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Key indicators

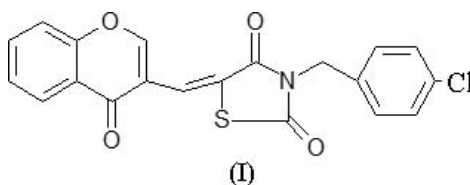
Single-crystal X-ray study
T = 293 K
Mean $\sigma(C-C)$ = 0.004 Å
R factor = 0.048
wR factor = 0.125
Data-to-parameter ratio = 13.7For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.3-(4-Chlorobenzyl)-5-(4-oxo-4*H*-chromen-3-yl-methylene)-1,3-thiazolidine-2,4-dione

In the title molecule, C₂₀H₁₂ClNO₄S, the benzopyran ring system and the thiazolidine ring are planar. The dihedral angle between the chlorobenzyl and thiazolidine rings is 74.42 (8)°. The crystal structure is stabilized by intermolecular C—H···O hydrogen bonds.

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Comment

Type 2 diabetes is a chronic and metabolic disease characterized by hyperglycemia and insulin resistance. In recent years, more effective orally active agents were discovered which effectively reduce insulin resistance. These agents have a common thiazolidine-2,4-dione substructure. 2,4-Thiazolidinediones provide many benefits to patients with type 2 diabetes by improving glycemic control and insulin sensitivity, thereby having the potential to decrease the risk of cardiovascular disease associated with insulin resistance (Fonseca, 2003). The chromone moiety forms the important component of pharmacophores of a number of biologically active molecules of synthetic as well as natural origin and many of them have useful medicinal applications (Singh *et al.*, 2002). The title compound, (I), is a chromonyl 2,4-thiazolidinedione and was synthesized for antidiabetic activity. Initially, the structure of (I) was evaluated by elementary analysis, ¹H NMR, mass and IR spectroscopic techniques. The crystal structure analysis of (I) was undertaken to elucidate the molecular conformation.



The benzopyran moiety is essentially planar (Fig. 1). In most of the flavones, the pyrone ring is distorted (Kendi *et al.*, 1996), but in (I) it is planar. The thiazolidine ring is planar within 0.012 (2) Å. The dihedral angle between the C15–C20 benzene ring and the thiazolidine ring is 74.42 (8)°. The C1=O1, C3=O2 and C6=O4 bonds have normal double-bond values of 1.207 (3), 1.211 (3) and 1.216 (3) Å, respectively. The strain caused by the ring fusion results in a slight widening of the angle O3–C8–C7 [121.4 (2)°] and narrowing of the angle C5–C6–C7 [114.9 (2)°] from the normal value of 120°. These angles are 122.9 (5) and 114.2 (6)° in 2'-methyl-3'-nitroflavone (Kendi *et al.*, 1996), and 121.2 (2) and 115.6 (2)° in morin (Cody & Luft, 1994). The molecular structure and crystal packing are stabilized by C—H···O hydrogen bonds

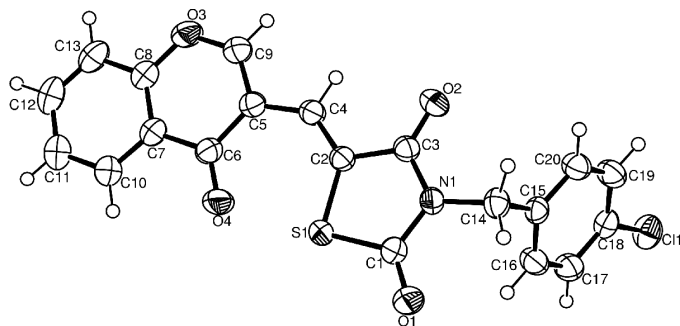


Figure 1

An ORTEP-3 (Farrugia, 1997) drawing of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

(Table 2). The intramolecular C—H...O hydrogen bond formed between atoms O4 and C10 is also seen in 7-hydroxy-2',6'-dimethoxyflavone (Wallet *et al.*, 1992) and 2-(2-ethoxy-carbonyl-1,4-benzodioxan-7-yl)-4H-1-benzopyranone (Özbey *et al.*, 1997).

Experimental

The chemical reagents used in the synthesis were purchased from E. Merck (Darmstadt, Germany) and Aldrich (Milwaukee, MI, USA). 3-(4-Dichlorobenzyl)thiazolidine-2,4-dione was synthesized according to the literature (Lo & Shropshire, 1957). A mixture of chromone-3-carboxaldehyde (0.3 g, 1.72 mmol) and 3-(4-dichlorobenzyl)thiazolidine-2,4-dione (0.415 g, 1.72 mmol) was refluxed in the presence of acetic acid (1 ml) and sodium acetate (0.235 g, 1.72 mmol) for 10 h. The crude product was crystallized from dimethylformamide (yield: 0.432 g, 63.2%; m.p: 524 K). IR (ν , cm^{-1}) (γ pyrone CO): 1638; ^1H NMR (DMSO- d_6 , 400 MHz): δ 4.88 (s, 2H, CH₂), 7.39 (d, 2H, 2', 6'-H), 7.50 (d, 2H, 3', 5'-H), 7.65 (ddd, 1H, 6-H), 7.82 (s, 1H, =CH), 7.83 (d, 1H, 8-H), 7.97 (ddd, 1H, 7-H), 8.21 (dd, 1H, $J_{5,6} = 7.60$ Hz, $J_{5,7} = 1.60$ Hz, 5-H), 9.03 (s, 1H, 2-H); ESMS (m/z): 398 ($M + 1$), 399 ($M + 2$), 400 ($M + 3$), 314.5 (100%), 286. Calculated for C₂₀H₁₂ClNO₄S: C 60.38, H 3.04, N 3.52, S 8.06%; found: C 60.83, H 3.15, N 3.61, S 7.89%.

Crystal data

C ₂₀ H ₁₂ ClNO ₄ S	$Z = 2$
$M_r = 398.82$	$D_x = 1.554 \text{ Mg m}^{-3}$
Triclinic, $P\bar{1}$	Cu $K\alpha$ radiation
$a = 8.7819$ (8) Å	Cell parameters from 25 reflections
$b = 10.2641$ (7) Å	$\theta = 19.2\text{--}42.6^\circ$
$c = 10.4074$ (12) Å	$\mu = 3.38 \text{ mm}^{-1}$
$\alpha = 112.034$ (8)°	$T = 293$ (2) K
$\beta = 98.297$ (8)°	Prism, colourless
$\gamma = 94.009$ (7)°	$0.48 \times 0.30 \times 0.15 \text{ mm}$
$V = 852.58$ (14) Å ³	

Data collection

Enraf–Nonius CAD-4 diffractometer	$R_{\text{int}} = 0.015$
Non-profiled ω scans	$\theta_{\text{max}} = 74.2^\circ$
Absorption correction: ψ scan (North <i>et al.</i> , 1968)	$h = 0 \rightarrow 10$
$T_{\text{min}} = 0.388$, $T_{\text{max}} = 0.596$	$k = -12 \rightarrow 12$
3583 measured reflections	$l = -12 \rightarrow 12$
3365 independent reflections	3 standard reflections
2864 reflections with $I > 2\sigma(I)$	frequency: 120 min
	intensity decay: 2%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0554P)^2 + 0.32999P]$
$R[F^2 > 2\sigma(F^2)] = 0.048$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.125$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.2$	$\Delta\rho_{\text{max}} = 0.62 \text{ e \AA}^{-3}$
3365 reflections	$\Delta\rho_{\text{min}} = -0.41 \text{ e \AA}^{-3}$
245 parameters	Extinction correction: SHELXL97
H-atom parameters constrained	Extinction coefficient: 0.0049 (6)

Table 1

Selected geometric parameters (Å, °).

C11—C18	1.743 (2)	O4—C6	1.216 (3)
S1—C2	1.752 (2)	N1—C1	1.381 (3)
S1—C1	1.768 (2)	N1—C3	1.383 (3)
O1—C1	1.207 (3)	N1—C14	1.472 (3)
O2—C3	1.211 (3)	C2—C4	1.341 (3)
O3—C9	1.332 (3)	C4—C5	1.450 (3)
O3—C8	1.380 (3)		
N1—C1—S1	111.23 (17)	C5—C6—C7	114.9 (2)
N1—C3—C2	110.65 (19)	C8—C7—C10	118.1 (2)
C9—C5—C4	116.9 (2)	C10—C7—C6	121.3 (2)
C4—C5—C6	124.8 (2)	O3—C8—C7	121.4 (2)
O4—C6—C5	123.1 (2)	O3—C8—C13	116.3 (2)
S1—C2—C4—C5	−1.1 (4)	C1—N1—C14—C15	100.8 (3)
C2—C4—C5—C6	−4.9 (4)	N1—C14—C15—C16	−65.7 (3)

Table 2

Hydrogen-bonding geometry (Å, °).

$D\text{—}H\cdots A$	$D\text{—}H$	$H\cdots A$	$D\cdots A$	$D\text{—}H\cdots A$
C4—H4...O2	0.93	2.42	2.836 (3)	107
C13—H13...O1 ⁱ	0.93	2.57	3.443 (4)	157
C14—H14A...O1	0.97	2.52	2.864 (3)	101
C14—H14B...O2 ⁱⁱ	0.97	2.42	3.361 (3)	164
C16—H16...O1	0.93	2.89	3.585 (4)	133
C19—H19...O4 ⁱⁱⁱ	0.93	2.71	3.351 (3)	127
C20—H20...O4 ⁱⁱⁱ	0.93	2.83	3.420 (3)	122

Symmetry codes: (i) $1 + x, 1 + y, z$; (ii) $-x, 2 - y, 1 - z$; (iii) $x, y, 1 + z$.

H atoms were placed in geometrically idealized positions and allowed to ride on their parent atoms, with C—H distances of 0.93 (aromatic) or 0.97 Å (methylene). The $U_{\text{iso}}(\text{H})$ values were set equal to $1.2U_{\text{eq}}(\text{parent atom})$.

Data collection: CAD-4 EXPRESS (Enraf–Nonius, 1994); cell refinement: CAD-4 EXPRESS; data reduction: XCAD4 (Harms & Wocadlo, 1995); program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEP-3 (Farrugia, 1997); software used to prepare material for publication: WinGX (Farrugia, 1999).

References

- Cody, V. & Luft, R. J. (1994). *J. Mol. Struct.* **317**, 89–97.
 Enraf–Nonius (1994). CAD-4 EXPRESS. Enraf–Nonius, Delft, The Netherlands.
 Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
 Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
 Fonseca, V. (2003). *Am. J. Med.* **115**, Suppl. 1, 42–48.
 Harms, K. & Wocadlo, S. (1995). XCAD4. University of Marburg, Germany.
 Kendi, E., Özbey, S., Tunçbilek, M. & Ertan, R. (1996). *Cryst. Res. Technol.* **31**, 611–615.

- Lo, C.-P. & Shropshire, E. (1957). *J. Org. Chem.* **22**, 999–1001.
- North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* **A24**, 351–359.
- Özbey, S., Kendi, E., Göker, H. & Ertan, R. (1997). *Acta Cryst.* **C53**, 1981–1983.
- Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
- Singh, G., Singh, L. & Ishar, P. S. (2002). *Tetrahedron*, **58**, 7883–7890.
- Wallet, J.-C., Gaydou, E. M., Espinosa, E., Osorno, O., Molins, E. & Miravittles, C. (1992). *Acta Cryst.* **C48**, 86–88.