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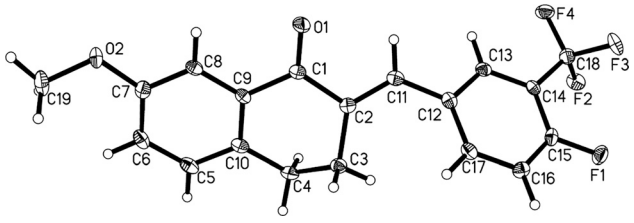
Crystal structure of (*E*)-2-(4-fluoro-3-(trifluoromethyl)benzylidene)-7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one, $C_{19}H_{14}F_4O_2$



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Abstract

$C_{19}H_{14}F_4O_2$, triclinic, $P\bar{1}$ (no. 2), a = 8.1539(7) Å, b = 8.8584(6) Å, c = 11.8025(9) Å, α = 73.186(7)°, β = 76.184(7)°, γ = 69.512(7)°, V = 755.39(11) Å^3, Z = 2, $R_{gt}(F)$ = 0.0436, $wR_{ref}(F^2)$ = 0.0965, T = 100 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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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.13 × 0.12 × 0.11 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.13 mm^{-1}
Diffractometer, scan mode:	SuperNova,
θ_{max}, completeness:	25.5°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	4729, 2802, 0.044
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2165
$N(param)_{refined}$:	227
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3]

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2988 (2)	0.3305 (2)	0.48684 (17)	0.0133 (4)
C2	0.1929 (2)	0.3765 (2)	0.60124 (16)	0.0131 (4)
C3	0.0556 (2)	0.2900 (2)	0.66472 (17)	0.0154 (4)
H3A	−0.046055	0.336418	0.622769	0.018*
H3B	0.016091	0.308112	0.745352	0.018*
C4	0.1307 (2)	0.1037 (2)	0.67046 (17)	0.0162 (4)
H4A	0.218474	0.054304	0.724099	0.019*
H4B	0.036067	0.053469	0.702984	0.019*
C5	0.2153 (2)	−0.0733 (2)	0.51930 (18)	0.0173 (4)
H5	0.158663	−0.145004	0.574691	0.021*
C6	0.2978 (2)	−0.1103 (2)	0.40935 (18)	0.0187 (5)
H6	0.296071	−0.205323	0.391527	0.022*
C7	0.3833 (2)	−0.0044 (2)	0.32589 (17)	0.0164 (4)
C8	0.3838 (2)	0.1365 (2)	0.35360 (17)	0.0144 (4)
H8	0.441305	0.207256	0.297862	0.017*
C9	0.2997 (2)	0.1742 (2)	0.46359 (16)	0.0126 (4)
C10	0.2144 (2)	0.0675 (2)	0.54957 (17)	0.0144 (4)
C11	0.2330 (2)	0.4869 (2)	0.63856 (16)	0.0148 (4)
H11	0.328592	0.521549	0.592644	0.018*
C12	0.1455 (2)	0.5600 (2)	0.74244 (16)	0.0140 (4)
C13	0.2469 (2)	0.6008 (2)	0.80319 (17)	0.0146 (4)
H13	0.368496	0.577884	0.778324	0.017*
C14	0.1689 (2)	0.6745 (2)	0.89955 (16)	0.0125 (4)
C15	−0.0127 (2)	0.7119 (2)	0.93335 (17)	0.0152 (4)
C16	−0.1169 (2)	0.6785 (2)	0.87378 (17)	0.0160 (4)
H16	−0.239140	0.706603	0.896725	0.019*

Table 2: (continued)

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C17	−0.0369 (2)	0.6024 (2)	0.77918 (17)	0.0150 (4)
H17	−0.106861	0.578852	0.738910	0.018*
C18	0.2747 (2)	0.7185 (2)	0.96570 (17)	0.0165 (4)
C19	0.4475 (3)	−0.1562 (3)	0.17480 (19)	0.0276 (5)
H19A	0.496952	−0.260926	0.226263	0.041*
H19B	0.507533	−0.155696	0.094191	0.041*
H19C	0.323735	−0.138634	0.177394	0.041*
F1	−0.09011 (13)	0.78448 (14)	1.02701 (10)	0.0217 (3)
F2	0.26292 (14)	0.64104 (13)	1.08269 (9)	0.0209 (3)
F3	0.22247 (14)	0.88031 (13)	0.96210 (10)	0.0243 (3)
F4	0.44808 (13)	0.67637 (14)	0.92155 (10)	0.0219 (3)
O1	0.37797 (17)	0.42131 (16)	0.41329 (12)	0.0189 (3)
O2	0.46868 (17)	−0.02713 (17)	0.21432 (12)	0.0220 (3)

Source of material

7−Methoxy-1-tetralone and 4-fluoro-3-(trifluoromethyl) benzaldehyde were dissolved in 10 mL methanol. Sodium hydroxide (aqueous solution, 25%) was added to the mixture and stirred for 3 h at room temperature. The in process-control was monitored by silica gel thin layer chromatography (TLC, 254 nm). When 7-methoxy-1-tetralone was disappeared, the precipitate was filtered from the reaction mixture and dissolved with dichloromethane. The organic phase was washed respectively with deionized water and brine, dried over anhydrous sodium sulfate and condensed under vacuum. The crude product was purified by silica-gel column chromatography (petroleum ether: ethyl acetate = 10:1, *v/v*). Crystals were obtained under ambient conditions *via* solvent evaporation in the mixed solvents of dichloromethane and methanol (1:1, *v/v*) and drying under vacuo at 60 °C 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) = 0.97 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

Inflammation is a very common and important basic pathological process [4]. This process can result in the excessive release of inflammatory mediators or cytokines such as NO, TNF-α, PGE2, and interleukin (IL)-6 [5, 6]. When stimulated in the brain, the body defenses by producing inflammation. Microglia is the resident immune competent cells of the CNS [7, 8]. Activated microglia-mediated inflammatory responses play a key role in the pathological development of inflammatory neurodegenerative diseases in the central nervous system (CNS) [4, 7, 8]. Despite distinct embryonic origins, microglia and resident tissue macrophages are related. Monocyte-derived macrophages are classified into phenotyopic subsets: M1, M2a, M2b and M2c. During inflammatory neurodegenerative diseases in CNS, the resident microglia become activated and polarized to a pro-inflammatory M1 phenotype [9]. It has been reported that the pro-inflammatory cytokines (tumor necrosis factor (TNF-α), interleukin (IL)-6, IL-1β) secreted from M1 microglia can compromise BBB functions by activating the nuclear factor κB (NF-κB) signaling pathway [4, 10, 11], leading to BBB disruption. Concomitantly, the BBB disruption can promote glial activation then boosts CNS inflammation [12]. Moreover, activated microglia can produce reactive oxygen species (ROS), which may indirectly trigger neuroinflammation by activating NF-κB [13]. Therefore, an NF-κB inhibitor may be a perspective drug for the treatment of inflammatory CNS neurodegenerative diseases.

3,4-Dihydronaphthalen-1(2*H*)-one (DHN)derivatives with antitumor and anti-inflammatory activities have been investigated as novel modulators of allergic and inflammatory responses [14]. But DHN derivatives have rarely been developed as anti-neuroinflammatory drugs [4]. We designed a series of new benzylidene-substituted DHN derivatives and synthesized them through Claisen−Schmidt condensation reactions.

The crystal structure analysis revealed that **F1–2** crystallized in the triclinic space group $P\bar{1}$. The ORTEP diagram is presented in the Figure. There is only one drug molecule in the asymmetric unit. Compared to the C(2)=C(11) olefinic bonds, 4-fluoro-3-(trifluoromethyl) phenyl and carbonyl groups adopt the Estereochemistry [15, 16]. Because of the sterical effects 3,4-dihydrobenzo[*b*]oxepin-5(2*H*)-one, the 7-methoxyphenyl and 4-fluoro-3-(trifluoromethyl)phenyl groups are not coplanar with each other. This twisted configuration may increase interactions with bioactive molecules, for the purposes of creating more potent biological activity [17]. Bond lengths and angles are all in the expected ranges [18].

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