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2-Amino-4-chloro-6-[*N*-methyl-*N*-(4-methylphenyl)amino]pyrimidine: formation *versus* fragmentation of hydrogen-bonded chains of edge-fused $R_2^2(8)$ rings in 4,6-disubstituted 2-aminopyrimidines

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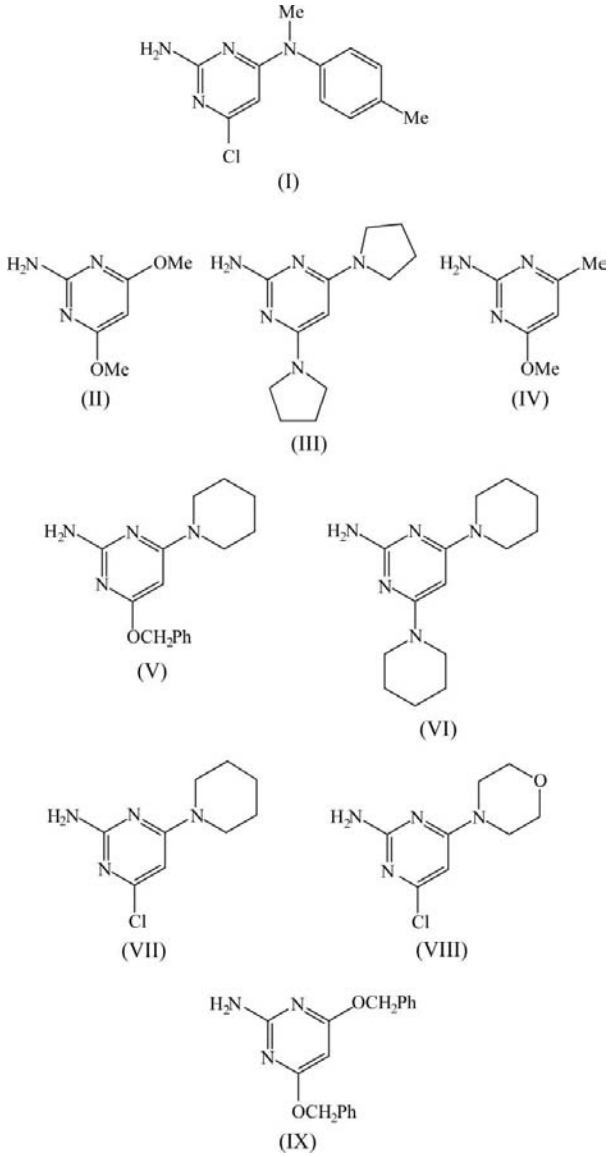
Molecules of the title compound, $C_{12}H_{13}ClN_4$, are linked by two independent N—H···N hydrogen bonds into a chain of edge-fused $R_2^2(8)$ rings. The significance of this study lies in its attempt to rationalize the patterns of supramolecular aggregation in the title compound and in a range of analogous 4,6-disubstituted 2-aminopyrimidines.

Comment

In recent years, we have reported the molecular and supramolecular structures of a number of 4,6-disubstituted 2-aminopyrimidines (Low *et al.*, 2002; Bowes *et al.*, 2003; Glidewell *et al.*, 2003; Melguizo *et al.*, 2003; Quesada *et al.*, 2002, 2004), which have proven to exhibit a very wide range of supramolecular aggregation patterns. We report here the structure of the title compound, (I) (Fig. 1), and we attempt a simple rationalization of some of the structural themes observed in earlier determinations. For the preparation of (I), which is intended for eventual use as an intermediate in the synthesis of a variety of fused heterocyclic derivatives, a solvent-free fusion method was used for the selective monosubstitution by *N*-methyl-4-toluidine of the 6-chloro substituent in the precursor compound 2-amino-4,6-dichloropyrimidine.

The molecules of (I) are linked into sheets by a combination of two independent N—H···N hydrogen bonds and one C—H···π(pyrimidine) hydrogen bond (Table 1). Amino atom N2 in the molecule at (x, y, z) acts as a hydrogen-bond donor to ring atoms N1 and N3 in the molecules at ($-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$) and ($-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$), respectively, so that molecules related by the 2_1 screw axis along ($\frac{1}{2}$, y, $\frac{3}{4}$) are linked into a $C(4)C(4)[R_2^2(8)]$ chain of rings (Bernstein *et al.*, 1995) (Fig. 2). In addition, aryl atoms C63 in the molecules at (x, y, z) and ($-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$) act as hydrogen-bond donors, respectively, to the pyrimidine rings of the molecules at ($-x, -y+1, -z+1$) and ($x+1, -y+\frac{3}{2}, z+\frac{1}{2}$), which are themselves components of the chains of rings along ($-\frac{1}{2}, -y, \frac{1}{4}$) and ($\frac{3}{2}, -y, \frac{5}{4}$), respectively. Hence, the C—H···π(pyrimidine) hydrogen bond links the chains of rings parallel to [010] into a sheet parallel to ($10\bar{2}$).



The formation of edge-fused chains of $R_2^2(8)$ as found in (I) occurs in a number of other simple 2-aminopyrimidines, but the disruption of such a chain formation appears to be readily accomplished, resulting either from steric factors arising from bulky substituents or from the presence of an alternative hydrogen-bond acceptor which can compete effectively with the pyrimidine ring N atoms. Chains of edge-fused $R_2^2(8)$ rings that are topologically identical to that in (I) are found both in

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the symmetrically disubstituted aminopyrimidines (II) and (III) (Low *et al.*, 2002) and in the unsymmetrically substituted compounds (IV) (Glidewell *et al.*, 2003) and (V) (Melguizo *et al.*, 2003), although the different space groups and Z' values mean that different symmetry operations relate the molecules within the chains.

However, in the structures of the related compounds (VI)–(IX), it is possible to discern only small fragments of a chain of edge-fused rings built from N—H···N hydrogen bonds. Thus, in (VI), whose constitution is similar to that of (III), the N—H···N hydrogen bonds generate only a centrosymmetric $R_2^2(8)$ dimer, *i.e.* a two-molecule fragment of the chain found in (I)–(V), and only one of the N—H bonds in (VI) is active in hydrogen-bond formation, although the dimers are further linked by a single C—H···π(pyrimidine) interaction (Quesada *et al.*, 2004). Compound (VII) crystallizes with $Z' = 2$ in the space group $P2_1/c$, and three independent N—H···N hydrogen bonds form an aggregate containing three edge-fused $R_2^2(8)$ rings, *i.e.* a four-molecule fragment of the chain, with again one of the N—H bonds playing no role in the hydrogen bonding (Bowes *et al.*, 2003). The morpholino analogue of (VII), *viz.* compound (VIII), crystallizes in two polymorphic forms, both in $P2_1/c$, with $Z' = 1$ and 2 (Bowes *et al.*, 2003). In each polymorph, paired N—H···N hydrogen bonds generate a two-component $R_2^2(8)$ fragment, and these are linked by N—H···O hydrogen bonds to form sheets of $R_2^2(8)$ and $R_6^6(40)$ rings in the $Z' = 1$ form, and chains of alternating $R_2^2(8)$ and $R_4^4(18)$ rings in the $Z' = 2$ form. Hence, all of the N—H bonds are active in hydrogen-bond formation here. Entirely analogous behaviour is exhibited by (IX), which is closely related to (II); paired N—H···N hydrogen bonds form an $R_2^2(8)$ dimer, again a two-molecule component of the chain found in (I)–(V), and N—H···O hydrogen bonds link these dimers into a chain of alternating $R_2^2(8)$ and $R_4^4(16)$ rings (Quesada *et al.*, 2002).

The disruption of the chain formation in (VIII) and (IX) can be interpreted straightforwardly in terms of the effective competition by the more electronegative O atoms as hydrogen-bond acceptors, leading to the replacement of some of the N—H···N hydrogen bonds by N—H···O hydrogen bonds. A more subtle question arises from the structural differences between (II) and (IX), where precisely the same sets of potential hydrogen-bond acceptors are present, arranged with the same relative dispositions; the original report on the structure of (IX), where the molecule has no internal symmetry in the crystal (Quesada *et al.*, 2002), emphasized the interplay between the conformations adopted by the benzyl substituents and the hydrogen-bond formation as a significant determinant of the overall crystal structure. The short-fragment formation by (VI) is readily understood in terms of steric factors, but a significant anomaly is apparent in the structure of (VII), where any steric factors might have been expected to be significantly less than those in (V). However, (VII) is in fact isomorphous and almost isostructural with the $Z' = 2$ polymorph of (VIII) (Bowes *et al.*, 2003) and it is entirely possible that a $Z' = 1$ polymorph of (VII) having a different overall aggregation pattern could also exist.

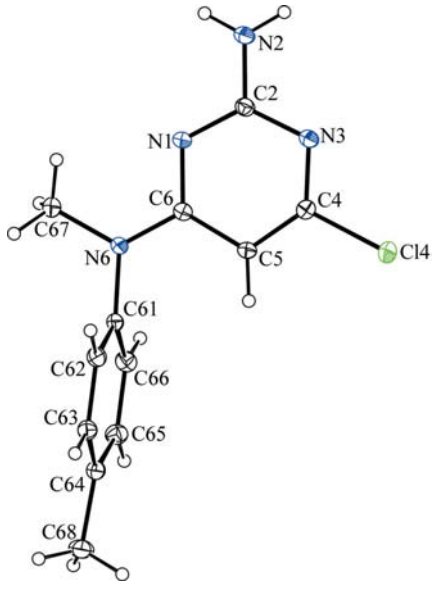

Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

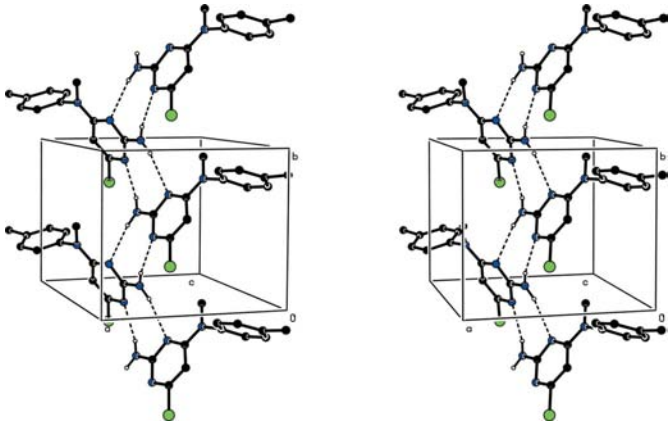

Figure 2
A stereoview of part of the crystal structure of (I), showing the formation of a hydrogen-bonded chain of edge-fused rings parallel to the [010] direction.

Experimental

A mixture of 2-amino-4,6-dichloropyrimidine (1.037 mmol) and *N*-methyl-4-toluidine (1.815 mmol) was placed in a test tube and heated at 473–483 K in an oil bath for 35 min. The reaction mixture was cooled to ambient temperature and the resulting solid was washed with an excess of a saturated aqueous solution of sodium hydrogen carbonate. The crude product was collected by filtration, washed successively with water and diethyl ether, and then dried in an oven at 333 K to give the title compound. Crystals suitable for single-crystal X-ray diffraction were obtained by slow evaporation of a solution in dimethyl sulfoxide (yield 92%, m.p. 473–475 K). HRMS: found 248.0822; $C_{12}H_{13}{}^{35}ClN_4$ requires: 248.0829.

Crystal data

$C_{12}H_{13}ClN_4$
$M_r = 248.71$
Monoclinic, $P2_1/c$
$a = 9.8184$ (5) Å
$b = 7.8683$ (7) Å
$c = 15.5719$ (16) Å
$\beta = 100.309$ (7)°
$V = 1183.57$ (17) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.30$ mm^{-1}
$T = 120$ (2) K
0.41 × 0.25 × 0.22 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.885$, $T_{max} = 0.936$
29284 measured reflections
2720 independent reflections
1933 reflections with $I > 2\sigma(I)$
$R_{int} = 0.058$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.048$
$wR(F^2) = 0.128$
$S = 1.10$
2720 reflections
156 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.44$ e Å^{-3}
$\Delta\rho_{min} = -0.30$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

Cg represents the centroid of the N1/C2/N3/C4–C6 ring.

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2A···N3^{i}	0.88	2.29	3.147 (3)	163
N2—H2B···N1^{ii}	0.88	2.47	3.333 (3)	168
C63—H63···Cg^{iii}	0.95	2.68	3.517 (2)	147

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) $-x, -y+1, -z+1$.

The space group $P2_1/c$ was uniquely assigned from the systematic absences. All H atoms were located in difference maps and then treated as riding atoms, with C—H distances of 0.95 (arene and pyrimidine) or 0.98 Å (CH_3) and N—H distances of 0.88 Å, and with $U_{iso}(H) = kU_{eq}$(carrier), where $k = 1.5$ for the methyl groups and $k = 1.2$ for all other H atoms.

Data collection: *COLLECT* (Hooft, 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, 2008); 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: SK3241). Services for accessing these data are described at the back of the journal.

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