Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(23):29-37
(http://www.derpharmachemica.com/archive.html)

Synthesis, Characterization, Crystal Structure and Hirshfeld Surface Analysis of 2-[1-(4-butylphenyl)-4,5-diphenyl-*1H*-imidazol-zyl]phenol

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ABSTRACT

The title compound 2-[1-(4-butylphenyl)-4,5-diphenyl-1H-imidazol-zyl]phenol has been synthesized by the reaction of appropriate mole quantities of 4-Butylaniline, benzil, ammonium acetate, salicylaldehyde in one pot reaction and characterized by Nuclear Magnetic Resonance (NMR) and IR techniques and finally the molecular structure was confirmed by single crystal X-ray diffraction studies. The title compound $C_{31}H_{28}N_2O$ crystallizes in the monoclinic crystal system, in $P2_1/n$ space group with unit cell parameters, a=10.0330(3) Å, b=14.7203(4) Å, c=16.9169(5) Å, β=101.596(1) Å and Z=4. The crystal structure of the title compound exhibit C–H···N and O–H···N hydrogen bonding interactions and contributes to the structural stability. Molecular structure is also stabilized by C–H···π interactions. Further, the Hirshfeld surface analysis; fingerprint plot reveals the percentage contribution from each individual molecular contact, and it shows that the H···H interactions has the major contribution (61.8%).

Keywords: Imidazole, One pot reaction, X-ray diffraction, Hirshfeld surface analysis, Fingerprint plots, C–H···π interactions

INTRODUCTION

Imidazoles and their derivatives display a wide range of biological properties, and they have commercial applications in various realms of therapy, including ulcerative, anti-hypertensive, antiviral, antibacterial, anti-tumor, antihistaminic and antihelminthic agents in veterinary medicine [1]. Keeping in view of their biological applications and continuation of our work on synthesis and single crystal study of novel heterocyclic compounds [2-4], we herein report the synthesis, spectral characterization and single crystal X-ray diffraction studies of 2-(1-(4-butylphenyl)-4,5-diphenyl-*1H*-imidazole 2-yl)phenol. The general procedure for the preparation of 2-(1-(4-butylphenyl)-4,5-diphenyl-*1H*-imidazole 2-yl)phenol has been appended in experimental part. The spectral results and X-ray structural conformations were discussed, further, the Hirshfeld surface analysis; fingerprint plots are also presented in order to quantify the interactions within the crystal structure.

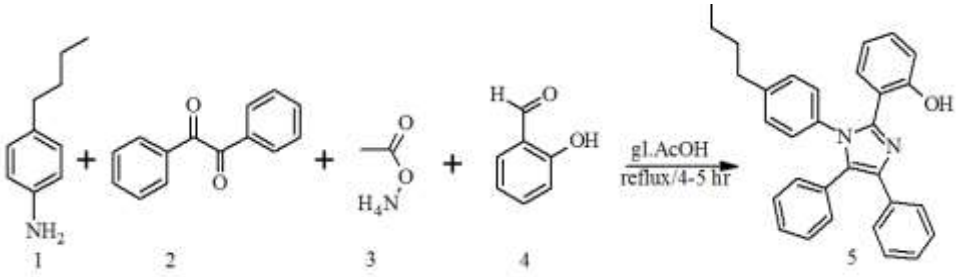
MATERIALS AND METHODS

The melting points were measured on a Boetius-Mikroheiztisch the company "VEB" weighing, Rapido Radebeul/VEB NAGEMA measured and are uncorrected. Thin Layer Chromatography (TLC) for the analysis was with aluminum foil fluorescent indicator from Merck KGaA (silica gel 60 F254, layer thickness 0.2 mm). Rf -values (run level relative to the solvent front). ^{1}H-NMR spectra were recorded on a "Gemini 2000" (400/100 MHz) and the spectra are shown in Figures 1 and 2. The ATR spectra were recorded on a FT-IR spectrometer "IFS 28" by "Bruker" and the corresponding spectrum is shown in Figure 3. Crystal structure was recorded by a Bruker Proteum X8 Single-crystal X-ray diffractometer.

Procedure for the preparation of 2-[1-(4-butylphenyl)-4,5-diphenyl-*1H*-imidazol-zyl]phenol

In a 250 ml round-bottom flask, a benzil (1 mmol, 2.1 g), butyl aniline (1 mmol, 1.49 g), ammonium acetate (1 mmol, 0.77 g) and salicylaldehyde (1 mmol, 1.22 g) were taken in glacial acetic acid (20 ml). The reaction mixture was then subjected to ultra-sonication for 30 mins and kept it for reflux for 4-5 h on heating mantle. The progress of the reaction was monitored by TLC (2:8 (v:v) ethyl acetate-pet ether mixture]. After the completion of the reaction, the mixture was cooled to room temperature and poured into ice cold water. The reaction mixture was quenched in water and neutralized by aqueous sodium bicarbonate solution and the product was extracted with ethyl acetate. The crude product was then recrystallized by hot ethanol to get fine crystals of analytically pure 2-[1-(4-butylphenyl)-4,5-diphenyl-*1H*-imidazol-zyl]phenol

with good yield (60-70%). M.P. 154°C. Reaction pathway for the synthesis of the title compound is shown in Scheme 1.



Scheme 1: Reaction pathway for the synthesis of the title compound

Physical and spectral data: IR (KBr) (v_{max}/cm^{-1}): 3614 (O-H), 1603 (C=N), 1590 (C=C), 1454 (C-C), 1255 (C-O), 1091 (=C-H). ^{1}H-NMR (400 MHz, DMSO): δ=0.860 (t, 3H, *J*=7.2 Hz), 1.246 (h, 2H, *J*=7.6Hz), 1.535 (p, *J*=6.8 Hz, 2H), 2.578 (t, *J*=7.6 Hz, 2H), 6.502 (t, *J*=7.6 Hz, 1H), 6.619 (d, *J*=8 Hz, 1H), 6.939 (d, *J*=8 Hz, 1H), 7.288 (m, *J*=4.4 Hz, 13H), 7.429 (d, *J*=7.6 Hz, 2H), 12.723 (s, Ar-OH, 1H), ppm. Mass spectra (LC-MS) of the compound 3a showed molecular ion peak at m/z=444 [M+1].

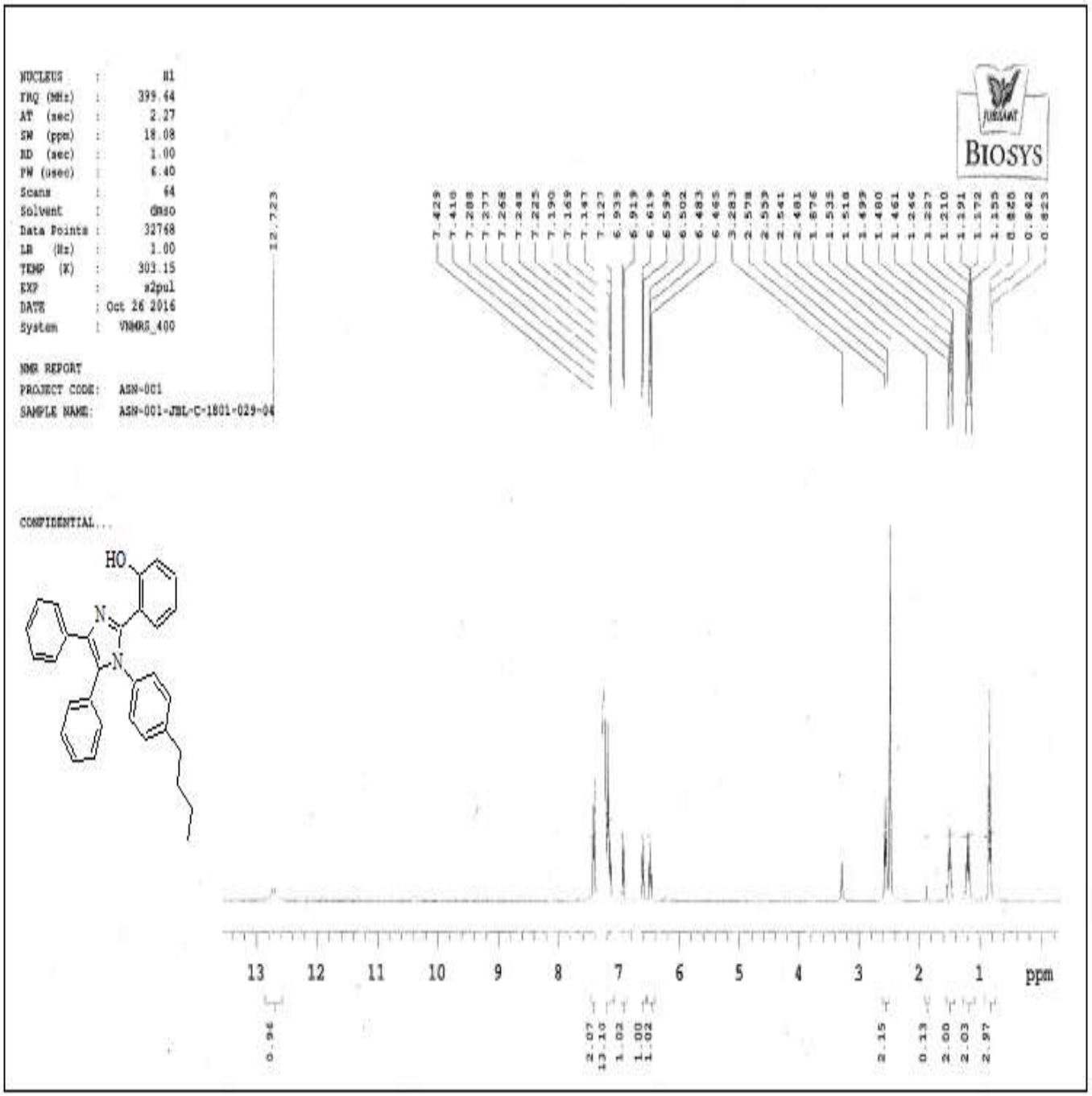


Figure 1: ^{1}H-NMR spectrum of 2-(1-(4-butylphenyl)-4,5-diphenyl-*1H*-imidazole-2-yl)phenol

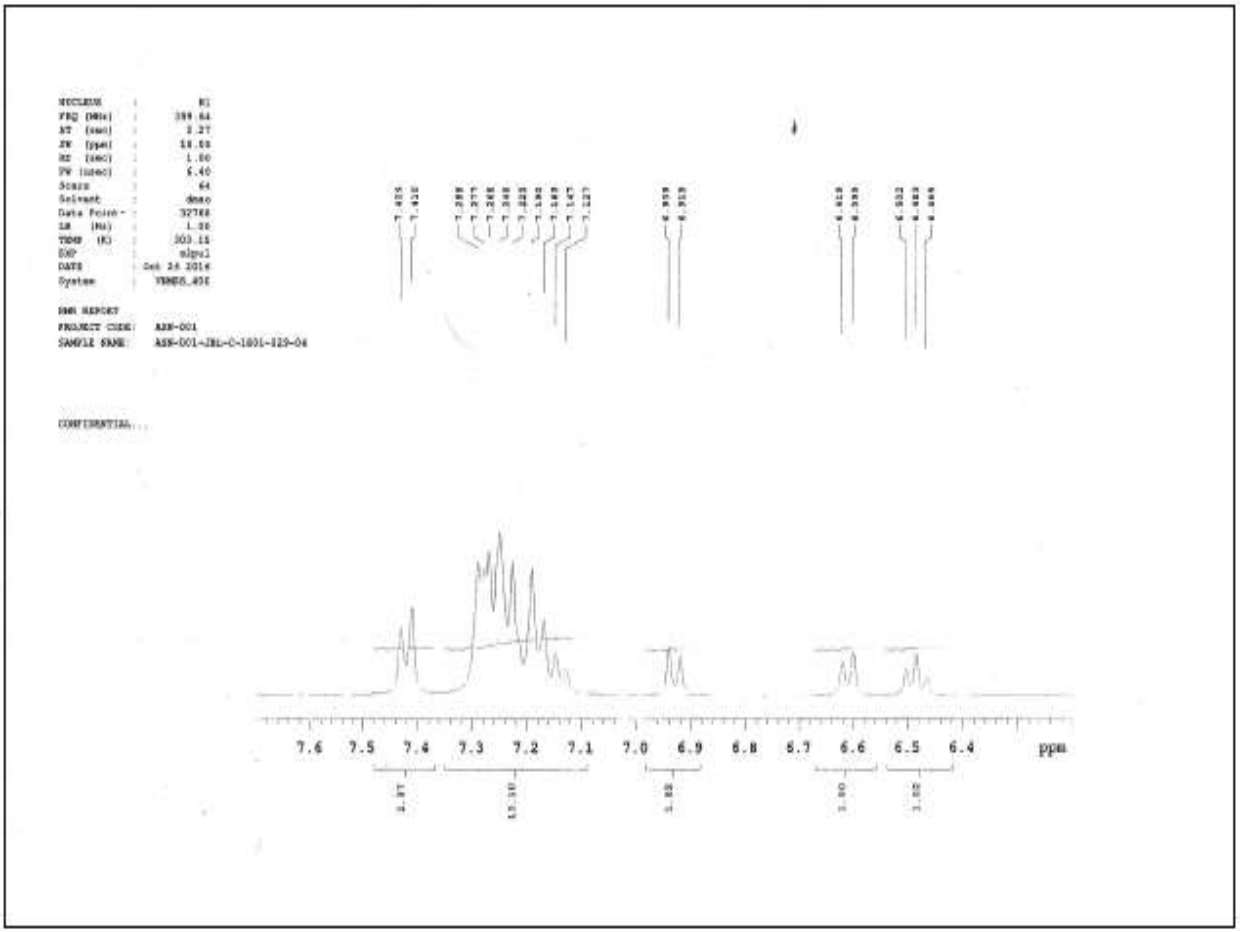


Figure 2: ^{1}H-NMR Enlarged spectrum of 2-(1-(4-butylphenyl)-4,5-diphenyl-*1H*-imidazole-2-yl)phenol

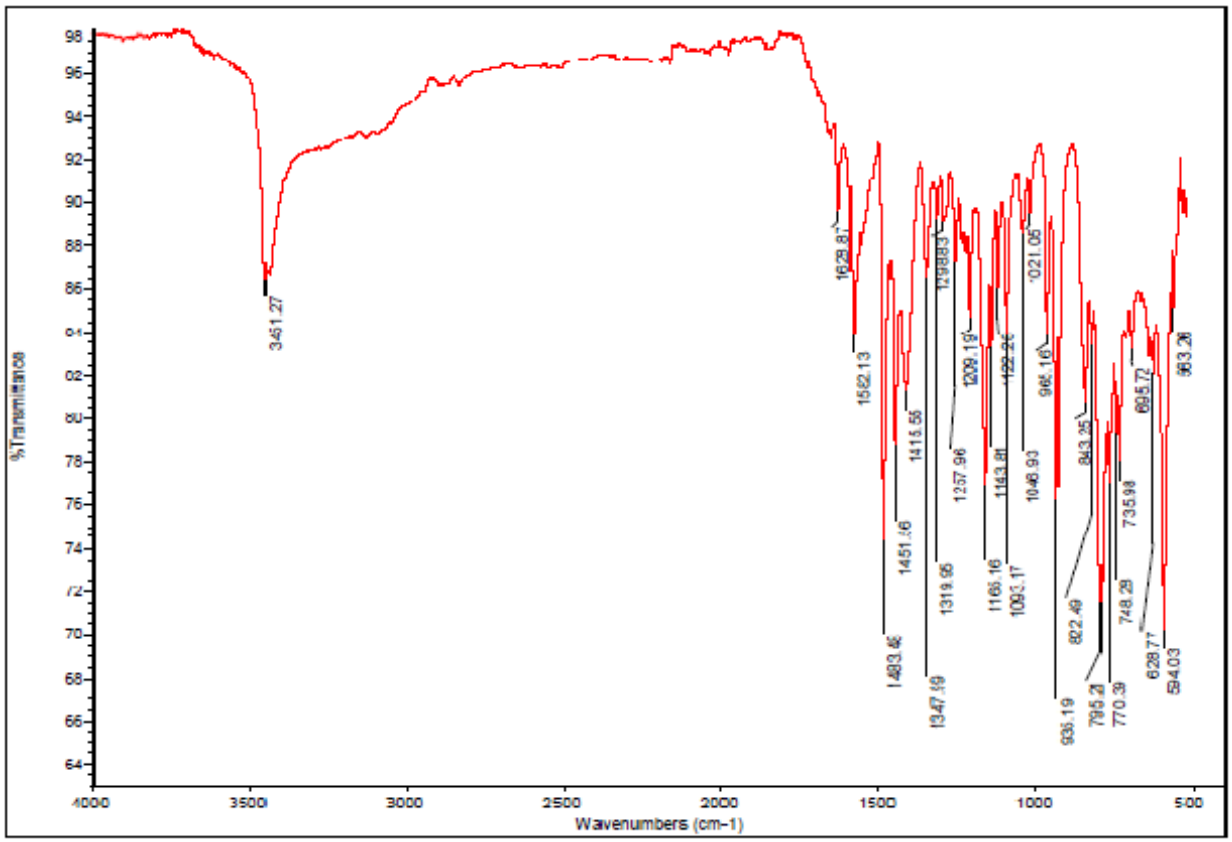


Figure 3: IR spectrum of 2-(1-(4-butylphenyl)-4,5-diphenyl-*1H*-imidazole-2-yl)phenol

Single crystal X-ray diffraction studies

Data collection and structure refinement: Rectangle shaped brown colored defect free single crystal of approximate dimension 0.29 × 0.25 × 0.19 mm was chosen for X-ray diffraction studies. X-ray intensity data for the title compound were collected at temperature 296 K on a Bruker Proteum2 CCD diffractometer with X-ray generator operating at 45 kV and 10 mA, using CuK_α radiation of wavelength 1.54178 Å. Data were collected for 24 frames per set with different settings of φ (0° and 90°), keeping the scan width of 0.5°, exposure time of 5 s, the sample to detector distance of 45.10 mm. The compound $C_{31}H_{28}N_2O$ crystallized in the monoclinic crystal system, in $P2_1/n$ space group. The complete intensity data sets were processed using Saint Plus [5]. All the frames could be indexed by using a primitive monoclinic lattice. The crystal structure was solved by direct methods and refined by full-matrix least squares method on F^2 using ShelXs and ShelXs programs [6]. All the non-hydrogen atoms were refined anisotropically and the hydrogen atoms were positioned geometrically, with C-H=0.93 Å and refined using a riding model with U_{iso}(H)=1.2 U_{eq}(C), U_{iso}(H)=1.5 U_{eq} (C_{methyl}). A total of 308 parameters are refined with 4024 unique reflections of 21883 observed reflections. After several cycles of refinement, the final difference Fourier map showed peaks of no chemical significance and the residual is saturated to 0.0576. The geometrical calculations were carried out using the program Platon [7]. The molecular and packing diagrams were generated using the software Mercury [8].

RESULTS AND DISCUSSIONS

Single crystal X-ray diffraction analysis confirms the molecular structure of the title compound $C_{31}H_{28}N_2O$. The ORTEP of the molecule with displacement ellipsoids drawn at 50% probability level with the O–H… N hydrogen bond exhibiting S(6) ring motif is shown in Figure 4. The details of the crystal data and structure refinement are as given in Table 1. The bond lengths and bond angles are in good agreement with the standard values, the list of selected bond lengths and bond angles are given in Tables 2 and 3. The conformation of the molecule can be described by the torsion angles. The list of torsion angles is given in Table 4.

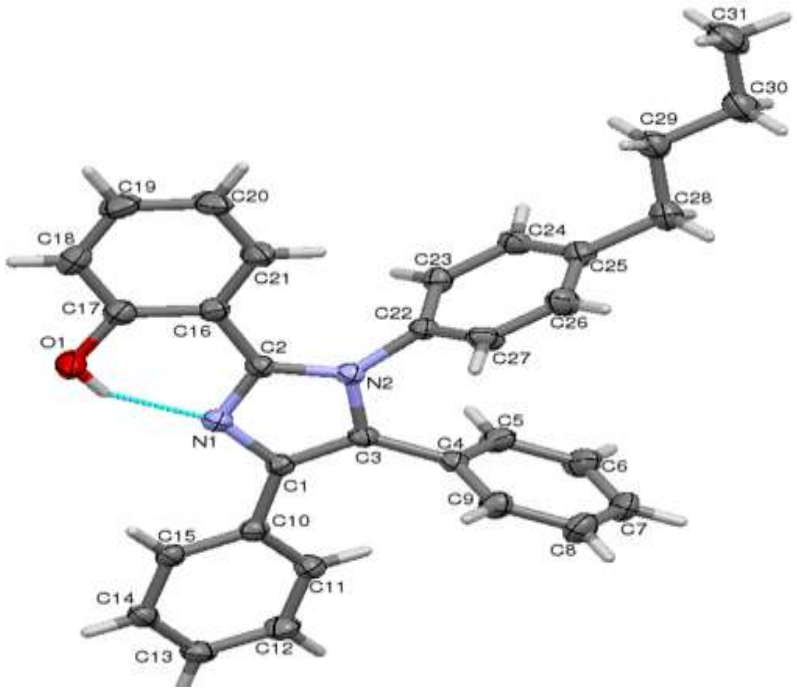


Figure 4: ORTEP of the molecule with thermal ellipsoids drawn at 50% probability with the O–H…N hydrogen bond exhibiting S(6) ring motif

Table 1: Crystal data and structure refinement details

Parameter	value
CCDC deposit No.	CCDC 1552249
Empirical formula	$C_{31}H_{28}N_2O$
Formula weight	444.55
Temperature	296 K
Wavelength	1.54178 Å
Crystal system, space group	Monoclinic, $P2_1/n$
Unit cell dimensions	a=10.0330(3) Å
	b=14.7203(4) Å
	c=16.9169(5) Å

	β=101.596(1)^o
Volume	2447.44(12) Å ^{3}
Z	4
Density(calculated)	1.207 Mg/m $^{-3}$
Absorption coefficient	0.565 mm^{-1}
*F*000	944
Crystal size	0.29 × 0.25 × 0.19 mm
θ range for data collection	5.41^o to 64.46^o
Index ranges	−11 ≤ h ≤ 11
	−16 ≤ k ≤ 17
	−19 ≤ l ≤ 19
Reflections collected	21883
Independent reflections	4024 [R int=0.0417]
Absorption correction	multi-scan
Refinement method	Full matrix least-squares on F^2
Data/restraints/parameters	4024/0/308
Goodness-of-fit on F^2	1.034
Final [I > 2 σ(I)]	*R*1=0.0576, w*R*2=0.1761
R indices (all data)	*R*1=0.0588, w*R*2=0.1782
Largest diff. peak and hole	0.372 and −0.256 e Å $^{-3}$

Table 2: Bond lengths (Å)

Atoms	Length	Atoms	Length
O1-C17	1.354(2)	C12-C13	1.389(3)
N1-C2	1.330(2)	C13-C14	1.383(3)
N1-C1	1.380(2)	C14-C15	1.388(3)
N2-C2	1.373(2)	C16-C17	1.413(3)
N2-C22	1.446(2)	C16-C21	1.406(3)
N2-C3	1.390(2)	C17-C18	1.393(3)
C1-C3	1.373(2)	C18-C19	1.379(3)
C1-C10	1.473(2)	C19-C20	1.386(3)
C2-C16	1.466(2)	C20-C21	1.379(3)
C3-C4	1.482(2)	C22-C27	1.383(2)
C4-C9	1.391(2)	C22-C23	1.382(2)
C4-C5	1.388(3)	C23-C24	1.388(3)
C5-C6	1.383(3)	C24-C25	1.388(3)
C6-C7	1.378(3)	C25-C28	1.512(3)
C7-C8	1.382(3)	C25-C26	1.390(3)
C8-C9	1.388(3)	C26-C27	1.390(3)
C10-C15	1.402(2)	C28-C29	1.522(3)
C10-C11	1.397(2)	C29-C30	1.525(3)
C11-C12	1.389(3)	C30-C31	1.517(3)

Table 3: Bond angles (°)

Atoms	Angle	Atoms	Angle
C1-N1-C2	107.64(14)	C12-C13-C14	119.32(17)
C2-N2-C3	107.49(14)	C13-C14-C15	120.38(17)
C2-N2-C22	131.50(14)	C10-C15-C14	120.83(16)
C3-N2-C22	120.94(13)	C2-C16-C17	118.71(16)
N1-C1-C3	108.92(14)	C17-C16-C21	117.94(16)

N1-C1-C10	121.20(15)	C2-C16-C21	123.29(16)
C3-C1-C10	129.87(15)	O1-C17-C16	122.97(16)
N1-C2-C16	122.06(15)	O1-C17-C18	117.22(17)
N2-C2-C16	128.22(15)	C16-C17-C18	119.80(17)
N1-C2-N2	109.67(14)	C17-C18-C19	120.73(18)
N2-C3-C1	106.27(14)	C18-C19-C20	120.34(19)
C1-C3-C4	132.33(15)	C19-C20-C21	119.61(19)
N2-C3-C4	121.38(14)	C16-C21-C20	121.56(18)
C3-C4-C5	120.54(15)	N2-C22-C27	119.63(15)
C5-C4-C9	119.10(16	C23-C22-C27	120.20(16)
C3-C4-C9	120.36(15)	N2-C22-C23	119.77(15)
C4-C5-C6	120.26(17)	C22-C23-C24	119.47(16)
C5-C6-C7	120.43(19)	C23-C24-C25	121.59(17)
C6-C7-C8	119.89(19)	C24-C25-C26	117.67(18)
C7-C8-C9	119.97(18)	C26-C25-C28	121.37(17)
C4-C9-C8	120.34(17)	C24-C25-C28	120.96(17)
C1-C10-C15	119.61(15)	C25-C26-C27	121.48(18)
C11-C10-C15	118.34(16)	C22-C27-C26	119.45(17)
C1-C10-C11	122.04(16)	C25-C28-C29	112.82(16)
C10-C11-C12	120.38(17)	C28-C29-C30	113.17(17)
C11-C12-C13	120.75(17)	C29-C30-C31	112.28(17)

Table 4: Torsion angles (°)

Atoms	Angle	Atoms	Angle
C1-N1-C2	107.64(14)	C12-C13-C14	119.32(17)
C2-N2-C3	107.49(14)	C13-C14-C15	120.38(17)
C2-N2-C22	131.50(14)	C10-C15-C14	120.83(16)
C3-N2-C22	120.94(13)	C2-C16-C17	118.71(16)
N1-C1-C3	108.92(14)	C17-C16-C21	117.94(16)
N1-C1-C10	121.20(15)	C2-C16-C21	123.29(16)
C3-C1-C10	129.87(15)	O1-C17-C16	122.97(16)
N1-C2-C16	122.06(15)	O1-C17-C18	117.22(17)
N2-C2-C16	128.22(15)	C16-C17-C18	119.80(17)
N1-C2-N2	109.67(14)	C17-C18-C19	120.73(18)
N2-C3-C1	106.27(14)	C18-C19-C20	120.34(19)
C1-C3-C4	132.33(15)	C19-C20-C21	119.61(19)
N2-C3-C4	121.38(14)	C16-C21-C20	121.56(18)
C3-C4-C5	120.54(15)	N2-C22-C27	119.63(15)

C5-C4-C9	119.10(16	C23-C22-C27	120.20(16)
C3-C4-C9	120.36(15)	N2-C22-C23	119.77(15)
C4-C5-C6	120.26(17)	C22-C23-C24	119.47(16)
C5-C6-C7	120.43(19)	C23-C24-C25	121.59(17)
C6-C7-C8	119.89(19)	C24-C25-C26	117.67(18)
C7-C8-C9	119.97(18)	C26-C25-C28	121.37(17)
C4-C9-C8	120.34(17)	C24-C25-C28	120.96(17)
C1-C10-C15	119.61(15)	C25-C26-C27	121.48(18)
C11-C10-C15	118.34(16)	C22-C27-C26	119.45(17)
C1-C10-C11	122.04(16)	C25-C28-C29	112.82(16)
C10-C11-C12	120.38(17)	C28-C29-C30	113.17(17)
C11-C12-C13	120.75(17)	C29-C30-C31	112.28(17)

The molecular structure consists of five membered imidazole ring as a central moiety which is attached by two phenyl rings at 4,5-position. The phenol and butylphenyl moiety are connected at the 2,3-positions of the imidazole ring.

The molecule is non-planar which is indicated by the dihedral angle values between the rings. Both the phenyl rings at 4, 5-position of imidazole ring and the butyl phenyl ring are twisted from the plane of the imidazole ring which is indicated by the dihedral angle values of 76.17(10)°, 18.50(9)° and 75.58(9)° of two phenyl ring and butyl phenyl ring with the imidazole ring respectively. Similarly, the dihedral angle value of 5.09(9)° between the phenol ring and the imidazole ring indicates that the phenol ring is almost planar with the imidazole ring. The butyl chain (C28-C29-C30-C31) attached to the phenyl ring (C22-C23-C24-C25-C26-C27) adopts +syn-clinal conformation which is indicated by the torsion angle value of 73.7(2)° along C24-C25-C28-C29.

The structure exhibits intramolecular hydrogen bonds of the type C–H···N and O–H···N. The C15–H15···N1 hydrogen bond has a length of 2.906(2) Å and an angle of 100°. Similarly, O1–H1···N1 hydrogen bond has a length of 2.5667(19) Å and an angle of 148°, these bonds are responsible for the stability of the molecule. The molecular structure also involves, C–H···π interactions; C(19)–H(19)···*Cg3 (Cg3* is the centroid of the ring C10/C11/C12/C13/C14/C15*)*, with a C–*Cg* distance of 3.649(2) Å, H···*Cg* distance of 2.80 Å, C–H···*Cg* angle of 153°, and with a symmetry code *1/2+x, 1/2-y, 1/2+z;* C(23)–H(23)···*Cg3*, with a C–*Cg* distance of 3.4391(19) Å, H···*Cg* distance of 2.59 Å, C–H···*Cg* angle of 152°, and with a symmetry code *1-x, 1-y, 1-z;* C(31)–H(31A)···*Cg*4 *(Cg*4 is the centroid of the ring C16/C17/C18/C19/C20/C21*)*, with *a* C–*Cg* distance of 3.777(3) Å, *H*···*Cg* distance of 2.92 Å, C–H···*Cg* angle of 149°, and with a symmetry code *1+x, y, z*; The packing of the molecules viewed along a-axis is as shown in Figure 5.

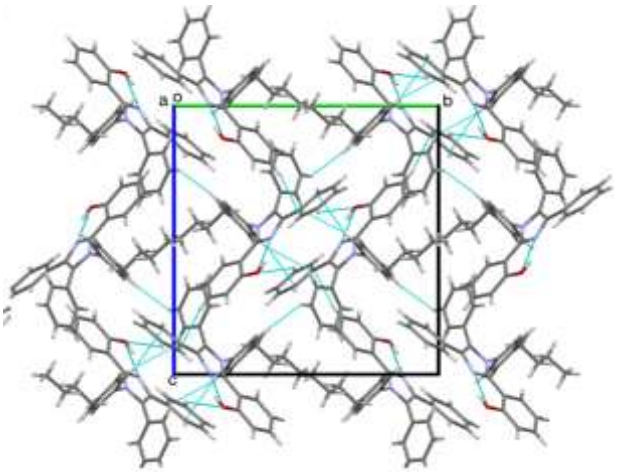


Figure 5: The packing of the molecules when viewed down the *a*-axis

Hirshfeld surface studies

Hirshfeld surface analysis is a computational tool, which helps to understand intermolecular interactions apart from their graphical visualization. Analysis and calculations of the Hirshfeld surface were carried out and finger print plots were plotted using the software Crystal Explorer version 3.0 [9]. The d_{norm} plots were mapped with color scale in between −0.050 au (blue) to 1.425 au (red) respectively. The expanded 2D

fingerprint plots [10,11] were displayed in the range of 0.6-2.8 Å with the d_e and d_i distance scales displayed on the graph axes.

The fingerprint plots reveal the percentage contribution of intermolecular contacts to the surface which can be represented in terms of color codes. The H···H (61.8%) contacts has maximum and C···N (0.1%) has minimum contributions. Similarly the C···H (30.8%), O···H (4.4%) and N···H (2.5%) contacts contribute to the total area of the surface as shown in Figure 6. These contacts are highlighted on the molecular surface using conventional mapping of d_{norm} and electrostatic potential as shown in the Figure 7. The regions with red and blue color represent the shorter and longer inter contacts [12-14].

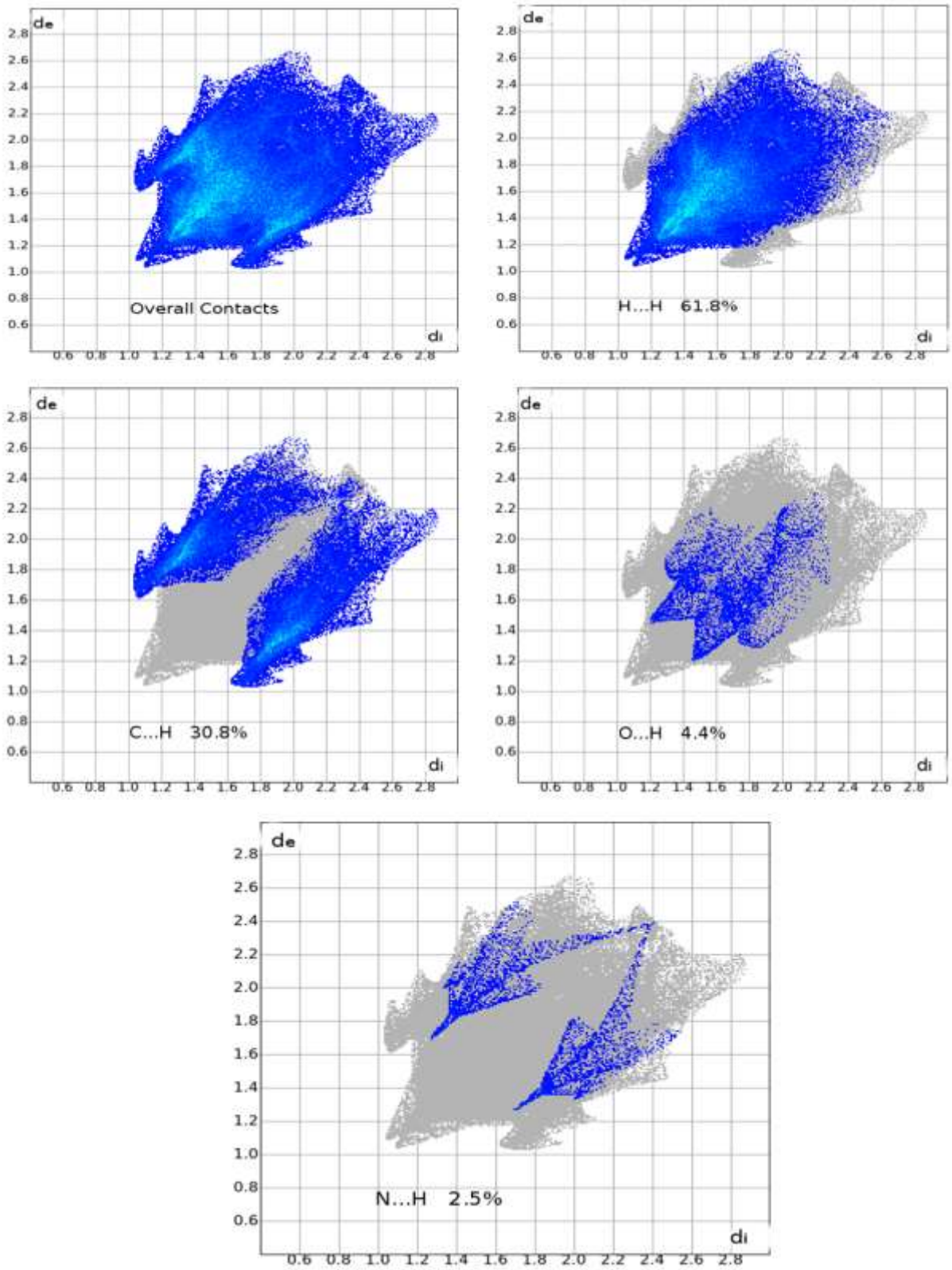


Figure 6: Fingerprint plots and corresponding surface area of the title compound showing the individual contribution of each interaction. d_i is the closest internal distance from a given point on the Hirshfeld surface and d_e is the closest external contacts

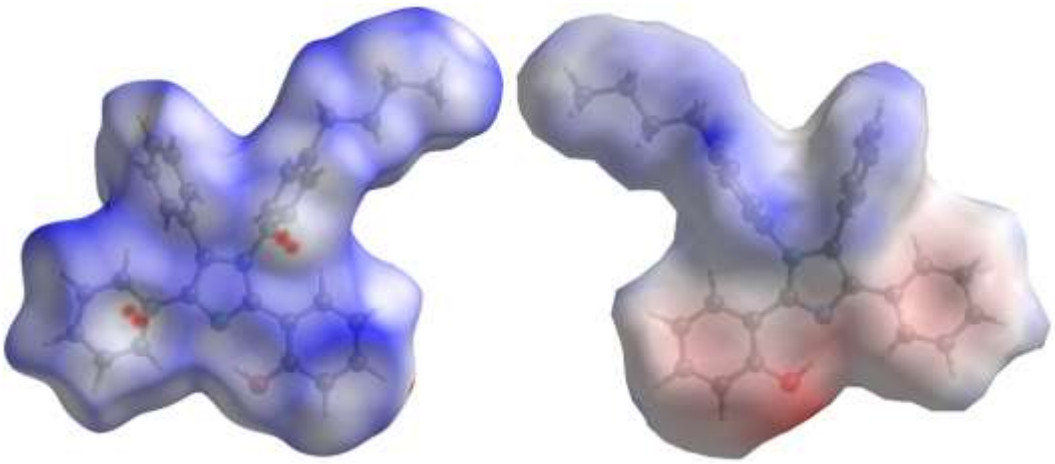


Figure 7: d_{norm} and electrostatic potential mapped on Hirshfeld surface visualizing the molecular contacts

CONCLUSION

The title compound $C_{31}H_{28}N_2O$ has been synthesized and the single crystals were grown by the slow evaporation method using ethanol as a solvent. The compound was characterized using the NMR, IR and the molecular structure of the compound was finally confirmed by the single crystal X-ray diffraction studies. The synthesized compound crystallized in the monoclinic crystal system, in $P2_1/n$ space group. The crystal and molecular structure of the compound is stabilized by the intra molecular C–H···N and OH···N hydrogen bond interactions. The molecular structure also involves C–H···π interactions, w–hich contributes to the crystal packing. The analysis of the Hirshfeld surface; fingerprint plots of the molecule confirms the presence of these interactions, the major share for the surface being from H···H (61.8%).

ACKNOWLEDGEMENT

The authors are thankful to the Institution of Excellence, Vijnana Bhavana, University of Mysore, Manasagangotri, Mysore, for providing the single-crystal X-ray diffraction data. One of author R. Anil Kumar acknowledges to UGC New Delhi for financial support received from BSR fellowship.

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