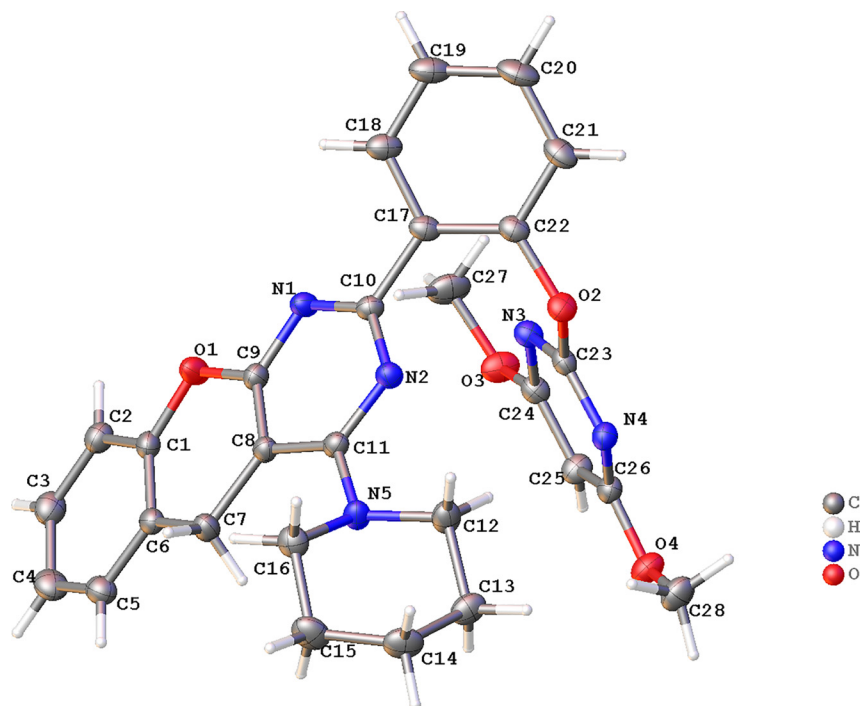


Dongtai Xie, Sufang Lei and Yuanxiang Li*

The crystal structure of 2-(2-((4,6-dimethoxypyrimidin-2-yl)oxy)phenyl)-4-(piperidin-1-yl)-5*H*-chromeno[2,3-*d*]pyrimidine, C₂₈H₂₇N₅O₄



<https://doi.org/10.1515/ncrs-2023-0511>

Received November 21, 2023; accepted December 30, 2023;
published online January 24, 2024

Abstract

C₂₈H₂₇N₅O₄, monoclinic, *P*₂₁/*c* (no. 14), *a* = 11.3563(15) Å, *b* = 17.547(2) Å, *c* = 12.8390(16) Å, β = 101.385(3)°, *V* = 2508.1(6) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0538, *wR*_{ref}(*F*²) = 0.1329, *T* = 292(2) K.

CCDC no.: 2308860

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.20 × 0.20 × 0.10 mm
Wavelength:	Mo <i>K</i> α radiation (0.71073 Å)
μ:	0.09 mm ^{−1}
Diffractometer, scan mode:	Bruker Apex Duo, φ and ω
θ _{max} , completeness:	27.0°, >99 %
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	14,614, 5449, 0.044
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2σ(<i>I</i> _{obs}), 2939
<i>N</i> (<i>param</i>) _{refined} :	336
Programs:	Bruker [1], SHELX [2–4], DIAMOND [5], Olex2 [6]

*Corresponding author: Yuanxiang Li, College of Chemistry and Materials Engineering, Huaihua University, Huaihua 418008, P.R. China, E-mail: hxyliyuanjun@163.com. <https://orcid.org/0000-0001-8917-9294>

Dongtai Xie, College of Chemistry and Materials Engineering, Huaihua University, Huaihua 418008, P.R. China

Sufang Lei, College of Biological and Food Engineering, Huaihua University, Huaihua 418008, P.R. China

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

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
C1	0.17728 (19)	0.27665 (12)	0.56693 (17)	0.0551 (5)
C2	0.0971 (2)	0.24144 (14)	0.48560 (17)	0.0662 (6)
H2	0.022092	0.262790	0.459805	0.079*
C3	0.1304 (2)	0.17439 (15)	0.44365 (18)	0.0742 (7)
H3	0.077794	0.150122	0.388995	0.089*
C4	0.2419 (2)	0.14333 (15)	0.48290 (19)	0.0786 (7)
H4	0.264408	0.097776	0.455353	0.094*
C5	0.3199 (2)	0.18013 (14)	0.56321 (18)	0.0690 (6)
H5	0.394791	0.158615	0.589189	0.083*
C6	0.29017 (18)	0.24792 (12)	0.60616 (16)	0.0532 (5)
C7	0.37539 (18)	0.28781 (12)	0.69300 (17)	0.0628 (6)
H7A	0.452785	0.292979	0.672537	0.075*
H7B	0.386581	0.257134	0.757051	0.075*
C8	0.33056 (17)	0.36523 (11)	0.71590 (15)	0.0494 (5)
C9	0.21584 (18)	0.38842 (13)	0.67250 (16)	0.0527 (5)
C10	0.24280 (17)	0.50487 (12)	0.74479 (14)	0.0489 (5)
C11	0.40089 (17)	0.42197 (12)	0.77654 (15)	0.0499 (5)
C12	0.59641 (18)	0.47693 (13)	0.85035 (19)	0.0707 (7)
H12A	0.583757	0.496962	0.917691	0.085*
H12B	0.574806	0.516186	0.796789	0.085*
C13	0.72641 (19)	0.45537 (15)	0.85922 (18)	0.0724 (7)
H13A	0.739684	0.439142	0.790245	0.087*
H13B	0.776501	0.499599	0.880900	0.087*
C14	0.7620 (2)	0.39222 (16)	0.93841 (19)	0.0827 (8)
H14A	0.761489	0.411086	1.009328	0.099*
H14B	0.843026	0.375657	0.936365	0.099*
C15	0.6773 (2)	0.32542 (16)	0.9148 (2)	0.0868 (8)
H15A	0.688820	0.300724	0.849914	0.104*
H15B	0.695664	0.288639	0.972072	0.104*
C16	0.54952 (19)	0.34998 (13)	0.90246 (16)	0.0658 (6)
H16A	0.497183	0.306465	0.882791	0.079*
H16B	0.535621	0.369446	0.969715	0.079*
C17	0.19220 (18)	0.58015 (13)	0.76475 (14)	0.0536 (5)
C18	0.07511 (19)	0.58296 (15)	0.78227 (16)	0.0675 (7)
H18	0.029905	0.538434	0.776973	0.081*
C19	0.0248 (2)	0.65030 (18)	0.80730 (18)	0.0815 (8)
H19	−0.053328	0.650773	0.819319	0.098*
C20	0.0897 (3)	0.71659 (18)	0.81449 (18)	0.0850 (8)
H20	0.056075	0.762040	0.831802	0.102*
C21	0.2059 (2)	0.71548 (14)	0.79580 (16)	0.0718 (7)
H21	0.250553	0.760237	0.800565	0.086*
C22	0.25494 (19)	0.64809 (13)	0.77023 (15)	0.0547 (5)
C23	0.39494 (19)	0.63025 (11)	0.65720 (16)	0.0499 (5)
C24	0.3302 (2)	0.59504 (12)	0.48912 (16)	0.0549 (5)
C25	0.44549 (19)	0.59362 (13)	0.47232 (16)	0.0605 (6)
H25	0.463224	0.581841	0.406489	0.073*
C26	0.53323 (19)	0.61072 (12)	0.55901 (17)	0.0546 (5)
C27	0.1226 (2)	0.57030 (17)	0.4302 (2)	0.0922 (9)
H27A	0.100392	0.617573	0.458638	0.138*
H27B	0.121288	0.530275	0.480891	0.138*
H27C	0.066736	0.558680	0.365704	0.138*
C28	0.74143 (19)	0.62000 (15)	0.63716 (18)	0.0805 (8)
H28A	0.727443	0.589569	0.695662	0.121*
H28B	0.742319	0.672924	0.656249	0.121*
H28C	0.817380	0.606409	0.620274	0.121*

Table 2: (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
N1	0.16781 (14)	0.45542 (10)	0.68711 (13)	0.0560 (5)
N2	0.35774 (14)	0.49187 (10)	0.78870 (12)	0.0514 (4)
N3	0.30243 (14)	0.61377 (9)	0.58206 (12)	0.0526 (4)
N4	0.51060 (15)	0.63006 (9)	0.65404 (13)	0.0525 (4)
N5	0.52072 (14)	0.40917 (10)	0.82101 (13)	0.0579 (5)
O1	0.13623 (12)	0.34326 (9)	0.60523 (12)	0.0699 (5)
O2	0.37364 (12)	0.65199 (8)	0.75377 (10)	0.0583 (4)
O3	0.24081 (13)	0.57683 (9)	0.40819 (10)	0.0732 (5)
O4	0.64781 (13)	0.60674 (10)	0.54673 (11)	0.0711 (5)

1 Source of materials

To a stirred mixture of 2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzaldehyde (0.519 g, 2 mmol), and malononitrile (0.1455 g, 2.2 mmol), piperidine (0.186 g, 2.2 mmol) in 15 mL EtOH was added. After stirring at room temperature for 30 min, 2-hydroxybenzaldehyde (0.269 g, 2.2 mmol) was added, and the mixture was stirred at room temperature for 10 h. After completion of the reaction, the solvent was evaporated to afford a crude mixture, which was further purified by flash chromatography (petroleum ether/ethyl acetate, V/V = 4:1) to get the title compound as a white solid (0.64 g, yield: 64 %). Crystals of the title compound were grown through slow evaporation of a petroleum ether/dichloromethane (V/V = 8:1) at 25/° for 3 days.

2 Experimental details

All H atoms were treated as riding, with C–H distances of 0.93 Å (aromatic), 0.97 Å (methylene) and 0.96 Å (methyl). The thermal factors of hydrogen atoms were set 1.2 times of their parent atoms (for aromatic and methylene) or 1.5 times of their parent atoms (for methyl).

3 Comment

As a continuation of our work on nitrogen-containing heterocyclic compounds which can be potentially applied in the fields of medical and organic chemistry [7], we have recently extended our synthesis work into deeper areas such as pyrimidine derivatives. The synthesis of pyrimidine-involved complexes are representing a challenge from both academic and industrial perspectives [8–10]. Especially, 5*H*-chromeno [2,3-*d*]pyrimidine derivatives have been emerged as promising and attractive scaffold in the development of potent anti-

tumor and antimicrobial agents in recent years. In a classical approach, the skeleton construction of 5*H*-chromeno[2,3-*d*]pyrimidine is accessible through three-component one-pot reaction in which ferric or sodium complexes were used as the catalyst. As an improved method with high yields, we have changed the earlier used 2-hydroxybenzaldehyde to 2-((4-hydroxy-6-methoxypyrimidin-2-yl)oxy)benzaldehyde. In this reaction, the catalysts can be avoided aiming to achieve the purpose of green environmental protection and economy. As a representative, the title compound was synthesized in a similar way with a yield up to 94 %. Herein, its crystal structure was reported.

The title molecule is shown in the figure. Relative to the middle benzene ring, the 5*H*-chromeno[2,3-*d*]pyrimidine and dimethoxypyrimidin moieties present a curved or highly distorted spatial configuration with the dihedral angle of 51.8(1)° between them. And each of the two parts are twisted away from the central benzen rings by 44.2(1)° and 64.5(1)°, respectively. It should be noted that the whole V-shaped spatial structure of the title compound is mainly determined by the spatial arrangement of each molecular group. For example, the distance between the N2 atom of pyrimidine and the ether O2 atom is only about 2.885(1) Å apart which is smaller than the van der Waals half-valence sum of these two atoms (3.28 Å) [11]. Due to the delocalization effects of the C17–C22 benzene and C23–C26/N3/N4 pyridine rings adjacent to the oxygen O2 atom, it may carry some π electrons which can interact with the pyridine N2 atoms via the $\pi \cdots \pi$ interaction. This delocalization can also be reflected by the two short C–O bond distances around O2 (1.364(2) and 1.407(2) Å), which is apparently shorter than the normal C–O single bond distance, for instance d_{C27-O3} and d_{C28-O4} is 1.430(2) Å in the title compound.

In the crystal packing, the DPPP molecules are mainly linked together by the intermolecular C–H $\cdots$ O, C–H $\cdots$ N and C–H $\cdots\pi$ stacking into the final three-dimensional network. Although several aromatic rings exist, no

apparent $\pi \cdots \pi$ stacking interactions are observed by a analysis of PLATON [12].

Author contribution: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: Huaihua Key Laboratory project (No. 2023R2206).

Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

References

1. Bruker. *SMART and SAINT*; Bruker AXS Inc.: Madison, WI, USA, **2003**.
2. Sheldrick G. M. *SHELXTL* – integrated space-group and crystal-structure determination. *Acta Crystallogr.* **2015**, A71, 3–8.
3. Sheldrick G. M. Crystal structure refinement with SHELXL. *Acta Crystallogr.* **2015**, C71, 3–8.
4. Sheldrick G. M. A short history of SHELX. *Acta Crystallogr.* **2008**, A64, 112–122.
5. Brandenburg K. *DIAMOND*; Crystal Impact GbR: Bonn, Germany, **2006**.
6. 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. Crystallogr.* **2009**, 42, 339–341.
7. Wang L. T., Lei S. F., Li Y. X. The crystal structure of 4,4'-dichloro-3,5'-diphenyl-1'*H*-1,3'-bipyrazole, $C_{18}H_{12}Cl_2N_4$. *Z. Kristallogr. N. Cryst. Struct.* **2023**, 238, 249–252.
8. Mirza-Aghayan M., Saeedi M., Boukherroub R. An efficient CuO/rGO/TiO₂ photocatalyst for the synthesis of benzopyranopyrimidine compounds under visible light irradiation. *New J. Chem.* **2022**, 46, 3817–3830.
9. Mostafavi M. M., Movahedi F. Synthesis, characterization, and heterogeneous catalytic activity of sulfamic acid functionalized magnetic IRMOF-3. *Eur. J. Inorg. Chem.* **2019**, 6, 787–793.
10. Brahmachari G., Das S. Sodium formate-catalyzed one-pot synthesis of benzopyranopyrimidines and 4-thio-substituted 4*H*-chromenes via multicomponent reaction at room temperature. *J. Heterocycl. Chem.* **2015**, 52, 653–659.
11. Rowland R. S., Taylor R. Intermolecular nonbonded contact distances in organic crystal structures: comparison with distances expected from van der Waals radii. *J. Phys. Chem.* **1996**, 100, 7384–7391.
12. Spek A. L. Structure validation in chemical crystallography. *Acta Crystallogr.* **2009**, D65, 148–155.