Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

N-(5-Chloro-1,3-thiazol-2-yl)-2,4-difluorobenzamide

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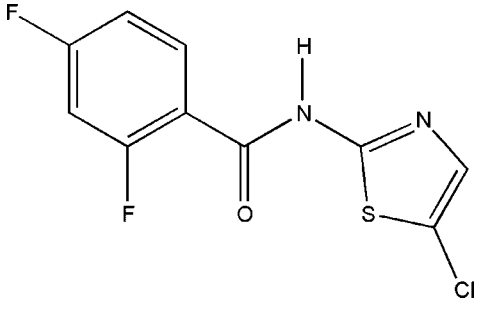
Received 27 March 2012; accepted 17 May 2012

Key indicators: single-crystal X-ray study; T = 296 K; mean σ(C–C) = 0.005 Å; R factor = 0.047; wR factor = 0.136; data-to-parameter ratio = 12.9.

The title compound, $C_{10}H_5ClF_2N_2OS$, was obtained by linking an amino heterocycle and a substituted benzoyl chloride. The dihedral angle between the two rings is 41.2 (2)° and the equalization of the amide C—N bond lengths reveals the existence of conjugation between the benzene ring and the thiazole unit. In the crystal, pairs of N—H···N hydrogen bonds link molecules into inversion dimers. Non-classical C—H···F and C—H···O hydrogen bonds stabilize the crystal structure.

Related literature

For synthesis and the biological activity of thiazolides, see: Ballard *et al.* (2011).



Experimental

Crystal data

$C_{10}H_5ClF_2N_2OS$ M_r = 274.68
Triclinic, $P\overline{1}$
a = 6.929 (2) Å
b = 7.330 (2) Å
c = 12.179 (4) Å
α = 101.669 (3)°
β = 98.277 (3)°
γ = 111.796 (3)°
V = 545.9 (3) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.55 mm^{-1}
T = 296 K
0.35 × 0.33 × 0.27 mm

Data collection

Bruker APEXII CCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.831, T_{max} = 0.866
3930 measured reflections
1998 independent reflections
1693 reflections with $I > 2\sigma(I)$
R_{int} = 0.028

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.136
S = 1.06
1998 reflections
155 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 1.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···N2^{i}	0.86	2.15	2.988 (3)	166
C4—H4···F2^{ii}	0.93	2.38	3.127 (4)	137
C4—H4···O3^{ii}	0.93	2.56	3.329 (4)	140

Symmetry codes: (i) $-x+2, -y+1, -z+1$; (ii) $x+1, y, z$.

Data collection: *APEX2* (Bruker, 2008); cell refinement: *SAINT* (Bruker, 2008); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

This research was supported by the earmarked fund for the China Agriculture Research System (CARS-38) and the open fund of the Key Laboratory of the New Animal Drug Project of Gansu Province and the Key Laboratory of Veterinary Pharmaceutical Development of the Ministry of Agriculture (1610322011011).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: RK2350).

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supplementary materials

Acta Cryst. (2012). E**68**, o1857 [doi:10.1107/S1600536812022477]

N-(5-Chloro-1,3-thiazol-2-yl)-2,4-difluorobenzamide

Xi-Wang Liu, Jian-Yong Li, Han Zhang, Ya-Jun Yang and Ji-Yu Zhang

Comment

Nitazoxanide, (2-acetyloloxy-*N*-(5-nitro-2-thiazolyl)benzamide), belonged to nitrothiazole analogue, was developed as a promising compound to treat both human and animal diseases (Ballard *et al.*, 2011). In this paper, we report the synthesis and structure of the title compound, which is a derivative of nitazoxanide. The conjugation between benzene ring and thiazole moiety confirmed the existance of amide anion, which is considered to directly inhibit the *PFOR* enzyme (key enzyme of central intermidiary matabolism in anaerobic organisms). The classical intermolecular hydrogen bonds N1—H1···N2^{i} forms centrosymmetrical dimers (Table 1). The non-classical intermolecular hydrogen bonds C4—H4···F2^{ii} and C4—H4···O3^{ii} stabilize molecular packing in crystal. Symmetry codes: (i) -*x*+2, -*y*+1, -*z*+1; (ii) *x*+1, *y*, *z*.

Experimental

The title compound was obtained according to routine method: to a solution of 5-chlorothiazol-2-amine (1 mmol) in distilled pyridine was added a equimolar amount of 2,4-difluorobenzoyl chloride with stirring. When addition was complete, the reaction mixture was allowed to stand at room temperature and stirred over night. The reaction was judged complete by *TLC* analysis. The crude product then seperated on dilution was filtered out, washed with 10% $NaHCO_3$ solution, then several times with water. The dry solid was purified by chromatography to give pure compound and the crystals were obtained by recrystalization from CH_3OH.

Refinement

The positions of all H atoms were determined geometrically and refined using a riding model with C—H = 0.93Å, N—H = 0.86Å and U_{iso}(H) = 1.2U_{eq}(C, N).

Computing details

Data collection: *APEX2* (Bruker, 2008); cell refinement: *SAINT* (Bruker, 2008); data reduction: *SAINT* (Bruker, 2008); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL* (Sheldrick, 2008).

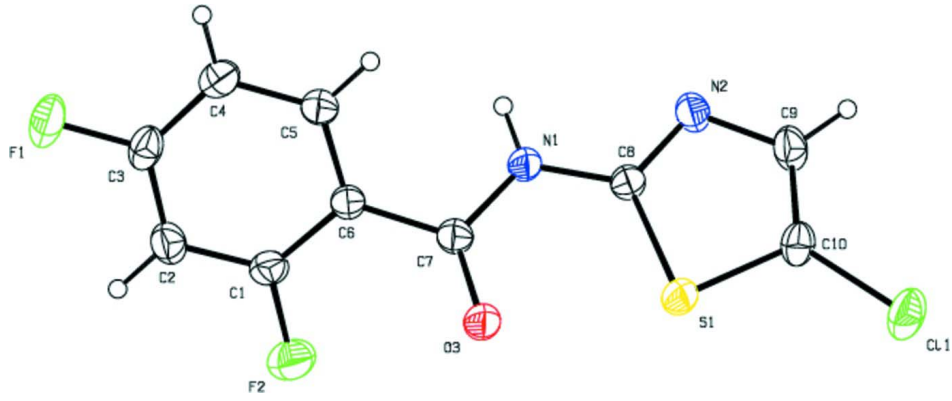

Figure 1

The molecular structure of title compound with the atom labels. Displacement ellipsoids are drawn at the 30% probability level. H atoms are presented as a small spheres of arbitrary radius.

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Crystal data

$C_{10}H_5ClF_2N_2OS$
$M_r = 274.68$
Triclinic, $P\overline{1}$
Hall symbol: -P 1
$a = 6.929$ (2) Å
$b = 7.330$ (2) Å
$c = 12.179$ (4) Å
$\alpha = 101.669$ (3)°
$\beta = 98.277$ (3)°
$\gamma = 111.796$ (3)°
$V = 545.9$ (3) Å^3
$Z = 2$
$F(000) = 276$
$D_x = 1.671$ Mg m^{-3}
Melting point = 428–429 K
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2870 reflections
$\theta = 3.1$–28.2°
$\mu = 0.55$ mm^{-1}
$T = 296$ K
Block, colourless
0.35 × 0.33 × 0.27 mm

Data collection

Bruker APEXII CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
φ– and ω–scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.831$, $T_{max} = 0.866$
3930 measured reflections
1998 independent reflections
1693 reflections with $I > 2\sigma(I)$
$R_{int} = 0.028$
$\theta_{max} = 25.5°$, $\theta_{min} = 3.1°$
$h = -8\rightarrow8$
$k = -8\rightarrow8$
$l = -14\rightarrow14$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.047$
$wR(F^2) = 0.136$
$S = 1.06$
1998 reflections
155 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0689P)^2 + 0.4949P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 1.25$ e Å^{-3}
$\Delta\rho_{min} = -0.33$ e Å^{-3}

Extinction correction: *SHELXL97* (Sheldrick, 2008), $Fc^{*}=kFc[1+0.001xFc^{2}\lambda^{3}/\sin(2\theta)]^{-1/4}$

Extinction coefficient: 0.53 (3)

Special details

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'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 (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	1.0517 (5)	0.7233 (5)	0.9365 (3)	0.0438 (7)
C2	1.2260 (5)	0.8083 (5)	1.0282 (3)	0.0494 (8)
H2	1.2296	0.8968	1.0958	0.059*
C3	1.3958 (5)	0.7579 (5)	1.0168 (3)	0.0467 (8)
C4	1.3945 (5)	0.6268 (5)	0.9182 (3)	0.0464 (7)
H4	1.5116	0.5954	0.9126	0.056*
C5	1.2153 (5)	0.5432 (5)	0.8280 (3)	0.0413 (7)
H5	1.2120	0.4530	0.7612	0.050*
C6	1.0387 (4)	0.5896 (4)	0.8336 (2)	0.0358 (6)
C7	0.8392 (5)	0.4900 (4)	0.7407 (2)	0.0390 (7)
C8	0.6940 (4)	0.3522 (4)	0.5350 (2)	0.0365 (6)
C9	0.5284 (5)	0.2099 (5)	0.3514 (3)	0.0505 (8)
H9	0.5166	0.1733	0.2722	0.061*
C10	0.3587 (5)	0.1551 (4)	0.3969 (3)	0.0447 (7)
Cl1	0.09389 (14)	0.01753 (14)	0.32522 (8)	0.0662 (4)
F1	1.5714 (3)	0.8434 (3)	1.10528 (18)	0.0673 (6)
F2	0.8890 (3)	0.7783 (4)	0.9458 (2)	0.0796 (8)
N1	0.8646 (4)	0.4602 (4)	0.62983 (19)	0.0376 (6)
H1	0.9916	0.5106	0.6191	0.045*
N2	0.7224 (4)	0.3246 (4)	0.4302 (2)	0.0449 (6)
O3	0.6609 (3)	0.4314 (4)	0.75914 (18)	0.0553 (6)
S1	0.43196 (11)	0.24360 (11)	0.54607 (6)	0.0421 (3)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0358 (15)	0.0438 (16)	0.0480 (17)	0.0122 (13)	0.0149 (13)	0.0095 (13)
C2	0.0483 (18)	0.0462 (17)	0.0386 (16)	0.0079 (14)	0.0089 (14)	0.0038 (13)
C3	0.0365 (15)	0.0494 (18)	0.0420 (16)	0.0035 (13)	0.0018 (12)	0.0198 (14)
C4	0.0377 (15)	0.0559 (19)	0.0504 (18)	0.0196 (14)	0.0119 (14)	0.0236 (15)
C5	0.0396 (15)	0.0447 (16)	0.0393 (15)	0.0156 (13)	0.0128 (12)	0.0123 (13)
C6	0.0329 (13)	0.0370 (14)	0.0339 (14)	0.0084 (11)	0.0107 (11)	0.0119 (11)
C7	0.0377 (15)	0.0413 (15)	0.0368 (15)	0.0135 (12)	0.0117 (12)	0.0121 (12)
C8	0.0339 (13)	0.0349 (14)	0.0372 (14)	0.0094 (11)	0.0101 (11)	0.0110 (11)
C9	0.0490 (18)	0.0455 (17)	0.0361 (16)	0.0020 (14)	0.0049 (13)	0.0052 (13)

C10	0.0414 (16)	0.0335 (15)	0.0440 (16)	0.0049 (12)	0.0006 (13)	0.0066 (12)
Cl1	0.0435 (5)	0.0572 (6)	0.0666 (6)	−0.0003 (4)	−0.0052 (4)	0.0058 (4)
F1	0.0444 (11)	0.0784 (14)	0.0528 (12)	0.0031 (10)	−0.0082 (9)	0.0204 (10)
F2	0.0495 (12)	0.0830 (16)	0.0895 (17)	0.0280 (11)	0.0141 (11)	−0.0104 (13)
N1	0.0304 (11)	0.0443 (13)	0.0336 (12)	0.0099 (10)	0.0091 (10)	0.0111 (10)
N2	0.0423 (13)	0.0449 (14)	0.0341 (13)	0.0058 (11)	0.0096 (11)	0.0062 (11)
O3	0.0349 (11)	0.0801 (17)	0.0385 (12)	0.0114 (11)	0.0119 (9)	0.0125 (11)
S1	0.0327 (4)	0.0449 (5)	0.0426 (5)	0.0098 (3)	0.0088 (3)	0.0114 (3)

Geometric parameters (Å, º)

C1—F2	1.343 (4)	C7—O3	1.220 (3)
C1—C2	1.366 (4)	C7—N1	1.371 (4)
C1—C6	1.393 (4)	C8—N2	1.306 (4)
C2—C3	1.374 (5)	C8—N1	1.379 (4)
C2—H2	0.9300	C8—S1	1.729 (3)
C3—F1	1.348 (3)	C9—C10	1.334 (5)
C3—C4	1.374 (5)	C9—N2	1.378 (4)
C4—C5	1.376 (4)	C9—H9	0.9300
C4—H4	0.9300	C10—Cl1	1.719 (3)
C5—C6	1.394 (4)	C10—S1	1.730 (3)
C5—H5	0.9300	N1—H1	0.8600
C6—C7	1.480 (4)		
F2—C1—C2	117.5 (3)	O3—C7—N1	120.7 (3)
F2—C1—C6	119.1 (3)	O3—C7—C6	123.3 (3)
C2—C1—C6	123.4 (3)	N1—C7—C6	116.0 (2)
C1—C2—C3	117.4 (3)	N2—C8—N1	121.3 (2)
C1—C2—H2	121.3	N2—C8—S1	115.8 (2)
C3—C2—H2	121.3	N1—C8—S1	122.9 (2)
F1—C3—C4	119.0 (3)	C10—C9—N2	115.1 (3)
F1—C3—C2	118.5 (3)	C10—C9—H9	122.5
C4—C3—C2	122.5 (3)	N2—C9—H9	122.5
C3—C4—C5	118.3 (3)	C9—C10—Cl1	127.8 (3)
C3—C4—H4	120.9	C9—C10—S1	111.6 (2)
C5—C4—H4	120.9	Cl1—C10—S1	120.56 (19)
C4—C5—C6	122.0 (3)	C7—N1—C8	122.4 (2)
C4—C5—H5	119.0	C7—N1—H1	118.8
C6—C5—H5	119.0	C8—N1—H1	118.8
C1—C6—C5	116.4 (3)	C8—N2—C9	110.0 (3)
C1—C6—C7	120.8 (3)	C8—S1—C10	87.44 (14)
C5—C6—C7	122.6 (3)		
F2—C1—C2—C3	−177.5 (3)	C1—C6—C7—N1	145.0 (3)
C6—C1—C2—C3	0.2 (5)	C5—C6—C7—N1	−40.5 (4)
C1—C2—C3—F1	178.6 (3)	N2—C9—C10—Cl1	178.5 (2)
C1—C2—C3—C4	−0.3 (5)	N2—C9—C10—S1	−0.6 (4)
F1—C3—C4—C5	−179.1 (3)	O3—C7—N1—C8	−4.4 (4)
C2—C3—C4—C5	−0.1 (5)	C6—C7—N1—C8	173.7 (2)
C3—C4—C5—C6	0.8 (4)	N2—C8—N1—C7	−179.6 (3)

F2—C1—C6—C5	178.1 (3)	S1—C8—N1—C7	−0.1 (4)
C2—C1—C6—C5	0.4 (4)	N1—C8—N2—C9	179.1 (3)
F2—C1—C6—C7	−7.1 (4)	S1—C8—N2—C9	−0.4 (3)
C2—C1—C6—C7	175.2 (3)	C10—C9—N2—C8	0.7 (4)
C4—C5—C6—C1	−0.9 (4)	N2—C8—S1—C10	0.1 (2)
C4—C5—C6—C7	−175.6 (3)	N1—C8—S1—C10	−179.4 (3)
C1—C6—C7—O3	−37.0 (4)	C9—C10—S1—C8	0.3 (3)
C5—C6—C7—O3	137.5 (3)	Cl1—C10—S1—C8	−178.9 (2)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···N2^{i}	0.86	2.15	2.988 (3)	166
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