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Crystal structure of (3*E*,5*E*)-3,5-bis(4-cyanobenzylidene)-1-((4-fluorophenyl)sulfonyl)piperidin-4-one, C₂₇H₁₈FN₃O₃S

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Abstract

C₂₇H₁₈FN₃O₃S, monoclinic, *P*₂₁/*c* (no. 14), *a* = 8.091(6) Å, *b* = 42.84(3) Å, *c* = 7.096(6) Å, β = 107.806(10)°, *V* = 2342(3) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0616, *wR*_{ref}(*F*²) = 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

Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	0.15 × 0.07 × 0.05 mm
Wavelength:	Mo Kα radiation (0.71073 Å)
μ:	0.18 mm ⁻¹
Diffractometer, scan mode:	Bruker SMART, φ and ω-scans
θ _{max} , completeness:	25.5°, >99%
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	12141, 4354, 0.085
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 2639
<i>N</i> (<i>param</i>) _{refined} :	316
Programs:	Bruker programs [1], SHELX [2, 3]

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-dione) is a yellow pigment extracted from the rhizome of turmeric, which has anti-inflammatory, anti-tumor, anti-oxidation 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 (3*E*,5*E*)-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 α,β-unsaturated keto groups and has a greater predilection or sequential interaction for bio-thiols resulting in a greater activity to

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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	0.4144(4)	0.05423(7)	0.8923(5)	0.0383(8)
C2	0.3696(5)	0.02551(7)	0.7924(5)	0.0423(8)
H2	0.2532	0.0183	0.7570	0.051*
C3	0.4956(5)	0.00785(8)	0.7457(5)	0.0473(9)
H3	0.4645	−0.0112	0.6747	0.057*
C4	0.6666(5)	0.01789(8)	0.8026(5)	0.0447(9)
C5	0.7138(5)	0.04582(7)	0.9054(5)	0.0452(9)
H5	0.8315	0.0525	0.9461	0.054*
C6	0.5876(4)	0.06378(7)	0.9476(5)	0.0412(8)
H6	0.6194	0.0830	1.0155	0.049*
C7	0.2767(4)	0.07219(7)	0.9406(5)	0.0414(8)
H7	0.1932	0.0602	0.9782	0.050*
C8	0.2542(4)	0.10341(7)	0.9382(5)	0.0375(8)
C9	0.0973(4)	0.11562(7)	0.9836(5)	0.0391(8)
C10	0.0547(4)	0.14970(7)	0.9537(4)	0.0371(7)
C11	0.1839(4)	0.17053(7)	0.8963(5)	0.0412(8)
H11A	0.1223	0.1889	0.8234	0.049*
H11B	0.2721	0.1781	1.0177	0.049*
C12	0.3705(4)	0.12645(7)	0.8759(5)	0.0439(8)
H12A	0.4630	0.1337	0.9946	0.053*
H12B	0.4267	0.1158	0.7877	0.053*
C13	−0.0974(4)	0.15965(7)	0.9680(5)	0.0426(8)
H13	−0.1668	0.1444	1.0048	0.051*
C14	−0.1714(4)	0.19136(8)	0.9338(5)	0.0420(8)
C15	−0.0730(5)	0.21821(8)	1.0024(5)	0.0469(9)
H15	0.0458	0.2163	1.0780	0.056*
C16	−0.1482(5)	0.24764(8)	0.9607(5)	0.0488(9)
H16	−0.0810	0.2658	1.0094	0.059*
C17	−0.3205(5)	0.25055(8)	0.8484(5)	0.0456(9)
C18	−0.4219(5)	0.22393(9)	0.7796(6)	0.0522(9)
H18	−0.5409	0.2258	0.7047	0.063*
C19	−0.3455(5)	0.19479(8)	0.8229(5)	0.0499(9)
H19	−0.4134	0.1767	0.7759	0.060*
C20	−0.4000(5)	0.28102(9)	0.8010(5)	0.0516(9)
C21	0.8016(5)	−0.00053(8)	0.7561(6)	0.0539(9)
C22	−0.0040(4)	0.12678(7)	0.4859(5)	0.0359(8)
C23	0.0195(4)	0.09466(7)	0.4719(5)	0.0415(8)
H23	0.1298	0.0865	0.4759	0.050*
C24	−0.1209(5)	0.07466(8)	0.4520(5)	0.0458(9)
H24	−0.1078	0.0527	0.4444	0.055*
C25	−0.2787(5)	0.08749(8)	0.4438(5)	0.0451(9)
C26	−0.3065(4)	0.11904(8)	0.4516(5)	0.0467(9)
H26	−0.4183	0.1270	0.4426	0.056*
C27	−0.1664(4)	0.13910(7)	0.4732(5)	0.0397(8)
H27	−0.1815	0.1610	0.4791	0.048*
F1	−0.4166(3)	0.06807(5)	0.4238(3)	0.0680(6)
N1	0.2715(3)	0.15380(6)	0.7715(4)	0.0397(6)
N2	0.9092(5)	−0.01436(8)	0.7186(6)	0.0778(11)
N3	−0.4593(4)	0.30522(8)	0.7653(5)	0.0687(10)
O1	0.0005(3)	0.09806(5)	1.0367(4)	0.0546(7)
O2	0.2994(3)	0.13803(5)	0.4493(4)	0.0555(7)
O3	0.1126(3)	0.18305(5)	0.4737(4)	0.0522(6)
S1	0.17615(10)	0.15208(2)	0.53075(13)	0.0405(2)

tumors rather than with normal cells. For example, 3,5-bis(2-fluorobenzylidene)-4-piperidone (EF24) is a more potent antitumor drug than curcumin that disrupts the microtubule cytoskeleton and inhibits HIF-1 [10].

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 dissymmetric compound. In this study, we report herein the crystal structure of (3*E*,5*E*)-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(4)°). 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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