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Two polymorphic forms of *N*-(4-chlorophenyl)-5-[(4-chlorophenyl)aminomethyl]-6-methyl-2-phenylpyrimidin-4-amine

Jerzy Cieplik,[a] Janusz Pluta,[a] Iwona Bryndal[b]* and Tadeusz Lis[b]

[a]Department of Organic Chemistry, Medical Academy, 9 Grodzka Street, 50-137 Wrocław, Poland, and [b]Faculty of Chemistry, University of Wrocław, 14 Joliot-Curie Street, 50-383 Wrocław, Poland
Correspondence e-mail: isia@wcheto.chem.uni.wroc.pl

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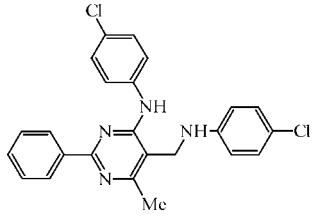
Two polymorphic forms of the title compound, $C_{24}H_{20}Cl_2N_4$, were obtained and characterized using X-ray crystal structure analysis. Colourless crystals of polymorph (I*a*) were obtained from the oily mother residue. Recrystallization of polymorph (I*a*) from an acetone–methanol mixture resulted in pale-yellow crystals of polymorph (I*b*). The major feature distinguishing the two polymorphic forms is their interaction modes, and hence their packing arrangements. In the crystal structure of polymorph (I*a*), there are N—H···N hydrogen bonds and also aromatic π–π stacking interactions between molecules. The molecules of polymorph (I*b*) are linked by N—H···Cl hydrogen bonds only.

Comment

Pyrimidine derivatives have very interesting biological properties and many applications in the areas of pharmaceuticals. For example, alkoxy- and amino-substituted 6-benzyloxy-5-nitropyrimidines are important as potential inhibitors of the human DNA-repair protein O^6-alkylguanine-DNA-transferase (Quesada *et al.*, 2002; Glidewell *et al.*, 2003). Several pyrimidine derivatives have been developed as agrochemicals (McCourt *et al.*, 2005), antiviral agents, such as AZT, which is the most widely used anti-HIV drug (Gilchrist, 1997), or antifolate drugs, such as TMP and DHFR (Feeney, 2000).

In order to discover more active pyrimidine compounds displaying immunomodulatory activity, we synthesized new 6-methyl-2-phenyl-5-substituted pyrimidine derivatives (Cieplik *et al.*, 1995). We report here the structures of two polymorphic forms of *N*-(4-chlorophenyl)-5-[(4-chlorophenyl)-aminomethyl]-6-methyl-2-phenylpyrimidin-4-amine, (I*a*) and (I*b*).

Polymorphs (I*a*) (Fig. 1) and (I*b*) (Fig. 2) crystallize in space group *Pbca* with $Z = 8$ and $P2_1/c$ with $Z = 4$, respectively. The bond lengths and angles for both polymorphs are in accordance with anticipated values (Quesada *et al.*, 2002, 2004). However, pronounced differences between these polymorphs are apparent in the conformation of the (4-chlorophenyl)-amino group about atom C51.



(I)

In both cases, the orientation of the N amide atoms with respect to each other is the result of an intramolecular N—H···N hydrogen bond between atoms N4 and N5, which generates an *S*(6) motif (Bernstein *et al.*, 1995). The C—N distances of the pyrimidine ring are in the range 1.329 (3)–

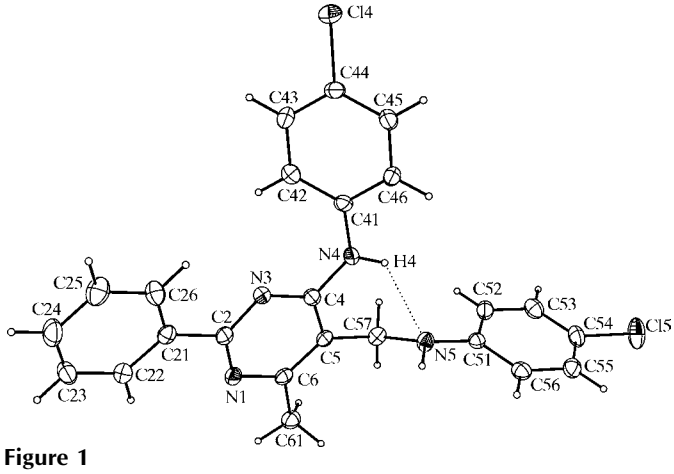


Figure 1
The molecule of polymorph (I*a*), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The dotted line indicates the intramolecular N—H···N hydrogen bond.

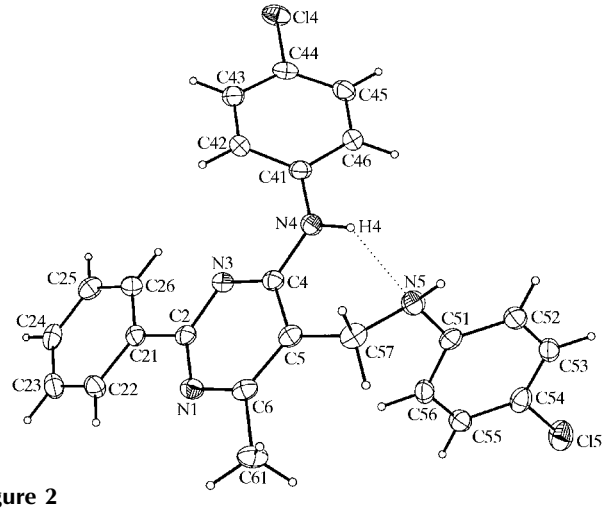


Figure 2
The molecule of polymorph (I*b*), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The dotted line indicates the intramolecular N—H···N hydrogen bond.

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1.360 (3) Å in (I*a*) and 1.329 (3)–1.353 (3) Å in (I*b*) (Table 1), with no significant bond fixation within the pyrimidine ring. In addition, the pyrimidine ring distances are comparable with the corresponding bonds in 4,6-disubstituted 2-aminopyrimidines (Quesada *et al.*, 2004). The phenyl ring is nearly coplanar with the pyrimidine ring: the angle between the least-squares planes through the pyrimidine and phenyl rings is 5.2 (2)° in (I*a*) and 6.4 (2)° in (I*b*). Aromatic atom C41 of the (4-chlorophenyl)amino group is also nearly coplanar with the pyrimidine ring, whereas atom C51 of the (4-chlorophenyl)-aminomethyl group deviates from the pyrimidine ring plane by −1.20 (1) Å in (I*a*) and −2.19 (1) Å in (I*b*). The C5—C57—N5—C51 torsion angle describing the orientation of aromatic atom C51 with respect to pyrimidine atom C5 is 179.8 (2)° in (I*a*) and 80.5 (2)° in (I*b*).

The molecules of (I*a*) are linked by N—H···N hydrogen bonds (Table 2), with amide atom N5 as a donor and ring atom N1 of the molecule at $(x-\frac{1}{2}, y, -z+\frac{1}{2})$ as acceptor in this linkage. Propagation of the hydrogen-bonding $C(7)$ motif generates a chain running along the *a* axis (Fig. 3). Between pyrimidine rings of adjacent molecules within a chain there is also an aromatic π–π stacking interaction, with an interplanar spacing of 3.47 (4) Å, a centroid–centroid separation of 3.71 (3) Å and a centroid offset of 1.31 Å. These chains run through each unit cell, but there is no direction-specific interaction between adjacent chains.

It is interesting to note that the aromatic π–π stacking interactions found in (I*a*) are absent in the structure of (I*b*) and molecules are linked by N—H···Cl hydrogen bonds only (Table 2). Amide atom N5 acts as a hydrogen-bond donor to atom Cl4 in the molecule at $(x, -y+\frac{3}{2}, z+\frac{1}{2})$. This hydrogen-bond motif, which can be described as $C(11)$, generates a chain running along the *c* axis (Fig. 4).

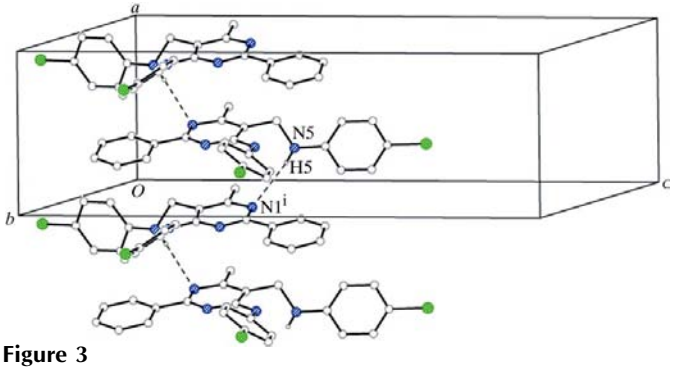

Figure 3
Part of the crystal structure of (I*a*), showing the chain formed *via* N—H···N hydrogen bonds. Dashed lines indicate intermolecular hydrogen bonds. [Symmetry code: (i) $x-\frac{1}{2}, y, -z+\frac{1}{2}$.]

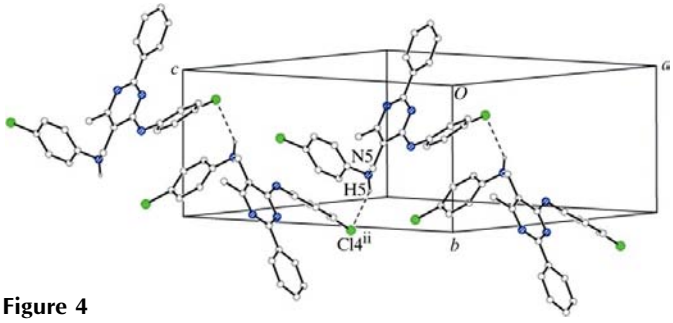

Figure 4
Part of the crystal structure of (I*b*), showing the chain formed *via* N—H···Cl hydrogen bonds. Dashed lines indicate intermolecular hydrogen bonds. [Symmetry code: (ii) $x, -y+\frac{3}{2}, z+\frac{1}{2}$.]

Experimental

Compound (I) was obtained as a yellow oil according to the procedure described previously by Cieplik *et al.* (1995). Colourless crystals of polymorph (I*a*) were grown by slow evaporation of a solution of the oily residue in an acetone–methanol mixture (1:4 *v*/*v*). Pale-yellow crystals of polymorph (I*b*) were obtained *via* recrystallization of (I*a*) from an acetone–methanol mixture (4:1 *v*/*v*).

Polymorph (I*a*)

Crystal data

$C_{24}H_{20}Cl_2N_4$
M_r = 435.34
Orthorhombic, *Pbca*
a = 7.378 (3) Å
b = 23.875 (6) Å
c = 23.984 (6) Å
V = 4225 (2) Å^3
Z = 8
D_x = 1.369 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 12344 reflections
θ = 4.5–27.5°
μ = 0.33 mm^{-1}
T = 100 (2) K
Plate, colourless
0.50 × 0.15 × 0.05 mm

Data collection

Kuma KM-4-CCD diffractometer
ω scans
34892 measured reflections
4829 independent reflections
3240 reflections with $I > 2\sigma(I)$
R_{int} = 0.075
θ_{max} = 27.5°
$h = -7 \rightarrow 9$
$k = -24 \rightarrow 31$
$l = -31 \rightarrow 29$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.075
$wR(F^2)$ = 0.148
S = 1.15
4829 reflections
278 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0597P)^2$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.58 e Å^{-3}
$\Delta\rho_{min}$ = −0.30 e Å^{-3}

Table 1
Comparison of bond lengths and torsion angles (Å, °) for polymorphs (I*a*) and (I*b*).

	(I*a*)	(I*b*)
N1—C2	1.344 (3)	1.337 (2)
C2—N3	1.334 (3)	1.337 (3)
N3—C4	1.329 (3)	1.329 (3)
C4—C5	1.416 (4)	1.421 (3)
C5—C6	1.385 (4)	1.389 (3)
C6—N1	1.360 (3)	1.353 (3)
C4—N4	1.368 (3)	1.377 (3)
N4—C41	1.412 (3)	1.409 (3)
C5—C57	1.506 (4)	1.524 (3)
C57—N5	1.458 (4)	1.468 (3)
N5—C51	1.401 (3)	1.399 (3)
N1—C2—C21—C22	−3.6 (4)	−1.5 (3)
N3—C4—N4—C41	−13.3 (4)	−0.8 (3)
C5—C4—N4—C41	166.9 (3)	179.6 (2)
C4—N4—C41—C42	−29.3 (5)	−39.4 (3)
C4—C5—C57—N5	61.9 (3)	40.5 (3)
C6—C5—C57—N5	−121.7 (3)	−144.4 (2)
C5—C57—N5—C51	179.8 (2)	80.5 (2)
C57—N5—C51—C52	33.1 (4)	−22.9 (3)
C57—N5—C51—C56	−148.8 (3)	159.4 (2)

Polymorph (I*b*)

Crystal data

$C_{24}H_{20}Cl_2N_4$
M_r = 435.34
Monoclinic, $P2_1/c$
a = 15.332 (4) Å
b = 7.993 (2) Å
c = 17.235 (4) Å
β = 104.06 (3)°
V = 2048.9 (9) Å^3
Z = 4
D_x = 1.411 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 16673 reflections
θ = 4.7–28.1°
μ = 0.34 mm^{-1}
T = 100 (2) K
Plate, pale yellow
0.16 × 0.15 × 0.10 mm

Data collection

Kuma KM-4-CCD diffractometer
ω scans
26386 measured reflections
4952 independent reflections
3895 reflections with $I > 2\sigma(I)$
R_{int} = 0.043
θ_{max} = 28.1°
$h = -20 \rightarrow 20$
$k = -8 \rightarrow 10$
$l = -22 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.145
S = 1.12
4952 reflections
278 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0769P)^2 + 0.4721P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.49 e Å^{-3}
$\Delta\rho_{min}$ = −0.30 e Å^{-3}

Table 2
Hydrogen-bonding geometry (Å, °) for polymorphs (I*a*) and (I*b*).

	D—H···A	D—H	H···A	D···A	D—H···A
(I*a*)	N4—H4···N5	0.84 (3)	2.31 (3)	2.940 (3)	132 (3)
	N5—H5···N1^{i}	0.84 (3)	2.54 (3)	3.274 (4)	147 (3)
(I*b*)	N4—H4···N5	0.88 (3)	2.07 (3)	2.786 (3)	138 (2)
	N5—H5···Cl4^{ii}	0.88 (3)	2.60 (3)	3.292 (2)	137 (2)

Symmetry codes: (i) $x - \frac{1}{2}, y, \frac{1}{2} - z$; (ii) $x, -y + \frac{3}{2}, z + \frac{1}{2}$.

The N-bonded H atoms were found in difference Fourier maps and refined with U_{iso}(H) = 1.2U_{eq}(N). The remaining H atoms were treated as riding, with C—H distances in the range 0.95–0.99 Å, and refined with U_{iso}(H) = 1.2U_{eq}(C), or 1.5U_{eq}(C) for methyl H atoms.

For both compounds, data collection: *CrysAlis CCD* (Oxford Diffraction, 2003); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2003); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* (Bruker, 1998); software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ3007). Services for accessing these data are described at the back of the journal.

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