

Marília S. Costa,<sup>a</sup> Nubia Boechat,<sup>a</sup> Vitor F. Ferreira,<sup>b</sup> Solange M. S. V. Wardell<sup>a</sup> and Janet M. S. Skakle<sup>c\*</sup>

<sup>a</sup>Fundação Oswaldo Cruz, Instituto de Tecnologia em Fármacos, Departamento de Síntese Orgânica, Manguinhos, CEP 21041-250 Rio de Janeiro, RJ, Brazil, <sup>b</sup>Universidade Federal Fluminense, Departamento de Química Orgânica, Instituto de Química, Outeiro de São João Baptista, CEP 24020-150 Niterói, RJ, Brazil, and <sup>c</sup>Department of Chemistry, College of Physical Sciences, University of Aberdeen, Meston Walk, Aberdeen AB24 3UE, Scotland

Correspondence e-mail: j.skakle@abdn.ac.uk

#### Key indicators

Single-crystal X-ray study  
 $T = 120$  K  
 Mean  $\sigma(C-C) = 0.004$  Å  
 $R$  factor = 0.062  
 $wR$  factor = 0.160  
 Data-to-parameter ratio = 15.2

For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

## 4-Difluoromethyl-1-(4-methylphenyl)-1H-1,2,3-triazole

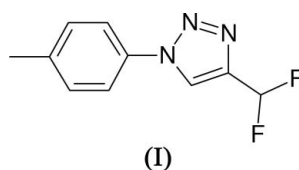
In the crystal structure of the title compound,  $C_{10}H_9F_2N_3$ , weak hydrogen bonding involving the triazole and difluoromethyl groups leads to the formation of chains along [010]. The benzene and triazole rings are essentially coplanar, with an angle of  $0.34$  ( $17^\circ$ ) between the planes defined by the two rings.

Received 11 April 2006

Accepted 11 April 2006

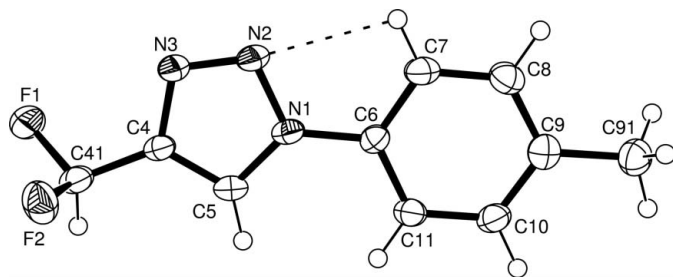
#### Comment

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains a leading cause of mortality worldwide. The World Health Organization estimates that about one-third of the world's population harbours latent infection of TB. Among such infected individuals, approximately eight million develop active TB, and almost two million of these die from the disease each year. 95% of new TB cases occur in developing countries. The current human immunodeficiency virus (AIDS) pandemic and resistance to the currently available drugs are proving major obstacles to the control of tuberculosis (Tewari *et al.*, 2004; World Health Organization, 2005; Tripathi *et al.*, 2005). Chemotherapy of TB started in the 1940s. Various drugs have been used against TB, including *para*-aminosalicylic acid, isoniazid, pyrazinamide, cycloserine, ethionamide, rifampicin and ethambutol. However, six decades have passed without any significant development of new chemical treatments of tuberculosis. TB really can be classed as a neglected disease.

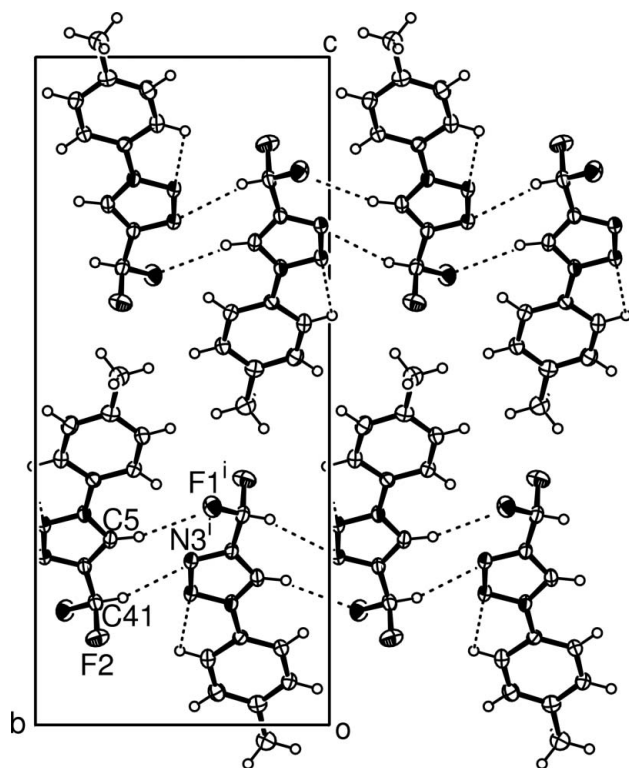


In pursuit of new drugs for TB, we have synthesized a series of 1-aryl-4-difluoromethyl-1,2,3-triazole derivatives and evaluated their inhibitory activities against *Mycobacterium tuberculosis*. All derivatives exhibited tuberculosis inhibitory activity; a full description of biological tests will be reported elsewhere (Costa, Boechat, Rangel *et al.*, 2006). The structure of 1-(4-methylphenyl)-4-difluoromethyl-1H-1,2,3-triazole, which exhibited 87% of inhibition at a concentration of  $40.0 \mu\text{g ml}^{-1}$ , is reported here.

The geometry of the title molecular structure (Fig. 1) was analysed with the aid of *PLATON* (Spek, 2003). The methyl group is almost coplanar with the aryl ring, with a torsion angle  $C7-C8-C9-C91 = 178.2$  ( $3^\circ$ ). Excluding the difluoromethyl group, the molecule is planar, with an angle between the planes defined by the triazole and aryl rings of



**Figure 1**  
The molecular structure of the title compound, showing displacement ellipsoids at the 50% probability level. H atoms are shown as circles of arbitrary radii and the dashed line indicates a weak hydrogen bond.



**Figure 2**  
Part of the structure of the title compound, showing the formation of hydrogen-bonded (dashed lines) chains along [010]. Ellipsoids and H atoms are shown as in Fig. 1. [Symmetry code: (i)  $\frac{3}{2} - x, -\frac{1}{2} + y, \frac{1}{2} - z$ ].

0.34 (17) Å. This is in marked contrast to the orientations in 1-(2,5-dimethoxyphenyl)-4-difluoromethyl-1*H*-1,2,3-triazole (Costa, Boechat, Ferreira, Wardell & Skakle, 2006), in which the substituent methoxy groups on the aryl ring cause a marked deviation from planarity.

With no scope for strong hydrogen bonding in the structure, weak hydrogen bonds exist (Table 1); an intramolecular hydrogen bond provides additional support between the triazole and aryl ring (C7–H7···N2). All other hydrogen bonds involve donors and acceptors within the triazole–difluoromethyl unit, and lead to the formation of chains along [010] (Fig. 2).

## Experimental

A solution of diazomalonaldehyde (5.0 mmol) in water (30 ml) was added dropwise to a stirred solution of 4-aminotoluene hydrochloride (4.5 mmol) in water (5 ml). The reaction mixture was stirred for 24 h at room temperature; the solid was collected, washed with cold water and crystallized from aqueous ethanol. The title compound was obtained in 93% yield as colourless solid, m.p. 351–352 K. Analysis calculated for  $C_{10}H_9F_2N_3$ : C 57.41, H 4.34, N 20.09%; found: C 57.45, H 4.37, N 19.97%. Full spectroscopic data are given in the CIF.

### Crystal data

$C_{10}H_9F_2N_3$	$Z = 4$
$M_r = 209.20$	$D_x = 1.492 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 4.6055$ (6) Å	$\mu = 0.12 \text{ mm}^{-1}$
$b = 9.4285$ (9) Å	$T = 120$ (2) K
$c = 21.459$ (3) Å	Cut blade, colourless
$\beta = 92.136$ (5)°	$0.22 \times 0.11 \times 0.03 \text{ mm}$
$V = 931.2$ (2) Å <sup>3</sup>	

### Data collection

Bruker–Nonius KappaCCD diffractometer	8742 measured reflections
$\varphi$ and $\omega$ scans	2112 independent reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	1262 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.636, T_{\max} = 1.000$	$R_{\text{int}} = 0.071$
	$\theta_{\max} = 27.7^\circ$

### Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F_o^2) + (0.0577P)^2 + 0.6473P]$
$R[F^2 > 2\sigma(F^2)] = 0.062$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.160$	$(\Delta/\sigma)_{\max} < 0.001$
$S = 1.03$	$\Delta\rho_{\max} = 0.24 \text{ e \AA}^{-3}$
2112 reflections	$\Delta\rho_{\min} = -0.32 \text{ e \AA}^{-3}$
139 parameters	
H-atom parameters constrained	

**Table 1**  
Hydrogen-bond geometry (Å, °).

D–H···A	D–H	H···A	D···A	D–H···A
C7–H7···N2	0.95	2.45	2.780 (3)	100
C5–H5···F1 <sup>i</sup>	0.93	2.52	3.421 (3)	164
C41–H41···N2 <sup>i</sup>	1.00	2.46	3.458 (3)	173
C41–H41···N3 <sup>i</sup>	1.00	2.47	3.403 (3)	155

Symmetry code: (i)  $-x + \frac{3}{2}, y - \frac{1}{2}, -z + \frac{1}{2}$ .

All H atoms were located in difference maps and then treated as riding atoms, with C–H distances of 0.93 Å (triazole), 0.95 Å (aryl), 1.00 Å (tertiary –CHF<sub>2</sub>) and 0.98 Å (methyl).  $U_{\text{iso}}$  values for the triazole and tertiary H were freely refined; otherwise  $U_{\text{iso}}(\text{H})$  values were set at  $1.2U_{\text{eq}}(\text{aryl C})$  or  $1.5U_{\text{eq}}(\text{methyl C})$ .

Data collection: COLLECT (Hooft, 1998); cell refinement: DENZO (Otwinowski & Minor, 1997) and COLLECT; data reduction: DENZO and COLLECT; program(s) used to solve structure: OSCAIL (McArdle, 2003) and SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: OSCAIL and SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEP-3 for Windows (Farrugia, 1997); software used to prepare material for publication: CIFTAB (Sheldrick, 1997).

We are indebted to the EPSRC for the use of both the Chemical Database Service at Daresbury, England, primarily for access to the Cambridge Structural Database (Fletcher *et*

al., 1996), and the X-ray service at the University of Southampton, England, for data collection.

## References

- Costa, M. S., Boechat, N., Ferreira, V. F., Wardell, S. M. V. & Skakle, J. M. S. (2006). *Acta Cryst.* **E62**, o2048–o2050.
- Costa, M. S., Boechat, N., Rangel, E. A., Ferreira, V. F., Junior, I. N., Lourenço, M. C. S. & Wardell, S. M. S. V. (2006). *Eur. J. Med. Chem.* In preparation.
- Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
- Fletcher, D. A., McMeeking, R. F. & Parkin, D. (1996). *J. Chem. Inf. Comput. Sci.* **36**, 746–749.
- Hooft, R. W. W. (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.
- McArdle, P. (2003). *OSCAIL for Windows*. Version 10. Crystallography Centre, Chemistry Department, National University of Ireland, Galway, Ireland.
- Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
- Sheldrick, G. M. (1997). *SHELXS97*, *SHELXL97* and *CIFTAB*. University of Göttingen, Germany.
- Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.
- Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
- Tewari, N., Tiwari, V. K., Tripathi, R. P., Chaturvedi, V., Srivastava, A., Srivastava, R., Shukla, P. K., Chaturvedi, A. K., Gaikwad, A., Sinha, S. & Srivastava, B. S. (2004). *Bioorg. Med. Chem. Lett.* **14**, 329–332.
- Tripathi, R. P., Tewari, N., Dwivedi, N. & Tiwari, V. K. (2005). *Med. Res. Rev.* **25**, 93–131.
- World Health Organization (2005). Report WHO/HTM/TB/2005. *Global Tuberculosis Control – Surveillance, Planning, Financing*. <http://www.who.int/tb>.