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Crystal structure of (*E*)-2-(4-fluoro-2-(trifluoromethyl)benzylidene)-7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one, C₁₉H₁₄F₄O₂

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.14 × 0.13 × 0.12 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.13 mm ⁻¹
Diffractometer, scan mode:	SuperNova, ω
$\theta_{\max}$, completeness:	25.5°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	7328, 2862, 0.027
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2364
$N(\text{param})_{\text{refined}}$:	227
Programs:	CrysAlis ^{PRO} [1], SHELX [2, 3]

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Abstract

C₁₉H₁₄F₄O₂, monoclinic, *C*2/*c* (no. 15), $a = 17.1519(13)$ Å, $b = 13.9810(8)$ Å, $c = 15.2299(9)$ Å, $\beta = 123.031(7)^\circ$, $V = 3061.9(4)$ Å³, $Z = 8$, $R_{\text{gt}}(F) = 0.0410$, $wR_{\text{ref}}(F^2) = 0.1010$, $T = 100(1)$ 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-Methoxy-3,4-dihydronaphthalen-1(2*H*)-one and 4-fluoro-2-(trifluoromethyl)benzaldehyde were dissolved in 10 mL of methanol. After the addition of 5 mL 25% NaOH solution, the mixture was stirred for 3 h at ambient temperature (monitored by TLC, 254 nm). The mixture was filtered and subsequently dissolved with ethyl acetate, and the organic phase was washed with water and brine, and finally dried over anhydrous sodium sulfate. After filtration, the filtrate was evaporated to dryness under vacuum and purified on a silica gel by column chromatography using petroleum ether/EtOAc (2:1, *v/v*) as the eluent. The title compound was recrystallized from dichloromethane and methanol (1:1, *v/v*) to attain suitable crystals.

Experimental details

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

Comment

Microglial cells function as the immune cells of the central nervous system (CNS), acting as primary mediators of

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	0.15858 (12)	0.32258 (13)	0.34683 (13)	0.0216 (4)
C2	0.13311 (12)	0.40869 (13)	0.38473 (12)	0.0216 (4)
C3	0.06355 (12)	0.39118 (13)	0.41445 (13)	0.0244 (4)
H3A	0.002668	0.379568	0.351814	0.029*
H3B	0.059398	0.447392	0.449029	0.029*
C4	0.09287 (12)	0.30525 (13)	0.48741 (13)	0.0252 (4)
H4A	0.151509	0.318790	0.552337	0.030*
H4B	0.046523	0.293022	0.503856	0.030*
C5	0.08278 (12)	0.12699 (14)	0.45434 (14)	0.0271 (4)
H5	0.063827	0.119032	0.500627	0.033*
C6	0.09002 (12)	0.04824 (14)	0.40523 (14)	0.0275 (4)
H6	0.076345	−0.012150	0.418954	0.033*
C7	0.11778 (11)	0.05825 (13)	0.33484 (13)	0.0232 (4)
C8	0.14015 (11)	0.14734 (13)	0.31668 (13)	0.0226 (4)
H8	0.160090	0.154448	0.271197	0.027*
C9	0.13271 (11)	0.22752 (13)	0.36722 (12)	0.0211 (4)
C10	0.10321 (12)	0.21842 (13)	0.43627 (13)	0.0226 (4)
C11	0.17173 (12)	0.49206 (13)	0.38675 (13)	0.0234 (4)
H11	0.211379	0.491860	0.362846	0.028*
C12	0.15803 (11)	0.58469 (13)	0.42303 (13)	0.0224 (4)
C13	0.13661 (11)	0.66879 (13)	0.36431 (13)	0.0217 (4)
C14	0.12213 (11)	0.75452 (14)	0.39928 (13)	0.0239 (4)
H14	0.107828	0.810213	0.359957	0.029*
C15	0.12959 (12)	0.75459 (13)	0.49395 (14)	0.0243 (4)
C16	0.15281 (12)	0.67566 (14)	0.55613 (14)	0.0270 (4)
H16	0.158728	0.678664	0.620505	0.032*
C17	0.16721 (12)	0.59111 (14)	0.52000 (13)	0.0248 (4)
H17	0.183564	0.536638	0.561494	0.030*
C18	0.12763 (12)	0.66818 (13)	0.26046 (14)	0.0251 (4)
C19	0.15224 (14)	−0.01821 (14)	0.21971 (15)	0.0314 (5)
H19A	0.110912	0.021932	0.161285	0.047*
H19B	0.153713	−0.080884	0.194888	0.047*
H19C	0.213632	0.008756	0.256636	0.047*
F1	0.11301 (8)	0.83847 (8)	0.52698 (8)	0.0353 (3)
F2	0.06892 (7)	0.60081 (8)	0.19533 (8)	0.0320 (3)
F3	0.20967 (7)	0.65053 (8)	0.27124 (8)	0.0339 (3)
F4	0.09746 (8)	0.75128 (8)	0.20967 (8)	0.0329 (3)
O1	0.19860 (9)	0.33000 (9)	0.30076 (10)	0.0296 (3)
O2	0.12024 (9)	−0.02482 (9)	0.28854 (10)	0.0289 (3)

inflammation. Neuroinflammation in the CNS mediated by overactivated microglia plays a key role in many neurodegenerative diseases [4–6]. M1 type microglial activation leads to proinflammatory effects by producing numerous cyto-mediators, such as proteases, proinflammatory cytokines and reactive oxygen species (ROS) [7]. Studies have shown that the inhibition of NF-κB signal pathway in microglia can reduce the expression of pro-inflammatory cytokines such as nitric oxide (NO), tumor necrosis factor-α (TNF-α), interleukin (IL)-1β and IL-6, and play an anti-neuroinflammatory effect [8–11]. Therefore, developing an

NF-κB inhibitor with anti-neuroinflammatory activities and low toxicity is a potential therapeutic strategy for treating inflammatory neurodegenerative CNS diseases [12].

3,4-Dihydronaphthalen-1(2*H*)-one (DHN) derivatives with anti-inflammatory activities have been investigated as potential Bcl-2 inhibitors and as anti-inflammatory agents that stabilize mast cells [13–15]. However, DHN derivatives have rarely been developed as anti-neuroinflammatory drugs. Therefore, our group designed and synthesized a new benzylidene-substituted DHN derivative which may have anti-neuroinflammatory activity. The synthesis succeeded by a Claisen–Schmidt condensation reaction.

Single-crystal structure analysis revealed that the title compound crystallized in the monoclinic space group *C2/c*. The ORTEP diagram is presented in Figure. Bond lengths and angles are all in the expected ranges [16]. There is one drug molecule in the asymmetric unit (see the Figure). According to the configuration at the C(2) = C(11) olefinic bond, the title molecule adopts the *E* stereochemistry [17]. Because of the distorting effect of 3,4-dihydronaphthalen-1(2*H*)-one, the 7-methoxyphenyl and 4-fluoro-2-(trifluoromethyl)phenyl groups are not coplanar with each other, with a dihedral angle of 29.37(3)°. This twist may increase the likelihood of interactions with bio molecules with the aim of creating more potent anti-neuroinflammatory activity [18].

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