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Crystal structure of (*E*)-7-fluoro-2-((6-methoxypyridin-3-yl)methylene)-3,4-dihydronaphthalen-1(2*H*)-one, C₁₇H₁₄FNO₂

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Abstract

C₁₇H₁₄FNO₂, monoclinic, *P*₂/c (no. 15), *a* = 7.3840(6) Å, *b* = 10.9208(8) Å, *c* = 16.7006(15) Å, β = 101.032(9)°, *V* = 1321.84(19) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0589, *wR*_{ref}(*F*²) = 0.1561, *T* = 100.00(18) K.

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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:	Yellow block
Size:	0.14 × 0.12 × 0.11 mm
Wavelength:	Mo Kα radiation (0.71073 Å)
μ:	0.10 mm ⁻¹
Diffractometer, scan mode:	SuperNova,
θ _{max} , completeness:	25.5°, >99%
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	5104, 2453, 0.056
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 1867
<i>N</i> (<i>param</i>) _{refined} :	191
Programs:	CrysAlis ^{PRO} [1], SHELX [2, 3]

Source of material

Firstly, according to the method described in the literature [4], 7-fluoro-3,4-dihydronaphthalen-1(2*H*)-one was synthesized. After that, 3.0 mmol of 7-fluoro-3,4-dihydronaphthalen-1(2*H*)-one and 3.0 mmol of 6-methoxynicotinaldehyde were dissolved in methanol (10 mL), and 20% sodium hydroxide (3.0 mL) solution was added. Subsequently, the above mixture was stirred for 3–5 h at room temperature and thin-layer chromatography was used to monitor the whole reaction process. After the reaction was completed, the supernatant was poured out and the reaction product was separated and purified using silica gel chromatography with petroleum ether/ethyl acetate (2:1, *v/v*) as eluent. Finally yellow crystals were obtained.

Experimental details

H atoms were placed in calculated positions and were included in the refinement with riding model approximation: *d*(C–H) = 0.96 Å (methyl), *U*_{iso}(H) = 1.5*U*_{eq}(C), *d*(C–H) = 0.97 Å (methylene), *U*_{iso}(H) = 1.2*U*_{eq}(C), and *d*(C–H) = 0.93 Å (aromatic), *U*_{iso}(H) = 1.2*U*_{eq}(C). Displacement ellipsoids in the Figure are drawn at the 30% probability level.

Comment

In recent years, it has been reported that 3,4-dihydronaphthalen-1(2*H*)-one (DHN) derivatives show

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

Atom	x	y	z	<i>U</i> _{iso} */ <i>U</i> _{eq}
C1	0.2117 (3)	0.00748 (19)	0.43809 (14)	0.0275 (5)
C2	0.2732 (3)	0.05060 (19)	0.52367 (13)	0.0253 (5)
C3	0.3043 (3)	0.18629 (19)	0.53626 (14)	0.0292 (5)
H3A	0.426850	0.206829	0.527593	0.035*
H3B	0.298193	0.206828	0.592197	0.035*
C4	0.1625 (3)	0.2624 (2)	0.47879 (14)	0.0325 (6)
H4A	0.042942	0.253385	0.494053	0.039*
H4B	0.197013	0.348159	0.484535	0.039*
C5	0.1106 (3)	0.3090 (2)	0.32763 (14)	0.0302 (6)
H5	0.098436	0.391404	0.339596	0.036*
C6	0.0910 (3)	0.2725 (2)	0.24683 (14)	0.0315 (6)
H6	0.066815	0.329268	0.204651	0.038*
C7	0.1083 (3)	0.1498 (2)	0.23084 (14)	0.0296 (6)
C8	0.1453 (3)	0.0637 (2)	0.29108 (14)	0.0277 (5)
H8	0.155816	−0.018492	0.278130	0.033*
C9	0.1672 (3)	0.10092 (19)	0.37264 (14)	0.0259 (5)
C10	0.1480 (3)	0.2247 (2)	0.39097 (14)	0.0268 (5)
C11	0.2970 (3)	−0.03436 (19)	0.58291 (14)	0.0270 (5)
H11	0.266007	−0.113631	0.565020	0.032*
C12	0.3636 (3)	−0.02293 (19)	0.67091 (13)	0.0259 (5)
C13	0.4783 (3)	0.0709 (2)	0.70770 (14)	0.0272 (5)
H13	0.512809	0.130932	0.674096	0.033*
C14	0.4925 (3)	−0.00514 (19)	0.83521 (14)	0.0264 (5)
C15	0.3800 (3)	−0.10489 (19)	0.80594 (14)	0.0281 (5)
H15	0.347781	−0.163197	0.841325	0.034*
C16	0.3188 (3)	−0.11358 (19)	0.72334 (14)	0.0273 (5)
H16	0.247123	−0.180150	0.701866	0.033*
C17	0.6720 (3)	0.1018 (2)	0.94663 (15)	0.0391 (6)
H17A	0.781281	0.097371	0.923508	0.059*
H17B	0.705472	0.097424	1.005009	0.059*
H17C	0.609516	0.177745	0.931174	0.059*
F1	0.08462 (19)	0.11296 (12)	0.15143 (8)	0.0386 (4)
N1	0.5424 (2)	0.08038 (16)	0.78830 (12)	0.0282 (5)
O1	0.2012 (2)	−0.10235 (13)	0.42069 (10)	0.0341 (4)
O2	0.5520 (2)	0.00144 (14)	0.91702 (9)	0.0336 (4)

many diverse biological activities. For instance, 2-benzylidene derivatives of DHN derivatives showed good tyrosine kinase inhibitory activity [5], and 4-amino derivatives of DHN had good anti-inflammatory effect [6]. In addition, some DHN derivatives could bind to the active pockets of the Bcl-2 protein and might be potential Bcl-2 inhibitors [7]. We found that DHN derivatives showed strong anti-neuroinflammatory properties by inhibiting the NF-κB signaling pathway with low toxicity in early studies [8]. In the present study, the title

compound, was synthesized by Claisen–Schmidt condensation reaction.

The analysis of the single-crystal structure of the title compound shows that only one molecule exists in the asymmetric unit (*cf.* the Figure). Bond lengths and angles are in the expected ranges. In the solid state, the 2-methoxypyridyl and 3,4-dihydronaphthalen-1(2*H*)-one groups adopt the *E* stereochemistry of the olefinic double bonds, as observed in other chemically-related compounds [9–14]. The dihedral angle between 2-methoxypyridyl group and the DHN ring is 40.36(3)°. The title molecule has an approximately linear structure.

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References

1. Rigaku OD. CRYALIS^{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. 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.* 2019, *C75*, 1157–1165.
5. Ryu I. Y., Choi I., Ullah S., Choi H., Chun P., Moon H. R. Tyrosinase inhibitory effects of derivatives of (*E*)-2- (substituted benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one. *Bull. Kor. Chem. Soc.* 2020, *41*, 1134–1139.
6. Barlow J. W., Walsh J. J. Synthesis and evaluation of 4-amino-3,4-dihydro-2*H*-naphthalen-1-one derivatives as mast cell stabilising and anti-inflammatory compounds. *Eur. J. Med. Chem.* 2008, *43*, 2891–2900.
7. Wang F. L., Zhang R. X., Cui Y., Sheng L. P., Sun Y. P. 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.
8. Sun Y., Zhou Y. Q., Liu Y. K., Zhang H. Q., Hou G. G., Meng Q. G., Hou Y. Potential anti-neuroinflammatory NF-κB inhibitors based on 3,4-dihydronaphthalen-1(2*H*)-one derivatives. *J. Enzym. Inhib. Med. Chem.* 2020, *35*, 1631–1640.

9. 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- κ B pathway activation. *Eur. J. Med. Chem.* 2019, 167, 187–199.
10. Li X. Y., Meng Q. G., Hou G. G. Crystal structure of (3*E*,5*E*)-3,5-bis(4-cyanobenzylidene)-1-((4-fluorophenyl) sulfonyl) piperidin-4-one, $C_{27}H_{18}FN_3O_3S$. *Z. Kristallogr. N. Cryst. Struct.* 2019, 234, 771–773.
11. Sun Y., Wang S. X., Hou G. G. Crystal structure of (3*E*,5*E*)-3,5-bis(3-nitrobenzylidene)-1-((4-(trifluoromethyl)phenyl)sulfonyl) piperidin-4-one-dichloromethane (2/1), $C_{53}H_{38}Cl_2F_6N_6O_{14}S_2$. *Z. Kristallogr. N. Cryst. Struct.* 2019, 234, 1047–1049.
12. Liu L. D., Liu S. L., Hou G. G. Crystal structure of 4-((*E*)-((*E*)-5-(2-fluorobenzylidene)-1-((4-fluorophenyl)sulfonyl)-4-oxopiperidin-3-ylidene)methyl)benzonitrile, $C_{26}H_{18}F_2N_2O_3S$. *Z. Kristallogr. N. Cryst. Struct.* 2018, 233, 1063–1065.
13. Zhang X. F., Wang H. Y., Zhao S. N., Zhang S. N., Zhao F. L., Meng Q. G. Crystal structure of (*E*)-2-(4-fluoro-3-(trifluoromethyl)benzylidene)-7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one, $C_{19}H_{14}F_4O_2$. *Z. Kristallogr. N. Cryst. Struct.* 2021, 236, 47–49.
14. Luan M. Z., Wang H. Y., Zhang M., Song J., Xu Y. R., Zhao F. L., Meng Q. G. Crystal structure of (*E*)-2-(4-fluoro-2-(trifluoromethyl)benzylidene)-7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one, $C_{19}H_{14}F_4O_2$. *Z. Kristallogr. N. Cryst. Struct.* 2021, 236, 245–247.