

2-Amino-4-chloro-5-formyl-6-[methyl(2-methylphenyl)amino]pyrimidine and 2-amino-4-chloro-5-formyl-6-[(2-methoxyphenyl)methylamino]pyrimidine are isostructural and form hydrogen-bonded sheets of $R_2^2(8)$ and $R_6^6(32)$ rings

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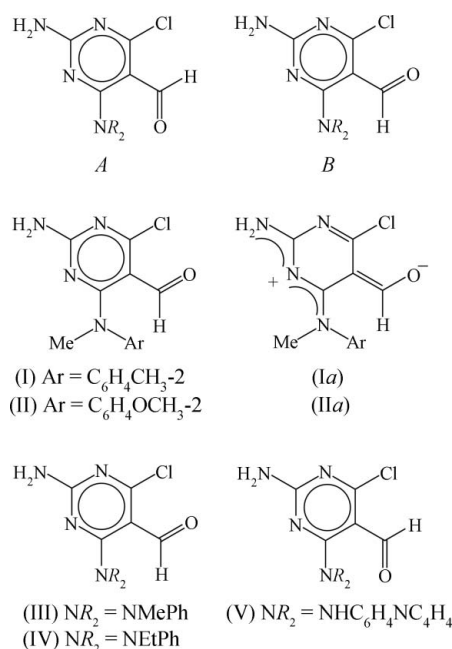
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2-Amino-4-chloro-5-formyl-6-[methyl(2-methylphenyl)amino]pyrimidine, $C_{13}H_{13}ClN_4O$, (I), and 2-amino-4-chloro-5-formyl-6-[(2-methoxyphenyl)methylamino]pyrimidine, $C_{13}H_{13}ClN_4O_2$, (II), are isostructural and essentially isomorphous. Although the pyrimidine rings in each compound are planar, the ring-substituent atoms show significant displacements from this plane, and the bond distances provide evidence for polarization of the electronic structures. In each compound, a combination of $N-H\cdots N$ and $N-H\cdots O$ hydrogen bonds links the molecules into sheets built from centrosymmetric $R_2^2(8)$ and $R_6^6(32)$ rings. The significance of this study lies in its observation of the isostructural nature of (I) and (II), and in the comparison of their crystal and molecular structures with those of analogous compounds.

Comment

We have recently reported the molecular and supramolecular structures of a number of N^6 -substituted 2-amino-4-chloro-5-formylpyrimidines (Cobo *et al.*, 2008). Two features of the molecular structures that vary independently amongst the 12 examples studied are the orientation of the formyl group and the shape of the pyrimidine ring, while in all cases the bond distances provide strong evidence for the development of polarized electronic structures. In the majority of the compounds studied earlier (Cobo *et al.*, 2008), the formyl orientation has the formyl C—H bond approximately parallel to the C—Cl bond, while in the remainder, the formyl C=O bond is approximately parallel to the C—Cl bond; these two

conformations are denoted *A* and *B*, respectively. For both conformers, examples were observed in which the pyrimidine rings were planar within experimental uncertainty, while in others these rings were significantly puckered into boat, screw-boat or twist-boat conformations. The puckering of the pyrimidine rings in these examples did not appear to inhibit to any degree the development of the polarized electronic structures, exactly as found in other heavily substituted pyrimidines previously reported (Low *et al.*, 2007; Melguizo *et al.*, 2003; Quesada *et al.*, 2003, 2004; Trilleras *et al.*, 2007). In all, of the 12 compounds previously studied, nine had formyl conformations of type *A* and three of type *B*; independently, five of them contained planar pyrimidine rings and seven contained puckered rings.



As a continuation of this study, we have now investigated two further examples, (I) and (II), which both turn out to have type *B* conformations and to contain planar pyrimidine rings. Compounds (I) and (II) were prepared by selective monosubstitution (Taylor & Gillespie, 1992; Quiroga *et al.*, 2008) of the 6-chloro substituent in 2-amino-4,6-dichloro-5-formylpyrimidine (Seela & Sterker, 1986), and their constitutions differ only in the identity of the substituent in the aryl ring, *i.e.* 2-methyl in (I) and 2-methoxy in (II) (Figs. 1 and 2). Compounds (I) and (II) crystallize in the same space group with fairly similar unit-cell dimensions; the coordinates of corresponding atoms are also similar, while the patterns of the hydrogen bonds are identical (Table 2). Accordingly, the compounds are isostructural and effectively isomorphous.

The corresponding bond distances and torsion angles for (I) and (II) are very similar (Table 1). The distances show many of the characteristics observed previously in other compounds of this type (Cobo *et al.*, 2008). Thus, the ring distances N1—C2 and C6—N1 and the exocyclic distances C2—N2 are all very similar, while the ring distances N3—C4 are, by some margin,

the shortest of all the N—C distances; the formyl C51—O51 bonds are long for their type [mean value (Allen *et al.*, 1987) 1.192 Å], while the C5—C51 bonds are short (mean value = 1.488 Å). Taken together these distances provide evidence for an important contribution to the overall electronic structures in (I) and (II) from the polarized forms (Ia) and (IIa). This is so despite the fact that the formyl O atom is not coplanar with the pyrimidine ring, as indicated by the non-zero values of the C4—C5—C51—O51 torsion angle (Table 1).

Although the pyrimidine ring in each of (I) and (II) is essentially planar, with the maximum deviation of a ring atom from the mean plane occurring in each compound for atom C5, displaced from the plane by 0.042 (3) Å in (I) and 0.048 (3) Å in (II), the substituent atoms attached to the pyrimidine ring all show significant deviations from the ring plane. In particular, the three adjacent substituent atoms Cl4,

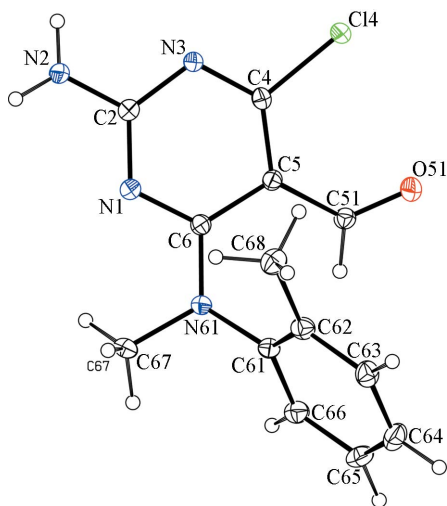


Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

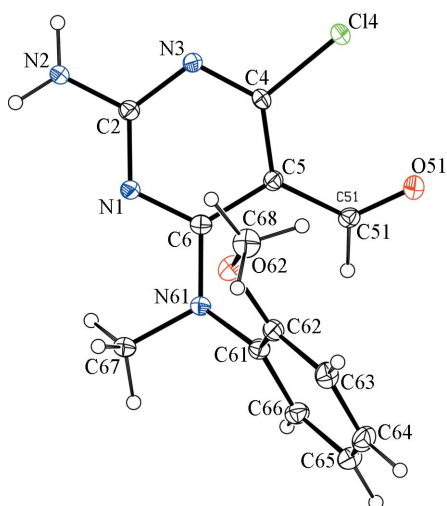


Figure 2
The molecular structure of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

C51 and N61 are displaced to alternate sides of the ring plane, with the central substituent atom C51 showing much the largest displacement in each compound (Table 1). Methoxy atom C68 in (II) is almost coplanar with the adjacent benzene ring, having a deviation from the ring plane of only 0.013 (4) Å; accordingly, the two exocyclic C—C—O angles associated with the methoxy substituent differ by *ca* 10°, as normally observed in such cases.

Compounds (I) and (II) exhibit identical patterns of hydrogen bonding (Table 2), with similar dimensions for the hydrogen bonds in the two compounds. The N—H...N hydrogen bond generates a centrosymmetric $R_2^2(8)$ (Bernstein *et al.*, 1995) motif, centred at (0, 0, $\frac{1}{2}$). The action of the N—H...O hydrogen bond is to link this dimeric unit at (0, 0, $\frac{1}{2}$) to the four adjacent dimers centred at ($-\frac{1}{2}$, $-\frac{1}{2}$, 0), ($-\frac{1}{2}$, $\frac{1}{2}$, 0), ($\frac{1}{2}$, $-\frac{1}{2}$, 1) and ($\frac{1}{2}$, $\frac{1}{2}$, 1), thereby generating a sheet parallel to (101) and built from alternating $R_2^2(8)$ and $R_6^6(32)$ rings (Fig. 3), in which both ring types are centrosymmetric. There are no direction-specific interactions between adjacent sheets; in particular, both C—H... π (arene) hydrogen bonds and aromatic π — π stacking interactions are absent, nor does the methoxy O atom in (II) play any part in the hydrogen bonding.

Within the hydrogen-bonded sheets formed in each of (I) and (II) there is a fairly short N—H...Cl contact (Table 2). However, it has been amply shown (Aakeröy *et al.*, 1999; Brammer *et al.*, 2001; Thallapally & Nangia, 2001) that Cl atoms covalently bonded to C atoms are very poor hydrogen-bond acceptors and that such contacts are probably no more than ordinary van der Waals contacts. It is thus safer to regard the N—H...Cl contacts in (I) and (II) as adventitious contacts consequent upon the geometry of the N—H...O hydrogen bonds and not of themselves structurally significant. In any event, such an interaction would not have any bearing on the overall forms of the hydrogen-bonded structures.

Of the analogues studied previously (Cobo *et al.*, 2008), those closest in constitution to (I) and (II) are (III), which differs from (I) and (II) only in carrying no substituent on the phenyl ring, and (IV), which is an isomer of (I). Compounds (III) and (IV) both adopt type *B* conformations, but while (III) contains a planar pyrimidine ring, in (IV) this ring adopts a boat conformation. Although dimers characterized by $R_2^2(8)$

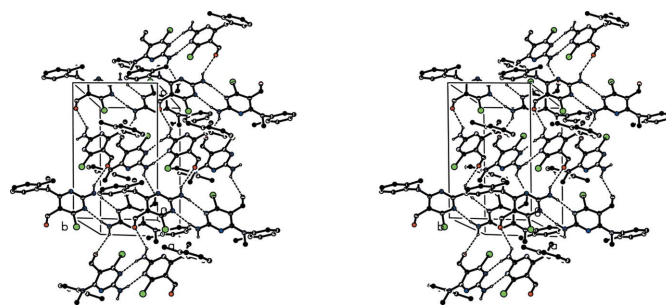


Figure 3
Stereoview of the crystal structure of (I), showing the formation of a hydrogen-bonded sheet of $R_2^2(8)$ and $R_6^6(32)$ rings parallel to (101). For the sake of clarity, H atoms bonded to C atoms have been omitted.

motifs and built from paired N—H...N hydrogen bonds can be identified in the structures of each of (III) and (IV), just as in (I) and (II), the further linking of these dimeric units in (III) and (IV) does not resemble that in (I) and (II). In (III), a combination of N—H...N and C—H... π (arene) hydrogen bonds leads to the formation of a chain of edge-fused rings, but the formyl O atom plays no role in the hydrogen bonding. In (IV), by contrast, a combination of N—H...N and N—H...O hydrogen bonds generates a chain of alternating centrosymmetric $R_2^2(8)$ and $R_4^4(16)$ rings.

The only other example in this series of a sheet of alternating $R_2^2(8)$ and $R_6^6(32)$ rings built from N—H...N and N—H...O hydrogen bonds, as in (I) and (II), was found in the structure of (V). This differs from (I) and (II), both in adopting a type A conformation and in the constitution of the NR₂ group bonded to C6. This substituent contains an N—H bond that forms an intramolecular N—H...O hydrogen bond to the formyl O atom but otherwise plays no role in the supramolecular aggregation.

Experimental

A solution containing 1 mmol of each of 2-amino-4,6-dichloro-5-formylpyrimidine, the appropriate secondary amine [methyl(2-methylphenyl)amine for (I) and methyl(2-methoxyphenyl)amine for (II)] and triethylamine as a base, in ethanol (5 ml), was heated under reflux for 3 h. The mixtures were cooled to ambient temperature and the resulting solid products were collected by filtration, washed with cold ethanol and dried in air before being recrystallized from ethanol to give yellow crystals of (I) and (II) suitable for single-crystal X-ray diffraction. Compound (I) (yield 80%, m.p. 456–458 K): MS (70 eV) m/z (%) 278/276 ($M + 2/M^+$, 13/42), 261/260 (55/17), 259 (100), 212 (13), 198 (23), 129/128 (31/8), 92/91 (6/20); HR–MS calculated for C₁₃H₁₃ClN₄O: 276.0778, found 276.0780. Compound (II) (yield 81%, m.p. 454–456 K): MS (70 eV) m/z (%) 294/292 ($M + 2/M^+$, 7/21), 263/261 (35/100), 234/233 (4/11), 131/129 (8/21); HR–MS calculated for C₁₃H₁₃ClN₄O₂ 292.0727, found 292.0727.

Compound (I)

Crystal data

C ₁₃ H ₁₃ ClN ₄ O	$V = 1284.75$ (19) Å ³
$M_r = 276.72$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 11.1502$ (8) Å	$\mu = 0.30$ mm ^{−1}
$b = 8.7271$ (8) Å	$T = 120$ (2) K
$c = 13.7129$ (13) Å	$0.47 \times 0.37 \times 0.26$ mm
$\beta = 105.676$ (7)°	

Data collection

Bruker–Nonius KappaCCD diffractometer	23784 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	2946 independent reflections
$T_{\min} = 0.874$, $T_{\max} = 0.927$	1999 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.059$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.051$	174 parameters
$wR(F^2) = 0.155$	H-atom parameters constrained
$S = 1.14$	$\Delta\rho_{\text{max}} = 0.38$ e Å ^{−3}
2946 reflections	$\Delta\rho_{\text{min}} = -0.46$ e Å ^{−3}

Compound (II)

Crystal data

C ₁₃ H ₁₃ ClN ₄ O ₂	$V = 1327.1$ (8) Å ³
$M_r = 292.72$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 11.301$ (4) Å	$\mu = 0.30$ mm ^{−1}
$b = 8.642$ (3) Å	$T = 120$ (2) K
$c = 14.568$ (5) Å	$0.27 \times 0.15 \times 0.10$ mm
$\beta = 111.13$ (3)°	

Data collection

Bruker–Nonius KappaCCD diffractometer	18363 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	3028 independent reflections
$T_{\min} = 0.939$, $T_{\max} = 0.971$	2010 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.103$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.061$	183 parameters
$wR(F^2) = 0.143$	H-atom parameters constrained
$S = 1.11$	$\Delta\rho_{\text{max}} = 0.52$ e Å ^{−3}
3028 reflections	$\Delta\rho_{\text{min}} = -0.43$ e Å ^{−3}

All H atoms were located in difference maps and then treated as riding atoms, with C—H distances of 0.95 (aromatic) or 0.98 Å (methyl) and N—H distances of 0.88 Å, and with $U_{\text{iso}}(\text{H}) = kU_{\text{eq}}(\text{carrier})$, where $k = 1.5$ for the methyl groups and $k = 1.2$ for all other H atoms.

For both compounds, 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

Table 1

Selected geometric parameters (Å, °) for (I) and (II).

(a) Selected distances and angles.

	(I)	(II)
N1—C2	1.331 (3)	1.336 (4)
C2—N3	1.355 (3)	1.342 (4)
N3—C4	1.307 (3)	1.314 (4)
C4—C5	1.382 (4)	1.387 (4)
C5—C6	1.437 (3)	1.425 (4)
C6—N1	1.328 (3)	1.328 (4)
C2—N2	1.320 (3)	1.322 (4)
C5—C51	1.460 (4)	1.461 (4)
C51—O51	1.212 (3)	1.208 (4)
C6—N61	1.351 (3)	1.369 (4)
C61—C62—O62	—	115.3 (3)
C63—C62—O62	—	125.1 (3)
C4—C5—C51—O51	24.5 (4)	20.8 (5)
N1—C6—N61—C61	−150.2 (2)	−145.5 (3)
C6—N61—C61—C62	52.9 (3)	51.2 (4)
C61—C62—O62—C68	—	−176.3 (3)
N1—C6—N61—C67	7.4 (3)	3.1 (4)

(b) Substituent-atom deviations from the pyrimidine plane.

Atom	(I)	(II)
N2	−0.093 (2)	−0.125 (3)
Cl4	0.106 (2)	0.106 (2)
C51	−0.368 (2)	−0.402 (3)
O51	0.218 (2)	0.331 (2)
N61	0.118 (2)	0.085 (2)

Table 2

Hydrogen bonds and short intermolecular contacts (Å, °) for (I) and (II).

Compound	<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
(I)	N2—H21...O51 ⁱ	0.88	2.38	3.052 (3)	134
	N2—H21...Cl1 ⁱ	0.88	2.58	3.377 (2)	152
	N2—H22...N3 ⁱⁱ	0.88	2.11	2.988 (3)	171
(II)	N2—H21...O51 ⁱ	0.88	2.55	3.125 (4)	124
	N2—H21...Cl1 ⁱ	0.88	2.58	3.375 (3)	150
	N2—H22...N3 ⁱⁱ	0.88	2.12	2.983 (4)	168

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

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: SK3279). Services for accessing these data are described at the back of the journal.

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