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Crystal structure and anti-inflammatory activity of (*E*)-7-fluoro-2-((5-methoxypyridin-3-yl)methylene)-3,4-dihydronaphthalen-1(2*H*)-one, $C_{17}H_{14}FNO_2$

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.14 × 0.12 × 0.10 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.10 mm ⁻¹
Diffractometer, scan mode:	SuperNova
$\theta_{\max}$, completeness:	25.5°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	5535, 2505, 0.025
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2103
$N(\text{param})_{\text{refined}}$:	191
Programs:	CrysAlis ^{PRO} [1], SHELX [2, 3]

Abstract

$C_{17}H_{14}FNO_2$, monoclinic, $C2/c$ (no. 15), $a = 15.5754(12)$ Å, $b = 7.4828(6)$ Å, $c = 23.0981(18)$ Å, $\beta = 90.797(7)^\circ$, $V = 2691.8(4)$ Å³, $Z = 8$, $R_{\text{gt}}(F) = 0.0442$, $wR_{\text{ref}}(F^2) = 0.1096$, $T = 100(1)^\circ$ 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.

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Source of material

7-Fluoro-3,4-dihydronaphthalen-1(2*H*)-one was synthesized according to the literature method [4]. 7-Fluoro-3,4-dihydronaphthalen-1(2*H*)-one (0.492 g, 3.0 mmol) and 5-methoxynicotinaldehyde (0.411 g, 3.0 mmol) were dissolved in 10 mL methanol, then 3.0 mL of a 20% NaOH solution was added. After that, the mixture was stirred at room temperature for 3–5 h. The reaction process was monitored by thin layer chromatograph (TLC). When the reaction was completed, the solvent was poured out and the residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (2:1, v/v) as the eluent to get yellow crystal.

Process of anti-inflammatory activity test: The anti-inflammatory activity of the title compound was evaluated by detecting the changes of NO secretion in lipopolysaccharide (LPS)-induced inflammatory model of RAW264.7 using ELISA method. Pyrrolidine dithiocarbamate (PDTC) was used as positive control. At the concentration of 6.0 μ M, the title compound had no obvious toxicity to RAW264.7 cells in the preliminary experiment. Firstly, RAW264.7 cells in logarithmic growth phase were added to 96 well plates and incubated for 12 h. Then, the target compound or PDTC was added and incubated for 2 h. After that, LPS was added at the concentration of 1.0 μ g/mL and incubated for 24 h sequentially. At last, the cell

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	0.92268 (10)	0.8407 (2)	0.49125 (6)	0.0196 (4)
C2	0.94668 (10)	0.8199 (2)	0.42924 (6)	0.0200 (4)
C3	0.90331 (10)	0.9449 (2)	0.38662 (7)	0.0227 (4)
H3A	0.914999	0.906136	0.347435	0.027*
H3B	0.926244	1.064529	0.391510	0.027*
C4	0.80623 (10)	0.9474 (2)	0.39604 (7)	0.0231 (4)
H4A	0.780845	1.041838	0.372688	0.028*
H4B	0.782004	0.834783	0.382931	0.028*
C5	0.70372 (11)	1.0496 (2)	0.47254 (7)	0.0249 (4)
H5	0.665552	1.080824	0.442911	0.030*
C6	0.68032 (11)	1.0772 (2)	0.52927 (7)	0.0263 (4)
H6	0.627101	1.125570	0.538174	0.032*
C7	0.73870 (11)	1.0306 (2)	0.57255 (7)	0.0257 (4)
C8	0.81698 (11)	0.9575 (2)	0.56156 (7)	0.0230 (4)
H8	0.854444	0.927294	0.591694	0.028*
C9	0.83971 (10)	0.9291 (2)	0.50374 (6)	0.0194 (4)
C10	0.78291 (10)	0.9763 (2)	0.45847 (7)	0.0200 (4)
C11	1.00023 (10)	0.6864 (2)	0.41680 (6)	0.0207 (4)
H11	1.016019	0.614675	0.448054	0.025*
C12	1.03804 (10)	0.6356 (2)	0.36119 (6)	0.0210 (4)
C13	1.06598 (10)	0.7593 (2)	0.31999 (7)	0.0237 (4)
H13	1.056781	0.880134	0.327027	0.028*
C14	1.11752 (11)	0.5383 (2)	0.26097 (7)	0.0244 (4)
H14	1.143356	0.504611	0.226588	0.029*
C15	1.09327 (10)	0.4054 (2)	0.29977 (7)	0.0224 (4)
C16	1.05361 (10)	0.4555 (2)	0.35049 (6)	0.0225 (4)
H16	1.037449	0.369456	0.377254	0.027*
C17	1.15159 (13)	0.1725 (3)	0.24205 (8)	0.0359 (5)
H17A	1.121016	0.212794	0.208109	0.054*
H17B	1.156175	0.044636	0.241253	0.054*
H17C	1.208012	0.224190	0.242867	0.054*
F1	0.71599 (7)	1.05995 (14)	0.62877 (4)	0.0383 (3)
N1	1.10507 (9)	0.71304 (19)	0.27123 (6)	0.0261 (3)
O1	0.96924 (7)	0.78370 (15)	0.53065 (5)	0.0252 (3)
O2	1.10640 (8)	0.22601 (16)	0.29239 (5)	0.0318 (3)

supernatants were collected from 96 well plates and the expression levels of NO secretion were detected by ELISA method with an ELISA kit (eBioScience, San Diego, CA).

Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with $d(\text{C-H}) = 0.96 \text{ \AA}$ (methyl), $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$, $d(\text{C-H}) = 0.97 \text{ \AA}$ (methylene), $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$, and $d(\text{C-H}) = 0.93 \text{ \AA}$ (aromatic), $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$. Displacement ellipsoids are drawn at the 30% probability level.

Comment

Recently, 3,4-dihydronaphthalen-1(2*H*)-one (DHN) derivatives have attracted more attention of many researchers due to its diverse biological activities such as anti-inflammatory, anti-tumor, and so on. It has been reported that some DHN derivatives could be investigated as novel modulators of allergic and inflammatory responses [5, 6]. In other reports, some benzylidene-substituted DHN derivatives could be used as potential Bcl-2 inhibitors and 4-amino derivatives of DHN could be investigated as anti-inflammatory agents that stabilize mast cells [7, 8]. In previous studies, we found that DHN derivatives might be explored as functional anti-neuroinflammatory agents [9]. In this study, the title compound was synthesised by Claisen–Schmidt condensation reactions and its anti-inflammatory activity was evaluated.

Single-crystal structure analysis reveals that there is only a drug molecule in the asymmetric unit of the title compound (*cf.* the figure). Bond lengths and angles are all in the expected ranges. In the solid state, 3-methoxypyridyl groups and DHN adopt the *E* stereochemistry of the olefinic double bonds [10–13]. The dihedral angles between 3-methoxypyridyl groups and DHN ring are 66.7(4)°. The title molecule shows a linear structure, and the nitrogen, fluorine and oxygen atoms of the molecule provide electron donors for biological activity [14–16].

According to the literatures, many diseases may be caused by inflammation which is triggered by the pro-inflammatory cytokines, such as NO, TNF- α , and IL-6. If the drug can inhibit the release of inflammatory factors, it will play an anti-inflammatory role [17, 18]. In this work, the inhibitory effect of title compound on NO release in mouse RAW264.7 cells induced by LPS was studied by ELISA method using PDTC as positive control. The express rate for NO production was 58.27 $\pm$ 4.19 and 49.70 $\pm$ 3.62% after treated by PDTC and the title compound, respectively. The experimental result showed that the title compound displayed potential inhibitory effects on LPS-induced NO secretion in mouse RAW264.7 cells.

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