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Crystal Structure and Hirshfeld Surface Analysis of (*E*)-1-(2,3-Dichlorobenzylidene)-2-Phenylhydrazine

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ABSTRACT

Schiff base analogue (*E*)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine was synthesized by condensation reaction of 2,3-dichlorobenzaldehyde and phenylhydrazine hydrochloride in the presence of sodium acetate in ethyl alcohol under reflux conditions. The structure of the title compound was determined by single crystal X-ray diffraction studies. The compound crystallizes in the orthorhombic crystal system with space group *Pcab* and unit cell parameters, $a=8.030(6)$ Å, $b=13.179(10)$ Å, $c=28.996(4)$ Å and $Z=8$. Crystal structure of the title compound is stabilized due to the C—H...Cl and C—H... π and π - π interactions.

Keywords: Schiff base, Condensation, X-ray diffraction, Crystal structure, Interactions

INTRODUCTION

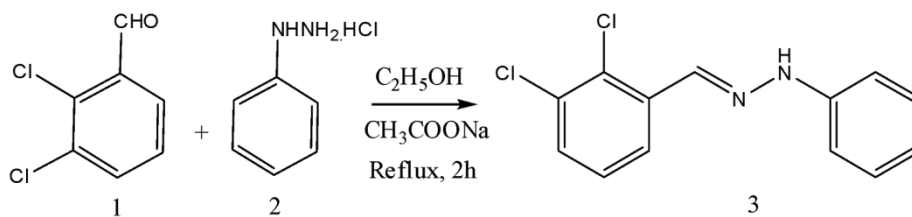
The study of Schiff base hydrazones is of vital importance due to their biological importance in the field of medicinal chemistry. Generally, the hydrazones serve as intermediates in the synthesis of varied number of organic and inorganic compounds. They have been used for the preparation of stable coordination complexes with most transition metal ions [1]. Hydrazones were extensively used as precursors in organic synthesis involving the construction of bioactive molecules such as pyrazolines [2,3], formylpyrazoles [4-6] and oxadiazoles [7]. Hydrazones are the essential class of compounds for the development of new chemical entities to treat various diseases of clinical importance. Hydrazones are well known for their wide spectrum of biological effects including antifungal [8], anticonvulsant [9] and analgesic activity [10]. In view of the synthetic utility and pharmaceutical applications associated with hydrazones, we herein report the synthesis, spectral and X-ray diffraction studies of (*E*)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine.

MATERIALS AND METHODS

The chemicals used were analytical grade from Sigma-Aldrich (India) and Merck Chemicals. Melting point was determined using open capillary and was uncorrected. ¹H NMR and ¹³C NMR spectra were recorded on Agilent-NMR 400 MHz and 100 MHz spectrometer using CDCl₃ as solvent. The Chemical shifts were expressed in δ ppm. Mass spectra were obtained on Mass Lynx SCN781 spectrometer TOF mode.

Synthesis of (*E*)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine

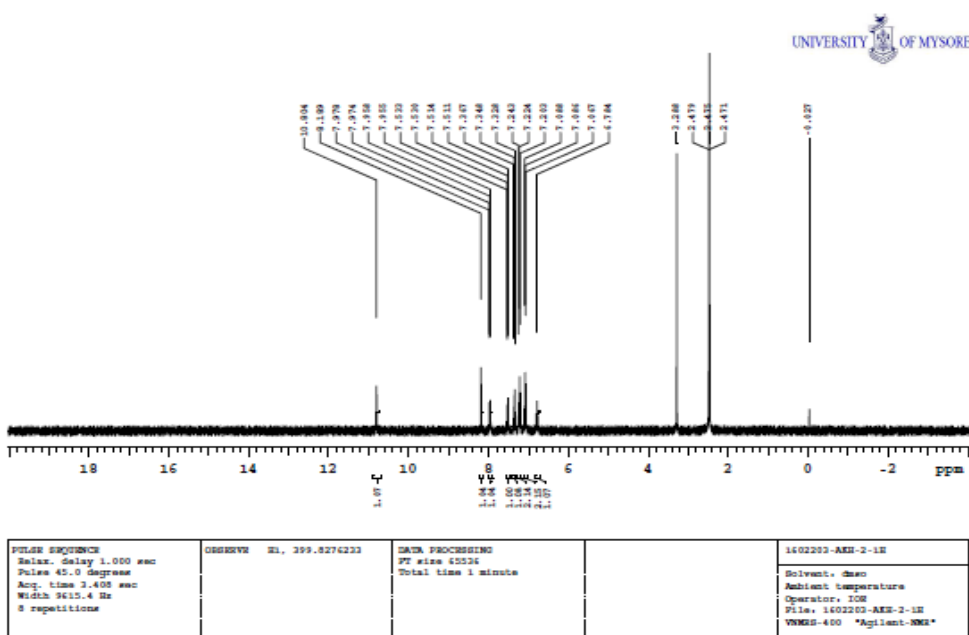
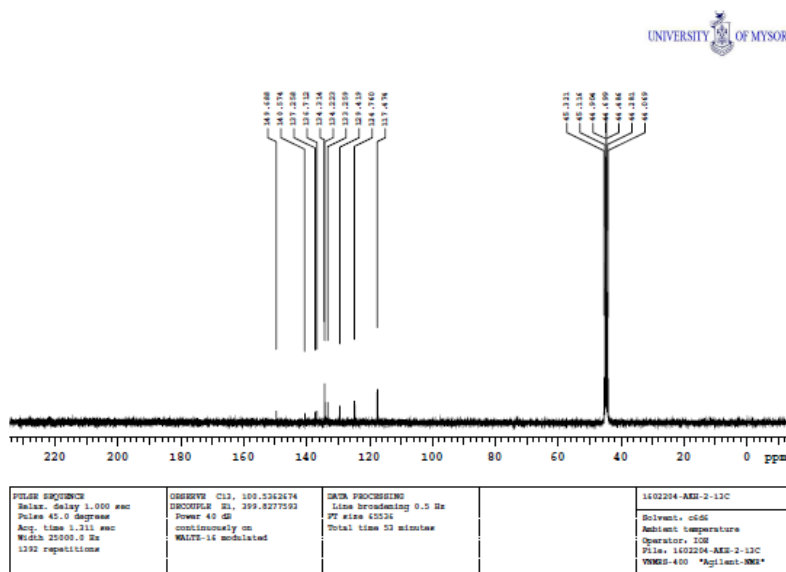
To the solution of 0.01 mol 2,3-dichlorobenzaldehyde (1) and 0.01 mol phenylhydrazine hydrochloride (2) in ethyl alcohol (20 ml), a saturated solution of sodium acetate in water was added drop-wise till to optimum pH of 7. Then, the mixture was refluxed on a water bath for 2 h. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was cooled to room temperature and poured into ice cold water. The solid separated was filtered, washed with ice cold water and dried. Colourless prism shaped crystals of title compound (*E*)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine, (3) were obtained by slow evaporation method by dissolving in methyl alcohol solvent, yield 90%, m.p. 108-110°C. The reaction pathway is depicted in Figure 1.

Figure 1: Pathway for the synthesis of (*E*)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine

Data, value and validation

Spectral data analysis

$^1\text{H NMR}$ (CDCl_3 , δ ppm): 10.80 (s, ^1H , CH=N), 8.19 (s, ^1H , NH), 6.78 (t, ^1H , Ar-H), 7.95-7.98 (dd, 2H, Ar-H), 7.511-7.53 (dd, 2H, Ar-H), 7.07-7.09 (d, ^1H , Ar-H), 7.32-7.36 (t, ^1H , Ar-H), 7.203-7.243 (d, ^1H , Ar-H) (Figure 1a). $^{13}\text{C NMR}$ (CDCl_3 , δ ppm): 117.47 (2C), 124.76 (2C), 129.4 (1C), 133.59 (1C), 134.22 (1C), 134.31(2C), 136.71(1C), 137.25(1C), 140.57(1C), 149.68(1C, C=N) (Figure 1b). MS (m/z): 268.97 (M+4, 10%), 266.97 (M+2, 63%), 264.97 (M^+ , 100%), 144.95, 133.05, 93.04 (Figure 1c).

Figure 1a: $^1\text{H NMR}$ spectrum of (*E*)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazineFigure 1b: $^{13}\text{C NMR}$ spectrum of (*E*)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine

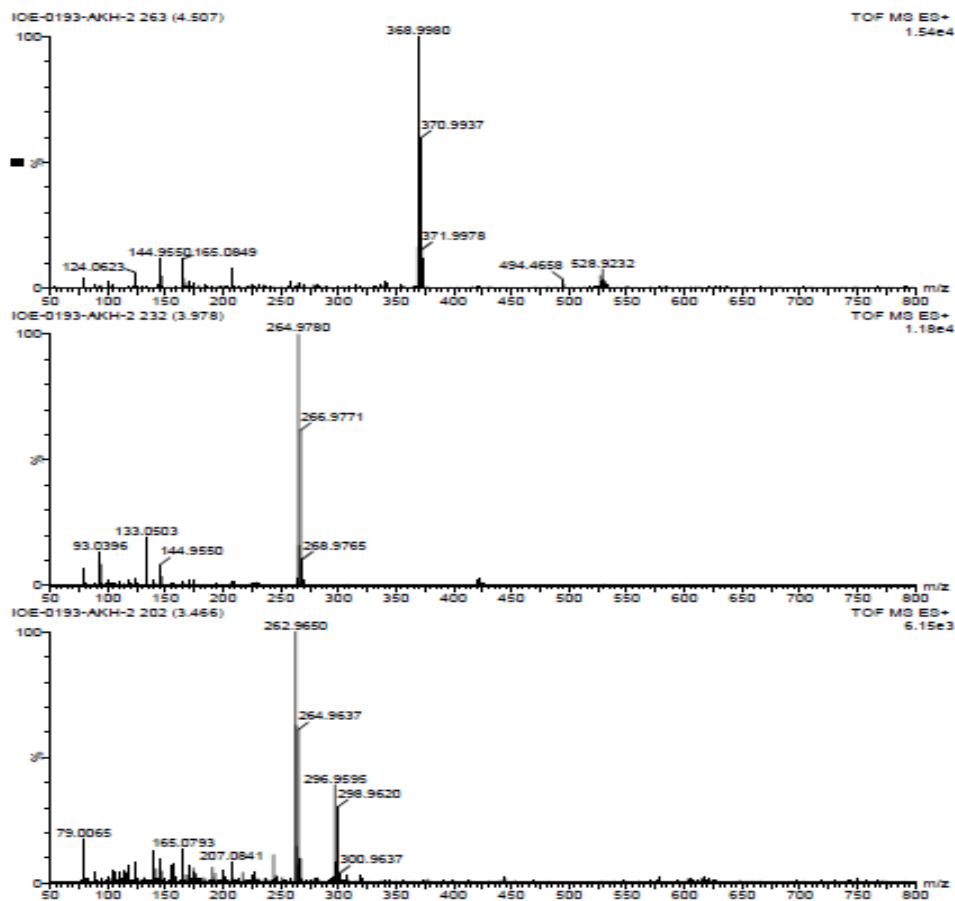


Figure 1c: Mass spectrum of (E)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine

Single crystal X-Ray diffraction studies

Data collection and structure solving procedures

A single crystal of dimension $0.29 \times 0.32 \times 0.35$ mm of the title compound was chosen for data collection and X-ray intensity were collected with χ fixed at 54° and ϕ , from 0° - 360° , scan width at 0.5° , exposure time of 3 s, the sample to detector distance of 50.0 mm at a temperature 293 K on Rigaku XtaLAB Mini X-ray diffractometer with MoK_α radiation of wavelength $\lambda=0.71073$ Å. A complete data set was processed by Crystal Clear [11]. The crystal structure was solved by direct methods and refined by full-matrix least squares method on F^2 using SHELX [12]. After several cycles of refinement, the final difference Fourier map showed peaks of no chemical significance and the residual is saturated to 0.0511. The geometrical calculations were carried out using PLATON [13]. The molecular and packing diagrams were generated using Mercury [14].

Hirshfeld surface procedures

In order to know the molecular interactions in the crystal, Hirshfeld surface analysis is carried out, using Crystal Explorer version 3.1 [15]. The 3D Hirshfeld surface mapped over a range of -0.5 to 1.5 Å is d_{norm} . The expanded 2D fingerprint plots are displayed in the range of 0.6 - 2.6 Å viewed with the d_e and d_i distance scales displayed on the graph axes. The d_e and d_i are the nearest distances to the nuclei from outside and inside the surface to the Hirshfeld surface, respectively. The short contacts information is shown effectively as red circular spots with negative values on the d_{norm} . The redistribution of electronic clouds in a molecule is represented as electrostatic potential (EP) plots and these 3D computer graphics generated using Crystal Explorer version 3.1 [15]. High electronegativity regions represented as red color, while blue colored regions represent electropositivity and plotted over a range of 0.008 - 0.008 a.u.

X-ray diffraction studies of the title compound shows 'E' configuration around C9-N10 double bond. The ORTEP of the molecule with displacement ellipsoids drawn at 50% probability level is shown in Figure 2. The packing of molecule when viewed along a and b -axes are shown in Figure 3. The crystal data and the structure refinement details are given in Table 1. Bond lengths, bond angles and the torsion angles are in good agreements with the standard values are given in Tables 1a-1c. In the title compound, (E)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine, a dihedral angle of $4.88(13)^\circ$ is formed between the mean planes of two phenyl rings, indicates that the two rings are in a plane. The +*anti periplanar* orientation of the molecule which is also evident from the torsion angle of $174.6(2)^\circ$ measured at the segment C9-N10-N11-C12, reveals the axial alignment of the rings. The Schiff base formation was confirmed through the bond formation between sp^2 hybridized carbon and nitrogen of imine group with a bond length of $1.277(3)$ Å. Contracted double bonds with shorter bond lengths usually observed at imine moiety of Schiff bases [16-18].

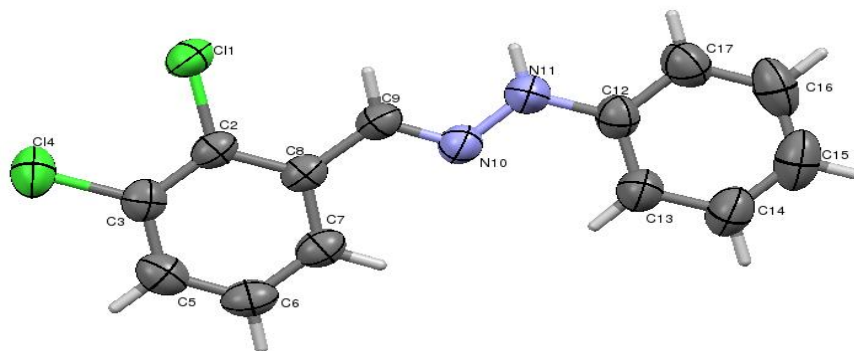


Figure 2: ORTEP of the molecule drawn at 50% probability of thermal ellipsoids

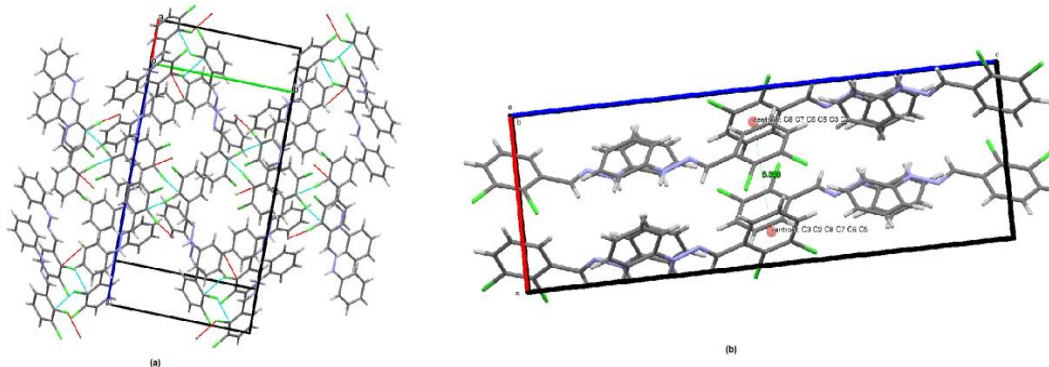
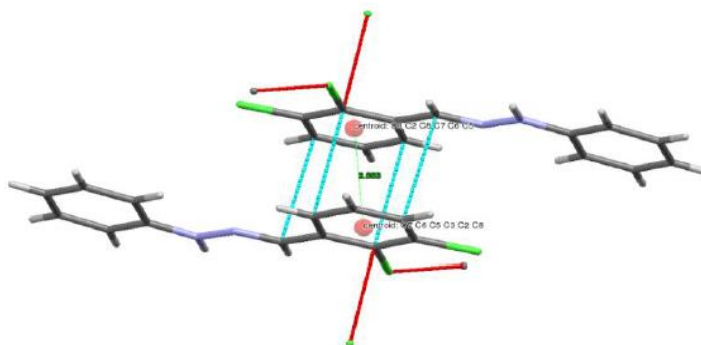
Figure 3(a): Packing of the molecule along the *a*-axis, (b) packing along *b*-axis and Cg1–Cg1 interaction distance of 5.388 Å

Figure 3(c): Cg1–Cg1 interaction distance 3.553 Å (Blue lines-van der Waal's forces, red lines hydrogen bonds)

Table 1: Crystal structure and refinement data

CCDC Number	1518995
Empirical formula	C ₁₃ H ₁₀ N ₂ Cl ₂
Formula weight	265.13 g mol ⁻¹
Temperature	293 K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, <i>Pcab</i>
Unit cell dimensions	<i>a</i> =8.030(6) Å
	<i>b</i> =13.179(10) Å
	<i>c</i> =23.656(18) Å
Volume	2504(3) Å ³
Z, calculated density	8, 1.407 Mg/m ³
Absorption coefficient	0.496 mm ⁻¹
<i>F</i> ₀₀₀	1088
Crystal size	0.29 × 0.32 × 0.35 mm
Limiting indices	-10 ≤ <i>h</i> ≤ 5, -5 ≤ <i>k</i> ≤ 16, -11 ≤ <i>l</i> ≤ 30
Reflections collected/unique	5018/2812 (R _{int} =0.0365)
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data/restraints/parameters	2812/0/155
Goodness-of-fit on <i>F</i> ²	1.025
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> ₁ =0.0511, <i>wR</i> ₂ =0.1460
<i>R</i> indices (all data)	<i>R</i> ₁ =0.0722, <i>wR</i> ₂ =0.1679
Largest diff. peak and hole	0.357 and -0.267 e. Å ⁻³

Table 1a: Bond lengths (Å)

Atoms	Length	Atoms	Length
C11-C2	1.728(3)	C6-C7	1.392(4)
C14-C3	1.728(3)	C7-C8	1.394(3)
N10-N11	1.354(3)	C8-C9	1.458(3)
N10-C9	1.277(3)	C12-C17	1.395(4)
N11-C12	1.388(3)	C12-C13	1.384(4)
C2-C8	1.398(3)	C13-C14	1.381(4)
C2-C3	1.389(3)	C14-C15	1.369(5)
C3-C5	1.380(3)	C15-C16	1.365(4)
C5-C6	1.364(4)	C16-C17	1.382(4)

Table 1b: Bond angles (°)

Atoms	Angle	Atoms	Angle
N10-N11-C12	119.8(2)	C7-C8-C9	120.64(19)
C11-C2-C8	120.27(18)	N10-C9-C8	119.7(2)
C3-C2-C8	120.5(2)	N11-C12-C13	121.4(2)
C11-C2-C3	119.25(17)	C13-C12-C17	119.2(2)
C2-C3-C5	120.0(2)	N11-C12-C17	119.4(2)
C14-C3-C2	120.61(18)	C12-C13-C14	120.1(3)
C14-C3-C5	119.39(18)	C13-C14-C15	120.7(3)
C3-C5-C6	120.7(2)	C14-C15-C16	119.3(3)
C5-C6-C7	119.7(2)	C15-C16-C17	121.6(3)
C6-C7-C8	121.0(2)	C12-C17-C16	119.1(3)
C2-C8-C9	121.2(2)		

Table 1c: Torsion angles (°)

Atoms	Angle	Atoms	Angle
C9-N10-N11-C12	174.6(2)	C3-C5-C6-C7	1.1(4)
N11-N10-C9-C8	-178.6(2)	C5-C6-C7-C8	-1.2(4)
N10-N11-C12-C17	178.2(2)	C6-C7-C8-C2	0.6(3)
N10-N11-C12-C13	-3.0(4)	C6-C7-C8-C9	178.3(2)
C11-C2-C3-C14	-1.8(3)	C2-C8-C9-N10	-179.3(2)
C11-C2-C8-C7	-179.46(17)	C7-C8-C9-N10	3.0(3)
C11-C2-C8-C9	2.8(3)	N11-C12-C13-C14	-179.9(3)
C3-C2-C8-C7	0.2(3)	C17-C12-C13-C14	-1.1(4)
C3-C2-C8-C9	-177.6(2)	N11-C12-C17-C16	179.4(3)
C8-C2-C3-C5	-0.3(3)	C13-C12-C17-C16	0.6(4)
C11-C2-C3-C5	179.35(18)	C12-C13-C14-C15	0.9(5)
C8-C2-C3-C14	178.58(18)	C13-C14-C15-C16	-0.2(5)
C14-C3-C5-C6	-179.24(19)	C14-C15-C16-C17	-0.3(5)
C2-C3-C5-C6	-0.4(4)	C15-C16-C17-C12	0.1(5)

The molecules exhibit no specific intermolecular hydrogen bonds, possesses C—H...Cg and C—Cl...Cg interaction and an intramolecular hydrogen bond interaction. Respective donor and acceptor parameters are as listed in Table 2. Two π - π interactions were observed from Cg(1)-->Cg(1) with distances and symmetry codes 5.388(4) Å (-1-x, 1-y, 1-z), 3.553(3) Å (-x, 1-y, 1-z) [Cg(1) is the centroid of C2-C3-C5-C6-C7-C8]. Absence of significant intermolecular interactions in title molecule, vander Waal's forces are purely responsible for molecular stability and the packing may be a result of C---H... π , Cg interactions (Figures 3b and 3c).

Table 2: Hydrogen bond and short contacts geometry (Å)

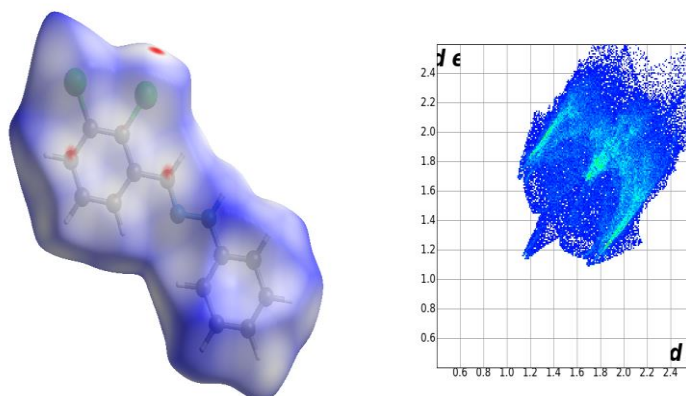
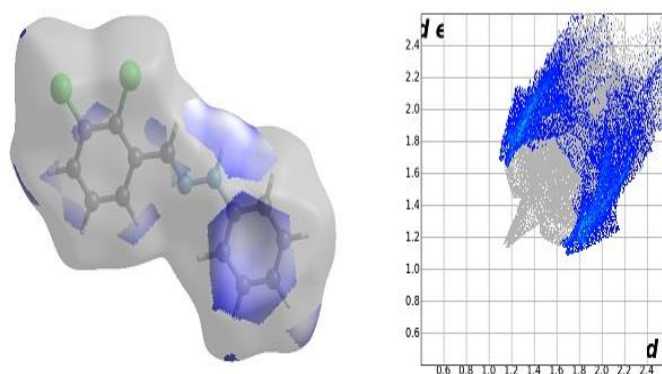
D—H/Cl...A	d(D—H/Cl)	d(H/Cl...A)	d(D...A)	<D—H/Cl...A
N11-H11...Cg2 ⁽ⁱ⁾	0.86	2.93	3.711(4)	152
C14-H14...Cg2 ⁽ⁱⁱ⁾	0.86	2.98	3.745(4)	140
C2-Cl1...Cg1 ⁽ⁱⁱⁱ⁾	3.373	4.895	145.44(9)	58.91
C9-H9...Cl1*	0.93	2.64	3.0356	106

Symmetry codes: (i) 1/2+x, 1-y, 1/2-z, (ii) -1/2+x, 1/2-y, z, (iii) 1/2+x, 3/2-y, z

*Intramolecular interaction. Cg1 and Cg2 are the centroids of C2-C3-C5-C6-C7-C8 and C12-C13-C14-C15-C16-C17

Hirshfeld surface analysis

The quantitative estimations of the atomic interactions shown as blue colored patches are superimposed on 2D and 3D Hirshfeld surfaces of the molecule in grey. The 3D and 2D Hirshfeld surfaces d_{norm} and the fingerprint plots are shown in Figure 4 and Figure 5a-5c respectively. Inter contacts are shown in these figures, which contribute to 2D Hirshfeld surface of the molecule are C...H (23%), Cl...H (25.5%), N...H (5.6%). The Cl...H interactions are higher than the C...H interactions; this may be attributed to the presence of two chlorine atoms in the asymmetric unit. The C...H and Cl...H interactions are shown as two blue spikes overlaid at the edges of the grey colour 2D fingerprint plot diagram of the whole molecule. Small red spots on the 3D plots indicate very weak D...H...A interactions (van der Waal's forces). This is also confirmed by the increased $d(\text{H...A})$ lengths of more than 2Å. Among the same atoms interactions H...H is maximum with 31.7% appears as a central spike in the 2D plot; N...N is minimum with 0.1%. The Cl...Cl 0.7%, C...C 4.5%, Cl...C 7.4% 2D Hirshfeld surfaces are observed for this molecule. The 3D Hirshfeld surface plots complementarily depicted this with blue patches on the grey colour envelop of the molecule. The electrostatic potentials mapped for the molecule using Crystal Explorer [15] is as shown in the Figure 6. Big red colour lobe at the two chlorine atoms of the molecule represents high electronegativity accumulated because of the formation of electronic clouds of the molecule near chlorine atoms; Cl4 is more electronegative and involves as donor atom for hydrogen bond (Table 2). Whereas ring Cg1 and Cl1 atom are electropositive and Cl1 is represented as red coloured cloud, which has become electron acceptor in the hydrogen bond with imine carbon C9---H9...Cl1. This donor and acceptor behaviours of the two chlorine atoms are shown in Figure 3(b). The electronegativity of the molecule is observed near the -NH group of the molecule, nitrogen atom of this part of the molecule also involved as hydrogen donor (Table 2). Thus electrostatic potential (EP) provides a visual method to predict reactive sites for electrophilic and nucleophilic bonding information of the molecules.

Figure 4: Hirshfeld surfaces associated with d_{norm} and finger print plot of the molecule considering all atomsFigure 5a: C-H, d_{norm} and finger print plot of the molecule

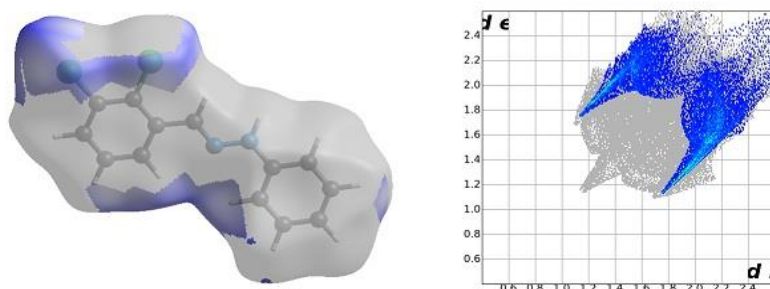
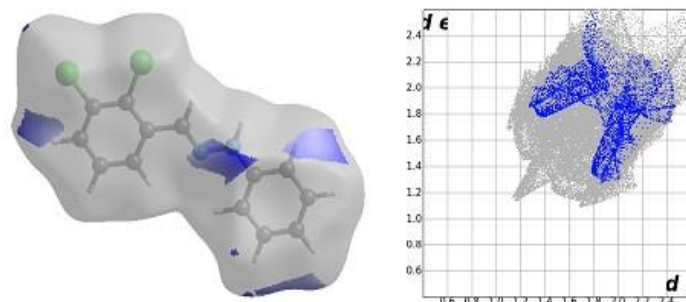
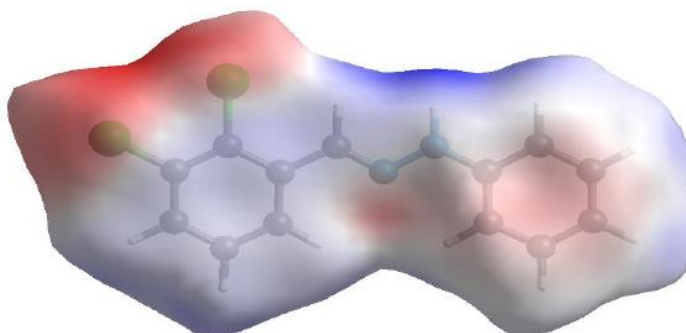
Figure 5b: Cl-H, d_{norm} and finger print plot of the moleculeFigure 5c: N-H, d_{norm} and finger print plot of the molecule

Figure 6: Electrostatic potential plot of the molecule

CONCLUSION

The title compound, (*E*)-1-(2,3-dichlorobenzylidene)-2-phenylhydrazine was synthesized. The crystal structure of the title compound was determined and analyzed by single crystal X-ray diffraction studies. The dihedral angle between the mean planes of two phenyl rings was $4.88(13)^\circ$. The molecular and crystal structure of the title compound is stabilized by the van der Waals' forces, intramolecular hydrogen bonds and C—H \cdots π , π - π interactions. The Hirshfeld surface analysis substantiates the findings of X-ray diffraction analysis.

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