2005

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

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Publication Details

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Abstract
The only specific interactions that influence the crystal packing of the title compound, C15H17ClN4O2, are weak C-H...N and C-H...Cl hydrogen bonds, even though there is a possibility of, for example, pi-pi stacking or halogen bonding. The dihedral angle between the mean planes of the imidazole and benzene rings is 59.82 (5) degrees. 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.

Keywords
methyl, 5, piperidyl, 1h, 2, 1, chlorophenyl, 4, nitro, imidazole

Disciplines
Engineering | Physical Sciences and Mathematics

Publication Details

This journal article is available at Research Online: http://ro.uow.edu.au/aiimpapers/1052
The only specific interactions that influence the crystal packing of the title compound, C₁₅H₁₇ClN₄O₂, 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-aminoimidazole 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-nitroimidazole 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; Suwnicki & Świerczek, 1996).

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

![Figure 1](image1.jpg)

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](image2.jpg)

The correlation between the C—N bond length and the sum of the valence angles around the amino N atom for 5-(cyclic)aminoimidazoles.
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
calculated 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,
2004a). The C—N—O 41 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, 2004b).

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 smaller the pyramidalization of
the N atom.

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)[R2(5)]
chains along the [001] direction}. These two kinds of weak
interactions close larger rings of molecules of motif R2(30)
(Fig. 3). The geometric details of these interactions are given
in Table 2. Interestingly, in this case no other specific inter-
atomic interactions (e.g. π—π stacking or halogen bonds) take
part in the formation of the supramolecular structure, even
though these interactions could compete successfully with
weak hydrogen bonding.

### 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 imida-
zo-moiety. Crystals of (I) suitable for X-ray data collection were
grown from a methanol solution.

#### Crystal data

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C15H17ClN4O2</td>
<td></td>
</tr>
<tr>
<td>M_r</td>
<td>320.78</td>
</tr>
<tr>
<td>Orthorhombic</td>
<td>P2_12_1</td>
</tr>
<tr>
<td>a</td>
<td>8.5841 (12) Å</td>
</tr>
<tr>
<td>b</td>
<td>9.0352 (12) Å</td>
</tr>
<tr>
<td>c</td>
<td>18.738 (2) Å</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>D_2</td>
<td>1.466 Mg m^-3</td>
</tr>
</tbody>
</table>

#### Data collection

- Kuma KM-4 CCD four-circle diffractometer
- Mo Kα radiation
- Cell parameters from 2320 reflections
- 4072 independent reflections
- 257 parameters
- R(int) = 0.027
- F(000) = 1453.3 (3) Å^3
- θmin = 3°–20°
- μ = 0.20 mm^-1
- T = 193 (1) K
- Needle, colourless
- 0.4×0.15×0.1 mm

#### Refinement

- R[F^2 > 2σ(F^2)] = 0.031
- wR(F^2) = 0.054
- S = 0.93
- 4096 reflections
- 257 parameters
- All H-atom parameters refined

#### Table 1

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length (Å)</th>
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<tr>
<td>C1—N1</td>
<td>1.438 (2)</td>
</tr>
<tr>
<td>C1—C11</td>
<td>1.391 (2)</td>
</tr>
<tr>
<td>C1—C2</td>
<td>1.427 (2)</td>
</tr>
<tr>
<td>C2—N3</td>
<td>1.301 (2)</td>
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<tr>
<td>C2—N1</td>
<td>1.383 (2)</td>
</tr>
<tr>
<td>C2—N51</td>
<td>1.376 (2)</td>
</tr>
<tr>
<td>C2—N4</td>
<td>1.383 (2)</td>
</tr>
<tr>
<td>C2—N41</td>
<td>1.383 (2)</td>
</tr>
<tr>
<td>C2—N51</td>
<td>1.361 (2)</td>
</tr>
</tbody>
</table>

#### Table 2

<table>
<thead>
<tr>
<th>Symmetry codes</th>
<th>Geometric parameters (Å, °)</th>
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<tr>
<td></td>
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<tr>
<td></td>
<td>1.383 (2)</td>
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<tr>
<td></td>
<td>N1—C5</td>
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<tr>
<td></td>
<td>1.391 (2)</td>
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<tr>
<td></td>
<td>N1—C11</td>
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<tr>
<td></td>
<td>1.438 (2)</td>
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<td>C2—N3</td>
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<td></td>
<td>1.301 (2)</td>
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<tr>
<td></td>
<td>C2—N1</td>
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<td>1.081 (1)</td>
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<td></td>
<td>C2—N51</td>
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<td></td>
<td>1.383 (2)</td>
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<td>C2—N4</td>
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<tr>
<td></td>
<td>C2—N51</td>
</tr>
<tr>
<td></td>
<td>1.361 (2)</td>
</tr>
</tbody>
</table>

Figure 3

The crystal packing of (I), viewed approximately along the [010]
direction. Hydrogen bonds are depicted as dashed lines. [Symmetry
codes: (iii) x, y, z; (iv) y + x, y, z; (iiii) z; (vi) y + x, y, z; (vii) 2x, y, z; (viii) z; (viii) x, 2y, z; z; for other
symmetry codes, see Table 2.]
The positions of the H atoms were freely refined \( |C - H| = 0.93 (2) - 1.02 (2) \AA. For each group of these atoms, i.e. for the methyl group, for each \( \text{CH}_2 \) 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.

### Table 2
Hydrogen-bond geometry (\( \AA, ^\circ \)).

<table>
<thead>
<tr>
<th></th>
<th>( D-H \cdot -A )</th>
<th>( D-H )</th>
<th>( H \cdot -A )</th>
<th>( D \cdot -A )</th>
<th>( D-H \cdot -A )</th>
</tr>
</thead>
<tbody>
<tr>
<td>C13-H13-N3i</td>
<td>0.97 (2)</td>
<td>2.45 (2)</td>
<td>3.424 (2)</td>
<td>180 (1)</td>
<td></td>
</tr>
<tr>
<td>C54-H54Cl14ii</td>
<td>0.98 (2)</td>
<td>3.06 (2)</td>
<td>3.705 (2)</td>
<td>125 (1)</td>
<td></td>
</tr>
<tr>
<td>C55-H55Cl14ii</td>
<td>0.97 (2)</td>
<td>2.95 (1)</td>
<td>3.564 (2)</td>
<td>122 (1)</td>
<td></td>
</tr>
</tbody>
</table>

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

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