STUDIES ON THE SYNTHESIS, STRUCTURAL CHARACTERIZATION, HIRSHFELD ANALYSISAND LIQUID CRYSTAL STUDY OF 5-PROPYLSULFANYL-1,3,4-THIADIAZOL-2-YLAMINE

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Abstract : Substituted 1,3,4-thiadiazoles named 5-Propylsulfanyl-1,3,4-thiadiazol-2-ylamine, have been synthesized , crystallized by solvothermal technique using autoclave and characterized by single crystal XRD, FT-IR, UV, elemental analysis, mass and 1H-NMR spectroscopy. The liquid crystalline phase studied using POM and to understand the intermolecular interactions and crystalline phase , Hirshfeld surface analysis was carried out. The compound has been crystallized in the triclinic crystal system in the $P\bar{1}$ space group . The geometrical parameters are a = 5.621(9) Å, b = 8.867(13) Å, c = 8.927(14) Å, α = 96.559 (14)°, β = 104.523(19)° , γ = 101.56(1)°, and Z =2. In the crystal structure cg-cg interactions are observed. Supramolecular architecture involves $R_2^2(8)$ graph-set motif.

IndexTerms **- Liquid crystal, Hirshfield, Single crystal XRD**

I. INTRODUCTION

Substituted 1,3,4-thiadiazoles exhibit a wide-ranging spectrum of biological activities including antioxidant[1], antimicrobial[2], antituberculosis[3], anti-inflammatory[4,5], anticonvulsants[6], antihypertensive[7-9], anticancer[10,11], antifungal activity[12]. antihepatitis B viral, antileishmanial, analgesic, antidiabetic, molluscicidal, diuretic, analgesic[13-17]. In that particularly 2-amino-5-sulfanyl-1,3,4-thiadiazole derivatives has effects on central nervous system[18] and acts as for antidepressant and anxiolytic agents[19]. The very familiar thiadiazole compound could be the acetazolamide; well-known carbonic anhydrase inhibitor, being used in treatment of glaucoma[20], high-altitude illness[21], epileptic seizures[22], idiopathic intracranial hypertension[23], hemiplegic migraine[24], cystinuria[25], obstructive sleep apnea[26], congenital myasthenic syndromes[27],etc.

Electron-deficient and good electron-accepting ability of 1,3,4-Thiadiazole reveals interesting electronic, optical and chemical properties. Thiadiazole core units formed nematic mesophases and possessed liquid crystalline properties [28,29]. Hence in current reserach, we included the investigation on liquid crystal property of synthesided molecule. Thiadiazole is an excellent candidate for organic bridging ligands to form functional coordination polymers. the polymeric metal-organic frameworks with a thiadiazole design exhibited applications in nonlinear optics, luminescence, electricity, magnetism, sorption, ion exchange, etc. [30,31]. 1,3,4-Thiadiazole-dithiolate/disulfide used as multidentate linkers or capacitance measurements in semiconductors[32,33] and as amperometric sensor [34,35].

Commonly, 1,3,4-thiadiazoles synthesized via general routes from cyclization of acylhydrazines with N,N′-diacylhydrazines and monoacylhydrazines. One-pot syntheses from acid hydrazides from using propylphosphonic anhydride(T_3P)[36], under microwave irradiation[37] ,by sulfur reagents like CS_2[38], isothiocyanate, dithiocarbamates [39], using phosphorus sulfides like P_2S_5 [40] and Lawesson's reagent were reported. Synthesis from thiohydrazines including thiosemicarbazides[41,42], dithiocarbazates, thioacylhydrazines, thiocarbazides, and bithioureas[43,44] were also reported. Transformation from 1,3,4-oxadiazoles,i.e., Replacement of −O− by −S− using thiocyanates or thiourea [45] viz. transformation of epoxides to episulfides is also remarkable.

II. Materials and methods

The chemical ingredients, viz., 5-amino-1,3,4-thiadiazole-2-thiol, 1-bromopropane, DMF and K_2CO_3 were obtained from Alfa-Aesar, India. The proposed structure of final compound was confirmed by ^{1}H-NMR spectra obtained using AGILENT (400 MHz) NMR spectrometer. FTIR spectra using Perkin-Elmer (model 337) USA. Mass spectral data by synapt *G2 HDMS* spectrometer using electron impact technique. Thin layer chromatography (TLC) was carried out on aluminum TLC plate (Silica gel 60). Elemental Analysis done by Perkin-Elmer (2400 Series II)

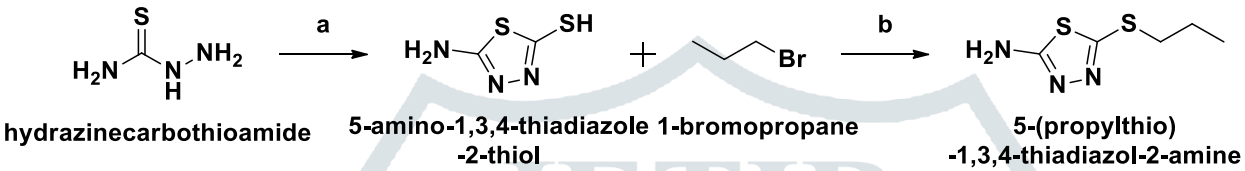
X-ray crystallography: A suitable crystal with approximate dimensions of 0.23 x 0.22 x 0.21 mm was used for X-ray diffraction study. X-ray intensity data were collected on Rigaku XtaLAB mini diffractometer equipped with Mo$K_\alpha$radiation of wavelength

0.71073 Å. The data collection was carried out for various settings of φ (0° - 90°) with scan width of 0.5°, 3s of exposure time. The sample to detector distance is about 50 mm. CrystalClear [46] program was used to process the entire data set. The crystal structure was solved using *SHELXS*-97 [47] and refinement against F^2 was carried out using *SHELXL*-97 [48] against F^2. A total of 92 parameters were refined with 1849 unique reflections which converges the residual factor to 0.0460. Geometrical calculations were done using *PLA*TON program [49]. Molecular graphics were generated by employing Mercury software [50].

III. Synthesis:

precursor thiosemicarbazide(4g,43.9mmol),CS_2 (4g,52.68mmol) and potassium hydroxide(36g, 65.85mmol) was refluxed in ethanol for about 8hours, then neutralize with con. HCl under stirring. The collected precipitate is purified using column chromatography to get desired product i.e., 5-Sulfanyl-1,3,4-thiadiazol-2-ylamine.

5-Sulfanyl-1,3,4-thiadiazol-2-ylamine (1g, 7.5mmol), 1-bromopropane (0.9ml, 7.5mmol) and potassium carbonate (3.1g,22.5mmol) was kept for reaction in DMF as solvent overnight . The reaction mixture was monitor by TLC by pet ether and ethyl acetate(2:1) as solvent mixture. After reaction completed water was added and crude product was precipitated. Then precipitate was washed with water and the obtained powdered precipitate is crystallized in autoclave using dmf as solvent . The fine pale yellow crystals were collected and characterized.



hydrazinecarbothioamide | 5-amino-1,3,4-thiadiazole -2-thiol | 1-bromopropane | 5-(propylthio) -1,3,4-thiadiazol-2-amine

(a)1) CS_2, KOH, EtOH, 75^{0}C , 8 h; 2) con. HCl, RT, 81%. (b)K_2CO_3, DMF, rt, overnight, 77%

scheme 1. synthesis of 5-(propylthio) -1,3,4-thiadiazol-2-amine

IV. Results and discussions

5-Propylsulfanyl-1,3,4-thiadiazol-2-ylamine . Yield: 77%; mp 117-119 °C; ^{1}H- NMR ($CDCl_3$, 400 MHz) δ 0.87 (t, 3H,CH3); 1.7 (m, 2H, CH2); 3.1 (t, 2H, SCH2); 5.1 (s, 2H, NH2).(**figure 1, figure 2**)

ESI–MS: m/z ,175.12 (**figure 3)**

CHN analysis; calculated for $C_5H_9N_3S_2$: C, 34.26; H, 5.18; N, 23.97; S, 36.59 obtained C, 34.06; H, 5.29; N, 24.32; S, 36.91

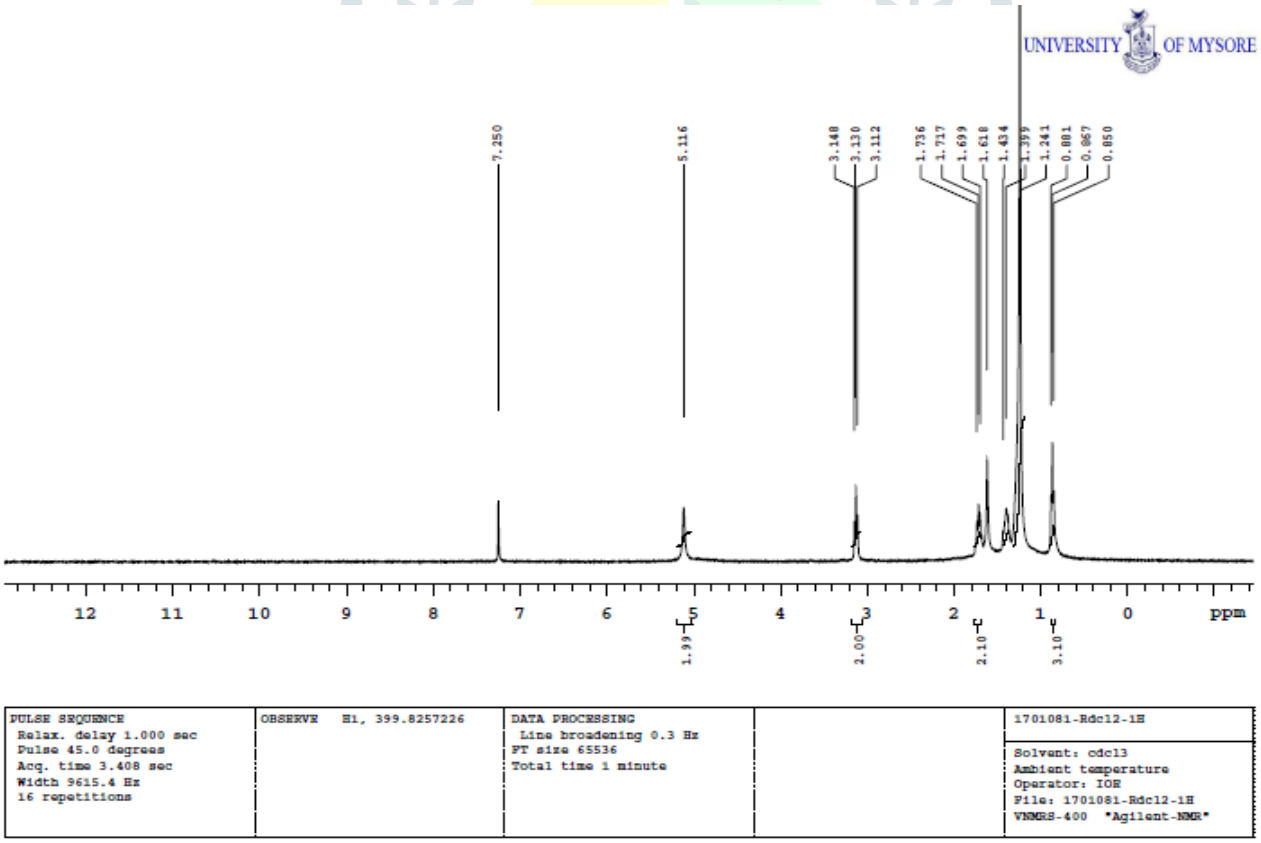


figure 1: ^{1}H- NMR spectra of 5-Propylsulfanyl-1,3,4-thiadiazol-2-ylamine

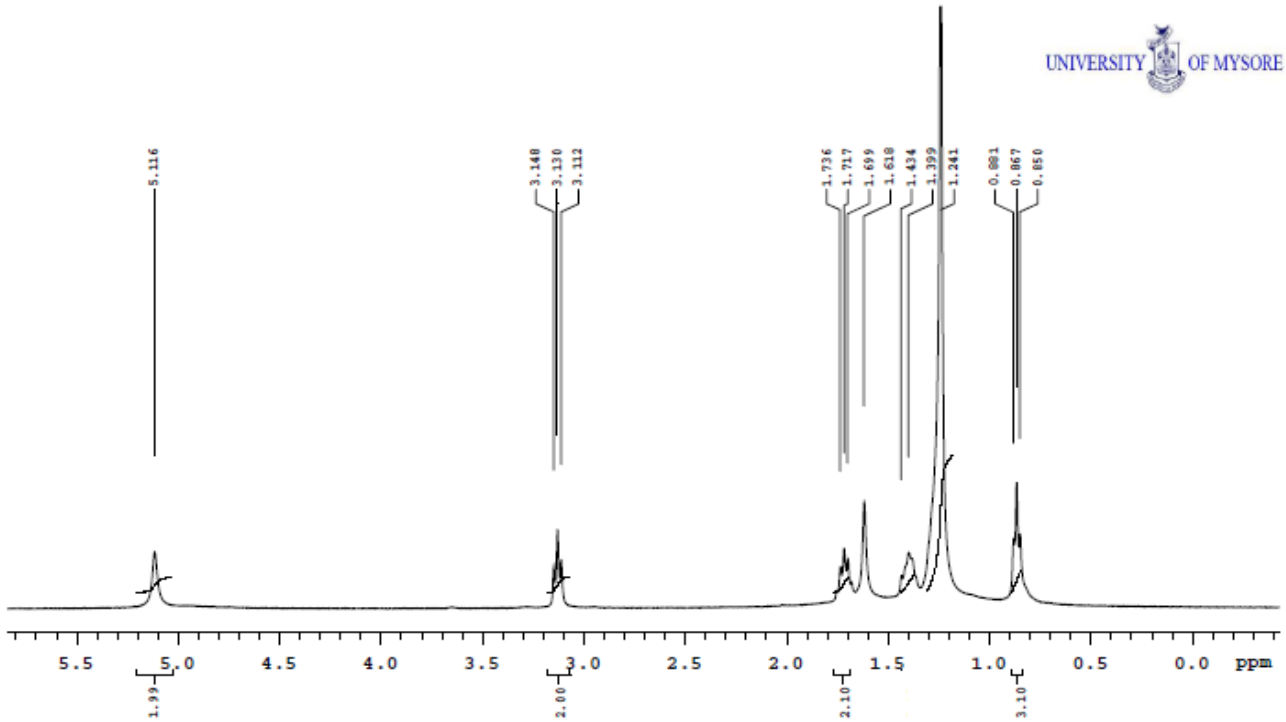


figure 2: expansion ^{1}H- NMR spectra of 5-Propylsulfanyl-1,3,4-thiadiazol-2-ylamine

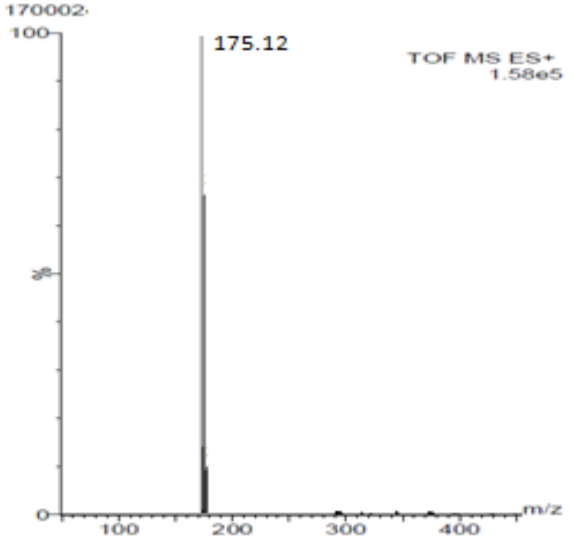


figure 3: mass spectra of 5-Propylsulfanyl-1,3,4-thiadiazol-2-ylamine

XRD:

The crystal data and refinement details are listed in **Table 1**. A few selected geometrical parameters are given in **Table 2**. The hydrogen bond geometry details are listed in **Table 3**.

CCDC number	1827424
Empirical formula	$C_5H_9N_3S_2$
Formula weight	175.27
Temperature	293 K
Wavelength	0.71073 Å
θ range	3.90° to 27.50°
Crystal system	Triclinic
Space group	$P\bar{1}$

Cell dimensions	a = 5.621(9) Å, b = 8.867(13) Å, c = 8.927(14) Å, α = 96.559(14)°, β = 104.523(19)°, γ = 101.56(1)°
Volume	415.6(11) Å^3
Z	2
Density(calculated)	1.401 Mg m $^{-3}$
Absorption coefficient	0.571 mm $^{-1}$
F_{000}	184
Crystal size	0.23 x 0.22 x 0.21 mm
Index ranges	$-7 \leq h \leq 7$ $-6 \leq k \leq 11$ $-9 \leq l \leq 11$
Reflections collected	2373
Independent reflections	1849
Absorption correction	Multi-scan
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	1849 / 0 / 92
Goodness-of-fit	1.034
Final [$I > 2\sigma(I)$]	R_1 = 0.0460, wR_2 = 0.1416
R indices (all data)	R_1 = 0.0529, wR_2 = 0.1513
Largest diff. peak and hole	0.447 and −0.388 e Å^{-3}

Table 1: Crystal data and refinement details.

Atoms	Bond length (Å)	Atoms	Bond angle and torsion angle (°)
S6-C2	1.734(3)	C2-S6-C5	86.5(1)
S6-C5	1.740(4)	N4-N3-C2	112.2(2)
S7-C8	1.801(4)	S6-C2-N1	121.5(2)
S7-C5	1.747(3)	S7-C5-N4	122.4(2)
N1-C2	1.353(4)	S7-C8-C9	109.3(2)
N3-N4	1.391(3)	C2-S6-C5-N4	0.4(2)
N3-C2	1.303(4)	C2-S6-C5-S7	−178.6(1)
N4-C5	1.291(3)	C2-N3-N4-C5	1.4(2)
C8-C9	1.515(4)	N3-N4-C5-S7	177.9(1)
C9-C10	1.525(5)	N4-N3-C2-S6	−1.1(2)

Table 2: Selected geometrical parameters.

The compound crystallizes in the triclinic crystal system in the space group $P\bar{1}$.The unit cell parameters are: a = 5.621(9) Å, b = 8.867(13) Å, c = 8.927(14) Å, α = 96.559 (14)°, β = 104.523(19)° , γ = 101.56(1)°, and Z =2.The *ORTEP* of the compound ($C_5H_9N_3S_2$) is shown in **Figure 4**. The thiadiazole ring in the structure is almost planar with a maximum r.m.s. deviation of 0.007(1) Å for S6. The planarity of the ring is also validated by the torsion angle values for the following atoms: C2-S6-C5-N4 = 0.4(2)°, C5-S6-C2-N3 = 0.4(2)°, C2-N3-N4-C5 = 1.4(2)°, N4-N3-C2-S6 = -1.1(2)°, and N3-N4-C5-S6 = -1.1(2)°. The thiadiazole ring is sp^2 hybridized with nearly trigonal geometry. This is confirmed by the bond angle values of S6-C2-N1 = 121.5(2)°, S7-C5-N4 = 122.4(2)°, S6-C5-S7 = 123.2(1)°, and N1-C2-N3 = 124.2(2)°. The two atoms N1 and S7 attached to the

thiadiazole ring are coplanar with the least-squares plane of the ring as indicated by the dihedral angles for N5-S6-C2-N1 = -178.2(2)° and C2-S6-C5-S7 = -178.6(1)° respectively.

In the structure two different types of *cg – cg* intermolecular interactions are observed between the centroids of the two thiadiazole rings. The geometry of the same could be given as*cg* (1) – *cg*(1)= 5.886(9) Å, α = 0.02(9)°, β = 57.4° and *cg* (1) – *cg*(1)=4.308(7) Å, α = 0.02(9)°, β = 33.9°. Intermolecular hydrogen bonds of the type N-H...N contacts connect the molecules to form a three dimensional network. **Figure 5** displays the packing of the molecules viewed down *b*axis. In the crystal structure supramolecular framework generates $R^2_2(8)$ graph-set motif [51] which involves N3A-H1A...N1 interactions. Bifurcated hydrogen bonds [52](H1B→N4 and H1B→ N3) are observed in the structure which are highlighted in **Figure 5**.

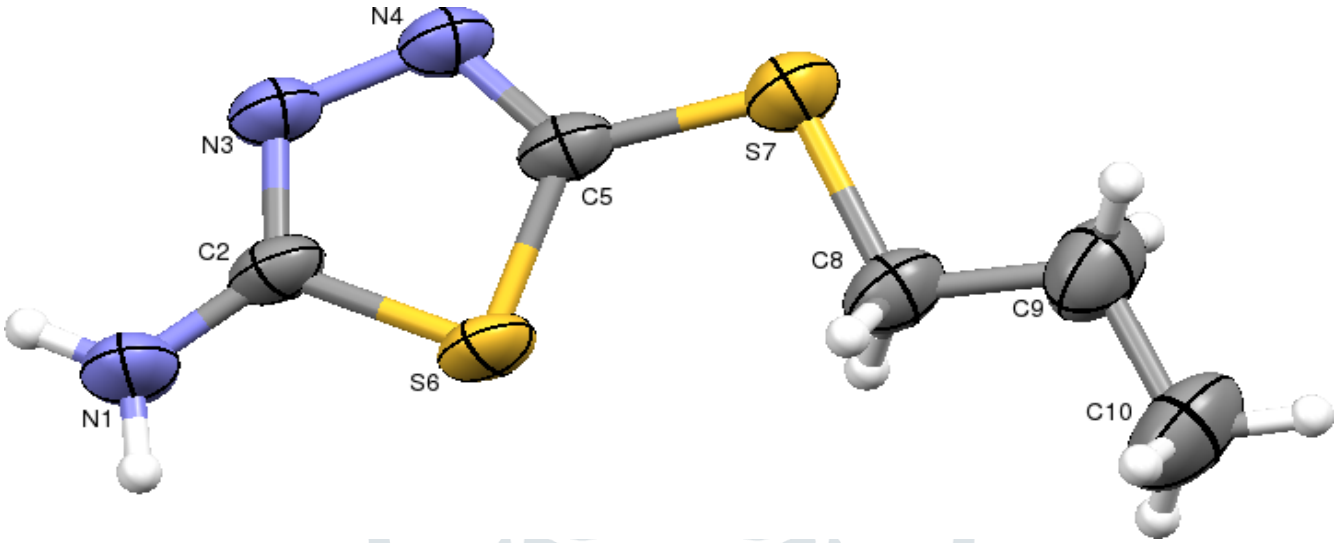
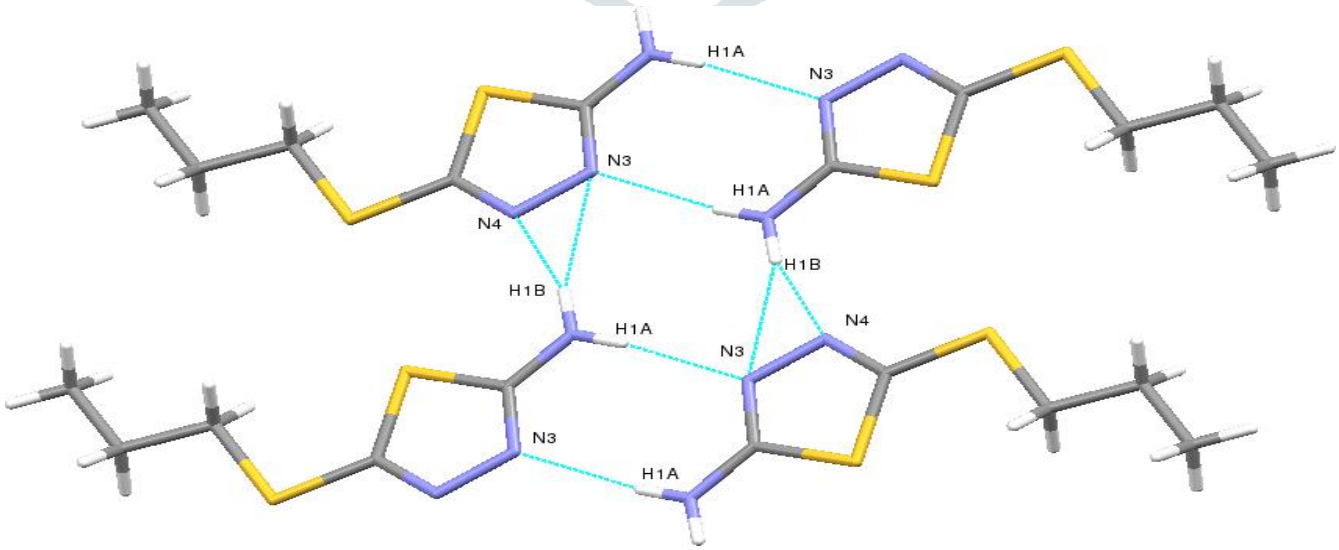


Figure 4: *ORTEP* of the compound with 50% probability displacement ellipsoids.

D-H...A	D-H	H...A	D...A	D-H...A
N1-H1A...N3[a]	0.86	2.14	2.994(6)	169
N1-H1B...N3[b]	0.86	2.56	3.394(6)	163
N1-H1B...N4[b]	0.86	2.19	2.999(6)	157

Table 3: Hydrogen bond geometry in Å and °.



Note: [a]and [b] indicates an intermolecular interactions with symmetry codes-1+*x, y, z,* and 1-*x, -y, 1-z* respectively.

Figure 5: Packing of the molecules viewed down *b* axis along with the formation of $R_2^2(8)$ graph-set motif via N-H...N hydrogen bonds.

Hirshfeld surface analysis

To explore the intermolecular interactions responsible for molecular packing in the crystal, Hirshfeld surface analysis was carried out. CrystalExplorer software [53] was used to generate molecular Hirshfeld surface and associated fingerprint plots. **Figure 6** shows the Hirshfeld surface of the compound mapped over d_{norm}. The bright red regions on the surface are due to contacts shorter than the van der Waals radii with negative d_{norm} value; blue regions on the surface are from contacts longer thanthe van der Waals radii with positive d_{norm}value; the white regions represent the contacts around the van der Waals radii with zero d_{norm} value [54]. The three bright red regions on the surface are due to N1-H1A...N3, N1-H1B...N3, and N1-H1B...N4 hydrogen bond interactions. **Figure 7** shows the associated fingerprint plots of the compound. **Figure 7a**depicts the total contribution from all the contacts to the total Hirshfeld surface area. A few other significant contributors to the total Hirshfeld surface area are: H-H (42.1%), N-H (25.5%), S-H (13.8%), S-S (6.0%), and C-H (5.6 %) contacts. The extended sharp spikes in **Figure 7c** are from N-H intermolecular interactions.

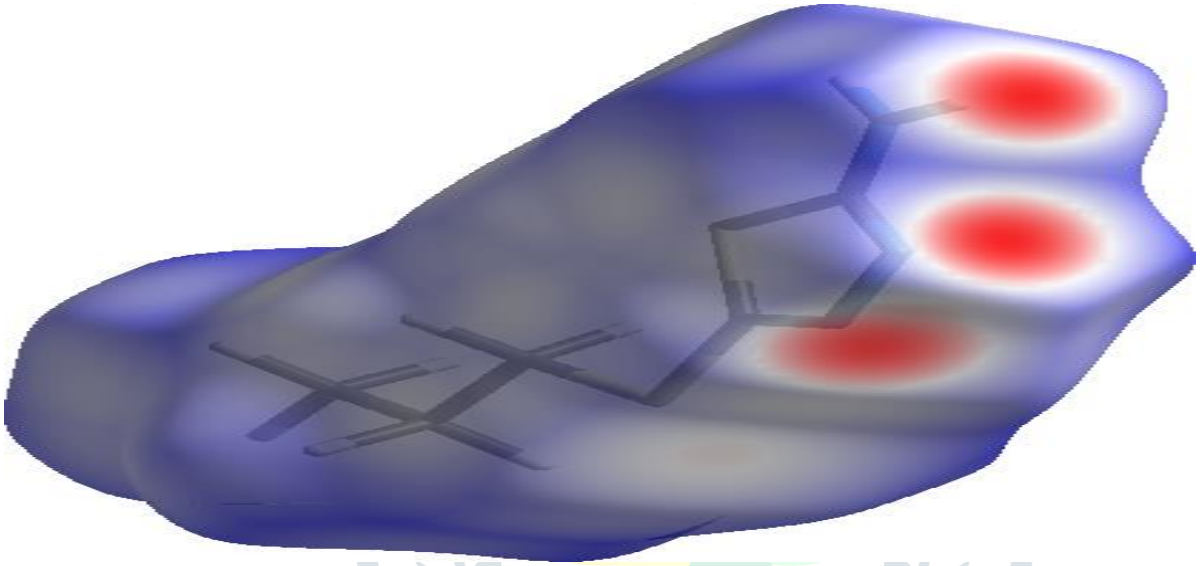


Figure 6. Hirshfeld surface mapped with the normalized contact distance d_{norm} showing N-H...N hydrogen bond interactions as red spots.

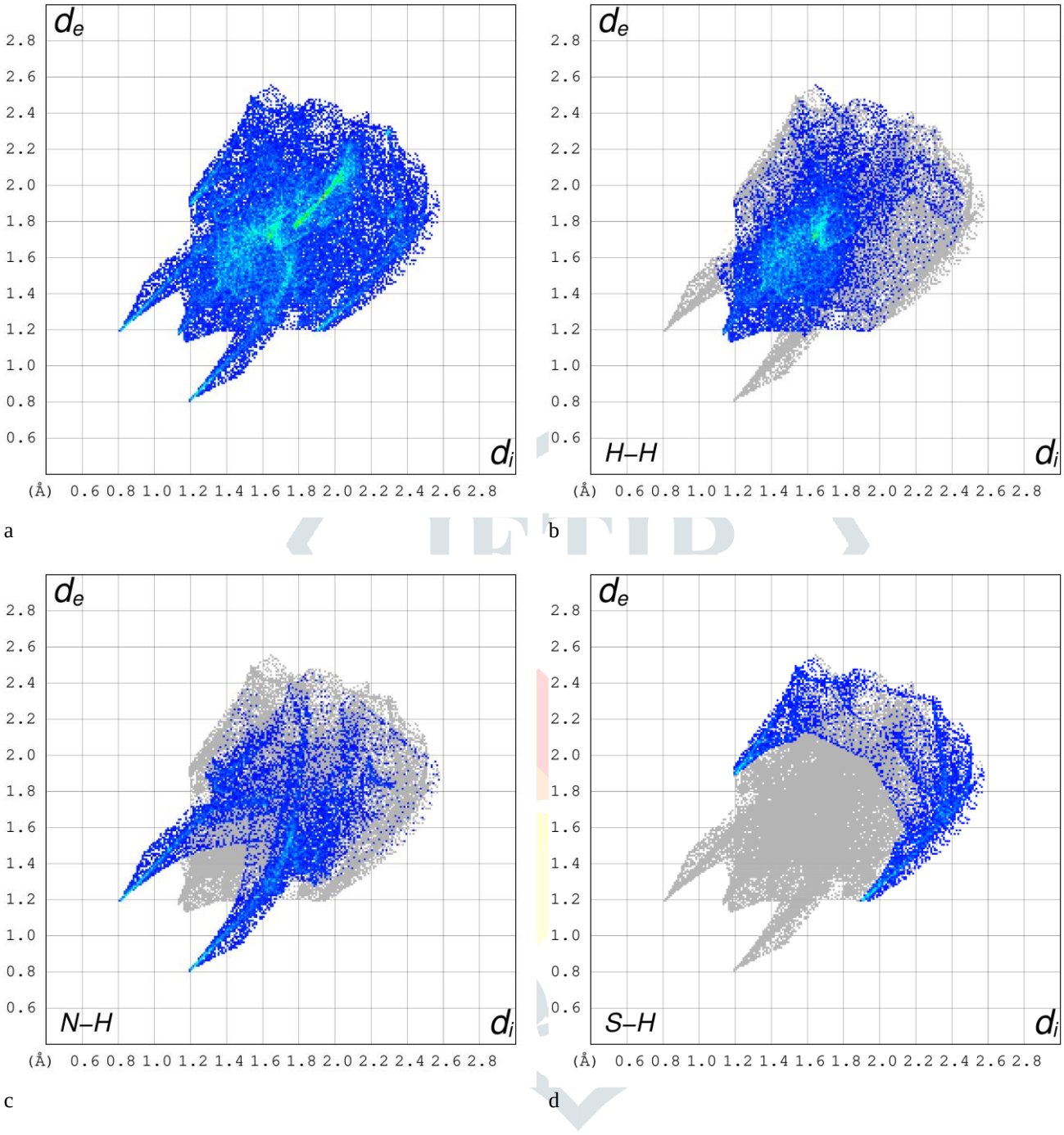
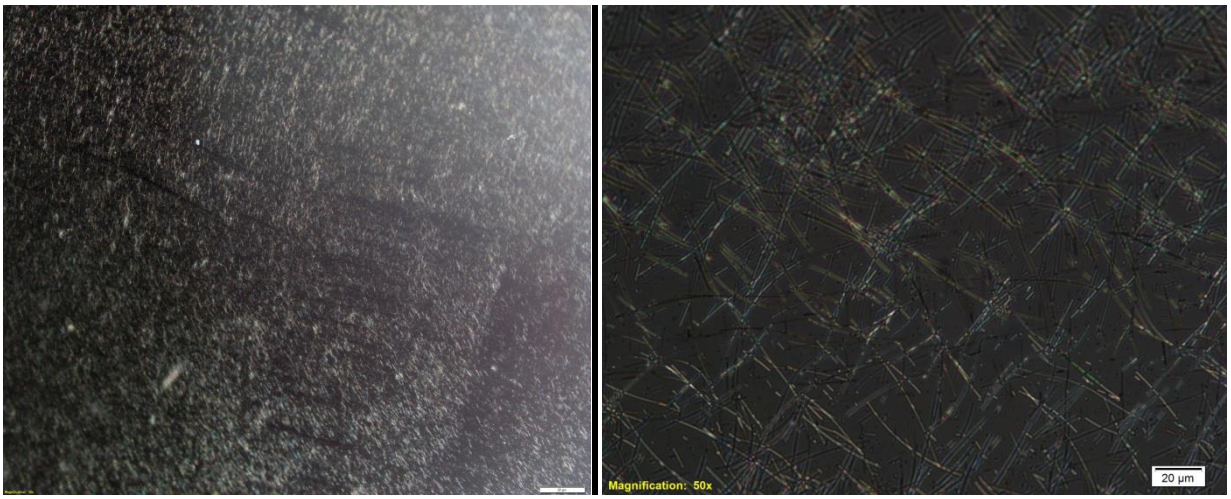


Figure 7: The fingerprint plots: From all the contacts (a), the decomposed plots resolved into H-H contacts (b), N-H contacts (c), and S-H contacts (d).

Liquid crystal behavior study : In the present work, link of alkyl group to the heterocyclic unit leads to molecule exhibit liquid crystal property. The change in phases under polarizing light has been done using polarizing optical microscope at different temperatures. The change from crystalline phase to smectic phase is obtained at 68^{o}C as shown in **figure 8** and Smectic to isotropic liquid state was observed at 117^{o}C.



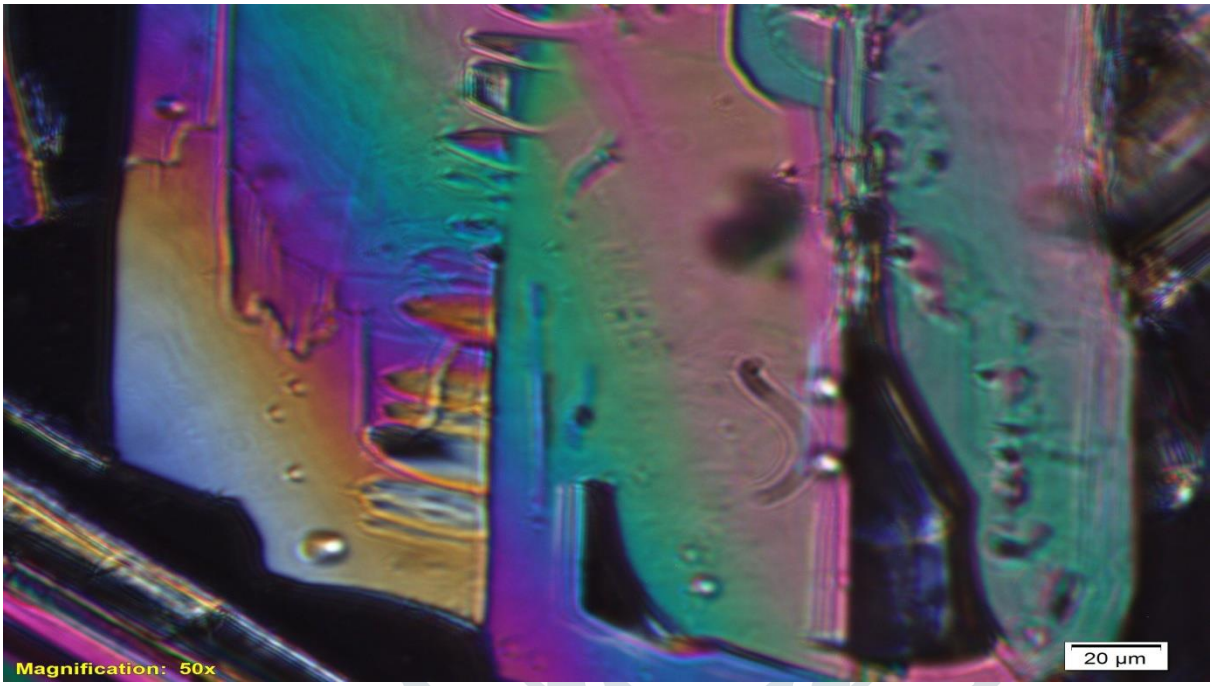


figure 8: liquid crystal study using POM

Conclusions

X-ray diffraction study reveals that intermolecular interactions of the type N-H...O are responsible for the molecular packing in the crystal. Hirshfeld surface analysis reinforces the presence of the same interactions. The synthesized smectic crystals may be further useful for optical applications. In future, further studies on liquid crystals will be carried out in order to find the effect of length of alkyl chains on the thermo-tropic liquid crystals.

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