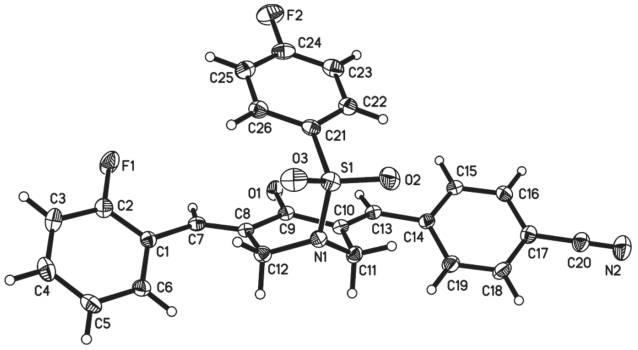
Lian-Dong Liu*, Shu-Lian Liu and Gui-Ge Hou

Crystal structure of 4-((*E*)-((*E*)-5-(2-fluorobenzylidene)-1-((4-fluorophenyl) sulfonyl)-4-oxopiperidin-3-ylidene)methyl)benzonitrile, $C_{26}H_{18}F_2N_2O_3S$



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Abstract

$C_{26}H_{18}F_2N_2O_3S$, monoclinic, $P2_1/c$ (no. 14), $a = 8.412(3)$ Å, $b = 22.056(8)$ Å, $c = 12.125(4)$ Å, $\beta = 102.316(5)°$, $V = 2198.0(14)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0475$, $wR_{ref}(F^2) = 0.1156$, $T = 173(2)$ K.

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The crystal structure is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Source of material

N-Methyl-4-piperidone (1.14 g, 0.01 mol), 2-fluorobenzaldehyde (1.24 mol, 0.01 mol) and 4-cyanobenzaldehyde (1.31 g, 0.01 mol) were dissolved in 15 mL of acetic acid. Dry HCl gas was passed through this mixture for 25 min. After stirring at room temperature for about 24 h, the mixture was added into 100 mL water, and then aqueous NaOH solution was added until the pH was adjusted to about 7. The mixture was filtered and subsequently washed by water to provide a yellow precipitate. The precipitates were purified on silica gel by column using methanol/petroleum ether/EtOAc (10:10:1, v/v/v) as the eluent to afford a yellow intermediate. Then, the yellow intermediate and 4-fluorophenylsulfonylfluoride (1.78 g, 0.01 mol) were dissolved in 50 mL of dichloromethane. Potassium carbonate (2.76 g, 0.02 mol) was added to the mixture and the mixture were stirred for about 12 h at room temperature. The precipitate was collected, washed with water and recrystallized from dichloromethane/methanol (1:1, *v*/*v*) to get light yellow crystals of title compound.

Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	0.26 × 0.25 × 0.05 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.20 mm^{-1}
Diffractometer, scan mode:	Bruker SMART, φ and ω-scans
θ_{max}, completeness:	25.5°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	11378, 4095, 0.034
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3110
$N(param)_{refined}$:	307
Programs:	Bruker programs [1], SHELX [2, 3]

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), $U_{iso}(H) = 1.2U_{eq}(C)$ and d(C—H) = 0.95 Å (aromatic), $U_{iso}(H) = 1.2U_{eq}(C)$.

Discussion

Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)1,6-heptadien-3,5-dion) has proved to be a powerful chemopreventive and anticancer agent, including anti-inflammatory, antibacterial, and antioxidant properties. However, the clinical use of curcumin has been limited because of its low anticancer activity and poor bioavailability [4]. In order to improve these defects, a novel class of curcumin analogues, (3*E*,5*E*)-3,5-bis(arylidene)-4-piperidone derivatives, has been reported as better antitumor agents [5–8]. Its pharmacophore is 1,5-diaryl-3-oxo-1,4-pentadienyl, which contains a α,β-unsaturated keto group and has a greater preference or sequential affinity for bio-thiols in contrast to

***Corresponding author: Lian-Dong Liu,** College of Chemistry, Chemical Engineering and Materials Science, Collaborative Innovation Center of Functionalized Probes for Chemical Imaging in Universities of Shandong, Key Laboratory of Molecular and Nano Probes, Ministry of Education, Shandong Provincial Key Laboratory of Clean Production of Fine Chemicals, Shandong Normal University, Jinan 250014, P.R. China, e-mail: lld369@sina.com
Shu-Lian Liu: Shandong Education Training Center of Quality and Technical Supervision, Jinan 250014, P.R. China
Gui-Ge Hou: School of Pharmacy, Binzhou Medical University, Yantai, Shandong 264003, P.R. China

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
F1	0.39138(19)	0.69104(6)	0.33479(12)	0.0567(4)
F2	0.6284(2)	0.67176(7)	−0.07671(13)	0.0642(5)
N1	0.9098(2)	0.49932(8)	0.36203(14)	0.0287(4)
N2	1.0896(3)	0.18516(11)	−0.0654(2)	0.0623(7)
O1	0.47692(18)	0.51400(7)	0.14691(13)	0.0376(4)
O2	1.13701(19)	0.50701(8)	0.26644(15)	0.0496(5)
O3	1.0843(2)	0.58965(8)	0.39257(14)	0.0477(5)
S1	1.02532(7)	0.54487(3)	0.30837(5)	0.03483(17)
C1	0.5109(2)	0.61043(9)	0.45075(18)	0.0282(5)
C2	0.4474(3)	0.66868(10)	0.4410(2)	0.0370(6)
C3	0.4388(3)	0.70506(12)	0.5313(2)	0.0455(6)
H3	0.3953	0.7449	0.5203	0.055*
C4	0.4952(3)	0.68229(12)	0.6391(2)	0.0464(7)
H4	0.4896	0.7065	0.7029	0.056*
C5	0.5594(3)	0.62475(11)	0.6538(2)	0.0417(6)
H5	0.5979	0.6093	0.7278	0.050*
C6	0.5677(3)	0.58948(10)	0.56101(18)	0.0341(5)
H6	0.6133	0.5500	0.5724	0.041*
C7	0.5110(3)	0.57439(9)	0.34961(17)	0.0279(5)
H7	0.4190	0.5790	0.2893	0.033*
C8	0.6254(2)	0.53571(9)	0.33204(17)	0.0250(5)
C9	0.5941(2)	0.50182(9)	0.22258(18)	0.0270(5)
C10	0.7093(2)	0.45183(9)	0.20863(17)	0.0273(5)
C11	0.8562(3)	0.44224(9)	0.30376(18)	0.0320(5)
H11A	0.8286	0.4128	0.3585	0.038*
H11B	0.9463	0.4250	0.2729	0.038*
C12	0.7842(2)	0.52497(10)	0.41614(17)	0.0301(5)
H12A	0.8236	0.5639	0.4528	0.036*
H12B	0.7648	0.4969	0.4756	0.036*
C13	0.6782(3)	0.42130(9)	0.11060(18)	0.0290(5)
H13	0.5859	0.4345	0.0564	0.035*
C14	0.7683(3)	0.37020(9)	0.07624(18)	0.0295(5)
C15	0.7667(3)	0.36228(9)	−0.03809(18)	0.0301(5)
H15	0.7067	0.3897	−0.0916	0.036*
C16	0.8503(3)	0.31550(10)	−0.07497(19)	0.0331(5)
H16	0.8481	0.3109	−0.1532	0.040*
C17	0.9383(3)	0.27491(10)	0.00278(19)	0.0348(5)
C18	0.9386(3)	0.28133(10)	0.1174(2)	0.0425(6)
H18	0.9972	0.2534	0.1706	0.051*
C19	0.8538(3)	0.32810(10)	0.1533(2)	0.0393(6)
H19	0.8533	0.3319	0.2313	0.047*
C20	1.0241(3)	0.22505(11)	−0.0344(2)	0.0428(6)
C21	0.9050(3)	0.58326(9)	0.19160(18)	0.0301(5)
C22	0.8874(3)	0.55904(10)	0.08393(19)	0.0367(5)
H22	0.9407	0.5222	0.0731	0.044*
C23	0.7924(3)	0.58846(11)	−0.0074(2)	0.0418(6)
H23	0.7786	0.5724	−0.0816	0.050*
C24	0.7188(3)	0.64138(11)	0.0126(2)	0.0427(6)
C25	0.7324(3)	0.66633(11)	0.1182(2)	0.0422(6)
H25	0.6783	0.7031	0.1282	0.051*
C26	0.8265(3)	0.63652(10)	0.20921(19)	0.0348(5)
H26	0.8374	0.6524	0.2833	0.042*

amino and hydroxy groups resulting in a greater chemosensitivity to tumors rather than with normal cells. Our interests lie in incorporation of different substituent groups on both sides of (3*E*,5*E*)-3,5-bis(arylidene)-4-piperidone. In addition, *N*-benzenesulfonyl substituents should improve antitumor activities and anti-inflammatory activity [9–13]. In this study, we report herein the crystal structure of 4-((*E*)-((*E*)-5-(2-fluorobenzylidene)-1-((4-fluorophenyl)sulfonyl)-4-oxopiperidin-3-ylidene)methyl)benzonitrile.

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. Derived from the crystal structure deterimination we learned that the C1—C7—C8—C9 torsion angle value is 177.29(3)° and the C9—C10—C13—C14 torsion angle value is 178.64(2)°. The 2-fluorophenyl group and the 4-cyano phenyl group on both sides of 3,5-bis(arylidene)-4-piperidone adopt the *E* stereochemistry of olefinic double bonds and the *E*, *E* isomer [14]. The 4-fluorophenyl group is almost coplanar with two substituated aryl rings on both sides of 3,5-bis(arylidene)-4-piperidone, which can be proved by the dihedral angles (12.207(4)° and 13.925(5)°, respectively). On the whole, the title molecule group looks like an "organic clip" [15]. The heteroatoms (F, N, O, S) can act as hydrogen bonding acceptors for biological macromolecules with the aim of creating more potent cytostatica [16].

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