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2-Methyl-5-(4-tolyl)-7-(trifluoromethyl)-pyrazolo[1,5-*a*]pyrimidine

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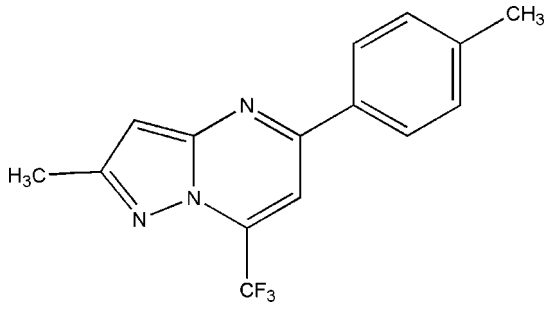
Key indicators: single-crystal X-ray study; T = 293 K; mean σ(C–C) = 0.003 Å; R factor = 0.057; wR factor = 0.227; data-to-parameter ratio = 19.8.

In the title compound, $C_{15}H_{12}F_3N_3$, the pyrazolo[1,5-*a*]-pyrimidine system ring is essentially planar with a maximum deviation from the mean plane of 0.014 (1) Å. The 4-tolyl group makes a dihedral angle of 14.1 (1)° with the pyrazolo[1,5-*a*]pyrimidine ring system. The crystal packing is stabilized mainly by van der Waals forces.

Related literature

For related pyrazolopyrimidine compounds, see: Wen *et al.* (2004, 2005); Oliveira-Campos *et al.* (2006). For related literature and the synthetic procedure, see: Martins *et al.* (2004, 2006). For the pharmacological activity, see: Almanza *et al.* (2001); Novinson *et al.* (1977); George (2001).



Experimental

Crystal data

$C_{15}H_{12}F_3N_3$
M_r = 291.28
Triclinic, $P\overline{1}$
a = 4.8715 (2) Å
b = 11.2655 (5) Å
c = 13.5584 (6) Å
α = 110.225 (3)°
β = 96.808 (3)°
γ = 99.835 (3)°
V = 675.13 (5) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.12 mm^{-1}
T = 293 (2) K
0.98 × 0.21 × 0.20 mm

Data collection

Bruker X8 APEXII diffractometer
Absorption correction: multi-scan (*XPREP*; Bruker, 2006)
T_{min} = 0.874, T_{max} = 0.977
16787 measured reflections
3757 independent reflections
2200 reflections with $I > 2\sigma(I)$
R_{int} = 0.040

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.227
S = 1.05
3757 reflections
190 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.40 e Å^{-3}
$\Delta\rho_{min}$ = −0.45 e Å^{-3}

Data collection: *APEX2* (Bruker, 2006); cell refinement: *SAINT* (Bruker, 2006); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: XU2373).

References

Almanza, C., Arriba, F. A., Cavalcanti, F. L., Gómez, L. A., Miralle, A., Merlos, M., Rafanell, J. G. & Forn, J. (2001). *J. Med. Chem.* **44**, 350–361.
Bruker (2006). *APEX2* (Version 2.1), *SAINT* (Version 7.34A) and *XPREP* (Version 2005/4). Bruker AXS Inc., Madison, Wisconsin, USA.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
George, C. F. P. (2001). *Lancet*, **358**, 1623–1626.
Martins, M. A. P., Cunico, W., Pereira, C. M. P., Sinhorin, A. P., Flores, A. F. C., Bonacorso, H. G. & Zanatta, N. (2004). *Curr. Org. Synth.* **1**, 391–403 and references therein.
Martins, M. A. P., Cunico, W., Scapin, E., Emmerich, D. J., Fiss, G. F., Rosa, F. A., Bonacorso, H. B., Zanatta, N. & Flores, A. F. C. (2006). *Lett. Org. Chem.* **3**, 358–362.
Novinson, T., Robins, R. K. & Matthews, T. R. (1977). *J. Med. Chem.* **20**, 296–299.
Oliveira-Campos, A. M. F., Rodrigues, L. M., Kaja, M., Guilardi, S., Franca, E. de F. & Ellena, J. (2006). *Acta Cryst.* E**62**, o5246–o5248.
Sheldrick, G. M. (1997). *SHELXL97* and *SHELXS97*. University of Göttingen, Germany.
Wen, L.-R., Wang, S.-W., Li, M. & Guo, W.-S. (2005). *Acta Cryst.* E**61**, o1459–o1460.
Wen, L.-R., Wang, S.-W., Xu, H.-Z., Zhang, X.-L., Li, M. & Liu, J.-H. (2004). *Acta Cryst.* E**60**, o1294–o1295.

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2-Methyl-5-(4-tolyl)-7-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidine

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S1. Comment

Pyrazolopyrimidine derivatives are important biologically active compounds obtained to showed anti-inflammatory (PGHS-2 inhibitors) (Almanza *et al.*, 2001) and antifungal activities (cAMP phosphodiasterase and xanthine oxidase inhibitors) (Novinson *et al.*, 1977). In addition, this scaffold have been found to be integral parts of potent nonbenzodiazepine hypnotic agents (George, 2001). Zaleplon is one example of a pyrazolopyrimidine derivative in clinical use (George, 2001). In a continuation of our study about synthesis and reactivity of pyrazolopyrimidine (Martins *et al.*, 2006) as well as trihalomethylated compounds (Martins *et al.*, 2004) we reported, in this communication, the crystal structure of the title compound, 2-methyl-5-(4-tolyl)-7-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidine.

The analysis showed that the pyrazolo[1,5-*a*]pyrimidine ring is essentially planar with maximum deviation from mean plane of 0.014 (1) Å. The 4-tolyl group makes a dihedral angle of 14.1 (1)° with respect to the pyrazolo[1,5-*a*]pyrimidine ring system. In addition, the dihedral angle between the five-membered ring and the fused six-membered ring is 0.84 (1)° in accordance with previous reports (Wen *et al.*, 2004; Wen *et al.*, 2005; Oliveira-Campos *et al.*, 2006). The crystal packing is stabilized mainly by van der Waals forces.

S2. Experimental

To a stirred solution of 1,1,1-trifluoro-4-methoxy-4-(4-tolyl)-but-3-en-2-one (0.244 g, 1.0 mmol) in acetic acid (5 ml) a solution containing the 5-methyl-3-amino-1*H*-pyrazole (0.097 g, 1.0 mmol) in acetic acid (5 ml) was added dropwise. The mixture was stirred under reflux for 16 h. After this time, the resultant solution was extracted with chloroform (3 × 10 ml), washed with distilled water (3 × 10 ml) and dried over magnesium sulfate. Finally, the solvent was removed under reduced pressure and a solid was obtained in good yield (79%). The product was purified by recrystallization from hexane, the slow evaporation of this solution at room temperature furnished the crystal used for the data collection.

S3. Refinement

All H atoms were refined using a riding model, with C—H distances set to 0.93 or 0.96 Å. U_{iso}(H) = xU_{eq}(C), with x = 1.5 for methyl groups and x = 1.2 otherwise.

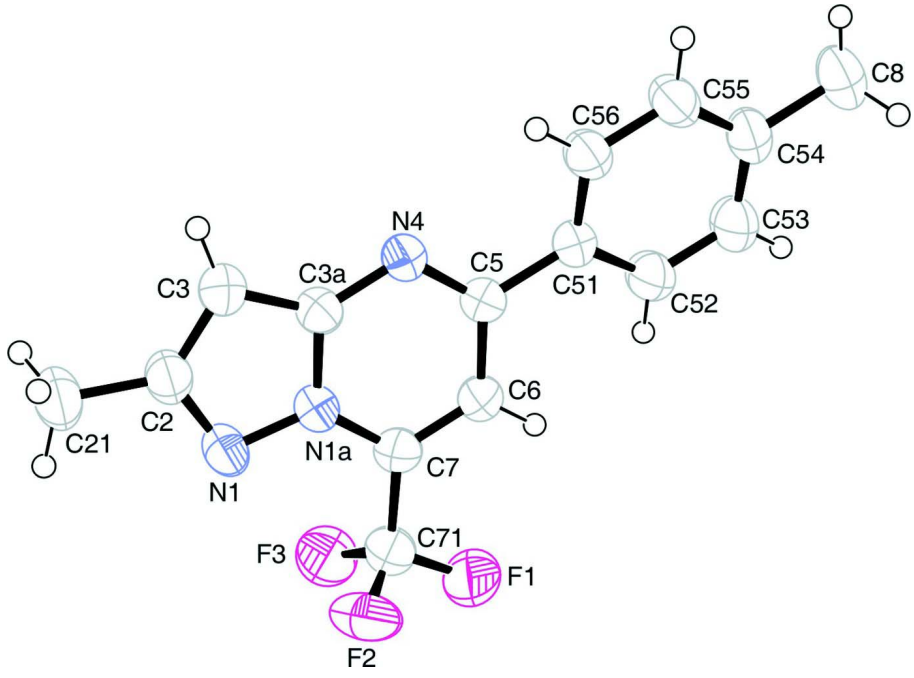

Figure 1

View of the asymmetric unit of the title compound, showing the atom labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary radii.

2-Methyl-5-(4-tolyl)-7-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidine

Crystal data

$C_{15}H_{12}F_3N_3$
$M_r = 291.28$
Triclinic, $P\overline{1}$
Hall symbol: -P 1
$a = 4.8715\ (2)$ Å
$b = 11.2655\ (5)$ Å
$c = 13.5584\ (6)$ Å
$\alpha = 110.225\ (3)°$
$\beta = 96.808\ (3)°$
$\gamma = 99.835\ (3)°$
$V = 675.13\ (5)$ Å^3
$Z = 2$
$F(000) = 300$
$D_x = 1.433$ Mg m^{-3}
Melting point = 415–416 K
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 150 reflections
$\theta = 3.0–24.6°$
$\mu = 0.12$ mm^{-1}
$T = 293$ K
Block, yellow
0.98 × 0.21 × 0.20 mm

Data collection

X8 APEXII diffractometer
Graphite monochromator
φ and ω scans
Absorption correction: multi-scan (*XPREP*; Bruker, 2006)
$T_{min} = 0.874$, $T_{max} = 0.977$
16787 measured reflections
3757 independent reflections
2200 reflections with $I > 2\sigma(I)$
$R_{int} = 0.040$
$\theta_{max} = 29.7°$, $\theta_{min} = 1.6°$
$h = -6\rightarrow6$
$k = -15\rightarrow15$
$l = -18\rightarrow18$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.057$
$wR(F^2) = 0.227$
$S = 1.05$
3757 reflections
190 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1373P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.40$ e Å^{-3}
$\Delta\rho_{min} = -0.45$ e Å^{-3}

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
N4	−0.1395 (3)	0.64063 (13)	0.15766 (10)	0.0437 (4)
C51	0.2301 (3)	0.60519 (16)	0.27094 (13)	0.0434 (4)
C5	0.0595 (3)	0.69036 (16)	0.24463 (12)	0.0427 (4)
N1A	−0.2415 (3)	0.85107 (14)	0.19699 (11)	0.0475 (4)
C3A	−0.2918 (3)	0.71919 (16)	0.13244 (13)	0.0443 (4)
C7	−0.0385 (4)	0.90322 (17)	0.28737 (15)	0.0517 (4)
N1	−0.4126 (3)	0.91420 (15)	0.15720 (13)	0.0560 (4)
C6	0.1130 (4)	0.82475 (17)	0.31325 (14)	0.0501 (4)
H6	0.2514	0.8577	0.3753	0.06*
C56	0.2277 (4)	0.48484 (18)	0.19505 (14)	0.0526 (5)
H56	0.1165	0.4575	0.1271	0.063*
C55	0.3880 (4)	0.40510 (18)	0.21898 (15)	0.0571 (5)
H55	0.381	0.3245	0.1668	0.069*
C52	0.4029 (4)	0.64261 (19)	0.37085 (15)	0.0584 (5)
H52	0.4097	0.723	0.4233	0.07*
C54	0.5592 (4)	0.44182 (19)	0.31862 (15)	0.0539 (5)
C3	−0.5081 (4)	0.69986 (19)	0.04969 (15)	0.0514 (4)
H3	−0.5939	0.622	−0.0068	0.062*
C2	−0.5725 (4)	0.81980 (18)	0.06756 (15)	0.0522 (5)
C53	0.5645 (5)	0.5626 (2)	0.39352 (16)	0.0631 (5)
H53	0.6796	0.5906	0.4608	0.076*
C8	0.7329 (5)	0.3537 (2)	0.34284 (18)	0.0700 (6)
H8A	0.7031	0.2754	0.2807	0.105*
H8B	0.6763	0.3327	0.4014	0.105*
H8C	0.9303	0.3967	0.3619	0.105*

C71	0.0064 (5)	1.0448 (2)	0.3532 (2)	0.0714 (6)
C21	−0.7881 (4)	0.8562 (2)	0.00171 (18)	0.0689 (6)
H21A	−0.7828	0.9471	0.0353	0.103*
H21B	−0.9738	0.8064	−0.0036	0.103*
H21C	−0.7457	0.8385	−0.0686	0.103*
F3	−0.2264 (3)	1.07474 (12)	0.38784 (11)	0.0893 (5)
F1	0.2076 (3)	1.07989 (12)	0.43939 (12)	0.1008 (6)
F2	0.0852 (3)	1.11914 (12)	0.29935 (14)	0.1004 (5)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N4	0.0444 (8)	0.0425 (8)	0.0452 (7)	0.0121 (6)	0.0056 (6)	0.0175 (6)
C51	0.0427 (9)	0.0434 (9)	0.0449 (9)	0.0114 (7)	0.0059 (6)	0.0177 (7)
C5	0.0430 (9)	0.0401 (9)	0.0447 (9)	0.0100 (6)	0.0078 (6)	0.0155 (7)
N1A	0.0449 (8)	0.0430 (8)	0.0557 (8)	0.0131 (6)	0.0048 (6)	0.0197 (7)
C3A	0.0449 (9)	0.0425 (9)	0.0476 (9)	0.0113 (7)	0.0081 (7)	0.0191 (7)
C7	0.0478 (10)	0.0399 (9)	0.0606 (11)	0.0105 (7)	0.0043 (8)	0.0121 (8)
N1	0.0507 (9)	0.0533 (10)	0.0723 (10)	0.0189 (7)	0.0068 (7)	0.0318 (8)
C6	0.0472 (10)	0.0425 (9)	0.0522 (10)	0.0106 (7)	−0.0016 (7)	0.0109 (8)
C56	0.0583 (11)	0.0473 (10)	0.0510 (10)	0.0183 (8)	0.0021 (8)	0.0168 (8)
C55	0.0628 (12)	0.0511 (11)	0.0613 (11)	0.0257 (9)	0.0107 (9)	0.0201 (9)
C52	0.0654 (12)	0.0500 (11)	0.0530 (10)	0.0179 (9)	−0.0029 (9)	0.0133 (8)
C54	0.0471 (10)	0.0617 (12)	0.0653 (11)	0.0200 (8)	0.0125 (8)	0.0346 (9)
C3	0.0495 (10)	0.0514 (10)	0.0526 (9)	0.0108 (7)	0.0018 (7)	0.0213 (8)
C2	0.0453 (9)	0.0570 (11)	0.0617 (11)	0.0134 (8)	0.0080 (8)	0.0310 (9)
C53	0.0654 (12)	0.0637 (13)	0.0580 (11)	0.0204 (9)	−0.0065 (9)	0.0233 (10)
C8	0.0662 (13)	0.0779 (14)	0.0844 (15)	0.0355 (11)	0.0151 (11)	0.0438 (12)
C71	0.0619 (13)	0.0448 (11)	0.0919 (16)	0.0169 (9)	−0.0039 (11)	0.0104 (11)
C21	0.0577 (12)	0.0765 (15)	0.0826 (14)	0.0196 (10)	0.0006 (10)	0.0442 (12)
F3	0.0826 (10)	0.0650 (9)	0.1014 (10)	0.0344 (7)	0.0122 (8)	0.0017 (7)
F1	0.0906 (11)	0.0543 (8)	0.1095 (11)	0.0197 (7)	−0.0302 (9)	−0.0132 (7)
F2	0.0970 (11)	0.0468 (8)	0.1534 (14)	0.0113 (7)	0.0153 (10)	0.0378 (8)

Geometric parameters (Å, º)

N4—C5	1.316 (2)	C52—C53	1.379 (3)
N4—C3A	1.351 (2)	C52—H52	0.93
C51—C56	1.387 (2)	C54—C53	1.382 (3)
C51—C52	1.391 (2)	C54—C8	1.502 (3)
C51—C5	1.475 (2)	C3—C2	1.385 (3)
C5—C6	1.435 (2)	C3—H3	0.93
N1A—C7	1.357 (2)	C2—C21	1.499 (3)
N1A—N1	1.3609 (19)	C53—H53	0.93
N1A—C3A	1.400 (2)	C8—H8A	0.96
C3A—C3	1.375 (2)	C8—H8B	0.96
C7—C6	1.351 (2)	C8—H8C	0.96
C7—C71	1.496 (3)	C71—F1	1.326 (2)

N1—C2	1.347 (2)	C71—F2	1.328 (3)
C6—H6	0.93	C71—F3	1.330 (3)
C56—C55	1.380 (2)	C21—H21A	0.96
C56—H56	0.93	C21—H21B	0.96
C55—C54	1.386 (3)	C21—H21C	0.96
C55—H55	0.93		

C5—N4—C3A	118.71 (14)	C53—C54—C8	121.90 (18)
C56—C51—C52	117.46 (16)	C55—C54—C8	120.90 (18)
C56—C51—C5	120.61 (15)	C3A—C3—C2	106.06 (16)
C52—C51—C5	121.91 (15)	C3A—C3—H3	127
N4—C5—C6	121.31 (15)	C2—C3—H3	127
N4—C5—C51	118.72 (14)	N1—C2—C3	113.05 (16)
C6—C5—C51	119.96 (15)	N1—C2—C21	117.78 (17)
C7—N1A—N1	127.00 (15)	C3—C2—C21	129.17 (17)
C7—N1A—C3A	120.58 (14)	C52—C53—C54	121.53 (17)
N1—N1A—C3A	112.42 (14)	C52—C53—H53	119.2
N4—C3A—C3	133.62 (16)	C54—C53—H53	119.2
N4—C3A—N1A	121.23 (15)	C54—C8—H8A	109.5
C3—C3A—N1A	105.15 (15)	C54—C8—H8B	109.5
C6—C7—N1A	118.36 (16)	H8A—C8—H8B	109.5
C6—C7—C71	123.34 (17)	C54—C8—H8C	109.5
N1A—C7—C71	118.31 (16)	H8A—C8—H8C	109.5
C2—N1—N1A	103.32 (14)	H8B—C8—H8C	109.5
C7—C6—C5	119.78 (16)	F1—C71—F2	107.13 (18)
C7—C6—H6	120.1	F1—C71—F3	106.74 (19)
C5—C6—H6	120.1	F2—C71—F3	107.32 (18)
C55—C56—C51	120.88 (17)	F1—C71—C7	110.86 (17)
C55—C56—H56	119.6	F2—C71—C7	112.3 (2)
C51—C56—H56	119.6	F3—C71—C7	112.17 (18)
C56—C55—C54	121.77 (17)	C2—C21—H21A	109.5
C56—C55—H55	119.1	C2—C21—H21B	109.5
C54—C55—H55	119.1	H21A—C21—H21B	109.5
C53—C52—C51	121.14 (17)	C2—C21—H21C	109.5
C53—C52—H52	119.4	H21A—C21—H21C	109.5
C51—C52—H52	119.4	H21B—C21—H21C	109.5
C53—C54—C55	117.20 (17)		

N4—C51—C5—C56	−14.5 (3)	N4—C51—C5—C52	166.90 (16)