Crystal structure of 2-chloro-*N*-[5-(4-fluorophenyl)-1,3,4-thiadiazol-2-yl]-nicotinamide, $C_{14}H_8ClFN_4OS$

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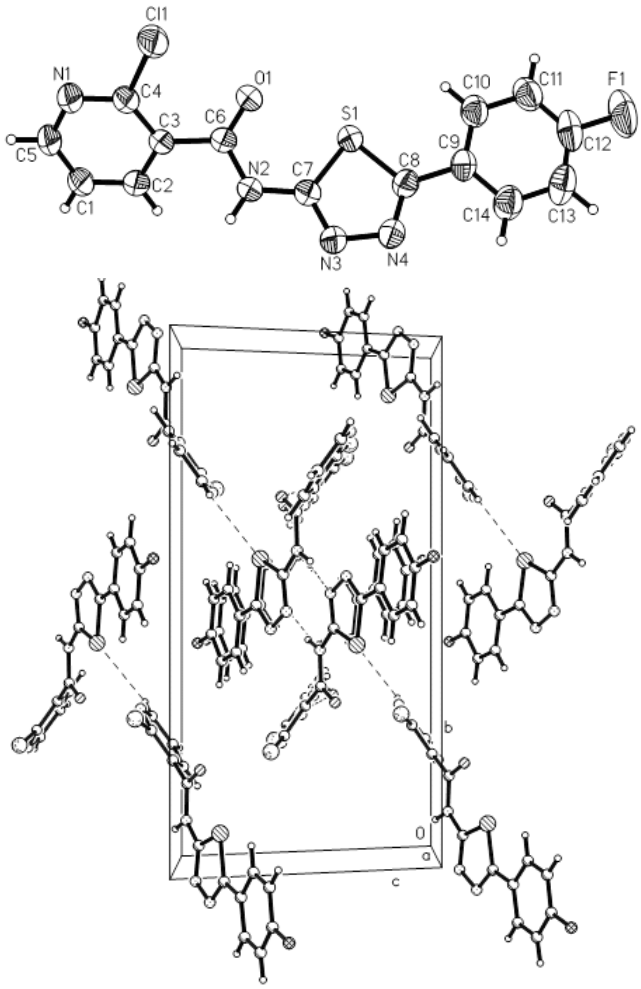

Abstract

$C_{14}H_8ClFN_4OS$, monoclinic, $P12_1/c1$ (no. 14), a = 7.451(4) Å, b = 19.628(9) Å, c = 10.519(5) Å, β = 110.137(7)°, V = 1444.4 Å^3, Z = 4, $R_{gt}(F)$ = 0.039, $wR_{ref}(F^2)$ = 0.098, T = 298 K.

Source of material

N,*N*-dicyclohexylcarbodiimide (5.7 mmol) was added to a cooled solution of 2-chloropyridine-3-carboxylic acid (5.6 mmol) and *N*-hydroxysuccinimide (5.6 mmol) in freshly distilled dioxane (30 ml). The reaction mixture was stirred overnight at room temperature. The insoluble material was filtered off and washed with cold dioxane. 5-(4-Fluorophenyl)-1,3,4-thiadiazol-2-amine (5.5 mmol) was added to the filtrate and the reaction mixture was stirred for 48 h at room temperature. The solvent was removed under reduced pressure. The residual was dissolved in ethyl acetate and the insoluble material was filtered off. The filtrate was washed successively with saturated Na_2CO_3 solution (20 ml), water (20 ml), 0.1 M HCl (20 ml) and water (20 ml). The organic layer evaporated in vacuo, the residual was recrystallized from methanol. Colorless block-shaped single crystals of the title compound suitable for X-ray diffraction analysis precipitated after several days (m.p. 199 - 201 °C). IR, ^{1}H-NMR and ESI-MS data are available in the CIF.

Experimental details

H atoms were positioned geometrically and refined using a riding model using U_{iso}(H) = 1.2 U_{eq}(C) for CH and CH_2 groups and U_{iso}(H) = 1.5 U_{eq}(C) for CH_3 groups.

Discussion

Recently, we have reported a few 1,3,4-thiadiazole compounds [1,2]. Some of the 1,3,4-thiadiazole derives have been found to have pharmacological and antitumor properties [3,4].

The molecule of the title compound displays a *trans* configuration with respect to the C=O and N—H bonds (figure, top). The planes of the phenyl ring and the 1,3,4-thiadiazole ring are not parallel with the dihedral angle of 4.20(2)°. The dihedral angle between the phenyl ring and the pyridyl ring is 45.83(4)°. The structure displays intermolecular N–H···N, C–H···O, and C–H···S hydrogen bonding (figure, bottom). All the bond lengths are within normal ranges and comparable to the values observed in the similar compounds [5-7].

Table 1. Data collection and handling.

Crystal:	colorless block, size 0.078 × 0.087 × 0.250 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	4.26 cm^{-1}
Diffractometer, scan mode:	Bruker SMART CCD, φ/ω
$2\theta_{max}$:	50°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	8573, 2492
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1599
$N(param)_{refined}$:	203
Programs:	SHELXS-97 [8], SHELXL-97 [9]

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Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(2)	4*e*	0.7170	0.3543	0.4294	0.063
H(1)	4*e*	0.9869	0.2868	0.5074	0.071
H(5)	4*e*	0.9872	0.1950	0.6398	0.074
H(11)	4*e*	–0.6891	0.4613	0.1053	0.079
H(10)	4*e*	–0.3710	0.4303	0.203	0.068
H(14)	4*e*	–0.2239	0.6278	0.2572	0.077
H(13)	4*e*	–0.5448	0.6572	0.1592	0.088
H(6)	4*e*	0.502(3)	0.428(1)	0.503(2)	0.052(8)

Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
S(1)	4*e*	0.00921(9)	0.42092(3)	0.32240(7)	0.0383(4)	0.0431(4)	0.0628(4)	0.0008(3)	0.0127(3)	–0.0003(3)
Cl(1)	4*e*	0.3836(1)	0.21657(4)	0.64377(8)	0.0484(4)	0.0829(6)	0.0947(6)	0.0078(4)	0.0357(4)	0.0353(4)
O(1)	4*e*	0.2229(2)	0.31053(8)	0.4016(2)	0.036(1)	0.047(1)	0.076(1)	–0.0029(8)	0.0138(9)	0.0035(9)
N(3)	4*e*	0.2510(3)	0.5166(1)	0.4187(2)	0.043(1)	0.043(1)	0.062(1)	0.001(1)	0.008(1)	0.001(1)
N(2)	4*e*	0.3933(3)	0.4085(1)	0.4580(2)	0.035(1)	0.039(1)	0.059(1)	–0.004(1)	0.009(1)	0.001(1)
N(1)	4*e*	0.7269(3)	0.2037(1)	0.6423(2)	0.039(1)	0.058(1)	0.076(2)	0.007(1)	0.019(1)	0.018(1)
F(1)	4*e*	–0.8283(2)	0.5797(1)	0.0674(2)	0.054(1)	0.136(2)	0.114(2)	0.038(1)	0.015(1)	0.027(1)
C(3)	4*e*	0.5583(3)	0.2997(1)	0.5146(2)	0.034(1)	0.039(1)	0.051(2)	–0.002(1)	0.013(1)	0.001(1)
C(6)	4*e*	0.3771(3)	0.3388(1)	0.4547(2)	0.039(2)	0.043(2)	0.051(2)	–0.002(1)	0.018(1)	0.004(1)
C(4)	4*e*	0.5728(3)	0.2422(1)	0.5948(2)	0.037(1)	0.050(2)	0.055(2)	0.000(1)	0.017(1)	0.007(1)
C(2)	4*e*	0.7185(3)	0.3163(1)	0.4825(3)	0.043(2)	0.047(2)	0.068(2)	–0.002(1)	0.020(1)	0.010(1)
C(8)	4*e*	–0.0622(4)	0.5057(1)	0.3063(2)	0.048(2)	0.043(1)	0.046(2)	0.004(1)	0.015(1)	–0.001(1)
N(4)	4*e*	0.0752(3)	0.5485(1)	0.3609(2)	0.049(1)	0.044(1)	0.065(1)	0.006(1)	0.012(1)	0.000(1)
C(1)	4*e*	0.8791(4)	0.2766(1)	0.5291(3)	0.036(2)	0.060(2)	0.084(2)	0.003(1)	0.024(2)	0.014(2)
C(7)	4*e*	0.2359(3)	0.4503(1)	0.4067(2)	0.040(1)	0.044(2)	0.047(2)	–0.002(1)	0.015(1)	0.001(1)
C(12)	4*e*	–0.6404(4)	0.5614(2)	0.1257(3)	0.050(2)	0.096(3)	0.064(2)	0.028(2)	0.019(2)	0.014(2)
C(5)	4*e*	0.8774(4)	0.2216(1)	0.6080(3)	0.035(2)	0.062(2)	0.085(2)	0.010(1)	0.016(2)	0.020(2)
C(11)	4*e*	–0.5947(4)	0.4944(2)	0.1365(3)	0.048(1)	0.080(2)	0.066(2)	0.005(2)	0.015(2)	0.015(2)
C(10)	4*e*	–0.4048(4)	0.4761(1)	0.1950(3)	0.050(1)	0.063(2)	0.056(2)	0.009(1)	0.015(1)	0.011(1)
C(9)	4*e*	–0.2646(4)	0.5253(1)	0.2416(2)	0.046(2)	0.055(2)	0.043(2)	0.010(1)	0.012(1)	0.004(1)
C(14)	4*e*	–0.3167(4)	0.5941(1)	0.2275(3)	0.060(2)	0.061(2)	0.062(2)	0.011(2)	0.008(2)	–0.003(1)
C(13)	4*e*	–0.5079(5)	0.6117(2)	0.1688(3)	0.072(2)	0.070(2)	0.068(2)	0.030(2)	0.011(2)	0.004(2)

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References

1. Li, S. H.; Li, G.; Huang, H. M.; Tu, G. G.; Liu, C. M.: (2*R*)-2-(Cinnamoylamino)-*N*-[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]-propanamide. Acta Crystallogr. **E64** (2008) o1887.
2. Li, S. H.; Huang, H. M.; Kuang, B. H.; Tu, G. G.; Liu, C. M.: (2*R*)-*N*-[5-(4-Chlorophenyl)-1,3,4-thiadiazol-2-yl]-2-(cinnamoylamino)-propanamide. Acta Crystallogr. **E64** (2008) o2006.
3. Tu, G. G.; Li, S. H.;Huang, H. M.; Li, G.; Xiong F.; Mai, X.; Zhu, H. W.; Kuang, B. H.; Xu, W. F.: Novel aminopeptidase Ninhibitors derived from 1,3,4-thiadiazole scaffold. Bioorg. Med. Chem. **16** (2008) 6663-6668.
4. Li, S. H.; Li, G.; Huang, H. M.; Xiong, F.;Liu, C. M.; Tu. G. G.: The synthesis and preliminary activity assay in vitro of peptide-like derivatives as APN inhibitors. Arch. Pharm. Res. **31** (2008) 1231-1239.
5. Song, X. J.; Zhang, S. H.; Li, Y. H.; Tan, X. H.; Wang, Y. G.: 1-(2,6-Difluorobenzoyl)-3-(1,3,4-thiadiazol-2-yl)urea. Acta Crystallogr. **E61** (2005) O2360-o2362.
6. Wan, R.; Han, F.; Zhang, J. J.; Cao, L.; Wang, J. T.: 3,5-Dimethyl-*N*-(5-*m*-tolyl-1,3,4-thiadiazol-2-yl)benzamide. Acta Crystallogr. **E63** (2007) o885-o886.
7. Yin, L.; Wan, R.; Han, F.; Wang, B.; Wang, J.: 2-Methoxy-*N*-[5-(2-methoxyphenyl)-1,3,4-thiadiazol-2-yl]benzamide hemihydrate. Acta Crystallogr. **E64** (2008) o1637.
8. Sheldrick, G. M.: SHELXS-97. Program for the Solution of Crystal Structures. University of Göttingen, Germany 1997.
9. Sheldrick, G. M.: SHELXL-97. Program for the Refinement of Crystal Structures. University of Göttingen, Germany 1997.