Journal of Chemical Crystallography, Vol. 35, No. 1, January 2005 (© 2005)
DOI: 10.1007/s10870-005-1156-5

Synthesis and X-ray structure of 3-(4-methyl phenyl)-2-(4-biphenyl)-1,3-thiazolidin-4-one

K. Jayalakshmi,(1) **M. Mahendra,**(2) **Basappa,**(1) **B.H. Doreswamy,**(2)
M.A. Sridhar,(2) **J. Shashidhara Prasad,**(2) **and K.S. Rangappa**(1)*

Received April 9, 2004; accepted August 2, 2004

The title compound ($C_{22}H_{19}NOS$) was synthesized, characterized and structure was determined by X-ray diffraction method. It crystallizes in the monoclinic space group $P2_1/c$ with cell parameters $a = 22.181(2)$ Å, $b = 6.0760(4)$ Å, $c = 13.349(3)$ Å, $\beta = 95.615(3)°$, and $Z = 4$. The final residual factor is 0.0625 for 1724 reflections with $I > 2\sigma(I)$. 4-thiazolidinone ring moiety shows twisted conformation.

KEY WORDS: 4-thiazolidinone; synthesis; crystal structure.

Introduction

4-thiazolidinone ring system comprises the broad spectrum for a number of biologically active compounds. In recent years, 4-thiazolidinones are the most extensively investigated class of compounds, which exhibits various biological activities, such as anticonvulsant,[1] antibacterial,[2] antifungal,[3] anti-inflammatory,[4] anticancer,[5] and antipsychotic[6] properties. Some of the reported 4-thiazolidinones have showed envelope or half-chair conformation with different configurations.[7–10] Their structural and conformational features are essential to correlate to the biological activity. As the part of our continuous research in the synthesis of nitrogen containing biologically active heterocyclic compounds,[11,12] the title compound has been synthesized and its structure is reported in this paper.

Experimental

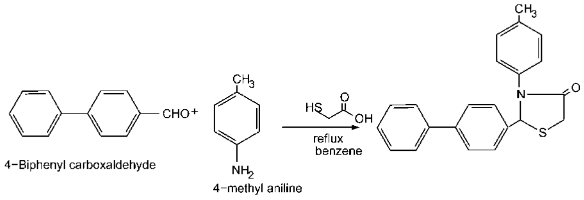
In a pilot experiment, a mixture of equimolar 4-biphenyl carboxaldehyde (0.1 molar) and 4-methyl aniline (0.1 molar) in dry benzene (20 mL) was refluxed for about 12–14 h until no more water was collected in a Dean–Stark trap. Thioglycolic acid (0.1 molar) was added to the reaction mixture and the reaction was carried out at reflux temperature until stoichiometric amount of water was collected in the Dean-Stark. The reaction mixture was concentrated to dryness under reduced pressure, the residue was taken up in ethyl acetate. The organic layer was successively washed with each 20 mL of 5% citric acid, distilled water, 5% sodium bicarbonate and finally by brine solution. The crude product obtained was recrystallized by methanol and further purified by column chromatography using silica gel (230–400 mesh). A transparent crystal was grown by slow evaporation method using HPLC methanol as a solvent.

The elemental analysis (C H N) of the reported compound agrees with the calculated

(1) Department of Studies in Chemistry, University of Mysore, Mysore, India.
(2) Department of Studies in Physics, University of Mysore, Mysore, India.
* To whom correspondence should be addressed; e-mail: rangappaks@yahoo.com.

values and was within ±4% of theoretical values. The IR spectra was taken on a Perkin-Elmer 399 spectrometer in KBr. ^{1}H NMR spectra (data reported in δ was recorded on a amx 400 MHz spectrometer with Me_4Si as internal reference. The ^{1}H NMR anaysis of the reported compound showed the C(5) methylenic protons, H_A and H_B of the thiazolidinone ring appeared as an AB system with a geminal proton coupling $J_{A,B}$ of 15.7 Hz. The proton lying at lower field showed a small coupling ($J = 2$ Hz) with the C(2)—H signal. This long-range coupling takes place through the eclipsing lone pair of the sulfur atom with the C—H_A bond of the thiazolidinone ring. The H_B proton appeared at higher field owing to the shielding effect of the nearly coplanar sulfur orbital.[13,14] Final confirmation regarding the whole structure and the absolute configuration at the new chiral atom C(2) was obtained by X-ray analysis of a suitable crystal of the title compound.

Anal. Calcd. for $C_{22}H_{19}NOS$; C, 76.56; H,5.548; N,4.058; Found C, 76.49; H, 5.54; N, 4.05; ν_{max} C=O 1678 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.2 (s, 3H, CH_3), 3.91 (d, $J = 15.7$ Hz, 1H, CH_2), 4.05 (d, $J = 15.7$ Hz, 1H, CH_2), 6.1(s, 1H, CH), 7.07–7.56 (m, 13H, Ar).



A single crystal of dimensions 0.2 mm × 0.25 mm × 0.25 mm was chosen for X-ray diffraction studies. The measurements were made on a DIPLabo Image Plate system with graphite monochromated radiation (MoKα). Thirty-six frames of data were collected by oscillation method. Successive frames were scanned in steps of 3°/min with an oscillation range of 5°. Image processing and data reduction were done by using Denzo.[15] All frames could be indexed with a monoclinic primitive cell. The structure was solved by direct methods using SHELXS-97.[16] All the non-hydrogen atoms were revealed in the first map itself. Full-matrix least-squares refinement (using SHELXL-97[17]) based on 1724 reflections ($I > 2\sigma(I)$) with isotropic temperature factors for all the atoms converged to the residual $R1 = 0.1224$. Subsequent refinements of non-hydrogen atoms with anisotropic thermal parameters and hydrogen atoms with the isotropic temperature factors were carried out. After eight cycles of refinement the residual converged to $R1 = 0.0625$. The details of crystal data and refinement are given in Table 1. The full crystallographic details are deposited in CCDC database under the reference number 232050 (see supplementary material).

Results and discussion

Table 2 gives the bond distances and bond angles of non-hydrogen atoms, respectively. The

Table 1. Crystallographic Details

CCDC No.	232050
Empirical formula	$C_{22}H_{19}NOS$
Formula weight	345.44
Temperature, K	293(2)
Wavelength, Å	0.71073
Crystal system	Monoclinic
Space group	$P2_1/c$
Cell dimensions	$a = 22.181(2)$ Å
	$b = 6.0760(4)$ Å
	$c = 13.349(3)$ Å
	$\beta = 95.615(3)°$
Volume, Å^3	1790.4(4)
Z	4
Density (calculated), Mg/m^3	1.282
Absorption coefficient, mm^{-1}	0.190
F_{000}	728
Theta range for data collection, Deg	3.48–22.46
Index ranges	$-12 \leq h \leq 13$
	$-6 \leq k \leq 6$
	$-23 \leq l \leq 23$
Reflections collected	3667
Independent reflections	2070 [R(int) = 0.0171]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2070/0/227
Goodness-of-fit on F^2	1.062
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0625$, $wR2 = 0.1748$
R indices (all data)	$R1 = 0.0720$, $wR2 = 0.1878$
Extinction coefficient	0.019(4)
Largest diff. peak and hole, e A^{-3}	0.548 and −0.350

Table 2. Bond Lengths (Å) and Bond Angles (Deg)

Atoms	Length	Atoms	Length
S1—C2	1.776(4)	C13—C14	1.375(5)
S1—C5	1.829(4)	C15—C14	1.382(5)
C3—C2	1.493(5)	C15—C16	1.383(5)
N4—C3	1.357(4)	C17—C12	1.382(5)
N4—C5	1.472(4)	C17—C16	1.378(5)
C5—C6	1.502(5)	C18—C15	1.504(5)
C6—C7	1.387(5)	C19—C9	1.480(5)
C7—C8	1.365(5)	C19—C20	1.429(7)
C9—C8	1.394(5)	C19—C24	1.348(6)
C9—C10	1.385(5)	C20—C21	1.393(8)
C11—C6	1.378(5)	C21—C22	1.419(10)
C11—C10	1.372(5)	C22—C23	1.330(10)
C12—N4	1.435(4)	C24—C23	1.376(7)
C12—C13	1.374(5)	O25—C3	1.220(4)
Atoms	**Angle**	**Atoms**	**Angle**
C2—S1—C5	93.97(16)	C13—C12—N4	121.1(3)
C3—C2—S1	108.5(3)	C13—C12—C17	118.9(3)
C3—N4—C5	117.7(3)	C13—C14—C15	121.3(4)
C3—N4—C12	122.0(3)	C14—C15—C16	117.1(3)
N4—C3—C2	113.3(3)	C14—C15—C18	122.0(4)
N4—C5—S1	105.2(2)	C16—C17—C12	119.6(3)
N4—C5—C6	113.6(3)	C16—C15—C18	120.9(4)
C6—C5—S1	110.6(2)	C17—C12—N4	120.0(3)
C7—C6—C5	122.1(3)	C17—C16—C15	122.2(3)
C7—C8—C9	121.7(3)	C19—C24—C23	124.8(5)
C8—C7—C6	121.1(3)	C20—C19—C9	120.3(4)
C8—C9—C19	121.9(3)	C20—C21—C22	118.0(7)
C10—C9—C8	116.7(4)	C21—C20—C19	120.2(6)
C10—C11—C6	121.3(3)	C22—C23—C24	118.4(6)
C10—C9—C19	121.3(4)	C23—C22—C21	121.8(7)
C11—C6—C5	120.3(3)	C24—C19—C9	123.1(4)
C11—C6—C7	117.6(3)	C24—C19—C20	116.5(5)
C11—C10—C9	121.5(3)	O25—C3—C2	122.7(3)
C12—N4—C5	119.3(3)	O25—C3—N4	123.9(3)
C12—C13—C14	120.9(3)		

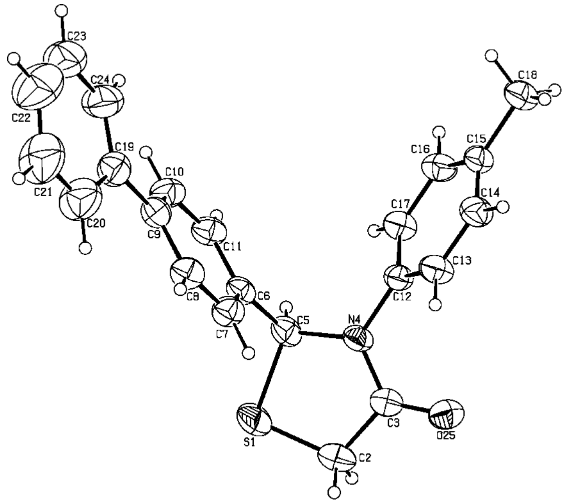


Fig. 1. ORTEP diagram of the molecule drawn at 50% probability.

bond distances and bond angles are in good agreement with the standard values. Figure 1 represents the ORTEP[18] diagram of the molecule with thermal ellipsoids drawn at 50% probability. The structure exhibits intermolecular hydrogen bonds of the type C—H···O. The intermolecular hydrogen bonds are bifurcated and represented by C5—H5···O25 (3.526 Å, 171°) and C17–H17···O25 (3.510 Å, 165°) with symmetry equivalent code $x, 1 + y, z$, respectively. These hydrogen bonds form an infinite chain like structure around the center of symmetry (i.e., at O25), when viewed parallel to the *ac* plane (Fig. 2). The X-ray molecular structure of the compound shows that the absolute configuration at chiral C-5

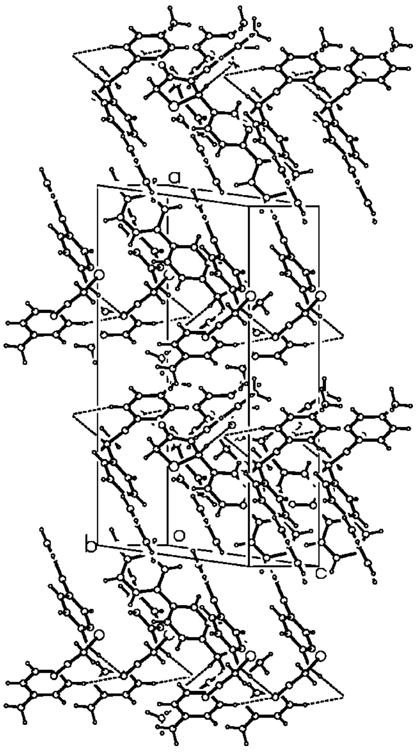


Fig. 2. Packing of the molecules parallel to the *ac* plane. Dashed lines represent the hydrogen bonds.

is *S*. The ring puckering analysis indicated that the thiazolidinone ring is just twisted on C5—S1 (the deviations from the best mean plane ranging from −0.0031 Å to −0.0749 Å) and the puckering amplitude Q2 is 0.1230 Å with no preferential symmetry. It was envelope in the thiazolidinone derivatives quoted before[7–10], which exhibited various biological activities. This conformational change can be attributed to the different steric hindrance of the substituents at N4 and C5, respectively, which shows pseudo-equatorial and pseudo-axial orientation with respect to the thiazolidinone ring plane. These are shown by torsion angles of S1—C5—C6—C7 (i.e., −57.2(4)°) and C3–N4–C12–C13 (i.e., 58.6(5)°). The above conformational features are necessary to rationalize the biological results and to determine the structure–activity relationship. The detailed activity studies are underway.

Acknowledgments

The authors would like to express their thanks to DST and UGC, Government of India for financial assistance under the project vides SP/I2/FOO/93 and 12-14/2002(SR-1) respectively. M. Mahendra thanks CSIR, Government of India for awarding Senior Research Fellowship.

Supplementary material CCDC-232050 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033; email: deposit@ccdc.cam.ac.uk.

References

1. Ragab, F.A.; Eid, N.M.; El-Tawab H.A. *Pharmazie*. **1997**, *52,* 926–929.
2. Pandeya, D.; Nair, K.B. *Pharmazie*. **1993**, *48,* 414–417.
3. Capan, G.; Ulusoy, N.; Ergenc, N.; Kiraz, M. *Montshefte Chemie* **1999**, *130,* 1399–1407.
4. Vigorita, M.G.; Ottaba, R.; Monforte, F.; Maccari, R.; Trovato, A.; Monfortre, M.T.; Taviano, M.F. *Bioorg. Med. Chem. Lett.* **2001**, *11,* 2791–2794.
5. Bhatt, J.J.; Shah, B.R.; Shah, H.P.; Trivedi, P.B.; Undavia N.K.; Desai N.C. *Indian J. Chem. B* **1994**, *33,* 189–192.
6. Hrib, N.J.; Jurcak, J.G.; Bregna, D.E.; Dunn, R.W.; Geyer, H.M.; Hartman, H.B.; Roehr, J.E.; Rogers, K.L.; Rush, D.K.; Szczepanik, A.M.; Szewczak, M.R.;Wilmot, C.A.; Conasay, P.G. *J. Med. Chem.* **1992**, *35, 14,* 2712–2715.
7. Diurno, M.; Mazzoni, O.; Piscopo, E.; Calignano, A.; Giordano, F.; Bolognese, A. *J. Med. Chem.* **1992**, *35,* 2910–2912.
8. Benetollo, F.; Bombieri, G.; Del Pra, A.; Basile, M.; Previtera, T.; Vigorita, M. G. *J. Cryst. Spectrosc. Res.* **1991**, *21,* 113.
9. Orsini, F.; Bombieri, G.; Benetollo, F.; Vigorita, M. G.; Previtera, T. *J. Chem. Crystallogr.* **1995**, *25,* 589.
10. Hickel, D.; Leger, J.M.; Carpy, A. *Acta Cryst.* **1983**, *C39,* 240–245.
11. Ravikumar, K.R.; Mallesh, H.; Basappa; Rangappa, K.S. *Eur. J. Med. Chem.* **2003**, *38,* 613–619.
12. Basappa, Sadashiva, M.P.; Mantelingu, K.; Swamy, N.S.; Rangappa, K.S. *Bioorg. Med. Chem.* **2003**, *11,* 1–6.
13. Vigotita, M.G.; Chimirri, A.; Grasso, S.; Fenech, G. *J. Heterocycl. Chem.* **1979**, *16,* 1257–1261.
14. Allingham, Y.; Cookson, R.C.; Crabb, T.A. *Tetrahedron* **1968**, *24,* 1989–1995.
15. Otwinowski, Z.; Minor, W. In *Methods in Enzymology*; Carter, C.W., Jr.; Sweet, R.M., Eds.; Academic Press: 1997, Vol. 276, p. 307.
16. Sheldrick, G.M. *SHELXS-97, Program for Crystal Structure Determination;* University of Göttingen: Germany, 1997.
17. Sheldrick, G.M. *SHELXL–97, Program for Refinement of Crystal Structure*; University of Göttingen: Germany, 1997.
18. Johnson, C.K. *ORTEP-II, A Fortran Thermal-Ellipsoid Plot Program*, Report ORNL-5138; Oak Ridge National Laboratory: Oak Ridge, Tennessee, USA, 1976.