Analysis of intermolecular interactions in 3-(4-fluoro-3-phenoxyphenyl)-1-((4-methylpiperazin-1-yl)methyl)-1H-1,2,4-triazole-5-thiol

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MS received 29 April 2014; revised 28 May 2014; accepted 15 July 2014

Abstract. In the present study, we have prepared and structurally characterized a derivative of 1,2,4 triazoles, namely 3-(4-fluoro-3-phenoxyphenyl)-1-((4-methylpiperazin-1-yl)methyl)-1H-1,2,4-triazole-5-thiol (**T-1**) via single crystal X-ray diffraction. The crystal structure was observed to be stabilized by the presence of various intermolecular interactions in the crystalline solid such as O-H...S, C-H...F, C-H...S, C-H...N, C-H...O, C-H... π , lp ... π and π ... π intermolecular interactions. The interaction energy of these interactions was evaluated through PIXEL method with decomposition of the total energy into the coulombic, polarization, dispersion and repulsion contribution. The study of the nature of H-bonds with sulfur reveals that stabilization due to contribution from polarization plays a significant role. It is noteworthy that the presence of the solvent molecules in the crystal structure were observed to provide stabilization to an otherwise destabilized molecular pair (comprising of two molecules of 1,2,4 triazoles in the asymmetric unit).

Keywords. 1,2,4-triazoles; crystal engineering; intermolecular interactions; Hirshfeld analysis; PIXEL; TURBOMOLE.

1. Introduction

Studying and analyzing intermolecular interactions plays a very pivotal role in the field of crystal engineering.¹ It facilitates the design of new materials with desirable properties and characteristics.² Presence of different kinds of intermolecular interactions in different crystal structures will lead to different chemical and biological activities and this is of great importance to pharmaceutical industries.³ The nature of intermolecular interactions in a crystal depends on the type of donor and acceptor atoms present in a particular molecule. In the presence of a strong acceptor and donor atom, the crystal packing will be predominantly controlled by the presence of strong hydrogen bonds such as O/N-H...O/N.⁴ In the past decade, the focus has shifted from strong intermolecular interactions to weak intermolecular interactions such as C-H...O/N,^{5–8} C-H...X (X = -F, -Cl, -Br, -I),^{9–14} C-H... π ¹⁵ and π ... π ^{16,17} and lp ... π ^{18,19} interactions present in the crystal structures. Weak

intermolecular interactions involving organic fluorine have received special attention due to its small size, electronegativity and lipophilic character.²⁰ It is due to this behaviour that more than 50% of pharmaceutical drugs contain fluorine and hence structural characterization of these compounds becomes very important.²¹

In the present study, we have prepared a derivative of 1, 2, 4-triazoles, namely 3-(4-fluoro-3-phenoxyphenyl)-1-((4-methylpiperazin-1-yl)methyl)-1H-1,2,4-triazole-5-thiol (**T-1**) (scheme 1). This compound was characterized via DSC (Differential Scanning Calorimetry) and single crystal XRD. 1, 2, 4-triazoles have widespread recognition due to its biological activities (namely antihypertensive, anti-bacterial and anti-viral).²² 1,2,4-triazoles have found its usefulness in industrial applications also.²³ Crystal structure analysis was performed on the prepared compound by analyzing the nature of intermolecular interactions present in the molecule. The role of these weak interactions in crystal packing and a quantitative assessment of the nature of these interactions using PIXEL^{24–31} constitute the main focus of this article. In addition, contribution of different intermolecular interactions over the Hirshfeld surface was also analyzed.³²

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Scheme 1. Chemical scheme depicting the preparation route for **T-1**.

2. Experimental

2.1 Synthesis

To a solution of 4-fluoro-3-phenoxybenzohydrazide (**I**, 0.01 mol) in methanol (150 mL), a solution of potassium thiocyanate (0.03 mol) in hydrochloric acid (3 mL) was added slowly with constant stirring. The reaction mixture was then evaporated to dryness on a steam bath. The residue was heated for an additional one hour in methanol (50 mL). The resulting solid was filtered off, washed with water/ethanol, dried and crystallized from ethanol to afford 2-(4-fluoro-3-phenoxybenzoyl)hydrazinecarbothioamide (**II**). In the next step, a mixture of **II** (0.01 mol) and sodium hydroxide solution (25 mL, 4%) was refluxed for 3 hours. The resulting solution was acidified after cooling and the precipitate thus obtained was filtered and recrystallized from ethanol-water to give 5-(4-fluoro-3-phenoxyphenyl)-4H-1,2,4-triazole-3-thiol (**III**). In the next step, **III** was added to a mixture of ethanol (15 mL), a solution of formaldehyde (40%, 1.5 mL) and 1-methylpiperazine (0.01 mol) and the reaction was stirred and refluxed for thirty minutes and was left overnight at room temperature. The resultant precipitate was filtered and recrystallized from aqueous dimethylformamide to obtain 3-(4-fluoro-3-phenoxyphenyl)-1-((4-methylpiperazin-1-yl) methyl)-1H-1,2,4-triazole-5-thiol (**T-1**).

The yield of the final product and the melting point of the compound were recorded (from DSC @ 5°C/min) (table S1 and figure S1).

2.2 Crystal growth

Suitable crystals of **T-1** of appropriate quality and size for single crystal X-ray diffraction was obtained

from slow evaporation method from ethanol at room temperature.

2.3 X-ray crystallography

Single crystal X-ray diffraction data of **T-1** were collected on a Bruker APEX-II diffractometer equipped with a CCD area detector using Mo K α radiation ($\lambda = 0.70173 \text{ \AA}$) in φ and ω scan modes at 100(2)K. Cell refinement and data reduction were performed using the program SAINT (Bruker AXS). The data were scaled and absorption correction was performed using SADABS (Bruker AXS). The crystal structure was solved by direct methods using SIR 92³³ and refined by least-squares methods on the basis of all observed reflections using SHELXL-2013³⁴ present in WinGx (version 2013.3).³⁵ Non-hydrogen atoms were refined with anisotropic displacement parameters. All the hydrogen atoms, except the hydrogen atoms attached to the solvent molecule, were then positioned geometrically and refined using a riding model with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}[\text{C}(sp^2)]$ and $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}[\text{C}(sp^3)]$. The hydrogen attached to the oxygen atom for one ethanol molecule (**solvent 2**) was then located from the difference electron density map and refined with isotropic displacement parameter while for the other solvent molecule (**solvent 1**) this could not be located. The disorder associated with the solvent molecules was modelled using the PART command in SHELXL97 and were refined for two independent positions, namely A and B ('A' depicting the higher occupancy).

The molecular connectivity and the crystal packing diagrams were generated using Mercury (CCDC) program.³⁶ Geometrical calculations were done using PARST³⁷ and PLATON.³⁸ The details of the crystal data, data collection and structure refinements are shown in table 1. The list of intermolecular interactions is given in table 3.

2.4 Theoretical calculations

The geometrical optimization of the molecule was performed at the B3LYP/6-311G** level of calculation using TURBOMOLE.^{39,40} For the purpose of the theoretical calculation, the two molecules in the asymmetric unit were extracted separately and then optimization was performed on each molecule with their solid state geometry as the starting point. Torsion angles of the isolated molecule in the gaseous state were then compared with those obtained experimentally in the solid state by X-ray diffraction (table 2).

The interaction energies of the intermolecular interactions in **T-1** were calculated with PIXELC module

Table 1. Crystallographic and refinement data.

Data	T-1
Formula	2(C ₂₀ H ₂₂ N ₅ F ₁ S ₁ O ₁), C ₂ H ₆ O, C ₂ H ₅ O
Formula Weight	890.10
Wavelength	0.71073
Temperature(K)	100(2) K
CCDC no	992599
Crystal System	Triclinic
Space Group	<i>P</i> 1
<i>a</i> (Å)	8.9055(3)
<i>b</i> (Å)	10.6993(3)
<i>c</i> (Å)	12.2617(4)
α (°)	104.596(2)
β (°)	91.314(2)
γ (°)	94.931(2)
<i>V</i> (cm³)	1125.23(6)
<i>Z</i>	1
Density(g cm⁻³)	1.314
μ (mm⁻¹)	0.181
<i>F</i>(000)	471
θ (min, max)	1.72, 25.00
Treatment of hydrogens	Fixed
<i>h</i>_{min,max}/<i>k</i>_{min,max}/<i>l</i>_{min,max}	−10, 10/ −12, 12/ −13, 14
No. of ref.	16080
No. unique ref./ obs. ref.	6976, 6420
No. of parameters	575
<i>R</i>_{all}, <i>R</i>_{obs}	0.0444, 0.0401
<i>wR</i>₂_{all}, <i>wR</i>₂_{obs}	0.0942, 0.0917
$\Delta\rho_{\text{min,max}}$ (e Å⁻³)	−0.372, 0.368
G. o. F	1.066

in the CLP computer program package (version 10.2.2012)^{41–43} with the total energies being partitioned into their coulombic, polarization, dispersion and repulsion contributions. For this purpose, hydrogen atoms were moved to their neutron value and an accurate electron density of the molecule was obtained at MP2/6-31G** with Gaussian 09.⁴⁴ Since the current investigation consists of four components (two molecules of 1, 2, 4-triazoles derivatives and two ethanol molecules), the PIXEL energy calculations were performed three times (**molecule 1** with **molecule 2**, **molecule 1** with **solvent 2** and **molecule 2** with **solvent 2**, figure 1) taking a

pair at a time as PIXELC module in CLP can handle only two components at a time. In this way the interaction energies for all the possible molecular pairs were obtained.⁴⁵ Since the hydrogen atom on the oxygen atom for **solvent 1** could not be located, the PIXEL calculations with the **solvent 1** could not be performed. For the sake of comparison, the interaction energy between the molecular pair (except for those which involves a disordered solvent molecule) was also calculated at DFT+Disp/B97-D level with higher aug-cc-pVTZ basis set using TURBOMOLE. The interaction energy was corrected for basis set superposition error with

Table 2. List of selected torsions (°) shown with red arrow in figure 2a in T-1.

	Torsion 1(°)	Torsion 2(°)	Torsion 2(°)	Torsion 4(°)	Torsion 5(°)
Solid state	67.4(3)	96.5(3)	166.4(3)	124.7(3)	129.4(3)
	68.3(3)'	101.5(3)'	160.2(3)'	61.3(3)'	19.7(4)'
Optimized at	68.9	100.3	179.2	70.3	67.2
DFT/B3LYP	68.8'	109.9'	179.0'	70.3'	14.8'

'Indicates second molecule in the asymmetric unit.

Figure 1. ORTEP drawn with 50% ellipsoidal probability of **T-1** with atom numbering scheme. C-atoms in purple are shown for the second molecule in the asymmetric unit. Hydrogen atoms were omitted for clarity and only the major conformer is shown for the disordered solvent molecules.

Boys-Bernardi counterpoise procedure.⁴⁶ The hydrogen atoms were moved to neutron values before the calculation. Table 3 contains all the intermolecular interactions present in **T-1** along with their respective interaction energies. It was observed that the molecular pairs have similar interaction energy in both solid (PIXEL) and gas phase (DFT-D).

The intermolecular interactions were further analyzed by Hirshfeld surfaces³² and 2D fingerprint⁴⁷ plots using Crystal Explorer 3.1.⁴⁸

3. Results and Discussion

ORTEP of **T-1** has been shown in figure 1. **T-1** crystallizes in the triclinic *P*1 space group with two molecules in the asymmetric unit along with two disordered ethanol molecules (the occupancy factor refines to a value of 0.810(6) for **solvent 1** and 0.681(14) for **solvent 2**) in the crystal. The molecule can be divided in three different parts. The central 1,2,4-triazole ring, the flexible fluorophenoxy group and the methyl piperazine moiety. Figure 2 shows the relevant torsions present in the crystal structure and the relevant torsion values are given in table 2. The two molecules in the asymmetric unit differ in their conformation around the fluorophenoxy group (**Torsion 4** and **5**, table 2, figure 2). The fluorophenoxy group is oriented *syn* with respect to the -SH group in one molecule and exhibits an *anti* in the other molecule (figure 2b) of the asymmetric unit.

Furthermore, except the fluorophenoxy, the remaining molecule exhibits similar molecular conformation in the solid state when compared with the isolated molecule (table 2).

The molecular structure of **T-1** consists of several hydrogen bond donors and acceptors. The hydrogen atom attached to sp^2 and sp^3 hybridized carbon can act as weak hydrogen bond donors. In term of the acceptor atoms, the molecule contains five nitrogen atoms in different electronic environments (three in central aromatic 1,2,4-triazole ring while two in terminal non-aromatic piperazine ring) in the molecule as strong H-bond acceptor along with one oxygen of fluorophenoxy part. Furthermore, the presence of -SH functional group in the molecule possesses moderate H-bond donor characteristics in addition to being an acceptor atom. The presence of aromatic rings and a fluorine atom in the molecule can also act as weak hydrogen bond acceptors and can result in the formation of C-H... π and π ... π interactions. Moreover, the presence of two ethanol molecules in the crystal structure introduces a strong hydrogen bond acceptor and donor atom for each solvent molecule. With these view points, one expects a cooperative interplay amongst all these intermolecular interactions in the formation of periodic arrangement of molecules inside the solid.

Figure 3a–c depicts the presence of different intermolecular interactions which connect the molecules in the crystal structure along with their respective interaction energies. The two molecules present in the asymmetric unit are connected by the presence of short N...N contacts ($d_{N1...N10} = 2.737(3)$ Å and $d_{N5...N6} = 2.813(3)$ Å, motif **XI** (table 3). The centroid-centroid distance for the interacting molecules is only 3.419 Å. The interaction energy calculated for this pair by PIXEL method (+3.34 kcal/mol, table 3) shows that these contacts are destabilizing in nature. The contact distance between the participating atoms is less by 13% than the sum of the van der Waals radius of nitrogen (3.1 Å). This results from the greater magnitude of the repulsion energy (+42.3 kcal/mol) towards the molecular pair **XI**. It is very interesting to note that albeit the presence of a destabilized molecular pair, the net stabilization originates owing to the presence of the solvent molecules around the given molecular pair (figure 3c) with the utilization of the O-H...S (I.E = −3.03 kcal/mol, Motif **XII**), weak C-H...O (I.E = −2.15 kcal/mol, Motif **XIII**) and C-H...N (I.E = −1.09 kcal/mol, Motif **XIV**) hydrogen bond. It is to be noted that the polarization contribution towards the ‘net’ interaction energy for motif **XII** is −5.64 kcal/mol which is 39% of the total stabilization energy. This signifies that the lone pairs on the sulfur atom are

Table 3. List of intermolecular interactions along with their interaction energies (kcal/mol).

Motif [#]	D-H...X	D...X (Å)	H...X (Å)	D-H...X Angle (°)	Symmetry code	Centroid Distance (Å)	E _{coal} (kcal/mol)	E _{pol} (kcal/mol)	E _{disp} (kcal/mol)	E _{rep} (kcal/mol)	E _{tot} (kcal/mol)	DFT-D (kcal/mol)
Intermolecular interactions involving molecule 1 and 2												
I	C40-H40...O1	3.331(3)	2.35	149	x, y-1, z	7.619	-2.67	-1.07	-8.67	4.82	-7.62	-8.93
2...1	C10...C33 ($\pi \cdots \pi$)	3.439(3)										
II	C3-H3B...S2	3.765(3)	2.90	137	x+1, y, z	9.350	-2.65	-1.57	-9.97	7.69	-6.50	-6.92
1...2	C25-H25B...N4	3.505(4)	2.66	134								
	C14-H14...N7	3.433(4)	2.64	130								
III	C26-H26B...O2	3.272(4)	2.37	140	x-1, y, z	8.906	-1.88	-0.93	-5.87	4.34	-4.37	-5.49
2...1												
IV	N2(<i>lp</i>)...C39	3.512(3)			x, y, z-1	10.701	-0.74	-0.50	-4.23	2.41	-3.03	-4.08
1...2	C6-H6B...C38	3.856(2)	3.00	136								
V	C19-H19...F2	3.197(4)	2.50	121	x-1, y+1, z	12.542	-1.02	-0.50	-4.08	2.67	-2.96	-3.17
1...2	C18-H18...C39	3.589(4)	2.86	134								
VI	C5-H5A...C15	3.712(4)	2.67	160	x, y-1, z-1	14.096	-1.50	-0.78	-5.30	4.75	-2.84	-4.18
1...1												
VII	C21-H21C...C27	3.835(3)	3.13	124	x, y+1, z	10.699	-0.74	-0.28	-3.48	2.12	-2.39	-2.93
2...2												
VIII	C37-H37...S1	3.686(3)	2.62	168	x+1, y, z+1	13.871	-1.74	-1.21	-3.65	4.34	-2.27	-1.64
2...1												
IX	C38-H38...S2	3.823(4)	2.87	147	x+1, y, z+1	14.989	-1.02	-0.62	-3.05	2.43	-2.27	-2.00
2...2												
X	C18-H18...F1	3.490(4)	2.65	134	x-1, y, z	8.905	-0.23	-0.19	-2.39	0.76	-2.05	-1.25
1...1												
XI	N1...N10	2.737(3)			x, y, z	3.419	-0.33	-8.36	-30.28	42.30	3.34	-0.73
1...2	N5...N6	2.813(3)										
Intermolecular interactions involving solvent with molecule 1 or 2												
XII	O4-H45...S2	3.282(3)	2.37	164	x+1, y+1, z	7.842	-4.58	-5.64	-4.18	11.40	-3.03	—
S2...2												

#1 and 2 refer to molecule 1 and 2 while s1 and s2 to solvent 1 and 2 from figure 1.

Table 3. (contd)

Motif [#]	D-H...X	D...X (Å)	H...X (Å)	D-H...X Angle (°)	Symmetry code	Centroid Distance (Å)	E _{coul} (kcal/mol)	E _{pol} (kcal/mol)	E _{disp} (kcal/mol)	E _{rep} (kcal/mol)	E _{tot} (kcal/mol)	DFT-D (kcal/mol)
XIII 2...S2	C33-H33...O4	3.302(4)	2.50	130	x, y-1, z	7.650	-1.67	-0.55	-1.34	1.39	-2.15	—
XIV S2...1	C44-H44B...N3	3.731(3)	2.72	155	x, y, z	5.610	-0.50	-0.43	-2.91	1.74	-1.09	—
XV S1...1	O3...S1	3.279(3)			x, +y, +z+1							—
XVI 1...S1	C16-H16...O3	3.451(3)	2.39	167	x, y, z							—

Figure 2. (a) Molecular structure showing selected torsion angles present in **T-1**; (b) Overlay of two molecules in the asymmetric unit of **T-1**.

deformed in the crystal environment with subsequent participation in the formation of hydrogen bonds. The electronic effects associated with the lone pairs on the sulfur atom has been viewed *via* inputs from electron density analysis in 4-methyl-3-thiosemicarbazide and these depict the redistribution of the valence electron density on the sulfur atom to accommodate the different intermolecular interactions.⁴⁹ However, the close approach of the donor oxygen and acceptor sulfur atom results in the repulsion contribution being of considerably higher magnitude, i.e., +11.4 kcal/mol. In the absence of the location of the hydrogen atom on solvent **1**, a short S1...O3 contact (motif **XV**) is observed which further necessitates the existence of a plausible O-H...S hydrogen bond. Therefore, the presence of solvent molecules around the molecular pair **XI** provides overall stabilization to the crystal structure and governs the existence of the destabilized molecular pair in **T-1**. In the crystal packing, the molecular pair **XI** propagates along the crystallographic *a*-axis with the utilization of motif **II** [I.E = -6.50kcal/mol, figure 3a and table 3) which consists of weak C-H...S, C-H...N hydrogen bonds (figure 4a). The molecular chain thus formed is connected *via* motif **I**, **V** and **VII** figure 4a and table 3. The motif **I** is the highest stabilized molecular pair with I.E. of -7.62 kcal/mol in the crystal packing and consists of weak C-H...O hydrogen bond along with $\pi \cdots \pi$ interaction (fig 3a and table 3). The motif **V** (I.E = -2.96kcal/mol) involves the presence of a weak C-H...O and C-H... π hydrogen bond whilst the presence of C-H... π hydrogen bonds links the molecules in motif **VII** (I.E = -2.39kcal/mol). Furthermore, the two weak C-H...S hydrogen bonds from motif **VIII** and **IX** with same stabilization energy (-2.27 kcal/mol, (figure 3a and b and table 3) connect

Figure 3. (a) Selected coordination environment around central molecule 1 (C-atoms are grey in colour) along with intermolecular interactions (shown by dotted lines) with symmetry equivalent molecules (represented with different colours of C-atoms). The Roman numbers indicate different molecular pairs and the corresponding symmetry code are mentioned in table 3. Hydrogen atoms not involved in interactions were omitted for clarity. (b) Selected coordination environment around central molecule 2 (C-atoms are purple in colour) along with intermolecular interactions (shown by dotted lines) with symmetry equivalent molecules (represented with different colours of C-atoms). The Roman numbers indicate different molecular pairs and the corresponding symmetry code are mentioned in table 3. Hydrogen atoms not involved in interactions were omitted for clarity. (c) Selected coordination environment of solvent molecule around two molecules of the asymmetric (C-atoms are grey and purple for molecule 1 and 2 respectively) along with intermolecular interactions (shown by dotted lines) which connect the molecule 1 and 2 with solvent molecules (represented with different colours of C-atoms, cyan for solvent 1 and green for solvent 2). The Roman numbers indicate different molecular pairs from table 3. Hydrogen atoms not involved in interactions were omitted for clarity except for the solvent molecules.

Figure 4. (a) Packing of molecules down the *ab* plane in **T-1** with the utilization of weak C-H...N, C-H...S, C-H... π hydrogen bonds. C-atoms in purple represent molecule 2 and C-atoms for solvent 1 and 2 are shown with cyan and green colour respectively. Same colour code has been followed in all the packing representations. The Roman numbers indicate different molecular pairs from table 3. (b) Packing view down the *ac*-plane showing the formation of molecular assembly by the utilization of weak C-H...O, C-H...S, C-H... π , C-H...F hydrogen bonds. The Roman numbers indicate different molecular pairs from table 3.

the two molecules in the asymmetric unit (motif **XI**) via the generation of a molecular chain down the crystallographic *ac* plane (figure 4b). Two such molecular chains are interconnected via weak C-H...O (motif **III**, I.E. = -4.37kcal/mol, table 3) and C-H...F (motif **X**, I.E. = -2.05 kcal/mol, table 3) in the crystal packing (figure 4b). Moreover, the presence of motif **IV** (I.E. = -3.03kcal/mol) which involves N(*lp*)... π and C-H... π interactions and motif **VI** (I.E. = -2.84kcal/mol, consists of weak C-H... π hydrogen bond) were also observed to stabilize the crystal packing in **T-1** (figure 3a and b and table 3). It is to be noted that S-H does not participate as a H-bond donor but both the sulfur atoms S1 and S2 in the two molecules of the asymmetric unit independently participate in the formation of numerous C-H...S intermolecular interactions wherein the distance is less than the sum of the van der Waals radii (3.0 Å) and the directionality ranges between 137–168°.

The nature of intermolecular interactions in **T-1** was further studied by Hirshfeld surfaces mapped with different properties e.g., d_i , d_e , d_{norm} , shape index,

Figure 5. Percentage distribution of the different intermolecular interactions present in the crystal structure.

curvedness (figure S2) and 2D-Fingerprint plots (figure S3). The contribution of the different intermolecular interactions over the Hirshfeld surfaces was also quantified from the decomposed 2D-Fingerprint plots. Figure 5 shows the percentage distribution of different intermolecular interaction present in the crystal structure obtained through 2D-fingerprint analysis. The maximum contribution is coming from the $H \cdots H$ interactions (54.7%) indicating that the interaction present in the crystal structure is dominantly of dispersive nature. This is followed by $H \cdots C(\pi)$, $H \cdots F$, $H \cdots O$, $H \cdots N$ and $H \cdots S$ which have a contribution of 16.1%, 9.1%, 8.7%, 4.9% and 4.1% respectively. This shows that the weaker interactions have a major role in the stabilization of the crystal packing of **T-1**.

4. Conclusions

In this study, a derivative of a 1,2,4-triazole was prepared and an in-depth crystal structure analysis was performed to study the nature of intermolecular interactions present in this compound. A cooperative interplay amongst the different intermolecular interactions involving all the atoms C, N, O, F, S with H was observed. The PIXEL method beautifully rationalizes the relationship between the nature of the participating atoms and the associated energetics for different molecular pairs extracted from the crystal packing. The quantification of the interaction energies brings out the contributory role of different interactions in the formation of the solid. The participation of sulfur in the formation of a relatively strong $O-H \cdots S$ and $C-H \cdots S$ H-bond depicts the stabilizing role of a lone pair of electrons on the sulfur atom which governs formation of such bonds. In the absence of the solvent molecule, the formation of the asymmetric unit comprising of multiple molecules of 1,2,4-triazole may be deemed difficult. This is reflected in the interaction energy being destabilizing for the molecular pair comprising of the two molecules 'only' in the asymmetric unit. This is

quite contradictory because there are innumerable cases wherein the asymmetric unit contains more than one molecule (excluding the solvent participation) in the crystal structure and which has an overall stabilizing effect. Thus such an analysis is imperative in modern day crystal structure analysis to delineate the role of 'stabilizing' and 'destabilizing' packing motifs in the crystal. The generation of new polymorphs may partly answer this problem and it is also of interest to explore the possibility of polymorphism in any crystalline solid.

Supplementary Information

The information on yield, melting point, DSC trace and the Hirshfeld surface depicting d_i , d_e , d_{norm} , shape index and curvedness and the associated 2D-Fingerprint plots are included in supplementary information. Supplementary information is available at www.ias.ac.in/chemsci.

Acknowledgements

PP thanks UGC for SRF fellowship. RS thanks IISER Bhopal for PhD scholarship. DC thanks IISER Bhopal for infrastructure and research facilities (experimental and computational) and DST for financial support.

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