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4-(4-Fluorophenyl)-3-(4-pyridyl)quinolin-2(1*H*)-one

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Key indicators

Single-crystal X-ray study
T = 295 K
Mean σ(C–C) = 0.003 Å
R factor = 0.057
wR factor = 0.174
Data-to-parameter ratio = 13.5

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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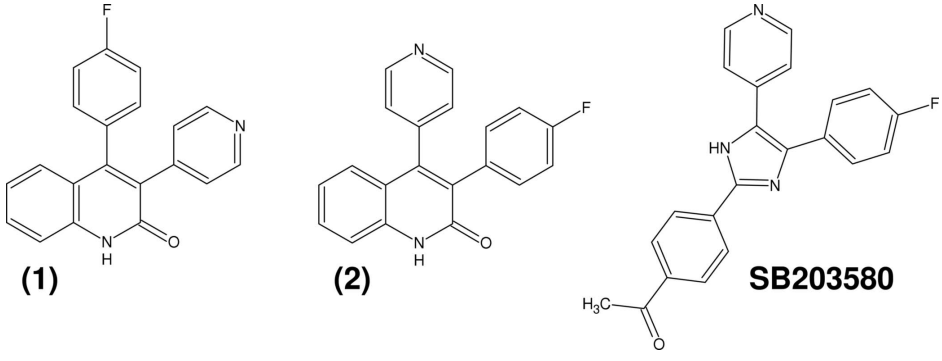
The title compound, $C_{20}H_{13}FN_2O$, has the quinolin-2(1*H*)-one unit in the lactam form. The molecules form dimers *via* N—H···O hydrogen bonds.

Comment

In this study, the title compound, (1), was prepared as an isomer of 3-(4-fluorophenyl)-4-(4-pyridyl)quinolin-2(1*H*)-one, (2) (Peifer, Schollmeyer *et al.*, 2006), which was actually developed as a novel ATP-competitive inhibitor of p38 mitogen-activated protein kinase (p38MAPK), a well characterized drug target in the cytokine signalling pathway (Kumar *et al.*, 2003). The compounds were designed by analogy to compound SB203580 (Cuenda *et al.*, 1995), in which the pyridine N atom accepts a key hydrogen-bond interaction from the protein. SB203580 and its derivatives contain a vicinal pyridine/fluorophenyl pharmacophore system connected to a five-membered ring (Peifer, Wagner & Laufer, 2006). In the present study, we formally replaced the five-membered core by a 3,4-diarylquinolin-2(1*H*)-one unit to study the impact of the modified molecular geometry on inhibitory activity towards the kinase. However, (2) was found to be biologically active in the *in vitro* p38MAPK assay (Laufer *et al.*, 2005), but by changing pyridine in the 3,4-diarylquinolin-2(1*H*)-one unit from position 4 as in compound (2) to position 3 as in compound (1), the activity vanished. Thus, we were particularly interested in the modified molecular geometry (Fig. 1). Interestingly, hydrogen bonding of NH and O of the lactam exclusively and not of the pyridine N atom appears in the crystal structure of (1) (Fig. 2), while in compound (2) the lactam NH and pyridine N are involved in hydrogen-bond interactions but not the lactam O atom (Peifer, Schollmeyer *et al.*, 2006).



The crystal structure analysis revealed that the quinolin-2(1*H*)-one unit is in the lactam form (see Fig. 1) and not in the tautomeric 4-(4-fluorophenyl)-3-pyridin-4-ylquinolin-2-ol

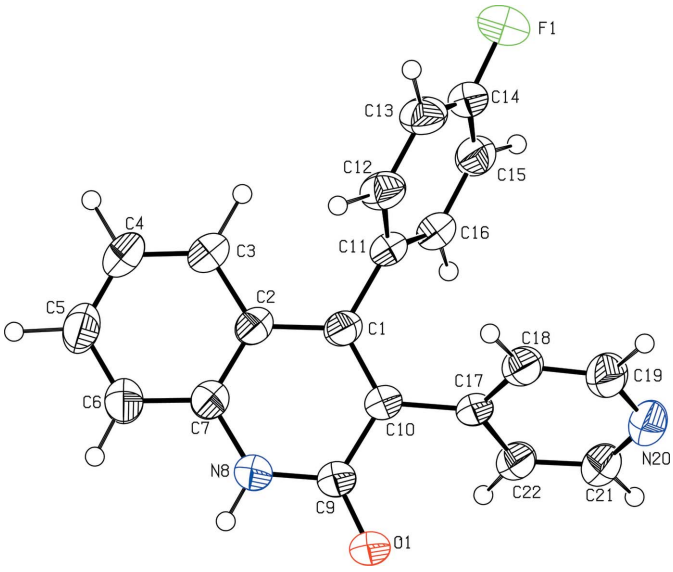


Figure 1
ORTEPII (Johnson, 1976) view of the molecular structure of (1). Displacement ellipsoids are drawn at the 50% probability level. H atoms are depicted as spheres of arbitrary size.

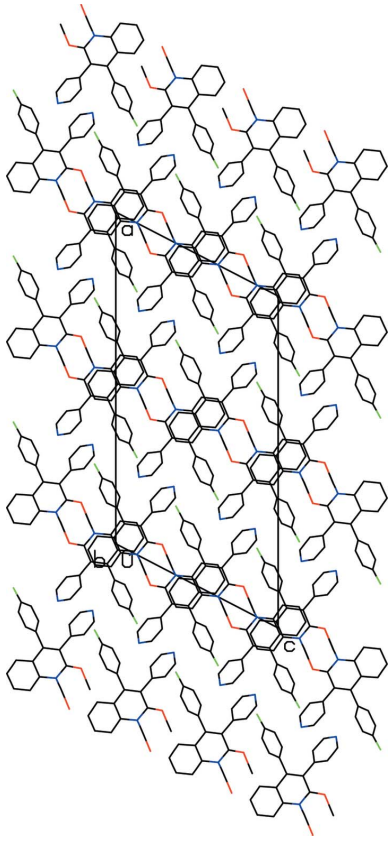
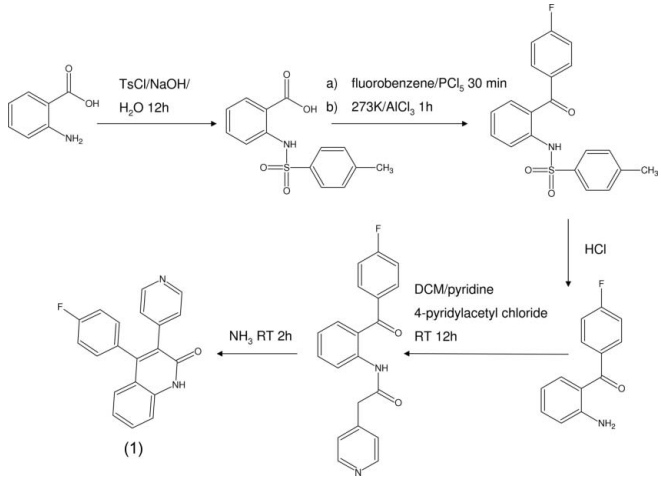


Figure 2
A packing diagram of (1), viewed along the *b* axis. Only important H atoms are shown, with their hydrogen bonds.

conformation. The NH group forms an intermolecular hydrogen bond to the lactam O atom, so that dimers are formed (see Fig. 2).

Experimental

Among the number of synthetic methods for preparing 3,4-diarylquinolin-2(1*H*)-one (Kadnikov & Larock, 2004; Fuerstner & Hupperts, 1995), in this study the ring closure to form the quinolin-2(1*H*)-one unit was achieved by a Knoevenagel reaction (see scheme below). The precursor was prepared as follows: 2-aminobenzoic acid (1.4 g) was protected by the phase transfer catalysis reaction of 2-{[(4-methylphenyl)sulfonyl]amino}benzoic acid with 4-methylbenzenesulfonyl chloride (1.9 g) in NaOH (0.5 g)/H_2O. This compound was reacted with fluorobenzene (20 ml) under Friedel–Crafts conditions to yield *N*-[2-(4-fluorobenzoyl)phenyl]-4-methylbenzenesulfonamide, which was deprotected by HCl (50 ml) to yield (2-aminophenyl)(4-fluorophenyl)methanone. Aminoacylation of this compound by pyridin-4-ylacetyl chloride (175 g) in dichloromethane followed by ring closure with ammonia (2 ml) and purification gave the title compound. Conditions and times of reactions are shown in the scheme below. Crystals of (1) suitable for X-ray analysis precipitated at 278 K from an ethanol solution by slow evaporation.



Crystal data

$C_{20}H_{13}FN_2O$
M_r = 316.33
Monoclinic, $C2/c$
a = 27.771 (2) Å
b = 8.2247 (4) Å
c = 15.2643 (12) Å
β = 117.466 (3)°
V = 3093.5 (4) Å^3
Z = 8
D_x = 1.358 Mg m^{-3}
Cu $K\alpha$ radiation
μ = 0.76 mm^{-1}
T = 295 (2) K
Plate, yellow
0.55 × 0.50 × 0.15 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\theta/2\omega$ scans
Absorption correction: ψ scan (*CORINC*; Dräger & Gattow, 1971)
T_{min} = 0.687, T_{max} = 0.894
3264 measured reflections
3135 independent reflections
2826 reflections with $I > 2\sigma(I)$
R_{int} = 0.030
θ_{max} = 73.9°
3 standard reflections
frequency: 60 min
intensity decay: 5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.174
S = 1.01
3135 reflections
232 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1237P)^2 + 1.2501P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.46 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0017 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N8—H8···O1^{i}	0.90 (1)	1.92 (1)	2.8148 (18)	177

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

H atoms were placed at calculated positions (except H8, which was located in a difference map). The individual U_{iso} values were freely refined. Positional parameters were refined using a riding model (C—H = 0.93 Å). The N8—H8 distance was refined.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: CORINC (Dräger & Gattow, 1971); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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