Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(12):286-291
(http://derpharmachemica.com/archive.html)

Hydrogen bonded supramolecular framework in a monoclinic polymorph of (*E*)-2-(1-(2-phenylhydrazono)ethyl)phenol

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ABSTRACT

Schiff base of 2-acetylphenolwas synthesized by the reaction of 2-acetylphenol and phenylhydrazine hydrochloride in the presence of sodium acetate in ethyl alcohol under reflux conditions. The crystal structure of the title compound was determined and analyzed by single crystal X-ray diffraction studies. The compound crystallizes in the monoclinic crystal system with space group $P2_1/n$ and unit cell parameters, a = 13.409 (4) Å, b = 10.665 (3) Å, c = 17.688 (4) Å; β=109.2(8)° and Z = 8. The crystal and molecular structure of the title compound is stabilized by the O—H···N and N—H···O hydrogen bond interactions.

Keywords: Schiff base, condensation, space group, crystal structure, hydrogen bond interactions.

INTRODUCTION

In recent times, interest in the study of Schiff base hydrazones has been increasing due to their biological importance in medicinal chemistry. The hydrazones were proved to be versatile intermediates in synthetic organic and inorganic chemistry. They have been used for the preparation of stable coordination complexes with most transition metal ions [1]. In organic synthesis, hydrazones were extensively used as precursors for the construction of bioactive molecules such as pyrazolines [2-4], formylpyazoles [5-7], oxadiazoles [8-9] and thiazolidinones [10]. Hydrazones constitute an essential class of compounds for the development of new chemical entities to treat various diseases of clinical importance. Hydrazones were known to exhibit wide spectrum of biological effects including antifungal [11], anti-inflammatory [12], anticonvulsant [13] and analgesic [14]. In view of the synthetic utility and pharmaceutical applications associated with hydrazones, herein we report the synthesis, spectral and X-ray diffraction studies of (*E*)-2-(1-(2-phenylhydrazono)ethyl)phenol.

MATERIALS AND METHODS

Chemicals used were obtained from Aldrich Chemicals Ltd., India and were used without further purification. Melting points were determined by an open capillary tube method and are uncorrected. The ^{1}H NMR spectra was recorded on Agilent-NMR 400 MHz spectrophotometer in $CDCl_3$ with TMS as an internal standard. The Chemical shifts are expressed in δ ppm. Mass spectra were obtained on Mass Lynx SCN781 spectrophotometer TOF mode.

Synthesis of (*E*)-2-(1-(2-phenylhydrazono) ethyl) phenol (3)

To the solution of2-acetylphenol, **1** (0.01 mol) in ethyl alcohol (20 mL), a solution of phenylhydrazine hydrochloride, **2** (0.01 mol) and sodium acetate (0.01 mol) in water:ethyl alcohol was added. Then the mixture was refluxed on a water bath for 1-2 h. The progress of the reaction was monitored by TLC. After completion of the

reaction, the mixture was poured into ice cold water. The solid separated was filtered, washed with ice cold water and dried to obtain the target molecule **3**. The reaction pathway is illustrated in **Figure 1**.

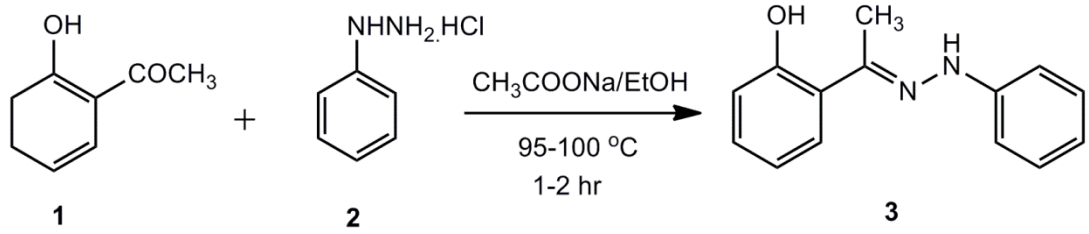

Figure 1.Reaction pathway for the synthesis of pyrazoline analogues

The solid obtained was dissolved in a minimum quantity of methyl alcohol at its boiling conditions to obtain the crystals of the product and the solution was kept aside undisturbed for slow evaporation of the solvent for three days. Colourless needle shaped crystals of the target molecule (*E*)-2-(1-(2-phenylhydrazono) ethyl) phenol, **3** formed were carefully separated from the solvent and dried.Yield 90%; m.p. 174-175 °C.

Spectral data: ^{1}HNMR ($CDCl_3$, δ ppm): 2.84 (s, 3H, CH_3), 6.10 (s, 1H, NH), 6.88-7.56 (m, 9H, Ar-H), 8.46 (s, 1H, OH). MS (m/z) for $C_{14}H_{14}N_2O$: 226 (M^+, 100%).

X-ray diffraction studies

A colourless needle shaped single crystal of dimension 0.20×0.24×0.30 mm of the title compound was selected for data collection and X-ray intensity were collected with χ fixed at 54° and φ, from 0° to 360°, scan width at 0.5°, exposure time of 3 sand the sample to detector distance of 50.0 mm at a temperature 293 K on Rigaku XtaLAB Mini X-ray diffractometer operating at 50 kV and 12 mA with MoK_α radiation of wavelength λ= 0.71073 Å.A complete data set was processed by *CRYSTAL CLEAR* [15]. All the frames could be indexed by using a primitive monoclinic lattice. The structure was solved by direct methods with R_{int} and R_{sigma} values of 0.051 and 0.064 respectively, and refined by full-matrix least squares method on F^2 using *SHELX* [16]. The geometrical calculations were carried out using *PLATON* [17].The molecular and packing diagrams were generated using *MERCURY* [18].

Data, Value and Validation

X-ray diffraction analysis revealed that the title compound is crystallized in the monoclinic crystal system with the space group $P2_1/n$, contradiction to the crystallization of the compound *o*-HydroxyacetophenonePhenylhydrazone with the space group $P2_1/c$ [19]. The *ORTEP* of the molecule with displacement ellipsoids drawn at 50 % probability level is shown in **Figure 2**.

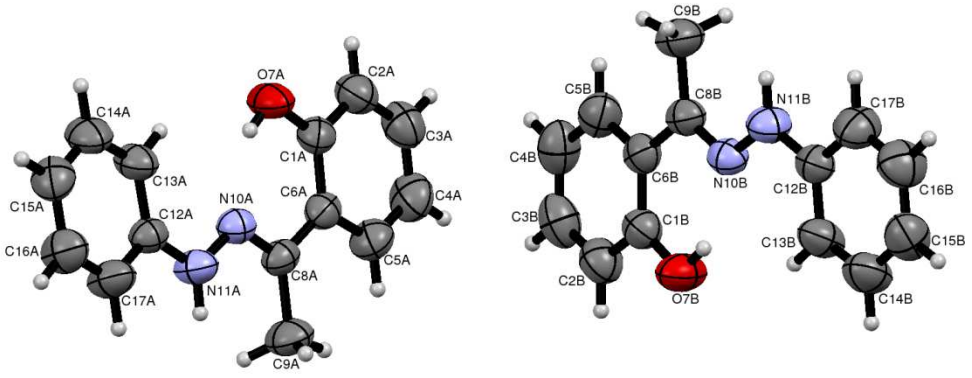

Figure 2.The*ORTEP* of the molecule with numbering scheme for non hydrogen atoms drawn at 50% probability level

The crystal data and the structure refinement details are given in **Table 1.** The bond lengths are listed in **Table 2** and bond angles are given in **Table 3**. The packing of molecules when viewed down along *a* axis shown in **Figure 3** shows that the molecules form layered stacking along (0 1 1) plane. The torsion angles are listed in **Table 4**.

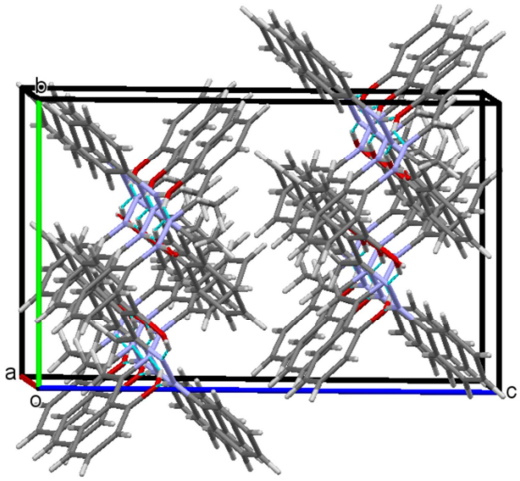

Figure 3.The packing of molecules when viewed down along *a* axis

Table 1.Crystal data and the details of structure refinement

CCDC Number	CCDC **1471488**
Empirical formula	$C_{14}H_{14}N_2O_1$
Formula weight	226.27 g mol^{-1}
Temperature	293 K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P $2_1/n$
Unit cell dimensions	*a* = 13.409 (4) Å
	b = 10.665 (3) Å
	c = 17.688 (4) Å
	β = 109.2 (8)°
Volume	2389.1 (1) $Å^3$
Z, calculated density	8, 1.258 Mg/m^3
Absorption coefficient	0.081 mm^{-1}
F_{000}	960
Crystal size	0.32×0.35×0.42 mm
Limiting indices	$-16 \le h \le 17$, $-12 \le k \le 13$, $-20 \le l \le 22$
Reflections collected / unique	10149 / 5390 (R_{int}= 0.052)
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5390/ 0 / 309
Goodness-of-fit on F^2	1.05
Final R indices [I>2sigma(I)]	*R*1 = 0.0683, *wR*2 = 0.1787
R indices (all data)	*R*1 = 0.1169, *wR*2 = 0.2199
Largest diff. peak and hole	0.27 and -0.17 e. $Å^{-3}$

Table 2. Bond lengths (Å)

C1A—O7A	1.347 (3)	C1B—O7B	1.354 (2)
C1A—C2A	1.378 (3)	C1B—C2B	1.381 (3)
C1A—C6A	1.407 (3)	C1B—C6B	1.409 (3)
C2A—C3A	1.370 (3)	C2B—C3B	1.365 (3)
C3A—C4A	1.368 (4)	C3B—C4B	1.359 (3)
C4A—C5A	1.377 (3)	C4B—C5B	1.373 (3)
C5A—C6A	1.392 (3)	C5B—C6B	1.397 (3)
C6A—C8A	1.475 (3)	C6B—C8B	1.468 (3)
C8A—N10A	1.288 (2)	C8B—N10B	1.294 (2)
C8A—C9A	1.491 (3)	C8B—C9B	1.497 (3)
N10A—N11A	1.356 (2)	N10B—N11B	1.358 (2)
N11A—C12A	1.386 (3)	N11B—C12B	1.384 (2)
C12A—C17A	1.377 (3)	C12B—C17B	1.379 (3)
C12A—C13A	1.387 (3)	C12B—C13B	1.388 (3)
C13A—C14A	1.375 (3)	C13B—C14B	1.370 (3)
C14A—C15A	1.368 (3)	C14B—C15B	1.363 (3)
C15A—C16A	1.358 (3)	C15B—C16B	1.372 (3)
C16A—C17A	1.368 (3)	C16B—C17B	1.369 (3)

Table 3. Bond angles (°)

O7A—C1A—C2A	117.1 (2)	O7B—C1B—C2B	117.4 (2)
O7A—C1A—C6A	122.6 (2)	O7B—C1B—C6B	122.1 (2)
C2A—C1A—C6A	120.3 (2)	C2B—C1B—C6B	120.5 (2)
C3A—C2A—C1A	121.2 (2)	C3B—C2B—C1B	120.9 (2)
C4A—C3A—C2A	119.9 (2)	C4B—C3B—C2B	120.2 (2)
C3A—C4A—C5A	119.3 (2)	C3B—C4B—C5B	119.8 (2)
C4A—C5A—C6A	122.6 (2)	C4B—C5B—C6B	122.4 (2)
C5A—C6A—C1A	116.6 (2)	C5B—C6B—C1B	116.2 (2)
C5A—C6A—C8A	121.2 (2)	C5B—C6B—C8B	121.2 (2)
C1A—C6A—C8A	122.2 (2)	C1B—C6B—C8B	122.5 (2)
N10A—C8A—C6A	116.9 (2)	N10B—C8B—C6B	117.1 (2)
N10A—C8A—C9A	121.9 (2)	N10B—C8B—C9B	121.9 (2)
C6A—C8A—C9A	121.2 (2)	C6B—C8B—C9B	121.0 (2)
C8A—N10A—N11A	118.3 (2)	C8B—N10B—N11B	119.1 (2)
N10A—N11A—C12A	121.4 (2)	N10B—N11B—C12B	120.6 (2)
C17A—C12A—N11A	118.2 (2)	C17B—C12B—N11B	118.5 (2)
C17A—C12A—C13A	118.8 (2)	C17B—C12B—C13B	118.2 (2)
N11A—C12A—C13A	123.0 (2)	N11B—C12B—C13B	123.2 (2)
C14A—C13A—C12A	119.2 (2)	C14B—C13B—C12B	119.3 (2)
C15A—C14A—C13A	121.6 (2)	C15B—C14B—C13B	122.0 (2)
C16A—C15A—C14A	118.7 (2)	C14B—C15B—C16B	119.0 (2)
C15A—C16A—C17A	121.2 (2)	C17B—C16B—C15B	119.8 (2)
C16A—C17A—C12A	120.5 (2)	C16B—C17B—C12B	121.6 (2)

Table 4.Torsion angles (°).

O7A—C1A—C2A—C3A	−179.7 (2)	O7B—C1B—C2B—C3B	−179.7 (2)
C6A—C1A—C2A—C3A	0.5 (3)	C6B—C1B—C2B—C3B	0.3 (3)
C1A—C2A—C3A—C4A	−0.1 (4)	C1B—C2B—C3B—C4B	−0.6 (4)
C2A—C3A—C4A—C5A	0.0 (4)	C2B—C3B—C4B—C5B	0.8 (4)
C3A—C4A—C5A—C6A	−0.3 (4)	C3B—C4B—C5B—C6B	−0.6 (4)
C4A—C5A—C6A—C1A	0.7 (3)	C4B—C5B—C6B—C1B	0.3 (3)
C4A—C5A—C6A—C8A	179.5 (2)	C4B—C5B—C6B—C8B	179.0 (2)
O7A—C1A—C6A—C5A	179.5 (2)	O7B—C1B—C6B—C5B	179.8 (2)
C2A—C1A—C6A—C5A	−0.7 (3)	C2B—C1B—C6B—C5B	−0.1 (3)
O7A—C1A—C6A—C8A	0.7 (3)	O7B—C1B—C6B—C8B	1.1 (3)
C2A—C1A—C6A—C8A	−179.5 (2)	C2B—C1B—C6B—C8B	−178.8 (2)
C5A—C6A—C8A—N10A	−174.6 (2)	C5B—C6B—C8B—N10B	−179.3 (2)
C1A—C6A—C8A—N10A	4.1 (3)	C1B—C6B—C8B—N10B	−0.7 (3)
C5A—C6A—C8A—C9A	7.1 (3)	C5B—C6B—C8B—C9B	1.5 (3)
C1A—C6A—C8A—C9A	−174.2 (2)	C1B—C6B—C8B—C9B	−179.8 (2)
C6A—C8A—N10A—N11A	179.7 (2)	C6B—C8B—N10B—N11B	−179.8 (2)
C9A—C8A—N10A—N11A	−2.0 (3)	C9B—C8B—N10B—N11B	−0.7 (3)
C8A—N10A—N11A—C12A	180.0 (2)	C8B—N10B—N11B—C12B	179.5 (2)
N10A—N11A—C12A—C17A	177.8 (2)	N10B—N11B—C12B—C17B	−176.7 (2)
N10A—N11A—C12A—C13A	−1.9 (3)	N10B—N11B—C12B—C13B	3.4 (3)
C17A—C12A—C13A—C14A	1.6 (3)	C17B—C12B—C13B—C14B	1.0 (3)
N11A—C12A—C13A—C14A	−178.6 (2)	N11B—C12B—C13B—C14B	−179.1 (2)
C12A—C13A—C14A—C15A	0.0 (4)	C12B—C13B—C14B—C15B	−0.2 (4)
C13A—C14A—C15A—C16A	−0.8 (4)	C13B—C14B—C15B—C16B	−0.3 (4)
C14A—C15A—C16A—C17A	0.0 (4)	C14B—C15B—C16B—C17B	−0.1 (4)
C15A—C16A—C17A—C12A	1.7 (4)	C15B—C16B—C17B—C12B	0.9 (4)
N11A—C12A—C17A—C16A	177.7 (2)	N11B—C12B—C17B—C16B	178.7 (2)
C13A—C12A—C17A—C16A	−2.5 (3)	C13B—C12B—C17B—C16B	−1.4 (3)

The compound (*E*)-2-(1-(2-phenylhydrazono)ethyl)phenol contains two molecules (A and B) in the asymmetric unit. The dihedral angle of 3.13 (1)° (in A) and 2.58 (1)° (in B) formed by the mean plane of hydroxyl phenyl ring C1→C6 (A/B) with the phenyl ring C12→C17 (A/B) indicates that the hydroxyl phenyl ring lies in the axial position with respect to the phenyl ring.

The molecules are linked through strong N—H···O hydrogen bond interactions along (0 0 2) plane as the nitrogen N11 (A) atom in the molecule at (x, y, z) of hydrazine group acts as donor to the oxygen O7 (B) atom at (2−*x*, 1−*y*, 1−*z*) and the nitrogen N11 (B) atom in the molecule at (x, y, z) of hydrazine group acts as donor to the oxygen O7 (A) atom at 1−*x*, 1−*y*, 1−*z* of the neighbouring molecules. A combination of these extensive hydrogen bond interactions listed in **Table 5** result in the formation of a three dimensional (3D)supramolecular network in the crystal, shown in **Figure 4.**

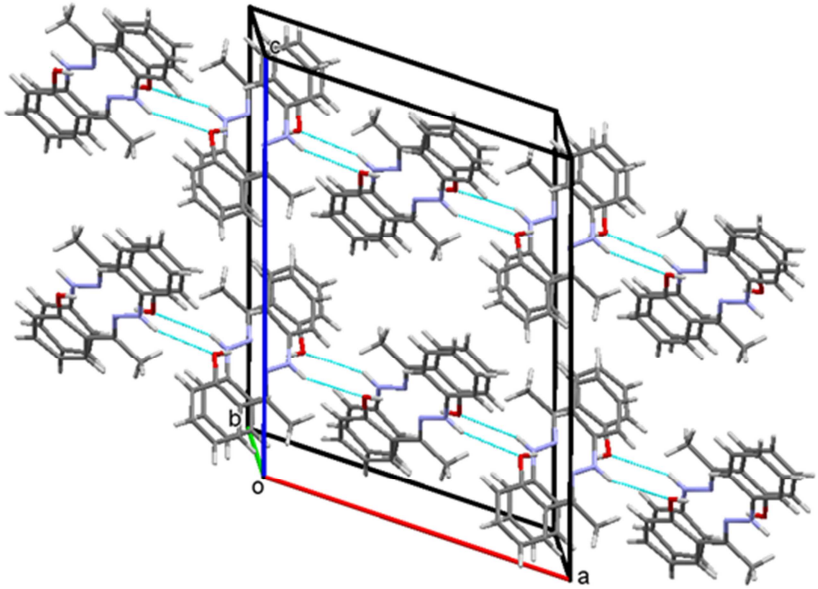

Figure 4.The $R_2^2(8)$ supramolecular network of molecules when viewed down along *b* axis. The dotted lines represent N—H···O hydrogen bond interactions along (002) plane

Table 5. Inter molecular and intra molecular hydrogen bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*	Symmetry codes
N11A—H11A···O7B	0.86	2.657	3.480	160	2−*x*, 1−*y*, 1−*z*
N11B—H11B···O7A	0.86	2.657	3.454	155	1−*x*, 1−*y*, 1−*z*
O7A—H7A···N10A	0.82	1.847	2.568	146	
O7B—H7B···N10B	0.82	1.843	2.565	146	

The molecules also exhibit $\pi\cdots\pi$ interactions between phenyl rings C12A→C17A and C12B→C17B with a *Cg2*···*Cg4* distance of 5.051 (2) Å, a dihedral angle of 83.3 (1)° between the mean planes of the rings C12A→C17A and C12B→C17B, a vertical distance from ring centroid *Cg2* to ring C12B→C17B being -1.416 (9) Å and a vertical distance from ring centroid *Cg4* to ring C12A→C17A being -4.913 (9) Å and symmetry code −1+*x*, *y*, 1+*z*, which play a vital role for the formation and strengthening of 3D supramolecular layered frame work.

The crystal and molecular structure is also stabilized by the O—H···N intra molecular hydrogen bond interactions (O7A—H7A···N10A and O7B—H7B···N10B) forming a six membered ring O7—H7—N10—C8—C6—C1 and inter molecular hydrogen bond interactions.

The Hirshfeld surface analysis [20−22] was carried out and the fingerprint plot [23] drawn by the computational methods implemented in *CRYSTAL EXPLORER* [24] to visualize the inter contacts in the molecular structure are shown in **Figures 5** and **6** respectively.

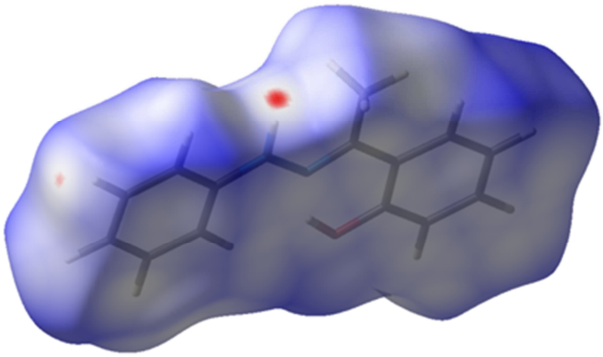

Figure 5.d_{norm}mapped on Hirshfeld surface of the molecule

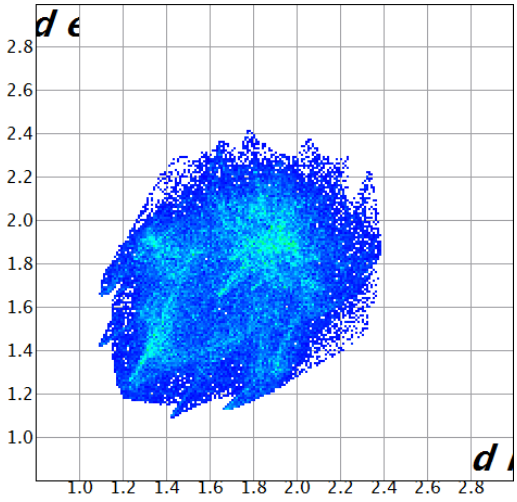

Figure 6.Finger print plot of the molecule considering all atoms

The inter contacts O···H show up as dark red spots which occur due to the hydrogen bond acceptors of N11A—H11A···O7B and N11B—H11B···O7A interactions. The inter contacts that contribute for the Hirshfeld surface of the molecule are H···H (56%), C···H (24%), O···H (8%), C···N (6%), which play a vital role in the stabilization of the crystal structure of the molecules.

Acknowledgements
The authors thank the National facility, Department of Studies in Physics, University of Mysore, Mysuru-570 006, India, for providing the X-ray intensity data.

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