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Synthesis, Crystal Structure and Hirshfeld Surface Analysis of 1-[5-methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]-3-p-tolyl-prop-2-en-1-one

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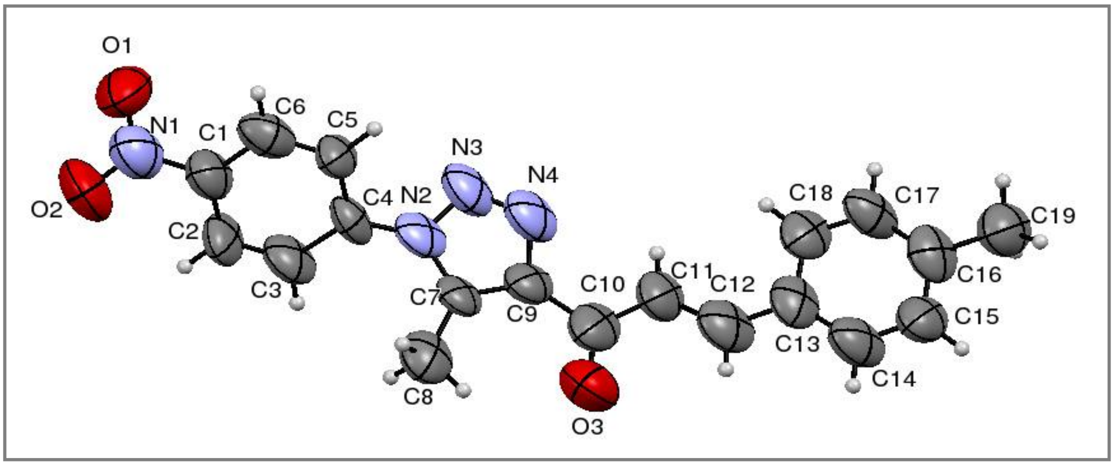
ABSTRACT

The title compound1-[5-methyl-1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl]-3-p-tolylprop-2-en-1-one is synthesized and the structure was confirmed by HNMR, IR, and single crystal X-ray diffraction. The title compound is a chalcone derivative which is known for potential pharmacological activities. The compound crystallizes in the monoclinic space group P21/c with cell parameters $a=8.2925(8)$ Å, $b=13.4045(12)$ Å, $c=15.5791(14)$ Å, $\alpha=90^o$, $\beta=94.584(5)^o$, $\gamma=15.5791(14)^o$, $Z=4$ *at 293 K. Hirshfeld surface analysis shows that the major intermolecular interaction is due to H…H contacts.*

Graphical Abstract



ORTEP diagram of the title compound

Keywords: Crystal structure, X-ray crystallography, Hirshfeld surface analysis, Chalcones, Triazoles, fingerprint plots.

INTRODUCTION

It has been reported in the literature that chalcone derivatives possess significant pharmacological activities [1], as well as they serve as important intermediate in the synthesis of various heterocycles[2]. Triazole is an important motif found in various biologically important heterocycles and is reported to exhibit significant anti-inflammatory, antimicrobial, analgesic, antioxidant and antiproliferative activity [3, 4]. With this background, in the present work, we have attempted to synthesize the title compound, 1-[5-methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]-3-p-tolylprop-2-en-1-one, which is a chalcone derivative, and belongs to the class of triazoles.Its structure has been confirmed using elemental analysis, IR,^{1}HNMR and X-ray diffraction techniques and intermolecular interactions are studied using Hirshfeld surface analysis.

MATERIALS AND METHODS

Synthesis: Chemicals were purchased from Sigma Aldrich Chemical Corporation. Melting point was determined in open capillary tube and is uncorrected. A solution of 1-(p-nitrophenyl)-5-methyl-4-acetyl-1,2,3-triazole(0.01 mol) an p-tolualdehyde(0.01 mol) in ethanol(20 ml) was treated with 10% KOH solution(2 ml). The mixture was stirred at room temperature for 4 hours and allowed to stand at room temperature for 24 hours. The precipitated crystals of *(E)*-1-[5-methyl-1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl]-3-p-tolylprop-2-en-1-one so obtained was collected by filtration, washed with cold ethanol and dried. Further purification was done by recrystallization from ethanol: D.M.F mixture. The scheme of synthesis is shown in figure 1.

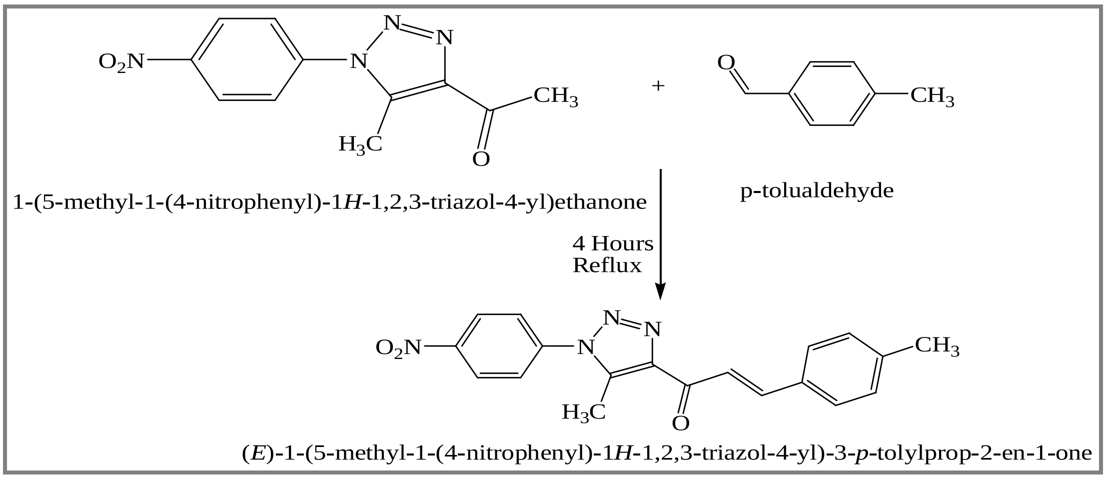


Figure 1. Scheme of synthesis of the title compound.

Spectroscopy: ^{1}HNMR spectra was recorded on a Bruker AMX-300/AMX-400 (300/400 MHz) spectrometer using DMSO-d6 as solvent and TMS as an internal standard. All chemical shifts values are reported in d scale downfield from TMS. Mass spectra of the compound was recorded in Agilent mass spectrometer operating at 20 eV and C, H, N analysis was carried out on a Schimadzu Elementar Vario-EL (Elementar-III) model. Homogeneity of the compound was checked by TLC on silica gel plates.

X-ray diffraction: White coloured crystal of the synthesized compound with approximate dimensions of 0.27×0.28×0.26 mm was used for X-ray diffraction study. X-ray diffraction data were collected on Bruker X calibur diffractometer equipped with Sapphire 3 CCD detector using Cu-K$_\alpha$ radiation. Data reduction and absorption correction were carried out using the APEX 2 package [5]. Crystal structure was solved by direct methods using *SHELXS-97* and was refined by full matrix least squares refinement against F^2using *SHELXL-97* [6]. Geometry, bond distances, bond angles, etc.

have been calculated using the rounded fractional coordinates. All su's are estimated from the variances of the (full) variance-covariance matrix. The cell e.s.d.'s are taken into account in the estimation of distances, angles and torsion angles. Weighted *R*-factors w*R* and all goodness of fit S are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. All the non-hydrogen atoms were refined anisotropically and the hydrogen atoms were placed at chemically acceptable positions.

The geometrical calculations were carried out using the program *PLATON* [**7**]. The molecular and packing diagrams were generated using the software *MERCURY* [**8**]. Hirshfeld surfaces, electrostatic potential and the associated 2D-fingerprint plots were calculated using *CRYSTAL EXPLORER 3.1* [**9**] with the generated CIF file of the structure.

RESULTS AND DISCUSSION

Spectral Analysis: After synthesis, the structure of the compound was initially confirmed using IR and ^{1}HNMR spectroscopy, and elemental analysis, the details of which are given below.

IR: The carbonyl absorption band was seen at 1685 cm^{-1} while the C-H stretching was observed at 3020cm^{-1}. Symmetric and asymmetric stretching of NO_2 was observed at 1560 and 1344 cm^{-1} respectively.

^{1}HNMR: In the ^{1}HNMR spectrum of the title compound, the CH_3 protons of the p-tolyl group appeared as singlet at δ, 2.3 integrating for three protons, while the triazolyl methyl protons came into resonance as a singlet at δ, 2.78. The olefinic protons appeared as two doublets at δ, 7.49 and 7.76 with coupling constant J=14.2Hz thereby indicating the trans-orientation. The signal due to aromatic protons of the p-tolyl and p-nitro phenyl group overlapped with each other and appeared as multiplets in the region of δ, 7.5-8.61 integrating for eight protons.

Elemental analysis: CHN elemental analysis was carried out in order to confirm the chemical composition of the synthesized compound. The obtained results are:

C, 65.5(65.51); H, 4.6(4.63); N, 16.1(16.08)

where the calculated percentages of elements are given in brackets. The differences between experimental and calculated percentages of Carbon (C), Hydrogen (H) and Nitrogen (N) are very small and within the experimental errors. This confirms that the product formation is in stoichiometric proportion. Further the mass spectrum of this compound showed the molecular ion peak at m/z 349 (M^++1) peak, thereby confirming the structure.

Yield: 86%. M.P. 186-88°C, Molecular Formula: $C_{19}H_{16}N_4O_3$ (348.36)

Single crystal X-ray diffraction: X-ray diffraction study reveals that the title compound crystallizes in the monoclinic crystal system in space group *P*21/c with cell parameters a = 8.2925(8)Å, b = 13.4045(12) Å, c = 15.5791(14) Å, α = 90°, β = 94.584(5)°, γ = 15.5791(14)°, Z = 4 and V= 1726.2(3) Å^3. A total of 238 parameters were refined with 2741 unique reflections which converged the residual to R=0.0673. The details of crystal data and structure refinement are given in table 1. Figure 2 shows the *ORTEP* diagram of the molecule with thermal ellipsoids drawn at 50% probability.

Selected bond lengths and bond angles, and torsion angles are listed in the table 2 and table 3 respectively. All the bond lengths and bond angles are comparable with compounds having similar structure reported earlier [**10, 11**].

Table 1. Crystal data and structure refinement details.

Formula	$C_{19} H_{17} N_4 O_3$
Formula Weight	349.37
Crystal System	Monoclinic
Space group	P21/c (No. 14)
Unit cell parameters	*a* = 8.2925(8)Å, *b* = 13.4045(12) Å, *c* = 15.5791(14) Å, α = 90°, β = 94.584(5)°, γ = 15.5791(14)°
Volume	1726.2(3) $Å^3$
Z	4
D(calculated)	1.344 g/cm^3
Absorption coefficient (Cu-K_α)	0.770 mm^{-1}
$F_{(000)}$	732
Crystal Size	0.27×0.28×0.26 mm
Data Collection	
Temperature	293 K
Radiation	Cu-K_α 1.54178 Å
θ range	4.4° to 64.5°
Dataset	-9 < h < 9; -15 < k < 15; -18 < l < 7
Total, Unique Data, R_{int}	8603, 2741, 0.029
Observed data [I > 2.0 sigma(I)]	1195
Refinement	
N_{ref}, N_{par}	2741, 238
Final R, wR2, S	0.0673, 0.1271, 1.1
Largest diffraction peak and hole	-0.48, 0.46 e $Å^{-3}$

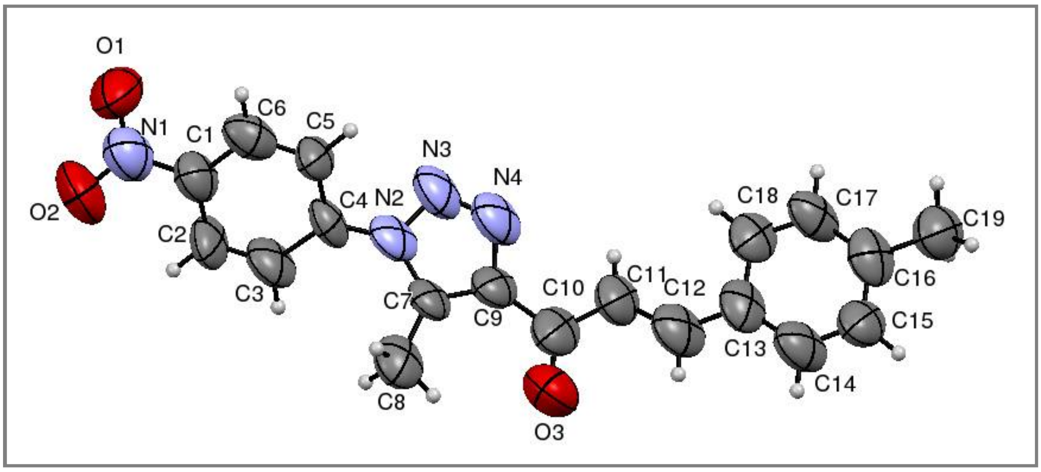


Figure 2. ORTEP diagram of the title compound with 50% probability ellipsoids.

Table 2. Selected Bond Lengths and Bond angles

Atoms	Bond length (Å)	Atoms	Bond angle (deg.)
O1-N1	1.244(15)	O1-N1-O2	118.4(12)
O2-N1	1.206(13)	O1-N1-C1	119.2(9)
O3-C10	1.197(19)	N3-N2-C7	106.8(9)
N1-C1	1.411(16)	N3-N2-C9	108.9(10)
N2-N3	1.352(14)	C2-C3-C4	124.8(9)
N2-C4	1.335(14)	N2-N3-N4	111.1(10)
N3 -N4	1.277(15)	N3-N2-C4	123.0(9)
N4-C9	1.393(16)	C2-C1-C6	119.0(10)
C1-C6	1.372(11)	O3-C10-C9	119.4(12)
C10-C11	1.440(17)	C10-C11-C12	123.7(13)
C13-C14	1.387(18)	C13-C14-C15	121.5(12)
C16-C19	1.484(16)	C15-C16-C19	121.7(12)

Table 3. Selected Torsion Angles

Atoms	Angle (deg.)	Atoms	Angle (deg.)
O1-N1-C1-C2	-167.8(11)	C1-C2-C3-C4	-4.0(18)
O1-N1-C1-C6	8.3(17)	N2-C4-C5-C6	174.9(9)
N3-N4-C9-C7	-0.4(9)	N3-N2-C4-C5	-45.5(12)
N3-C2-C4-C3	131.6(10)	C10-C11-C12-C13	-178.6(8)
C4-N2-C7-C8	-3.9(11)	C14-C15-C16-C19	179.3(8)

The three rings found in the structure –nitrophenyl ring C1–C6, triazol ring N2-N3-N4-C7-C9, and methylphenyl ring C13-C18 are all highly planar and *sp2* hybridized. The maximum deviation from the mean plane in these rings are for atoms C3(-0.022(11) Å), N2(-0.009(9) Å), and, C14(-0.012(13) Å) respectively. The dihedral angle between least square planes containing nitrophenyl and triazol rings is46.2(5)° (*syn-clinal* configuration); nitrophenyl and methylphenyl rings is 47.9(5)° (*syn-clinal* configuration); and, triazol and methylphenyl rings is 19.4(4)° (*syn-periplanar* configuration). Interactions between C3-H3-methylphenyl rings provide stability to the crystal structure.

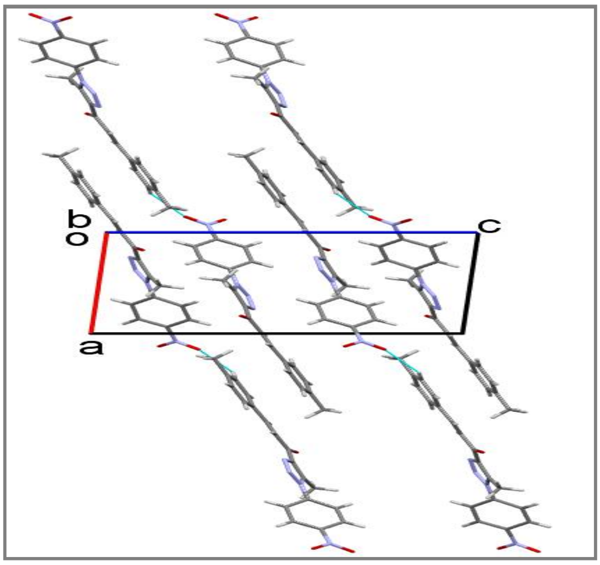


Figure 3. Packing diagram of the molecule viewed along the crystallographic *b* axis.

Figure 3 shows the packing diagram of the molecule viewed along the crystallographic *b* axis. It is observed that the molecules are arranged in a head-to-tail fashion in the form of inter-penetrating layers. Inter molecular distance in each layer is 3.481 Å as measured between atoms O2 and C19 of nearest neighbouring molecules. Layer spacing is found to be 4.455 Å when measured between C1 and C10 atoms belonging to molecules of adjacent layers. The methylphenyl rings of molecules in neighbouring layers are inclined at an angle of 80.41° while triazol rings are inclined at an angle of 22.28°. Hydrogen bond geometry details showing intra-molecular hydrogen bonds are provided in table 4. There are no inter-molecular hydrogen bonds in the crystal structure. Short contacts between H15 and O2 link molecules in each layer while short contacts between C10-H8C and C5-H18 link molecules of adjacent layers. These provide stability to the crystal structure.

Table 4. Hydrogen-bond geometry (Å, deg.)

Nr Typ	D --- H....A	D - H	H...A	D...A	D...A
1	C(8) --H(8A) ..O(3)	0.96	2.48	3.134(16)	125
2	C(11) --H(11) ..N(4)	0.93	2.47	2.854(16)	105
3	C(12) --H(12) ..O(3)	0.93	2.56	2.874(16)	100

Hirshfeld surface Analysis: The Hirshfeld electrostatic potential (3D d_{norm} surface) mapped using DFT theory over the range of 0.065 to 0.075 a.u. is shown in figure 4. Here, the molecular electrostatic potential implies the total charge distribution of the molecule, which is a physical property. A portion of a molecule with a negative electrostatic potential is susceptible to an electrophilic attack - more negative the potential, higher is the susceptibility to electrophilic attack. Thus, the Hirshfeld surface analysis provides a medium to understand the electron density which in turn is useful for determining the electrophilic and nucleophilic reactivities as well as hydrogen-bonding interactions. In Figure 4, the different values of the electrostatic potential at the surface are represented by different colours. Red and blue areas refer to the regions of negative and positive potentials and correspond to the electron–rich and electron–poor regions respectively [12].

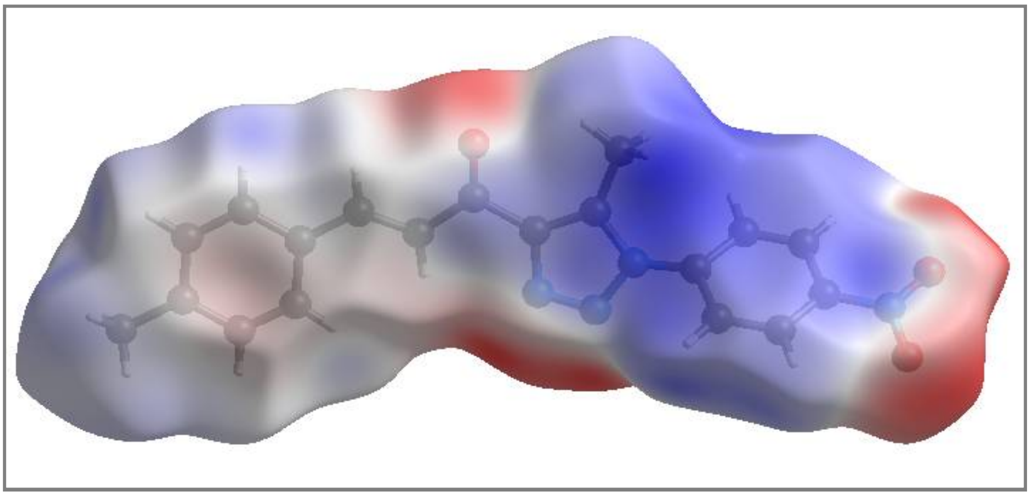


Figure 4. The electrostatic potential mapped on Hirshfeld surface of the title compound.

The associated 2D-fingerprint plots of the Hirshfeld surface are shown in figure 5. The fingerprint plot provides an overview of intermolecular contacts in the crystal, which is a combination of d_i and d_e. Here, d_e refers to the distance from the point to the nearest nucleus external to the surface, and d_i refers to the distance to the nearest nucleus internal to the surface, at each point on the Hirshfeld surface [13]. The parameter d_{norm} displays a surface with a red-white-blue colour scheme, in which bright red spots highlight shorter contacts, white areas represent contacts around the Van der Waals separation, and blue regions are devoid of close contacts. The contribution of various intermolecular contacts to the Hirshfeld surface is shown in the table 5. From the table, we observe that the major contribution to Hirshfeld surface comes from H...H (30.3%), C...H (14.9%), O...H (12.6%), and, H...C (12.0%) contacts. These contacts are highlighted by a conventional mapping of d_{norm} on the molecular Hirshfeld surface shown in figure 5.

Table 5. Percentage of various intermolecular contacts contributed to the Hirshfeld surface.

Intercontacts	Contribution (%)	Intercontacts	Contribution (%)
O...O	0.5	C...O	0.9
O...N	1.2	C...N	1.0
O...C	0.5	C...C	2.2
O...H	12.6	C...H	14.9
N...O	1.4	H...O	11.4
N...N	0.9	H...N	3.8
N...C	1.0	H...C	12.0
N...H	5.4	H...H	30.3

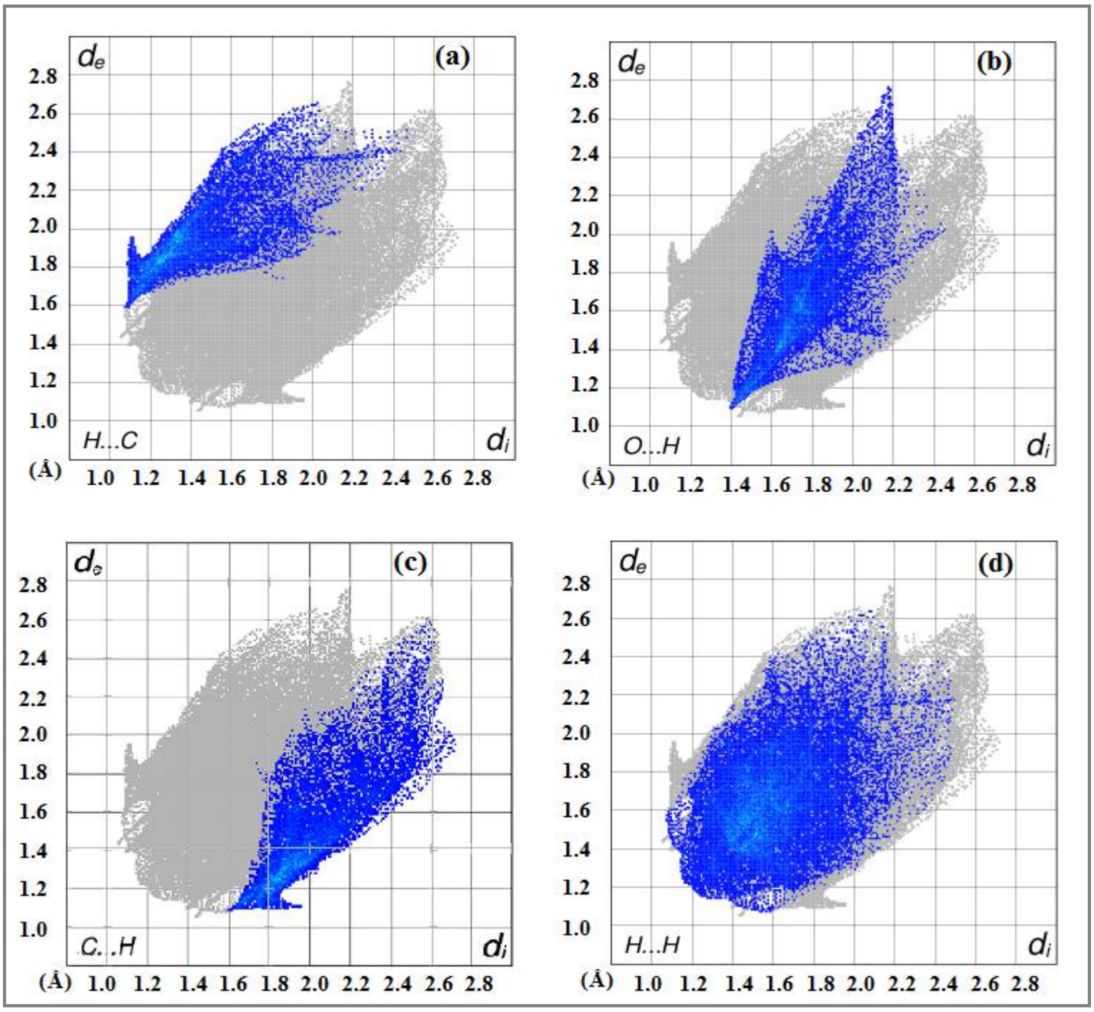


Figure 5. Fingerprint plot of the title compound resolved into (a) H...C, (b) O...H, (c) C...H, and, (d) H...H contacts showing the percentage of contacts contributing to the total Hirshfeld surface area of the molecule.

APPLICATION

Literature survey reveals that chalcone derivatives with triazole moiety show significant pharamacological applications and are helpful in synthesis of biologically important heterocycles [1-4, 14]. The present work helps us to understand the properties of one such derivative and synthesize more efficient materials.

CONCLUSION

In view of pharamacological importance of chalcone derivatives with triazole moiety, the title compound was synthesized and its structure was confirmed using IR, ^{1}HNMR, and elemental analysis. Further, the use of single crystal X-ray diffraction technique revealed that the compound crystallizes in monoclinic crystal system with space group P21/c. Hirshfeld surface analysis shows that intermolecular interactions of type H…H are major contributors to the Hirshfeld surface.

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