Sheng-Nan Zhang, Feng-Lan Zhao and Qing-Guo Meng*

Crystal structure of (*E*)-7-hydroxy-2-((6-methoxypyridin-3-yl)methylene)-3,4-dihydronaphthalen-1(2*H*)-one, C₁₇H₁₅NO₃

Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	0.14 × 0.12 × 0.11 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.10 mm ⁻¹
Diffractometer, scan mode:	SuperNova, CCD plate scans
$\theta_{\max}$, completeness:	25.5°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	6179, 2512, 0.024
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2118
$N(\text{param})_{\text{refined}}$:	192
Programs:	CrysAlis ^{PRO} [1], SHELX [2,3]

<https://doi.org/10.1515/ncrs-2021-0382>

Received October 4, 2021; accepted October 22, 2021;
published online November 3, 2021

Abstract

C₁₇H₁₅NO₃, monoclinic, $P2_1/n$ (no. 14), $a = 4.3970(3)$ Å, $b = 13.8942(8)$ Å, $c = 22.0484(14)$ Å, $\beta = 91.099(6)^\circ$, $V = 1346.75(15)$, $Z = 4$, $R_{\text{gt}}(F) = 0.0412$, $wR_{\text{ref}}(F^2) = 0.1003$, $T = 150$ K.

CCDC no.: 2078244

Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Source of material

Five milliliters (25%) of sodium hydroxide aqueous solution was added dropwise to the mixture of 7-hydroxy-3,4-dihydronaphthalen-1(2*H*)-one and 6-methoxynicotinaldehyde in 10 mL methanol and stirred at room

temperature for 3 h. The in process-control was monitored by silica gel thin layer chromatography (TLC, 254 nm). When the reaction was stopped, the precipitate was filtered from the reaction mixture and dissolved with ethyl acetate. The organic phase was washed successively with water and brine, and dried over anhydrous sodium sulfate. After filtration, the ethyl acetate solution was condensed *in vacuo* to yield a white solid, which was purified by silica-gel column chromatography (petroleum ether: ethyl acetate = 1:2, *v/v*). Crystals of the title compound were obtained by recrystallization in dichloromethane and methanol (1:1, *v/v*) system and dried under *vacuo* at 65 °C for 3 h.

Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with $d(\text{C-H}) = 0.97$ Å (methylene), $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$, and $d(\text{C-H}) = 0.93$ Å (aromatic), $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$.

Comment

Existing studies have used 3,4-dihydronaphthalen-1(2*H*)-one (DHN) derivatives that showed anti-tumor and anti-inflammatory activities as novel allergic and inflammatory responses modifiers [4–7] and as potential retinoic acid (RA)-metabolizing enzymes inhibitors to treat skin diseases and cancer. However, DHN derivatives are rarely developed as

*Corresponding author: Qing-Guo Meng, School of Pharmacy, Collaborative Innovation Center of Advanced Drug Delivery System and Biotech Drugs in Universities of Shandong, Key Laboratory of Molecular Pharmacology and Drug Evaluation (Yantai University), Ministry of Education, Yantai University, Yantai, P. R. China, E-mail: qingguomeng@163.com

Sheng-Nan Zhang and Feng-Lan Zhao, School of Pharmacy, Collaborative Innovation Center of Advanced Drug Delivery System and Biotech Drugs in Universities of Shandong, Key Laboratory of Molecular Pharmacology and Drug Evaluation (Yantai University), Ministry of Education, Yantai University, Yantai, P. R. China. <https://orcid.org/0000-0003-2395-1346> (S.-N. Zhang)

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	0.4103 (3)	0.59130 (11)	0.32499 (7)	0.0209 (3)
C2	0.2800 (3)	0.62282 (11)	0.38360 (7)	0.0208 (3)
C3	0.2984 (4)	0.55204 (11)	0.43536 (7)	0.0230 (4)
H3A	0.160627	0.571695	0.466893	0.028*
H3B	0.503212	0.551673	0.452488	0.028*
C4	0.2146 (3)	0.45095 (11)	0.41360 (7)	0.0222 (3)
H4A	0.242599	0.405774	0.446782	0.027*
H4B	0.001897	0.449622	0.401130	0.027*
C5	0.4936 (3)	0.32575 (11)	0.35329 (7)	0.0226 (4)
H5	0.429679	0.279271	0.380596	0.027*
C6	0.6726 (4)	0.29884 (11)	0.30550 (7)	0.0240 (4)
H6	0.725640	0.234559	0.300547	0.029*
C7	0.7744 (3)	0.36760 (11)	0.26460 (7)	0.0209 (3)
C8	0.6895 (3)	0.46246 (11)	0.27141 (7)	0.0206 (3)
H8	0.755823	0.508562	0.244088	0.025*
C9	0.5041 (3)	0.48944 (11)	0.31927 (7)	0.0188 (3)
C10	0.4070 (3)	0.42076 (11)	0.36142 (7)	0.0185 (3)
C11	0.1545 (3)	0.71073 (11)	0.38609 (7)	0.0222 (4)
H11	0.138271	0.742258	0.348966	0.027*
C12	0.0392 (3)	0.76505 (10)	0.43746 (7)	0.0205 (3)
C13	0.1408 (4)	0.75574 (11)	0.49728 (7)	0.0260 (4)
H13	0.283352	0.707946	0.505846	0.031*
C14	−0.1518 (4)	0.87792 (11)	0.53065 (7)	0.0239 (4)
C15	−0.2689 (4)	0.89500 (12)	0.47248 (8)	0.0334 (4)
H15	−0.410710	0.943597	0.465416	0.040*
C16	−0.1707 (4)	0.83881 (11)	0.42625 (7)	0.0261 (4)
H16	−0.243654	0.849544	0.386960	0.031*
C17	−0.1111 (4)	0.92834 (13)	0.63415 (8)	0.0343 (4)
H17A	−0.161393	0.867427	0.651909	0.051*
H17B	−0.182775	0.979394	0.659500	0.051*
H17C	0.105531	0.933248	0.630514	0.051*
N1	0.0488 (3)	0.81053 (9)	0.54364 (6)	0.0250 (3)
O1	0.9577 (3)	0.34428 (8)	0.21739 (5)	0.0277 (3)
H1	0.994506	0.286436	0.218249	0.042*
O2	0.4448 (3)	0.64764 (8)	0.28244 (5)	0.0302 (3)
O3	−0.2526 (3)	0.93570 (9)	0.57523 (5)	0.0348 (3)

anti-neuroinflammatory drugs, so the synthesis and crystal structure of novel benzylidene-substituted DHN derivatives with anti-neuroinflammatory activities are of great significance. Our group synthesized some of these compounds and studied their anti-neuroinflammatory activity [8–12].

Single crystal structure analysis revealed that the title compound crystallized in the monoclinic space group *P*₂/*n*. The ORTEP diagram is presented in the Figure. Bond lengths and angles are all in the expected ranges. There is only one drug molecule in the asymmetric unit. The C(2)=C(11) olefinic bond adopts the *E* stereochemistry [13, 14]. Because of the sterical effect of 3,4-dihydronaphthalen-1(2*H*)-1, 7-hydroxyphenyl and 6-methoxypyridin-3-yl groups both are not coplanar with each other, showing a dihedral angle

of approximately 52°. This twisted configuration may increase likelihood of interactions with bioactive molecules [15].

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

Research funding: This work was supported by Science and Technology Innovation Development Plan of Yantai (No. 2020XDRH105) and the National Natural Science Foundation of China (No. 81473104).

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

References

1. Rigaku OD. CrysAlis^{PRO}; Rigaku Oxford Diffraction Ltd: Yarnton, Oxfordshire, England, 2017.
2. Sheldrick G. M. A short history of *SHELX*. *Acta Crystallogr.* 2008, *A64*, 112–122.
3. Sheldrick G. M. Crystal structure refinement with *SHELXL*. *Acta Crystallogr.* 2015, *C71*, 3–8.
4. Wang F. L., Zhang R. X., Cui Y., Sheng L. P., Sun Y. P., Tian W., Liu X., Liang S. Z. Design, synthesis and biological evaluation of 3,4-dihydronaphthalen-1(2*H*)-one derivatives as Bcl-2 inhibitors. *Res. Chem. Intermed.* 2017, *43*, 5933–5942.
5. Barlow J. W., Zhang T., Woods O., Byrne A. J., Walsh J. J. Novel mast cell-stabilising amine derivatives of 3,4-dihydronaphthalen-1(2*H*)-one and 6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-one. *Med. Chem.* 2011, *7*, 213–223.
6. Zhang J. Q., Zhang Q., Xu Y. R., Li H. X., Zhao F. L., Wang C. M., Liu Z., Liu P., Liu Y. N., Meng Q. G., Zhao F. Synthesis and *in vitro* anti-inflammatory activity of C20 epimeric ocotillol-type triterpenes and protopanaxadiol. *Planta Med.* 2019, *85*, 292–301.
7. Kirby A. J., Le L. R., Maharlouie F., Mason P., Nicholls P. J., Smith H. J., Simons C. Inhibition of retinoic acid metabolising enzymes by 2-(4-aminophenylmethyl)-6-hydroxy-3,4-dihydronaphthalen-1(2*H*)-one and related compounds. *J. Enzym. Inhib. Med. Chem.* 2003, *18*, 27–33.
8. Zhang X. F., Meng Q. G. Crystal structure of (*E*)-2-((2-methoxy-3-pyridyl) methylene)-7-fluoro-3,4-dihydronaphthalen-1(2*H*)-one, C₁₇H₁₄FNO₂. *Z. Kristallogr. N. Cryst. Struct.* 2021, *236*, 507–509.
9. Luan M. Z., Meng Q. G. Crystal structure of (*E*)-7-methoxy-2-((5-methoxypyridin-3-yl)methylene)-3,4-dihydronaphthalen-1(2*H*)-one, C₁₈H₁₇NO₃. *Z. Kristallogr. N. Cryst. Struct.* 2021, *236*, 387–389.
10. Sun Y., Gao Z. F., Wang C. H., Hou G. G. Synthesis, crystal structures and anti-inflammatory activity of fluorine-substituted 1,4,5,6-tetrahydrobenzo[*h*]quinazolin-2-amine derivatives. *Acta Crystallogr. C Struct. Chem.* 2019, *75*, 1157–1165.
11. Sun Y., Zhou Y. Q., Liu Y. K., Zhang H. Q., Hou G. G., Meng Q. G., Hou Y. Potential anti-neuroinflammatory NF-001082B inhibitors based on 3,4-dihydronaphthalen-1(2*H*)-one derivatives. *J. Enzym. Inhib. Med. Chem.* 2020, *35*, 1631–1640.

12. Wang L., Meng Q. G., Jiang N., Wei L., Wang C. H. Crystal structure of (*E*)-7-methoxy-2-((6-methoxypyridin-3-yl)methylene)-3,4-dihydronaphthalen-1(2*H*)-one, $C_{18}H_{17}NO_3$. *Z. Kristallogr. N. Cryst. Struct.* 2021, 236, 1069–1071.
13. Yao B. R., Sun Y., Chen S. L., Suo H. D., Zhang Y. L., Wei H., Wang C. H., Zhao F., Cong W., Xin W. Y., Hou G. G. Dissymmetric pyridyl-substituted 3,5-bis(arylidene)-4-piperidones as anti-hepatoma agents by inhibiting NF-kappaB pathway activation. *Eur. J. Med. Chem.* 2019, 167, 187–199.
14. Li N., Xin W. Y., Yao B. R., Wang C. H., Cong W., Zhao F., Li H. J., Hou Y., Meng Q. G., Hou G. G. Novel dissymmetric 3,5-bis(arylidene)-4-piperidones as potential antitumor agents with biological evaluation *in vitro* and *in vivo*. *Eur. J. Med. Chem.* 2018, 147, 21–33.
15. Li N., Yao B. Y., Wang C. H., Meng Q. G., Hou G. G. Synthesis, crystal structure and activity evaluation of novel 3,4-dihydro-1-benzoxepin-5(2*H*)-one derivatives as protein-tyrosine kinase (PTK) inhibitors. *Acta Crystallogr. C* 2017, C73, 1003–1009.