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

Key Laboratory of the New Animal Drug Project, Gansu Province, Key Laboratory of Veterinary Pharmaceutical Development, Ministry of Agriculture, Lanzhou Institute of Animal Science and Veterinary Pharmaceutics of CAAS, Lanzhou 730050, People's Republic of China

Correspondence e-mail: lijy1971@163.com

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).
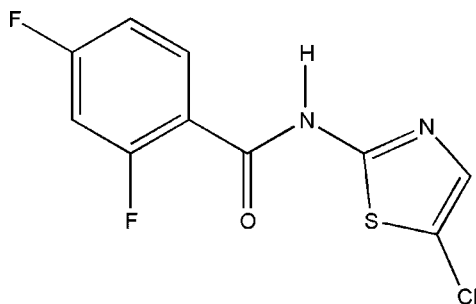
Experimental

Crystal data

$C_{10}H_5ClF_2N_2OS$

M_r = 274.68

Triclinic, $P\bar{1}$

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

$0.35 \times 0.33 \times 0.27$ 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.

References

Ballard, T. E., Wang, X., Olekhnovich, I., Koerner, T., Seymour, C., Salamoun, J., Warthan, M., Hoffman, P. S. & Macdonald, T. L. (2011). ChemMedChem, **6**, 362–377.

Bruker (2008). APEX2 and SAINT. Bruker AXS Inc., Madison, Wisconsin, USA.

Sheldrick, G. M. (1996). SADABS. University of Göttingen, Germany.

Sheldrick, G. M. (2008). Acta Cryst. A**64**, 112–122.

supporting information

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

S1. 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*.

S2. 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.

S3. 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 $U_{iso}(H) = 1.2U_{eq}(C, N)$.
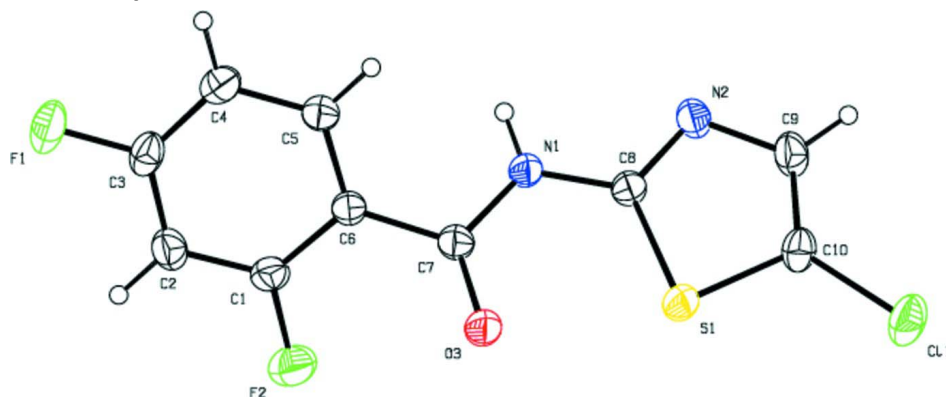

Figure 1

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.

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

Crystal data

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

Data collection

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

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.047$	$w = 1/[\sigma^2(F_o^2) + (0.0689P)^2 + 0.4949P]$
$wR(F^2) = 0.136$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.06$	$(\Delta/\sigma)_{max} < 0.001$
1998 reflections	$\Delta\rho_{max} = 1.25$ e Å^{-3}
155 parameters	$\Delta\rho_{min} = -0.33$ e Å^{-3}
0 restraints	Extinction correction: *SHELXL97* (Sheldrick, 2008), Fc*=kFc[1+0.001xFc$^2\lambda^3$/sin(2θ)]$^{-1/4}$
Primary atom site location: structure-invariant direct methods	Extinction coefficient: 0.53 (3)
Secondary atom site location: difference Fourier map	

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···N2ⁱ	0.86	2.15	2.988 (3)	166
C4—H4···F2ⁱⁱ	0.93	2.38	3.127 (4)	137
C4—H4···O3ⁱⁱ	0.93	2.56	3.329 (4)	140

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