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

<https://doi.org/10.1515/ncrs-2021-0245>

Received June 15, 2021; accepted July 13, 2021;

published online August 2, 2021

Abstract

C₁₇H₁₅NO₃, triclinic, $P\bar{1}$ (no. 2), $a = 7.5016(4)$ Å, $b = 13.6750(8)$ Å, $c = 14.8557(9)$ Å, $\alpha = 115.469(6)^\circ$, $\beta = 91.726(5)^\circ$, $\gamma = 97.325(5)^\circ$, $V = 1358.48(15)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0442$, $wR_{\text{ref}}(F^2) = 0.1095$, $T = 100$ K.

CCDC no.: 2078640

The molecular structure is shown in the figure. Displacement ellipsoids are drawn at the 40% probability level.

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Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	0.13 × 0.12 × 0.10 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.10 mm ⁻¹
Diffractometer, scan mode:	SuperNova
θ_{max} , completeness:	25.5°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	9244, 5038, 0.025
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 4080
$N(\text{param})_{\text{refined}}$:	383
Programs:	CrysAlis ^{PRO} [1], SHELX [2, 3]

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

Source of material

Drop 5 mL (25%) sodium hydroxide aqueous solution to 7-hydroxy-3,4-dihydronaphthalen-1(2*H*)-one and 6-methoxypicolinaldehyde, then add 10 mL methanol and stir at room temperature for 3 h. Silica gel thin layer method was used to monitor the process control chromatography (TLC, 254 nm). When the reaction was stopped, the precipitate was filtered from the reaction and dissolved with ethyl acetate. The organic phase was washed successively by water and brine, and dried with anhydrous sodium sulfate. After filtration, the ethyl acetate was condensed under vacuo to yield a white solid, which was purified by silica gel column chromatography (petroleum ether: ethyl acetate = 1:2, v/v). Appropriate crystals of the title compound were obtained by recrystallization from dichloromethane and methanol (1:1, v/v) and dried in 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), $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$.

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	0.6511 (2)	0.37693 (13)	0.02118 (11)	0.0175 (3)
C2	0.4853 (2)	0.33607 (13)	0.05593 (11)	0.0182 (4)
C3	0.4599 (2)	0.21732 (14)	0.03643 (12)	0.0228 (4)
H3A	0.334953	0.194165	0.042426	0.027*
H3B	0.534525	0.209552	0.086724	0.027*
C4	0.5094 (2)	0.14321 (14)	−0.06736 (12)	0.0227 (4)
H4A	0.504387	0.069222	−0.073809	0.027*
H4B	0.421911	0.141177	−0.117786	0.027*
C5	0.8061 (2)	0.11105 (14)	−0.14522 (12)	0.0208 (4)
H5	0.765646	0.035969	−0.173143	0.025*
C6	0.9747 (2)	0.14846 (14)	−0.16421 (12)	0.0212 (4)
H6	1.046478	0.098841	−0.203713	0.025*
C7	1.0359 (2)	0.26065 (14)	−0.12384 (11)	0.0188 (4)
C8	0.9297 (2)	0.33332 (13)	−0.06384 (11)	0.0183 (4)
H8	0.970838	0.408287	−0.036556	0.022*
C9	0.7604 (2)	0.29542 (13)	−0.04355 (11)	0.0174 (4)
C10	0.6955 (2)	0.18273 (13)	−0.08550 (11)	0.0188 (4)
C11	0.3764 (2)	0.40996 (14)	0.10176 (11)	0.0191 (4)
H11	0.418808	0.479991	0.108651	0.023*
C12	0.2038 (2)	0.40092 (13)	0.14284 (11)	0.0177 (4)
C13	−0.0323 (2)	0.29892 (14)	0.17238 (12)	0.0203 (4)
C14	−0.1197 (2)	0.38971 (15)	0.22199 (12)	0.0239 (4)
H14	−0.228044	0.383070	0.249224	0.029*
C15	−0.0391 (2)	0.48863 (15)	0.22875 (12)	0.0240 (4)
H15	−0.092044	0.551250	0.260781	0.029*
C16	0.1232 (2)	0.49391 (14)	0.18691 (12)	0.0210 (4)
H16	0.177496	0.559801	0.188568	0.025*
C17	−0.0400 (2)	0.10651 (15)	0.10537 (14)	0.0297 (4)
H17A	−0.030161	0.099968	0.038791	0.045*
H17B	−0.114177	0.042343	0.102317	0.045*
H17C	0.078006	0.113579	0.136486	0.045*
C18	0.7915 (2)	0.87256 (13)	0.49960 (11)	0.0183 (4)
C19	0.9319 (2)	0.79937 (13)	0.47370 (11)	0.0184 (4)
C20	0.9193 (2)	0.71556 (15)	0.51506 (13)	0.0258 (4)
H20A	1.033228	0.688049	0.510952	0.031*
H20B	0.826312	0.654267	0.474908	0.031*
C21	0.8751 (2)	0.76514 (15)	0.62350 (12)	0.0245 (4)
H21A	0.859672	0.708543	0.646730	0.029*
H21B	0.974653	0.820803	0.664974	0.029*
C22	0.5825(2)	0.81246 (14)	0.70147 (12)	0.0219 (4)
H22	0.602239	0.775285	0.739679	0.026*
C23	0.4317(2)	0.86352 (14)	0.71286 (12)	0.0225 (4)
H23	0.351119	0.860032	0.758138	0.027*
C24	0.3998 (2)	0.92010 (13)	0.65701 (12)	0.0198 (4)
C25	0.5171 (2)	0.92188 (13)	0.58793 (11)	0.0186 (4)
H25	0.495005	0.958266	0.549320	0.022*
C26	0.6691 (2)	0.86950 (13)	0.57534 (11)	0.0176 (4)
C27	0.7060 (2)	0.81539 (13)	0.63387 (12)	0.0193 (4)
C28	1.0580 (2)	0.81543 (13)	0.41681 (11)	0.0172 (3)
H28	1.041033	0.868530	0.395372	0.021*
C29	1.2178 (2)	0.76286 (13)	0.38312 (11)	0.0176 (4)
C30	1.4004 (2)	0.63949 (14)	0.37863 (13)	0.0224 (4)
C31	1.5203 (2)	0.66874 (14)	0.32111 (13)	0.0249 (4)
H31	1.622063	0.635261	0.301572	0.030*
C32	1.4822 (2)	0.74872 (14)	0.29457 (12)	0.0229 (4)

Table 2: (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
H32	1.558203	0.770683	0.256145	0.027*
C33	1.3285 (2)	0.79681 (14)	0.32566 (11)	0.0203 (4)
H33	1.300573	0.851035	0.308087	0.024*
C34	1.3078 (2)	0.52660 (18)	0.45777 (18)	0.0454 (6)
H34A	1.305991	0.587024	0.522152	0.068*
H34B	1.340584	0.465398	0.466487	0.068*
H34C	1.190225	0.506202	0.421826	0.068*
N1	0.12467 (16)	0.30214 (11)	0.13616 (9)	0.0189 (3)
N2	1.25470 (17)	0.68363 (11)	0.40945 (10)	0.0201 (3)
O1	0.69851 (14)	0.47535 (9)	0.04534 (8)	0.0232 (3)
O2	1.20095 (14)	0.29427 (10)	−0.14626 (9)	0.0258 (3)
H2	1.227398	0.360985	−0.114419	0.039*
O3	−0.11985 (14)	0.20131 (10)	0.16273 (9)	0.0255 (3)
O4	0.77477 (14)	0.93468 (9)	0.46041 (8)	0.0217 (3)
O5	0.25137 (14)	0.97224 (10)	0.67322 (9)	0.0251 (3)
H5A	0.241687	0.998242	0.633132	0.038*
O6	1.43737 (15)	0.55831 (10)	0.40217 (10)	0.0338 (3)

Comment

In inflammatory neurodegenerative diseases of the central nervous system (CNS), the microglia are activated and polarized into pro-inflammatory M1 phenotype. Neuroinflammation is a mediator and key factor in the progression of brain diseases [4]. The inflammatory process may lead to excessive release of inflammatory mediators or cytokines, such as tumor necrosis factor- α (TNF- α), interleukin (IL)-6, and so on [5]. Existing studies have showed that 3,4-dihydronaphthalene-1(2*H*)-one (DHN) derivatives have anti-tumor and anti-inflammatory activity as modifiers for allergic and inflammatory responses, however, few studies on DHN derivatives against neuroinflammation have been conducted. Thus it is promising to synthesize novel pyridine substituted derivatives to fight neuroinflammation [6]. Some DHN derivatives had been designed and synthesized as anti-inflammatory agents [7, 8]. Our group investigated DHN derivatives based on pyridine groups and tested their anti-neuroinflammatory activity. The results showed that the methoxy substituted compounds have better activity.

The title compound crystallizes in the triclinic space group $P\bar{1}$. Bond lengths and angles are all in the expected ranges [9]. There are two drug molecules in the asymmetric unit. 6-Methoxypyridine and carbonyl groups adopt the E stereochemistry. Because of the distorting effect of 3,4-dihydronaphthalene-1(2*H*)-one, the 7-hydroxyphenyl and 6-methoxy pyridine groups are not coplanar. This twisted configuration may increase the likelihood of interactions

with bioactive molecules, for the purposes of creating more potent biological activity [10].

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. Gao C. L., Hou G. G., Liu J., Ru T., Xu Y. Z., Zhao S. Y., Ye H., Zhang L. Y., Chen K. X., Guo Y. W., Pang T., Li X. W. Synthesis and target identification of benzoxepane derivatives as potential anti-inflammatory agents for ischemic stroke. *Angew. Chem. Int. Ed.* 2020, 59, 2429–2439.
5. Li N., Xin W. Y., Yao B. R., Cong W., Wang C. H., Hou G. G. *N*-Phenylsulfonyl-3,5-bis(arylidene)-4-piperidone derivatives as activation NF- κ B inhibitors in hepatic carcinoma cell lines. *Eur. J. Med. Chem.* 2018, 155, 531–544.
6. Zhou Y. Q., Hou G. G., Meng Q. G., Hou Y. Crystal structure and anti-inflammatory activity of (3*E*,5*E*)-1-((4-chlorophenyl)sulfonyl)-3-(pyridin-4-ylmethylene)-5-(2-(trifluoromethyl)benzylidene)piperidin-4-one, $C_{25}H_{18}ClF_3N_2O_3S$. *Z. Kristallogr. N. Cryst. Struct.* 2020, 235, 411–413.
7. Zhang X. F., Meng Q. G. Crystal structure of (3*E*,5*E*)-2-((2-methoxy-3-pyridyl)methylene)-7-fluoro-3,4-dihydronaphthalen-1(2*H*)-one, $C_{17}H_{14}FNO_2$. *Z. Kristallogr. N. Cryst. Struct.* 2021, 236, 507–509.
8. Luan M. Z., Wang H. Y., Zhang M., Song J., Hou G. G., Zhao F. L., Meng Q. G. Crystal structure of (*E*)-2-(3,5-bis(trifluoromethyl)benzylidene)-7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one, $C_{20}H_{14}F_6O_2$. *Z. Kristallogr. N. Cryst. Struct.* 2021, 236, 61–63.
9. Xiong C. L., Lan Y. D., Song X. Y., Xiong W. M., Nie X. L. Crystal structure of methyl 4-acetoxy-3,5-dimethoxybenzoate, $C_{12}H_{14}O_6$. *Z. Kristallogr. N. Cryst. Struct.* 2021, 236, 573–575.
10. Sun Y., Liu Y. K., Li J. D., Meng Q. G., Hou G. G. Crystal structure and anti-inflammatory activity of (3*E*,5*E*)-3-(2-fluorobenzylidene)-1-((4-fluorophenyl)sulfonyl)-5-(pyridin-3-ylmethylene)piperidin-4-one, $C_{24}H_{18}F_2N_2O_3S$. *Z. Kristallogr. N. Cryst. Struct.* 2020, 235, 377–379.