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

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(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.

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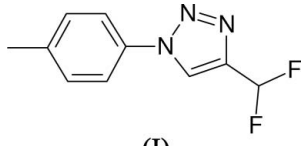
In the crystal structure of the title compound, $C_{10}H_9F_2N_3$, weak hydrogen bonding involving the triazole and difluoromethyl groups leads to the formation of chains along [010]. The benzene and triazole rings are essentially coplanar, with an angle of 0.34 (17)° between the planes defined by the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

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.



(I)

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-1*H*-1,2,3-triazole, which exhibited 87% of inhibition at a concentration of 40.0 μg 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)°. Excluding the difluoromethyl group, the molecule is planar, with an angle between the planes defined by the triazole and aryl rings of

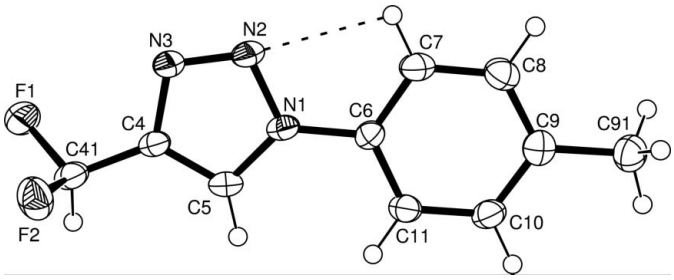


Figure 1
The molecular structure of the title compound, showing displacement ellipsoids at the 50% probability level. H atoms are shown as circles of arbitrary radii and the dashed line indicates a weak hydrogen bond.

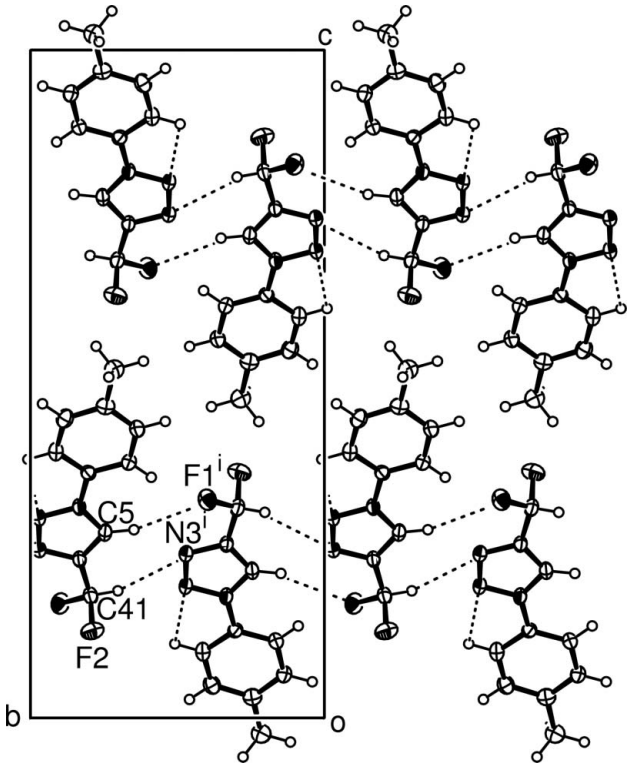


Figure 2
Part of the structure of the title compound, showing the formation of hydrogen-bonded (dashed lines) chains along [010]. Ellipsoids and H atoms are shown as in Fig. 1. [Symmetry code: (i) $\frac{3}{2} - x, -\frac{1}{2} + y, \frac{1}{2} - z$].

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

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

Data collection

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

Refinement

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

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^{i}	0.93	2.52	3.421 (3)	164
C41—H41···N2^{i}	1.00	2.46	3.458 (3)	173
C41—H41···N3^{i}	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_2) and 0.98 Å (methyl). U_{iso} values for the triazole and tertiary H were freely refined; otherwise U_{iso}(H) values were set at $1.2U_{eq}$(aryl C) or $1.5U_{eq}$(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).

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

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