (II) are triclinic. For each, the space group $P\overline{1}$ was selected and confirmed by the subsequent structure analysis. All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H = 0.95 (aromatic and formyl), 0.98 (CH_3) or 0.99 Å (CH_2), and N—H = 0.86 Å, and with $U_{iso}(H) = kU_{eq}$(carrier), where $k = 1.5$ for the methyl groups and 1.2 for all other H atoms.

For both compounds, data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX/LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *OSCAIL* (McArdle, 2003) 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: SK3170). Services for accessing these data are described at the back of the journal.

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