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4-Difluoromethyl-1-(2,5-dimethoxyphenyl)-1*H*-1,2,3-triazole

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.002 Å
R factor = 0.042
wR factor = 0.110
Data-to-parameter ratio = 15.0

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

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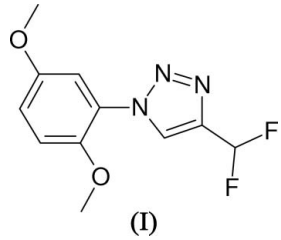
In the title compound, $C_{11}H_{11}F_2N_3O_2$, the aryl and triazole rings are both planar, but at an angle of 45.27 (4)° to each other.

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 this 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 new series of 1-aryl-4-difluoromethyl-1,2,3-triazole derivatives and evaluated their inhibitory activities against *M. tuberculosis*. All derivatives exhibited tuberculosis inhibitory activity at high concentrations (MIC > 6.5 g ml^{-1}); a full description of the biological tests will be reported elsewhere (Costa, Boechat, Rangel *et al.*, 2006). The structure of the title compound, (I), which exhibited 74% of inhibition at a concentration of 80.0 μg ml^{-1}, is reported below.



(I)

$C_{11}H_{11}F_2N_3O_2$ (Fig. 1) crystallizes in the space group $P2_1/c$; the geometry of the structure was analysed with the aid of *PLATON* (Spek, 2003). Both the triazole and the aryl rings are planar and the methoxy groups are nearly coplanar with the aryl ring, with torsion angles C8—C7—O7—O71 = 4.7 (2)° and C9—C10—O10—C101 = 6.7 (2)°. The angle between the

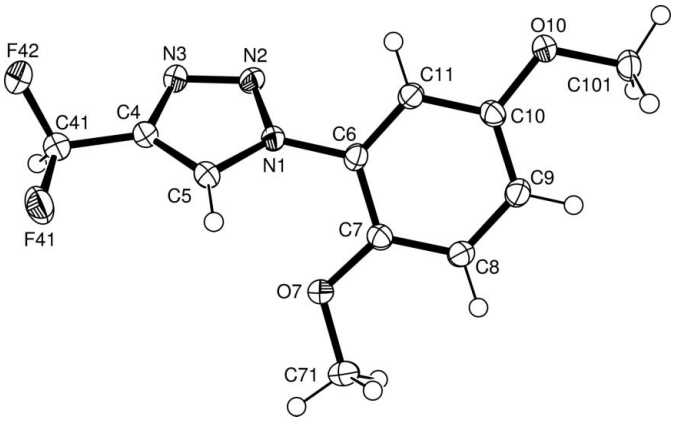


Figure 1
The molecular structure of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown as circles of arbitrary radii.

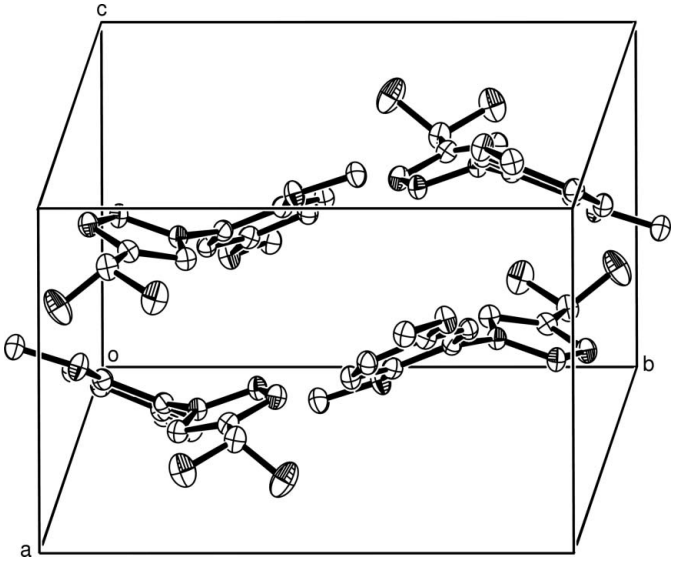


Figure 2
The unit-cell contents, showing the relative orientation of the triazole and aryl groups. Ellipsoids are represented as in Fig. 1. H atoms have been omitted.

planes defined by the triazole and aryl rings is 45.27 (4)° (Fig. 2). Comparison with 1-(4-methylphenyl)-4-difluoromethyl-1*H*-1,2,3-triazole (Costa, Boechat, Ferreira *et al.*, 2006) indicates that the presence of the methoxy groups, *ortho* and *meta* to the triazole, leads to this deviation from coplanarity.

Experimental

A solution of diazomalonaldehyde (5.0 mmol) in water (30 ml) was added dropwise to a stirred solution of 2,5-dimethoxyaniline 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 98% yield as a white solid (m.p. 351–352 K). ^{1}H NMR (500 MHz, $CDCl_3$/Me_4Si): δ 3.89 (*s*, 3H, $2OCH_3$), 6.95 (*t*, 1H, CHF_2, J = 55.0 Hz), 7.04 (*dd*, 2H, J = 2.0 e 7.0 Hz, arom.), 7.63 (*dd*, 2H, J = 2.0 e 7.0 Hz, arom.), 8.14 (*sl*, 1H, triazole). ^{19}F NMR (376.0 MHz, $CDCl_3$/$CFCl_3$): δ −112.2 (2F, CHF_2). Full spectroscopic data are given in the CIF. Analysis calculated for $C_{11}H_{11}F_2N_3O_2$: C 51.77, H 4.34, N 16.46%; found: C 51.78, H 4.36, N 16.49%.

Crystal data

$C_{11}H_{11}F_2N_3O_2$
M_r = 255.23
Monoclinic, $P2_1/c$
a = 13.4574 (6) Å
b = 11.4815 (5) Å
c = 7.3719 (2) Å
β = 105.247 (3)°
V = 1098.95 (7) Å^3
Z = 4
D_x = 1.543 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.13 mm^{-1}
T = 120 (2) K
Shard, colourless
0.14 × 0.12 × 0.05 mm

Data collection

Nonius KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.822, T_{max} = 1.000
14882 measured reflections
2510 independent reflections
1975 reflections with $I > 2\sigma(I)$
R_{int} = 0.053
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.110
S = 1.06
2510 reflections
167 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0488P)^2 + 0.501P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.021 (3)

All H atoms were located in difference maps and then treated as riding atoms with C—H distances of 0.95 (aryl), 1.00 (methine), 1.01 (triazole) and 0.98 Å (methyl), and with U_{iso}(H) values of $1.2U_{eq}$(aryl) or $1.5U_{eq}$(methyl); U_{iso} values for the triazole and methine H atoms were freely refined.

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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