

Crystal structure analysis of 6-amino-5-(6-fluoro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione

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Abstract : The crystal structure of 6-amino-5-(6-fluoro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (C₂₂H₁₆FN₅O₃). The compound crystallizes in Monoclinic P2₁/c space group with unit cell parameters at 296(2) K as follows: a = 13.3119(5) Å, b = 10.7033(4) Å, c = 13.8141(4) Å, α = 90°, β = 91.8261(12)°, γ = 90°. Crystal data were collected using BRUKER SMART APEX II CCD X-ray diffractometer. The structure was solved by direct methods and refined on F² by full-matrix least-squares procedures to the final R₁ of 0.0384 using SHELXL programs.

Key Words : isoxazole, quinolone, pyrimidine and crystal structure.

Introduction

Spiro-pyrrolidine derivatives are unique tetracyclic 5-HT_{2A} receptor antagonists^{1,2}. These derivatives possess anticancer³ and anti-influenza virus⁴ activities. Highly functionalized pyrrolidines have gained much interest in the past few years as they constitute the main structural element of many natural and synthetic pharmacologically active compounds⁵. Optically active pyrrolidines have been used as intermediates, chiral ligands or auxiliaries in controlled asymmetric synthesis^{6,7}. In view of this importance and in continuation of our work on the crystal structure analysis of spiro-pyrrolidine derivatives, the crystal structure of the title compound has been carried out and the results are presented here.

Experimental

X-ray Structure Determination

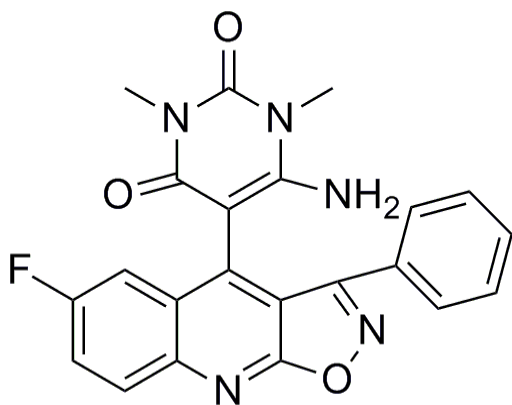
Single crystal of the compound suitable for x-ray diffraction was obtained by slow evaporation method. Three dimensional intensity data were collected on a Bruker⁸ SMART APEX CCD Diffractometer using graphite monochromatized Mo-Kα radiation (λ = 0.71073 Å) at Department of chemistry, IIT, Chennai, India. The structure was solved by direct methods and refined on F² by full-matrix least-squares procedures using the SHELXL programs⁹. All the non-hydrogen atoms were refined using isotropic and later anisotropic thermal parameters. The hydrogen atoms were included in the structure factor calculation at idealized positions by using a riding model, but not refined. Images were created with ORTEP-3⁹. The crystallographic data for the compound are listed in Table 1.

Table 1: Crystal data and structure refinement of the titled compound

Compound	Parameters
Empirical formula	C ₂₂ H ₁₆ F N ₅ O ₃
Formula weight	417.4
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 13.3119(5) Å alpha = 90°. b = 10.7033(4) Å beta = 91.8261(12)°. c = 13.8141(4) Å gamma = 90°
Volume	1967.25(12) Å ³
Z, Calculated density	4, 1.409Mg/m ³
Absorption coefficient	0.104 mm ⁻¹
F(000)	864
Crystal size	0.35 x 0.20 x 0.16 mm
Theta range for data collection	2.41 to 25.00°.
Limiting indices	-15<=h<=15, -12<=k<=11, -16<=l<=16
Reflections collected / unique	14836 / 3469 [R(int) = 0.0214]
Completeness to theta = 25.00	100.00%
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3469 / 0 / 290
Goodness-of-fit on F ²	1.435
Final R indices [I>2sigma(I)]	R1 = 0.0384 , wR2 = 0.1049
R indices (all data)	R1 = 0.0526, wR2 = 0.1127
Largest diff. peak and hole	0.179 and -0.182e. Å ⁻³

Synthesis of the compound

A mixture of 5-F isatin (1 mmol), 6-amino-1, 3-dimethyl uracil (1 mmol), isoxazole (1 mmol) and *p*-TSA.H₂O (0.20 mmol) in water (3 mL) were charged in a 25 mL round bottomed flask and the mixture was heated at reflux. The resulting solution was stirred for 3.5 hour. The consumption of the starting material was monitored by TLC. The precipitated solid was filtered and washed with ethanol (5-7 mL), dried under vacuum to obtain pure product in good yield (81 %).



Results and Discussion

The symmetric unit of the title compound is shown in Fig. 1. The two fused phenyl and cyclopentane rings are approximately planar, making dihedral angle of $1.47(17)^\circ$ and $1.56(17)^\circ$, respectively. The molecule is twisted with the benzene ring and the mean plane through the fused two triazole ring system be inclined to one another by $87.06(18)^\circ$ and $89.5(2)^\circ$, respectively. The methylene groups assume a twisted conformation, as can be seen from the torsion angle $C26-C27-C28-C29 = 173.5(6)^\circ$ and $C20-C21-C22-C23 = -176.5(4)^\circ$, indicating a(+) Anti-periplanar and (-) Anti-periplanar conformation for this group. Atoms O1 and O2 deviated from the respective two phenyl rings by -0.012 \AA and -0.061 \AA , respectively.

In the crystal, molecules are linked by C---H...N hydrogen bond to form chains propagating along the b axis direction. The crystal packing is further stabilizing by C---H...Cl intermolecular interactions. The chains are linked by slipped parallel $\pi \dots \pi$ interactions, involving inversion related chloromethylphenoxy methyl rings, forming slabs parallel to the bc plane $Cg^4-Cg^1 = 3.903 \text{ \AA}$, inter-planar distance = $-3.5087(15) \text{ \AA}$, slippage = 1.708 \AA Cg^4 is the centroid of ring (C2-C3-C4-C6-C7-C8). The selected bond lengths and angles are listed in table 3 and 4, respectively.

Table 2: Hydrogen-bond geometry [\AA]

Distance (\AA)				Angle ($^\circ$)
D—H...A	D—H	H...A	D...A	D—H...A
C9---H9A...N6	0.97	2.51	3.382(4)	149
C39---H39...Cl2	0.93	2.79	3.715(3)	170

Symmetry code: i. x, y, 1+z, ii. x,1+y,-1+z

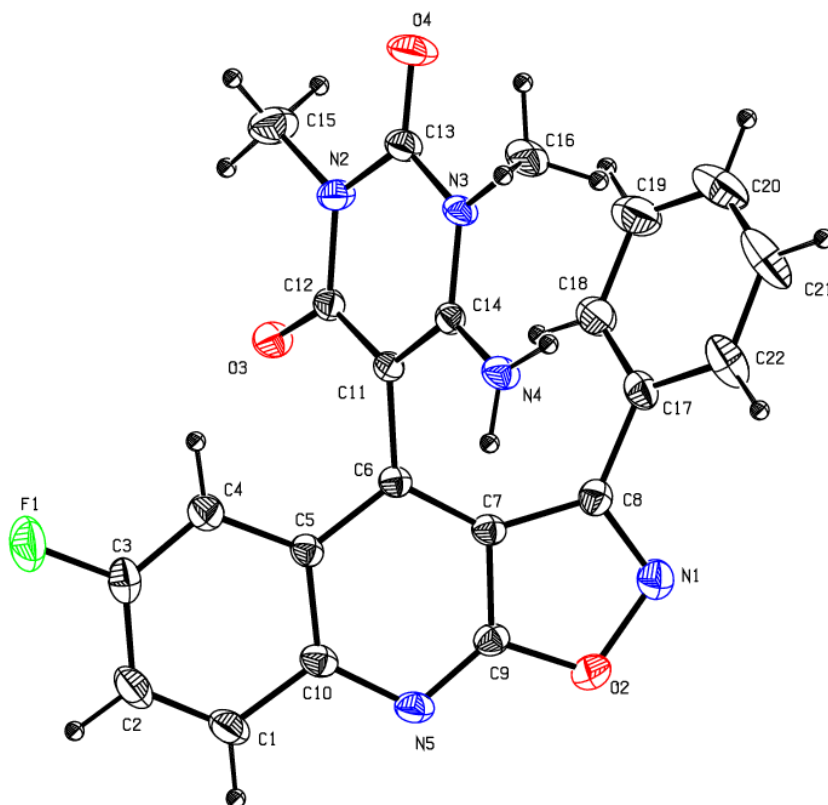


Fig.1. The molecular structure of the title compound, with the atom-numbering scheme. The displacement ellipsoids are drawn at 30% probability level. H atoms are shown as spheres of arbitrary radius.

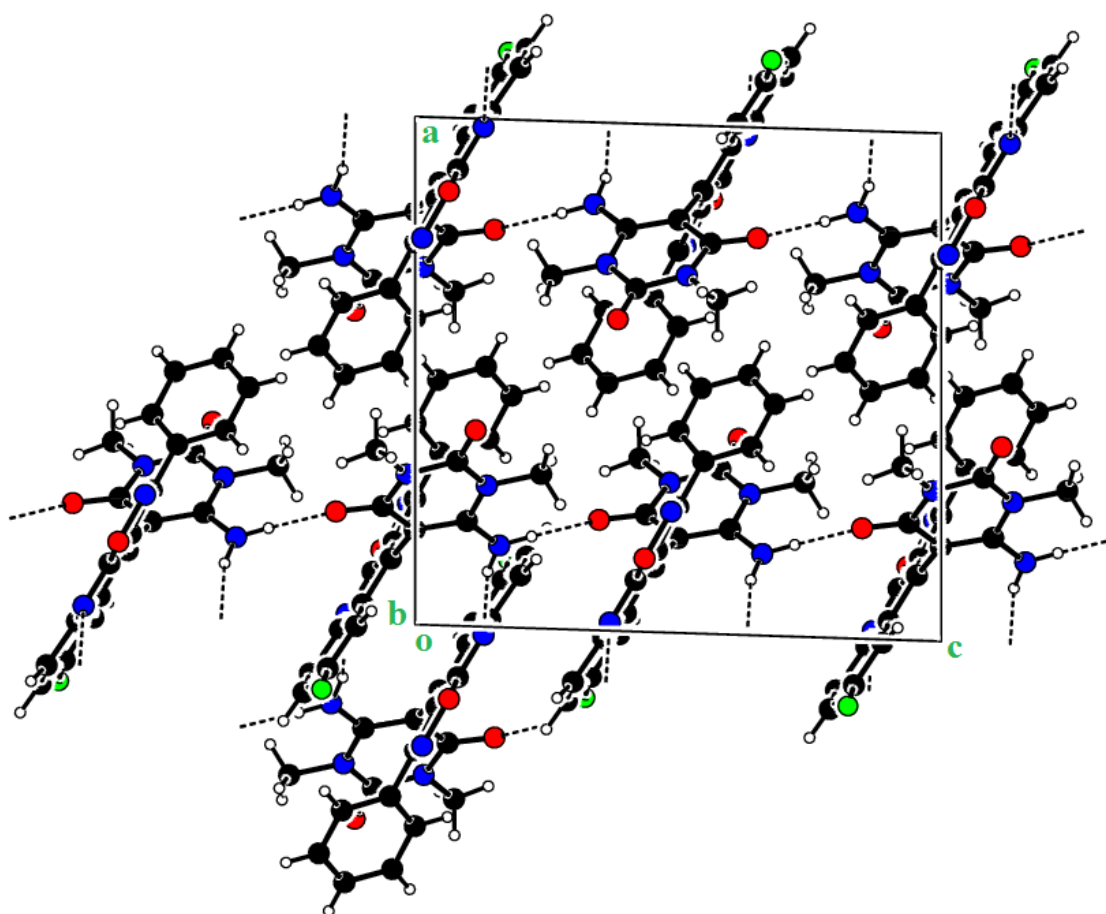


Fig.2. The crystal packing of the title compound, viewed along b axis, showing C---H...N hydrogen bonds. The hydrogen bonds are shown as dashed lines (see Table 2 for details).

Table 3: Selected Bond lengths (Å) Table 4: Selected Bond angles (°)

Bond	Length (Å)	Bond	Angle (°)
C(1)-C(2)	1.349(3)	C(2)-C(1)-C(10)	120.68(17)
C(1)-C(10)	1.416(2)	C(1)-C(2)-C(3)	119.15(16)
C(2)-C(3)	1.390(3)	C(4)-C(3)-F(1)	118.74(17)
C(3)-C(4)	1.346(2)	C(4)-C(3)-C(2)	123.64(17)
C(3)-F(1)	1.361(2)	F(1)-C(3)-C(2)	117.62(15)
C(4)-C(5)	1.419(2)	C(3)-C(4)-C(5)	118.82(16)
C(5)-C(6)	1.422(2)	C(4)-C(5)-C(6)	121.54(14)
C(5)-C(10)	1.426(2)	C(4)-C(5)-C(10)	118.43(14)
C(6)-C(7)	1.384(2)	C(6)-C(5)-C(10)	120.02(14)
C(6)-C(11)	1.478(2)	C(7)-C(6)-C(5)	115.25(13)
C(7)-C(9)	1.398(2)	C(7)-C(6)-C(11)	121.50(13)
C(7)-C(8)	1.443(2)	C(5)-C(6)-C(11)	123.24(14)
C(8)-N(1)	1.309(2)	C(6)-C(7)-C(9)	119.14(14)
C(8)-C(17)	1.478(2)	C(6)-C(7)-C(8)	137.13(14)
C(9)-N(5)	1.3039(19)	C(9)-C(7)-C(8)	103.73(14)
C(9)-O(2)	1.3613(19)	N(1)-C(8)-C(7)	111.07(14)

C(10)-N(5)	1.373(2)	N(1)-C(8)-C(17)	119.34(14)
C(11)-C(14)	1.3924(18)	C(7)-C(8)-C(17)	129.56(15)
C(11)-C(12)	1.413(2)	N(5)-C(9)-O(2)	121.08(14)
C(12)-O(3)	1.2390(16)	N(5)-C(9)-C(7)	128.71(15)
C(12)-N(2)	1.3971(19)	O(2)-C(9)-C(7)	110.20(14)
C(13)-O(4)	1.2111(18)	N(5)-C(10)-C(1)	117.48(15)
C(13)-N(2)	1.3755(18)	N(5)-C(10)-C(5)	123.34(14)
C(13)-N(3)	1.390(2)	C(1)-C(10)-C(5)	119.17(16)
C(14)-N(4)	1.331(2)	C(14)-C(11)-C(12)	120.18(13)
C(14)-N(3)	1.3719(18)	C(14)-C(11)-C(6)	120.60(13)
C(15)-N(2)	1.465(2)	C(12)-C(11)-C(6)	118.79(12)
C(16)-N(3)	1.4597(17)	O(3)-C(12)-N(2)	118.53(13)
C(17)-C(22)	1.380(2)	O(3)-C(12)-C(11)	124.90(14)
C(17)-C(18)	1.383(2)	N(2)-C(12)-C(11)	116.57(12)
C(18)-C(19)	1.373(2)	O(4)-C(13)-N(2)	122.02(15)
C(19)-C(20)	1.361(3)	O(4)-C(13)-N(3)	121.63(13)

Conclusion

The crystal structure analysis of a novel quinolone compound was studied using x-ray diffraction method. In the crystal, molecules are linked via C---H...N hydrogen bonds, forms chains. The crystal packing is further stabilized by C---H... π and π --- π intermolecular interactions.

Acknowledgments

The authors thank the Department of chemistry, IIT, Chennai, India, for X-ray intensity data collection.

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