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2-Chloro-4-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidineKevin D. Bunker,^a Curtis Moore,^b Cynthia L. Palmer,^a Arnold L. Rheingold^b and Alex Yanovsky^{a*}

^aPfizer Global Research and Development, La Jolla Labs, 10770 Science Center Drive, San Diego, CA 92121, USA, and ^bDepartment of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093, USA
Correspondence e-mail: alex.yanovsky@pfizer.com

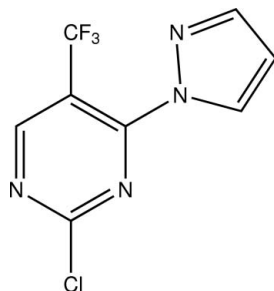
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Key indicators: single-crystal X-ray study; $T = 100$ K; mean $\sigma(\text{C}-\text{C}) = 0.004$ Å; R factor = 0.033; wR factor = 0.082; data-to-parameter ratio = 9.7.

The reaction of 2,4-dichloro-5-(trifluoromethyl)pyrimidine with 1*H*-pyrazole gave two structural isomers in a 1:1 ratio that were separable by chromatography. The title compound, $\text{C}_8\text{H}_4\text{ClF}_3\text{N}_4$, was the first product to elute and was characterized in the present study to confirm that substitution by the pyrazolyl group had occurred at position 4. The molecule (with the exception of the F atoms) is essentially planar, with a mean deviation of 0.034 Å from the least-squares plane through all non-H and non-F atoms. The bond angles in the pyrimidine ring show a pronounced alternating pattern with three angles, including those at the two N atoms being narrower, and the remaining three wider than 120°.

Related literature

For the structures of similar pyrazolylpyrimidine derivatives, see: Peresypkina *et al.* (2005); Liu *et al.* (2005); Brunet *et al.* (2007). For statistics on endocyclic angular distortions in triazine derivatives similar to those observed in the title compound, see: Allington *et al.* (2001).



Experimental

Crystal data

$\text{C}_8\text{H}_4\text{ClF}_3\text{N}_4$
 $M_r = 248.60$
 Orthorhombic, $P2_12_12_1$
 $a = 5.5776$ (3) Å
 $b = 7.7117$ (4) Å
 $c = 21.8335$ (12) Å
 $V = 939.12$ (9) Å³
 $Z = 4$
 Cu $K\alpha$ radiation
 $\mu = 3.90$ mm⁻¹
 $T = 100$ K
 $0.40 \times 0.21 \times 0.10$ mm

Data collection

Bruker APEXII CCD diffractometer
 Absorption correction: multi-scan (SADABS; Bruker, 2001)
 $T_{\min} = 0.305$, $T_{\max} = 0.697$
 3416 measured reflections
 1402 independent reflections
 1273 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.030$
 $\theta_{\text{max}} = 61.9^\circ$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.033$
 $wR(F^2) = 0.082$
 $S = 1.02$
 1402 reflections
 145 parameters
 H-atom parameters constrained
 $\Delta\rho_{\text{max}} = 0.21$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.22$ e Å⁻³
 Absolute structure: Flack (1983), 503 Friedel pairs
 Flack parameter: 0.05 (2)

Data collection: APEX2 (Bruker, 2007); cell refinement: SAINT (Bruker, 2007); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: SHELXTL (Sheldrick, 2008); software used to prepare material for publication: SHELXTL.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: EZZ213).

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2-Chloro-4-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine

Kevin D. Bunker, Curtis Moore, Cynthia L. Palmer, Arnold L. Rheingold and Alex Yanovsky

S1. Comment

The reaction of 2,4-dichloro-5-(trifluoromethyl)pyrimidine with 1*H*-pyrazole gave two structural isomers in a 1:1 ratio that were separable by chromatography. The title compound was the first product to elute and was characterized in the present study to confirm substitution by N-pyrazolyl group to have occurred at position 4 (Fig. 1).

The molecule (with the exception of the F atoms) is essentially planar: the maximum displacement of the N1 atom from the plane, drawn through all non-F and non-H atoms, is equal to 0.076 (4) Å. Other pyrazolylpyrimidine derivatives were also shown to have planar molecules (Peresypkina *et al.*, 2005; Liu *et al.*, 2005; Brunet *et al.*, 2007).

The geometry of the pyrimidine ring is characterized by alternating of bond angle distortions: angles at the N3, N4 and C5 atoms [112.8 (3); 116.1 (3); 115.4 (3)°] are all narrower, whereas the remaining angles in the ring at the C4, C6 and C7 atoms [121.2 (3); 124.7 (3); 129.7 (3)°] are wider than 120°. Such angular distortions were also observed in other pyrimidine structures (see, for instance, the above quoted papers). The study by Allington *et al.* (2001) contains analysis of some statistics on similar angular distortions in the triazine derivatives.

The dramatic difference between the exocyclic bond angles C4—C5—C8 127.1 (3)° and C6—C5—C8 117.5 (3)° can be attributed to the repulsion of the CF₃-group from pyrazolyl substituent (the F1⋯N1 and F2⋯N1 distances are 2.720 (3) Å and 2.774 (3) Å respectively).

S2. Experimental

2-Chloro-4-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine and 4-chloro-2-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine. To a *N,N*-dimethylacetamide (46.0 ml) solution of pyrazole (726 mg, 10.7 mmol) and potassium carbonate (3.84 g, 27.8 mmol) was added 2,4-dichloro-5-trifluoromethyl-pyrimidine (2.01 g, 1.250 ml, 9.27 mmol) by syringe in one shot at rt. The mixture was stirred overnight and monitored by TLC (20% EtOAc/heptane). After consumption of starting material, the reaction mixture was diluted with water and extracted with EtOAc (3×). The organic layers were combined, dried, and concentrated. The crude residue was subjected to flash chromatography (silica gel, 0-40% EtOAc/heptane), and three major bands eluted. The first major band was isolated to give 460 mg (20%) of 2-chloro-4-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine. The second band was also collected to give 460 mg (20%) of 4-chloro-2-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine. The third band was found to be 2,4-di(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine and was not isolated. X-ray quality crystals of the first product to elute were grown in DCM/heptane upon slow evaporation.

2-chloro-4-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine: ¹H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 6.56 (dd, J=2.77, 1.51 Hz, 1 H) 7.89 (d, J=0.76 Hz, 1 H) 8.59 (dd, J=2.77, 0.76 Hz, 1 H) 8.96 (s, 1 H). ¹³C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 109.96 (s, 1 C) 111.39 - 112.97 (m, 1 C) 117.69 - 126.63 (m, 1 C) 130.42 (s, 1 C) 145.57 (s, 1 C) 155.57 (s, 1 C) 160.86 (q, J=7.09 Hz, 1 C) 163.04 (s, 1 C).

4-chloro-2-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine: ^1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 6.57 (dd, $J=2.77, 1.51$ Hz, 1 H) 7.90 (d, $J=1.01$ Hz, 1 H) 8.59 (dd, $J=2.77, 0.50$ Hz, 1 H) 8.92 (s, 1 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 110.22 (s, 1 C) 121.68 (q, $J=272.65$ Hz, 1 C) 120.34 (q, $J=33.99$ Hz, 1 C) 130.23 (s, 1 C) 145.59 (s, 1 C) 156.64 (s, 1 C) 158.07 (q, $J=5.14$ Hz, 1 C) 161.02 (s, 1 C).

S3. Refinement

All H atoms were placed in geometrically calculated positions (C—H 0.93 Å) and included in the refinement in riding motion approximation. The $U_{\text{iso}}(\text{H})$ were set to $1.2U_{\text{eq}}$ of the carrying atom.

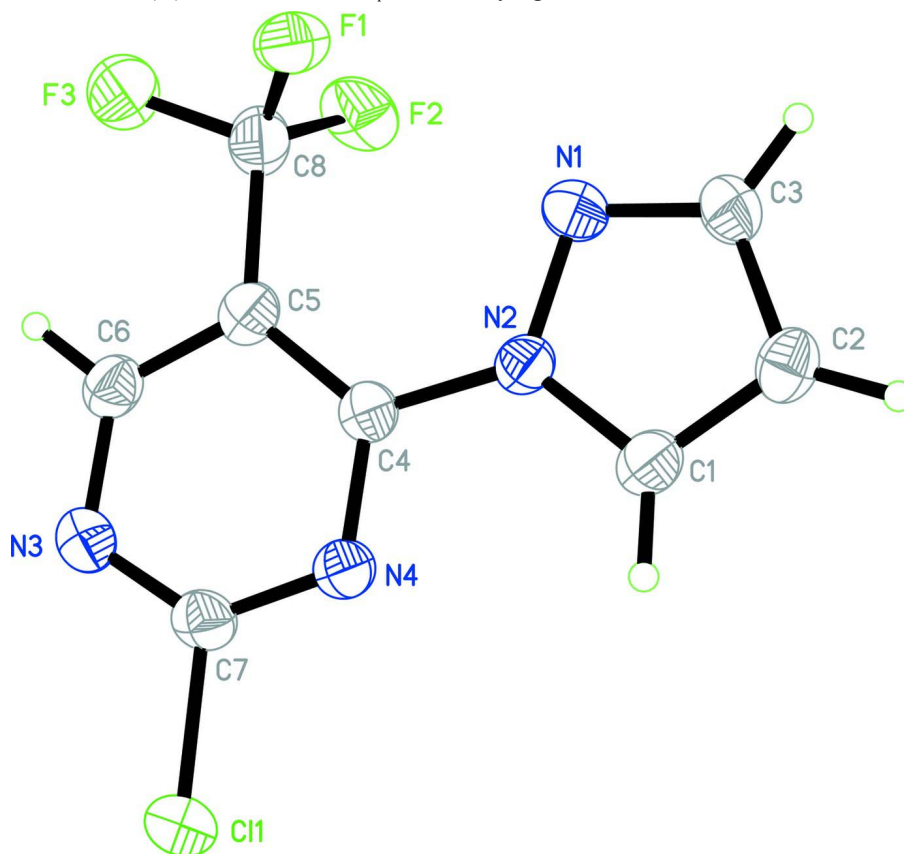


Figure 1

Molecular structure of the title compound, showing 50% probability displacement ellipsoids and atom numbering scheme. H atoms are drawn as circles with arbitrary small radius.

2-Chloro-4-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)pyrimidine

Crystal data

$\text{C}_8\text{H}_4\text{ClF}_3\text{N}_4$

$M_r = 248.60$

Orthorhombic, $P2_12_12_1$

Hall symbol: P 2ac 2ab

$a = 5.5776$ (3) Å

$b = 7.7117$ (4) Å

$c = 21.8335$ (12) Å

$V = 939.12$ (9) Å³

$Z = 4$

$F(000) = 496$

$D_x = 1.758$ Mg m⁻³

Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å

Cell parameters from 2204 reflections

$\theta = 4.1\text{--}61.5^\circ$

$\mu = 3.90$ mm⁻¹

$T = 100$ K

Rod, colourless

$0.40 \times 0.21 \times 0.10$ mm

Data collection

Bruker APEXII CCD diffractometer	3416 measured reflections
Radiation source: fine-focus sealed tube	1402 independent reflections
Graphite monochromator	1273 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{\text{int}} = 0.030$
Absorption correction: multi-scan (SADABS; Bruker, 2001)	$\theta_{\text{max}} = 61.9^\circ$, $\theta_{\text{min}} = 4.0^\circ$
$T_{\text{min}} = 0.305$, $T_{\text{max}} = 0.697$	$h = -6 \rightarrow 6$
	$k = -8 \rightarrow 8$
	$l = -25 \rightarrow 24$

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.033$	$w = 1/[\sigma^2(F_o^2) + (0.048P)^2]$
$wR(F^2) = 0.082$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.02$	$(\Delta/\sigma)_{\text{max}} = 0.001$
1402 reflections	$\Delta\rho_{\text{max}} = 0.21 \text{ e } \text{\AA}^{-3}$
145 parameters	$\Delta\rho_{\text{min}} = -0.22 \text{ e } \text{\AA}^{-3}$
0 restraints	Absolute structure: Flack (1983), 503 Friedel pairs
Primary atom site location: structure-invariant direct methods	Absolute structure parameter: 0.05 (2)
Secondary atom site location: difference Fourier map	

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds 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 (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
Cl1	0.18059 (15)	0.39628 (9)	0.50346 (4)	0.0390 (2)
F1	0.7206 (4)	1.0219 (2)	0.35103 (8)	0.0430 (5)
F2	0.4712 (4)	0.9283 (2)	0.28305 (8)	0.0450 (5)
F3	0.3535 (5)	1.0974 (2)	0.35501 (11)	0.0629 (7)
N1	0.8456 (5)	0.7028 (3)	0.30856 (11)	0.0326 (6)
N2	0.7484 (5)	0.5994 (3)	0.35248 (10)	0.0262 (5)
N3	0.1542 (5)	0.7067 (3)	0.45907 (11)	0.0308 (6)
N4	0.4754 (5)	0.5271 (3)	0.42520 (10)	0.0272 (6)
C1	0.8693 (6)	0.4455 (4)	0.35742 (13)	0.0312 (7)
H1A	0.8338	0.3531	0.3848	0.037*
C2	1.0494 (6)	0.4503 (4)	0.31581 (13)	0.0312 (7)
H2A	1.1661	0.3635	0.3079	0.037*
C3	1.0253 (6)	0.6127 (4)	0.28693 (13)	0.0332 (7)
H3A	1.1282	0.6524	0.2552	0.040*
C4	0.5510 (6)	0.6502 (3)	0.38708 (12)	0.0250 (6)

C5	0.4336 (6)	0.8113 (4)	0.38345 (13)	0.0283 (6)
C6	0.2380 (6)	0.8301 (3)	0.42115 (13)	0.0304 (7)
H6A	0.1561	0.9381	0.4204	0.037*
C7	0.2831 (6)	0.5640 (3)	0.45766 (12)	0.0296 (7)
C8	0.4981 (7)	0.9624 (4)	0.34258 (14)	0.0378 (8)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C11	0.0460 (5)	0.0364 (3)	0.0347 (4)	−0.0015 (3)	0.0081 (4)	0.0070 (3)
F1	0.0604 (15)	0.0304 (8)	0.0382 (10)	−0.0103 (9)	0.0101 (10)	−0.0007 (7)
F2	0.0489 (13)	0.0564 (12)	0.0298 (10)	0.0079 (10)	−0.0012 (8)	0.0164 (8)
F3	0.0824 (18)	0.0377 (10)	0.0685 (14)	0.0283 (12)	0.0320 (13)	0.0215 (10)
N1	0.0390 (16)	0.0315 (12)	0.0272 (14)	0.0008 (12)	0.0052 (12)	0.0051 (10)
N2	0.0341 (15)	0.0238 (10)	0.0208 (11)	0.0022 (11)	−0.0010 (10)	0.0006 (9)
N3	0.0295 (15)	0.0341 (13)	0.0288 (14)	0.0000 (12)	0.0027 (11)	−0.0013 (10)
N4	0.0355 (16)	0.0256 (10)	0.0205 (12)	−0.0014 (11)	−0.0022 (11)	−0.0010 (9)
C1	0.043 (2)	0.0259 (14)	0.0242 (14)	0.0034 (13)	−0.0011 (14)	−0.0004 (11)
C2	0.0343 (19)	0.0304 (14)	0.0288 (16)	0.0047 (12)	−0.0038 (14)	−0.0053 (12)
C3	0.038 (2)	0.0353 (15)	0.0262 (15)	0.0021 (15)	0.0067 (13)	−0.0006 (13)
C4	0.0296 (16)	0.0269 (13)	0.0185 (13)	−0.0009 (11)	−0.0032 (13)	−0.0021 (11)
C5	0.0361 (18)	0.0272 (14)	0.0215 (14)	0.0029 (12)	−0.0055 (14)	−0.0006 (12)
C6	0.0332 (18)	0.0269 (13)	0.0312 (15)	0.0043 (12)	−0.0014 (14)	−0.0001 (11)
C7	0.038 (2)	0.0311 (15)	0.0198 (13)	−0.0031 (13)	−0.0031 (13)	0.0008 (11)
C8	0.050 (2)	0.0337 (15)	0.0300 (17)	0.0120 (15)	0.0064 (15)	0.0052 (13)

Geometric parameters (Å, °)

C11—C7	1.732 (3)	N4—C4	1.331 (4)
F1—C8	1.336 (4)	C1—C2	1.355 (5)
F2—C8	1.334 (4)	C1—H1A	0.9500
F3—C8	1.345 (4)	C2—C3	1.408 (4)
N1—C3	1.308 (4)	C2—H2A	0.9500
N1—N2	1.360 (3)	C3—H3A	0.9500
N2—C1	1.369 (4)	C4—C5	1.406 (4)
N2—C4	1.392 (4)	C5—C6	1.374 (5)
N3—C7	1.315 (4)	C5—C8	1.511 (4)
N3—C6	1.345 (4)	C6—H6A	0.9500
N4—C7	1.316 (4)		
C3—N1—N2	104.4 (2)	N2—C4—C5	125.9 (3)
N1—N2—C1	111.6 (3)	C6—C5—C4	115.4 (3)
N1—N2—C4	122.2 (2)	C6—C5—C8	117.5 (3)
C1—N2—C4	126.2 (2)	C4—C5—C8	127.1 (3)
C7—N3—C6	112.8 (3)	N3—C6—C5	124.7 (3)
C7—N4—C4	116.1 (3)	N3—C6—H6A	117.6
C2—C1—N2	106.8 (3)	C5—C6—H6A	117.6
C2—C1—H1A	126.6	N3—C7—N4	129.7 (3)

N2—C1—H1A	126.6	N3—C7—C11	115.5 (2)
C1—C2—C3	104.7 (3)	N4—C7—C11	114.7 (2)
C1—C2—H2A	127.6	F2—C8—F1	107.9 (3)
C3—C2—H2A	127.6	F2—C8—F3	106.4 (3)
N1—C3—C2	112.6 (3)	F1—C8—F3	105.3 (3)
N1—C3—H3A	123.7	F2—C8—C5	113.4 (3)
C2—C3—H3A	123.7	F1—C8—C5	113.9 (3)
N4—C4—N2	112.9 (2)	F3—C8—C5	109.6 (3)
N4—C4—C5	121.2 (3)		
