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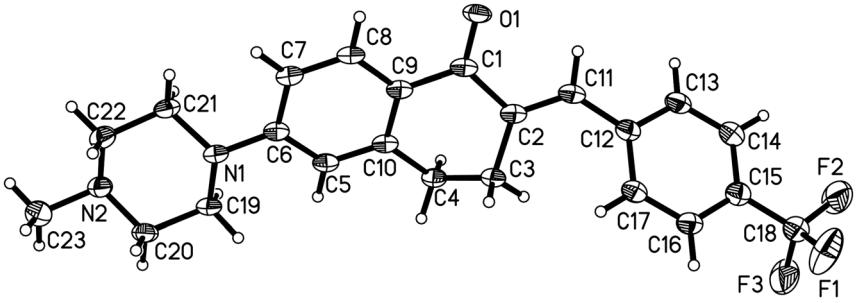
Crystal structure of (*E*)-6-(4-methylpiperazin-1-yl)-2-(4-(trifluoromethyl)benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one, $C_{23}H_{23}F_3N_2O$



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Abstract

$C_{23}H_{23}F_3N_2O$, monoclinic, *Cc* (no. 14), a = 19.6605(5) Å, b = 15.1474(3) Å, c = 6.4603(1) Å, β = 96.704(2)°, V = 1910.76(7) Å^3, Z = 4, R_{gt}(F) = 0.0567, wR_{ref}(F^2) = 0.1746, T = 293 K.

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The crystal structure is shown in the Figure 1. Displacement ellipsoids are drawn at the 50 % probability level. There is a drug molecule.

Table 1 contains details on crystal structure and measurement conditions.

The list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.16 × 0.13 × 0.12 mm
Wavelength:	Cu*K*α radiation (1.54178 Å)
μ:	0.89 mm^{-1}
Diffractometer, scan mode:	Rigaku, φ and ω scans
θ_{max}, completeness:	74.3°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	9,625, 3,779, 0.031
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs} > 2 σ(I_{obs}), 3,421
$N(param)_{refined}$:	264
Programs:	Rigaku,[1] SHELX.[2,3]

1 Source of material

Based on the literature synthesis,[4,5] *N*-methylpiperazine (16.02 g, 0.16 mol), potassium carbonate (27.80 g, 0.20 mol) and *N*,*N*-dimethylformamide (6 mL) were added into a 250 mL round flask. The mixture was stirred and reacted under an oil bath at 353 K for 4 h. After that, the temperature was raised to 383 K, and 6-fluoro-1-tetralone (3.35 g, 0.02 mol) was added. The reaction was continued for another 5 h. After filtration and spin evaporation, the residue was purified on a silica gel column chromatography (dichloromethane: methanol = 30:1, *v*: *v*) to afford the intermediate. Next, the intermediate (0.24 g, 1.0 mmol) and 4-(trifluoromethyl) benzaldehyde (0.34 g, 2.0 mmol) were dissolved in 3 mL methanol. A 25 % sodium hydroxide solution (3 mL) was used as a catalyst. The system was reacted on ice for 10 min and then stirred at room temperature for 2 days. The reaction was stopped when it was monitored by thin-layer chromatography (TLC) that the intermediate had been completely consumed. Then the precipitate obtained by suction filtration was rinsed with 50 % methanol. After drying, a dichloromethane and methanol solution (4 mL, 1:1,

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v: *v*) of the powder was kept at room temperature to obtain clear light colourless crystals after a few days.

2 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).

3 Comment

Previous studies revealed that 3,4-dihydronaphthalene-1(2*H*)-one compounds have excellent anti-inflammatory and anti-tumor activity.[6,7] The aldehyde group is drawn into the compound to obtain $\hat{I}\pm,\hat{I}^2$-unsaturated ketone by condensation, which increases the active site of the compound.[8] Fluorine is the most electronegative element and its inclusion in a molecule has a very strong effect on the acidity or basicity of proximal functional groups.[9,10] In addition, some research indicates that the introduction of a nitrogen-containing heterocycle at the end of the compound may reduce the toxicity and increase the biological activity of the compound.[11,12] Therefore, we introduced a trifluoromethyl group at the C(15) position and a *N*-methylpiperazine substituent at C(6) position to obtain the target compound, (*E*)-6-(4-methylpiperazin-1-yl)-2-(4- (trifluoromethyl)benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one.

Single crystal structure analysis shows that there is only one molecule in the asymmetric unit of the title compound (*cf.* Figure 1). The bond lengths and bond angles are within the normal range. The parent nucleus of the molecule is 3,4-dihydronaphthalene-1(2*H*)-one. The $\hat{I}\pm,\hat{I}^2$-unsaturated ketone was obtained at the C(2) position through the Claisen–Schmidt condensation reaction.[13] The bond lengths of O(1) = C(1) and C(2) = C(11) are 1.229(2) Å and 1.343(2) Å, respectively. The torsion angle of O(1) = C(1)–C(2) = C(11) is about −3.2(2)° and the torsion angle of C(1)–C(2) = C(11)–C(12) is about 172.26(16)°. Trifluoromethyl is substituted as an electron-withdrawing group at the C(15) position.[14] The bond length of C(15)–C(18) is 1.493(3) Å. The 3,4-dihydronaphthalene-1(2*H*)-one and the benzene ring connected to the trifluoromethyl group are not coplanar, and the dihedral angle is about 49.28(3)°. There is a *N*-methylpiperazine substitution at the C(6) position. The bond length of N(2)–C(23) is 1.457(2) Å. The torsion angle of N(1)–C(19)–C(20)–N(2) is about 56.70(19)°, and the torsion angle of N(1)–C(21)–C(22)–N(2) is about −57.2(2)°. The dihedral angle between the 3,4-dihydronaphthalene-1(2*H*)-one and the *N*-methylpiperazine is about 17.854(69)°. The *N* atom in *N*-methylpiperazine has a lone pair of electrons and can easily act as a hydrogen-bond acceptor or form hydrogen-bond interactions. The *N*-methylpiperazine ring adopts a "chair" configuration.[15] Overall, the molecule has a linear structure.[16]

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