

N-(2,3,5,6-Tetrafluoropyridin-4-yl)formamide

Bailey D. Newell,^a Colin D. McMillen^b and John P. Lee^{a*}

^aThe University of Tennessee at Chattanooga, Department of Chemistry and Physics, #2252, 615 McCallie Avenue, Chattanooga, TN 37403, USA, and ^bClemson University, Department of Chemistry, Clemson, SC 29634, USA.

*Correspondence e-mail: John-Lee@utc.edu

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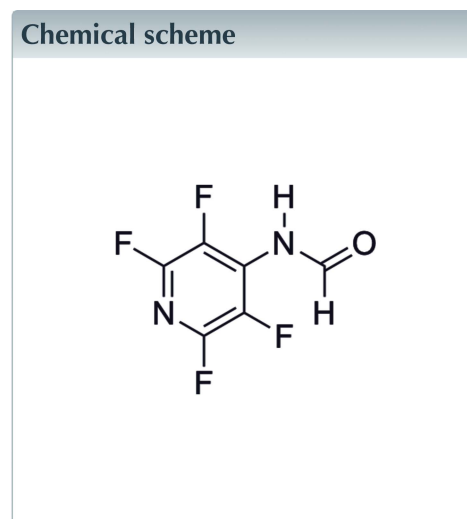
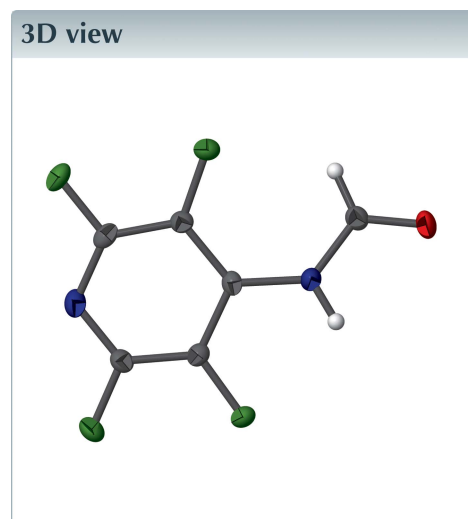
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Keywords: crystal structure; amide bond; perfluorinated pyridine; formamide; hydrogen bonding.

CCDC reference: 2196118

Structural data: full structural data are available from iucrdata.iucr.org

The title compound, C₆H₂F₄N₂O, displays amide bond lengths of 1.218 (3) Å and 1.366 (3) Å for the C=O and C–N bonds, respectively. The C_p–N–C–O (p = pyridine) torsion angle of 179.0 (2)° indicates an anti-conformation for the grouping. Intermolecular hydrogen bonding is observed between the amine N–H group and the carbonyl O atom, which generates chains of molecules propagating along the *b*-axis direction.



Structure description

The title compound, *N*-(2,3,5,6-tetrafluoropyridin-4-yl)formamide, (I), contains a perfluorinated pyridine heterocycle and a formamide group *para* to the pyridine N atom. These groups have shown utility in independent biochemical applications. For example, fluoroaromatic compounds are used in positron emission tomography (Hashizume *et al.*, 1996) and pyridine rings can act as the bioisosteres of amides (Sun *et al.*, 2019). The structure reported here combines these components and could be of interest for biochemical applications. A search of the CCDC shows no structures that contain a pyridine ring functionalized with a formamide group in the 4-position (Groom *et al.*, 2016).

The crystal structure of (I) represents the first example of a perfluorinated pyridine ring with a formamide functional group (Fig. 1). The amide bond lengths for (I) are 1.218 (3) Å and 1.366 (3) Å for the C=O and C–N bonds, respectively, which are in good agreement with the corresponding bonds in the related compounds *N*-phenylformamide (Omondi *et al.*, 2014), *N*-(2,6-difluorophenyl)formamide (Omondi *et al.*, 2009*b*), and *N*-(2,6-dibromophenyl)formamide (Omondi *et al.*, 2009*a*). As observed in other structures, the amide bond lengths for (I) are consistent with little to no N=C/C–O bond resonance contribution. The formamide group and pyridine ring in (I) are somewhat twisted with a dihedral angle of 13.21 (5)°. This is similar to *N*-phenyl-

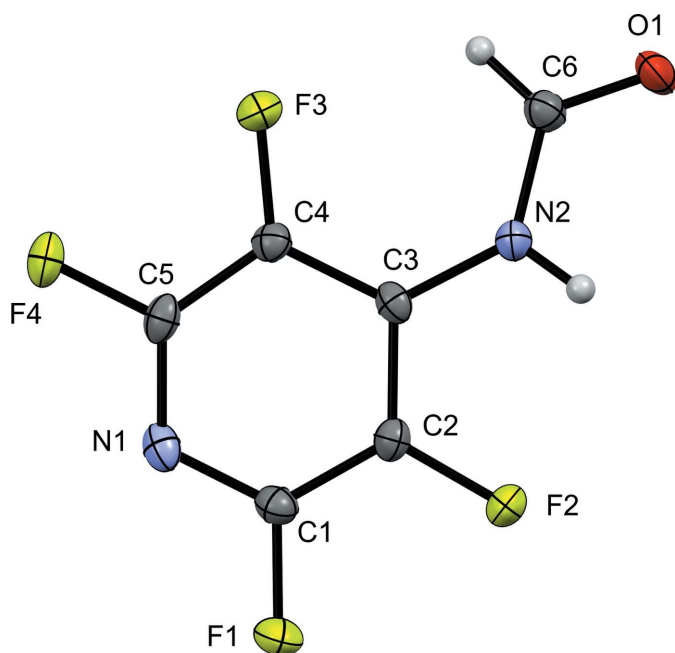


Figure 1
Displacement ellipsoid perspective view (50% probability) for the title structure showing the atom-numbering scheme.

formamide (Omondi *et al.*, 2014) (dihedral angle between the benzene ring and formamide groups = 10.5°) but in contrast to *N*-(2,6-difluorophenyl)formamide (Omondi *et al.*, 2009b) and *N*-(2,6-dibromophenyl)formamide (Omondi *et al.*, 2009a) where the equivalent dihedral angles are 58.4 and 83.2° , respectively. The latter structures indicate that the steric effects likely increase from H to F to Br; however, this large deviation from planarity is not observed in (I). Furthermore, the torsion angle of $179.0(2)^\circ$ for C3–N2–C6–O1 in (I) indicates a near *anti*-conformation, but in structures with a benzene ring, the carbonyl–benzene conformation is *syn* regardless of aromatic substituents (Omondi *et al.*, 2009a,b, 2014). Taken together, these indicate that the pyridine ring is

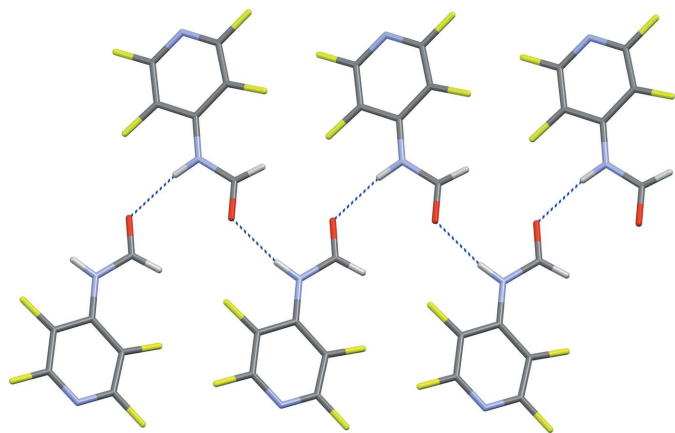


Figure 2
Intermolecular hydrogen bonding forming a chain propagating along the *b*-axis direction where hydrogen bonds are represented with dashed lines.

Table 1
Hydrogen-bond geometry (\AA , $^\circ$).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$N2-H2\cdots O1^i$	0.87 (3)	1.96 (3)	2.814 (3)	171 (3)

Symmetry code: (i) $-x, y - \frac{1}{2}, -z + \frac{3}{2}$.

playing a role in the structure beyond the sterics of the aromatic ring substituents. The pyridyl related compounds *N*-(3,5-dichloro-2-pyridyl)formamide (Resinger *et al.*, 2005) and formyl(2-pyridyl)amine (Bock *et al.*, 1996) also show an *anti*-conformation for the carbonyl and pyridine ring as well as near coplanarity of the functional groups as observed for the title compound.

In the extended structure of (I) the molecules are linked by $N-H\cdots O$ hydrogen bonds with a bond angle of $171(3)^\circ$ (Table 1), which suggests evidence of intermediate–strong hydrogen bonding (Arunan *et al.*, 2011). The hydrogen bonding generates chains of molecules propagating along the *b*-axis direction in the extended structure (Fig. 2) with adjacent molecules in the chain related by 2_1 screw axis symmetry. Neighboring sets of chains form an L shape through a nearly orthogonal (84°) orientation of the pyridine rings in each chain (Fig. 3). This brings about short contacts between the pyridyl nitrogen atoms and the π systems of these orthogonal pyridine rings ($N\cdots\text{centroid} = 3.502 \text{ \AA}$; shortest $N\cdots C = 3.032 \text{ \AA}$).

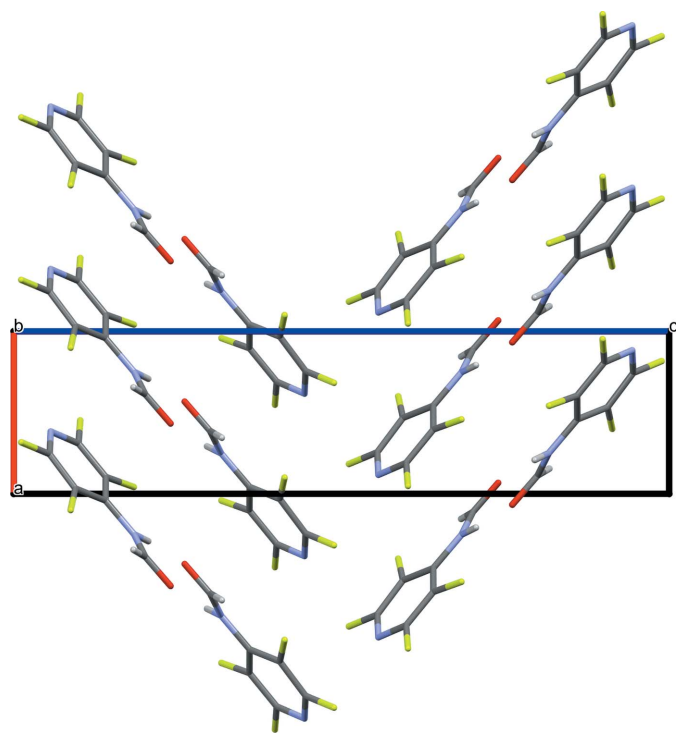


Figure 3
Extended structure as viewed looking down the *b*-axis showing the L-shape that is formed by the orthogonal pyridine rings of neighboring chains.

Table 2

Experimental details.

Crystal data	
Chemical formula	C ₆ H ₂ F ₄ N ₂ O
<i>M_r</i>	194.10
Crystal system, space group	Orthorhombic, <i>P</i> 2 ₁ 2 ₁ 2 ₁
Temperature (K)	100
<i>a</i> , <i>b</i> , <i>c</i> (Å)	5.1183 (4), 6.2707 (6), 20.6294 (16)
<i>V</i> (Å ³)	662.11 (10)
<i>Z</i>	4
Radiation type	Mo <i>K</i> α
μ (mm ⁻¹)	0.21
Crystal size (mm)	0.28 × 0.06 × 0.05
Data collection	
Diffractionmeter	Bruker D8 Venture Photon 2
Absorption correction	Multi-scan (<i>SADABS</i> ; Bruker, 2018)
<i>T_{min}</i> , <i>T_{max}</i>	0.897, 1.000
No. of measured, independent and observed [<i>I</i> > 2σ(<i>I</i>)] reflections	3556, 1309, 1200
<i>R_{int}</i>	0.029
(sin θ/λ) _{max} (Å ⁻¹)	0.618
Refinement	
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> [<i>F</i> ²], <i>S</i>	0.028, 0.066, 1.09
No. of reflections	1309
No. of parameters	122
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
Δρ _{max} , Δρ _{min} (e Å ⁻³)	0.14, -0.19
Absolute structure	Flack <i>x</i> determined using 424 quotients [(<i>I</i> ⁺) - (<i>I</i> ⁻)] / [(<i>I</i> ⁺) + (<i>I</i> ⁻)] (Parsons <i>et al.</i> , 2013)
Absolute structure parameter	-0.1 (6)

Computer programs: *APEX3* and *SAINT* (Bruker, 2018), *SHELXT2014/5* (Sheldrick, 2015a), *SHELXL2016/6* (Sheldrick, 2015b), and *SHELXTL* (Sheldrick, 2008).

Synthesis and crystallization

A 50 ml round-bottom flask was charged with 2,3,5,6-tetrafluoropyridin-4-amine (0.1078 g, 0.6491 mmol), *p*-toluene-sulfonic acid (0.0046 g, 0.027 mmol), trimethyl orthoformate (0.28 ml, 2.6 mmol), and toluene (5 ml). A Dean–Stark apparatus was filled with toluene (10 ml), and the solution was refluxed for 16 h. A homogenous colorless solution was

obtained. Crystals were obtained by dichloromethane layered with hexanes, yielding orange needles. ¹⁹F{¹H} NMR (CDCl₃, δ): 91.1 (2F, *d*, -CF), 154.9 (2F, *d*, -CF). ¹H NMR (CDCl₃, δ): 9.00 (1H, *s*, -O=CH), 7.70 (1H, *s*, -NH).

Refinement

Crystal data, data collection, and structure refinement details are summarized in Table 2.

Funding information

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full crystallographic data

IUCrData (2022). 7, x220804 [https://doi.org/10.1107/S2414314622008045]

***N*-(2,3,5,6-Tetrafluoropyridin-4-yl)formamide**

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N*-(2,3,5,6-Tetrafluoropyridin-4-yl)formamideCrystal data*

C₆H₂F₄N₂O

M_r = 194.10

Orthorhombic, *P*2₁2₁2₁

a = 5.1183 (4) Å

b = 6.2707 (6) Å

c = 20.6294 (16) Å

V = 662.11 (10) Å³

Z = 4

F(000) = 384

D_x = 1.947 Mg m⁻³

Mo *Kα* radiation, λ = 0.71073 Å

Cell parameters from 2461 reflections

θ = 3.4–26.0°

μ = 0.21 mm⁻¹

T = 100 K

Column, colourless

0.28 × 0.06 × 0.05 mm

Data collection

Bruker D8 Venture Photon 2
diffractometer

Radiation source: Incoatec IμS

φ and ω scans

Absorption correction: multi-scan
(SADABS; Bruker, 2018)

T_{min} = 0.897, *T_{max}* = 1.000

3556 measured reflections

1309 independent reflections

1200 reflections with *I* > 2σ(*I*)

R_{int} = 0.029

θ_{max} = 26.0°, θ_{min} = 3.4°

h = -6→6

k = -7→7

l = -25→25

Refinement

Refinement on *F*²

Least-squares matrix: full

R [*F*² > 2σ(*F*²)] = 0.028

wR (*F*²) = 0.066

S = 1.09

1309 reflections

122 parameters

0 restraints

Primary atom site location: dual

Secondary atom site location: difference Fourier
map

Hydrogen site location: mixed

H atoms treated by a mixture of independent
and constrained refinement

w = 1/[σ²(*F_o*²) + (0.0317*P*)² + 0.041*P*]

where *P* = (*F_o*² + 2*F_c*²)/3

(Δ/σ)_{max} < 0.001

Δρ_{max} = 0.14 e Å⁻³

Δρ_{min} = -0.19 e Å⁻³

Absolute structure: Flack *x* determined using

424 quotients [(*F*⁺)-(*F*)]/[(*F*⁺)+(*F*)] (Parsons *et al.*, 2013)

Absolute structure parameter: -0.1 (6)

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.

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
F1	0.9516 (3)	−0.1033 (2)	0.60146 (7)	0.0280 (4)
F2	0.5417 (3)	−0.0546 (2)	0.68314 (6)	0.0218 (4)
F3	0.3999 (3)	0.6218 (2)	0.58674 (7)	0.0246 (4)
F4	0.8168 (3)	0.5429 (2)	0.51143 (7)	0.0246 (4)
O1	−0.0674 (4)	0.4673 (3)	0.73924 (8)	0.0239 (4)
N1	0.8836 (4)	0.2207 (3)	0.55635 (10)	0.0194 (5)
N2	0.2513 (4)	0.3050 (3)	0.68341 (10)	0.0176 (5)
H2	0.208 (6)	0.193 (5)	0.7052 (15)	0.030 (8)*
C1	0.8095 (5)	0.0761 (4)	0.59878 (12)	0.0186 (6)
C2	0.6040 (5)	0.0998 (4)	0.64033 (11)	0.0172 (5)
C3	0.4581 (5)	0.2879 (4)	0.64007 (11)	0.0153 (5)
C4	0.5327 (5)	0.4385 (4)	0.59394 (11)	0.0168 (5)
C5	0.7440 (5)	0.3963 (4)	0.55472 (11)	0.0188 (6)
C6	0.1120 (5)	0.4818 (4)	0.70070 (12)	0.0195 (6)
H6	0.155131	0.616615	0.682599	0.023*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.0275 (9)	0.0267 (8)	0.0299 (8)	0.0124 (7)	0.0063 (8)	0.0033 (6)
F2	0.0255 (8)	0.0183 (7)	0.0215 (7)	0.0018 (7)	0.0038 (7)	0.0059 (6)
F3	0.0292 (9)	0.0193 (7)	0.0253 (8)	0.0059 (7)	0.0041 (8)	0.0053 (6)
F4	0.0272 (8)	0.0280 (8)	0.0187 (7)	−0.0051 (7)	0.0039 (7)	0.0064 (6)
O1	0.0232 (10)	0.0228 (9)	0.0255 (9)	0.0014 (9)	0.0100 (9)	−0.0038 (7)
N1	0.0152 (11)	0.0287 (11)	0.0143 (10)	−0.0001 (9)	−0.0007 (10)	−0.0007 (8)
N2	0.0183 (11)	0.0174 (10)	0.0170 (10)	−0.0002 (9)	0.0036 (11)	0.0011 (8)
C1	0.0167 (13)	0.0196 (12)	0.0195 (12)	0.0029 (10)	−0.0009 (12)	−0.0008 (10)
C2	0.0183 (13)	0.0185 (12)	0.0149 (12)	−0.0013 (10)	−0.0003 (12)	0.0013 (9)
C3	0.0146 (11)	0.0197 (11)	0.0117 (11)	−0.0002 (10)	−0.0011 (11)	−0.0029 (8)
C4	0.0182 (13)	0.0176 (11)	0.0146 (11)	0.0010 (11)	−0.0021 (11)	0.0005 (9)
C5	0.0211 (13)	0.0220 (12)	0.0132 (12)	−0.0055 (11)	−0.0026 (12)	0.0026 (10)
C6	0.0198 (14)	0.0183 (12)	0.0205 (12)	0.0005 (11)	0.0016 (13)	−0.0021 (9)

Geometric parameters (\AA , $^\circ$)

F1—C1	1.341 (3)	N2—C3	1.390 (3)
F2—C2	1.348 (3)	N2—H2	0.87 (3)
F3—C4	1.343 (3)	C1—C2	1.365 (3)
F4—C5	1.335 (3)	C2—C3	1.396 (3)
O1—C6	1.218 (3)	C3—C4	1.394 (3)
N1—C5	1.313 (3)	C4—C5	1.376 (4)
N1—C1	1.316 (3)	C6—H6	0.9500
N2—C6	1.366 (3)		
C5—N1—C1	116.0 (2)	N2—C3—C2	118.0 (2)

C6—N2—C3	128.9 (2)	C4—C3—C2	115.4 (2)
C6—N2—H2	113 (2)	F3—C4—C5	119.8 (2)
C3—N2—H2	118 (2)	F3—C4—C3	121.1 (2)
N1—C1—F1	116.7 (2)	C5—C4—C3	119.1 (2)
N1—C1—C2	124.4 (2)	N1—C5—F4	116.3 (2)
F1—C1—C2	118.9 (2)	N1—C5—C4	125.0 (2)
F2—C2—C1	121.0 (2)	F4—C5—C4	118.7 (2)
F2—C2—C3	118.9 (2)	O1—C6—N2	120.2 (2)
C1—C2—C3	120.1 (2)	O1—C6—H6	119.9
N2—C3—C4	126.5 (2)	N2—C6—H6	119.9
C5—N1—C1—F1	-179.4 (2)	N2—C3—C4—F3	-1.1 (4)
C5—N1—C1—C2	-0.8 (4)	C2—C3—C4—F3	176.8 (2)
N1—C1—C2—F2	-179.1 (2)	N2—C3—C4—C5	179.8 (2)
F1—C1—C2—F2	-0.6 (3)	C2—C3—C4—C5	-2.3 (3)
N1—C1—C2—C3	-0.7 (4)	C1—N1—C5—F4	-179.5 (2)
F1—C1—C2—C3	177.9 (2)	C1—N1—C5—C4	0.7 (4)
C6—N2—C3—C4	-15.2 (4)	F3—C4—C5—N1	-178.2 (2)
C6—N2—C3—C2	167.0 (2)	C3—C4—C5—N1	0.9 (4)
F2—C2—C3—N2	-1.3 (3)	F3—C4—C5—F4	2.0 (3)
C1—C2—C3—N2	-179.8 (2)	C3—C4—C5—F4	-178.9 (2)
F2—C2—C3—C4	-179.3 (2)	C3—N2—C6—O1	179.0 (2)
C1—C2—C3—C4	2.2 (3)		

Hydrogen-bond geometry (Å, °)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
N2—H2 \cdots O1 ⁱ	0.87 (3)	1.96 (3)	2.814 (3)	171 (3)

Symmetry code: (i) $-x, y-1/2, -z+3/2$.