Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2-Methyl-6-(trifluoromethyl)imidazo-[1,2-*a*]pyridine-3-carbonitrile

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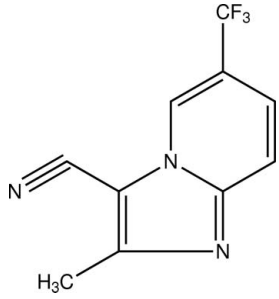
Received 16 December 2010; accepted 31 January 2011

Key indicators: single-crystal X-ray study; T = 297 K; mean σ(C–C) = 0.002 Å; disorder in main residue; R factor = 0.049; wR factor = 0.130; data-to-parameter ratio = 16.0.

In the title compound, $C_{10}H_6F_3N_3$, the imidazo[1,2-*a*]pyridine group is essentially planar with a maximum deviation of 0.021 (1) Å. The F atoms in the trifluoromethyl group and the methyl H atoms are each disordered over two sets of sites with refined site occupancies of 0.68 (1):0.32 (1). In the crystal, molecules are linked into infinite chains through two C—H···N interactions forming $R_2^2(12)$ and $R_2^2(8)$ hydrogen-bond ring motifs. These chains are stacked along the *a* axis.

Related literature

For the biological activity of imidazole derivatives, see: Biftu *et al.* (2006); Elhakmoui *et al.* (1994); Fisher & Lusi (1972); Gudmundsson & Johns (2003, 2007); Kaminski *et al.* (1989); Rewankar *et al.* (1975); Rupert *et al.* (2003). For graph-set descriptions of hydrogen-bond ring motifs, see: Bernstein *et al.* (1995).



Experimental

Crystal data

$C_{10}H_6F_3N_3$
M_r = 225.18
Monoclinic, $P2_1/c$
a = 5.6871 (3) Å
b = 8.5437 (5) Å
c = 20.5403 (13) Å
β = 96.653 (4)°
V = 991.31 (10) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.13 mm^{-1}
T = 297 K
0.43 × 0.22 × 0.07 mm

Data collection

Bruker APEXII DUO CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2009)
T_{min} = 0.945, T_{max} = 0.991
10175 measured reflections
2820 independent reflections
1720 reflections with $I > 2\sigma(I)$
R_{int} = 0.029

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.130
S = 1.03
2820 reflections
176 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.13 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
C1—H1A···N3^{i}	0.93	2.45	3.384 (2)	176
C4—H4A···N2^{ii}	0.93	2.53	3.428 (2)	163

Symmetry codes: (i) $-x, -y+1, -z+1$; (ii) $-x+2, -y, -z+1$.

Data collection: *APEX2* (Bruker, 2009); cell refinement: *SAINT* (Bruker, 2009); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2009).

HKF and MMR thank USM for the Research University Grant (No. 1001/PFIZIK/ 811160).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: FL2329).

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‡ Thomson Reuters ResearcherID: A-3561-2009.

supporting information

Acta Cryst. (2011). E**67**, o573 [doi:10.1107/S1600536811003928]

2-Methyl-6-(trifluoromethyl)imidazo[1,2-*a*]pyridine-3-carbonitrile

Hoong-Kun Fun, Mohd Mustaqim Rosli, D. J. Madhu Kumar, D. Jagadeesh Prasad and G. K. Nagaraja

S1. Comment

The imidazole nucleus is a widely used pharmacophore in medicinal compounds due to its broad spectrum of biological activities. Moreover imidazole derivatives are isosteres of naturally-occurring nucleotides which allow them to interact easily with the biopolymers of the living systems. It has been known that imidazo[1,2-a]pyridine derivatives exhibit diverse biological activities (Gudmundsson & Johns, 2003) and were used as antiviral (Elhakmoui *et al.*, 1994), antiulcer (Kaminski *et al.*, 1989), antibacterial (Rewankar *et al.*, 1975), antifungal (Fisher & Lusi, 1972), antiprotozoal (Biftu *et al.*, 2006), antiherpes (Gudmundsson & Johns, 2007) and anti-inflammatory (Rupert *et al.*, 2003) compounds.

All bond lengths and angles in the compound are within normal range. The imidazo[1,2-a] pyridine group is planar with maximum deviation of -0.021 (1)Å for atom N1 (Fig. 1). The F atoms in the trifluoromethyl group and the methyl H atoms are disordered over two positions with refined site occupancies of 0.68 (1):0.32 (1).

In the crystal structure, the molecules form infinite chains through C1—H1A···N3^{i} and C4—H4A···N2^{ii} (Table 1) interactions. These interactions also form $R^2_2(12)$ and $R^2_2(8)$ hydrogen ring motifs, respectively (Bernstein *et al.*, 1995). The chains are stacked along the *a*-axis (Fig. 2).

S2. Experimental

A mixture of 5-(trifluoromethyl) pyridin-2-amine (0.01mol) and dimethylacetamide dimethyl acetal (0.03mol) was refluxed for 24 hr at 900 C. The resultant product was recrystallized from ethanol. The product so obtained (0.01mol) was refluxed with bromoacetonitrile (0.01mol) in toluene at 600 C. The product was then removed by evaporation of toluene under reduced pressure and it was isolated by column chromatography using ethyl acetate as an eluent. It was then recrystallized by slow evaporation from ethanol to give crystals suitable for x-ray analysis.

S3. Refinement

H atoms were placed in calculated positions [C–H = 0.93–0.96 Å] and refined as riding with U_{iso}(H) = 1.2$_{eq}$(C) or 1.5U_{eq}(methyl C). A rotating group model was used for the methyl group. The F atoms in trifluoromethyl group and the H atoms in methyl group are disordered over two position with refined site occupancies of 0.68 (1):0.32 (1).

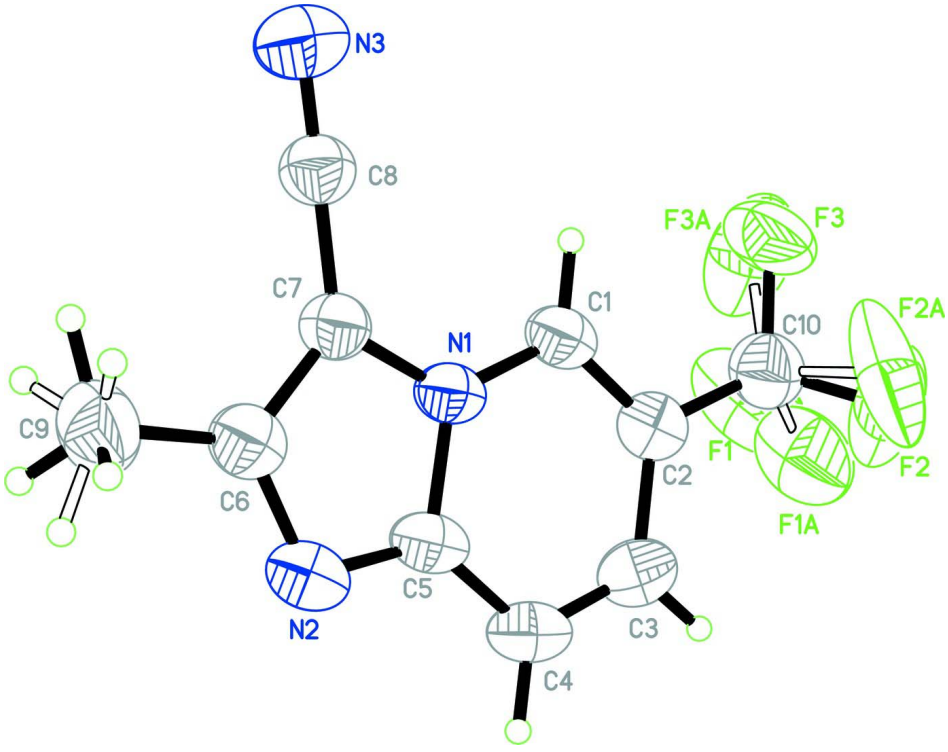

Figure 1

The molecular structure of (I), showing 30% probability displacement ellipsoids and the atom-numbering scheme. Open bonds show minor components.

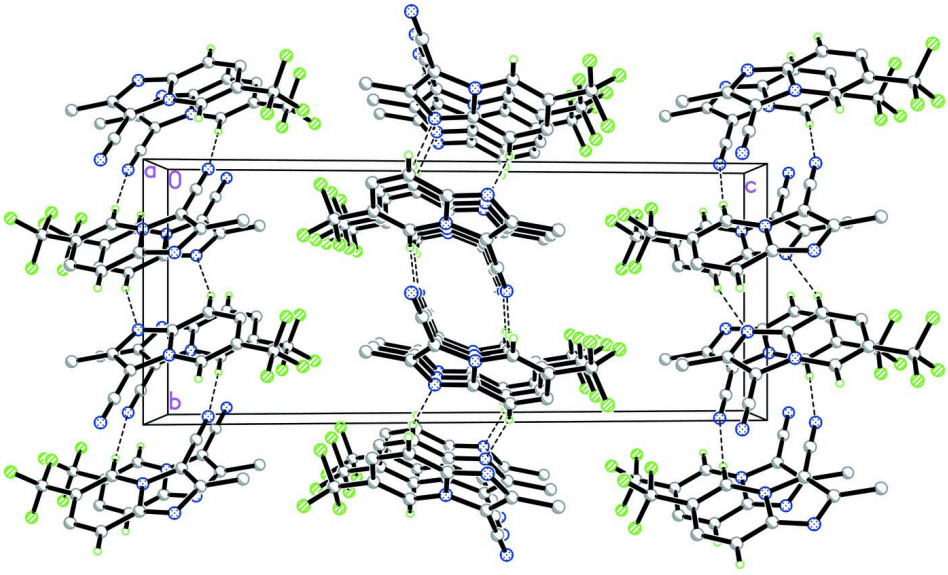

Figure 2

The crystal packing of (I) viewed along the a axis showing molecular chains stacked down the a-axis. Dashed lines indicate hydrogen bonds. H atoms not involved in the hydrogen bond interactions have been omitted for clarity. Only major components are shown.

2-Methyl-6-(trifluoromethyl)imidazo[1,2-*a*]pyridine-3-carbonitrile

Crystal data

$C_{10}H_6F_3N_3$
$M_r = 225.18$
Monoclinic, $P2_1/c$
Hall symbol: -P 2ybc
$a = 5.6871\ (3)$ Å
$b = 8.5437\ (5)$ Å
$c = 20.5403\ (13)$ Å
$\beta = 96.653\ (4)°$
$V = 991.31\ (10)$ Å^3
$Z = 4$
$F(000) = 456$
$D_x = 1.509$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2837 reflections
$\theta = 2.6–25.3°$
$\mu = 0.13$ mm^{-1}
$T = 297$ K
Plate, colourless
0.43 × 0.22 × 0.07 mm

Data collection

Bruker APEXII DUO CCD area-detector diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2009)
$T_{min} = 0.945$, $T_{max} = 0.991$
10175 measured reflections
2820 independent reflections
1720 reflections with $I > 2\sigma(I)$
$R_{int} = 0.029$
$\theta_{max} = 29.8°$, $\theta_{min} = 2.6°$
$h = -7\rightarrow7$
$k = -11\rightarrow11$
$l = -28\rightarrow28$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.049$
$wR(F^2) = 0.130$
$S = 1.03$
2820 reflections
176 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
$w = 1/[\sigma^2(F_o^2) + (0.0575P)^2 + 0.0655P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.13$ e Å^{-3}
$\Delta\rho_{min} = -0.22$ e Å^{-3}

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 $F^2 > 2$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}	Occ. (<1)
C10	0.2247 (4)	0.2282 (2)	0.30231 (9)	0.0633 (5)	
F1	0.1174 (15)	0.0950 (4)	0.2794 (3)	0.1138 (18)	0.675 (13)
F2	0.3304 (7)	0.2905 (11)	0.2575 (3)	0.134 (2)	0.675 (13)
F3	0.0427 (9)	0.3205 (5)	0.3079 (2)	0.0858 (13)	0.675 (13)

F1A	0.246 (3)	0.1157 (11)	0.2609 (4)	0.097 (3)	0.325 (13)
F2A	0.329 (2)	0.3390 (12)	0.2678 (6)	0.131 (4)	0.325 (13)
F3A	0.0178 (17)	0.271 (2)	0.3077 (6)	0.141 (5)	0.325 (13)
N1	0.46963 (19)	0.24647 (12)	0.47742 (6)	0.0410 (3)	
N2	0.7873 (2)	0.15187 (14)	0.54049 (6)	0.0528 (3)	
N3	0.1553 (2)	0.49667 (17)	0.57317 (7)	0.0660 (4)	
C1	0.3230 (3)	0.27046 (16)	0.42094 (8)	0.0447 (4)	
H1A	0.1888	0.3328	0.4206	0.054*	
C2	0.3776 (3)	0.20129 (17)	0.36531 (7)	0.0478 (4)	
C3	0.5809 (3)	0.10468 (18)	0.36599 (8)	0.0541 (4)	
H3A	0.6161	0.0581	0.3274	0.065*	
C4	0.7237 (3)	0.07997 (17)	0.42235 (8)	0.0530 (4)	
H4A	0.8554	0.0153	0.4228	0.064*	
C5	0.6712 (2)	0.15294 (16)	0.48021 (8)	0.0455 (4)	
C6	0.6634 (3)	0.24616 (17)	0.57735 (8)	0.0486 (4)	
C7	0.4662 (2)	0.30593 (16)	0.54019 (7)	0.0432 (3)	
C8	0.2918 (3)	0.40991 (17)	0.55779 (7)	0.0468 (4)	
C9	0.7402 (3)	0.2770 (2)	0.64782 (8)	0.0654 (5)	
H9A	0.7533	0.1797	0.6713	0.098*	0.675 (13)
H9B	0.6256	0.3425	0.6654	0.098*	0.675 (13)
H9C	0.8910	0.3287	0.6523	0.098*	0.675 (13)
H9D	0.8904	0.2278	0.6603	0.098*	0.325 (13)
H9E	0.6250	0.2353	0.6738	0.098*	0.325 (13)
H9F	0.7547	0.3878	0.6549	0.098*	0.325 (13)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C10	0.0701 (12)	0.0666 (11)	0.0522 (10)	0.0091 (10)	0.0024 (9)	−0.0014 (8)
F1	0.131 (3)	0.0749 (15)	0.117 (3)	0.001 (2)	−0.065 (3)	−0.0194 (17)
F2	0.085 (2)	0.255 (7)	0.0643 (18)	0.003 (3)	0.0218 (15)	0.049 (3)
F3	0.093 (3)	0.095 (2)	0.0627 (18)	0.0467 (16)	−0.0183 (18)	−0.0041 (12)
F1A	0.116 (6)	0.093 (4)	0.071 (3)	0.011 (4)	−0.032 (4)	−0.018 (3)
F2A	0.213 (10)	0.090 (5)	0.082 (5)	−0.027 (4)	−0.018 (5)	0.050 (3)
F3A	0.039 (3)	0.302 (15)	0.081 (5)	0.003 (6)	0.002 (3)	0.042 (8)
N1	0.0356 (6)	0.0390 (6)	0.0485 (7)	0.0048 (5)	0.0053 (5)	0.0016 (5)
N2	0.0445 (7)	0.0524 (7)	0.0604 (8)	0.0094 (6)	0.0009 (6)	0.0029 (6)
N3	0.0590 (8)	0.0662 (9)	0.0748 (10)	0.0127 (7)	0.0158 (7)	−0.0053 (7)
C1	0.0389 (7)	0.0421 (7)	0.0524 (9)	0.0057 (6)	0.0024 (7)	0.0051 (6)
C2	0.0468 (8)	0.0463 (8)	0.0498 (9)	0.0012 (6)	0.0043 (7)	0.0004 (6)
C3	0.0525 (9)	0.0530 (9)	0.0580 (10)	0.0038 (7)	0.0117 (8)	−0.0084 (7)
C4	0.0432 (8)	0.0486 (8)	0.0680 (10)	0.0103 (7)	0.0096 (8)	−0.0042 (7)
C5	0.0371 (7)	0.0400 (7)	0.0593 (9)	0.0067 (6)	0.0046 (7)	0.0022 (6)
C6	0.0451 (8)	0.0471 (8)	0.0532 (9)	0.0008 (6)	0.0045 (7)	0.0036 (6)
C7	0.0403 (7)	0.0434 (7)	0.0462 (8)	0.0040 (6)	0.0064 (6)	0.0027 (6)
C8	0.0435 (8)	0.0466 (8)	0.0509 (8)	0.0023 (6)	0.0078 (7)	0.0010 (6)
C9	0.0651 (11)	0.0746 (12)	0.0540 (10)	0.0025 (9)	−0.0037 (9)	0.0045 (8)

Geometric parameters (Å, º)

C10—F3A	1.249 (10)	C2—C3	1.420 (2)
C10—F2	1.273 (4)	C3—C4	1.351 (2)
C10—F1A	1.298 (7)	C3—H3A	0.9300
C10—F3	1.316 (4)	C4—C5	1.405 (2)
C10—F1	1.350 (5)	C4—H4A	0.9300
C10—F2A	1.359 (9)	C6—C7	1.379 (2)
C10—C2	1.491 (2)	C6—C9	1.486 (2)
N1—C1	1.3635 (19)	C7—C8	1.4095 (19)
N1—C7	1.3880 (18)	C9—H9A	0.9600
N1—C5	1.3931 (17)	C9—H9B	0.9600
N2—C5	1.3340 (19)	C9—H9C	0.9600
N2—C6	1.3571 (19)	C9—H9D	0.9600
N3—C8	1.1442 (17)	C9—H9E	0.9600
C1—C2	1.354 (2)	C9—H9F	0.9600
C1—H1A	0.9300		
F3A—C10—F1A	115.7 (7)	C2—C3—H3A	119.8
F2—C10—F3	104.8 (4)	C3—C4—C5	119.33 (13)
F2—C10—F1	109.4 (4)	C3—C4—H4A	120.3
F3—C10—F1	102.0 (4)	C5—C4—H4A	120.3
F3A—C10—F2A	108.3 (9)	N2—C5—N1	111.00 (12)
F1A—C10—F2A	95.5 (7)	N2—C5—C4	130.66 (13)
F3A—C10—C2	115.4 (6)	N1—C5—C4	118.32 (14)
F2—C10—C2	114.5 (3)	N2—C6—C7	110.63 (14)
F1A—C10—C2	111.4 (4)	N2—C6—C9	122.40 (14)
F3—C10—C2	113.7 (3)	C7—C6—C9	126.97 (14)
F1—C10—C2	111.5 (2)	C6—C7—N1	106.29 (12)
F2A—C10—C2	108.4 (5)	C6—C7—C8	129.98 (14)
C1—N1—C7	131.48 (12)	N1—C7—C8	123.71 (13)
C1—N1—C5	122.71 (12)	N3—C8—C7	178.02 (17)
C7—N1—C5	105.77 (12)	C6—C9—H9A	109.5
C5—N2—C6	106.31 (12)	C6—C9—H9B	109.5
C2—C1—N1	118.37 (13)	C6—C9—H9C	109.5
C2—C1—H1A	120.8	C6—C9—H9D	109.5
N1—C1—H1A	120.8	C6—C9—H9E	109.5
C1—C2—C3	120.76 (15)	H9D—C9—H9E	109.5
C1—C2—C10	119.84 (14)	C6—C9—H9F	109.5
C3—C2—C10	119.40 (14)	H9D—C9—H9F	109.5
C4—C3—C2	120.49 (14)	H9E—C9—H9F	109.5
C4—C3—H3A	119.8		
C7—N1—C1—C2	176.78 (13)	C6—N2—C5—N1	−0.64 (16)
C5—N1—C1—C2	−0.6 (2)	C6—N2—C5—C4	177.88 (15)
N1—C1—C2—C3	0.7 (2)	C1—N1—C5—N2	178.33 (12)
N1—C1—C2—C10	−178.43 (14)	C7—N1—C5—N2	0.40 (16)
F3A—C10—C2—C1	−22.2 (11)	C1—N1—C5—C4	−0.4 (2)

F2—C10—C2—C1	120.0 (5)	C7—N1—C5—C4	−178.32 (13)
F1A—C10—C2—C1	−156.7 (8)	C3—C4—C5—N2	−177.24 (15)
F3—C10—C2—C1	−0.4 (4)	C3—C4—C5—N1	1.2 (2)
F1—C10—C2—C1	−115.0 (5)	C5—N2—C6—C7	0.64 (17)
F2A—C10—C2—C1	99.5 (6)	C5—N2—C6—C9	−178.97 (14)
F3A—C10—C2—C3	158.6 (11)	N2—C6—C7—N1	−0.40 (16)
F2—C10—C2—C3	−59.1 (5)	C9—C6—C7—N1	179.19 (14)
F1A—C10—C2—C3	24.1 (8)	N2—C6—C7—C8	−178.74 (14)
F3—C10—C2—C3	−179.6 (3)	C9—C6—C7—C8	0.8 (3)
F1—C10—C2—C3	65.8 (5)	C1—N1—C7—C6	−177.68 (14)
F2A—C10—C2—C3	−79.7 (6)	C5—N1—C7—C6	0.00 (15)
C1—C2—C3—C4	0.1 (2)	C1—N1—C7—C8	0.8 (2)
C10—C2—C3—C4	179.24 (15)	C5—N1—C7—C8	178.48 (13)
C2—C3—C4—C5	−1.0 (2)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C1—H1*A*···N3^{i}	0.93	2.45	3.384 (2)	176
C4—H4*A*···N2^{ii}	0.93	2.53	3.428 (2)	163

Symmetry codes: (i) −*x*, −*y*+1, −*z*+1; (ii) −*x*+2, −*y*, −*z*+1.