*Available online at* www.joac.info

ISSN: 2278-1862

**Journal of Applicable Chemistry**

2016, 5 (5): 1113-1119

(International Peer Reviewed Journal)

# Synthesis and Crystal structure of 4-(3-chlorophenyl)-N3, N5-bis (2,6-fluorophenyl)-2,6-dimethyl-pyridine-3,5-dicarboxamide using Hirshfeld Surface Analysis

**S. Neetha[1*], Arun Mishra[2], M. A. Sridhar[3], J. Shashidhara Prasad [3] and Anamik Shah[2]**

1. Department of Physics, The National Institute of Engineering, Mysuru, **INDIA**
2. Department of Studies in Chemistry, Saurashtra University, Rajkot, **INDIA**
3. Department of Studies in Physics, University of Mysore, Mysuru, **INDIA**

Email: neethagowda@gmail.com

Accepted on 17th September 2016

## ABSTRACT

*The title compound, $C_{27}H_{20}ClF_2N_3O_2$, crystallizes in the monoclinic crystal system and space group $P2_1/a$ with cell parameters a = 10.0610(11) Å, b = 11.012(2) Å, c = 22.402(5) Å, β = 102.731°, V = 2420.0(8) Å$^3$ for Z = 4. The structure exhibits inter-molecular hydrogen bonds of the type N—H...O.*

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

## INTRODUCTION

Pyridine is a simple aromatic heterocyclic organic compound used as a precursor to agrochemicals and pharmaceutical. It is structurally related to benzene, wherein one CH group in the aromatic six-membered ring is replaced by a nitrogen atom. The pyridine ring occurs in many important compounds, including nicotinamides. 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. In addition it is a denaturant for antifreeze mixtures and is sometimes used as a ligand in coordination chemistry. 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 (0.02 mol), 4-methoxybenzaldehyde (0.01 mol) 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 it was further refluxed on a water bath for a period of 10--12 h. The completion was monitored by TLC (Merck $60F_{254}$). A solid mass was

obtained. The product was then filtered and washed with ether. It was recrystalized from Ethanol + Acetone. 4-(3-chloro phenyl)-N3, N5-bis (2-fluoro phenyl)-2,6-dimethyl-1,4-dihydro pyridine-3, 5-dicarboxamide (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 crystallized as dihydropyridine, but due to aromatization, dihydropyridine loses the proton and converts into pyridine structure. The Schematic diagram of the synthesized compound is shown in fig.1.

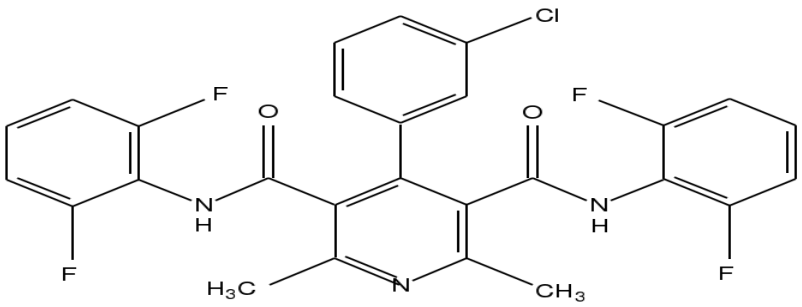


**Fig 1.** The Schematic diagram of the compound

## 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 DIPLabo Image Plate system equipped with a normal focus, 3 kW sealed X-ray source (graphite monochromated $MoK_{\alpha}$). 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° per minute 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 monoclinic 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 converge the residual R1 to 0.1298. 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 0.0962. The details of crystal data and refinement are given in Table 1.

**Table 1.** Crystal data and structure refinement table

| | |
|---|---|
| CCDC | 691262 |
| Empirical formula | $C_{27}H_{18}ClF_4N_3O_2$ |
| Formula weight | 527.89 |
| Temperature | 293(2)K |
| Wavelength | 0.71073Å |
| Crystal system | Monoclinic |

| | |
|---|---|
| Space group | $P2_1/a$ |
| Cell dimensions | a= 10.0610(11)Å<br>b= 11.012(2)Å<br>c= 22.402(5)Å<br>β = 102.731(11)° |
| Volume | 2420.9(8)Å$^3$ |
| Z | 4 |
| Density(calculated) | 1.448 Mg/m$^3$ |
| Absorption coefficient | 0.220 mm$^{-1}$ |
| $F_{000}$ | 1080 |
| Crystal size | 0.3 x 0.25 x 0.25 mm |
| Theta range for data collection | 2.07° to 24.99° |
| Index ranges | −10≤ h≤ 10<br>-11≤ k≤ 11<br>-26≤ l≤ 26 |
| Reflections collected | 6075 |
| Independent reflections | 3475[$R_{int}$ = 0.0385] |
| Absorption correction | None |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3475 / 0 / 337 |
| Goodness-of-fit on $F^2$ | 1.081 |
| Final R indices [I>2 σ(I)] | R1 = 0.0962, wR2 =0.2754 |
| R indices (all data) | R1 = 0.1298, wR2 = 0.3088 |
| Extinction coefficient | 0.018(4) |
| Largest diff. peak and hole | 0.677 and -0.728 e.Å$^{-3}$ |

Table2 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 | 1.218(5) | O10-C9-N11 | 124.6(4) |
| C13-F18 | 1.287(9) | F18-C13-C12 | 119.2(6) |
| C17-F19 | 1.236(1) | F19-C17-C16 | 117.4(8) |
| C22-Cl26 | 1.730(5) | C21-C22-Cl26 | 118.9(4) |
| C27-O28 | 1.217(5) | O28-C27-N29 | 124.4(4) |
| N29-C30 | 1.428(6) | N29-C27-C5 | 113.2(4) |
| C31-F36 | 1.259(1) | F36-C31-C30 | 117.9(6) |
| C35-F37 | 1.292(8) | F37-C35-C30 | 120.0(5) |

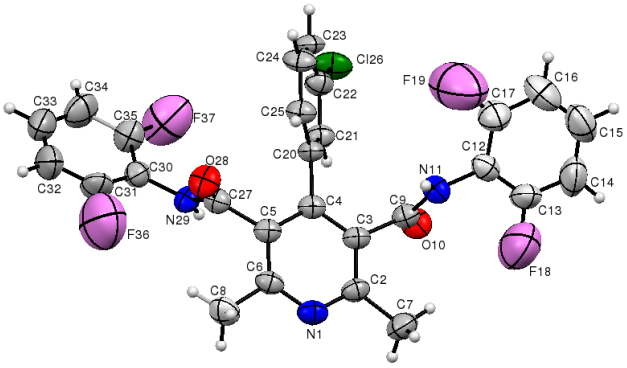


**Figure 2.** The ORTEP diagram of compound

The dihedral angles between the least squares planes of pyridine ring and phenyl rings bridged by C-N groups are 24.5(3)° and 29.0(3)° respectively, while that of pyridine and the phenyl ring is 59.9(2)°. The pyridine ring is planar. The atom C14 deviates from Cremer and Pople plane by 0.021(9)Å, defined by C12-C13-C14-C15-C16-C17. The torsion angles about C30-N29-C27-C5 and C3-C9-N11-C12 are 178.6(4)° and 177.6(4)° respectively, give *anti-periplanar* conformation. The torsion angle about C3-C4-C20-C21 being 60.2(6)° gives *syn-clinal* conformation (Table 3)

**Table 3.** Selected Torsion Angles (deg)

| Atoms | Torsion Angles | Atoms | Torsion Angles |
|---|---|---|---|
| N1-C2-C3-C9 | -179.3(4) | C4-C3C9-O10 | -98.0(5) |
| C4-C5-C27-O28 | -98.2(6) | C5-C4-C20-C21 | -119.8(5) |
| C5-C4-C20-C21 | -119.8(5) | C13-C12-C17-F19 | 174.8(7) |
| C17-C12-C13-F18 | -179.4(7) | C27-C5-C6-N1 | 177.5(4) |
| C31-C30-C35-F37 | 176.5(6) | C35-C30-C31-F36 | 179.0(7) |

The molecule exhibits inter-molecular hydrogen bonds of the type N-H..O. N11-H11..O10 and N29-H29..O28, have lengths of 2.886(5)Å and 2.860(5)Å with angles of 165° and 160°, respectively with symmetry codes *1/2+x,1/2-y, z* and *-1/2+x,1/2-y, z*. Packing of the molecules down *b* axis shown in fig. 3.

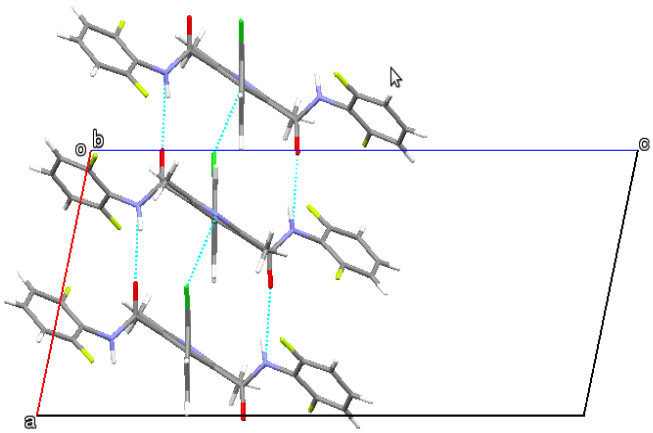


**Figure 3.** The packing view of the molecules down the b axis. The cyan lines indicate hydrogen bonds

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

| D-H...A | D-H | H...A | D...A (Å) | D-H...A (°) |
|---|---|---|---|---|
| N11-H11-O10 | 0.86 | 2.05 | 2.886(5) | 165 |
| N29-H29-O28 | 0.86 | 2.04 | 2.860(5) | 160 |

**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.

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, H...H (31%), F...H (18.5 %), C...H (16.2%), H...O (10.2%), H...Cl (9.8%), N...H (3.5%) and others (10.8%). 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.

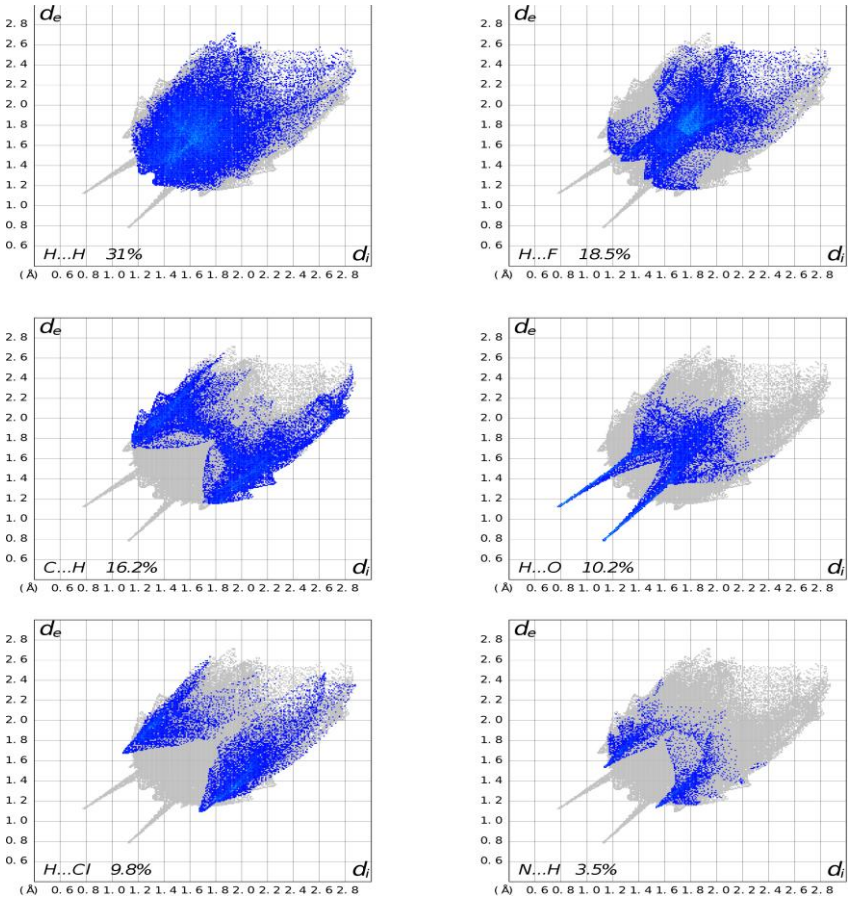


**Figure 4:** Fingerprint plot of the title compound

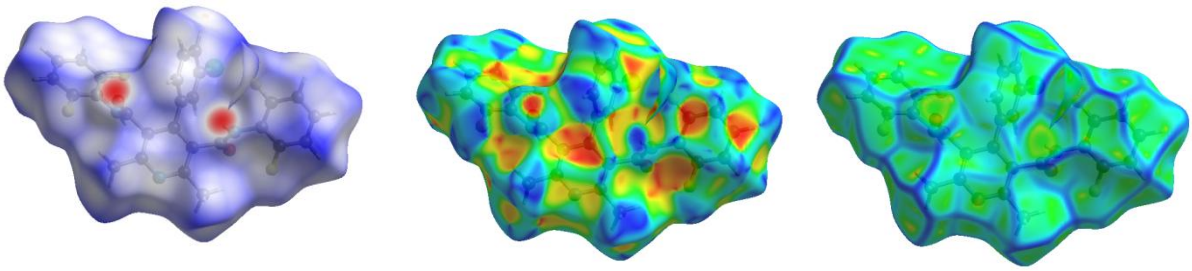

**Figure 5:** $d_{norm}$, shape index and curvedness mapped on Hirshfeld surface.

## 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.

## ACKNOWLEDGEMENTS

The authors would like to thank Department of Studies in Physics, Manasagangotri, University of Mysore, Mysuru and Department of Chemistry, Saurashtra University, Rajkot for providing the laboratory facility.

## REFERENCES

[1] K. Poreba, A. Opolski, J. Wietrzyk, M. Kowalska, *Arch. Pharm.*, **2001,** 334, 219–223.
[2] A. Gangjee, O. Adaira, S. F. Queener, *Bioorg Med. Chem.*, **2001,** 9, 2929–2935.
[3] A. Perez-Rebolledo, J. D. Ayala, G. M. de Lima, N. Marchini et al., *Eur. J. Med. Chem.*, **2005,** 40, 467- 472.
[4] X. Liu, M. L. Go, *Bioorg. Med. CHem*, **2006,** 14, 153–163.
[5] S. Huang, R. Lin, Y. Yu, Y. Lu, et al., *Bioorg. Med. Chem. Lett.*, **2007,** 17, 1243–1245.
[6] A. Bazgira, M. M. Khannaposhtani, A. A. Soorki, *Bioorg. Med. Chem. Lett.*, **2008,** 18, 5800– 5803.
[7] V. Nair, G. Chi, Q. Shu, J. Julander, D. F. Smee, *Bioorg. Med. Chem. Lett.*, **2009,** 19, 1425–1427.
[8] J. Cerbulis, M. W. Taylor, *Anal. Chem.*, **1963,** 35(1), 114.
[9] Z. Otwinowski et al. in *Methods in Enzymology*, 276, C.W. Carter Jr., R.M. Sweet (Eds), p. 307, Academic Press, New York, **1997**.
[10] S. Mackay et al. *maXus Computer Program for the Solution and Refinement of Crystal Structures*, Bruker Nonius, The Netherlands, **1999**.
[11] G.M. Sheldrick, SHELXS97 and SHELXL97, *Program for Crystal Structure Solution*. Germany; University of Gö ttingen, **1997**.
[12] S. K. Wolff, D. J. Grimwood, J. J. McKinnon, D. Jayatilaka and M. A. Spackamn, Crystal Explorer 3.0, University of Westren Australia, Perth, **2007**.
[13] N. Latha Rani, C.S. Karthik, P. Mallu, L. Mallesha, M.A. Sridhar. Synthesis, Crystal Structure and Hirshfeld Study of 3, 3'-dinitrobenzophenone, *J. Applicable Chem*, **2016**, 5(1), 231-241.

## AUTHORS' ADDRESSES

1. **Dr. Neetha S**
Assistant Professor, Department of Physics,
The National Institute of Engineering, Mysuru 570 011, India.
Email: neethagowda@gmail.com
2. **Dr. Arun Mishra**
Department of Studies in Chemistry,
Saurashtra University, Rajkot, India,
Ph: 91-281-2581013
3. **Dr. M.A. Sridhar**
Professor, Department of Studies in Physics,
University of Mysuru, Mysuru 570 006, India
Email: mas@physics.uni-mysore.ac.in, 0821-2419333
4. **Dr. J. Shashidhara Prasad**
Former Vice-Chancellor,
University of Mysore, Mysuru 570 006, India
Email: jsp@physics.uni-mysore.ac.in, 0821-2419333
5. **Dr. Anamik Shah**
Professor, Department of Studies in Chemistry,
Saurashtra University, Rajkot, India
Email: anamik_shah@hotmail.com, 91-281-2581013