The title compound, N-(2,3,5,6-tetrafluoropyridin-4-yl)formamide, \( \text{C}_6\text{H}_2\text{F}_4\text{N}_2\text{O} \), displays amide bond lengths of 1.218 (3) Å and 1.366 (3) Å for the \( \text{C}=\text{O} \) and \( \text{C}—\text{N} \) bonds, respectively. The \( \text{C}_p—\text{N—C—O} \) (\( p = \text{pyridine} \)) torsion angle of 179.0 (2)° indicates an anti-conformation for the grouping. Intermolecular hydrogen bonding is observed between the amine \( \text{N—H} \) group and the carbonyl \( \text{O} \) atom, which generates chains of molecules propagating along the \( b \)-axis direction.

Structure description

The title compound, \( \text{N-(2,3,5,6-tetrafluoropyridin-4-yl)formamide} \), (I), contains a perfluorinated pyridine heterocycle and a formamide group \( \text{para} \) to the pyridine \( \text{N} \) atom. These groups have shown utility in independent biochemical applications. For example, fluoroaromatic compounds are used in positron emission tomography (Hashizume \textit{et al.}, 1996) and pyridine rings can act as the bioisosteres of amides (Sun \textit{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 \textit{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 \( \text{C}=\text{O} \) and \( \text{C}—\text{N} \) bonds, respectively, which are in good agreement with the corresponding bonds in the related compounds \( \text{N-phenylformamide} \) (Omondi \textit{et al.}, 2014), \( \text{N-(2,6-difluorophenyl)formamide} \) (Omondi \textit{et al.}, 2009b), and \( \text{N-(2,6-dibromophenyl)formamide} \) (Omondi \textit{et al.}, 2009a). As observed in other structures, the amide bond lengths for (I) are consistent with little to no \( \text{N—C—O} \) 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 \( \text{N-phenyl-} \)
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Data reports

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., 2009) and N-(2,6-dibromophenyl)formamide (Omondi et al., 2009) 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)° 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 playing a role in the structure beyond the steric 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⋯O hydrogen bonds with a bond angle of 171 (3)° (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 21 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⋯centroid = 3.502 Å; shortest N⋯C = 3.032 Å).

![Figure 1](image1) Displacement ellipsoid perspective view (50% probability) for the title structure showing the atom-numbering scheme.

![Figure 2](image2) Intermolecular hydrogen bonding forming a chain propagating along the b-axis direction where hydrogen bonds are represented with dashed lines.

![Figure 3](image3) 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 1

|       | D—H⋯A | D—H | H⋯A | D⋯A | D—H⋯A |
|-------|-------|-----|-----|-----|-------|
| N2—H2⋯O1 | 0.87 (3) | 1.96 (3) | 2.814 (3) | 171 (3) |

Symmetry code: (i) −x, y −1/2, −z + 1/2

Table 1

Hydrogen-bond geometry (Å, °).

for the data reports 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., 2009) and N-(2,6-dibromophenyl)formamide (Omondi et al., 2009) 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)° 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 playing a role in the structure beyond the steric 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.

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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. $^{19}$F$[1H]$ NMR (CDCl$_3$, $\delta$): 91.1 (2F, d, –CF), 154.9 (2F, d, –CF). $^1$H NMR (CDCl$_3$, $\delta$): 9.00 (1H, s, –O–CH), 7.70 (1H, s, –NH).

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References

Arunan, E., Desiraju, G. R., Klein, R. A., Sadlej, J., Scheiner, S., Alkorta, I., Clary, D. C., Crabtree, R. H., Dannenberg, J. J., Hobza, P., Kjaergaard, H. G., Legon, A. C., Mennucci, B. & Nesbitt, D. J. (2011). Pure Appl. Chem. 83, 1637–1641.

Bock, H., Van, T. T. H., Solouki, B., Schödel, H., Artus, G., Herdtwech, E. & Hermann, W. A. (1996). Liebigs Ann. pp. 403–407. DOI: 10.1002/jlac.199619960316.

Bruker (2018). APEX3, SAINT and SADABS. Bruker AXS Inc., Madison, Wisconsin, USA.

Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). Acta Cryst. B72, 171–179.

Hashizume, T., Hashimoto, N. & Miyake, Y. (1996). Japan Patent JP 08310973 A.

Omondi, B., Fernandes, M. A., Levendis, D. C. & Layh, M. (2014). Acta Cryst. B70, 106–114.

Omondi, B., Levendis, D. C., Layh, M. & Fernandes, M. A. (2009a). Acta Cryst. C65, 160–162.

Omondi, B., Levendis, D. C., Layh, M. & Fernandes, M. A. (2009b). Acta Cryst. C65, 470–475.

Parsons, S., Flack, H. D. & Wagner, T. (2013). Acta Cryst. B69, 249–259.

Resinger, A., Wentrup, C., Byriel, K. A. & Kennard, C. H. L. (2005). Acta Cryst. E61, o2053–o2054.

Sheldrick, G. M. (2008). Acta Cryst. A64, 112–122.

Sheldrick, G. M. (2015a). Acta Cryst. A71, 3–8.

Sheldrick, G. M. (2015b). Acta Cryst. C71, 3–8.

Sun, S., Jia, Q. & Zhang, Z. (2019). Bioorg. Med. Chem. Lett. 29, 2535–2550.
full crystallographic data

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

Bailey D. Newell, Colin D. McMillen and John P. Lee

*C6H2F4N2O*  
Mr = 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*₂ = 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 *μ*S  
φ and *ω* scans  
Absorption correction: multi-scan  
(SADABS; Bruker, 2018)  
*T*ₘᵡᵣᵢₜ = 0.897, *T*ₘₐₓ = 1.000  
3556 measured reflections

**Refinement**

Refinement on *F*²  
Least-squares matrix: full  
*R* = 0.028  
*wR*(*F*) = 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*²) + (0.0317*P)² + 0.041*P]"  
where *P* = (*F*² + 2*F*c²)/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 [(*I*)−(*I*)]/[(*I*)+(*I*)] (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 (Å²)**

|     | x         | y         | z         | Uiso*/Ueq |
|-----|-----------|-----------|-----------|-----------|
| 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 (Å²)**

|     | U₁₁| U₂₂| U₃₃| U₁₂| U₁₃| U₂₃ |
|-----|----|----|----|----|----|----|
| 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 (Å, °)**

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

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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, °)

| D—H···A | D—H | H···A | D···A | D—H···A |
|---------|------|-------|-------|---------|
| N2—H2···O1 † | 0.87 (3) | 1.96 (3) | 2.814 (3) | 171 (3) |

Symmetry code: (i) −x, y−1/2, −z+3/2.