Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

6-Chloro-1-(3,5-dimethylphenylsulfonyl)-1*H*-benzimidazol-2(3*H*)-one

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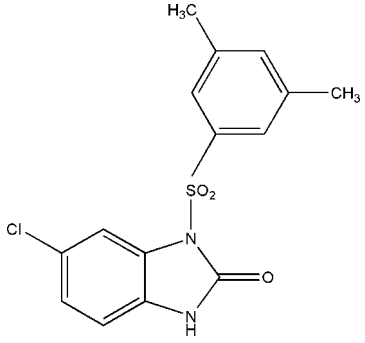
Received 28 November 2008; accepted 15 December 2008

Key indicators: single-crystal X-ray study; T = 293 K; mean σ(C–C) = 0.005 Å; R factor = 0.057; wR factor = 0.133; data-to-parameter ratio = 18.3.

The title compound, $C_{15}H_{13}ClN_2O_3S$, is one of a series of N^1-benzyl-1,3-dihydro-2*H*-benzimidazol-2-one derivatives, a new class of non-nucleoside HIV-1 reverse transcriptase inhibitors. The dihedral angle between the two pharmacophoric groups, the dimethylbenzene ring and the benzimidazolone ring system, is 88 (1)°, giving a butterfly-like conformation to the molecule. The molecular packing is characterized by a bifurcated N—H···(O,O) hydrogen bond and short Cl···O contacts of 3.122 (2) Å. In addition, π–π stacking of the benzimidazolone rings is also present, with interplanar separations of 3.95 (1) Å.

Related literature

For the role of the substituents on the benzene nucleus in anti-HIV-1 compounds, see: Barreca *et al.* (2007). For related literature, see: Barreca *et al.* (2005); Beddoes *et al.* (1986); Liu *et al.* (2007).



Experimental

Crystal data

$C_{15}H_{13}ClN_2O_3S$
M_r = 336.78
Monoclinic, $P2_1/c$
a = 12.173 (3) Å
b = 14.036 (3) Å
c = 8.949 (2) Å
β = 95.77 (2)°
V = 1521.3 (6) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.40 mm^{-1}
T = 293 (2) K
0.5 × 0.4 × 0.3 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Absorption correction: none
3964 measured reflections
3634 independent reflections
3214 reflections with $I > 2\sigma(I)$
R_{int} = 0.014
3 standard reflections
frequency: 120 min
intensity decay: 1%

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.133
S = 1.19
3634 reflections
199 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2···O1^{i}	0.86	2.18	2.852 (3)	135
N2—H2···O2^{i}	0.86	2.39	3.075 (3)	138

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

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *XCAD4* (Harms & Wocadlo, 1995); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: FJ2178).

References

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.
Barreca, L. M., Rao, A., De Luca, L., Iraci, N., Monforte, A. M., Maga, G., De Clercq, E., Pannecouque, C., Balzarini, J. & Chimirri, A. (2007). *Bioorg. Med. Chem. Lett.* **17**, 1956–1960.
Barreca, L. M., Rao, A., De Luca, L., Zappala, M., Monforte, A. M., Maga, G., Pannecouque, C., De Clercq, E., Balzarini, J., Chimirri, A. & Monforte, P. (2005). *J. Med. Chem.* **48**, 3433–3437.
Beddoes, R. L., Dalton, L., Joule, J. A., Mills, O. S., Street, J. D. & Watt, C. I. F. (1986). *J. Chem. Soc. Perkin Trans. 2*, pp. 787–797.
Enraf–Nonius (1989). *CAD-4 Software*. Enraf–Nonius, Delft, The Netherlands.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Harms, K. & Wocadlo, S. (1995). *XCAD4*. University of Marburg, Germany.
Liu, Y., Gribble, G. W. & Jasinski, J. P. (2007). *Acta Cryst.* E**63**, o735–o737.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

supplementary materials

Acta Cryst. (2009). E**65**, o159 [**doi:10.1107/S1600536808042694**]

6-Chloro-1-(3,5-dimethylphenylsulfonyl)-1*H*-benzimidazol-2(3*H*)-one

F. Meneghetti, G. Bombieri, P. Logoteta and L. De Luca

Comment

In the course of previous studies on new anti-HIV agents, some of us reported the synthesis and anti-HIV activity of a series of N1-benzyl-1,3-dihydro-2*H*-benzimidazol-2-ones, a new class of non-nucleoside HIV-1 reverse transcriptase inhibitors (NNRTIs) (Barreca *et al.* 2005). More recently molecular modeling studies led to the discovery of N1-phenylsulfonyl-1,3-dihydro-2*H*-benzimidazol-2-ones as highly potent NNRTIs active at nanomolar concentration (Barreca *et al.* 2007). In this paper we report the results of the X-ray structure determination of 6-chloro-1-(3,5-dimethylphenylsulfonyl)-1,3-dihydro-2*H*-benzimidazol-2-one (I) the most potent derivative of the series, active against wild-type and mutant HIV-1 strains (Barreca *et al.*, 2007). On this respect, its geometrical features defined by X-ray analysis (Fig. 1), could be an useful tool to understand the structure-activity relationship of this class of compounds. The bicyclic part of the molecule consists of an aromatic ring (C2 to C7) and an imidazol-2(3*H*)-one nucleus approximately planar. This bicyclic fragment makes a dihedral angle of 88 (1)° with the dimethylphenyl ring. Such geometry is in agreement with the best docked conformation previously calculated (Barreca *et al.*, 2007) and match well with the pharmacophoric model proposed for the interactions with the macromolecule. As previously observed in other *N*-(phenylsulfonyl)indoles (Liu *et al.*, 2007) and *N*-phenylsulfonamides, (Beddoes *et al.*, 1986) the N atom lone pair eclipses the sulfonyl group; accordingly the corresponding torsion angle O(2)—S(1)—N(1)—C(7) is 48.4 (2)°. In the crystal packing are present two intermolecular hydrogen bonds (Fig. 2) between N2—H2 and $O1^{I}$ at a distance of 2.18 (2) Å, angle 134.2 (2)° and N2—H2 with $O2^{I}$ of 2.39 (2) Å, angle 137.9 (4)°, forming a biforcated linkage with the adjacent molecule at *x*; 1/2 - *y*; *z* + 1/2. The crystal structure is also stabilized by π-π stacking of the benzimidazolone moieties [3.95 (1) Å] and by short intermolecular $Cl(1)\cdots O(3)^{I}$ contacts [3.122 (2) Å].

Experimental

The compound I has been synthesized as previously reported (Barreca *et al.*, 2007). Single crystals were obtained at room temperature by slow evaporation of a $CHCl_3$ solution.

Refinement

All non-H-atoms were refined anisotropically. Hydrogen atoms were introduced at calculated positions, in their described geometries and allowed to ride on the attached carbon atom with fixed isotropic thermal parameters (1.2Ueq and 1.5Ueq of the parent carbon atom for aromatic H-atoms and methyls H-atoms, respectively).

Figures

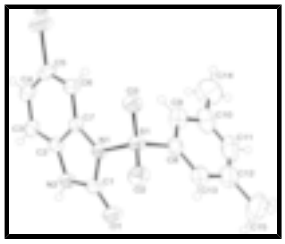


Fig. 1. : The molecular structure of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 40% probability level.

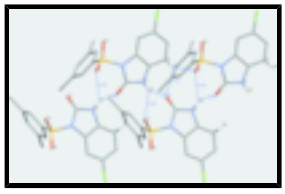


Fig. 2. : Packing diagram of the title compound, showing the intermolecular interactions as dotted lines.

6-Chloro-1-(3,5-dimethylphenylsulfonyl)-1*H*-benzimidazol-2(3*H*)-one

Crystal data

$C_{15}H_{13}ClN_2O_3S$	F_{000} = 696
M_r = 336.78	D_x = 1.470 Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation λ = 0.71073 Å
Hall symbol: -P 2ybc	Cell parameters from 25 reflections
a = 12.173 (3) Å	θ = 9–10º
b = 14.036 (3) Å	μ = 0.40 mm^{-1}
c = 8.949 (2) Å	T = 293 (2) K
β = 95.77 (2)º	Prism, colourless
V = 1521.3 (6) Å^3	0.5 × 0.4 × 0.3 mm
Z = 4	

Data collection

Enraf–Nonius CAD-4 diffractometer	θ_{max} = 28.0º
Monochromator: graphite	θ_{min} = 3.3º
T = 293(2) K	h = −16→15
Non–profiled ω/2θ scans	k = 0→18
Absorption correction: none	l = 0→11
3964 measured reflections	3 standard reflections
3634 independent reflections	every 120 min
3214 reflections with $I > 2\sigma(I)$	intensity decay: 1%
R_{int} = 0.014	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map

Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.057$	H-atom parameters constrained
$wR(F^2) = 0.133$	$w = 1/[\sigma^2(F_o^2) + (0.0188P)^2 + 1.7615P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.19$	$(\Delta/\sigma)_{max} = 0.003$
3634 reflections	$\Delta\rho_{max} = 0.23$ e Å^{-3}
199 parameters	$\Delta\rho_{min} = -0.27$ e Å^{-3}
Primary atom site location: structure-invariant direct methods	Extinction correction: none

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.78957 (6)	0.45343 (4)	0.18441 (6)	0.04124 (17)
Cl1	0.89540 (9)	0.73749 (6)	0.67132 (11)	0.0776 (3)
O3	0.81132 (18)	0.55252 (13)	0.1756 (2)	0.0524 (5)
O1	0.80048 (19)	0.25911 (13)	0.3298 (2)	0.0545 (5)
N2	0.85398 (19)	0.32965 (15)	0.5597 (2)	0.0426 (5)
H2	0.8602	0.2802	0.6166	0.051*
N1	0.83211 (18)	0.42285 (14)	0.3607 (2)	0.0371 (4)
O2	0.83888 (19)	0.38810 (15)	0.0896 (2)	0.0567 (5)
C2	0.8705 (2)	0.42257 (18)	0.6105 (3)	0.0387 (5)
C8	0.6470 (2)	0.4341 (2)	0.1704 (3)	0.0508 (6)
C7	0.85543 (19)	0.48366 (17)	0.4866 (2)	0.0351 (5)
C1	0.8269 (2)	0.32671 (17)	0.4093 (3)	0.0417 (5)
C4	0.9024 (2)	0.5555 (2)	0.7717 (3)	0.0519 (7)
H4	0.9177	0.5817	0.8670	0.062*
C6	0.8637 (2)	0.58080 (18)	0.5011 (3)	0.0425 (5)
H6	0.8547	0.6215	0.4188	0.051*
C3	0.8955 (2)	0.4574 (2)	0.7537 (3)	0.0464 (6)
H3	0.9074	0.4166	0.8356	0.056*
C5	0.8864 (2)	0.61419 (19)	0.6469 (3)	0.0491 (6)
C13	0.6006 (3)	0.3614 (3)	0.0822 (4)	0.0734 (10)
H13	0.6452	0.3204	0.0334	0.088*
C9	0.5842 (3)	0.4951 (3)	0.2471 (4)	0.0671 (9)

H9	0.6174	0.5437	0.3060	0.081*
C11	0.4255 (4)	0.4091 (4)	0.1443 (5)	0.0941 (15)
H11	0.3495	0.3998	0.1362	0.113*
C10	0.4705 (3)	0.4829 (4)	0.2352 (5)	0.0858 (12)
C12	0.4884 (4)	0.3499 (3)	0.0666 (6)	0.0954 (15)
C15	0.4332 (5)	0.2721 (4)	−0.0324 (8)	0.152 (2)
H15A	0.3928	0.2305	0.0274	0.229*
H15B	0.4884	0.2362	−0.0772	0.229*
H15C	0.3835	0.3005	−0.1099	0.229*
C14	0.4004 (4)	0.5506 (5)	0.3165 (7)	0.1339 (17)
H14A	0.4464	0.5843	0.3924	0.201*
H14B	0.3454	0.5152	0.3626	0.201*
H14C	0.3650	0.5953	0.2462	0.201*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0549 (4)	0.0401 (3)	0.0290 (3)	0.0002 (3)	0.0055 (2)	0.0037 (2)
Cl1	0.1068 (7)	0.0451 (4)	0.0801 (6)	−0.0057 (4)	0.0058 (5)	−0.0229 (4)
O3	0.0702 (13)	0.0436 (10)	0.0431 (10)	−0.0050 (9)	0.0043 (9)	0.0112 (8)
O1	0.0876 (15)	0.0359 (9)	0.0394 (10)	−0.0034 (9)	0.0039 (9)	−0.0019 (8)
N2	0.0592 (13)	0.0362 (10)	0.0325 (10)	0.0004 (9)	0.0044 (9)	0.0061 (8)
N1	0.0522 (12)	0.0326 (9)	0.0266 (9)	0.0025 (8)	0.0046 (8)	0.0029 (7)
O2	0.0803 (14)	0.0593 (12)	0.0319 (9)	0.0065 (11)	0.0119 (9)	−0.0046 (8)
C2	0.0415 (12)	0.0424 (13)	0.0326 (11)	−0.0008 (10)	0.0060 (9)	0.0002 (9)
C8	0.0551 (16)	0.0537 (16)	0.0421 (14)	−0.0006 (13)	−0.0025 (12)	0.0088 (12)
C7	0.0357 (11)	0.0383 (12)	0.0316 (11)	0.0015 (9)	0.0055 (8)	−0.0022 (9)
C1	0.0570 (15)	0.0357 (12)	0.0327 (11)	0.0021 (11)	0.0068 (10)	0.0021 (9)
C4	0.0551 (16)	0.0606 (17)	0.0398 (13)	−0.0041 (13)	0.0039 (11)	−0.0130 (12)
C6	0.0491 (14)	0.0375 (12)	0.0410 (13)	0.0005 (11)	0.0051 (10)	−0.0003 (10)
C3	0.0521 (15)	0.0540 (15)	0.0332 (12)	−0.0012 (12)	0.0040 (10)	0.0017 (11)
C5	0.0524 (15)	0.0400 (13)	0.0557 (16)	−0.0051 (11)	0.0096 (12)	−0.0138 (12)
C13	0.076 (2)	0.0580 (19)	0.080 (2)	−0.0021 (17)	−0.0227 (19)	0.0045 (17)
C9	0.0559 (18)	0.089 (3)	0.0559 (18)	−0.0019 (17)	0.0029 (14)	−0.0021 (17)
C11	0.060 (2)	0.121 (4)	0.096 (3)	−0.021 (2)	−0.016 (2)	0.039 (3)
C10	0.063 (2)	0.123 (4)	0.072 (2)	0.008 (2)	0.0080 (19)	0.015 (2)
C12	0.081 (3)	0.079 (3)	0.117 (4)	−0.011 (2)	−0.033 (3)	0.016 (3)
C15	0.138 (5)	0.115 (4)	0.186	−0.035 (4)	−0.075 (4)	−0.004 (4)
C14	0.080 (3)	0.185	0.140 (5)	0.021 (4)	0.027 (3)	−0.019 (5)

Geometric parameters (Å, °)

S1—O3	1.419 (2)	C6—C5	1.388 (4)
S1—O2	1.423 (2)	C6—H6	0.9300
S1—N1	1.6667 (19)	C3—H3	0.9300
S1—C8	1.749 (3)	C13—C12	1.368 (6)
Cl1—C5	1.746 (3)	C13—H13	0.9300
O1—C1	1.210 (3)	C9—C10	1.388 (5)
N2—C1	1.354 (3)	C9—H9	0.9300

N2—C2	1.389 (3)	C11—C12	1.367 (7)
N2—H2	0.8600	C11—C10	1.395 (7)
N1—C7	1.419 (3)	C11—H11	0.9300
N1—C1	1.421 (3)	C10—C14	1.512 (7)
C2—C3	1.376 (3)	C12—C15	1.520 (7)
C2—C7	1.399 (3)	C15—H15A	0.9600
C8—C13	1.375 (4)	C15—H15B	0.9600
C8—C9	1.376 (5)	C15—H15C	0.9600
C7—C6	1.372 (3)	C14—H14A	0.9600
C4—C5	1.385 (4)	C14—H14B	0.9600
C4—C3	1.389 (4)	C14—H14C	0.9600
C4—H4	0.9300		
O3—S1—O2	120.41 (13)	C4—C3—H3	121.1
O3—S1—N1	105.25 (11)	C4—C5—C6	123.8 (3)
O2—S1—N1	106.81 (11)	C4—C5—Cl1	119.1 (2)
O3—S1—C8	109.74 (14)	C6—C5—Cl1	117.1 (2)
O2—S1—C8	109.40 (14)	C12—C13—C8	119.6 (4)
N1—S1—C8	103.86 (12)	C12—C13—H13	120.2
C1—N2—C2	111.5 (2)	C8—C13—H13	120.2
C1—N2—H2	124.2	C8—C9—C10	119.0 (4)
C2—N2—H2	124.2	C8—C9—H9	120.5
C7—N1—C1	109.87 (18)	C10—C9—H9	120.5
C7—N1—S1	127.94 (16)	C12—C11—C10	122.8 (4)
C1—N1—S1	120.99 (16)	C12—C11—H11	118.6
C3—C2—N2	130.5 (2)	C10—C11—H11	118.6
C3—C2—C7	121.3 (2)	C9—C10—C11	117.8 (4)
N2—C2—C7	108.2 (2)	C9—C10—C14	119.5 (5)
C13—C8—C9	122.0 (3)	C11—C10—C14	122.7 (4)
C13—C8—S1	120.2 (3)	C11—C12—C13	118.7 (4)
C9—C8—S1	117.7 (2)	C11—C12—C15	119.7 (5)
C6—C7—C2	122.1 (2)	C13—C12—C15	121.5 (5)
C6—C7—N1	132.8 (2)	C12—C15—H15A	109.5
C2—C7—N1	105.1 (2)	C12—C15—H15B	109.5
O1—C1—N2	129.2 (2)	H15A—C15—H15B	109.5
O1—C1—N1	125.6 (2)	C12—C15—H15C	109.5
N2—C1—N1	105.1 (2)	H15A—C15—H15C	109.5
C5—C4—C3	119.6 (2)	H15B—C15—H15C	109.5
C5—C4—H4	120.2	C10—C14—H14A	109.5
C3—C4—H4	120.2	C10—C14—H14B	109.5
C7—C6—C5	115.5 (2)	H14A—C14—H14B	109.5
C7—C6—H6	122.3	C10—C14—H14C	109.5
C5—C6—H6	122.3	H14A—C14—H14C	109.5
C2—C3—C4	117.7 (2)	H14B—C14—H14C	109.5
C2—C3—H3	121.1		

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···O1^{i}	0.86	2.18	2.852 (3)	135 (1)

N2—H2···O2^{i}	0.86	2.39	3.075 (3)	138 (1)

Symmetry codes: (i) *x*, −*y*+1/2, *z*+1/2.

Fig. 1

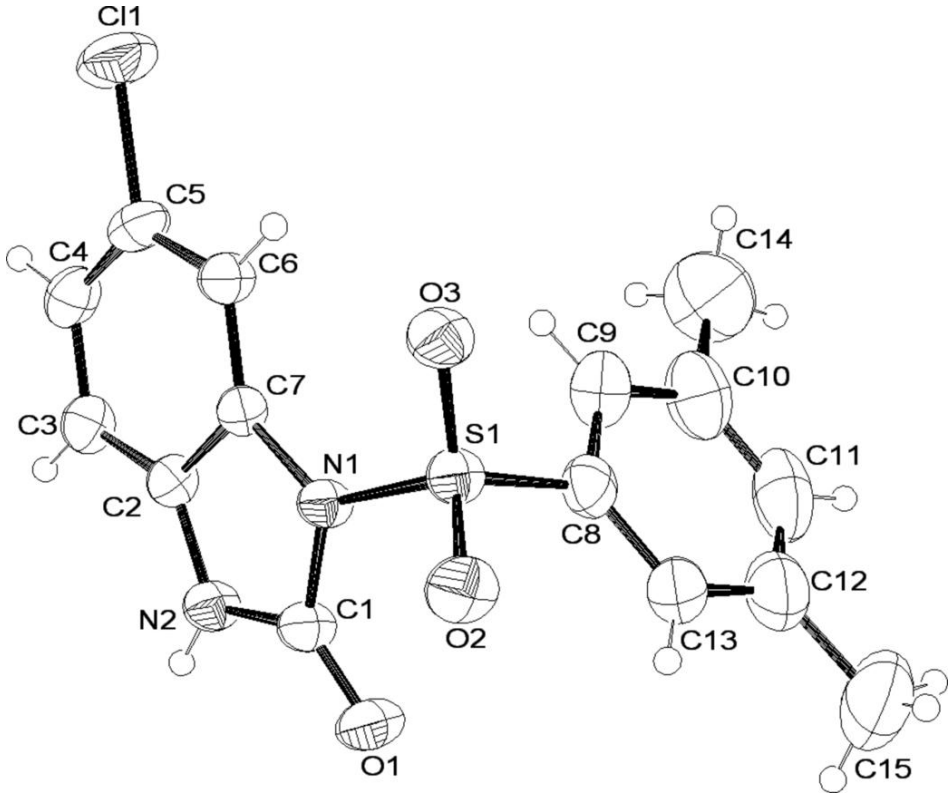


Fig. 2