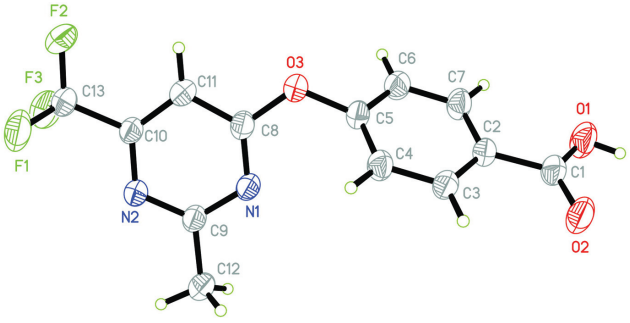
Wen-Neng Wu*, Qiang Fei, Yong-Hui Ge and Xiu-Hai Gan

Crystal structure of 4-((2-methyl-6-(trifluoromethyl)pyrimidin-4-yl)oxy)benzoic acid, $C_{13}H_9F_3N_2O_3$



https://doi.org/10.1515/ncrs-2020-0020
Received January 08, 2020; accepted February 29, 2020; available online March 25, 2020

Abstract

$C_{13}H_9F_3N_2O_3$, monoclinic, $P2_1/c$ (no. 14), $a = 8.6952(7)$ Å, $b = 19.6715(18)$ Å, $c = 8.0995(8)$ Å, $\beta = 110.691(3)°$, $V = 1296.0(2)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0558$, $wR_{ref}(F^2) = 0.1358$, $T = 298(2)$ K.

CCDC no.: 1965889

The molecular structure is shown in the figure. 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 block
Size:	0.30 × 0.27 × 0.10 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.14 mm^{-1}
Diffractometer, scan mode:	CCD, φ and ω
θ_{max}, completeness:	25.0°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	6503, 2290, 0.066
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1237
$N(param)_{refined}$:	191
Programs:	Bruker [1], SHELX [2]

Source of material

All solvents were dried by standard methods in advance and distilled before use. 4-Chloro-2-methyl-6-(trifluoromethyl)pyrimidine (0.01 mol), Cs_2CO_3 (0.02 mol), and ethyl 4-hydroxybenzoate (0.012 mol) were added in a 100 mL three-necked round-bottomed flask. The samples were reacted for 2–3 h at room temperature, and the solvent was removed. Water was added to the residue, the precipitate formed was filtered off and recrystallized from ethanol to yield 70% of methyl 4-((2-methyl-6-(trifluoromethyl)-pyrimidin-4-yl)oxy)benzoate. **^{1}H NMR** (DMSO-*d*6, ppm) δ: 8.06 (d, 2H, $J = 9.0$ Hz, Ph-H), 6.67 7.58 (s, 1H, pyrimidine-H), 7.42 (d, 2H, $J = 9.0$ Hz, Ph-H), 3.87 (s, 3H, CH3O), 2.51 (s, 3H, CH3); **^{13}C NMR** (DMSO-*d*6, ppm) δ: 170.05, 169.67, 165.95, 156.71 (q, $J = 35.25$ Hz), 155.97, 131.60, 127.75, 122.39, 121.78 (q, $J = 272.85$ Hz), 103.83, 52.69, 25.82; **HRMS (ESI):** Calcd. for $C_{14}H_{11}F_3N_2O_3$ $[M+H]^+$: 313.0797; found: 313.0795. Methyl 4-((2-methyl-6-(trifluoromethyl)pyrimidin-4-yl)oxy)benzoate (0.01 mol), THF (10 mL), KOH (0.02 mol), and H_2O (5 mL) were added. The samples were reacted for 6 h at room temperature, and the solvent was removed. Water was added to the residue and acidified with concentrated hydrochloric acid to pH 2–3. The precipitate formed was filtered off and recrystallized from ethanol to yield 70% of title compound. Colorless single crystals were grown and obtained in ethanol after 8 h. **^{1}H NMR** (DMSO-*d*6, ppm) δ: 12.56 (s, 1H), 7.80 (d, 2H, $J = 8.4$ Hz, Ph-H), 7.48 (s, 1H, pyrimidine-H), 6.83 (d, 2H, $J = 8.4$ Hz, Ph-H), 2.35 (s, 3H, CH3); **^{13}C NMR** (DMSO-*d*6, ppm) δ: 167.63, 162.69, 162.06, 151.96 (q, $J = 35.25$ Hz), 131.98, 122.09 (q, $J = 273.00$ Hz), 121.82, 115.56, 111.07, 25.90; **HRMS (ESI):** Calcd. for $C_{13}H_9F_3N_2O_3$ $[M+H]^+$: 299.0640; found: 299.0638.

Experimental details

The room-temperature structure was refined using full-matrix least-squares as implemented in the SHELXL program [2]. H atoms were constrained to ride on their pivot atoms.

Corresponding author: Wen-Neng Wu, Food and Pharmaceutical Engineering Institute, Guiyang University, Guiyang, Guizhou, P.R. China, e-mail: wuwenneng123@126.com. https://orcid.org/0000-0001-8704-226X
Qiang Fei and Yong-Hui Ge: Food and Pharmaceutical Engineering Institute, Guiyang University, Guiyang 550003, Guizhou, P.R. China
Xiu-Hai Gan: Key Laboratory of Functional Organic Molecule, Guizhou Education University, Guiyang 550018, Guizhou, P.R. China

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

Atom	x	y	z	U_{iso}*/U_{eq}
F1	0.0828(2)	0.81901(13)	1.3721(3)	0.1159(9)
F2	−0.0740(2)	0.83549(12)	1.1076(3)	0.1119(8)
F3	0.0187(2)	0.73781(13)	1.1919(3)	0.1068(8)
N1	0.4796(3)	0.83773(12)	1.0814(3)	0.0539(6)
N2	0.3434(3)	0.78537(13)	1.2559(3)	0.0606(7)
O1	0.8158(2)	0.95736(13)	0.4385(3)	0.0912(8)
H1	0.8943	0.9705	0.4133	0.137*
O2	0.9716(3)	0.99741(13)	0.7010(3)	0.0903(8)
O3	0.3322(2)	0.90623(11)	0.8472(2)	0.0673(6)
C1	0.8430(4)	0.96901(17)	0.6009(4)	0.0653(9)
C2	0.7139(3)	0.94836(14)	0.6706(4)	0.0557(8)
C3	0.7361(3)	0.95991(15)	0.8464(4)	0.0600(8)
H3	0.8344	0.9784	0.9215	0.072*
C4	0.6131(3)	0.94408(15)	0.9102(4)	0.0606(8)
H4	0.6274	0.9519	1.0279	0.073*
C5	0.4690(3)	0.91658(14)	0.7975(4)	0.0571(8)
C6	0.4459(3)	0.90429(16)	0.6236(4)	0.0659(9)
H6	0.3481	0.8852	0.5490	0.079*
C7	0.5691(3)	0.92053(15)	0.5612(4)	0.0661(9)
H7	0.5542	0.9125	0.4434	0.079*
C8	0.3410(3)	0.86677(15)	0.9872(4)	0.0552(8)
C9	0.4763(3)	0.79749(15)	1.2135(4)	0.0546(8)
C10	0.2060(3)	0.81714(16)	1.1579(4)	0.0558(8)
C11	0.1957(3)	0.85940(16)	1.0215(4)	0.0607(8)
H11	0.0990	0.8817	0.9560	0.073*
C12	0.6342(3)	0.76481(16)	1.3207(4)	0.0727(9)
H12A	0.6190	0.7391	1.4146	0.109*
H12B	0.7160	0.7992	1.3695	0.109*
H12C	0.6694	0.7350	1.2472	0.109*
C13	0.0579(4)	0.8031(2)	1.2070(5)	0.0748(10)

Comment

Pyrimidine compounds and their derivatives have been playing a significant role in the pharmaceutical and pesticide chemistry [3, 4]. In recent years, many pyrimidine compounds have displayed applications as antifungal, antibacterial, insecticidal, herbicidal, and antiviral agents [5–10]. A series of pyrimidine derivatives have been synthesized, which show novel structure and herbicidal activity [11].

The title structure crystallises in the monoclinic space group $P2_1/c$ with one molecule in the asymmetric unit. All bond lengths and angles are within normal ranges. The angle subtended by C(5), O(3) and C(8) is 121.5(2)°. The bond lengths of C(1)-O(1) and C(1)-O(2) are 1.272(3) and 1.257(3) Å respectively, in accordance with the single- and double-bond characters of these bonds, respectively. The hydroxy H atom could be located on a difference Fourier map. In the structure of the title compound there are two intermolecular hydrogen bonds, O(1)—H(1)···O(2) [D···A 2.638(4) Å, DHA = 164.9°] and C(12)—H(12A)···N(1) [D···A 3.513(4) Å, DHA = 159.9°].

Acknowledgements: We gratefully acknowledge support by China Postdoctoral Science Foundation (NO.: 2017M623070), the National Natural Science Foundation of China (NO.: 31701821), the Guizhou Science and Technology Fund Project (NO.: [2019]1015), Guiyang University Hospital Research Project (NO.: 2017ZD10), The Guizhou province Biological and Pharmaceutical engineering Research Centerand (NO.: QJHKY[2019]051), and the Construction Project of Key Laboratories from the Education Department of Guizhou Province (No.: QJHKY[2018]001).

References

1. Bruker. SMART, SAINT and SADABS. Brucker AXS Inc., Madison, Wisconsin, USA (1998).
2. Sheldrick, G. M.: A short history of SHELX. Acta Crystallogr. **A64** (2008) 112–122.
3. Shi, J. T.; Gong, Y. L.; Wang, Y.; Chen, Y.; Ding, S.; Liu, J.: Synthesis, structure and biological activity of 2-[2-(4-fluorobenzylidene)hydrazinyl]-4-(1-methyl-1*H*-indol-3-yl)thieno[3,2-*d*]pyrimidine. Chin. J. Struct. Chem. **38** (2019) 1530–1536.
4. Chen, Q.; Zhu, X. L.; Jiang, L. L.; Liu, Z. M.; Yang, G. F.: Synthesis, antifungal activity and CoMFA analysis of novel 1,2,4-triazolo[1,5-*a*] pyrimidine derivatives. Eur. J. Med. Chem. **43** (2008) 595–603.
5. Wu, W. N.; Chen, M. H.; Wang, R.; Tu, H. T.; Yang, M. F.; Ouyang, G. P.: Novel pyrimidine derivatives containing an amide moiety: design, synthesis, and antifungal activity. Chem. Pap. **73** (2019) 719–729.
6. Fang, Z.; Zheng, S.; Chan, K. F.; Yuan, W.; Guo, Q.; Wu, W. Y.; Liu, Y. K.; Lu, Y. J.; Leung, Y. C.; Chan, T. H.; Wong, K. Y.; Sun, N.: Design, synthesis and antibacterial evaluation of 2,4-disubstituted-6-thiophenyl-pyrimidines. Eur. J. Med. Chem. **161** (2019) 141–153.
7. Triloknadh, S.; Rao, C. V.; Nagaraju, K.; Krishna, N. H.; Ramaiahb, C. V.; Rajendra, W.; Trinath, D.; Suneetha, Y.: Design, synthesis, neuroprotective, antibacterial activities and docking studies of novel thieno[2,3-*d*]pyrimidine-alkyne Mannich base and oxadiazole hybrids. Bioorg. Med. Chem. Lett. **28** (2018) 1663–1669.
8. Liu, X. H.; Wang, Q.; Sun, Z. H.; Wedge, D. P. E.; Estep, J. J.; Tan, C. X.; Weng, J. Q.: Synthesis and insecticidal activity of novel pyrimidine derivatives containing urea pharmacophore against *Aedes Aegypti*. Pest Manag. Sci. **73** (2017) 953–959.
9. Shen, Z. H.; Sun, Z. H.; Becnel, J. J.; Estep, A.; David, D. E.; Tan, C. X.; Wen, J. Q.; Han, L.; Liu, X. H.: Synthesis and mosquiticidal activity of novel hydrazone containing pyrimidine derivatives against *Aedes aegypt*. Lett. Drug Des. Discov. **15** (2018) 951–956.
10. Chen, X. M.; Wang, S. H.; Cui, D. L.: The synthesis and herbicidal activity of 5-(substituted-phenyl)-4,6-dioxo-4,5,6,7-tetrahydropyrazolo(3,4-*d*)pyrimidines. J. Heterocycl. Chem. **52** (2015) 607–610.
11. Wang, Y. Y.; Xu, F. Z.; Zhu, Y. Y.; Song, B. A.; Liu, D. X.; Yu, G.; Chen, S. H.; Xue, W.; Wu, J.: Pyrazolo[3,4-*d*]pyrimidine derivatives containing a Schiff base moiety as potential antiviral agents. Bioorg. Med. Chem. Lett. **28** (2018) 2979–2984.