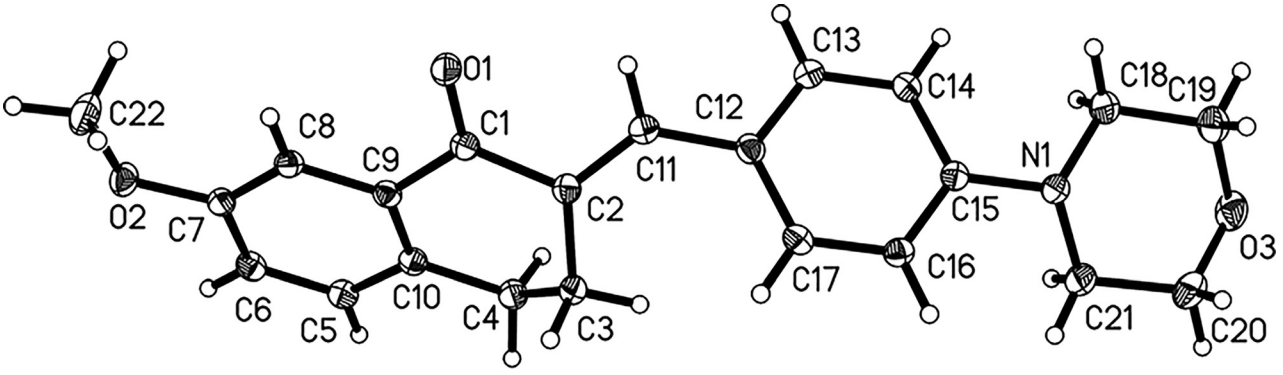
Xiao-Qian Yuan, Le-Hui Zhao, Jia-Jing Zhang and Gui-Ge Hou*

Crystal structure of (*E*)-7-methoxy-2-(4-morpholinobenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one, $C_{22}H_{23}NO_3$



https://doi.org/10.1515/ncrs-2022-0578
Received December 11, 2022; accepted February 1, 2023;
published online February 14, 2023

Abstract

$C_{22}H_{23}NO_3$, triclinic, $P\bar{1}$ (no. 2), a = 9.6505(4) Å, b = 9.9712(5) Å, c = 10.0845(4) Å, α = 68.177(4)°, β = 88.106(3)°, γ = 79.234(4)°, V = 884.30(7) Å^3, Z = 2, $R_{gt}(F)$ = 0.0424, $wR_{ref}(F^2)$ = 0.1150, T = 293 K.

CCDC no.: 2213129

The crystal structure is shown in the figure. Displacement ellipsoids are drawn at the 35% probability level. 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:	0.14 × 0.12 × 0.10 mm
Wavelength:	Cu *K*α radiation (1.54178 Å)
μ:	0.70 mm^{-1}
Diffractometer, scan mode:	SuperNova
θ_{max}, completeness:	71.7°, 98%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	7276, 3309, 0.020
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3057
$N(param)_{refined}$:	237
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3]

Source of material

Referring to the literature synthesis methods [4, 5], a substituted benzene was synthesized with succinic anhydride with the aid of Friedel–Crafts reaction, hydrazine hydrate discount, and dehydration condensation to generate an intermediate, 7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one. Dissolve the intermediate (0.50 g, 2.83 mmol) and 4-morpholinobenzaldehyde (0.54 g, 2.83 mmol) in 10 mL of methanol and stir in an ice-salt bathtub at 268 K until clarified, then add 5 mL of 25% NaOH solution and switch to room temperature after 5 min of response and proceed to stir for 30 min, all through during the response is monitored by using thin-layer chromatography (TLC). After the reaction, the solvent used to be eliminated by way of filtration, and the filter residue used to be purified with the aid of silica gel column chromatography (dichloromethane: methanol = 40:1), v/v) to acquire yellow crystals.

***Corresponding author: Gui-Ge Hou**, School of Pharmacy, The Key Laboratory of Prescription Effect and Clinical Evaluation of State Administration of Traditional Chinese Medicine of China, Binzhou Medical University, Yantai, 264003, P. R. China, E-mail: guigehou@163.com. https://orcid.org/0000-0002-9493-3981
Xiao-Qian Yuan, **Le-Hui Zhao and Jia-Jing Zhang**, School of Pharmacy, The Key Laboratory of Prescription Effect and Clinical Evaluation of State Administration of Traditional Chinese Medicine of China, Binzhou Medical University, Yantai, 264003, P. R. China

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.13613 (14)	1.28453 (14)	0.40430 (14)	0.0261 (3)
C2	0.17012 (14)	1.12605 (14)	0.42281 (14)	0.0261 (3)
C3	0.15672 (15)	1.09227 (14)	0.29104 (14)	0.0284 (3)
H3A	0.057698	1.106826	0.264755	0.034*
H3B	0.198623	0.990186	0.310535	0.034*
C4	0.23050 (16)	1.19182 (15)	0.16749 (14)	0.0300 (3)
H4A	0.331698	1.164829	0.187346	0.036*
H4B	0.211047	1.176880	0.080745	0.036*
C5	0.18949 (15)	1.46108 (15)	0.00942 (14)	0.0288 (3)
H5	0.225165	1.434287	−0.065838	0.035*
C6	0.14430 (15)	1.60727 (15)	−0.01370 (14)	0.0296 (3)
H6	0.150160	1.678344	−0.103881	0.035*
C7	0.08943 (14)	1.64965 (14)	0.09805 (14)	0.0273 (3)
C8	0.08396 (14)	1.54429 (14)	0.23332 (14)	0.0263 (3)
H8	0.048519	1.571874	0.308188	0.032*
C9	0.13254 (14)	1.39536 (14)	0.25613 (14)	0.0252 (3)
C10	0.18284 (14)	1.35157 (15)	0.14429 (14)	0.0265 (3)
C11	0.21903 (15)	1.02845 (15)	0.55285 (14)	0.0285 (3)
H11	0.222624	1.068008	0.622618	0.034*
C12	0.26754 (15)	0.86875 (15)	0.60073 (14)	0.0277 (3)
C13	0.38400 (16)	0.80370 (15)	0.69564 (15)	0.0324 (3)
H13	0.426162	0.862579	0.728681	0.039*
C14	0.43931 (16)	0.65489 (15)	0.74260 (15)	0.0306 (3)
H14	0.519810	0.616687	0.802709	0.037*
C15	0.37553 (14)	0.56086 (14)	0.70071 (13)	0.0252 (3)
C16	0.25475 (14)	0.62462 (15)	0.60907 (14)	0.0268 (3)
H16	0.208241	0.564903	0.581459	0.032*
C17	0.20379 (14)	0.77442 (15)	0.55922 (14)	0.0274 (3)
H17	0.125201	0.813647	0.496535	0.033*
C18	0.54895 (17)	0.35136 (16)	0.84990 (17)	0.0373 (4)
H18A	0.535619	0.391290	0.924653	0.045*
H18B	0.630268	0.383507	0.797197	0.045*
C19	0.57666 (19)	0.18589 (17)	0.91663 (18)	0.0422 (4)
H19A	0.662697	0.152025	0.976116	0.051*
H19B	0.499698	0.154258	0.977448	0.051*
C20	0.4663 (2)	0.17133 (18)	0.7235 (2)	0.0458 (4)
H20A	0.387567	0.139010	0.780905	0.055*
H20B	0.477125	0.127184	0.651841	0.055*
C21	0.43312 (18)	0.33615 (16)	0.64969 (16)	0.0370 (4)
H21A	0.506030	0.368169	0.583134	0.044*
H21B	0.343988	0.364978	0.595721	0.044*
C22	−0.0197 (2)	1.84410 (17)	0.17131 (17)	0.0499 (5)
H22A	−0.098099	1.795850	0.206489	0.075*
H22B	−0.052313	1.948675	0.132776	0.075*
H22C	0.048284	1.818881	0.248199	0.075*
N1	0.42445 (12)	0.40773 (12)	0.75373 (12)	0.0280 (3)
O1	0.11542 (12)	1.32345 (11)	0.50666 (10)	0.0343 (3)
O2	0.04439 (12)	1.79790 (10)	0.06203 (10)	0.0347 (3)
O3	0.59014 (12)	0.12118 (11)	0.81196 (13)	0.0442 (3)

Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with *d*(C–H) = 0.96 Å (methyl), U_{iso}(H) = 1.5U_{eq}(C), *d*(C–H) = 0.97 Å (methylene), U_{iso}(H) = 1.2U_{eq}(C), and *d*(C–H) = 0.93 Å (aromatic), U_{iso}(H) = 1.2U_{eq}(C).

Comment

In recent research, curcumin was modified to 3,4-dihydronaphthalen-1(2*H*)-one (DHN) derivatives to improve their water solubility, metabolic degradation, and bioavailability [6]. The substituents of DHN can be halogen, methoxyl, substituted phenyl, heterocyclic, etc. Some DHN derivatives substituted with methoxy inhibited the activation of NF-**kappa**B signaling pathway to exert low toxicity and anti-neuroinflammatory effects [7]. In this experiment, the title compound was synthesized by the Claisen–Schmidt condensation reaction between 7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one and 4-morpholinobenzaldehyde.

Single-crystal structure analysis reveals that there is one DHN molecule in the asymmetric unit (*cf*. the Figure). The parent nucleus is the 3,4-dihydronaphthalen-1(2*H*)-one and the 7 position of the aromatic ring is substituted by methoxyl group. In DHN molecule, the *E* stereochemistry of the olefinic double bond is adopted [8, 9]. Bond length of C(2) = C(11) olefinic bond is 1.3454(19) Å. The torsion angle of C(1)–C(2)–C(11)–C(12) is 176.53(13)°, while the torsion angle of C(3)–C(2)–C(11)–C(12) is 1.5(2)°. The entire molecule forms a linear structure under the action of the olefin bond bridging [10]. Bond lengths and angles are all in the expected ranges [11]. On one side of the molecule is a methoxy-substituted DHN, while on the other side is a 4-morpholine substituted phenyl group. In parent nucleus DHN, there are two methylene groups, which affect the coplanar properties of DHN molecules. Because of the distorting effect of DHN, the 4-morpholinobenzylidene and 3,4-dihydronaphthalen-1(2*H*)-one is not coplanar with each other, and the dihedral angles is about 68.3(3)°. In addition, the morpholine ring takes a “chair” configuration. The active groups, such as carbonyl group, morpholine group and methoxy group in the molecule contribute to the anti-inflammatory activity of the compound [12].

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 College Youth Innovation Science and Technology Support Programme of Shandong Province (No. 2020KJK003) and Key Support Projects (Inheritance and Development of Traditional Chinese Medicine) of the State Administration of Traditional Chinese Medicine (No. 2021-242).

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. Katila P., Shrestha A., Shrestha A., Shrestha R., Park P. H., Lee E. S. Introduction of amino moiety enhances the inhibitory potency of 1-tetralone chalcone derivatives against LPS-stimulated reactive oxygen species production in RAW 264.7 macrophages. *Bioorg. Chem.* 2019, *87*, 495–505.
5. Sun Y., Gao Z., Wang C., 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.
6. Nelson K. M., Dahlin J. L., Bisson J., Graham J., Pauli G. F., Walters M. A. The essential medicinal chemistry of curcumin. *J. Med. Chem.* 2017, *60*, 1620–1637.
7. 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.
8. Zhang Y.-L., Liu S.-L., Hou G.-G., Wang L., Zhang X.-F. Crystal structure of (*E*)-7-bromo-2-(3,5-dimethoxybenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one, $C_{19}H_{17}BrO_3$. *Z. Kristallogr. N. Cryst. Struct.* 2022, *237*, 907–909.
9. Zhang Y.-L., Liu S.-L., Hou G.-G., Zhang X.-F., Wang L., Xin W.-Y. Crystal structure of (*E*)-7-bromo-2-(4-methoxybenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one, $C_{18}H_{15}BrO_2$. *Z. Kristallogr. N. Cryst. Struct.* 2022, *237*, 945–947.
10. Wang L., Meng Q.-G., Hou G.-G. Crystal structure of (*E*)-7-methoxy-2-((6-methoxypyridin-2-yl) methylene)-tetralone, $C_{18}H_{17}NO_3$. *Z. Kristallogr. N. Cryst. Struct.* 2021, *236*, 1023–1025.
11. Turner A. B., Harrison W. T. A. 5–Hydroxy-6,7-dimethoxy-2-[(*E*)-1-(4-methoxyphenyl)methylidene]-3,4-dihydro-2*H*-napthalen-1-one. *Acta Crystallogr.* 2006, *E62*, o386–o387.
12. Zhang X. F., Luan M. Z., Yan W. B., Zhao F. L., Hou Y., Hou G. G., Meng Q. G. Anti-neuroinflammatory effects of novel 5,6-dihydrobenzo [*h*]quinazolin-2-amine derivatives in lipopolysaccharide-stimulated BV2 microglial cells. *Eur. J. Med. Chem.* 2022, *235*, 114322.