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Crystal structure of (3E,5E)-3,5-bis(4-cyanobenzylidene)-1-((4-fluorophenyl)sulfonyl)piperidin-4-one, C$_{27}$H$_{18}$FN$_{3}$O$_{3}$S

Abstract

C$_{27}$H$_{18}$FN$_{3}$O$_{3}$S, monoclinic, $P2_1/c$ (no. 14), $a = 8.091(6)$ Å, $b = 42.84(3)$ Å, $c = 7.096(6)$ Å, $\beta = 107.806(10)^\circ$, $V = 2342(3)$ Å$^3$, $Z = 4$, $R_{int} = 0.0616$, $wR_{ref} = 0.1321$, $T = 173(2)$ 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.

Source of material

4-Piperidone hydrochloride hydrate (0.77 g, 5.0 mmol) and 4-cyanobenzaldehyde (1.31 mol, 10.0 mmol) were dissolved in 25 mL of acetic acid. Dry HCL gas was passed through this mixture for 25 min. After stirring at room temperature for about 36 h, the mixture was added into 100 mL acetone. The precipitate was filtered and subsequently washed by acetone to provide a yellow intermediate. Then, the yellow intermediate and 4-fluorophenylsulfonylfluoride (0.89 g, 5.0 mol) were dissolved in 50 mL of dichloromethane. Potassium carbonate (2.76 g, 0.02 mol) was added and the mixture was stirred for 12 h at room temperature. The precipitate was collected, washed with water and recrystallized from dichloromethane/methanol (2:1, v/v) to get light yellow crystals of the title compound.

Experimental details

All H atoms were placed in idealized positions and treated as riding on their parent atoms, with $d$(C–H) = 0.99 Å (methylene), $U_{iso}$(H) = 1.2 $U_{eq}$(C) and $d$(C–H) = 0.95 Å (aromatic), $U_{iso}$(H) = 1.2 $U_{eq}$(C).

Discussion

Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)1,6-heptadien-3,5-dion) is a yellow pigment extracted from the rhizome of turmeric, which has anti-inflammatory, anti-tumor, antioxidation and other activities. However, the clinical application of curcumin is limited due to its low anticancer activity and poor bioavailability [4]. In order to improve these defects, a new class of curcumin analogs (3E,5E)-3,5-bis(arylidene)-4-piperidones (BAP) have been reported as better antitumor agents [5–9]. The pharmacophore of BAP is 1,5-diaryl-3-oxo-1,4-pentadienyl, which contains two $\alpha,\beta$-unsaturated keto groups and has a greater predilection or sequential interaction for bio-thiols resulting in a greater activity to...
Our interests lie in incorporation of strong electron-withdrawing substituent groups on both sides of BAP. In addition, we expect that inflammatory activity [11–13]. In previous study, crystal structure and bioactivity of 4-((E)−((E)−5-(2-fluorobenzylidene)-1-(4′-fluorophenyl)sulfonyl)-4-oxopiperidin-3-ylidene)methyl)benzonitrile (BAP-1) was reported [7, 14], which is a disymmetric compound. In this study, we report herein the crystal structure of (3E,5E)-3,5-bis(4-cyanobenzylidene)-1-((4-fluorophenyl)sulfonyl)piperidin-4-one.

There is one molecule in the asymmetric unit of the title crystal structure (cf. the figure). Bond lengths and angles are all in the expected ranges. Single-crystal structure analysis reveals that two 4-cyano phenyl groups on both sides of 3,5-bis(arylidene)-4-piperidone are symmetric compared with central piperidin-4-one. The piperidin-4-one moiety shows the typical folding. The E stereochemistry of olefinic double bonds is adopted [15]. And the dihedral angles between two 4-cyano phenyl groups is 37°. The 2-fluorophenyl group is almost coplanar with 1,5-diaryl-3-oxo-1,4-pentadienyl moiety, which can be proved by the dihedral angles (16.36(9)°). On the whole, the title molecule looks like an “organic clip” [16]. The heteroatoms (F, N, O, S) can act as hydrogen bonding acceptors for biological macromolecules with the aim of creating more potent cytostatica [17].

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References


