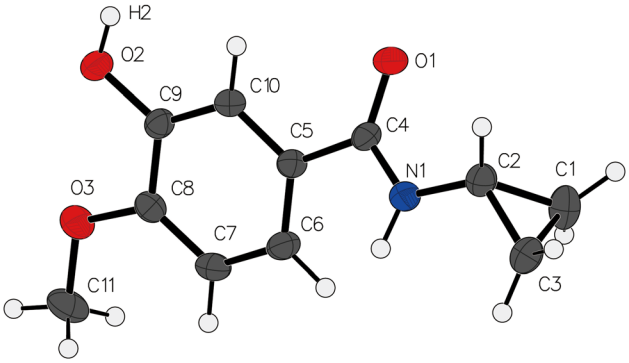
Hongjuan Tong*, Xiaona Xu, Zhoujing Zhu and Bin Liu

Crystal structure of *N*-cyclopropyl-3-hydroxy-4-methoxybenzamide, $C_{11}H_{13}NO_3$



https://doi.org/10.1515/ncrs-2023-0379
Received August 19, 2023; accepted September 8, 2023;
published online September 21, 2023

Abstract

$C_{11}H_{13}NO_3$, monoclinic, $P2_1/n$ (no. 14), a = 8.0478(3) Å, b = 9.8093(4) Å, c = 13.1602(5) Å, β = 104.712(2)°, V = 1004.85(7) Å^3, Z = 1, $R_{gt}(F)$ = 0.0395, $wR_{ref}(F^2)$ = 0.1010, T = 170 K.

CCDC no.: 2288223

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:	0.19 × 0.12 × 0.08 mm
Wavelength:	Mo *Kα* radiation (0.71073 Å)
μ:	0.10 mm^{-1}
Diffractometer, scan mode:	D8 VENTURE, φ and ω
θ_{max}, completeness:	26.4°, 99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	8509, 2027, 0.042
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1606
$N(param)_{refined}$:	145
Programs:	Bruker [1], SHELX [2, 3], Olex2 [4]

1 Source of materials

A mixture of 3-hydroxy-4-methoxybenzoic acid (1.68 g, 10 mmol), cyclopropanamine (1.71 g, 30 mmol), 2-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HATU) (4.18 g, 11 mmol) and *N*,*N*-diisopropylethyl-amine (2.58 g, 20 mmol) was dissolved in *N*,*N*-dimethylformamide (20 mL). The mixture was stirred for 4 h at 40 °C, until the TLC indicated the reaction was completed. The mixture was diluted with brine, and then extracted with ethyl acetate (3 × 30 mL). The organic phase was washed with brine (30 mL), dried with anhydrous sodium sulphate, and then concentrated under pressure. The title compound was separated by silica-gel column chromatography with ethyl acetate-petroleum ether (50 %). The target product was obtained as a white solid. Yield: 87.0 %.

2 Experimental details

In the refinement process, the positions of hydrogen atoms were treated as idealized riding atoms, with their coordinates determined based on the surrounding atoms. The U_{iso} values were set to 1.2 times the U_{eq} values of the parent atoms. The crystal structure was solved using the ShelXT software [2], and refinement was performed using ShelXL [3] within the Olex2 software platform [4].

3 Comment

Benzamide derivatives have been investigated for their diverse biological properties [5, 6]. The acquisition of the accurate crystal structure of benzamide derivatives holds significant potential in the exploration of novel drug candidates. The scientific community has made substantial progress in documenting a multitude of relevant structural data [7–13].

In the depicted molecular structure within the figure of the manuscript, the central benzene ring is substituted by a

***Corresponding author: Hongjuan Tong**, Xianyang Key Laboratory of Molecular Imaging and Drug Synthesis, School of Pharmacy, Shaanxi Institute of International Trade & Commerce, Xianyang, Shaanxi, China, E-mail: dearthj@126.com. https://orcid.org/0000-0001-7219-8018
Xiaona Xu, School of Pharmaceutical & Chemical Engineering, Xianyang Vocational Technical College, Xianyang, Shaanxi, China
Zhoujing Zhu and Bin Liu, Xianyang Key Laboratory of Molecular Imaging and Drug Synthesis, School of Pharmacy, Shaanxi Institute of International Trade & Commerce, Xianyang, Shaanxi, China. https://orcid.org/0000-0003-2852-7739 (B. Liu)

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.4365 (2)	0.71964 (17)	0.15235 (12)	0.0362 (4)
H1A	0.353326	0.716007	0.196268	0.043*
H1B	0.464628	0.812527	0.132444	0.043*
C2	0.5755 (2)	0.61482 (15)	0.17137 (11)	0.0283 (4)
H2A	0.689294	0.644862	0.161749	0.034*
C3	0.4314 (2)	0.60753 (16)	0.07497 (12)	0.0311 (4)
H3A	0.344869	0.534648	0.070964	0.037*
H3B	0.456142	0.631144	0.007157	0.037*
C4	0.68371 (18)	0.52159 (15)	0.34720 (11)	0.0238 (3)
C5	0.66359 (18)	0.41563 (14)	0.42465 (11)	0.0236 (3)
C6	0.50854 (19)	0.35148 (15)	0.42081 (12)	0.0270 (3)
H6	0.409783	0.373050	0.366226	0.032*
C7	0.49726 (19)	0.25558 (15)	0.49673 (12)	0.0276 (3)
H7	0.390040	0.213519	0.494456	0.033*
C8	0.64067 (19)	0.22093 (14)	0.57549 (11)	0.0246 (3)
C9	0.79705 (19)	0.28715 (14)	0.58093 (11)	0.0241 (3)
C10	0.80620 (18)	0.38377 (15)	0.50650 (11)	0.0243 (3)
H10	0.911804	0.429633	0.511015	0.029*
C11	0.4855 (2)	0.05878 (18)	0.65113 (13)	0.0376 (4)
H11A	0.440197	0.012234	0.583902	0.056*
H11B	0.402867	0.127530	0.661257	0.056*
H11C	0.504583	−0.007863	0.708412	0.056*
N1	0.57891 (17)	0.51331 (13)	0.25076 (10)	0.0274 (3)
H1	0.511 (2)	0.4389 (19)	0.2331 (14)	0.043 (5)*
O1	0.79438 (13)	0.61218 (11)	0.37228 (8)	0.0321 (3)
O2	0.93602 (14)	0.25167 (11)	0.66074 (8)	0.0302 (3)
H2	1.026 (3)	0.300 (2)	0.6538 (16)	0.058 (7)*
O3	0.64497 (14)	0.12376 (11)	0.65087 (8)	0.0309 (3)

N-cyclopropyl moiety, a hydroxyl group and the methoxy group. Notably, the C4–N1–C2 bond angle in the amide group is determined to be 122.61(13)°. Furthermore, the benzene ring plane exhibits a significant torsion angle of 58.56° with respect to the cyclohexyl plane.

Within the crystal lattice, molecular association is enhanced through the formation of a O2–H2…O1 hydrogen bonding interaction. The angle between these hydrogen bonds is measured as 174(3)°, with a corresponding bond length of 1.79(3) Å.

Acknowledgements: This work was financially supported by the projects of Natural Science Foundation of Shannxi Province (2021JM-561), Scientific research plan project of Shaanxi Provincial Department of Education (22JK0277), Key Laboratory of Molecular Imaging and Drug Synthesis of Xianyang city (2021QXNL-PT-0008), Doctoral research fund project of Xianyang Vocational and Technical College (2021BK01) and the scientific research fund project of Xianyang Vocational and Technical College (2020KJB02).

References

1. Bruker. SAINT, APEX2 and SADABS; Bruker AXS Inc.: Madison, WI, USA, 2012.
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. 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.
5. McGuire R. T., Lundrigan T., MacMillan J. W. M., Robertson K. N., Yadav A. A., Stradiotto M. Mapping dual-base-enabled nickel-catalyzed aryl amidations: application in the synthesis of 4-quinolones. *Angew. Chem. Int. Ed.* 2022, *61*, e202200352.
6. Oliveira C., Gaspar A., Gomes L. R., Low J. N., Borges F., Cagide F. Structural elucidation of a series of benzamide derivatives. *Magn. Reson. Chem.* 2018, *56*, 216–223.
7. Wu L., Wang T., Gao C., Huang W., Qu J., Chen Y. Skeletal reconstruction of 3-alkylidenepyrrolidines to azepines enabled by Pd-catalyzed C–N bond cleavage. *ACS Catal*. 2021, *11*, 1774–1779.
8. Durant F., Renard P., Evrard G., Michel A. Molecular structure of benzamide neuroleptics. Ⅲ. *N*-(8–Benzyl-1αH,5αH-nortropan-3α-yl)-2,6-dimethoxybenzamide, $C_{23}H_{28}N_2O_3$. *Acta Crystallogr.* 1985, *C41*, 1361–1362.
9. Furuya T., Iwanami S., Takenaka A., Sasada Y. Structure of *cis-N*-(1-benzyl-2-methyl-3-pyrrolidinyl)-5-chloro-2-methoxybenzamide. *Acta Crystallogr*. 1986, *C42*, 1071–1073.
10. Nasir M. M. F., Hassan I. N., Yamin B. M., Daud W. R. W., Kassim M. B. 3-(3–Methoxybenzoyl)-1,1-diphenylthiourea. *Acta Crystallogr*. 2011, *E67*, o1947–o1948.
11. Gomes L. R., Low J. N., Oliveira C., Cagide F., Borges F. Crystal structures of three 3,4,5-trimethoxybenzamide-based derivatives. *Acta Crystallogr*. 2016, *E72*, 675–682.
12. Zhang J., Guo S., Guo Y., Yang Y. The crystal structure of N-cyclopentyl-3-hydroxy-4-methoxybenzamide, $C_{13}H_{17}NO_3$. *Z. Kristallogr. N. Cryst. Struct.* 2022, *237*, 551–553.
13. Zhang J., Zhao X., Cai C. The crystal structure of *N*-cyclohexyl-3-hydroxy-4-methoxybenzamide, $C_{14}H_{19}NO_3$. *Z. Kristallogr. N. Cryst. Struct.* 2022, *237*, 543–545.