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2-Amino-3-methyl-6-[methyl(phenyl)-amino]-5-nitropyrimidin-4(3*H*)-one: polarized molecules within hydrogen-bonded sheets

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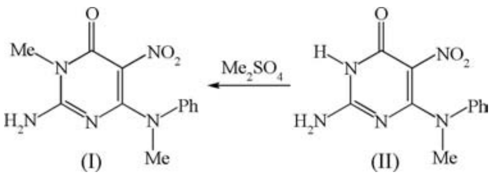
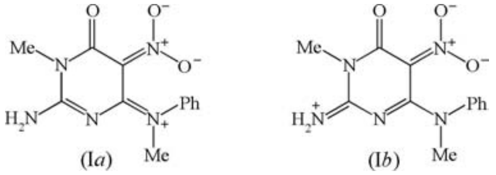
The pyrimidinone ring in the title compound, $C_{12}H_{13}N_5O_3$, is effectively planar, despite the presence of five substituents. The bond distances provide evidence for significant polarization of the electronic structure, with charge separation, and the molecules are linked into sheets by a combination of N—H···O and N—H···π(arene) hydrogen bonds. Comparisons are made with the molecular and supramolecular structures of the precursor compound 2-amino-6-[methyl(phenyl)amino]-5-nitropyrimidin-4(3*H*)-one.

Comment

We report here the structure of the title compound, (I) (Fig. 1), which was prepared by methylation under basic conditions of the precursor (II), whose structure we reported previously (Rodríguez *et al.*, 2007). Compounds (I) and (II) have both been prepared as potential intermediates for the synthesis of benzo-fused pyrimidine derivatives which resemble the well known benzodiazepines, and which have also shown related pharmacological properties, as anti-anxiety or antidepressive agents (Dlugosz & Machon, 1990), and have been regarded as candidates for anti-HIV-1 inhibitors (Di Braccio *et al.*, 2001).



Despite the high degree of substitution of the pyrimidine ring in (I), this ring is effectively planar, with a maximum deviation from the mean plane of only 0.038 (2) Å (for atom C4). Significant distortion from planarity is quite commonly observed in highly substituted pyrimidines (Low *et al.*, 2007; Melguizo *et al.*, 2003; Quesada *et al.*, 2003, 2004; Trilleras *et al.*, 2007, 2009; Cobo *et al.*, 2008). The conformation of the molecular skeleton can be defined in terms of just four torsion angles (Table 1), which show that both the nitro group and the phenyl ring deviate significantly from the plane of the pyrimidine ring; the dihedral angles between the pyrimidine ring and the nitro and phenyl groups are, respectively, 49.8 (2) and 64.0 (2)°. The molecules of (I) thus have no internal symmetry so that, as crystallized, they are conformationally chiral; the centrosymmetric space group accommodates equal numbers of the two conformational enantiomers. The overall conformation of (I) is remarkably similar to that of unmethylated compound (II), where the corresponding values of the key torsion angles, listed in the same order as given in Table 1, are −49.4 (5), 161.7 (4), −6.1 (5) and −51.5 (5)° (Rodríguez *et al.*, 2007).



The bond distances within the substituted pyrimidine part of the molecule show a number of unusual values (Table 1). Firstly, the C4—C5 and C5—C6 bonds, which are formally single and double bonds, respectively, have almost identical lengths. Secondly, the C5—N51 distance is short for its type [mean value (Allen *et al.*, 1987) = 1.468 Å; lower quartile value = 1.460 Å], while the N—O distances are both somewhat long for their type (mean value = 1.210 Å; upper quartile value = 1.218 Å). Thirdly, the four C—N distances between atoms N21 and N61 span a fairly small range, despite one of them being formally a double bond and the rest of them single bonds. These observations taken together indicate that the polarized forms (I*a*) and (I*b*) (see scheme) are both significant contributors to the overall electronic structure, in addition to the localized form (I).

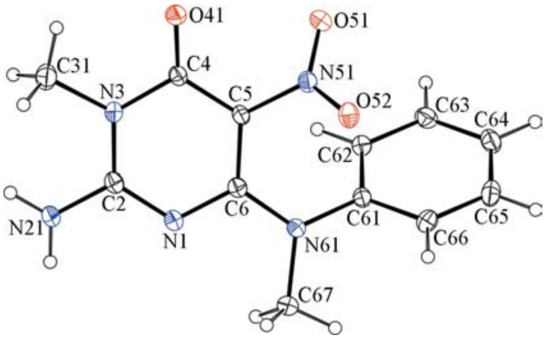


Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

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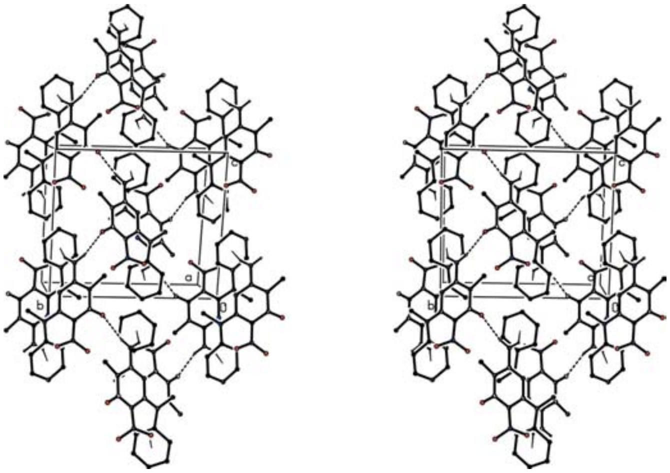

Figure 2
A stereoview of part of the crystal structure of (I), showing the formation of a hydrogen-bonded sheet lying parallel to $(10\overline{1})$. For the sake of clarity, H atoms bonded to C atoms have been omitted.

The molecules of compound (I) are linked into sheets by a combination of one N—H$\cdots\pi$(arene) hydrogen bond and one N—H$\cdots$O hydrogen bond (Table 2). Pairs of molecules related by inversion are linked by the N—H$\cdots\pi$(arene) hydrogen bond to form a centrosymmetric dimer unit and this dimer can conveniently be regarded as the basic building block from which the hydrogen-bonded sheet is constructed. This reference dimer unit, centred at $(0, \frac{1}{2}, \frac{1}{2})$, is directly linked by N—H$\cdots$O hydrogen bonds to four further dimers, *viz.* those centred at $(-\frac{1}{2}, 0, 0)$, $(-\frac{1}{2}, 1, 0)$, $(\frac{1}{2}, 0, 1)$ and $(\frac{1}{2}, 1, 1)$, so that propagation by the space group of the two hydrogen bonds generates a thick sheet lying parallel to $(10\overline{1})$ (Fig. 2). There are no direction-specific interactions between adjacent sheets; in particular, aromatic π–π stacking interactions are absent from the structure of (I).

Despite the close similarities between the conformations of (I) and (II) and thus the overall molecular shapes, these compounds have different crystallization properties. While (I) crystallizes in the centrosymmetric space group $P2_1/n$ with both conformational enantiomers present, (II) crystallizes in the Sohnke space group $P2_12_12_1$ with just a single enantiomer present in each crystal (Rodríguez *et al.*, 2007). Although the molecule of (II) contains three N—H bonds, only two of them are involved in hydrogen-bond formation. The supramolecular aggregation of (II) in fact depends upon two independent three-centre N—H$\cdots$(O)$_2$ systems, which link molecules related by a 2_1 screw axis into a ribbon of edge-fused rings containing rings of $R_2^1(6)$, $R_1^2(6)$ and $R_2^2(6)$ (Bernstein *et al.*, 1995) types. Thus, although the molecule of (II) participates in more N—H bonds than that of (I), the hydrogen-bonded aggregation in (II) is one-dimensional, as opposed to two-dimensional in compound (I).

Experimental

Solid sodium hydroxide (2.85 mmol) was added to a solution of 2-amino-6-(*N*-methylanilino)-5-nitropyrimidin-4(3*H*)-one (2.37 mmol) in dimethylformamide (25 ml). This mixture was heated at 363 K for a period of 1 h and then held at 333 K while one equivalent of dimethyl sulfate was added dropwise, following which the entire mixture was stirred overnight. The reaction mixture was poured on to ice–water (100 ml) and neutralized with 20% aqueous hydrochloric acid. The resulting solution was extracted with ethyl acetate (4 × 20 ml), and the combined organic extracts were dried over anhydrous sodium sulfate. Subsequent removal of the solvent under reduced pressure gave the title compound (yield 97%, m.p. 549–551 K). Crystals suitable for single-crystal X-ray diffraction were grown from a solution in dimethyl sulfoxide.

Crystal data

$C_{12}H_{13}N_5O_3$
$M_r = 275.27$
Monoclinic, $P2_1/n$
$a = 9.158$ (2) Å
$b = 12.178$ (3) Å
$c = 11.103$ (2) Å
$\beta = 105.207$ (18)°
$V = 1194.9$ (5) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.11$ mm^{-1}
$T = 120$ K
0.46 × 0.22 × 0.21 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{\min} = 0.942$, $T_{\max} = 0.976$
29059 measured reflections
2743 independent reflections
1816 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.057$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.050$
$wR(F^2) = 0.154$
$S = 1.08$
2743 reflections
183 parameters
H-atom parameters constrained
$\Delta\rho_{\max} = 0.41$ e Å^{-3}
$\Delta\rho_{\min} = -0.37$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.319 (3)	C2—N21	1.336 (3)
C2—N3	1.353 (3)	C4—O41	1.231 (3)
N3—C4	1.398 (3)	C5—N51	1.431 (3)
C4—C5	1.406 (3)	N51—O51	1.228 (2)
C5—C6	1.395 (3)	N51—O52	1.222 (2)
C6—N1	1.339 (3)	C6—N61	1.356 (3)
C4—C5—N51—O51	−55.4 (3)	N1—C6—N61—C67	−15.6 (3)
N1—C6—N61—C61	151.52 (19)	C6—N61—C61—C62	−46.9 (3)

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

Cg represents the centroid of the C61–C66 ring.

D—H$\cdots$*A*	*D*—H	H$\cdots$*A*	*D*$\cdots$*A*	*D*—H$\cdots$*A*
N21—H21$\cdots$*Cg*$^{\rm i}$	0.88	2.72	3.401 (2)	135
N21—H22$\cdots$O41$^{\rm ii}$	0.88	2.13	2.884 (2)	143

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

All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H distances of 0.95 (aromatic) or 0.98 Å (methyl) and N—H distances of 0.88 Å, and with $U_{\rm iso}({\rm H}) = kU_{\rm eq}$(carrier), where $k = 1.5$ for the methyl groups, which were permitted to rotate but not to tilt, 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: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DN3119). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Burla, M. C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G. L., De Caro, L., Giacovazzo, C., Polidori, G. & Spagna, R. (2005). *J. Appl. Cryst.* **38**, 381–388.

Cobo, J., Trilleras, J., Quiroga, J., Marchal, A., Nogueras, M., Low, J. N. & Glidewell, C. (2008). *Acta Cryst.* B**64**, 596–609.

Di Braccio, M., Grossi, G., Roma, G., Vargiu, L., Mura, M. & Marongiu, M. E. (2001). *Eur. J. Med. Chem.* **36**, 935–949.

Dlugosz, A. & Machon, Z. (1990). *Pharmazie*, **45**, 491–492.

Duisenberg, A. J. M., Hooft, R. W. W., Schreurs, A. M. M. & Kroon, J. (2000). *J. Appl. Cryst.* **33**, 893–898.

Duisenberg, A. J. M., Kroon-Batenburg, L. M. J. & Schreurs, A. M. M. (2003). *J. Appl. Cryst.* **36**, 220–229.

Hooft, R. W. W. (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.

Low, J. N., Trilleras, J., Cobo, J., Marchal, A. & Glidewell, C. (2007). *Acta Cryst.* C**63**, o681–o684.

Melguizo, M., Quesada, A., Low, J. N. & Glidewell, C. (2003). *Acta Cryst.* B**59**, 263–276.

Quesada, A., Marchal, A., Low, J. N. & Glidewell, C. (2003). *Acta Cryst.* C**59**, o102–o104.

Quesada, A., Marchal, A., Melguizo, M., Low, J. N. & Glidewell, C. (2004). *Acta Cryst.* B**60**, 76–89.

Rodríguez, R., Cobo, J., Nogueras, M., Low, J. N. & Glidewell, C. (2007). *Acta Cryst.* C**63**, o697–o700.

Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.

Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.

Trilleras, J., Quiroga, J., Cobo, J. & Glidewell, C. (2009). *Acta Cryst.* C**65**, o11–o14.

Trilleras, J., Quiroga, J., Low, J. N., Cobo, J. & Glidewell, C. (2007). *Acta Cryst.* C**63**, o758–o760.