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Synthesis and Crystal Structure of 4-(N, N-Dimethylphenyl)-N3-(6-Fluorophenyl)-N5-(2,6-Fluorophenyl)-2,6-Dimethyl-Pyridine-3,5-Dicarboxamide Using Hirshfeld Surface Analysis

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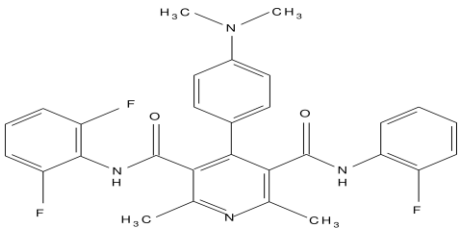
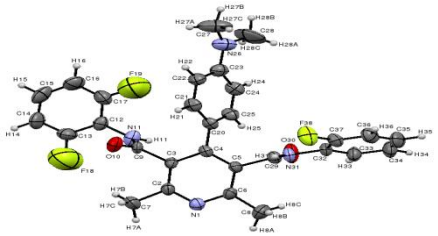
ABSTRACT

The title compound, $C_{29}H_{25}F_3N_4O_2$, crystallizes in the triclinic crystal system and space group P-1 with cell parameters a=9.918(3)Å, b=11.332(6)Å, c = 12.730(6)Å, α=77.838(12)°, β = 70.42(3)°, γ=75.68(3)°, V = 1293.3(10)Å^3 for Z = 2. The structure exhibits inter-molecular hydrogen bonds of the type N—H...O.

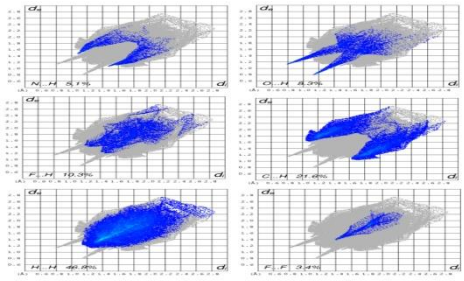
Graphical Abstract



The Schematic diagram of the compound



The ORTEP diagram of the compound



Fingerprint plot of the title compound.

Keywords: Pyridine, crystal structure, hydrogen bond, Hirshfeld surface analysis.

INTRODUCTION

Pyridine used as a precursor to agrochemicals and pharmaceutical is a simple aromatic heterocyclic organic compound. Structurally related to benzene, wherein one CH group in the aromatic six-membered ring is replaced by a nitrogen atom. Pyridines and some pyridine fused ring systems have attracted great attention as potential chemotherapeutic agents [1-7]. Pyridine acts as reagent for detection of acid on paper chromatograms [8]. It is also used as a solvent or intermediary in numerous industries including producing piperidine, rubber products, polycarbonate resins, medicines, vitamins, food flavorings, herbicides, pesticides, explosives, paints, dyes, adhesives and waterproofing for fabrics, antihistamine steroids, sulfa antibiotics. With this background, the title compound was synthesized and characterized. The study of X-ray diffraction and Hirshfeld surface analysis along with fingerprint plots confirm the structure of the compound and nature of the intermolecular interactions respectively.

MATERIALS AND METHODS

Synthesis and Method of Crystallization: Acetoacetanilide (0.02mol) and N,N-dimethyl benzaldehyde (0.01mol) were dissolved in 25 mL methanol and heated on water bath till the solid disappeared in the reaction mass. Concentrated ammonia (3 mL) was added to the reaction and was further refluxed on a water bath for a period of 10-12 h. The completion was monitored by TLC (Merck 60 F_{254}). After completion of reaction it was allowed to come to room temperature and solid mass appeared in the flask. The product was filtered and washed with ether. It was recrystallized from Ethanol + Acetone.

4-(N,N-dimethylphenyl)-N3, N5-bis (2-fluorophenyl)-2, 6-dimethyl-1,4-dihydropyridine-3, 5-dicarboxa mide (2.5 g) was taken in 30 mL solvent mixture [Ethanol+DMF(7.5:2.5)]. 1 g of charcoal was added and heated on a heating device for 6 min. The solution was filtered while hot through Whatman 41 filter paper. The solution was kept in a stopper conical flask slightly opened. The crystals were grown by thin film evaporation. The compound was synthesized and crystalized as dihydropyridine, but due to aromatization, dihydropyridine loses the proton and converts into pyridine structure.

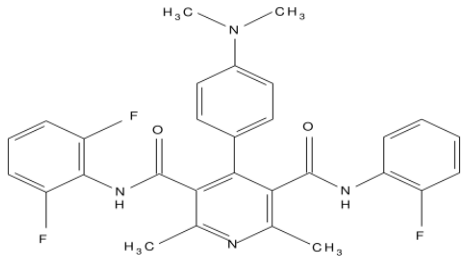


Fig 1. The Schematic diagram of the compound

Table 1. Crystal data and structure refinement table

CCDC	1578868
Empirical formula	$C_{29}H_{25}F_3N_4O_2$
Formula weight	518.53
Temperature	293(2)K
Wavelength	0.71073Å
Crystal system	Triclinic
Space group	P -1

Cell dimensions	a= 9.918(3)Å b= 11.332(6)Å c= 12.730(6)Å α=77.838(12)° β= 70.42(3)° γ=75.68(3)°
Volume	1293.3(10)Å^3
Z	2
Density(calculated)	1.332 Mg/m^3
Absorption coefficient	0.100 mm^{-1}
F_{000}	540
Crystal size	0.3 x 0.25 x 0.25 mm
Theta range for data collection	2.36° to 24.99°
Index ranges	−10≤ h≤ 10 -11≤ k≤ 11 -15≤ l≤ 15
Reflections collected	3941
Independent reflections	3007[R_{int} = 0.0572]
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3007 / 0 / 348
Goodness-of-fit on F^2	1.840
Final R indices [I>2 σ(I)]	R1 = 0.1098, wR2 =0.2776
R indices (all data)	R1 = 0.1669, wR2 = 0.3249
Extinction coefficient	0.043(12)
Largest diff. peak and hole	0.453 and -0.523 e.Å^{-3}

RESULTS AND DISCUSSION

Crystal Structure Determination: A single crystal of the title compound with dimensions 0.30x0.25x0.25 mm was chosen for the X-ray diffraction study. The data were collected on a DIP Labo Image Plate system equipped with a normal focus, 3 kW sealed X-ray source (graphite monochromated MoK_α). The crystal to detector distance was fixed at 120 mm with the detector area of 441 x 240 mm^2. Thirty six frames of data were collected at room temperature by the oscillation method. Each exposure of the image plate was set to 400s. Successive frames were scanned in steps of 5° min^{-1} with an oscillation range of 5°. Image processing and data reduction were done using Denzo [9]. The reflections were merged with Scalepack [10]. All the frames could be indexed using a triclinic lattice. Absorption correction was not applied. The structure was solved by direct methods using SHELXS-97 [11]. Least-squares refinement using SHELXL-97 [11] with isotropic temperature factors for all the non-hydrogen atoms converged the residual R1 to 0.1669. Subsequent refinements were carried out with anisotropic thermal parameters for non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms which were placed at chemically acceptable positions. The hydrogen atoms were allowed to ride on their parent atoms. After eight cycles of refinement the residual converged to 0.1098. The details of crystal data and refinement are given in table 1. Table 2 gives the list of selected bond lengths and bond angles respectively which are in good agreement with the standard values. The ORTEP of the molecule with thermal ellipsoids is shown in Fig. 2.

Table 2. Selected bond lengths and bond angles (Å)

Atoms	Length	Atoms	Angle
C9-O10	1.228(7)	O10-C9-N11	121.6(5)
C13-F18	1.313(1)	F18-C13-C12	117.1(8)
C17-F19	1.260(9)	F19-C17-C16	118.7(8)
C23-N26	1.400(9)	C22-C23-N26	121.8(7)
C27-N26	1.436(1)	O30-C29-N31	123.4(5)
C29-030	1.223(8)	N31-C32-C33	123.4(5)
N31-C32	1.409(7)	F38-C37-C36	119.4(6)
C37-F38	1.354(7)	F38-C37-C32	116.7(5)

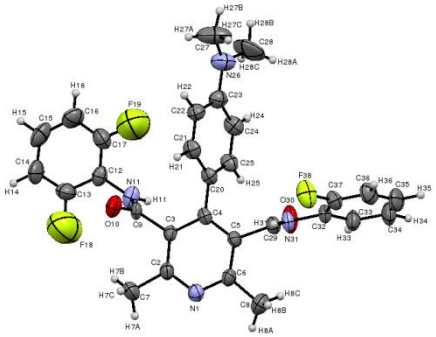


Figure 2. The ORTEP diagram of the compound

The dihedral angles between the least squares planes of pyridine ring and phenyl rings bridged by C-N groups are 9.9(4)° and 77.1(3)° respectively, while that of pyridine and phenyl ring is 58.4(3)°. The atom C20 deviates from Cremer and Pople's plane by 0.021(7)Å, defined by C20-C21-C22-C23-C24-C25. The torsion angles about C12-N11-C9-C3 and C32-N31-C29-C5 are 178.2(5)° and 171.3(6)° respectively, give *anti-periplanar* conformation and C3-C4-C20-C25 give *-anti-clinal* conformation for torsion angle being -119.3(7)°.

Table 3. Selected Torsion Angles (deg)

Atoms	Torsion Angles	Atoms	Torsion Angles
N1-C2-C3-C9	179.1(6)	C4-C3-C9-O10	-112.1(7)
C4-C5-C29-O30	-82.0(9)	C5-C4-C20-C21	-125.5(7)
C17-C12-C13-F18	-170.1(9)	C29-C5-C6-N1	-178.5(7)
N31-C32-C37-F38	-2.3(9)		

The molecule exhibits inter-molecular hydrogen bonds of the type N-H...O. N11-H11...O30 and N31-H31...O10, have lengths of 2.827(9)Å and 2.944(8) Å with angles of 149° and 163°, respectively, with symmetry codes *-x,1-y, -z* and *1-x,1-y, -z*. Packing of the molecules down *b* axis shown in Fig. 3.

Table 4. Hydrogen bond geometry (Å, deg.)

D-H...A	D-H	H...A	D...A (Å)	D-H...A (°)
N11-H11-O30	0.86	2.05	2.827(9)	149
N31-H31-O10	0.86	2.04	2.944(8)	163

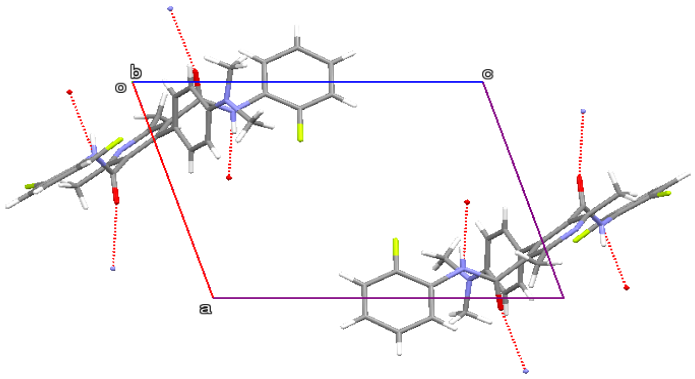


Figure 3. The packing view of the molecules down the b axis. The red lines indicate hydrogen bonds.

Hirshfeld Surface Analysis: The intermolecular interaction of the title compound is quantified using Hirshfeld surface analysis [12-13]. The shape of the Hirshfeld surface is characteristic of the molecule and its crystalline environment.

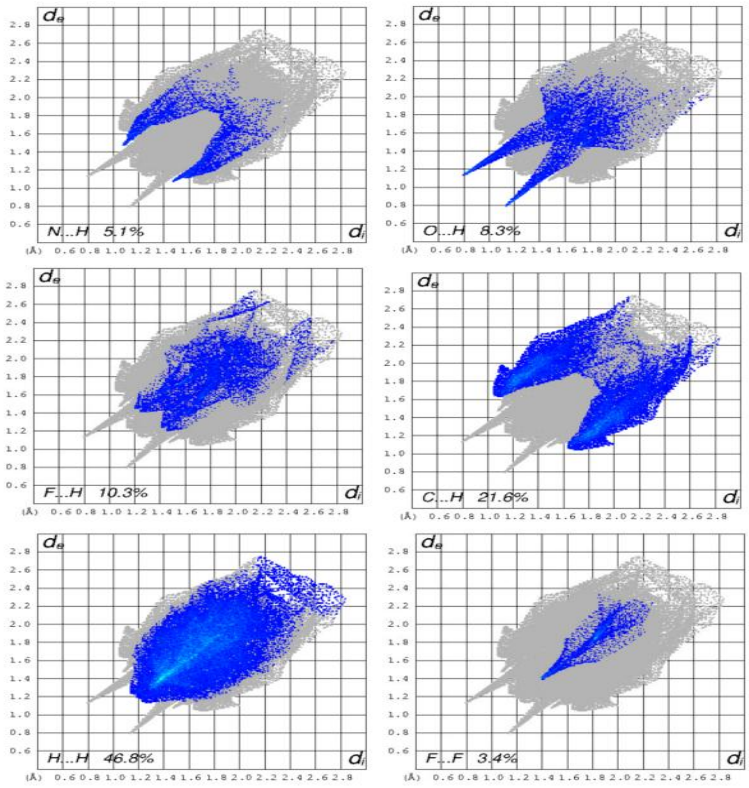


Figure 4. Fingerprint plot of the title compound

The distances $d_{e,}$ is the closest external contacts with percentage of various intermolecular contacts and $d_{i,}$ the closest internal distance from given point on the Hirshfeld surface mapped provide a three-dimensional picture of intermolecular close contacts in a crystal. They are also used to generate a fingerprint plot Fig 4, a concise two-dimensional summary of intermolecular interactions and the relative contributions to the Hirshfeld surface (in percentage) for major intermolecular contacts associated with the title compound. The contribution of the intercontacts to the Hirshfeld surfaces are, N...H (5.1%), O...H (8.3%), F...H (10.3

%), C...H (21.6%), H...H (46.8%), F...F (3.4%), and others (4.5%). These intercontacts are highlighted by conventional mapping of d_{norm} on molecular Hirshfeld surfaces are shown in fig. 5. The red spots over the surface indicate the intercontacts involved in hydrogen bond, while H...H bonding is the major contributor in crystal packing. In fig. 5, the shape index and curvedness shows characteristic packing arrangement and the ways in which adjacent molecules contact one another. The shape index surface clearly shows that the two sides of the molecules are involved in same contacts with neighboring molecules and curvedness plots show flat surface patches characteristic of planar stacking.

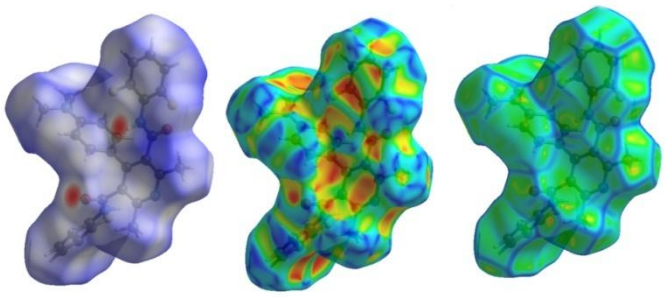


Figure 5. d_{norm},shape index and curvedness mapped on Hirshfeld surface.

APPLICATIONS

Literature survey shows that the pyridine derivatives have numerous applications. This research work is useful for the creation of a library. Whenever there is a need for molecule with these properties, we can make use of the title compound.

CONCLUSIONS

The present work helps us to understand the molecular structure and the intermolecular interactions of the synthesized compound. The structure was confirmed by, X-ray diffraction. Further, from the Hirshfeld surface analysis and its associated fingerprint plot, it can be concluded that the major contribution to the total surface area is from H...H interactions.

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