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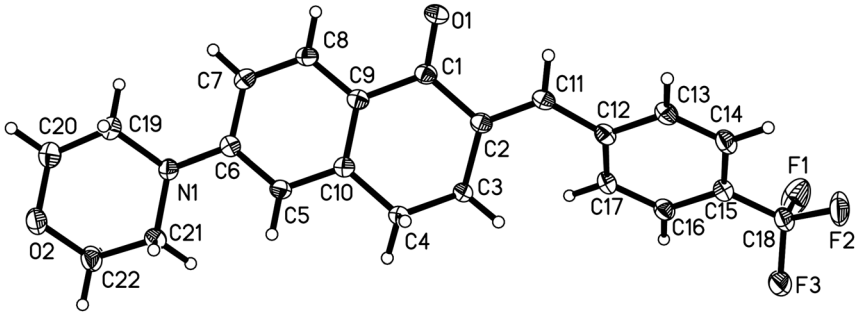
Crystal structure of (*E*)-6-morpholino-2-(4-(trifluoromethyl)benzylidene)-3,4-dihydronaphthalen-1(*2H*)-one, $C_{22}H_{20}F_3NO_2$



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Abstract

$C_{22}H_{20}F_3NO_2$, monoclinic, $P2_1/c$ (no. 14), a = 18.2286(3) Å, b = 15.0613(3) Å, c = 6.4904(1) Å, β = 94.082(2)°, V = 1777.40(5) Å^3, Z = 4, $R_{gt}(F)$ = 0.0388, $wR_{ref}(F^2)$ = 0.1082, T = 293 K.

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

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:	Clear light colourless block
Size:	0.15 × 0.12 × 0.10 mm
Wavelength:	CuKα radiation (1.54178 Å)
μ:	0.96 mm^{-1}
Diffractometer, scan mode:	Rigaku, φ and ω scans
θ_{max}, completeness:	74.4°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	9161, 3516, 0.021
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, $I_{obs} > 2\sigma(I_{obs})(I_{obs})$, 3,304
$N(param)_{refined}$:	254
Programs:	Rigaku,[1] SHELX[2,3]

1 Source of material

According to the synthesis method in reference[4–6], morphine (27.86 g, 0.32 mol) and potassium carbonate (55.4 g, 0.40 mol) were weighed into a 500 mL round-bottled flask and *N*,*N*-dimethylformamide (25.0 mL) was added to react at 313 K for 12 h. Then 6-fluoro-3,4-dihydronaphthalen-1(*2H*)-one (6.56 g, 0.04 mol) was added to the system at 393 K reflux reaction. Thin-Layer Chromatography (TLC, Dichloromethane:Methyl alcohol = 15:1, v:v) monitored the reaction process, and the reaction was stopped after 6 h. After the reaction system was restored to room temperature, solid-liquid separation was separated and the filter cake was washed white with dichloromethane (20.0 mL). The solvent was spun off and then separated by column chromatography with dichloromethane:methyl alcohol (30:1, v:v) as eluent to obtain the intermediate 6-morpholino-3,4-dihydronaphthalen-1(*2H*)-one. The intermediate (2.31 g, 0.01 mol) and 4-(trifluoromethyl)benzaldehyde (3.48 g, 0.02 mol) were dissolved in methanol (20.0 mL) and followed by 25 % sodium hydroxide solution (10.0 mL) as catalyst at 293 K for 24 h. Then it was washed and precipitated with petroleum ether and ultrasonic with acetone for 15 min. Dichloromethane (5.0 mL) and methanol alcohol (5.0 mL) were added for recrystallization at room temperature to obtain transparent crystal of (*E*)-6-morpholino-2-(4-(trifluoromethyl) benzylidene)-3,4-dihydronaphthalen-1(*2H*)-one.

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2 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) = 1.2 U_{eq}(C), and d(C–H) = 0.93 Å (aromatic), U_{iso}(H) = 1.2 U_{eq}(C).

3 Comment

3,4–Dihydronaphthalen-1(*2H*)-one derivatives have been reported in many articles and are considered as a new kind anti-inflammatory, anti-tumor modifier[7,8] and have also been shown to be active ingredients for the prevention of Alzheimer's disease and dementia.[9] The study found that there is an active pocket on the right side of it,[10] and small molecule drugs with different effects can be obtained by splicing different active functional groups. The introduction of benzene improves catalytic activity[11] and the electron-withdrawing group has been shown to have excellent anti-inflammatory and anti-tumor effects.[12] At the same time, nitrogen-containing heterocyclic compounds also have good biological activity and are the main pharmacophore of small molecule compounds. Morpholine fragments play a key role in the treatment of malignant tumors.[13] Therefore, we introduced morpholine and electron-absorbing group trifluoromethyl in the synthesis to further improve the activity of 3,4-dihydronaphthalen-1(*2H*)-one derivatives. The intermediate was obtained by nucleophilic substitution reaction with morpholine and 6-fluoro-3,4-dihydronaphthalen-1(*2H*)-one, and then the target compound was obtained by Claisen–Schmidt reaction with 4-(trifluoromethyl)benzaldehyde.

Single crystal structure analysis revealed that the title compound is monoclinic with only one drug molecule in the asymmetric unit (*cf.* Figure 1) and is consistent with previously reported compounds.[14] 3,4-Dihydronaphthalone is the main pharmacophore, followed by the introduction of morpholine at C6 position and 4-(trifluoromethyl)benzaldehyde at C2 position to form *α*,*β*-unsaturated ketone. In this molecule, the bond lengths of C(1)=O(1), C(1)–C(2), C(2)–C(3) and C(3)–C(4) located on the parent nucleus are 1.2246(15) Å, 1.5030(17) Å, 1.5033(16) Å, 1.5225(16) Å. The dihedral angle between these two planes is 14.69(3)°. At the same time, double bonds can be introduced at the C2 position through Claisen–Schmidt reaction, which allows the parent nucleus to be coplanar with *p*-trifluorobenzyl group. The bond length between C(2)=C(11) is 1.3459(17) Å, and the torsion angle of O(1)=C(1)–C(2)=C(11) is about 1.56(18)°. It is worth noting that the bond lengths of C(18)–F(1), C(18)–F(2), C(18)–F(3) are essentially the same. They are 1.3351(17) Å, 1.3326(16) Å, 1.3365(16) Å, respectively.[15–17] In addition, C(19)–N(1) and C(21)–N(1) on morphin has a bond length of about 1.4726(16) Å and 1.4675(16) Å. The morphin ring adopts a "chair" configuration.[16]

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