

|           |             |          |             |
|-----------|-------------|----------|-------------|
| N2—C2     | 1.387 (2)   | C5—C6    | 1.378 (3)   |
| C8—N1     | 1.304 (2)   | C10—F    | 1.331 (4)   |
| C8—C9     | 1.488 (3)   |          |             |
| C9—S—C1   | 96.69 (9)   | C3—C2—C7 | 122.4 (2)   |
| N2—C1—C10 | 111.71 (10) | N2—C2—C7 | 104.2 (2)   |
| N2—C1—S   | 102.52 (12) | N1—C7—C6 | 129.8 (2)   |
| C10—C1—S  | 108.60 (10) | N1—C7—C2 | 110.7 (2)   |
| C8—N2—C2  | 106.76 (14) | C6—C7—C2 | 119.5 (2)   |
| C8—N2—C1  | 120.38 (15) | C8—N1—C7 | 103.82 (15) |
| C2—N2—C1  | 132.87 (15) | C4—C3—C2 | 117.0 (2)   |
| N1—C8—N2  | 114.6 (2)   | C3—C4—C5 | 121.4 (2)   |
| N1—C8—C9  | 130.4 (2)   | C6—C5—C4 | 121.6 (2)   |
| N2—C8—C9  | 115.0 (2)   | C5—C6—C7 | 118.1 (2)   |
| C8—C9—S   | 105.40 (13) | F—C10—C1 | 111.8 (2)   |
| C3—C2—N2  | 133.5 (2)   |          |             |

Symmetry code: (i)  $x, \frac{1}{2} - y, z$ .

The structure was solved by direct methods and refined using full-matrix least-squares techniques with all non-H atoms anisotropic. The H atoms were located from difference maps and refined isotropically. The C—H bonds range from 1.05 (4) to 0.94 (2) Å, while  $U_{eq}$  ranges from 2 (1) to 5.9 (5) Å<sup>2</sup>. The space-group determination was a little difficult as there was a choice between  $P2_1$  or  $P2_1/m$  and neither the systematic absences nor statistical calculations based on the absolute value of  $E^2 - 1$  could determine which was correct. The best results were obtained in the centrosymmetric space group with the F atom and H10C occupancy factors set to 0.5. This is because the central part of the molecule lies on a symmetry mirror plane and the —CH<sub>2</sub>F and the —CH<sub>3</sub> groups are positioned symmetrically on either side of the molecule, thus generating the crystallographic disorder.

All calculations were performed on a MicroVAX 3400 and on a DEC-alpha 3000/400.

Data collection: *P3/V Software* (Siemens, 1989). Cell refinement: *P3/V Software*. Data reduction: *SHELXTL-Plus* (Sheldrick, 1990). Program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *SHELXTL-Plus*. Software used to prepare material for publication: *PARST95* (Nardelli, 1995) and *SHELXL93*.

We thank the Italian MURST and the Centro Diffratometria a Raggi-X of the University of Messina, Italy.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1235). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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## 1-[3,5-Bis(trifluoromethyl)phenyl]-1H,3H-thiazolo[3,4-a]benzimidazole

GIUSEPPE BRUNO,<sup>a</sup> ANNA MARIA MONFORTE,<sup>b</sup> FRANCESCO NICOLÓ,<sup>a</sup> ROSARIO SCOPELLITI<sup>a</sup> AND MARIA ZAPPALÁ<sup>b</sup>

<sup>a</sup>Dipartimento di Chimica Inorganica, Chimica Analitica e Chimica Fisica, Università di Messina, 98166 Vill. Sant'Agata, Messina, Italy, and <sup>b</sup>Dipartimento Farmaco-Chimico, Università di Messina, 98168 Viale Annunziata, Messina, Italy. E-mail: bruno@medif0.unime.it

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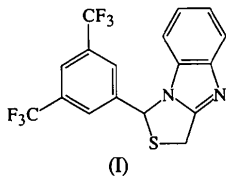
## Abstract

The crystal structure of the title compound, C<sub>17</sub>H<sub>10</sub>F<sub>6</sub>N<sub>2</sub>S, has been determined. The thiazole ring fused with the benzimidazole system is in an envelope conformation, while the two trifluoromethyl groups at positions 3 and 5 of the phenyl substituent are dynamically disordered because of their rotation along the Csp<sup>3</sup>—Csp<sup>2</sup> bond.

## Comment

In the course of our studies on new anti-HIV agents, we reported the synthesis and anti-HIV activity of a series of 1-aryl-1H,3H-thiazolo[3,4-a]benzimidazoles, a new class of non-nucleoside HIV-1 reverse transcriptase

inhibitors (Chimirri, Grasso, Monforte, Monforte & Zappalá, 1991*a,b*; Bruno *et al.* 1996). In this paper, we report the results of the X-ray structure determination of 1-(3,5-difluoromethylphenyl)-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazole, (I), as part of a wider structural and pharmacological study on thiazolo[3,4-*a*]benzimidazole derivatives aimed at obtaining information concerning the effect on anti-HIV activity of the nature and position of the substituents on the aromatic ring at C1.



The title compound, (I), has a chiral centre at C1. Thus, in the crystalline state described by the centrosymmetric space group  $P2_1/c$ , we have a perfect racemic mixture. Fig. 1 shows the *R* enantiomer and the atom-numbering scheme. The benzimidazole system is planar owing to the wide electron  $\pi$  delocalization, confirmed by the sums of the valency angles around N2 and C8 [359.8 (2) and 360.0 (2)°, respectively] and by the bond lengths involving the N atoms of the imidazole ring [C8—N1 = 1.312 (3), N2—C8 = 1.360 (3), N2—C2 = 1.385 (3), C7—N1 = 1.394 (3) Å] which are intermediate between expected C=N and C—N values. This electron delocalization extends its influence to the C1 and C9 atoms as can be seen from the torsion angles C9—C8—N1—C7 [−176.8 (3)°] and C1—N2—C2—C3 [−3.8 (5)°] and the bond distance C8—C9 [1.478 (4) Å]. The ring puckering parameters (Cremer & Pople, 1975) for the thiazole prove the envelope conformation [ $\varphi = -1.1$  (9)°] with the S atom displaced by 0.350 (1) Å from the weighted least-squares plane defined by the remaining atoms of the ring.

The 3,5-difluoromethylphenyl group linked through C10 to C1 is rotated with respect to the plane through all atoms except S of the thiazolobenzimidazole system, as

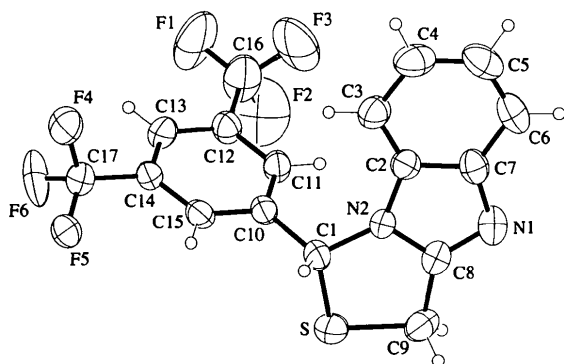


Fig. 1. View of the title compound with displacement ellipsoids at the 50% probability level. For clarity, only the higher occupancy positions of the CF<sub>3</sub> groups are shown.

indicated by the angle of 73.14 (6)° between the phenyl group and the central part of the molecule; the molecule therefore assumes a butterfly-like conformation. This arrangement decreases the steric effects and maximizes the intermolecular hydrogen interactions mentioned below. The crystal packing is mainly determined by van der Waals interactions and by weak hydrogen bonds involving the H11 atom bonded to C11 and the N1 atom of an adjacent molecule [H11···N1<sup>i</sup> = 2.461, C11···N1<sup>i</sup> = 3.379 (3), C11—H11···N1<sup>i</sup> = 169.3 (3), (i) 2−*x*, 1−*y*, 1−*z*]; the molecules are related by an inversion centre and show the typical head-to-tail disposition.

The F atoms of the disordered trifluoromethyl groups are involved in several weak hydrogen-bonding interactions [F···H contacts ranging from 2.25 (2) to 2.98 (2) Å] but these are not able to hinder the rotation. As a result of this rotational disorder, the C—F bond distances are not well determined [1.230 (10)–1.377 (9) Å].

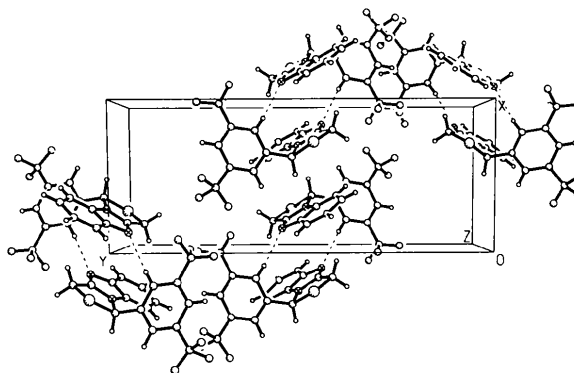


Fig. 2. Packing in the unit cell viewed down *c*. Dotted lines show the hydrogen-bonding interactions and cross-hatched circles indicate N atoms.

## Experimental

The title compound was obtained as described earlier (Chimirri *et al.*, 1991*b*) and recrystallized from ethanol.

### Crystal data

C<sub>17</sub>H<sub>10</sub>F<sub>6</sub>N<sub>2</sub>S  
*M<sub>r</sub>* = 388.33  
 Monoclinic  
 $P2_1/c$   
 $a = 8.281$  (2) Å  
 $b = 20.914$  (4) Å  
 $c = 9.549$  (2) Å  
 $\beta = 97.46$  (2)°  
 $V = 1639.8$  (6) Å<sup>3</sup>  
 $Z = 4$   
 $D_x = 1.573$  Mg m<sup>−3</sup>  
 $D_m$  not measured

Mo  $K\alpha$  radiation  
 $\lambda = 0.71073$  Å  
 Cell parameters from 35 reflections  
 $\theta = 5$ –15°  
 $\mu = 0.264$  mm<sup>−1</sup>  
 $T = 293$  (2) K  
 Prismatic  
 0.20 × 0.12 × 0.08 mm  
 Colourless

### Data collection

Siemens R3m/V diffractometer  
 $\omega/2\theta$  scans

1839 observed reflections  
 $[I > \sigma(I)]$   
 $R_{int} = 0.0181$

Absorption correction:  $\theta_{\max} = 24^\circ$   
 $\psi$  scan (Kopfmann & Huber, 1968)  $h = -1 \rightarrow 10$   
 $T_{\min} = 0.708$ ,  $T_{\max} = 0.831$   $k = -1 \rightarrow 24$   
 $l = -11 \rightarrow 11$   
 3467 measured reflections monitored every 97 reflections  
 2577 independent reflections intensity decay: 1%

### Refinement

Refinement on  $F^2$  Extinction correction:  $SHELXL93$  (Sheldrick, 1993)  
 $R[F^2 > 2\sigma(F^2)] = 0.0377$   
 $wR(F^2) = 0.0860$  Extinction coefficient: 0.0053 (8)  
 $S = 0.964$  Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)  
 1839 reflections  
 291 parameters  
 $w = 1/[\sigma^2(F_o^2) + (0.0416P)^2]$  where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\max} = 0.001$   
 $\Delta\rho_{\max} = 0.170 \text{ e } \text{Å}^{-3}$   
 $\Delta\rho_{\min} = -0.147 \text{ e } \text{Å}^{-3}$

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters ( $\text{Å}^2$ )

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$$

|      | x            | y            | z            | $U_{eq}$    |
|------|--------------|--------------|--------------|-------------|
| S    | 0.72936 (11) | 0.46944 (4)  | 0.15816 (7)  | 0.0548 (3)  |
| C1   | 0.6329 (3)   | 0.52643 (12) | 0.2691 (2)   | 0.0373 (7)  |
| N2   | 0.7100 (3)   | 0.51068 (9)  | 0.4106 (2)   | 0.0361 (5)  |
| C8   | 0.7999 (3)   | 0.45633 (13) | 0.4319 (3)   | 0.0411 (7)  |
| C9   | 0.8122 (4)   | 0.41796 (12) | 0.3038 (3)   | 0.0504 (8)  |
| C2   | 0.7044 (3)   | 0.53861 (13) | 0.5414 (3)   | 0.0370 (7)  |
| C7   | 0.7974 (3)   | 0.49750 (14) | 0.6356 (3)   | 0.0427 (7)  |
| N1   | 0.8569 (3)   | 0.44609 (11) | 0.5647 (2)   | 0.0498 (6)  |
| C3   | 0.6305 (4)   | 0.59320 (13) | 0.5843 (3)   | 0.0489 (8)  |
| C4   | 0.6544 (4)   | 0.60636 (15) | 0.7272 (3)   | 0.0605 (9)  |
| C5   | 0.7480 (4)   | 0.5663 (2)   | 0.8218 (3)   | 0.0616 (9)  |
| C6   | 0.8189 (4)   | 0.5123 (2)   | 0.7797 (3)   | 0.0559 (9)  |
| C10  | 0.6604 (3)   | 0.59436 (12) | 0.2252 (2)   | 0.0338 (6)  |
| C11  | 0.8075 (3)   | 0.62469 (12) | 0.2638 (3)   | 0.0395 (7)  |
| C12  | 0.8314 (3)   | 0.68650 (13) | 0.2193 (3)   | 0.0438 (7)  |
| C16  | 0.9866 (5)   | 0.7200 (2)   | 0.2676 (5)   | 0.0778 (11) |
| F1†  | 0.9979 (10)  | 0.7781 (3)   | 0.2315 (9)   | 0.151 (4)   |
| F2‡  | 1.1072 (8)   | 0.6904 (4)   | 0.2118 (9)   | 0.146 (3)   |
| F3‡  | 1.0329 (9)   | 0.7124 (3)   | 0.4030 (6)   | 0.125 (3)   |
| F1'‡ | 0.9660 (18)  | 0.7560 (8)   | 0.3847 (12)  | 0.150 (6)   |
| F2'‡ | 1.1136 (14)  | 0.6889 (5)   | 0.287 (2)    | 0.149 (12)  |
| F3'‡ | 1.0063 (19)  | 0.7672 (7)   | 0.1801 (15)  | 0.097 (6)   |
| C13  | 0.7083 (4)   | 0.71792 (13) | 0.1330 (3)   | 0.0465 (8)  |
| C14  | 0.5617 (3)   | 0.68795 (12) | 0.0949 (2)   | 0.0393 (7)  |
| C17  | 0.4299 (4)   | 0.7234 (2)   | 0.0050 (3)   | 0.0521 (8)  |
| F4†  | 0.3661 (13)  | 0.7685 (4)   | 0.0765 (11)  | 0.066 (2)   |
| F5†  | 0.3096 (10)  | 0.6888 (4)   | -0.0566 (7)  | 0.085 (2)   |
| F6†  | 0.4929 (10)  | 0.7552 (4)   | -0.0974 (5)  | 0.088 (2)   |
| F4'† | 0.450 (2)    | 0.7348 (10)  | -0.1259 (12) | 0.138 (10)  |
| F5'† | 0.297 (2)    | 0.6859 (10)  | -0.0029 (17) | 0.098 (6)   |
| F6'† | 0.385 (3)    | 0.7769 (8)   | 0.060 (3)    | 0.089 (8)   |
| C15  | 0.5366 (3)   | 0.62640 (13) | 0.1414 (2)   | 0.0382 (7)  |

† Site occupancy = 0.70. ‡ Site occupancy = 0.30.

Table 2. Selected geometric parameters ( $\text{Å}$ ,  $^\circ$ )

|           |            |          |           |
|-----------|------------|----------|-----------|
| S—C9      | 1.821 (3)  | N2—C2    | 1.385 (3) |
| S—C1      | 1.844 (3)  | C8—N1    | 1.312 (3) |
| C1—N2     | 1.455 (3)  | C8—C9    | 1.478 (4) |
| C1—C10    | 1.507 (3)  | C2—C7    | 1.401 (3) |
| N2—C8     | 1.360 (3)  | C7—N1    | 1.394 (3) |
| C9—S—C1   | 95.26 (12) | N1—C8—C9 | 131.0 (2) |
| N2—C1—C10 | 114.1 (2)  | N2—C8—C9 | 115.2 (2) |
| N2—C1—S   | 102.5 (2)  | C8—C9—S  | 104.6 (2) |

|          |           |          |           |
|----------|-----------|----------|-----------|
| C10—C1—S | 110.9 (2) | C3—C2—N2 | 133.1 (2) |
| C8—N2—C2 | 107.4 (2) | N2—C2—C7 | 103.9 (2) |
| C8—N2—C1 | 119.6 (2) | N1—C7—C6 | 129.8 (3) |
| C2—N2—C1 | 132.8 (2) | N1—C7—C2 | 111.1 (2) |
| N1—C8—N2 | 113.8 (2) | C8—N1—C7 | 103.8 (2) |

Reflection intensities were evaluated by profile fitting of a 96-step peak scan over  $2\theta$  shells (Diamond, 1969) and then corrected for Lorentz-polarization effects.

The structure was solved by direct methods and refined using full-matrix least squares with all non-H atoms anisotropic. H atoms were included in calculated positions using a riding model with a common value for  $U_{eq}$ .

Rotational disorder of the two  $\text{CF}_3$  groups was handled by splitting them into two staggered positions and fixing their occupancy site; since the F atoms displayed the usual high librational motion associated with terminal  $\text{CF}_3$  groups, the repeated attempts by the least-squares programs to position them too close to the central C atoms failed. Finally some weak restraints (the C—F bond lengths were forced to a refined unique mean value and the F-atom  $U_{ij}$  components approximated to isotropic behaviour) were adopted to correct their geometry.

Data collection: P3/V (Siemens, 1989). Cell refinement: P3/V. Data reduction: *SHELXTL-Plus* (Sheldrick, 1990). Program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *SHELXTL-Plus*. Software used to prepare material for publication: *PARST95* (Nardelli, 1995) and *SHELXL93*.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1245). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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