Molecular Crystals and Liquid Crystals

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl20

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Version of record first published: 17 Dec 2009

To cite this article: S. Doreswamy, C. V. Kavitha, M. A. Sridhar, K. S. Rangappa & J. Shashidhara Prasad (2009): Crystal and Molecular Structure of 3-(2-(1-Hydroxycyclohexyl)-2-(4-methoxyphenyl)ethyl)-2-(4-p-methylphenyl)-1,3-thiazolidin-4-one, Molecular Crystals and Liquid Crystals, 515:1, 171-178

To link to this article: http://dx.doi.org/10.1080/15421400903290873

Mol. Cryst. Liq. Cryst., Vol. 515, pp. 171–178, 2009

ISSN: 1542-1406 print/1563-5287 online
DOI: 10.1080/15421400903290873

Crystal and Molecular Structure of 3-(2-(1-Hydroxycyclohexyl)-2-(4-methoxyphenyl) ethyl)-2-(4-p-methylphenyl)-1,3-thiazolidin-4-one

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The compound 3-(2-(1-hydroxycyclohexyl)-2-(4-methoxyphenyl)ethyl)-2-(4-methylphenyl)-thiazolidin-4-one was synthesized. The compound crystallizes in the orthorhombic system with space group Pbca *and cell parameters are* a = *11.795(1) Å,* b = *11.727(1) Å,* c = *33.964(9) Å, Z* = *8, V* = *4697.9(2) Å*^{3}*. The final residual factor is* R1 = *0.0647. The molecule exhibits intermolecular hydrogen bond of type O-H* $\cdots$ *O.*

Keywords: anti-cancer; anti-diabetic; thiazolidine

INTRODUCTION

The structural and therapeutic diversity of small heterocyclic molecules has fascinated organic and medicinal chemists. In recent years, 4-thiazolidinones and oxazolidinones have been the most extensively investigated class of compounds. 4-thiazolidinones have a wide spectrum of biological activity [1]. Hence, there is interest in their synthesis and structural investigation. Thiazolidinones are found to possess interesting profiles viz., anti-HIV [2], anti-diabetic [3], anti-cancer activity [4]. Recently, we have reported the one-pot, three-component synthesis, and antimicrobial studies of various 2,3-disubstituted 1,3-thiazolidin-4-ones including the title compound, as analogs of venlafaxine. The title compound showed potent antimicrobial activity against various bacteria and fungi. In vitro antimicrobial results revealed that this compound may serve as a

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new class of antimicrobial agent. This prompted us to study the molecular structure of the compound 3-(2-(1-hydroxycyclohexyl)-2-(4-methoxyphenyl)ethyl)-2-p-methylphenyl-thiazolidin-4-one.

SYNTHESIS

The compound was synthesized as per the procedure given in reference [5]. A schematic diagram of the molecule is shown in Fig. 1.

CRYSTAL STRUCTURE DETERMINATION

A single crystal of the title compound with dimensions $0.2\,\text{mm} \times 0.3\,\text{mm} \times 0.2\,\text{mm}$ was chosen for an X-ray diffraction study. The data were collected on a Diplabo Image Plate system equipped with a normal focus sealed X-ray tube (graphite monochromated MoKα). The crystal to detector distance is fixed at 120 mm with a detector area of $441 \times 240\,\text{mm}^2$. Thirty-six frames of data were collected by the oscillation method. Each exposure of the image plate was set to a period of 400 s. Successive frames were scanned in steps of 5° per minute with oscillation range of 5°. Image processing and data reduction were done using Denzo [6]. The reflections were merged using scalepack. All the frames could be indexed using primitive orthorhombic system. The structure was solved by direct methods using SHELXS-97 [7]. Least squares refinement using SHELXL-97 [8] with isotropic temperature factors for all the non-hydrogen atoms converged the residual $R1$ to 0.1796. Subsequent refinements were carried out with anisotropic thermal parameters for non-hydrogen atoms and isotropic temperature factors for all hydrogen atoms which were placed at chemically acceptable positions. The hydrogen atoms were allowed to ride on their parent atoms. The final residual value after the refinement is 0.0647.

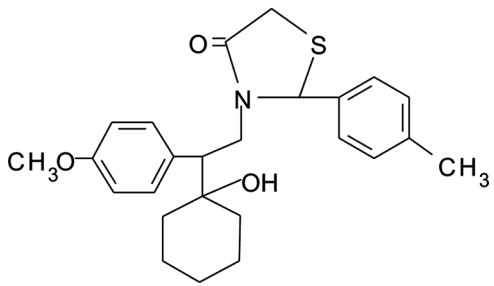

FIGURE 1 Schematic diagram of the molecule.

TABLE 1 Crystal and Structure Refinement Data

CCDC No.	701150
Empirical formula	$C_{25}\ H_{31}\ N\ O_3\ S$
Formula weight	425.57
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	*Pbca*
Cell dimensions	$a = 11.795(1)$ Å
	$b = 11.727(1)$ Å
	$c = 33.964(3)$ Å
Volume	4697.9(7) Å^3
Z	8
Density (calculated)	1.203 Mg/m^3
Absorption coefficient	0.163 mm^{-1}
F_{000}	1824
Crystal size	$0.2 \times 0.3 \times 0.2$ mm
θ range for data collection	2.10° to 25.02°
Index ranges	$-13 \leq h \leq 13$
	$-13 \leq k \leq 13$
	$-40 \leq I \leq 40$
Reflections collected	5594
Independent reflections	3402 [R(int) = 0.0218]
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3402/0/274
Goodness-of-fit on F^2	1.149
Final R indices [I > 2σ<r(I)]	$R1 = 0.0647$, $wR2 = 0.1580$
R indices (all data)	$R1 = 0.0909$, $wR2 = 0.1964$
Extinction coefficient	0.017(2)
Largest diff. Peak and hole	0.528 and –0.462 eÅ^{-3}

The details of the crystal data and refinement are given in Table 1. Table 2 gives the atomic coordinates and equivalent thermal parameters. Tables 3 and 4 give the bond lengths and bond angles of the non-hydrogen atoms.

An ORTEP [9] drawing of the molecule at 50% probability is shown in Fig. 2. The ring puckering analysis [10] of the thiazolidine ring in the molecule indicates that the ring is twisted on C23-S22 with a puckering amplitude $Q2 = 0.131(3)$ Å [11]. The weighted average absolute torsion angle is 8.86(13,127)°. The first number within the parentheses indicates internal esd and the second number indicates the external esd [13]. The atoms S22 and C21 deviate from the Cremer and Pople plane defined by the atoms N18, C19, C21, S22, C23 by 0.082(2) Å and −0.058(4) Å, respectively. The ring puckering analysis for the cyclohexane ring indicates that the cyclohexane ring exhibits

TABLE 2 Atomic Coordinates and Equivalent Thermal Parameters of the Non-Hydrogen Atoms

Atom	x	y	z	U_{eq}
Cl	0.0438(3)	−0.1461(3)	0.1805(2)	0.117(2)
O2	0.1027(2)	−0.2411(2)	0.16378(9)	0.0935(8)
C3	0.2179(2)	−0.2351(3)	0.16285(9)	0.0655(8)
C4	0.2737(3)	−0.3278(2)	0.14695(9)	0.0631(8)
C5	0.3894(2)	−0.3303(2)	0.14466(8)	0.0570(7)
C6	0.4558(2)	−0.2396(2)	0.15845(7)	0.0496(7)
C7	0.3976(3)	−0.1483(3)	0.17449(9)	0.0603(8)
C8	0.2815(3)	−0.1447(3)	0.1769(1)	0.0687(9)
C9	0.5830(2)	−0.2361(2)	0.15365(7)	0.0484(7)
C10	0.6485(2)	−0.3314(2)	0.17577(7)	0.0497(7)
O11	0.6261(2)	−0.4395(2)	0.15752(6)	0.0620(6)
C12	0.7751(2)	−0.3073(3)	0.17604(8)	0.0589(8)
C13	0.8428(3)	−0.3926(3)	0.2007(1)	0.0719(9)
C14	0.7986(3)	−0.3964(3)	0.2426(1)	0.084(1)
C15	0.6727(3)	−0.4238(3)	0.2430(1)	0.081(1)
C16	0.6058(3)	−0.3399(3)	0.21822(8)	0.0657(8)
C17	0.6132(2)	−0.2316(2)	0.10938(8)	0.0573(7)
N18	0.5608(2)	−0.1345(2)	0.08942(6)	0.0585(7)
C19	0.6113(3)	−0.0326(3)	0.08891(9)	0.0725(9)
O20	0.7037(2)	−0.0133(2)	0.10417(7)	0.0932(8)
C21	0.5439(4)	0.0569(3)	0.0673(1)	0.106(1)
S22	0.41206(9)	−0.00429(8)	0.05404(3)	0.0883(4)
C23	0.4546(3)	−0.1486(3)	0.06822(8)	0.0634(8)
C24	0.4648(3)	−0.2282(3)	0.03354(8)	0.0633(8)
C25	0.5617(3)	−0.2355(3)	0.01118(9)	0.082(1)
C26	0.5665(4)	−0.3054(4)	−0.0215(1)	0.095(1)
C27	0.4758(5)	−0.3711(3)	−0.0325(1)	0.099(1)
C28	0.3815(4)	−0.3661(4)	−0.0099(2)	0.123(2)
C29	0.3748(3)	−0.2976(4)	0.0231(1)	0.098(1)
C30	0.4841(5)	−0.4468(4)	−0.0686(2)	0.153(2)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij}\left(a_i^* a_j^*\right)(a_\mathrm{i} \cdot a_\mathrm{j}).$$

chair conformation. The C10-O11 bond lies in the axial plane of the Cremer and Pople plane defined by atoms C10, C12, C13, C14, C15, C16 as indicated by angle 3.9(2)°. The C10-C9 bond lies in the equatorial plane of the Cremer and Pople plane mentioned above as indicated by angle 66.9(2)°. The title molecule has chiral centres at C9 and C23 in *R* and *S* configurations respectively. Since the molecule has crystallized in a centrosymmetric space group, we can surmise that the compound is a racemic mixture.

The torsion angles of 145.9(3)° about N18-C23-C24-C29 and 85.0 (3)° about S22-C23-C24-C25 indicates +*anti*-clinal and +*syn*-clinal

TABLE 3 Bond Lengths (Å)

Atoms	Length	Atoms	Length
Cl-O2	1.430(4)	C15-C16	1.517(4)
O2-C3	1.362(3)	C17-N18	1.463(4)
C3-C4	1.381(4)	N18-C19	1.336(4)
C3-C8	1.383(4)	N18-C23	1.453(4)
C4-C5	1.367(4)	C19-O20	1.227(4)
C5-C6	1.402(4)	C19-C21	1.506(5)
C6-C7	1.383(4)	C21-S22	1.771(4)
C6-C9	1.509(3)	S22-C23	1.830(3)
C7-C8	1.373(4)	C23-C24	1.508(4)
C9-C17	1.546(4)	C24-C25	1.375(4)
C9-C10	1.553(4)	C24-C29	1.383(5)
C10-O11	1.436(3)	C25-C26	1.380(5)
C10-C12	1.520(4)	C26-C27	1.371(5)
C10-C16	1.531(4)	C27-C28	1.352(7)
C12-C13	1.531(4)	C27-C30	1.517(5)
C13-C14	1.513(5)	C28-C29	1.382(6)
C14-C15	1.519(4)		

TABLE 4 Bond Angles (°)

Atoms	Angle	Atoms	Angle
C3–O2-C1	117.0(3)	C15-C16-C10	113.2(2)
O2-C3-C4	116.4(3)	N18-C17-C9	112.3(2)
O2-C3-C8	124.9(3)	C19-N18-C23	118.7(3)
C4-C3-C8	118.7(3)	C19-N18-C17	120.9(3)
C5-C4-C3	121.0(3)	C23-N18-C17	120.3(2)
C4-C5-C6	121.5(3)	O20-C19-N18	123.8(3)
C7-C6-C5	116.2(3)	O20-C19-C21	123.0(3)
C7-C6-C9	120.9(2)	N18-C19-C21	113.2(3)
C5-C6-C9	122.7(2)	C19-C21-S22	107.8(3)
C8-C7-C6	122.8(3)	C21-S22-C23	93.8(2)
C7-C8-C3	119.7(3)	N18-C23-C24	112.9(3)
C6-C9-C17	109.6(2)	N18-C23-S22	105.1(2)
C6-C9-C10	115.0(2)	C24-C23-S22	112.9(2)
C17-C9-C10	112.3(2)	C25-C24-C29	117.4(3)
O11-C10-C12	110.4(2)	C25-C24-C23	122.4(3)
O11-C10-C16	106.8(2)	C29-C24-C23	120.2(3)
C12-C10-C16	109.2(2)	C24-C25-C26	121.0(3)
O11-C10-C9	109.6(2)	C27-C26-C25	121.4(4)
C12-C10-C9	111.0(2)	C28-C27-C26	117.6(4)
C16-C10-C9	109.8(2)	C28-C27-C30	122.5(5)
C10-C12-C13	113.2(2)	C26-C27-C30	120.0(5)
C14-C13-C12	110.7(3)	C27-C28-C29	122.2(4)
C13-C14-C15	110.7(3)	C28-C29-C24	120.4(4)
C16-C15-C14	111.4(3)		

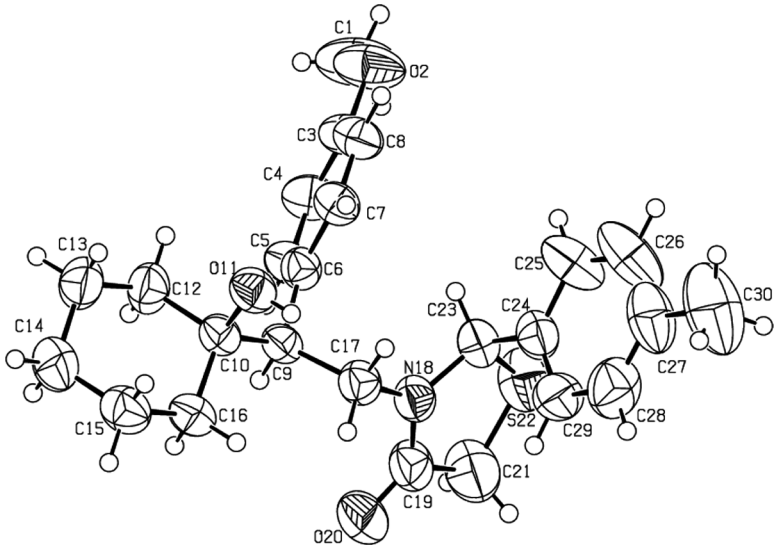

FIGURE 2 ORTEP of the molecule at 50% probability.

conformations, respectively. Similarly, the torsion angle about C7-C6-C9-C10 is 120.6(3)° indicating +*anti*-clinal conformation. The torsion angle about C5-C6-C9-C17 is 63.7(3)°, which indicates +*syn*-clinal conformation. The torsion angle about C17-N18-C23-C24 −63.9(3)°, which indicates −*syn*-clinal conformation. The bond angle C21-S22-C23 is 93.8(2)°. The bond angles C19-N18-C17, C23-N18-C17, and C19-N18-C23 are 120.9(3)°, 120.3(2)°, and 118.7(3)°, respectively. The bond length of C21-S22 is 1.771(4) Å and that of S22-C23 is 1.830(3) Å. The bond lengths of C23-N18 and C17-N18 are 1.453(4) Å and 1.463(4) Å, respectively, and the bond length of C19-N18 is 1.336(4) Å, which indicates double bond nature [12]. The bond length of C19-O20 is 1.227(4) Å. The atoms S22 and N18 are on the same side of the mean plane of thiazolidine ring having deviations 0.071(1) Å and 0.047(2) Å, respectively. The deviations of atoms C21 and C23 from the mean plane of thiazolidine ring is −0.062(4) Å and −0.074(3) Å, respectively, indicating that they are deviated in the direction opposite to S22 and N18 atoms with respect to the mean plane of the thiazolidine ring. Since the deviations of all four atoms is very small, we can assume that they are in the mean plane of the thiazolidine ring. The C1 is in the mean plane of methoxy phenyl ring and has a deviation 0.005(6) Å with respect to the mean plane. The dihedral angle between the plane of 1,3-thiazolidine-4-one and

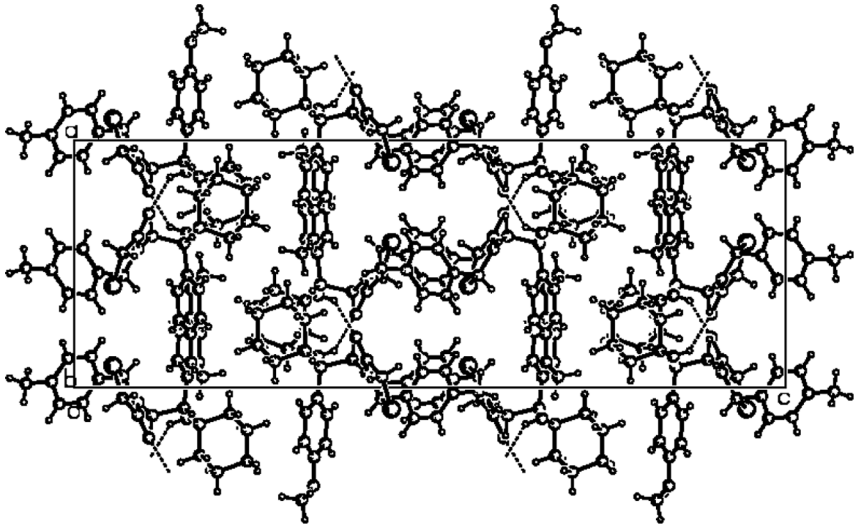

FIGURE 3 Packing of molecules down *b*.

the plane of methoxy phenyl is 46.8(2)°. The dihedral angle between the plane of 1,3-thiazolidine-4-one and the plane of methylphenyl is 78.7(2)°. The dihedral angle between the plane of methoxy phenyl and the plane of methylphenyl is 31.9(2)°. The structure exhibits intermolecular hydrogen bond of the type O11-H11 $\cdots$ O20 with symmetry code 3/2-*x*, $-1/2+y$,*z*, bond length 2.839(3) Å and bond angle 134°. The packing of molecules down *b* axis is shown in Fig. 3.[1]

ACKNOWLEDGMENTS

The authors would like to express their thanks to DST, Government of India for financial assistance under the projects SP/I2/FOO/93 and DV6/15/DST/2005-06.

[1]CCDC 701150 contains the supplementary crystallographic data for this article. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retriving.html or from The Cambridge crystallpgraphic data center, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: +44(0)1223-336033; E-mail: deposit@ccdc.cam.ac.uk

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