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5-Methyl-1,2,4-triazolo[1,5-*a*]pyrimidine-6-carbonitrile

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.004 Å
R factor = 0.053
wR factor = 0.147
Data-to-parameter ratio = 14.6

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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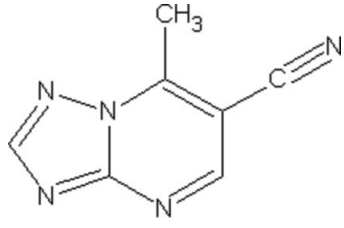
The title compound, $C_7H_5N_5$, was designed and synthesized as a potential antitumour agent. The molecules are located on crystallographic mirror planes. The electron-accepting 6-cyano group has no effect on the π-electron cloud of the heterocyclic system. The molecular packing is governed by C—H···N intermolecular hydrogen bonds, which link the molecules into chains running along the *c* axis.

Comment

1,2,4-Triazolo[1,5-*a*]pyrimidines have long been known to possess a variety of biological properties (Ram, 1988), antitumour activity being one of the most important. The molecular mechanism of the cytotoxic action of such planar heterocyclic molecules typically lies in an intercalative interaction with adjacent base pairs of nuclear DNA. Extension of the planarity of the molecule by the addition of π-electron-containing substituents coplanar with the heterocyclic system usually results in potentiation of this activity. Thus, we were prompted to prepare a series of derivatives having substituents with a +*M* or –*M* effect bonded to the pyrimidine ring of the heterocyclic system. As the electrostatic energy is known to be the dominant contributor to the overall intercalative binding energy, we were interested in the determination and comparison of both the molecular and electronic structures of the respective derivatives using theoretical and experimental methods. In this communication, we report the crystal structure of the title 5-methyl-6-cyano derivative, (I).



(I)

The molecular structure and atom-numbering scheme for (I) are shown in Fig. 1. The molecules lie on crystallographic mirror planes (at $y = \frac{1}{4}$ and $\frac{3}{4}$); thus they are exactly planar, as required by symmetry. As noted above, the main interest in such planar DNA-intercalating molecules is to obtain precise structural data and electron-density distribution, indispensable for subsequent modelling of the drug–DNA interaction and computation of the intercalative binding energy. As revealed by a search of the Cambridge Structural Database (CSD; Allen, 2002), the π-electron distribution within the [1,2,4]triazolo[1,5-*a*]pyrimidine substructure is almost insen-

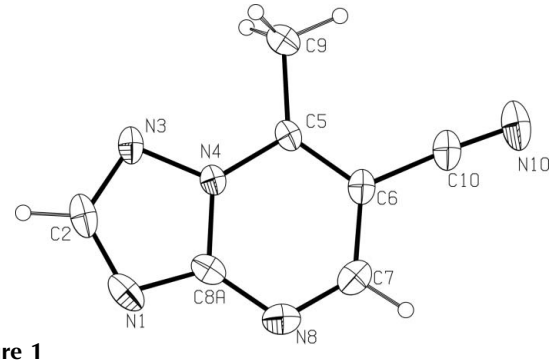


Figure 1
A displacement ellipsoid plot, at the 35% probability level, of (I), with the atom-labelling scheme. H atoms are drawn as small circles of arbitrary size.

sitive to the electron-releasing or -accepting nature of the subsituents; this is also seen in the present derivative, (I), for which the bond lengths within the ring system (Table 1) differ to within 6σ, as compared with some 23 other derivatives found in the search of the CSD.

The crystal packing of (I) is controlled by two hydrogen bonds, C2—H2···N10^{i} and C7—H7···N3^{ii} (symmetry codes are given in Table 2), which link the molecules into chains running parallel to the *c* axis. On the other hand, despite the planarity of the molecules, it seems that no significant π–π stacking interactions are observed. The stacking shows only a partial overlap of the five-membered rings: the centroid···centroid distance for the stacked five-membered rings is 3.6806 (15) Å, while that for the six-membered rings is 4.2894 (18) Å; the five- and six-membered rings are at $(1-x, \frac{1}{2}+y, 1-z)$ and $(-x, \frac{1}{2}+y, 1-z)$, respectively.

Experimental

The synthesis of (I) has been described in detail elsewhere (Černuchová *et al.*, 2005). In short, a solution of (*E*)-2-ethoxymethylene-3-oxabutanenitrile (1 g, 7.2 mmol) and 3-amino-1,2,4-triazole (0.60 g, 7.2 mmol) in toluene (15 ml) was refluxed for 30 min. After cooling the reaction mixture, the precipitate which formed was filtered off and recrystallized from toluene to afford (I) as orange crystals (78% yield; m.p. 418–419 K).

Crystal data

$C_7H_5N_5$
M_r = 159.16
Monoclinic, $P2_1/m$
a = 7.105 (2) Å
b = 6.413 (2) Å
c = 8.190 (3) Å
β = 96.82 (3)°
V = 370.5 (2) Å^3
Z = 2
D_x = 1.427 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 20 reflections
θ = 7–20°
μ = 0.10 mm^{-1}
T = 296 (2) K
Prism, orange
0.30 × 0.20 × 0.15 mm

Data collection

Siemens *P*4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
1628 measured reflections
1165 independent reflections
723 reflections with $I > 2\sigma(I)$
R_{int} = 0.040
θ_{max} = 30.0°
$h = -1 \rightarrow 9$
$k = -1 \rightarrow 9$
$l = -11 \rightarrow 11$
3 standard reflections
every 97 reflections
intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.053
$wR(F^2)$ = 0.147
S = 1.03
1165 reflections
80 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0688P)^2 + 0.0536P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C8*A*	1.321 (3)	C5—C9	1.482 (3)
N1—C2	1.350 (4)	C6—C7	1.414 (3)
C2—N3	1.323 (3)	C6—C10	1.437 (3)
N3—N4	1.368 (3)	C7—N8	1.306 (3)
N4—C5	1.360 (3)	N8—C8*A*	1.354 (3)
N4—C8*A*	1.390 (3)	C10—N10	1.136 (3)
C5—C6	1.372 (3)		
C8*A*—N1—C2	102.7 (2)	N3—N4—C8*A*	109.65 (18)
N3—C2—N1	117.5 (2)	N1—C8*A*—N8	129.6 (2)
C2—N3—N4	100.9 (2)	N1—C8*A*—N4	109.2 (2)
C5—N4—N3	126.10 (18)	N8—C8*A*—N4	121.2 (2)
C5—N4—C8*A*	124.25 (19)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2···N10^{i}	0.93	2.47	3.366 (4)	161
C7—H7···N3^{ii}	0.93	2.42	3.265 (4)	151

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

Methyl H atoms were located in a difference Fourier map and refined isotropically. Atoms H2 and H7 were refined with fixed geometry (C—H = 0.93 Å), riding on their parent atoms, with $U_{iso}(H) = 1.2U_{eq}(C)$.

Data collection: *XSCANS* (Siemens, 1991); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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