

3,6-Di(*p*-chlorophenyl)-2,7-dihydro-1,4,5-thiadiazepine: Crystal Structure and Decoding Intermolecular Interactions with Hirshfeld Surface Analysis

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Abstract In 3,6-di(*p*-chlorophenyl)-2,7-dihydro-1,4,5-thiadiazepine, C₁₆H₁₂Cl₂N₂S, which crystallizes in the triclinic space group, P-1, with $a = 8.4012(13)$ Å, $b = 9.2087(15)$ Å, $c = 10.4974(17)$ Å, $\alpha = 69.835(3)^\circ$, $\beta = 77.091(4)^\circ$, $\gamma = 81.820(4)^\circ$, $V = 741.2(2)$ Å³ and $Z = 2$, the seven-membered ring adopts a distorted boat conformation. The structure was solved by direct methods and refined by full-matrix least squares based on F^2 with weight $w = 1/[\sigma^2(F_o^2) + (0.0018P)^2 + 1.5600P]$ where $P = (F_o^2 + 2F_c^2)/3$. The new d_{norm} Hirshfeld surface and the breakdown of fingerprint plots were used for visualizing and exploring of title compound for quantifying intermolecular interactions in crystal lattice.

Keywords Thiadiazepine · Crystal structure · Hirshfeld surface

Introduction

As part of a continuing search for study on conformations of medium-sized heterocyclic compounds containing heteroatoms and synthesis of 3,6-disubstituted-2,7-dihydro-1,4,5-thiadiazepine as ligands for bioheterocycles complexes preparation [1–10], we have now prepared and reported

the structures of 3,6-di(*p*-chlorophenyl)-2,7-dihydro-1,4,5-thiadiazepine (Scheme 1). The intermolecular interaction in the crystal structure has also been investigated by using Hirshfeld Surface Computational Method.

Experimental

Preparation of 3,6-di(*p*-chlorophenyl)-2,7-dihydro-1,4,5-thiadiazepine

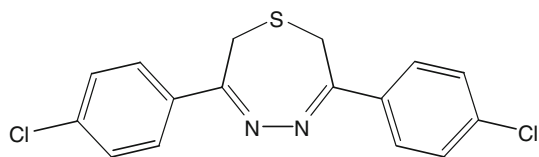
To a stirred solution of 1-(4-chlorophenyl)-2-thiocyanatoethanone (1.00 mmol, 0.212 g) in ethanol (5 mL) was added hydrazine hydrate 80% (1 mL) in one portion. The reaction mixture was heated at reflux for 28 h. The resulting solution was cooled and then poured into water (50 mL) and acidified with HCl (3 M) to pH 6. The solid residue was filtered off and washed with water (20 mL) and then suitable crystals of 3,6-di(*p*-chlorophenyl)-2,7-dihydro-1,4,5-thiadiazepine for single-crystal X-ray diffraction were obtained from ethanol. Yield (68%), mp: 198(°) ¹H NMR (100 MHz, CDCl₃): δ 3.46 (dd, 4H, 2CH₂), 7.79 (dd, 8H, 8CH) IR (KBr disc) ν : 1580, 1490, 1320, 1089, 833 cm⁻¹, EIMS m/z 339(M + 4⁺).

X-ray Diffraction

Crystal data, as well as details of data collection and structure refinement are listed in Table 1. Data were collected on a colorless prism crystal mounted and centered on a glass capillary which was put on a Bruker Apex II diffractometer equipped with graphite monochromated MoK α radiation ($\lambda = 0.71073$ Å). Intensities of 7180 reflections were measured using Bruker SMART 1000 CCD area detector, giving 3230 unique reflections.

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Scheme 1 Structure of 3,6-di(*p*-chlorophenyl)-2,7-dihydro-1,4,5-thiadiazepine

The final unit cell was determined from 898 reflections in the range of $2.10^\circ < \theta < 26.98^\circ$. The diffraction data were collected at 120 K with the φ and ω scans techniques. A semi-empirical absorption correction was applied. The data were integrated using the SAINT suite of software and corrected for the effects of absorption using SADABS [11]. The structure was solved by direct methods and refined by full-matrix least squares based on F^2 with weight $w = 1/[\sigma^2(F_o^2) + (0.0018P)^2 + 1.5600P]$ where $P = (F_o^2 + 2F_c^2)/3$ using the SHELXTL ver. 5.1 software [12]. All non-hydrogen atoms were refined with anisotropic displacement

parameters. The H(C) atom positions were calculated and refined in isotropic approximation in riding model with the $U_{iso}(H)$ parameters equal to $1.2 U_{eq}(C_i)$ where $U_{(C_i)}$ are the equivalent thermal parameters of the carbon atoms to which corresponding H atoms are bonded.

Crystallographic information has been deposited with the Cambridge Crystallographic Data Centre (CCDC number = 672457). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html. (Or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk.)

Hirshfeld Surface Computational Method

Molecular Hirshfeld surfaces partition crystal space into smooth, non-overlapping, interlocking molecular volumes [13]. Inside the Hirshfeld surface the electron distribution due to a sum of spherical atoms for the molecule (the promolecule) dominates the corresponding sum over the

Table 1 Crystal data and structure refinement for title compound

<i>Crystal data</i>	
$C_{16}H_{12}Cl_2N_2S$	$Z = 2$
$M_r = 335.24$	$D_x = 1.502 \text{ Mg/m}^3$
Triclinic, P-1	MoK α radiation
$a = 8.4012(13) \text{ \AA}$	Wavelength of incident radiation: 0.71073 \AA
$b = 9.2087(15) \text{ \AA}$	$\theta = 2.10\text{--}26.98^\circ$
$c = 10.4974(17) \text{ \AA}$	$T = 120(2) \text{ K}$
$\alpha = 69.835(3)^\circ$	$\mu = 0.572 \text{ mm}^{-1}$
$\beta = 77.091(4)^\circ$	Cell parameters from 898 reflections
$\gamma = 81.820(4)^\circ$	$0.3 \times 0.2 \times 0.2 \text{ mm}$
$V = 741.2(2) \text{ \AA}^3$	
<i>Data collection</i>	
Bruker SMART 1000 CCD diffractometer	3230 Independent reflections
φ and ω scans	$R_{int} = 0.0438$
Absorption correction: Semi-empirical from equivalents (SADABS; Sheldrick, 1998a)	$\theta_{max} = 30^\circ$
$T_{min} = 0.842$, $T_{max} = 0.889$	1662 reflections with $I > \sigma(I)$
7180 measured reflections	$-10 \leq h \leq 10$
	$-11 \leq k \leq 11$
	$-13 \leq l \leq 13$
<i>Refinement</i>	
Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0018P)^2 + 1.5600P]$, where $P = (F_o^2 + 2F_c^2)/3$
Final R indices [for 1662 rfln with $I > 2\sigma(I)$]	$(\Delta/\sigma)_{max} < 0.001$
$R_1 = 0.0645$, $wR_2 = 0.1328$	$\Delta\rho_{max} = 0.453 \text{ e.\AA}^{-3}$
$wR(F^2) = 0.172$	$\Delta\rho_{min} = -0.447 \text{ e.\AA}^{-3}$
$S = 1.004$	
3230 reflections	
190 parameters	

crystal (the procrystal), and the Hirshfeld surface is defined implicitly where the ratio of promolecule to procrystal electron densities equals 0.5. As it depends intimately on the molecular geometry, the location and orientation of nearest and more distant neighboring molecules, and the nature (radial extent) of specific atom types that make close contacts with the molecule in question, the Hirshfeld surface reflects in considerable detail the immediate environment of a molecule in a crystal. Any number of different properties such as various intermolecular interactions, packing behavior in different phases, effects of pressure and temperature on crystal structure and polymorphic molecular crystal structure [13–16], can be encoded on the Hirshfeld surfaces, and some of these have been explored in detail. For a given crystal structure and set of spherical atomic electron densities, the Hirshfeld surface is unique, and it is this property that suggests the possibility of gaining additional insight into the polymorphism of molecular crystals [17].

For each point on the surface, two colored distance properties are defined: d_e , the distance from the point to the nearest nucleus external to the surface, and d_i , the distance to the nearest nucleus internal to the surface.

2D fingerprint plots [13] are derived from the Hirshfeld surface by plotting the fraction of points on the surface as a function of the pair (d_i , d_e). Each point on the standard 2D graph represents a bin formed by discrete intervals of d_i and d_e ($0.01 \times 0.01 \text{ \AA}$), and the points are colored as a function of the fraction of surface points in that bin, with a range from blue (relatively few points) through green (moderate fraction) to red (highest fraction).

Results and Discussion

The molecular structure of title compound, (I), is depicted in Fig. 1, with the atomic numbering scheme, and selected bond lengths and angles are given in Table 2.

Fig. 1 A molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level

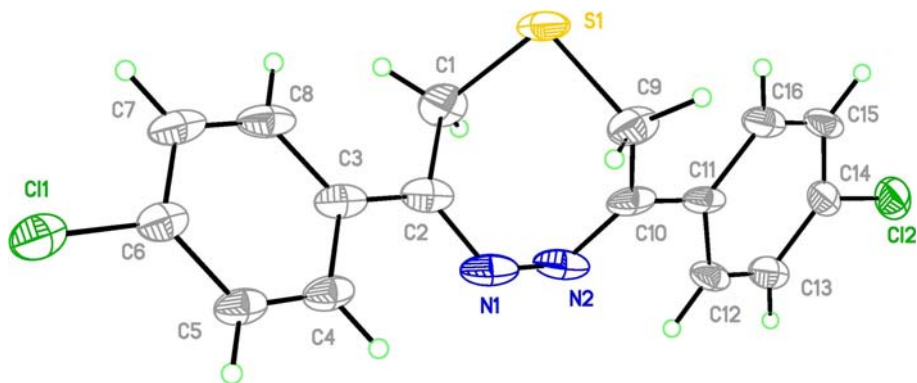


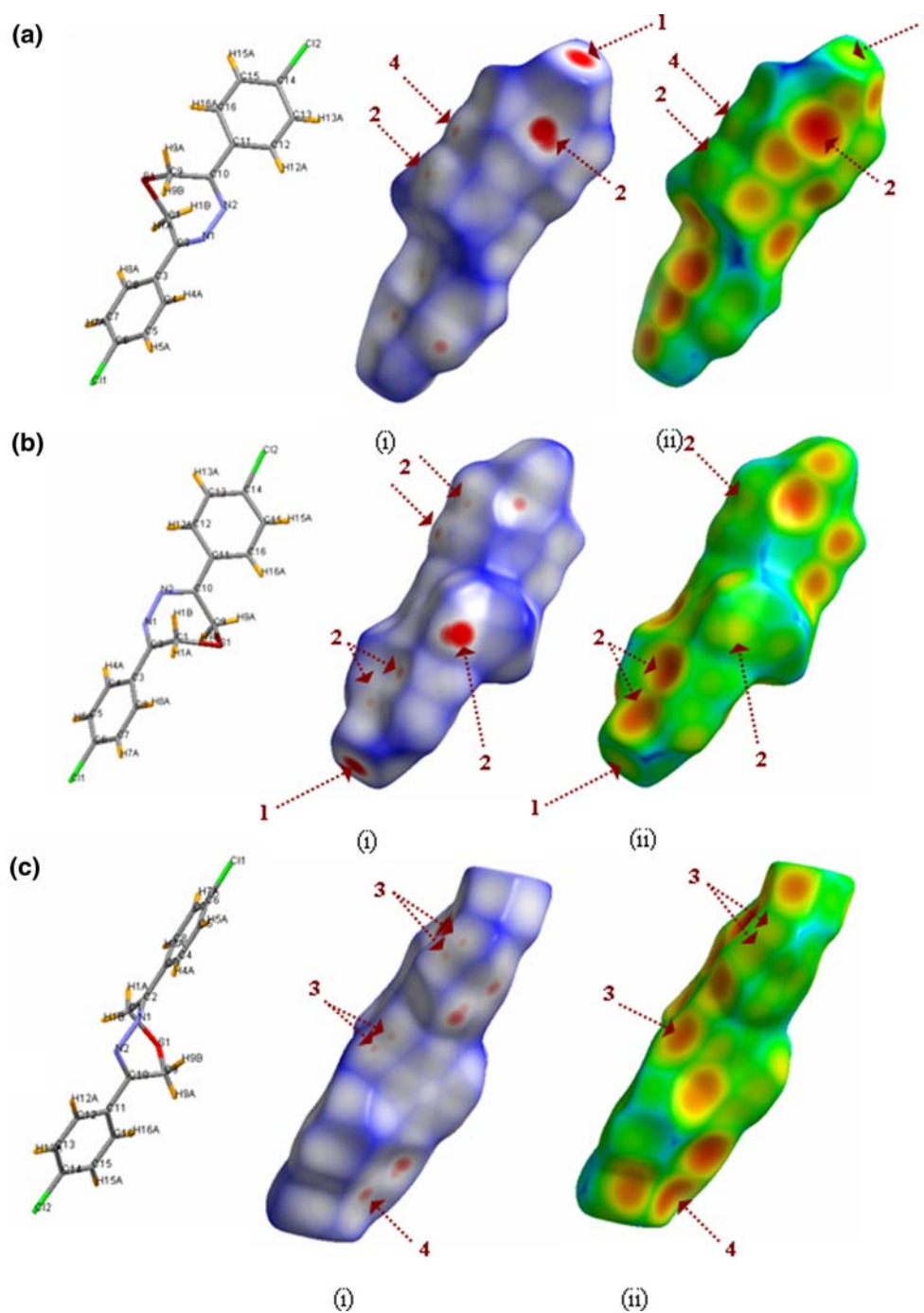
Table 2 Selected bond lengths (Å) and angles (°) for (I)

S(1)–C(1)	1.812(5)	C(1)–S(1)–C(9)	98.3(2)
S(1)–C(9)	1.813(5)	C(2)–N(1)–N(2)	117.8(4)
Cl(1)–C(6)	1.727(5)	C(10)–N(2)–N(1)	117.3(4)
Cl(2)–C(14)	1.727(5)	C(2)–C(1)–S(1)	109.4(3)
N(1)–C(2)	1.281(6)	C(11)–C(10)–C(9)	122.2(4)
N(1)–N(2)	1.396(6)	C(16)–C(11)–C(12)	117.9(5)
N(2)–C(10)	1.282(6)	C(16)–C(11)–C(10)	121.5(4)
C(1)–C(2)	1.512(6)	C(12)–C(11)–C(10)	120.5(4)
C(11)–C(16)	1.390(6)	N(1)–C(2)–C(1)	119.9(5)
C(11)–C(12)	1.408(6)	C(3)–C(2)–C(1)	122.4(4)
C(2)–C(3)	1.478(7)	C(8)–C(3)–C(4)	117.6(5)
C(3)–C(8)	1.388(6)	C(8)–C(3)–C(2)	122.7(4)
C(3)–C(4)	1.400(6)	C(4)–C(3)–C(2)	119.7(4)
C(4)–C(5)	1.371(6)	C(13)–C(14)–C(15)	119.8(5)
C(14)–C(15)	1.386(7)	C(13)–C(14)–Cl(2)	120.0(4)
C(5)–C(6)	1.379(6)	C(15)–C(14)–Cl(2)	120.2(4)
C(15)–C(16)	1.384(7)	C(16)–C(15)–C(14)	119.9(4)

The compound (I) has a thiadiazepine seven-membered ring, which is commonly considered unstable because the high strain in seven-membered ring. The torsion angle studies indicate that the seven-membered ring in the title compound adopts a distorted boat shaped conformation. The two substituted *p*-chlorophenyl ring systems in (I) are flat. The two aromatic rings, *p*-chlorophenyl, of (I), although not orthogonal to each other, adopt a relatively large dihedral angle to each other, $50.3(9)^\circ$. The distance between S–C(1) is longer than the normal S–C(sp^3) distance of $1.81(2) \text{ \AA}$ [18]. The N(1)–N(2) distance of $1.39(5) \text{ \AA}$, corresponds to a normal N(sp^2)–N(sp^2) distance [18].

For the first time in our research into the applications of Hirshfeld surface-based tools, we make use of Crystal Explorer [19], a new computer program for calculation and display of Hirshfeld surfaces and 2D fingerprint plots, to comprising the most common intermolecular interactions

Fig. 2 The Hirshfeld surface of (I), (a), (b) and (c), mapped with d_{norm} (i) and the d_e (ii) property in three orientation. The molecules beside the surfaces have been added for clarity



of inorganic and organic compounds. The new d_{norm} surface and the breakdown of fingerprint plots [20] (existing new techniques and tools based on the Hirshfeld surface and already incorporated in Crystal Explorer computer program) was used for visualizing and exploring of title compound structure for decoding and quantifying intermolecular interactions in crystal lattice.

As above mentioned the new d_{norm} (normalized contact distance, Eq. 1) surface and the breakdown of fingerprint

plots [20] were used for visualizing and exploring of title compound for quantifying intermolecular interactions in crystal lattice.

$$d_{\text{norm}} = \frac{d_i - r_i^{\text{vdW}}}{r_i^{\text{vdW}}} + \frac{d_e - r_e^{\text{vdW}}}{r_e^{\text{vdW}}} \quad (1)$$

In title compound, owing to the presence of N, Cl, S and H atoms in molecule structure, a large numbers of van der Waals interactions, ($\text{H}\cdots\text{H}$, $\text{Cl}\cdots\text{Cl}$, $\text{C}\cdots\text{H}$, $\text{Cl}\cdots\text{S}$,

N...H and S...H) have been observed in crystal lattice. Figure 2 shows the Hirshfeld surfaces 3D maps (d_c and d_{norm}) of synthesized compound that have been colour coded.

As be shown in the Fig. 7, 2D fingerprint plot has been constructed and break downed. By using above mentioned 3D maps and 2D diagrams, we can realize and compare the kinds of intermolecular interactions in the crystal lattice of title compound.

The regions in Fig. 2a, b labeled 1 are associated with Cl...Cl contacts (Cl(1) at $(-2 + x, y, 1 + z)$ and Cl(2) at (x, y, z)) 3.26(3) Å (see Fig. 3). In this case, d_{norm} focuses attention on Cl...Cl contact which is not apparent on the d_c surface.

C-H... π contacts from alkyl atom C(9) in the molecule at $(x, y, 1 + z)$, acts as a donor to the C3/C4-C7/8 aryl ring in the molecule at $(-2 + x, y, 1 + z)$, can be seen in regions labelled 2 in Fig. 2a, b(i and ii) (see Fig. 4).

Yellow concave area classified 3 in Fig. 2c(ii) and a pair of pale-red regions labelled 3 in Fig. 2c(i) reveal the weak intermolecular interaction from nitrogen atoms, (N(1) and N(2)), of seven-membered ring, at $(2 - x, -y, 1 - z)$, and hydrogen atom of *p*-chlorophenyl ring, H(5A) at (x, y, z) , 2.86(5) and 2.96(7) Å (Fig. 5).

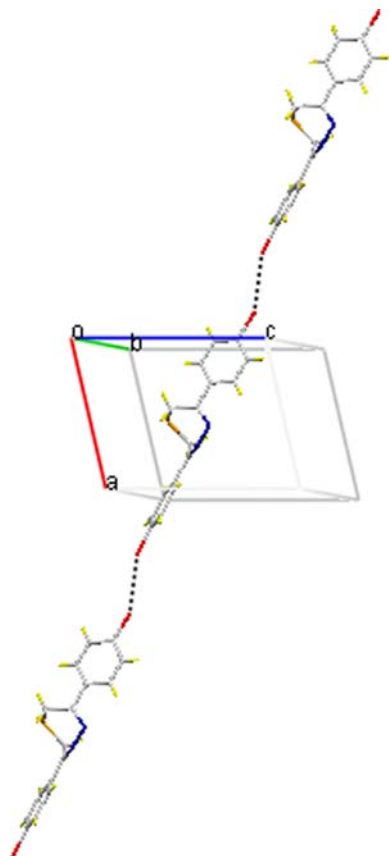


Fig. 3 Part of the crystal structure of (I), showing the formation of a chain along [100] generated by the Cl...Cl contacts

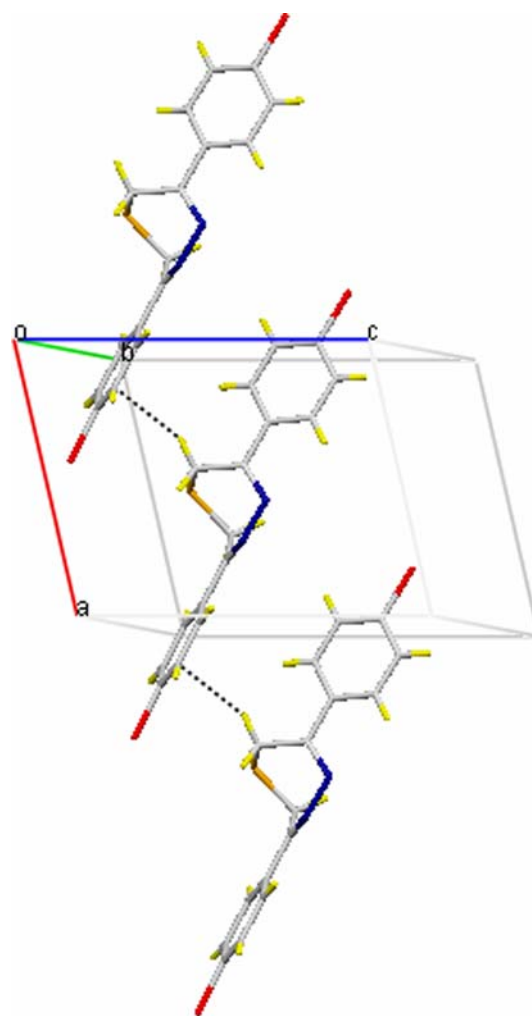


Fig. 4 Part of the crystal structure of (I), showing the formation of a chain along [100] generated by the C-H... π interactions

The areas in Fig. 2a, c(i and ii) labelled 4 are weak Cl...H interactions with the range of 3.08(8) to 3.21(8) Å in the crystal network (see Fig. 6).

Figure 7 illustrates the decomposing of finger print plot for (I) in crystal lattice, highlighting separately the H...H, Cl...Cl, C-H... π , Cl...H, Cl...S, N...H and S...H intermolecular contacts; to provide context, the outline of the full fingerprint is shown in grey. This analysis allows separation of contributions from different interaction kinds, which commonly overlap in the full fingerprint.

From this simple analysis, it immediately emerges that title compound are noticeably contribute in C-H... π interactions (28.1% area) more than other contacts. Figure 8 shows the relative contributions to the Hirshfeld surface area due to H...H, Cl...Cl, Cl...H, Cl...S, N...H and S...H contacts for (I).

Fig. 5 Part of the crystal structure of (I), showing the formation of a chain along [100] generated by the N...H interactions

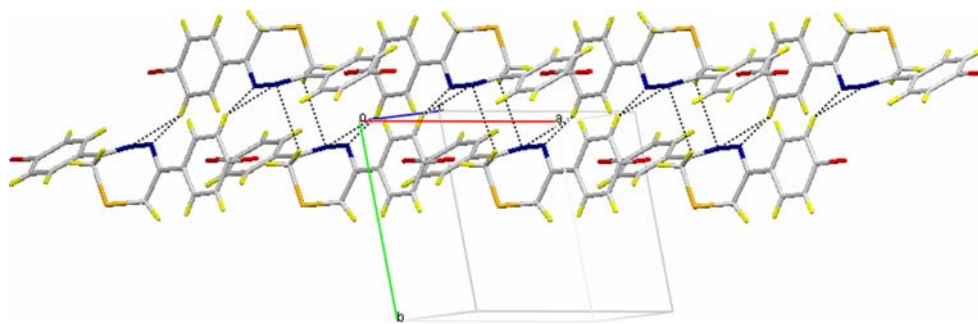
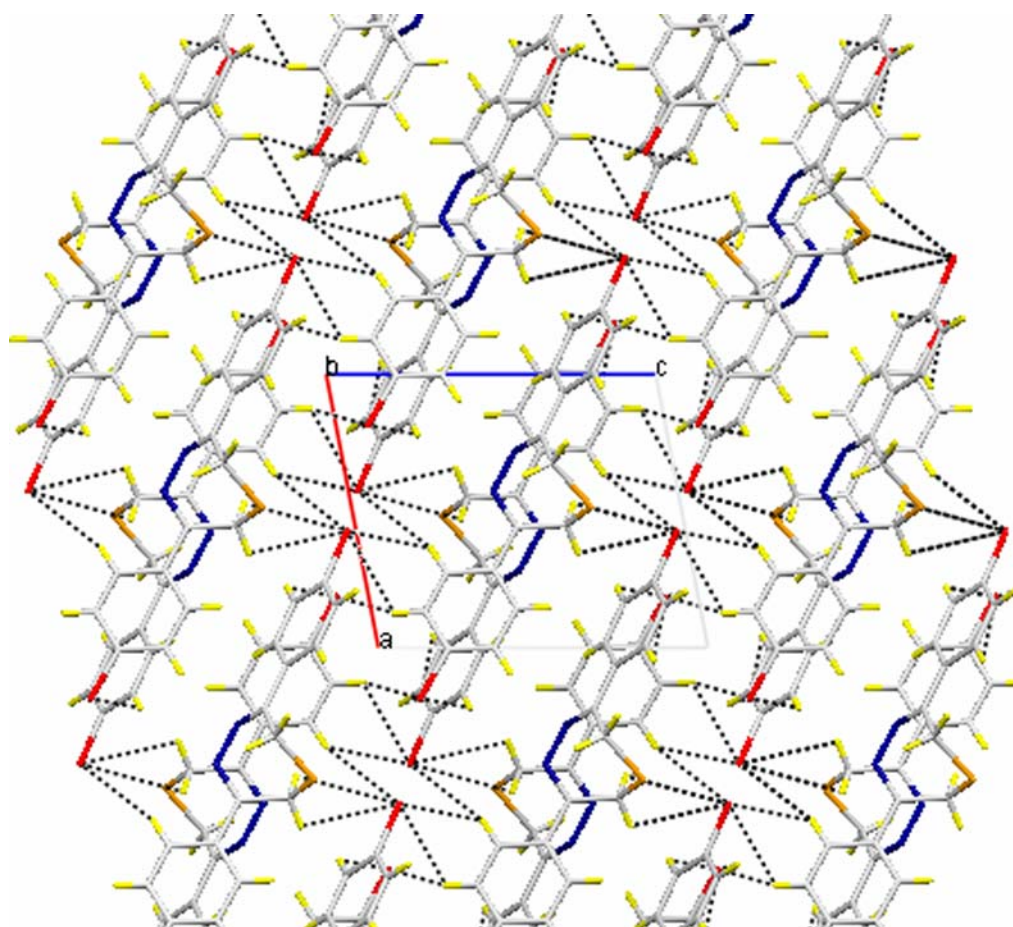


Fig. 6 A view of Cl...H interactions along the crystallographic plane ac



Conclusion

In this paper, 3,6-di(*p*-chlorophenyl)-2,7-dihydro-1,4,5-thiadiazepine has been synthesized, crystallized and characterized by IR spectrophotometer, ^1H NMR, EIMS and X-ray single

crystallography. Hirshfeld surface and 2D finger print plots were used for visualizing, exploring and quantifying intermolecular interactions in crystal lattice. This analysis showed noticeably contribute in C-H... π interactions more than other contacts (H...H, Cl...Cl, Cl...H, Cl...S, N...H and S...H).

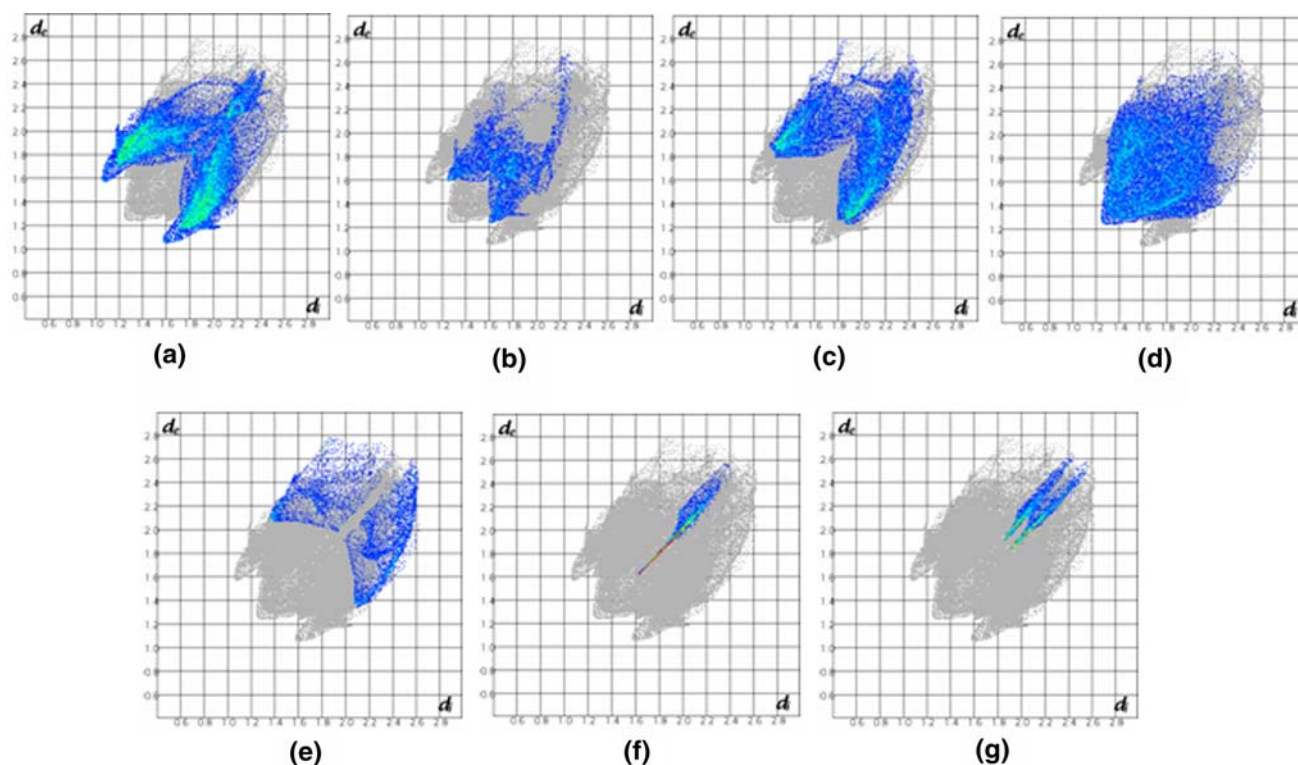


Fig. 7 Fingerprint plots for title complex resolved into C-H... π (a), N...H (b), Cl...H (c), H...H (d), S...H (e), Cl...Cl (f) and Cl...S (g) intermolecular contacts. The full fingerprint appears beneath each decomposed plots as a *grey shadow*

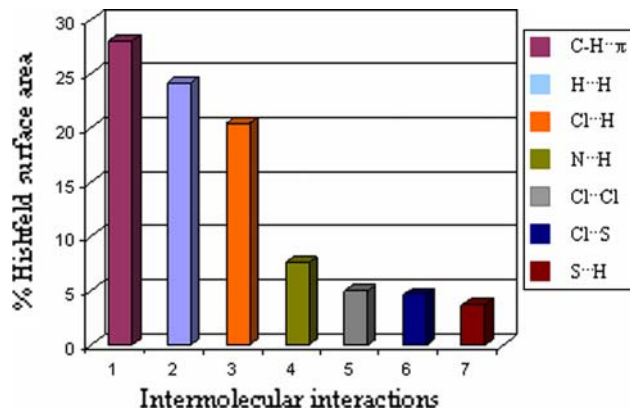


Fig. 8 Relative contributions to the Hirshfeld surface area for the various intermolecular contacts (C-H... π , N...H, Cl...H, H...H, S...H, Cl...Cl and Cl...S in title compound

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