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Crystal structure of (3*E*,5*E*)-3,5-bis(3-nitrobenzylidene)-1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-one — dichloromethane (2/1), C₅₃H₃₈Cl₂F₆N₆O₁₄S₂

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Abstract

C₅₃H₃₈Cl₂F₆N₆O₁₄S₂, triclinic, *P* $\bar{1}$ (no. 2), $a = 12.1975(6)$ Å, $b = 13.9973(7)$ Å, $c = 16.3818(10)$ Å, $\alpha = 69.365(5)^\circ$, $\beta = 76.620(5)^\circ$, $\gamma = 77.292(4)^\circ$, $V = 2516.8(3)$ Å³, $Z = 2$, $R_{\text{gt}}(F) = 0.0540$, $wR_{\text{ref}}(F^2) = 0.1413$, $T = 100.02(10)$ K.

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The asymmetric unit of 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.

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Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	0.13 × 0.11 × 0.09 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.31 mm ^{−1}
Diffractometer, scan mode:	SuperNova,
θ_{max} , completeness:	29.6°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	32642, 12083, 0.039
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 9426
$N(\text{param})_{\text{refined}}$:	748
Programs:	CrysAlis ^{PRO} [1], SHELX [2, 3]

Source of material

3-Nitrobenzaldehyde (1.51 mol, 10.0 mmol) and 4-piperidone hydrate hydrochloride (0.77 g, 5.0 mmol) were dissolved in 25 mL of acetic acid. Dry HCL gas was passed through the mixture for 25 min. After stirring at room temperature overnight, the mixture was added into 100 mL acetone. The precipitate was filtered and washed by cold acetone to obtain a yellow intermediate. Then, the yellow intermediate, 4-(trifluoromethyl)benzenesulfonylchloride (1.22 g, 5.0 mol) and potassium carbonate (2.76 g, 0.02 mol) were mixed in 50 mL of dichloromethane. The mixture was 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 the title compound.

Experimental details

All H atoms were placed in idealized positions and treated as riding on their parent atoms, with $d(\text{C}–\text{H}) = 0.97$ Å (methylene), $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ and $d(\text{C}–\text{H}) = 0.93$ Å (aromatic), $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$.

Comment

Curcumin, 1,7-bis(4-hydroxy-3-methoxyphenyl)1,6-heptadien-3,5-dione, has been extensively investigated for its anti-inflammatory activity, anti-tumor, anti-oxidation and other activities. However, its clinical application was limited due to its low bioactivities, poor aqueous solubility and relatively low bioavailability [4]. In order to improve these defects, a series of novel curcumin analogs (such as

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
C1	0.8280(2)	0.59233(17)	0.62487(15)	0.0155(5)
H1A	0.903306	0.553515	0.614371	0.019*
H1B	0.771714	0.547615	0.637103	0.019*
C2	0.81726(19)	0.63143(17)	0.70176(15)	0.0144(4)
C3	0.7305(2)	0.72551(17)	0.70534(15)	0.0153(5)
C4	0.65484(19)	0.76653(17)	0.63694(15)	0.0145(5)
C5	0.68973(19)	0.73525(17)	0.55463(15)	0.0140(4)
H5A	0.640507	0.688521	0.556361	0.017*
H5B	0.680813	0.795930	0.503175	0.017*
C6	0.88242(19)	0.59230(17)	0.76486(15)	0.0143(4)
H6	0.870004	0.627684	0.805534	0.017*
C7	0.9708(2)	0.50104(17)	0.77835(15)	0.0149(5)
C8	1.0674(2)	0.50570(19)	0.80817(15)	0.0172(5)
H8	1.074939	0.565246	0.818064	0.021*
C9	1.1517(2)	0.42030(19)	0.82273(15)	0.0188(5)
C10	1.1425(2)	0.32790(19)	0.81352(16)	0.0209(5)
H10	1.199264	0.270953	0.826024	0.025*
C11	1.0455(2)	0.32291(18)	0.78498(15)	0.0183(5)
H11	1.036940	0.261847	0.778232	0.022*
C12	0.9616(2)	0.40866(18)	0.76653(15)	0.0164(5)
H12	0.898171	0.404876	0.745999	0.020*
C13	0.5572(2)	0.82874(17)	0.65510(16)	0.0162(5)
H13	0.547154	0.841296	0.708656	0.019*
C14	0.46498(19)	0.87946(17)	0.60396(15)	0.0154(5)
C15	0.45007(19)	0.85943(17)	0.52943(16)	0.0164(5)
H15	0.501062	0.809941	0.508405	0.020*
C16	0.3589(2)	0.91410(18)	0.48789(16)	0.0183(5)
C17	0.2794(2)	0.98875(18)	0.51577(17)	0.0208(5)
H17	0.220000	1.025684	0.485074	0.025*
C18	0.2918(2)	1.00611(18)	0.59105(17)	0.0198(5)
H18	0.238796	1.054039	0.612694	0.024*
C19	0.3826(2)	0.95265(18)	0.63425(17)	0.0183(5)
H19	0.389460	0.965427	0.684717	0.022*
C20	0.77964(19)	0.61476(17)	0.41905(15)	0.0138(4)
C21	0.7972(2)	0.50770(18)	0.44643(16)	0.0170(5)
H21	0.857179	0.470219	0.476209	0.020*
C22	0.7238(2)	0.45745(18)	0.42871(16)	0.0190(5)
H22	0.733721	0.385674	0.447072	0.023*
C23	0.6354(2)	0.51491(18)	0.38337(16)	0.0172(5)
C24	0.6180(2)	0.62231(19)	0.35600(16)	0.0173(5)
H24	0.558055	0.659757	0.326090	0.021*
C25	0.6908(2)	0.67280(18)	0.37381(15)	0.0157(5)
H25	0.680585	0.744577	0.355818	0.019*
C26	0.5533(2)	0.4599(2)	0.36834(17)	0.0212(5)
C27	1.03724(19)	0.10536(17)	0.02346(16)	0.0157(5)
H27A	1.055584	0.114441	−0.039419	0.019*
H27B	1.071374	0.036332	0.054594	0.019*
C28	1.08701(19)	0.18383(17)	0.04234(15)	0.0142(4)
C29	1.0148(2)	0.28708(17)	0.03753(15)	0.0154(5)
C30	0.90077(19)	0.30703(17)	0.00905(15)	0.0138(4)
C31	0.8543(2)	0.21691(17)	0.00460(16)	0.0161(5)
H31A	0.773954	0.221683	0.030108	0.019*
H31B	0.860914	0.222279	−0.056965	0.019*
C32	1.1905(2)	0.16554(18)	0.06454(15)	0.0163(5)
H32	1.210249	0.217132	0.079333	0.020*

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
C33	1.27624(19)	0.07284(17)	0.06803(16)	0.0155(5)
C34	1.3482(2)	0.04095(18)	0.13117(16)	0.0161(5)
H34	1.342198	0.077973	0.169709	0.019*
C35	1.4287(2)	−0.04716(18)	0.13503(16)	0.0168(5)
C36	1.4420(2)	−0.10540(18)	0.07936(17)	0.0197(5)
H36	1.495312	−0.165121	0.084910	0.024*
C37	1.3731(2)	−0.07167(18)	0.01516(17)	0.0187(5)
H37	1.381512	−0.107980	−0.024315	0.022*
C38	1.2913(2)	0.01627(18)	0.00935(16)	0.0173(5)
H38	1.245842	0.037960	−0.034184	0.021*
C39	0.84731(19)	0.40559(17)	−0.01441(15)	0.0144(4)
H39	0.882813	0.453253	−0.006396	0.017*
C40	0.7409(2)	0.44833(17)	−0.05086(15)	0.0152(5)
C41	0.6887(2)	0.54784(18)	−0.04940(15)	0.0159(5)
H41	0.720846	0.583960	−0.025271	0.019*
C42	0.5895(2)	0.59180(18)	−0.08397(15)	0.0166(5)
C43	0.5381(2)	0.54235(19)	−0.12167(16)	0.0197(5)
H43	0.471349	0.573714	−0.144578	0.024*
C44	0.5899(2)	0.44457(19)	−0.12393(17)	0.0211(5)
H44	0.557440	0.409431	−0.148760	0.025*
C45	0.6894(2)	0.39842(18)	−0.08967(16)	0.0180(5)
H45	0.722910	0.332939	−0.092407	0.022*
C46	0.8910(2)	0.10002(18)	0.22637(16)	0.0181(5)
C47	0.9802(2)	0.0470(2)	0.27252(18)	0.0250(6)
H47	1.024579	−0.011735	0.261458	0.030*
C48	1.0023(2)	0.0825(2)	0.33492(18)	0.0252(6)
H48	1.061800	0.047851	0.366116	0.030*
C49	0.9354(2)	0.16991(19)	0.35076(16)	0.0198(5)
C50	0.8486(2)	0.22436(18)	0.30242(17)	0.0204(5)
H50	0.806399	0.284625	0.311862	0.024*
C51	0.8251(2)	0.18911(18)	0.24045(16)	0.0193(5)
H51	0.766307	0.224384	0.208705	0.023*
C52	0.9523(2)	0.2032(2)	0.42391(17)	0.0245(6)
C53	0.1851(3)	0.7656(2)	0.3153(2)	0.0375(7)
H53A	0.112049	0.746175	0.348322	0.045*
H53B	0.204990	0.812879	0.338939	0.045*
Cl1	0.28922(9)	0.65486(6)	0.32854(7)	0.0584(3)
Cl2	0.17403(7)	0.82736(6)	0.20381(5)	0.03666(18)
F1	0.59999(15)	0.36509(13)	0.36398(14)	0.0420(5)
F2	0.51409(16)	0.50912(14)	0.29292(12)	0.0403(4)
F3	0.46382(16)	0.44716(17)	0.43253(12)	0.0489(5)
F4	0.94753(13)	0.30517(12)	0.40120(10)	0.0275(3)
F5	0.86952(19)	0.17980(18)	0.49448(12)	0.0556(6)
F6	1.05067(17)	0.16023(14)	0.45113(13)	0.0467(5)
N1	0.80908(16)	0.68418(14)	0.54688(12)	0.0136(4)
N2	1.25620(19)	0.42942(19)	0.84814(14)	0.0251(5)
N3	0.34320(18)	0.89041(17)	0.41104(14)	0.0221(5)
N4	0.91333(17)	0.11597(15)	0.05104(13)	0.0164(4)
N5	1.50686(18)	−0.07743(16)	0.19928(14)	0.0202(4)
N6	0.53398(18)	0.69507(16)	−0.07935(14)	0.0197(4)
O1	0.72015(15)	0.76400(13)	0.76350(11)	0.0218(4)
O2	0.97763(13)	0.61624(12)	0.45446(11)	0.0165(3)
O3	0.86026(14)	0.78291(12)	0.38867(11)	0.0171(3)
O4	1.32487(17)	0.35070(17)	0.87119(15)	0.0381(5)
O5	1.26983(16)	0.51577(16)	0.84366(14)	0.0318(5)
O6	0.39888(17)	0.81163(15)	0.39672(13)	0.0317(5)

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
O7	0.27415(16)	0.94992(15)	0.36508(12)	0.0286(4)
O8	1.04822(15)	0.35323(13)	0.05388(12)	0.0214(4)
O9	0.73760(15)	0.07112(14)	0.15476(12)	0.0237(4)
O10	0.91760(16)	−0.05283(13)	0.16630(12)	0.0245(4)
O11	1.57554(17)	−0.15676(15)	0.20459(13)	0.0319(5)
O12	1.49989(16)	−0.02156(14)	0.24370(13)	0.0268(4)
O13	0.57484(16)	0.73538(13)	−0.04039(12)	0.0255(4)
O14	0.44863(16)	0.73480(15)	−0.11349(13)	0.0298(4)
S1	0.86809(5)	0.67870(4)	0.44758(4)	0.01307(12)
S2	0.85863(5)	0.05059(4)	0.15021(4)	0.01771(13)

3*E*,5*E*-3,5-bis(arylidene)-4-piperidones (BAPs)) were previously synthesized as better antitumor and anti-inflammatory agents in our laboratory [5, 6]. BAPs have greater predilection or sequential interaction for bio-thiols resulting in a greater activity to tumors rather than with normal cell because BAPs contain two α,β -unsaturated keto groups [7]. Our interests lie in incorporation of strong electron-withdrawing substituent groups (such as −NO₂) on both sides of BAPs. Meanwhile, strong electron-withdrawing trifluoromethyl group was introduced into *N*-benzenesulfonyl substituents of BAPs. We want to be able to improve antitumor and anti-inflammatory activity [8].

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) and (3*E*,5*E*)-3,5-bis(4-cyanobenzylidene)-1-((4-fluorophenyl)sulfonyl)piperidin-4-one (BAP-2) were reported [9, 10].

There are two BAPs molecules and a dichloromethane molecule in the asymmetric unit of the title crystal structure (*cf.* the figure). Bond lengths and angles all in the expected ranges [10]. Single-crystal structure analysis reveals that configurations of two BAPs molecules are different. In one molecule, two 3-nitro phenyl groups on both sides of 3,5-bis(arylidene)-4-piperidone are symmetric compared with central piperidin-4-one, which adopt the *E* stereochemistry of olefinic double bonds. And the dihedral angles between two 4-nitro phenyl groups is 24.53(6)°. The 4-trifluoromethylphenyl group bend towards the side of carbonyl group. The molecule looks like an “organic clip” [11]. In the other molecules, two 3-nitro phenyl groups take the *trans*-configuration. Meanwhile, 4-trifluoromethylphenyl group stretch in the other direction of carbonyl group, which is different with the first molecule. In title compound, the peripheric heteroatoms (such as F, N, O, S) can act as hydrogen bonding acceptors

for bioactive molecules with the aim of creating more potent biological activity [12, 13].

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