Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

6-(3,4-Difluorobenzoyl)-3-[2-(4-pyridyl)ethyl]-1,3-benzothiazol-2(3*H*)-one

Süheyla Özbey[a]* and Nesrin Gökhan[b]

[a]Hacettepe University, Faculty of Engineering, Department of Engineering Physics, Beytepe 06800, Ankara, Turkey, and [b]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 06100 Sıhhiye, Ankara, Turkey
Correspondence e-mail: sozbey@hacettepe.edu.tr

Received 9 July 2004
Accepted 9 August 2004
Online 18 September 2004

A new type of benzothiazolinone derivative with potential pharmacological activity, *viz*. 6-(3,4-difluorobenzoyl)-3-[2-(4-pyridyl)ethyl]-1,3-benzothiazol-2(3*H*)-one, $C_{21}H_{14}F_2N_2O_2S$, has been prepared and studied by NMR, IR and single-crystal X-ray diffraction techniques. The molecule is not planar, the pyridine and difluorobenzene moieties being located above and below the benzothiazole ring system. The carbonyl O atoms are involved in an intramolecular hydrogen-bond-type interaction.

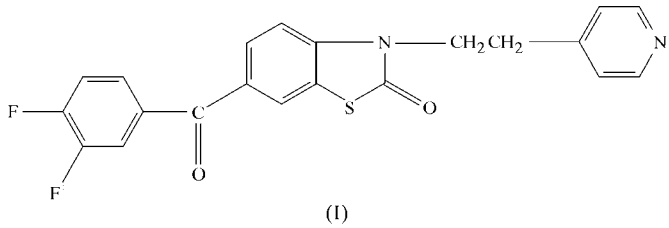
Comment

Benzothiazole derivatives possess a broad spectrum of pharmacological activity, including antibacterial, antifungal (Delmas *et al.*, 2002; Kanoongo *et al.*, 1990; Karalı *et al.*, 2004; Lakhan *et al.*, 2000), dopaminergic (Weinstock *et al.*, 1987), anticonvulsant (Chopade *et al.*, 2002), antiadrenergic (Di Nunno *et al.*, 2000) and analgesic anti-inflammatory activities (Gökhan *et al.*, 2004; Khedekar *et al.*, 2003). The medicinal importance of these derivatives prompted us to synthesize a 3-substituted-2-benzothiazolinone derivative and clarify its structure.

It has been stated that 2-hydroxybenzothiazole may also exist in the tautomeric form (Katritzky, 1985). The vinylpyridine group therefore may be bonded to the 6-acyl-2-benzothiazolinone moiety through both the N and the O atoms, depending on whether the molecule existed in the hydroxy or the ketone form, and a mixture of N-substituted or O-substituted benzothiazolinone derivatives may be generated. The present work has been carried out in order to determine the stereochemistry of the reactive tautomeric form.

The title compound, (I), was synthesized by the reaction of 6-(3,4-difluorobenzoyl)benzothiazolin-2-one with 4-vinylpyridine. The structure of (I) was suggested by IR, ^{1}H NMR and elemental analysis. In order to obtain information about the stereochemistry of the molecule and to confirm the assigned structure, an X-ray analysis was undertaken. The biological activity of (I) is under investigation.

The molecular structure and atom-numbering scheme are shown in Fig. 1, and the arrangement of the molecules in the unit cell is shown in Fig. 2. Selected bond lengths and angles are listed in Table 1. The benzothiazole ring system is planar, the greatest deviations from the least-squares plane of the system being those of atoms C3 [−0.016 (2) Å] and C1 [0.0142 (2) Å]. The dihedral angle between the planes associated with the benzene and thiazoline rings is only 0.55 (8)°. This value is close to those found for other structures including a benzothiazole ring system [*e.g.* 0.3 (1)° (Ćaleta *et al.*, 2004) and 2.3 (4)° (Castiñeiras *et al.*, 2000)].



(I)

The pyridylethyl moiety at atom N1 is rotated around the N1—C8 and C9—C10 bonds, giving C7—N1—C8—C9 and C8—C9—C10—C14 torsion angles of 81.9 (3) and 98.3 (3)°. The dihedral angle between the ring planes is 1.08 (9)°, so that the pyridine ring is almost parallel to the benzothiazole ring system. The difluorobenzene moiety is nearly planar, and atoms F1 and F2 lie −0.043 (2) and 0.56 (2) Å from the mean plane of the benzene ring atoms. The carbonyl group at atom C4 is inclined with respect to the benzothiazole system; atom O2 lies 0.853 (2) Å from the mean ring plane. The dihedral angle between the plane defined by atoms O2, C4, C15 and C16 and the plane of the benzene ring is 33.3 (1)°.

In the thiazoline ring, the S1—C1 bond is longer than the S1—C2 bond [1.746 (2) Å *versus* 1.784 (2) Å] and is also longer than the accepted value for an S—Csp^2 single bond [1.762 Å for O=C—S—C; Allen *et al.*, 1987]. The difference between the S1—C1 and S1—C2 bond lengths can be attributed to the fact that carbonyl atom O1 is bonded to atom C1, whereas atom C2 belongs to the aromatic ring. The S—C distances are in agreement with those found for other structures containing benzothiazolinone, such as 2-hydroxybenzothiazole [1.7767 (13) and 1.7479 (13) Å; Flakus *et al.*, 2002] and methyl 3-[5-choloro-2-oxo-2*H*-1,3-benzothiazol-3-yl]propano-

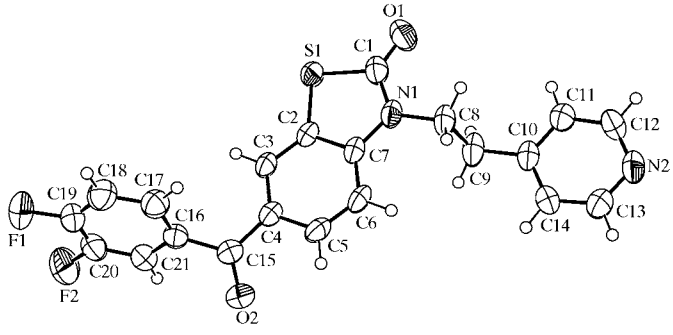


Figure 1
The molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level.

 DOI: 10.1107/S0108270104019730

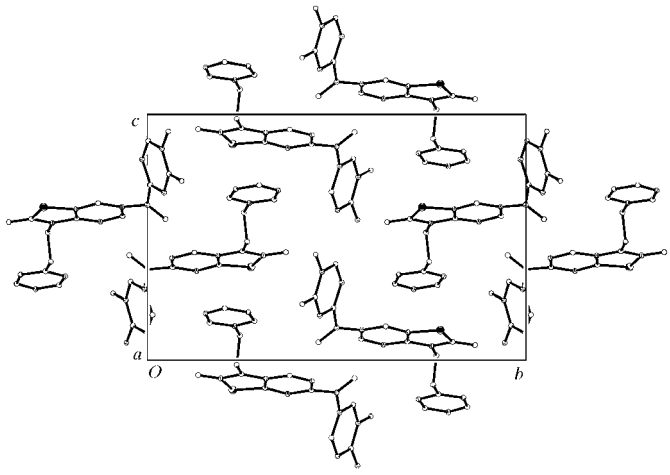


Figure 2
The crystal packing of (I), projected on to the *bc* plane.

ate [1.776 (3) and 1.742 (3) Å; Aydın *et al.*, 2002]. The N1—C1 [1.377 (3) Å] and N1—C7 [1.380 (3) Å] bond lengths are within the usual range for Csp^2—Nsp^2 bonds, while the N1—C8 bond length [1.464 (2) Å] is close to the average length of Csp^3—Nsp^2 bonds (Allen *et al.*, 1987). These values are comparable to those of other structures {1.3589 (16) and 1.3911 (16) Å in 2-hydroxybenzothiazole, and 1.362 (4), 1.401 (4) and 1.469 (3) Å in methyl 3-[5-choloro-2-oxo-2*H*-1,3-benzothiazol-3-yl]propanoate}. The sum of the angles about atom N1 (360°) indicates a planar sp^2 environment.

In this structure, the orientations of carbonyl atoms O2 and O1 toward the benzothiazole and ethyl groups, respectively, are consistent with an intramolecular hydrogen-bond-type interaction. In this manner, carbonyl groups are involved in the formation of a five-membered ring structure [C5···O2 = 2.830 (3) Å, C5—H5···O2 = 95°, C8···O1 = 2.835 (3) Å and C8—H8*B*···O1 = 100°]. The crystal packing of (I) is shown in Fig. 2. There are no intermolecular hydrogen bonds, but the F atoms of the phenyl substituent are involved in short intermolecular contacts [F1···F1^{i} = 2.814 (3) Å and S1···F2^{ii} = 3.347 (2) Å; symmetry codes: (i) $-x, -y, -z$; (ii) $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$].

Experimental

For the synthesis of (I), 4-vinylpyridine (7.5 mmol) was added to 6-(3,4-difluorobenzoyl)benzothiazolin-2-one (2.5 mmol). The reaction mixture was heated under reflux in an oil bath until molten and then for an additional 2 h at 353 K. On addition of a cold alcohol–water mixture, the product separated and the resulting precipitate was collected by filtration (Gökhan *et al.*, 1999) (yield 61.41%; m.p. 399–401 K). The crude product was recrystallized from ethanol–water. IR (KBr, cm^{-1}): ν 1692 (lactam C=O), 1649 (aromatic ketone); ^{1}H NMR ($CDCl_3$): δ 3.071–3.109 (*t*, 2H, CH_2–Ar), 4.243–4.280 (*t*, 2H, N–CH_2), 7.026–7.047 (*d*, *J* = 8.4 Hz, 1H, benzothiazolin-2-one H-4), 7.162–7.173 (*d*, *J* = 4.4 Hz, 2H, pyridine H-2, H-6), 7.315–7.339 (*t*, 1H, benzene H-5′), 7.53–7.57 (*s*, 1H, benzene H-2′), 7.624–7.674 (*t*, 1H, benzene H-6′), 7.728–7.754 (*d*, *J* = 10 Hz, benzothiazolin-2-one H-5), 7.922–7.926 (*s*, 1H, benzothiazolin-2-one H-7), 8.529–8.543 (*d*, *J* = 8 Hz, 2H, pyridine H-3, H-5). Analysis calculated for $C_{21}H_{14}F_2N_2O_2S$: N 7.07, S 8.09%; found: N 6.93, S 7.81%.

Crystal data

$C_{21}H_{14}F_2N_2O_2S$
M_r = 396.4
Monoclinic, $P2_1/n$
a = 7.2985 (15) Å
b = 19.4347 (19) Å
c = 12.6638 (16) Å
β = 93.020 (1)°
V = 1793.8 (5) Å^3
Z = 4
D_x = 1.468 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 11–18.1°
μ = 0.22 mm^{-1}
T = 295 (2) K
Prism, colourless
0.54 × 0.42 × 0.12 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.852, T_{max} = 0.974
3924 measured reflections
3636 independent reflections
2575 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 26.3°
$h = -9 \rightarrow 0$
$k = -24 \rightarrow 0$
$l = -15 \rightarrow 15$
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.120
S = 1.02
3636 reflections
253 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0601P)^2 + 0.5076P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

S1—C2	1.746 (2)	C15—C16	1.500 (3)
S1—C1	1.784 (2)	N2—C13	1.311 (3)
C7—N1	1.380 (3)	N2—C12	1.319 (3)
N1—C1	1.377 (3)	F2—C20	1.347 (3)
N1—C8	1.464 (2)	C8—C9	1.522 (3)
O1—C1	1.204 (3)	F1—C19	1.353 (3)
O2—C15	1.219 (2)	C10—C9	1.505 (3)
C15—C4	1.480 (3)		
C2—S1—C1	91.49 (10)	O1—C1—N1	125.9 (2)
N1—C7—C2	112.95 (17)	N1—C1—S1	108.94 (15)
C1—N1—C7	115.86 (16)	N1—C8—C9	111.37 (17)
C7—C2—S1	110.72 (15)	N2—C12—C11	124.7 (2)
C13—N2—C12	115.0 (2)	C14—C10—C11	116.13 (19)
C10—C11—C12	119.6 (2)	N2—C13—C14	125.2 (2)
C16—C15—C4—C3	−35.4 (3)	C7—N1—C8—C9	81.9 (3)
C4—C15—C16—C17	−45.7 (3)	C14—C10—C9—C8	98.3 (3)
C1—N1—C8—C9	−96.6 (2)	N1—C8—C9—C10	178.9 (2)

H atoms were placed in idealized positions and refined using a riding model [U_{iso}(H) = 1.3U_{eq}(C), C—H = 0.93 Å (aromatic) and C—H = 0.97 Å (ethyl)].

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *XCAD*4 (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV1196). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. S1–83.

Aydın, A., Arıcı, C., Akkurt, M., Akkoç, Y. & Şahin, M. F. (2002). *Anal. Sci.* **18**, 1401–1402.

Ćaleta, I., Grdiša, M., Mrvoš-Sermek, D., Cetina, M., Tralić-Kulenović, V., Pavelić, K. & Karminski-Zamola, G. (2004). *Farmaco*, **59**, 297–305.

Castiñeiras, A., Gómez, M. C. & Sevillano, P. (2000). *J. Mol. Struct.* **554**, 301–306.

Chopade, R. S., Bahekar, R. H., Khedekar, P. B., Bhusari, K. P. & Rao, A. R. R. (2002). *Arch. Pharm.* **335**, 381–388.

Delmas, F., Di Giorgio, C., Robin, M., Azas, N., Gasquet, M., Detang, C., Costa, M., Timon-David, P. & Galy, J. P. (2002). *Antimicrob. Agents*, **46**, 2588–2594.

Di Nunno, L., Franchini, C., Scilimati, A., Sinicropi, M. S. & Tortorella, P. (2000). *Tetrahedron: Asymmetry*, **11**, 1571–1583.

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.

Flakus, H. T., Miros, A. & Jones, P. G. (2002). *J. Mol. Struct.* **604**, 29–44.

Gökhan, N., Aktay, G. & Erdoğan, H. (2004). *Turk. J. Chem.* **28**, 123–132.

Gökhan, N., Erdoğan, H., Durlu, T. & Demirdamar, R. (1999). *Arch. Pharm. Pharm. Med. Chem.* **332**, 43–49.

Harms, K. & Wocadlo, S. (1995). *XCAD*4. University of Marburg, Germany.

Kanoongo, N., Singh, R. V., Tandon, J. P. & Goyal, R. B. (1990). *J. Inorg. Biochem.* **38**, 57–67.

Karalı, N., Cesur, N., Gürsoy, A., Ateş, O., Özden, S., Otuk, G. & Birteksöz, S. (2004). *Indian J. Chem. Sect. B*, **43**, 212–216.

Katritzky, A. R. (1985). In *Handbook of Heterocyclic Chemistry*. Oxford: Pergamon Press.

Khedekar, P. B., Bahekar, R. H., Chopade, R. S., Umathe, S. N., Rao, A. R. R. & Bhusari, K. P. (2003). *Arzneim. Forsch.* **53**, 640–647.

Lakhan, R., Sharma, B. P. & Shukla, B. N. (2000). *Farmaco*, **55**, 331–337.

North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.

Sheldrick, G. M. (1997). *SHELXL*97 and *SHELXS*97. University of Göttingen, Germany.

Weinstock, J., Gaitanopoulos, D. E., Stringer, O. D., Franz, R. G., Hieble, J. P., Kinter, L. B., Mann, W. A., Flaim, K. E. & Gessner, G. (1987). *J. Med. Chem.* **30**, 1166–1176.