

4-[4-(4-Fluorophenyl)-1,2-oxazol-5-yl]pyridine

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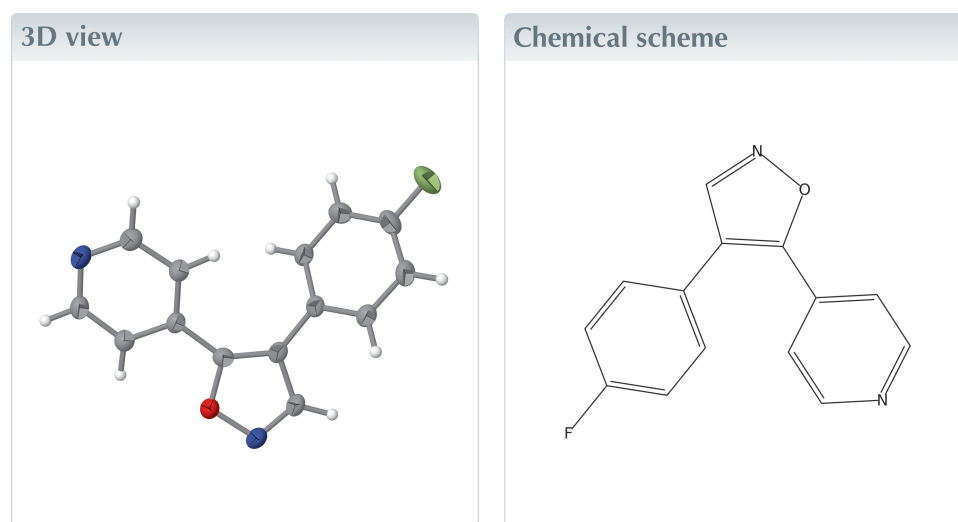
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Keywords: crystal structure; pyridine; isoxazole; MAP kinase inhibitor.

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

The title compound, C₁₄H₉FN₂O, crystallizes in the monoclinic space group *P2₁/c*. The dihedral angles between the central isoxazole ring and the 4-fluorophenyl and pyridine rings are 37.51 (10) and 12.11 (15)°, respectively.



Structure description

The title compound, C₁₄H₉FN₂O, (Fig. 1), was synthesized to extend our study on the role of the hydrogen-bonding heteroatom-Lys53 interaction between pyridin-4-yl-substituted five-membered heterocyclic ring inhibitors and the p38 α mitogen-activated protein (MAP) kinase (Abu Thaher *et al.*, 2009). For the structure of a regioisomer of the title compound, see Koch *et al.* (2025).

The isoxazole ring (C1–C3, O4, N5) makes dihedral angles of 37.51 (10) and 12.11 (15)° with 4-fluorophenyl (C6–C11) and pyridine (C12–C14, N15, C16, C17) rings, respectively. The 4-fluorophenyl ring makes a dihedral angle of 41.82 (9)° with the pyridine ring. In the crystal, the π -hydrogen–nitrogen bond (C1–H1...N15, Table 1) leads to the formation of chains along the *c*-axis direction. The packing is shown in Fig. 2.

Synthesis and crystallization

3-(Dimethylamino)-2-(4-fluorophenyl)-1-(pyridin-4-yl)prop-2-en-1-one (500 mg) was dissolved in methanol (8 ml) and water (4 ml). Sodium carbonate (106 mg) and hydroxylamine hydrochloride (123 mg) were added. The pH was adjusted to 5 by dropwise addition of acetic acid. The reaction mixture was heated to reflux temperature for 2.5 h. After cooling to room temperature, the pH was set to 7 by addition of ammonium hydroxide solution. Ice was added to the mixture and the title compound crystallized slowly as colorless needles (180 mg).

Refinement

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

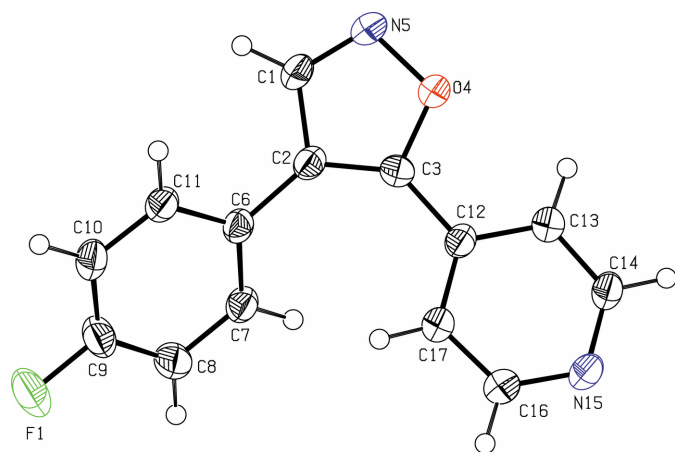


Figure 1
View of the title compound. Displacement ellipsoids are drawn at the 50% probability level.

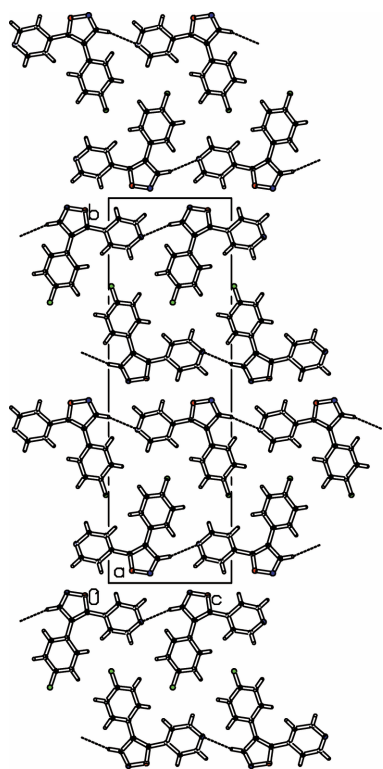


Figure 2
Part of the packing diagram. View along the *a*-axis direction. Hydrogen bonds are shown as dashed lines.

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

<i>D</i> —H··· <i>A</i>	<i>D</i> —H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> —H··· <i>A</i>
C1—H1···N15 ⁱ	0.95	2.54	3.459 (4)	164

Symmetry code: (i) *x*, *y*, *z* + 1.

Table 2
Experimental details.

Crystal data	
Chemical formula	C ₁₄ H ₉ FN ₂ O
<i>M_r</i>	240.23
Crystal system, space group	Monoclinic, <i>P</i> 2 ₁ / <i>c</i>
Temperature (K)	193
<i>a</i> , <i>b</i> , <i>c</i> (Å)	3.9252 (18), 29.539 (4), 9.642 (4)
β (°)	102.06 (2)
<i>V</i> (Å ³)	1093.3 (7)
<i>Z</i>	4
Radiation type	Cu <i>K</i> α
μ (mm ⁻¹)	0.88
Crystal size (mm)	0.30 × 0.05 × 0.05
Data collection	
Diffractometer	Enraf–Nonius CAD-4
Absorption correction	—
No. of measured, independent and observed [<i>I</i> > 2 σ (<i>I</i>)] reflections	2383, 2077, 1387
<i>R</i> _{int}	0.048
(<i>sin</i> θ / λ) _{max} (Å ⁻¹)	0.609
Refinement	
<i>R</i> [<i>F</i> ² > 2 σ (<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.055, 0.157, 1.06
No. of reflections	2077
No. of parameters	164
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{\text{max}}$, $\Delta\rho_{\text{min}}$ (e Å ⁻³)	0.28, -0.27

Computer programs: *CAD-4 Software* (Enraf–Nonius, 1989), *CORINC* (Dräger & Gattow, 1971), *SHELXT2014* (Sheldrick, 2015a), *SHELXL2019/3* (Sheldrick, 2015b) and *PLATON* (Spek, 2009).

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full crystallographic data

IUCrData (2025). **10**, x251107 [https://doi.org/10.1107/S2414314625011071]

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Crystal data $C_{14}H_9FN_2O$ $M_r = 240.23$ Monoclinic, $P2_1/c$ $a = 3.9252$ (18) Å $b = 29.539$ (4) Å $c = 9.642$ (4) Å $\beta = 102.06$ (2)° $V = 1093.3$ (7) Å³ $Z = 4$ $F(000) = 496$ $D_x = 1.459$ Mg m⁻³Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å

Cell parameters from 25 reflections

 $\theta = 21\text{--}29^\circ$ $\mu = 0.88$ mm⁻¹ $T = 193$ K

Needles, colourless

0.30 × 0.05 × 0.05 mm

Data collection

Enraf–Nonius CAD-4

diffractometer

Radiation source: rotating anode

Graphite monochromator

 $\omega/2\theta$ scans

2383 measured reflections

2077 independent reflections

1387 reflections with $I > 2\sigma(I)$ $R_{\text{int}} = 0.048$ $\theta_{\text{max}} = 70.0^\circ$, $\theta_{\text{min}} = 3.0^\circ$ $h = -4 \rightarrow 0$ $k = 0 \rightarrow 36$ $l = -11 \rightarrow 11$

3 standard reflections every 60 min

intensity decay: 2%

*Refinement*Refinement on F^2

Least-squares matrix: full

 $R[F^2 > 2\sigma(F^2)] = 0.055$ $wR(F^2) = 0.157$ $S = 1.06$

2077 reflections

164 parameters

0 restraints

Primary atom site location: structure-invariant

direct methods

Hydrogen site location: inferred from neighbouring sites

H-atom parameters constrained

 $w = 1/[\sigma^2(F_o^2) + (0.078P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$ $(\Delta/\sigma)_{\text{max}} < 0.001$ $\Delta\rho_{\text{max}} = 0.28$ e Å⁻³ $\Delta\rho_{\text{min}} = -0.27$ e Å⁻³

Extinction correction: SHELXL-2019/3

(Sheldrick, 2015b),

 $F_c^* = kF_c[1 + 0.001 \times F_c^2 \lambda^3 / \sin(2\theta)]^{-1/4}$

Extinction coefficient: 0.0051 (10)

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. Hydrogen atoms were placed at calculated positions and were refined in the riding-model approximation with C–H = 0.95 Å, and with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{C})$.

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	0.9320 (6)	0.22890 (6)	0.9777 (2)	0.0623 (7)
C1	0.4161 (9)	0.43647 (9)	0.8975 (3)	0.0366 (7)
H1	0.448981	0.431370	0.996651	0.044*
C2	0.4831 (7)	0.40304 (9)	0.7999 (3)	0.0285 (6)
C3	0.4057 (7)	0.42489 (8)	0.6731 (3)	0.0295 (6)
O4	0.2967 (6)	0.46779 (6)	0.69270 (19)	0.0385 (6)
N5	0.3058 (8)	0.47453 (8)	0.8374 (2)	0.0439 (7)
C6	0.6013 (7)	0.35668 (8)	0.8417 (3)	0.0275 (6)
C7	0.4785 (8)	0.31866 (9)	0.7610 (3)	0.0311 (6)
H7	0.316577	0.322411	0.673623	0.037*
C8	0.5878 (8)	0.27570 (9)	0.8056 (3)	0.0377 (7)
H8	0.505879	0.249920	0.749620	0.045*
C9	0.8192 (9)	0.27122 (9)	0.9338 (3)	0.0398 (7)
C10	0.9413 (8)	0.30723 (10)	1.0186 (3)	0.0376 (7)
H10	1.096255	0.302943	1.107434	0.045*
C11	0.8325 (8)	0.35024 (9)	0.9712 (3)	0.0324 (7)
H11	0.916967	0.375771	1.027989	0.039*
C12	0.4195 (7)	0.41517 (8)	0.5250 (3)	0.0278 (6)
C13	0.2652 (8)	0.44483 (9)	0.4176 (3)	0.0329 (7)
H13	0.153322	0.471542	0.440137	0.040*
C14	0.2755 (8)	0.43522 (9)	0.2785 (3)	0.0358 (7)
H14	0.166021	0.455787	0.207181	0.043*
N15	0.4307 (7)	0.39864 (8)	0.2382 (2)	0.0366 (6)
C16	0.5827 (8)	0.37062 (9)	0.3421 (3)	0.0355 (7)
H16	0.695501	0.344424	0.316372	0.043*
C17	0.5861 (8)	0.37730 (9)	0.4841 (3)	0.0318 (6)
H17	0.700583	0.356340	0.553090	0.038*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.0842 (17)	0.0341 (10)	0.0623 (13)	0.0099 (10)	0.0010 (11)	0.0143 (8)
C1	0.0539 (19)	0.0356 (15)	0.0222 (13)	−0.0003 (14)	0.0121 (12)	0.0010 (11)
C2	0.0333 (15)	0.0302 (14)	0.0229 (12)	−0.0042 (12)	0.0076 (11)	−0.0009 (10)
C3	0.0337 (16)	0.0244 (13)	0.0299 (14)	−0.0010 (11)	0.0058 (11)	−0.0018 (10)
O4	0.0618 (15)	0.0301 (10)	0.0245 (9)	0.0069 (10)	0.0113 (9)	0.0013 (8)
N5	0.072 (2)	0.0360 (13)	0.0254 (12)	0.0057 (13)	0.0152 (12)	−0.0034 (10)
C6	0.0312 (15)	0.0297 (14)	0.0229 (13)	−0.0016 (11)	0.0084 (11)	0.0027 (10)
C7	0.0356 (16)	0.0327 (14)	0.0234 (13)	−0.0035 (12)	0.0024 (11)	0.0004 (11)
C8	0.0460 (19)	0.0280 (14)	0.0373 (15)	−0.0045 (13)	0.0047 (14)	−0.0016 (11)
C9	0.047 (2)	0.0298 (15)	0.0414 (17)	0.0023 (13)	0.0067 (14)	0.0100 (12)
C10	0.0429 (18)	0.0402 (16)	0.0268 (13)	0.0023 (14)	0.0009 (12)	0.0060 (11)

C11	0.0392 (17)	0.0329 (15)	0.0244 (13)	-0.0029 (12)	0.0049 (11)	-0.0008 (11)
C12	0.0321 (15)	0.0286 (13)	0.0223 (12)	-0.0046 (11)	0.0047 (10)	0.0000 (10)
C13	0.0402 (17)	0.0306 (14)	0.0273 (13)	0.0020 (12)	0.0055 (12)	0.0013 (10)
C14	0.0468 (18)	0.0345 (14)	0.0239 (13)	-0.0003 (13)	0.0024 (12)	0.0032 (11)
N15	0.0481 (16)	0.0386 (13)	0.0232 (11)	-0.0012 (12)	0.0075 (10)	-0.0018 (10)
C16	0.0426 (18)	0.0350 (15)	0.0298 (14)	0.0018 (13)	0.0100 (12)	-0.0016 (11)
C17	0.0382 (17)	0.0313 (14)	0.0254 (12)	0.0014 (12)	0.0054 (11)	0.0008 (11)

Geometric parameters (Å, °)

F1—C9	1.364 (3)	C9—C10	1.366 (4)
C1—N5	1.297 (3)	C10—C11	1.387 (4)
C1—C2	1.426 (4)	C10—H10	0.9500
C1—H1	0.9500	C11—H11	0.9500
C2—C3	1.359 (3)	C12—C17	1.394 (4)
C2—C6	1.475 (3)	C12—C13	1.394 (4)
C3—O4	1.363 (3)	C13—C14	1.380 (4)
C3—C12	1.469 (3)	C13—H13	0.9500
O4—N5	1.403 (3)	C14—N15	1.337 (4)
C6—C7	1.394 (3)	C14—H14	0.9500
C6—C11	1.395 (4)	N15—C16	1.340 (3)
C7—C8	1.379 (4)	C16—C17	1.381 (4)
C7—H7	0.9500	C16—H16	0.9500
C8—C9	1.379 (4)	C17—H17	0.9500
C8—H8	0.9500		
N5—C1—C2	113.3 (2)	C9—C10—C11	118.1 (3)
N5—C1—H1	123.3	C9—C10—H10	120.9
C2—C1—H1	123.3	C11—C10—H10	120.9
C3—C2—C1	103.1 (2)	C10—C11—C6	121.2 (3)
C3—C2—C6	133.3 (2)	C10—C11—H11	119.4
C1—C2—C6	123.6 (2)	C6—C11—H11	119.4
C2—C3—O4	109.5 (2)	C17—C12—C13	116.8 (2)
C2—C3—C12	137.3 (2)	C17—C12—C3	123.1 (2)
O4—C3—C12	113.1 (2)	C13—C12—C3	120.0 (2)
C3—O4—N5	109.05 (19)	C14—C13—C12	119.8 (3)
C1—N5—O4	104.9 (2)	C14—C13—H13	120.1
C7—C6—C11	118.3 (2)	C12—C13—H13	120.1
C7—C6—C2	122.9 (2)	N15—C14—C13	123.8 (3)
C11—C6—C2	118.7 (2)	N15—C14—H14	118.1
C8—C7—C6	121.2 (2)	C13—C14—H14	118.1
C8—C7—H7	119.4	C14—N15—C16	116.1 (2)
C6—C7—H7	119.4	N15—C16—C17	124.3 (3)
C9—C8—C7	118.1 (3)	N15—C16—H16	117.8
C9—C8—H8	120.9	C17—C16—H16	117.8
C7—C8—H8	120.9	C16—C17—C12	119.2 (2)
F1—C9—C10	118.5 (3)	C16—C17—H17	120.4
F1—C9—C8	118.5 (3)	C12—C17—H17	120.4

C10—C9—C8	123.0 (3)		
N5—C1—C2—C3	0.7 (4)	C7—C8—C9—C10	0.7 (5)
N5—C1—C2—C6	-178.3 (3)	F1—C9—C10—C11	178.3 (3)
C1—C2—C3—O4	-0.7 (3)	C8—C9—C10—C11	-1.6 (5)
C6—C2—C3—O4	178.1 (3)	C9—C10—C11—C6	0.9 (5)
C1—C2—C3—C12	176.7 (3)	C7—C6—C11—C10	0.6 (4)
C6—C2—C3—C12	-4.5 (6)	C2—C6—C11—C10	177.4 (3)
C2—C3—O4—N5	0.6 (3)	C2—C3—C12—C17	-10.5 (5)
C12—C3—O4—N5	-177.6 (2)	O4—C3—C12—C17	166.9 (3)
C2—C1—N5—O4	-0.4 (4)	C2—C3—C12—C13	170.4 (3)
C3—O4—N5—C1	-0.1 (3)	O4—C3—C12—C13	-12.2 (4)
C3—C2—C6—C7	-38.6 (5)	C17—C12—C13—C14	1.6 (4)
C1—C2—C6—C7	140.1 (3)	C3—C12—C13—C14	-179.2 (3)
C3—C2—C6—C11	144.8 (3)	C12—C13—C14—N15	-0.7 (5)
C1—C2—C6—C11	-36.6 (4)	C13—C14—N15—C16	-0.2 (4)
C11—C6—C7—C8	-1.5 (4)	C14—N15—C16—C17	0.2 (5)
C2—C6—C7—C8	-178.1 (3)	N15—C16—C17—C12	0.7 (5)
C6—C7—C8—C9	0.9 (5)	C13—C12—C17—C16	-1.5 (4)
C7—C8—C9—F1	-179.1 (3)	C3—C12—C17—C16	179.3 (3)

Hydrogen-bond geometry (Å, °)

<i>D—H...A</i>	<i>D—H</i>	<i>H...A</i>	<i>D...A</i>	<i>D—H...A</i>
C1—H1...N15 ⁱ	0.95	2.54	3.459 (4)	164

Symmetry code: (i) *x, y, z+1*.