Single crystal X-ray diffraction signature, Hirshfeld surface analysis and global reactivity parameters of 3,5-dichloropyridin-4-amine

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Abstract - The title compound 3,5-dichloropyridin-4-amine (DCPA) was purchased from commercial source; single crystals were grown at room temperature by slow evaporation in methanol as solvent and solid state structure authenticated by spectroscopic signature like SCXRD technique. 3,5-dichloropyridin-4-amine (DCPA) crystallizes in the orthorhombic with space group *Pna2₁*, *a* =13.3133(9) Å, *b* = 12.9286(11) Å, *c* = 3.8678(3) Å and *α* = *β* = *γ* =90°Volume/Å^3 = 665.73(9), Z = 4. The crystal structure displays one dimensional supramolecular architecture featuring C(6) chains of N_2-H_3…N_1 hydrogen bonds running parallel to [0 1 -1]. The qualitative and quantitative analysis of intermolecular interactions in solid state DCPA was performed with assistance of 3D-Hirshfeld surfaces and 2D-finger print plots along with single crystal X-ray analysis. Global reactivity parameters are calculated from energy difference between the HOMO and LUMO;the plots revealed that charge delocalization within molecule.

Keywords:3,5-dichloropyridin-4-amine, SCXRD, Hirshfeld surfaces, HOMO and LUMO energies.

I. INTRODUCTION

Pyridine scaffolds are key building blocks for agrochemicals, pharmaceutical compounds and are often part of biomolecules such as eponymous pyridine nucleotides and alkaloids. It is also widely used as solvent and reagent in industry. Halogen substituted scaffolds possesses benchmark in biological activities such as anticancer [1], antiviral [2], anti-tuberculosis [3], anti-malarial [4,5], antifungal agents and anti-diabetic agents [6].

From the above significance of pyridine motifs have motivated towards the crystallization, solid state structure authenticationas well as calculation of global reactivity parameters of 3,5-dichloropyridin-4-amine (DCPA) along with Hirshfeld surface and finger print analysis it would be more useful.

II. EXPERIMENTAL

3,5-dichloropyridin-4-amine was purchased from Alfa Aesar and suitable crystals were grown from methanol by slow evaporation at room temperature.

2.1 X-ray crystallography

A suitable prism shape crystal was selected and which is mounted on a Bruker APEX-II CCD diffractometer using graphite monochromated MoKa (λ = 0.71073 Å) radiation and CCD detector. The crystal data was collected at 296 K. The structure was solved using Olex2 software with the olex2.solve [7] structure solution program using Charge Flipping and the structure was refined with the ShelXL [8] refinement package using Least Squares minimization. All the non-hydrogen atoms were revealed in the first difference Fourier map itself and were refined anisotropically. All carbon bound H atoms were positioned geometrically, with C-H = 0.93 Å and refined using a riding model with $U_{iso}(H) = 1.2U_{eq}(C)$. The nitrogen bound H atoms were located in a difference map and were freely refined. All the geometrical calculations were carried out using the program PLATON [9] within the WinGX suite [10]. The molecular and packing diagrams were generated using the software MERCURY [11].The crystallographic data and refinement parameters are listed in Table 1.

2.2 Hirshfeld surface analysis

Crystal Explorer 3.1 [18] is a graphical tool which accepts CIF file as input file for the generation of 3D-Hirshfeld surfaces [12-14] and the related 2D fingerprint plots [15-17]are unique for every crystal structure. 3D-Hirshfeld surfaces and 2D fingerprint plots assist to identify the type and nature of packing of molecules in their solid-state. The d_{norm} surface mapped with rainbow colour scheme, bright red colour code denotes with-ve symbol (shows contacts shorter than the sum of van der Waals radii), +ve symbol mark with blue colour code represent longer than the sum of vander Waals radii and zero symbol mark as white color code signifies intermolecular distances close to van der Waals contacts.

III. RESULTS AND DISCUSSION

3.1 Crystal structure analysis

The molecular structure of 3,5-dichloropyridin-4-amine (DCPA) determined by SCXRD is depicted in Figure 1. The 3,5-dichloropyridin-4-amine (DCPA) molecule is almost planar (r.m.s. deviation for the non-H atoms = 0.006 Å), and, the crystal structure displays one dimensional supramolecular architecture featuring C(6) chains of N_2-H_3…N_1 hydrogen bonds (Table 2 and Figure 2) running parallel to [0 1 -1].

3.2 Hirshfeld surface analysis

The 3D-Hirshfeld surfaces and 2D-finger prints plots of DCPAsketch in Fig.3, illustrate d_{norm}(A), shape index (B) and curvedness (C) mapped over in the range of -0.454 (red) to 1.218 (blue) Å au, -1.0 (concave) to 1.0 Å au (convex) and -4.0 (flat) to 0.4 Å au (singular), respectively. The predominant interactions between the NH_2 group as well as the nitrogen of pyridine ring visualized as bright red spot marked as point A on d_{norm} surface(show in Fig.3) and those interactions are obviously seen in Fig.4. In the 2D fingerprint plots (Fig.5), the interaction of N-H···N look like two separate spikes noticeable as a and b almost equal lengths (Fig.5) are characteristics of nearly equal H(donor)···N(acceptor) distances and generate a one dimensional C(6) chains propagating along the [0 1 -1] direction. The upper spike (Fig.5) corresponds to the donor spike (H atom of NH_2 group interacting with N-atoms of the pyridine ring), with the lower spike being an acceptor spike (N-atoms of the pyridine ring interacting with H-atom of NH_2 group). The wings marked in Fig.5 (circled with black) are due to the Cl···H contacts. A significant difference in terms of H···H contacts appears as spikes (marked as red circles in Fig.5). The relative contribution of the different interactions to the Hirshfeld surface was calculated for DCPA. It is evident that the H···H contacts can account for about 15.9% of the Hirshfeld surface area; the remaining contribution was mostly due to N···H 13.1%, Cl···H 39.9%, H···C 7.4%, Cl···Cl 7.0% and C···C 6.7% interactions, with only minor contribution from other interactions.

IV. FRONTIER MOLECULAR ORBITAL ANALYSIS

HOMO-LUMO orbital calculations was performed with Tonto program implemented in Crystal Explorer 3.1 package by DFT method at Becke88LYP/6-31G(d) basic set. The diagrammatic representation of frontier orbitals shown in Figure 6, which reveals the HOMO (energy: 6.88 eV) is π nature is confirmed over the molecule and LUMO (energy: 1.01 eV) is localized over pyridine ring, partially on chloro groups except amino group, these revels that delocalization with in molecule and the HOMO-LUMO energy gap is 5.86 eV. The global chemical descriptors (which calculated from the energies of HOMO and LUMO's) associated with a molecular system are: ionization potential (I) = $-E_{HOMO}$= 6.88eV, electron affinity (A) = $-E_{LUMO}$= 1.01eV, chemical potential (μ) = -3.945eV, the global hardness (η) = 2.93eV,softness (ν)= 0.34eV, electronegativity (χ) = 3.945eV and electrophilicity index (ω) = 22.88eV[19, 20]. The measure of chemical potential is negative (-3.945eV) reflecting DCPA molecule stable.

V. CONCLUSION

Solid state structure of 3,5-dichloropyridin-4-amine (DCPA) has been characterized by single crystal X-ray diffraction technique. The X-ray diffraction studies shows that the title compound crystallizes in the orthorhombic with space group $Pna2_1$, Volume/$Å^3$ = 665.73(9), Z = 4, a =13.3133(9) Å, b = 12.9286(11) Å, c = 3.8678(3) Å and $\alpha = \beta = \gamma$ =90°. The crystal structure displays one dimensional supramolecular architecture featuring C(6) chains of N_2-H_3…N_1 hydrogen bonds running parallel to [0 1 -1].The qualitative and quantitative measure of intermolecular interactions for DCPA molecule also performed with grateful assistance of CrystalExplorer3.1 package while performing the 3D-Hirshfeld surface and 2D-fingerprint plots. The conclusion drawn from global reactivity parameters reflects DCPA is stable, those calculated from energy gap of HOMO and LUMO.

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SUPPLEMENTARY MATERIAL

The cif file of the title compound have been assigned CCDC number **1826125**and can be obtained free of cost on application to CCDC 12 Union Road, Cambridge CB21 EZ, UK. (Fax: (+44) 1223 336-033: e-mail: data_request@ccdc.cam.ac.uk).

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FIGURES

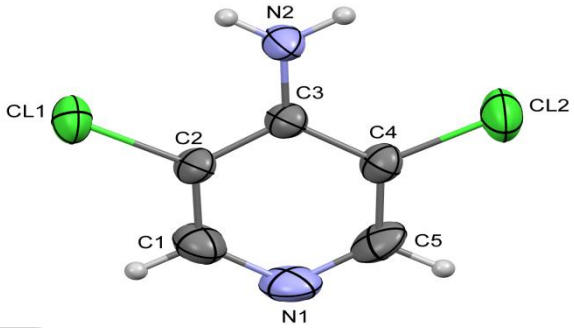

Figure 1: ORTEP view of the DCPA with atom numbering scheme for non-hydrogen atoms.

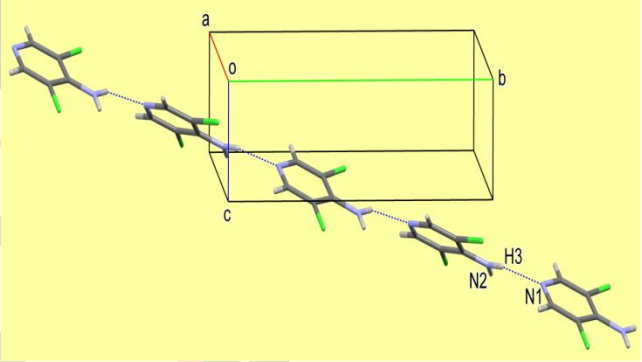

Figure 2. Crystal packing of DCPA.

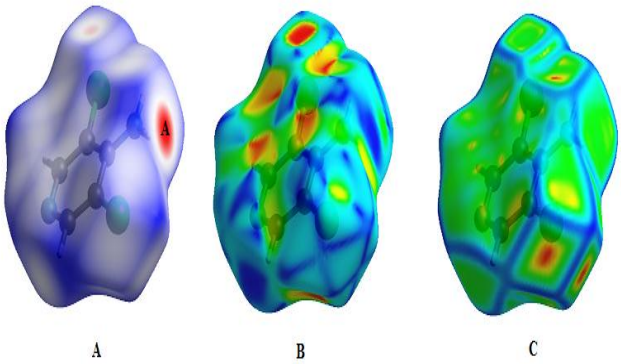

Figure 3. Hirshfeld surface of DCPA.

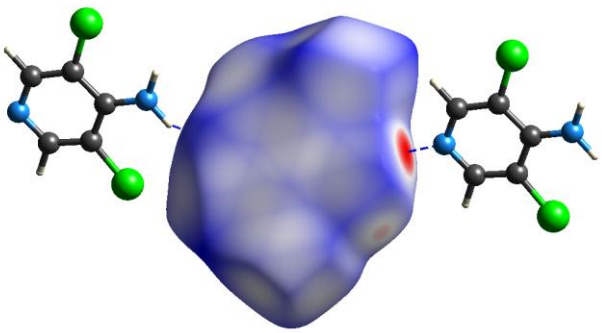

Figure 4. N-H---N intermolecular interactions mapped over d_{norm} surface

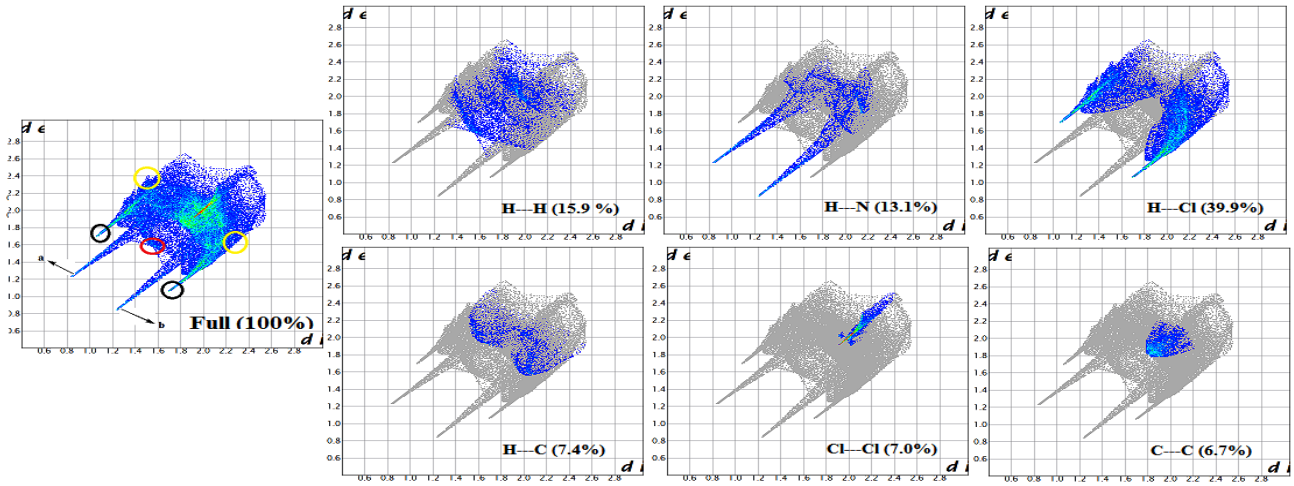

Figure 5. 2D finger plots of DCPA.

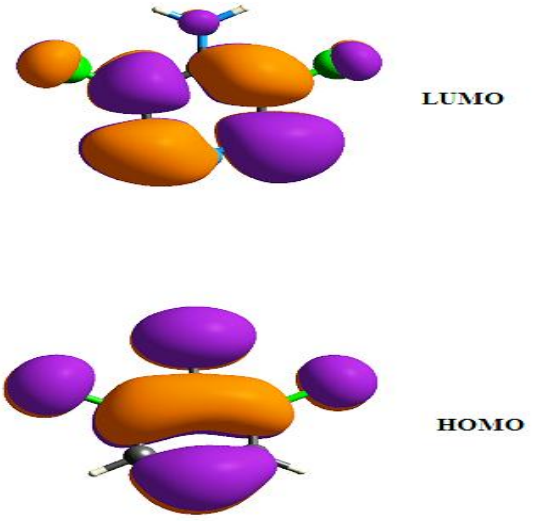

Figure 6. HOMO-LUMO plots of DCPA.

TABLES

Table 1 Crystal data and structure refinement for 3,5-dichloropyridin-4-amine (DCPA)

Empirical formula	$C_5H_4Cl_2N_2$
Formula weight	163.00
Temperature/K	296.15
Crystal system	orthorhombic
Space group	$Pna2_1$
a/Å	13.3133(9)
b/Å	12.9286(11)
c/Å	3.8678(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	665.73(9)
Z	4
ρ_{calc}g/cm^3	1.626
μ/mm^{-1}	0.874
F(000)	328.0
Crystal size/mm^3	0.27 × 0.25 × 0.22
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	6.12 to 52.72
Index ranges	-16 ≤ h ≤ 12, -6 ≤ k ≤ 16, -3 ≤ l ≤ 4
Reflections collected	1517
Independent reflections	985 [R_{int} = 0.0233, R_{sigma} = 0.0393]
Data/restraints/parameters	985/3/90
Goodness-of-fit on F^2	1.079
Final R indexes [I>=2σ (I)]	R_1 = 0.0462, wR_2 = 0.1155
Final R indexes [all data]	R_1 = 0.0521, wR_2 = 0.1232
Largest diff. peak/hole / e Å^{-3}	0.32/-0.47
Flack parameter	0.02(14)

Table 2 Hydrogen bond geometry in DCPA(Å, º)

D-H…A	D-H	H…A	D…A	D-H…A
N2-H3…N1^{i}	0.90	2.13	2.9351	148
i: 1/2-x,1/2+y,1/2+z				