Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

1-Amino-6-chloro-2-(1*H*-pyrrol-2-yl)benzimidazole (RS 1350)

Augusto Pifferi,[a] Mercedes Camalli,[a]* Romano Silvestri,[b] Gabriella De Martino,[b] Silvio Massa[c] and Marino Artico[b]

[a]Istituto di Strutturistica Chimica-CNR, PO Box 10 I-00016 Monterotondo Stazione, Roma, Italy, [b]Istituto Pasteur-Fondazione Cenci Bolognetti, Dipartimento di Studi Farmaceutici, Universitá di Roma 'La Sapienza', Box 36 Roma 62,P.le Aldo Moro 5,I-00185, Roma, Italy, and [c]Dipartimento Farmaco Chimico Tecnologico, Universitá di Siena, Via Aldo Moro, I-53100, Siena, Italy

Correspondence e-mail: mercedes.camalli@mlib.cnr.it

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.006 Å
R factor = 0.042
wR factor = 0.070
Data-to-parameter ratio = 8.2

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

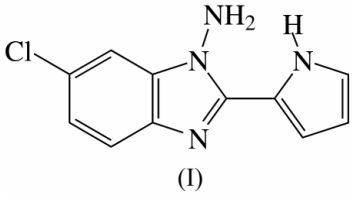
Received 4 June 2001
Accepted 28 June 2001
Online 10 August 2001

The title compound (RS 1350), $C_{11}H_9ClN_4$, was recently synthesized by a Smiles rearrangement of 1-[(5-chloro-2-nitrophenyl)sulfonyl]-1*H*-pyrrole-2-carbohydrazide or 1-(5-chloro-2-nitrophenyl)-1*H*-pyrrole-2-carbohydrazide in powdered iron–glacial acetic acid medium. From the crystallographic analysis, it is observed that, in the title compound, the benzimidazole moiety is planar and forms a dihedral angle of 3.8 (2)° with the pyrrole ring. The near planarity of the two rings indicates an extended conjugation.

Comment

HIV-1 reverse transcriptase (RT), the enzyme which catalyses the transcription of viral single-stranded RNA into double-stranded DNA, is the most investigated target in searching for anti-AIDS drugs. In the last decade, many RT inhibitors were synthesized and some were selected as lead compounds for clinical trials (Artico, 1996; Pedersen & Pedersen, 1999). Two classes of RT inhibitors were identified (Vandamme *et al.*, 1998). The nucleoside analogues (NRTIs) act as competitive inhibitors or DNA chain terminator. The non-nucleoside analogues (NNRTIs) are allosteric inhibitors of the RT enzyme which bind to a hydrophobic pocket in the enzyme–DNA complex close to the active site (Spence *et al.*, 1995; Vandamme *et al.*, 1998; De Clercq, 1998). Despite their different structures, NNRTIs adopt a common 'butterfly-like' active conformation, having two π-electron-donor regions between a lipophilic site (Schaefer *et al.*, 1993). The major problem related to NNRTIs concerns the rapid development of mutations in the RT, with failure of therapy. The synthesis of NNRTIs active on a wide panel of viral resistant mutants useful in anti-AIDS drug combination strategies is a current goal. Our engagement in the field of anti-AIDS chemotherapy (Silvestri *et al.*, 1994, 1995, 1997, 1998; Silvestri, Artico *et al.*, 2000; Silvestri, Pifferi *et al.*, 2000; Artico *et al.*, 1994, 1995, 2000; Artico, Silvestri, Massa *et al.*, 1996; Artico, Silvestri, Pagnozzi, Stefancich, Massa & La Colla, 1996; Ettorre *et al.*, 2001) led to the discovery of the pyrrolo[1,2-*b*][1,2,5]benzothiadiazepin-10(11*H*)ones (PBTDs), a novel class of NNRTIs endowed with anti-HIV-1 RT activity comparable with that of nevirapine (Artico, Silvestri, Pagnozzi, Stefancich, Massa, Loi *et al.*, 1996). Pursuing our research on novel PBTDs active toward resistant mutants, we planned the synthesis of 7-chloro-11-hydrazinopyrrolo[1,2-*b*][1,2,5]benzothiadiazepin-10(11*H*)one 5,5-dioxide, (IV), by iron powder–acetic acid reduction of 1-[(5-chloro-2-nitrophenyl)sulfonyl]-1*H*-pyrrole-2-carbohydrazide, (II) (Silvestri, Pifferi *et al.*, 2000). Unexpectedly instead of (IV), the reaction furnished 1-amino-6-chloro-2-(1*H*-pyrrol-2-yl)benzimidazole, (I), as the sole product. We supposed that (II) underwent Smiles rearrangement to give

(I). In fact, 1-[(5-chloro-2-nitrophenyl)sulfonyl]-1*H*-pyrrole-2-carbohydrazide, (II), possesses the structural features required to achieve Smiles rearrangement, *i.e.* (i) a strongly electron-withdrawing *ortho*-nitro group activating the aromatic ring; (ii) the sulfonyl group as a good leaving group; (iii) the nucleophilicity; (iv) the acidity of the $CONHNH_2$ entering group (Truce *et al.*, 1971).



(I)

We decided to confirm unambiguously the structure of (I) by crystallographic analysis. The benzimidazole moiety is planar, with Cl1 and N2 deviating from it by −0.030 (2) and 0.038 (3) Å, respectively. The angle between the planar benzimidazole moiety and the pyrrole ring is 3.8 (2)°. No unusual features were found in the geometry of the rings. The near planarity of the benzimidazole and the pyrrole rings indicate extended conjugation. The NH_2 group adopts a pyramidal configuration.

Experimental

The title compound was synthesized according to Silvestri, Pifferi *et al.* (2000).

Crystal data

$C_{11}H_9ClN_4$
M_r = 232.67
Orthorhombic, *Pbca*
a = 10.065 (2) Å
b = 23.178 (4) Å
c = 9.077 (3) Å
V = 2117.5 (9) Å^3
Z = 8
D_x = 1.460 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 32 reflections
θ = 2.9–16.0°
μ = 0.34 mm^{-1}
T = 293 K
Prism, brown
0.30 × 0.20 × 0.15 mm

Data collection

Siemens *P*3 automatic four circle diffractometer
$\theta/2\theta$ scans
5213 measured reflections
4669 independent reflections
1194 reflections with $F > 3\sigma(F)$
R_{int} = 0.063
θ_{max} = 35.1°
$h = 0 \rightarrow 16$
$k = 0 \rightarrow 37$
$l = 0 \rightarrow 14$
3 standard reflections
every 97 reflections
intensity decay: none

Refinement

Refinement on F
R = 0.042
wR = 0.070
S = 0.97
1194 reflections
145 parameters
H-atom parameters constrained
$w = 1/(0.2+F+0.0792F^2)$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

The crystal diffracted quite weakly at room temperature which reduced the number of reflections with significant intensities. The positions of the H atoms were calculated geometrically at a distance of 0.96 Å from the corresponding C or N atom, and a riding model was used during their refinement.

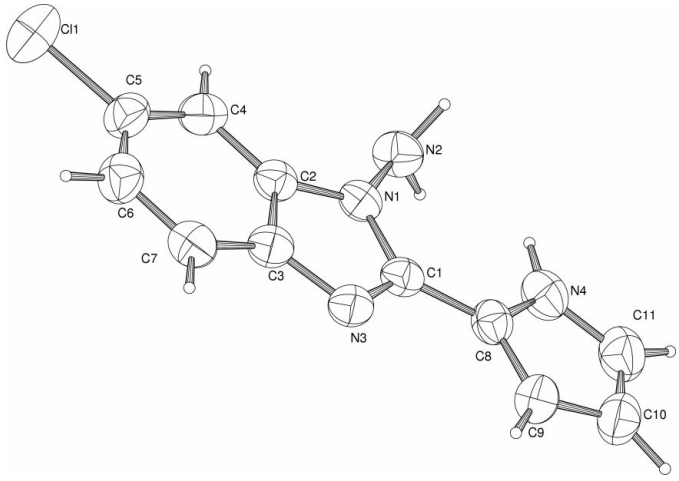


Figure 1
The molecular structure of (I). Displacement ellipsoids are shown at the 50% probability level.

Data collection: *R*3*m*/*V* (Siemens, 1989); cell refinement: *R*3*m*/*V*; data reduction: *XDISK* (Siemens, 1989); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *CAOS* (Camalli & Spagna, 1994); molecular graphics: *CAOS*; software used to prepare material for publication: *CAOS*.

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