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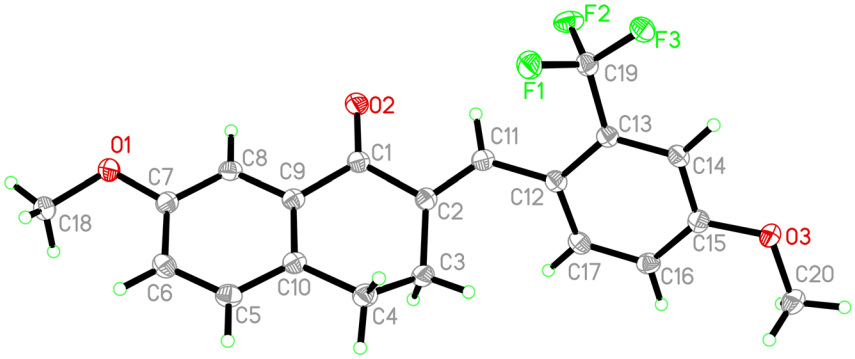
Crystal structure of (*E*)-7-methoxy-2-(4-methoxy-2-(trifluoromethyl)benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one, $C_{20}H_{17}F_3O_3$



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Abstract

$C_{20}H_{17}F_3O_3$, monoclinic, $P2_1/c$ (no. 14), a = 9.0684(4) Å, b = 13.1942(6) Å, c = 13.7883(7) Å, β = 96.250(5)°, V = 1639.97(13) Å^3, Z = 4, $R_{gt}(F)$ = 0.0415, $wR_{ref}(F^2)$ = 0.1125, T = 100 K.

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The crystal structure is shown in the figure. Displacement ellipsoids are drawn at the 40% 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:	0.15 × 0.13 × 0.12 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.12 mm^{-1}
Diffractometer, scan mode:	SuperNova,
θ_{max}, completeness:	25.5°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	7489, 3045, 0.033
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2677
$N(param)_{refined}$:	237
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3]

Source of material

7-Methoxy-3,4-dihydronaphthalen-1(2*H*)-one (0.86 g, 4.90 mmol) and 4-methoxy-2-(trifluoromethyl)benzaldehyde (1.0 g, 4.90 mmol) were dissolved in 10 mL acetic acid. Then dry hydrogen chloride gas was flowed continuously into the solution for 45 min. After gas insertion, the reaction system was stirred at room temperature for 7 days. The response endpoint was detected by thin layer chromatography (TLC). When the reaction was stopped, the precipitate was filtered from the reaction system, then it was dissolved in distilled water and regulated to a neutral pH with saturated aqueous Na_2CO_3 solution. The precipitate was filtered from the system and dissolved with dichloromethane. The organic phase was washed successively with deionized water and brine, dried over anhydrous sodium sulfate and condensed under

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.65903 (18)	0.85750 (12)	0.75806 (11)	0.0233 (4)
C2	0.52023 (17)	0.87935 (12)	0.80475 (11)	0.0227 (4)
C3	0.47743 (18)	0.98904 (12)	0.81346 (12)	0.0271 (4)
H3A	0.404935	0.994976	0.859948	0.033*
H3B	0.431623	1.012871	0.750752	0.033*
C4	0.61089 (19)	1.05553 (12)	0.84653 (12)	0.0273 (4)
H4A	0.581050	1.126148	0.842785	0.033*
H4B	0.645118	1.040365	0.914076	0.033*
C5	0.83547 (19)	1.11643 (12)	0.77025 (12)	0.0260 (4)
H5	0.822365	1.179616	0.797941	0.031*
C6	0.95318 (18)	1.10252 (12)	0.71576 (12)	0.0261 (4)
H6	1.018474	1.155375	0.707433	0.031*
C7	0.97262 (18)	1.00806 (12)	0.67346 (11)	0.0240 (4)
C8	0.87565 (18)	0.92996 (12)	0.68672 (11)	0.0234 (4)
H8	0.888982	0.867084	0.658471	0.028*
C9	0.75768 (17)	0.94476 (11)	0.74228 (11)	0.0215 (3)
C10	0.73627 (17)	1.03941 (12)	0.78504 (11)	0.0229 (4)
C11	0.45120 (18)	0.79930 (12)	0.83858 (11)	0.0233 (4)
H11	0.492558	0.736336	0.827811	0.028*
C12	0.31823 (17)	0.79841 (11)	0.89061 (11)	0.0220 (3)
C13	0.30686 (17)	0.73063 (11)	0.96888 (11)	0.0205 (3)
C14	0.18284 (17)	0.72872 (11)	1.01812 (11)	0.0223 (3)
H14	0.177658	0.683316	1.069226	0.027*
C15	0.06522 (17)	0.79426 (11)	0.99190 (11)	0.0227 (4)
C16	0.07080 (18)	0.85976 (12)	0.91389 (12)	0.0247 (4)
H16	−0.008410	0.902745	0.894950	0.030*
C17	0.19630 (18)	0.86046 (12)	0.86423 (12)	0.0250 (4)
H17	0.198868	0.904022	0.811408	0.030*
C18	1.16961 (19)	1.06935 (12)	0.58758 (13)	0.0315 (4)
H18A	1.102901	1.117475	0.554077	0.047*
H18B	1.237668	1.045225	0.544134	0.047*
H18C	1.223877	1.101359	0.642947	0.047*
C19	0.43031 (17)	0.65857 (12)	1.00020 (11)	0.0240 (4)
C20	−0.16949 (19)	0.85596 (13)	1.02981 (15)	0.0336 (4)
H20A	−0.131895	0.923978	1.035071	0.050*
H20B	−0.238349	0.845630	1.077069	0.050*
H20C	−0.218968	0.845282	0.965470	0.050*
F1	0.56347 (10)	0.70360 (7)	1.01402 (7)	0.0332 (3)
F2	0.44254 (11)	0.58498 (7)	0.93359 (7)	0.0335 (3)
F3	0.41204 (11)	0.61127 (7)	1.08397 (7)	0.0306 (3)
O1	1.08689 (13)	0.98608 (8)	0.61966 (9)	0.0311 (3)
O2	0.69183 (14)	0.77092 (8)	0.73599 (9)	0.0321 (3)
O3	−0.04984 (12)	0.78627 (8)	1.04735 (8)	0.0268 (3)

vacuum. The crude product was purified by silica-gel column chromatography (petroleum ether: ethyl acetate = 10:1, *v*:*v*). Single crystal was obtained under ambient conditions *via* solvent evaporation in the mixed solvents of dichloromethane and methanol (1:1, *v*:*v*) and drying under *vacuo* at 333 K for 3 h.

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), and *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

3,4-Dihydronaphthalen-1(2*H*)-ones (DHNs) derivatives with antitumor and anti-inflammatory activities have been investigated as novel modulators of allergic and inflammatory responses [4, 5]. Our interests lie in developing these derivatives as anti-neuroinflammatory drugs. In this study, we designed and synthesized a new DHNs derivative through Claisen–Schmidt condensation reaction and we obtained a new single crystal by introducing trifluoromethyl.

The title compound contains one drug molecule in the asymmetric unit (cf. the figure). Bond lengths and angles are all in the expected ranges [6]. The title molecule has an approximately linear structure. The parent nucleus is 3,4-dihydronaphthalen-1(2*H*)-one and the 7 position of the aromatic ring are methoxylated. The third and fourth positions of the parent nucleus are two methylene saturated carbons. The olefinic double bonds between 3,4-dihydronaphthalen-1(2*H*)-one and 4-methoxy-2-(trifluoromethyl)benzaldehyde groups and carbonyl group form a and b unsaturated ketones. With respect to the C(2) = C(11) olefinic bonds, 4-methoxy-2-(trifluoromethyl) benzaldehyde and carbonyl groups adopt the *E* stereochemistry [7–9]. Because of the distorting effect of 3,4-dihydronaphthalen-1(2*H*)-one, the 7-methoxyphenyl and 4-methoxy-2-(trifluoromethyl)benzaldehyde groups are not coplanar with each other, with a dihedral angle of approximately 60.6° [10]. This twisted configuration may increase the likelihood of interactions with bioactive molecules or the purposes of creating more potent biological activity [11, 12].

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References

[1] Rigaku O. D. *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] 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. Enzyme Inhib. Med. Chem.* 2020, *35*, 1631–1640.
[5] 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-κB pathway activation. *Eur. J. Med. Chem.* 2019, *167*, 187–199.
[6] Zingales S. K., Moore M. E., Goetz A. D., Padgett C. W. Crystal structure of (*E*)-2-[(2-bromopyridin-3-yl)methylidene]-6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one and 3-[(*E*)-(6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalen-2-ylidene)methyl]pyridin-2(1*H*)-one. *Acta Crystallogr.* 2016, *E72*, 955–958.
[7] 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.
[8] 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.
[9] 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.* 2017, *C73*, 1003–1009.
[10] 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.
[11] Yang Q. W., Wang N., Zhang J., Chen G., Xu H., Meng Q. G., Du Y., Yang X., Fan H. Y. *In vitro* and *in silico* evaluation of stereoselective effect of ginsenosideisomers on platelet P2Y12 receptor. *Phytomedicine* 2019, *64*, 152899.
[12] Yao B. R., Li N., Wang C. H., Hou G. G., Meng Q. G., Yan K. Novel asymmetric 3,5-bis(arylidene)piperidin-4-one derivatives: synthesis, crystal structures and cytotoxicity. *Acta Crystallogr.* 2018, *C74*, 659–665.