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1-(4-Chlorophenyl)-2-methyl-4-nitro-5-(1-piperidyl)-1*H*-imidazole

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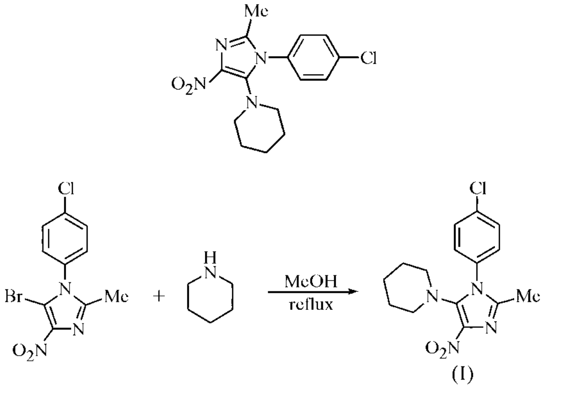
The only specific interactions that influence the crystal packing of the title compound, $C_{15}H_{17}ClN_4O_2$, are weak C—H···N and C—H···Cl hydrogen bonds, even though there is a possibility of, for example, π–π stacking or halogen bonding. The dihedral angle between the mean planes of the imidazole and benzene rings is 59.82 (5)°. The length of the C—N bond connecting the imidazole and piperidine fragments is correlated with the degree of pyramidalization of the piperidine N atom.

Comment

Nitroimidazoles have been intensively investigated as radiosensitizers of hypoxic tumour cells and as veterinary drugs (Smithen & Hardy, 1982). In particular, 4-nitro-5-amino-imidazole derivatives have been relatively widely studied, due to their expected radiosensitizing activity combined with good water solubility (see, for example, Wolska *et al.*, 1993, 1994). More recently, in the crystal structure of 1,2-dimethyl-5-morpholino-4-nitroimidazole hydrate, the interesting case of



centrosymmetric–non-centrosymmetric ambiguity was found (Kubicki *et al.*, 2003). Moreover, a number of simple 4-nitro-imidazole derivatives have been used for studying different intermolecular interactions (see, for example, Kubicki, 2005, and references therein). The structure of another 5-amino-4-nitroimidazole, the title compound, (I), is reported here. The ability of 4-nitroimidazoles to undergo nucleophilic substitution has been widely investigated (see, for example, Mąkosza, 1992) and provides a convenient way of modifying azole derivatives. Some amino derivatives have also been synthesized in this way (Mąkosza & Białecki, 1998; Suwiński & Świerczek, 1996).

Fig. 1 shows a displacement ellipsoid representation of (I). The benzene and imidazole rings are almost perfectly planar,

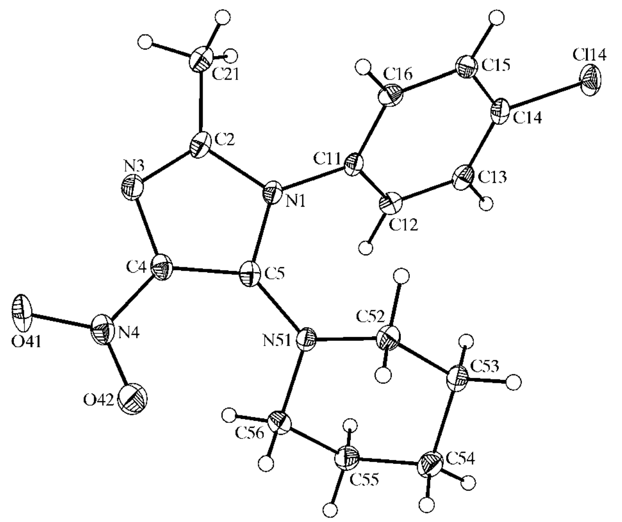


Figure 1
A view of the molecule of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

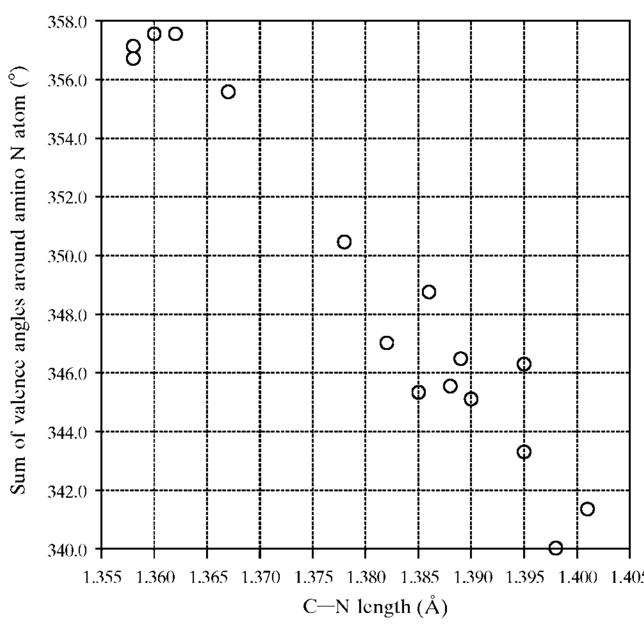


Figure 2
The correlation between the C—N bond length and the sum of the valence angles around the amino N atom for 5-(cyclic)aminoimidazoles.

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the maximum deviations from the least-squares planes being not larger than 0.015 (1) Å. The dihedral angle between the mean planes of these rings is 59.82 (5)°. The nitro group is also significantly twisted out of the imidazole plane, the dihedral angle between the appropriate planes being 14.7 (2)°. This value is larger than in similar compounds and is probably caused by the presence of the bulky substituent at position 5. The C—N—O angles are asymmetric, and this asymmetry is typical of 5-substituted 4-nitroimidazole derivatives (Kubicki, 2004*a*). The C4—N4—O41 angle (*cis* with respect to imidazole ring atom N3) is smaller than the angle *trans* to N3 (C4—N4—O42) by 1.1°. For 5-H derivatives, this asymmetry in C—N—O angles is also observed, but in reverse, *i.e.* the *cis* angle is larger than the *trans* one (Kubicki, 2004*b*).

The molecular geometry of (I) is quite typical. In this type of compound, there is an interesting correlation between the C5—N51 bond length and the sum of the bond angles around N51: the longer the bond, the larger the pyramidalization of the N atom, *i.e.* the smaller the sum of the bond angles. For 16 fragments of 5-(cyclic)aminoimidazoles found in the Cambridge Structural Database (CSD; November 2004 version, February 2005 updates; Allen, 2002), the correlation coefficient is 0.98 (Fig. 2), and the data for (I) fit perfectly into this relation. It might also be noted that there is no such correlation between the C5—N51 bond length and the angles around atom C5.

The piperidine ring is in a chair conformation. The asymmetry parameters (Duax & Norton, 1975) show only minor distortions from ideal C_{3d} symmetry (the maximum value of the ΔC_2 parameter is 3.83°, and of ΔC_s is −3.15°).

In the crystal structure of (I), there are infinite chains of molecules extending along the [100] direction, created by C—H···N3 hydrogen bonds. Using graph-set notation (Etter *et al.*, 1990; Bernstein *et al.*, 1995), this motif can be described as a *C*(7) chain. Neighbouring chains are connected by weak three-centred C—H···Cl hydrogen bonds {$C(12)[R_2^1(5)]$ chains along the [001] direction}. These two kinds of weak interactions close larger rings of molecules of motif $R_4^4(30)$ (Fig. 3). The geometric details of these interactions are given in Table 2. Interestingly, in this case no other specific interatomic interactions (*e.g.* π–π stacking or halogen bonds) take part in the creation of the supramolecular structure, even though these interactions could compete succesfully with weak hydrogen bonding.

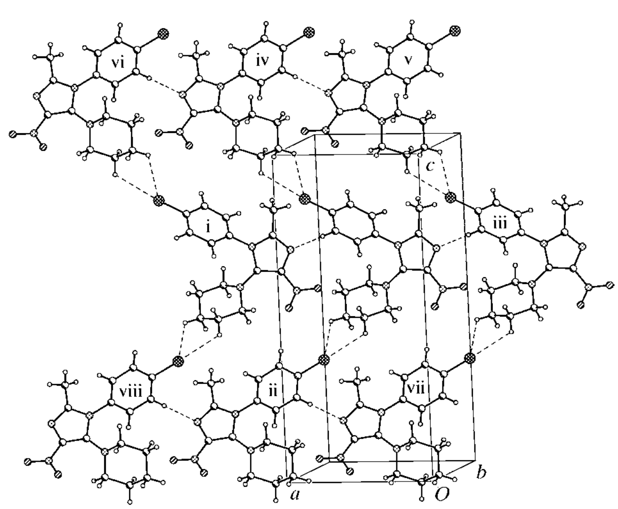

Figure 3
The crystal packing of (I), viewed approximately along the [010] direction. Hydrogen bonds are depicted as dashed lines. [Symmetry codes: (iii) $-1 + x, y, z$; (iv) $\frac{3}{2} - x, -y, \frac{1}{2} + z$; (v) $\frac{3}{2} - x, -y, \frac{1}{2} + z$; (vi) $\frac{5}{2} - x, -y, \frac{1}{2} + z$; (vii) $\frac{1}{2} - x, -y, -\frac{1}{2} + z$; (viii) $\frac{5}{2} - x, -y, -\frac{1}{2} + z$; for other symmetry codes, see Table 2.]

Experimental

The title compound was synthesized by nucleophilic replacement of bromine at the 5-position of the imidazole ring by piperidine (see scheme). The reaction was carried out in boiling methanol with an excess of piperidine over 24 h with a high yield. In contrast with the reactivity of the 1-alkyl derivative, in which double substitution of the bromo and nitro groups was observed (Kulkarni *et al.*, 1987), the arene substituent significantly decreases the reactivity of the imidazole moiety. Crystals of (I) suitable for X-ray data collection were grown from a methanol solution.

Crystal data

$C_{15}H_{17}ClN_4O_2$
$M_r = 320.78$
Orthorhombic, $P2_12_12_1$
$a = 8.5841$ (12) Å
$b = 9.0352$ (12) Å
$c = 18.738$ (2) Å
$V = 1453.3$ (3) Å^3
$Z = 4$
$D_x = 1.466$ Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 2320 reflections
$\theta = 3$–20°
$\mu = 0.28$ mm^{-1}
$T = 90$ (1) K
Needle, colourless
0.4 × 0.15 × 0.1 mm

Data collection

Kuma KM-4 CCD four-circle diffractometer
ω scans
Absorption correction: multi-scan (SORTAV; Blessing, 1989)
$T_{min} = 0.958$, $T_{max} = 0.972$
15516 measured reflections
4072 independent reflections
3298 reflections with $I > 2\sigma(I)$
$R_{int} = 0.027$
$\theta_{max} = 30.0°$
$h = -12 \rightarrow 12$
$k = -12 \rightarrow 12$
$l = -25 \rightarrow 23$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.031$
$wR(F^2) = 0.054$
$S = 0.93$
4069 reflections
257 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.021P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.008$
$\Delta\rho_{max} = 0.25$ e Å^{-3}
$\Delta\rho_{min} = -0.22$ e Å^{-3}
Absolute structure: Flack (1983), with 1654 Friedel pairs
Flack parameter: −0.03 (4)

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.383 (2)	N3—C4	1.376 (2)
N1—C5	1.391 (2)	N4—O42	1.234 (2)
N1—C11	1.438 (2)	N4—O41	1.239 (2)
C2—N3	1.301 (2)	C5—N51	1.361 (2)
C2—N1—C5	108.1 (1)	O42—N4—C4	118.9 (1)
C2—N1—C11	124.7 (1)	O41—N4—C4	117.8 (1)
C5—N1—C11	127.1 (1)	C5—N51—C56	120.7 (1)
C2—N3—C4	105.0 (1)	C5—N51—C52	121.2 (1)
O42—N4—O41	123.2 (1)	C56—N51—C52	114.9 (1)

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

D—H···A	D—H	H···A	D···A	D—H···A
C13—H13···N3^{i}	0.97 (2)	2.45 (2)	3.424 (2)	180 (1)
C54—H54B···Cl14^{ii}	0.98 (2)	3.06 (2)	3.705 (2)	125 (1)
C55—H55B···Cl14^{ii}	0.97 (2)	2.95 (1)	3.564 (2)	122 (1)

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

The positions of the H atoms were freely refined [C—H = 0.93 (2)–1.02 (2) Å. For each group of these atoms, *i.e.* for the methyl group, for each CH_2 group and for ring H atoms, one common U_{iso}(H) parameter was refined.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2002); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *Stereochemical Workstation Operation Manual* (Siemens, 1989); software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: TA1498). Services for accessing these data are described at the back of the journal.

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