X-ray Structure Analysis Online

Crystal Structure of an Unexpected Derivative of Curcumin: 2-[2-(4-Acetoxy-3-methoxyphenyl)ethyl]benzothiazole

M. Concepción Lozada,* Raúl G. Enríquez,† Benjamin Ortíz,** Dino Gnecco,*** and Manuel Soriano-García**†**

**Departamento de Sistemas Biológicos, UAM-Xochimilco. Calzada del Hueso 1100, Col. Villa Quietud, Coyoacan, 04960, Mexico D. F.*
***Instituto de Química, UNAM, Circuito Exterior, Ciudad Universitaria, Coyoacan, México D. F. 04510, Mexico*
****Centro de Química del Instituto de Ciencias, BUAP, Puebla 72000, México*

$C_{18}H_{15}NO_3S$ is orthorhombic, $P2_12_12_1$. The unit-cell dimensions at 293 K are a = 7.182(1), b = 11.100(1), c = 20.644(2)Å, V = 1645.7(3)Å^3, D_x = 1.313 g/cm^3, and Z = 4. The R value is R = 0.0552 for 1493 reflections with $I > 2\sigma(I)$. The title compound has two independent rings: a phenyl ring and a benzothiazole ring bridge *via* an ethyl moiety. Apart from the C–H···O intermolecular interactions, the molecules in the crystal are packed at normal van der Waals distances.

(Received November 12, 2007; Accepted March 24, 2008; Published on web September 10, 2009)

The benzothiazole derivatives are of biological and industrial interest. For example, the benzothiazole derivatives were synthesized in order to explore the structural requirements of serotonin 5-HT_{2B} receptor antagonists.[1] Some benzothiazols possess the activity as inhibitors of the enzyme cyclooxygenase.[2]

The general methodology for the synthesis of benzothiazole derivatives is the reaction of 2-aminothiophenol with carboxylic acids or its derivatives by employing vigorous reaction conditions, or by using of microwave irradiation.[3] The condensation of aldehydes with 2-aminothiophenol in an acid or basic medium affords the corresponding benzothiazoline, which after an $FeCl_3$ or scandium triflate assisted dehydrogenation treatment[4] gives the 2-substituted benzothiazol.

In the present paper we report on a the structural modification of the (1*E*,6*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione (curcumin) derivative reacted with 2-aminothiophenol to obtain the 2-[2-(4-acetoxy-3-methoxypheny l)ethyl]benzothiazole **1**. This reaction occurs with the loss of a part of the curcumin molecule. The synthesis and the spectroscopic data have been reported elsewhere.[5] Colorless crystals were grown by slow evaporation from an acetone-hexane solution.

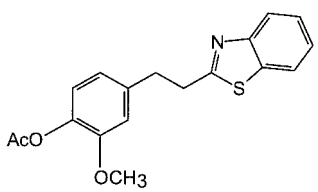

Fig. 1 Chemical structure of 2-[2-(4-acetoxy-3-methoxyphenyl)-ethyl]benzothiazole.

† To whom correspondence should be addressed.
E-mail: habib@servidor.unam.mx and soriano@servidor.unam.mx

X-ray data for crystals of the title compound were collected by graphite-monochromatized Mo K_α radiation at 293 K. No

Table 1 Crystal and experimental data

Formula: $C_{18}H_{15}NO_3S$
Formula weight = 325.38
Crystal system: orthorhombic
Space group: $P2_12_12_1$ $Z = 4$
a = 7.182(1)Å
b = 11.100(1)Å
c = 20.644(2)Å
V = 1645.7(3)Å^3
D_x = 1.313 g/cm^3
μ(Mo K_α) = 0.210 mm^{-1}
T = 293 K
Light yellow
F(0 0 0) = 680
0.27 × 0.26 × 0.10 mm
Radiation: Mo K_α
ω scans with θ_{max} = 32.62°
R (F^2) = 0.0552 [1493 reflections with $I > 2\sigma(I)$]
wR (F^2) = 0.0672 [1493 reflections with $I > 2\sigma(I)$]
$(\Delta/\sigma)_{max}$ = 0.004
$(\Delta\rho)_{max}$ = 0.155 eÅ^{-3}
$(\Delta\rho)_{min}$ = –0.134 eÅ^{-3}
No. of reflections measured = 22847
No. of reflections used = 1493
No. of parameters = 226
Goodness-of-fit = 0.940
Measurement: Bruker Smart Apex CCD diffractometer
Program system: SMART V 5.625 and SAINT V 6.23C
Structure determination: direct methods (SHELXS-97)
Refinement: full matrix least-squares (SHELXL-97)

CCDC 664778 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ca.uk/data_request/cif.

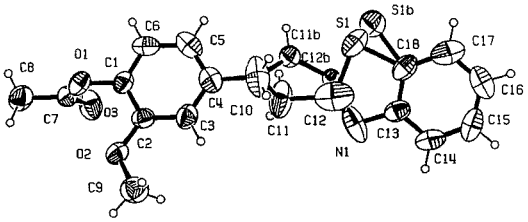

Fig. 2 Molecular structure of 2-[2-(4-acetoxy-3-methoxyphenyl)ethyl]benzothiazole Thermal ellipsoids are drawn at the 30% probability level.

Table 2 Final atomic coordinates and equivalent isotropic temperature factors (Å^2)

Atom	*x*	*y*	*z*	U_{eq}
O1	0.9926(3)	0.76718(15)	0.40610(7)	0.0867(6)
O2	1.0535(3)	0.94396(17)	0.32274(7)	0.0945(6)
O3	1.1568(3)	0.63847(17)	0.34645(9)	0.1205(8)
N1	0.3708(5)	0.9132(4)	0.0519(2)	0.1452(17)
C1	0.8658(5)	0.7849(3)	0.35500(13)	0.0768(8)
C2	0.8937(4)	0.8796(3)	0.31323(15)	0.0772(8)
C3	0.7638(5)	0.9028(2)	0.26604(13)	0.0908(9)
C4	0.6051(5)	0.8355(3)	0.25974(15)	0.1033(10)
C5	0.5837(5)	0.7399(3)	0.30242(17)	0.1096(11)
C6	0.7102(5)	0.7156(3)	0.35023(14)	0.0924(9)
C7	1.1376(5)	0.6926(3)	0.39512(13)	0.0802(9)
C8	1.2652(3)	0.6879(2)	0.45141(11)	0.1104(10)
C9	1.0773(4)	1.0499(2)	0.28681(12)	0.1168(10)
C10	0.4576(7)	0.8635(4)	0.21136(19)	0.1767(19)
S1	0.1075(6)	0.8276(2)	0.11761(8)	0.1238(11)
C11	0.5017(10)	0.8457(6)	0.1549(3)	0.154(3)
C12	0.3327(15)	0.8811(9)	0.0997(4)	0.168(5)
S1B	0.0016(11)	0.8043(5)	0.1103(2)	0.1115(18)
C11B	0.3361(17)	0.8049(9)	0.1793(6)	0.075(4)
C12B	0.297(2)	0.8341(12)	0.1118(7)	0.052(4)
C13	0.2047(6)	0.9251(3)	0.01584(18)	0.0882(9)
C14	0.2056(5)	0.9763(2)	-0.0435(2)	0.1097(11)
C15	0.0399(7)	0.9820(3)	-0.07619(16)	0.1160(13)
C16	-0.1222(5)	0.9397(3)	-0.0527(2)	0.1250(15)
C17	-0.1212(6)	0.8869(3)	0.0077(2)	0.1213(13)
C18	0.0463(7)	0.8801(3)	0.04220(13)	0.0916(10)

The occupancy factors for C11, C12, S1 and C11B, C12B, S1B are 0.726 and 0.274, respectively. $U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}(a_i^* a_j^*)(\boldsymbol{a}_i \cdot \boldsymbol{a}_j)$.

absorption correction was applied. The structure was solved by direct methods and refined by full-matrix least-squares with anisotropic temperature factors for the non-hydrogen atoms. The occupancy factors for C11, C12, S1 and C11B, C12B, S1B are 0.726 and 0.274, respectively. The positions of all H atoms were calculated geometrically, and a riding model was used in the refinement, with C–H distances in the range of 0.93 – 0.98 Å and $U_{iso}(H) = 1.2U_{eq}(C)$. The software used to prepare the material for publication was PARST97.[6] The chemical and molecular structures for **1** are shown in Figs. 1 and 2, respectively. Table 1 summarizes the crystal and experimental data. Atomic positional parameters for non-hydrogen atoms are given in Table 2. The bond angles for non-H atoms are listed in Table 3.

Table 3 Selected bond distances (Å)

N1 - C12	1.085(9)	N1 - C13	1.412(4)
N1 - C12B	1.608(17)	C4 - C10	1.489(4)
C10 - C11	1.224(5)	C10 - C11B	1.274(11)
S1 - C18	1.719(4)	S1 - C12	1.762(9)
C11 - C12	1.710(11)	S1B - C18	1.669(6)
C11B-C12B	1.459(16)	C13 - C14	1.350(3)
C13 - C18	1.356(4)	C14 - C15	1.369(3)
C15 - C16	1.346(4)	C16 - C17	1.378(4)
C17 - C18	1.400(4)		

The title compound has two independent rings, a phenyl ring and a benzothiazole ring bridge *via* an ethyl moiety. S1 and C12 atoms of the benzothiazole ring are disordered. C10–C11 is abnormally short due to the fact that these two atoms are disordered. The bond lengths of both phenyl rings (C1–C6 and C13–C18) are normal. The bond angles for the C1–C6 and C13–C18 rings were found to be between 116.7(3), 122.3(3)° and 117.6(4), 123.9(4)°, respectively. The C–N–C angle in the benzothiazole ring is 107.3(8)°, which agrees with the corresponding value found in *N*,*N*-(2-benzothiazole)(2-pyridylmethyl)amine.[7] The molecular conformation is characterized by a dihedral angle of only 27.1(1), 26.1(1)° between the mean planes of the phenyl ring and C12–C18, N1, S1 and the C12B–C18, N1, S1B rings, respectively.

The molecule is stabilized by three C–H···O intermolecular contacts of <3.40 Å [C9···O3 (–*x*+2, +*y*+1/2, –*z*+1/2); C5···O3 (*x*–1, +*y*, +*z*); C14···O2 (–*x*+3/2, –*y*+2, –*z*–1/2)]. Apart from the C–H···O intermolecular interactions, the molecules in the crystal are packed at normal van der Waals distances.

Acknowledgements

RGE acknowledges support from the CONACyT (37821-N and 40959-Q) and DGAPA (UNAM) (IN232202).

References

1. G. Giorgioni, B. Accorroni, A. Stefano, G. Marucci, A. Siniscalchi, and F. Claudi, *Med. Chem. Res.*, **2005**, *14*, 57.
2. R. Paramashivappa, P. Pahani Kumar, P. V. Subba Rao, and A. Srinivasa Rao, *Bioorg. Med. Chem. Lett.*, **2003**, *13*, 657.
3. A. K. Chakraborti, C. Selvam, G. Kaur, and S. Bhagat, *Synlett.*, **2004**, *5*, 851.
4. T. Itoh, K. Nagata, H. Ishikawa, and A. Ohsawa, *Heterocycles*, **2004**, *63*, 2769.
5. S. Shishodia, G. Sethi, and B. B. Aggarwal, *Ann. N. Y. Acad. Sci.*, **2005**, *1056*, 206.
6. M. Nardelli, *J. Appl. Cryst.*, **1995**, *28*, 659.
7. Z-F. Chen, Y-Z. Tang, S-M. Shi, X-W. Wang, H. Liang, and K-B. Yu, *Acta Cryst.*, **2003**, *E59*, o1461.