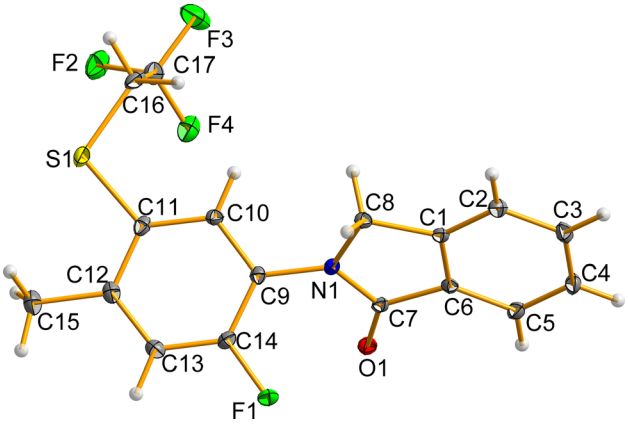
Jing Zhang and Lixin Zhang*

The crystal structure of 2-(2-fluoro-4-methyl-5-((2,2,2-trifluoroethyl)thio)phenyl)isoindolin-1-one, $C_{17}H_{13}F_4NOS$



https://doi.org/10.1515/ncrs-2023-0042
Received January 27, 2023; accepted February 10, 2023;
published online March 1, 2023

Abstract

$C_{17}H_{13}F_4NOS$, triclinic, $P\bar{1}$ (no. 2), a = 6.1249(7) Å, b = 9.9306(10) Å, c = 13.1754(13) Å, α = 83.116(8)°, β = 80.305(9)°, γ = 73.204(9)°, V = 754.08 Å^3, Z = 2, $R_{gt}(F)$ = 0.0460, $wR_{ref}(F^2)$ = 0.1078, T = 150 K.

CCDC no: 2234414.

Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Colourless needle
Size:	0.14 × 0.11 × 0.08 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.26 mm^{-1}
Diffractometer, scan mode:	SuperNova, ω
θ_{max}, completeness:	25.0°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	4888, 2652, 0.031
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2036
N(param)$_{refined}$:	218
Programs:	CrysAlis^{PRO} [1], Olex2 [2], SHELX [3]

1 Source of materials

The 2-(chloromethyl)-*N*-(2-fluoro-4-methyl-5-((2,2,2-trifluoroethyl)thio)phenyl)benzamide (CTPB) was synthesized according to the literature method [4]. Sodium hydride (60% in oil, 0.15 g, 3.75 mmol) was washed with hexane three times and the washed sodium hydride was added to a stirred solution of CTPB (1.00 g, 2.56 mmol) in dry tetrahydrofuran (20 mL) at room temperature. The reaction mixture was continuously stirred at room temperature for 6 h and the reaction was monitored by TLC. After the reaction was complete, the reaction solution was poured into 0.1 N hydrochloric acid, which was then brought to basic using aqueous sodium bicarbonate solution, and extracted with ethyl acetate. The organic layer was collected, and distilled under reduced pressure. The remaining substance was purified by flash column chromatography using petroleum ether: ethyl acetate (20:1, v/v) to give a white solid (0.69 g, 75.9% yield), M.p.: 85.1–86.5 °C. 5.80 mg of white solid was taken and dissolved in 10 mL of dichloromethane and 5 mL of ethanol was added. After slow volatilization for three days, crystals of the title compound were obtained.

2 Experimental details

The hydrogen atom positions were fixed geometrically at the calculated distances and allowed to ride on the parent atoms. The U_{iso} of the H-atoms were set to 1.2 and 1.5 times U_{eq} of the parent atoms with C–H = 0.93 Å (aromatic) and C–H = 0.97 Å (aliphatic).

3 Comment

Isoindolin-1-ones can be found in various natural and synthetic products that show a wide range of biological activities

***Corresponding author: Lixin Zhang**, College of Chemical Engineering, University of Science and Technology Liaoning, Anshan, 114051, Liaoning Province, P. R. China; and Institute of Functional Molecules, Shenyang University of Chemical Technology, Shenyang, 110142, Liaoning Province, P. R. China, E-mail: zhanglixin@syuct.edu.cn
Jing Zhang, College of Chemical Engineering, University of Science and Technology Liaoning, Anshan, 114051, Liaoning Province, P. R. China; and Institute of Functional Molecules, Shenyang University of Chemical Technology, Shenyang, 110142, Liaoning Province, P. R. China. https://orcid.org/0000-0003-4952-3550

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
S1	0.18420 (12)	0.45943 (8)	0.88482 (6)	0.0299 (2)
F1	1.0196 (3)	0.50923 (15)	0.60674 (12)	0.0295 (4)
F2	0.1815 (3)	0.18028 (19)	1.02542 (13)	0.0454 (5)
F3	0.1931 (4)	0.05626 (19)	0.90021 (15)	0.0564 (6)
F4	0.4719 (3)	0.14536 (17)	0.90564 (13)	0.0410 (4)
O1	1.2038 (3)	0.21223 (18)	0.61478 (13)	0.0235 (4)
N1	0.8326 (3)	0.2969 (2)	0.57365 (15)	0.0181 (5)
C1	0.8841 (4)	0.1918 (2)	0.42068 (19)	0.0184 (6)
C2	0.8680 (5)	0.1430 (3)	0.3288 (2)	0.0236 (6)
H2	0.728041	0.165367	0.303476	0.028*
C3	1.0672 (5)	0.0595 (3)	0.2756 (2)	0.0259 (6)
H3	1.059601	0.024370	0.214316	0.031*
C4	1.2765 (5)	0.0280 (3)	0.3122 (2)	0.0256 (6)
H4	1.408173	−0.026069	0.274375	0.031*
C5	1.2925 (4)	0.0757 (3)	0.4041 (2)	0.0228 (6)
H5	1.432562	0.053408	0.429404	0.027*
C6	1.0931 (4)	0.1579 (2)	0.45783 (19)	0.0174 (6)
C7	1.0608 (4)	0.2224 (2)	0.55712 (19)	0.0189 (6)
C8	0.7021 (4)	0.2852 (3)	0.49284 (19)	0.0202 (6)
H8A	0.637340	0.376686	0.458536	0.024*
H8B	0.579140	0.242068	0.520800	0.024*
C9	0.7342 (4)	0.3878 (2)	0.65465 (19)	0.0182 (6)
C10	0.5348 (4)	0.3750 (3)	0.71954 (19)	0.0209 (6)
H10	0.467375	0.305299	0.710621	0.025*
C11	0.4366 (4)	0.4661 (3)	0.7973 (2)	0.0225 (6)
C12	0.5317 (5)	0.5750 (3)	0.8103 (2)	0.0233 (6)
C13	0.7278 (5)	0.5868 (3)	0.7444 (2)	0.0240 (6)
H13	0.793895	0.658067	0.751200	0.029*
C14	0.8259 (4)	0.4944 (3)	0.6691 (2)	0.0216 (6)
C15	0.4248 (5)	0.6771 (3)	0.8931 (2)	0.0316 (7)
H15A	0.265369	0.719900	0.886532	0.047*
H15B	0.504101	0.748972	0.885453	0.047*
H15C	0.437121	0.627302	0.959923	0.047*
C16	0.1204 (5)	0.3001 (3)	0.8621 (2)	0.0306 (7)
H16A	−0.044331	0.312885	0.878949	0.037*
H16B	0.162634	0.284809	0.789203	0.037*
C17	0.2417 (5)	0.1721 (3)	0.9229 (2)	0.0364 (8)

[5–10]. Many references showed crystal structures of the derivatives with the isoindolin-1-one group [11–20].

As shown in the figure, in the main moiety of title compound, the nitrogen atom on isoindole-1-one connects a phenyl group, and the dihedral angle between isoindole-1-one plane and phenyl plane (C9 → C14) is 55.04°. All C–C bond lengths in aromatic rings range from 1.373 to 1.407 Å. All of C–C single bond lengths are between 1.484 and 1.513 Å. N–C bonds are 1.374 and 1.468 Å. The C–S bonds are 1.779 and 1.804 Å. All bond lengths and angles are within a reasonable range [11–18]. In the crystal, title molecules are linked by hydrogen bonds, which are the major intermolecular force to maintain the stability of the crystal structure. The angle of hydrogen bond C(8)–H(8B)···O(1) is 160°, and the length is 2.50 Å. The angle of hydrogen bond C(16)–H(16B)···O(1) is 163°, and the length is 2.44 Å.

Author contribution: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.
Research funding: None declared.
Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

References

1. Agilent Technologies: CrysAlis^{PRO} *Software System (Version 171.38.43f)*; Agilent Technologies UK Ltd: Oxford, UK, 2015.
2. Dolomanov O. V., Bourhis L. J., Gildea R. J., Howard J. A. K., Puschmann H. OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* 2009, *42*, 339–341.
3. Sheldrick G. M. Crystal structure refinement with SHELXL. *Acta Crystallogr.* 2015, *C71*, 3–8.
4. Kalugin V. E., Shestopalov A. M. The synthesis of 3-cyano-2-(organylamino)thieno[3,2-*c*]isoquinoline derivatives. *Russ. Chem. Bull.* 2019, *68*, 588–596.
5. Ghosh S., Cho S. J. Structural insights from molecular modeling of isoindolin-1-one derivatives as PI3Kγ inhibitors against gastric carcinoma. *Biomedicines* 2022, *10*, 813.
6. Kumar J. S., Naimisha R., Thirupataiah B., Reddy G. S., Bung N., Roy A., Bulusu G., Mishra A., Yadav P. N., Misra P., Pal M. Sonochemical synthesis and biological evaluation of isoquinolin- 1(2*H*)-one/ isoindolin-1-one derivatives: discovery of a positive ago-allosteric modulator (PAAM) of $5HT_{2C}$R. *Bioorg. Chem.* 2022, *129*, 106202.
7. Bhatia R. K. Isoindole derivatives: propitious anticancer structural motifs. *Curr. Top. Med. Chem.* 2017, *17*, 189–207.
8. Zhao J., Liu J., Shen Y., Tan Z., Zhang M., Chen R., Zhao J., Zhang D., Yu L., Dai J., Stachybotrysams A.-E. prenylated isoindolinone derivatives with anti-HIV activity from the fungus stachybotrys chartarum. *Phytochem. Lett.* 2017, *20*, 289–294.
9. Wang K., Bao L., Qi Q., Zhao F., Ma K., Pei Y., Liu H. Erinacerins C–L, isoindolin-1-ones with α-glucosidase inhibitory activity from cultures of the medicinal mushroom *Hericium erinaceus*. *J. Nat. Prod.* 2015, *78*, 146–154.
10. El-Tamany E. S. H., Sowellim S. Z., Hamed A. A., Radwan A. S. Synthesis and antimicrobial activity of some isoindole derivatives. *Res. Chem. Intermed.* 2015, *41*, 2675–2685.
11. Mukherjee A. K., Guha S., Khan M. W., Kundu N. G., Helliwell M. Two (*Z*)-*N*-aryl-3-benzylideneisoindolin-1-ones. *Acta Crystallogr.* 2000, *C56*, 85–87.
12. Zeng D., Xing A. P., Wei J. J., Chu Y. X., Zhang S. L. Crystal structure of 3-((1*H*-benzo[*d*]imidazol-2-yl)amino)-2-(1*H*-benzo[*d*] imidazol-2-yl) isoindolin-1-one, $C_{22}H_{16}N_6O$. *Z. Kristallogr. N. Cryst. Struct.* 2019, *234*, 249–251.
13. Ha K. Crystal structure of 2-(tricyclo [3.3.1.1(3, 7)] decan-1-yl)-3-(tricyclo [3.3.1.1(3, 7)]-decan-1-ylimino) isoindolin-1-one, $C_{28}H_{34}N_2O$. *Z. Kristallogr. N. Cryst. Struct.* 2013, *228*, 107–108.

14. Zheng Y., Wu J. L. 2-(4-Hydroxybiphenyl-3-yl) isoindolin-1-one. *Acta Crystallogr.* 2010, *E66*, o448.
15. Liu S., Zhang X. L., Zhang W. H., Zhu H. J. 3-Hydroxy-3-phenylisoindolin-1-one 0.33-hydrate. *Acta Crystallogr.* 2009, *E65*, o3011.
16. Li W., Yin H., Wen L., Cui J., Wang D. 3-Ethoxy-2-(1,3-thiazol-2-yl) isoindolin-1-one. *Acta Crystallogr.* 2009, *E65*, o2594.
17. Urban J., Ludvík J., Fábry J., Dušek M., Fejfarová K. 2-(2-Hydroxyethyl)-3-[(2-hydroxyethyl) imino] isoindolin-1-one. *Acta Crystallogr.* 2009, *E65*, o2092–o2093.
18. Wang J., Johnson D. M., Tiekink E. R. Crystal structure of 2-(3-oxo-1, 3-dihydro-2-benzofuran-5-yl)-3-(2-oxopropyl) isoindolin-1-one, $C_{19}H_{15}NO_4$. *Z. Kristallogr. N. Cryst. Struct.* 2008, *223*, 27–28.
19. Fun H. K., Shen Y. M., Xu J. H., Chantrapromma S. 3-Benzyl-4,5,6,7-tetrachloro-3-hydroxy-2-(3-hydroxypropyl) isoindolin-1-one. *Acta Crystallogr.* 2007, *E63*, o944–o945.
20. Chowdhury K., Mukhopadhyay R., Mukherjee M., Broder C. K., Kundu N. G. (*Z*)-3-Acetonylidene-2,3-dihydro-1*H*-isoindolin-1-one. *Acta Crystallogr.* 2001, *E57*, o421–o423.